

2.7.4.7.2 本文中には含めないが、引用する図表

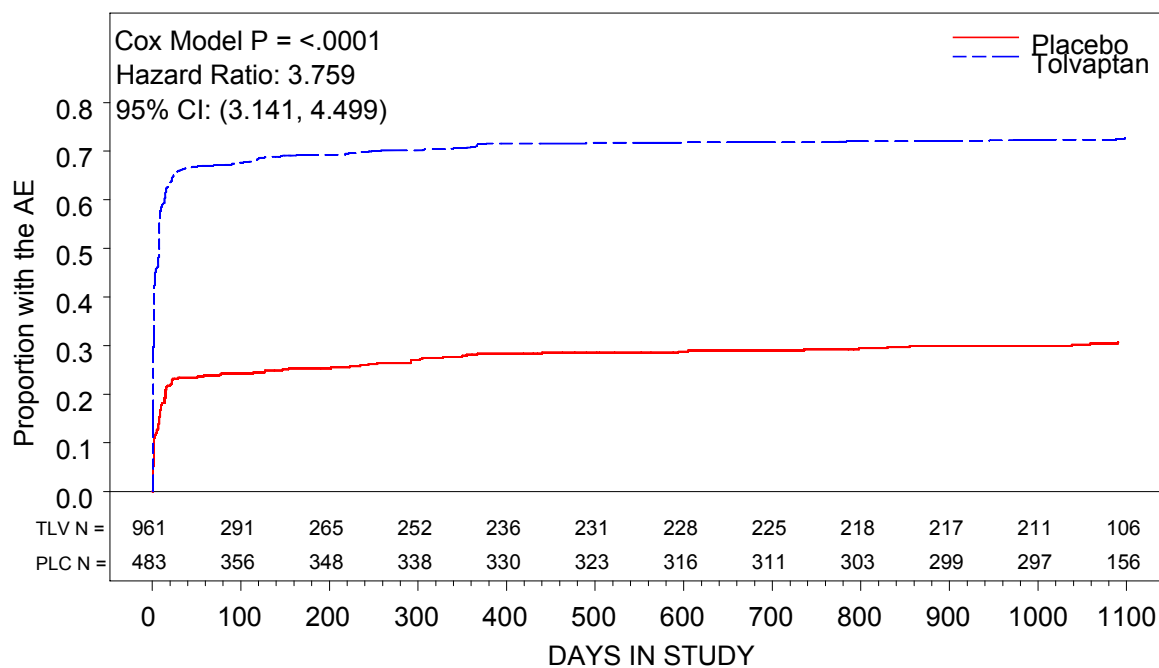


図 2.7.4.7-1 Kaplan-Meier Curves of Time to First Treatment-emergent Adverse Events in the Urination CMQ

PLC = placebo, TLV = tolvaptan.

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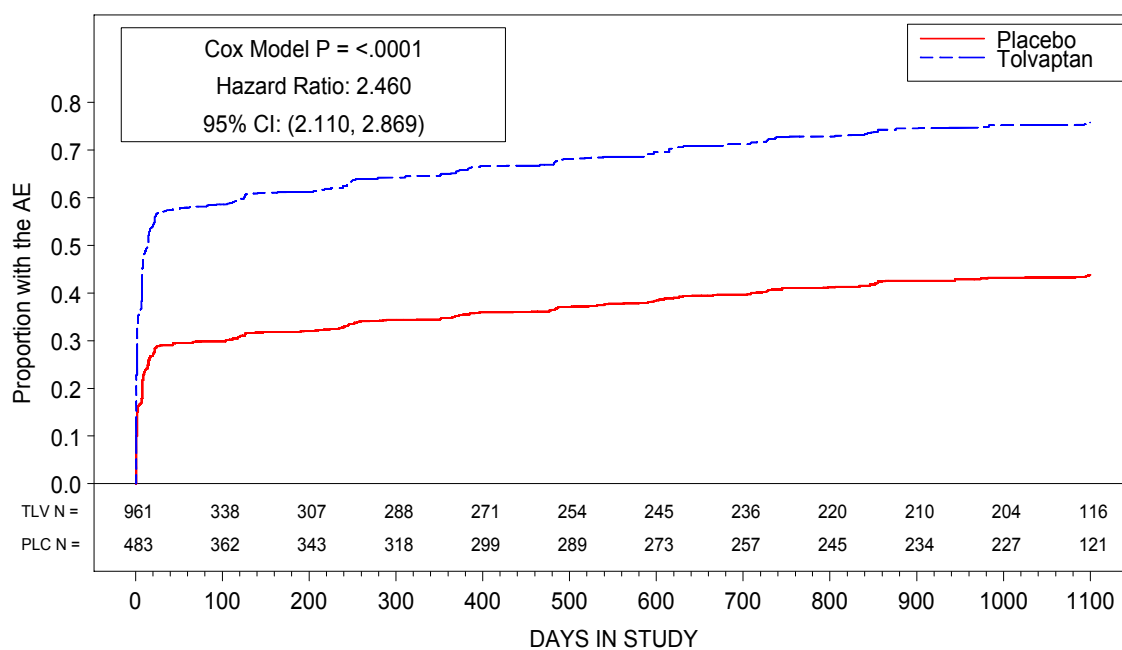


図 2.7.4.7-2 Kaplan-Meier Curves of Time to First Treatment-emergent Adverse Events in the Dehydration CMQ

PLC = placebo, TLV = tolvaptan.

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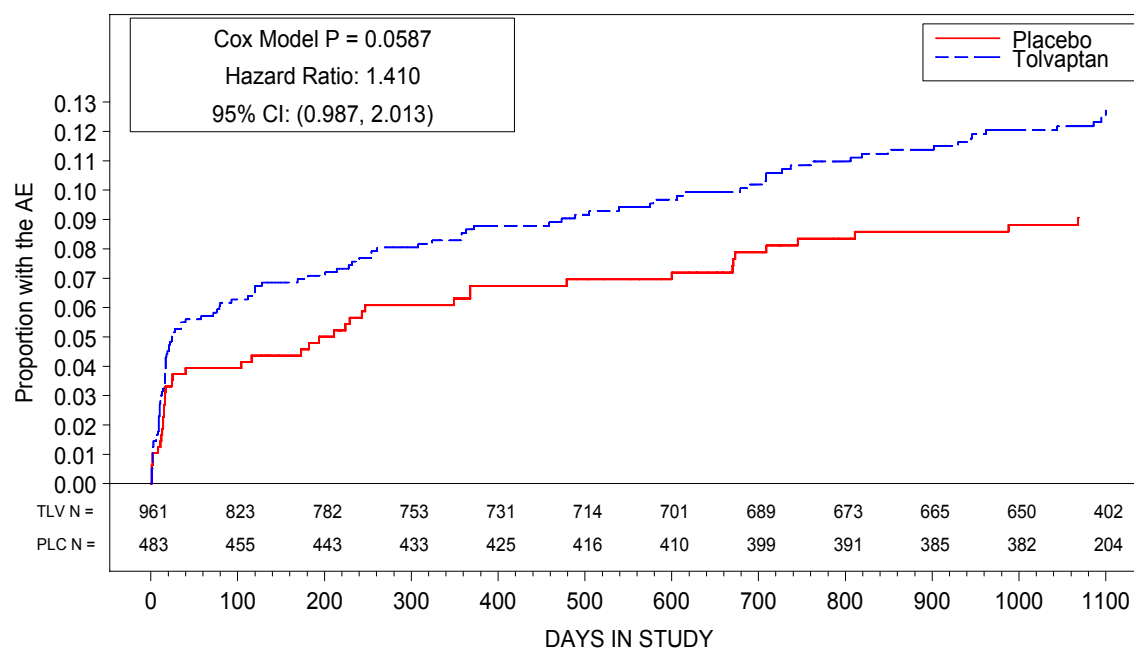


図 2.7.4.7-3 Kaplan-Meier Curves of Time to First Treatment-emergent Adverse Events of Dizziness

PLC = placebo, TLV = tolvaptan.

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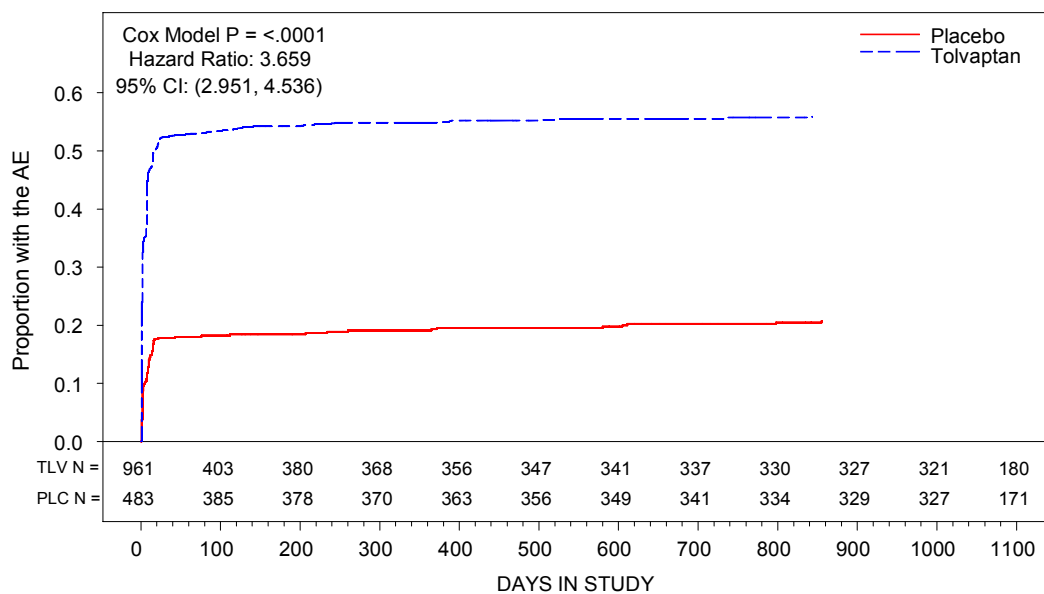


図 2.7.4.7-4 Kaplan-Meier Curves of Time to First Treatment-emergent Adverse Events of Thirst

PLC = placebo, TLV = tolvaptan.

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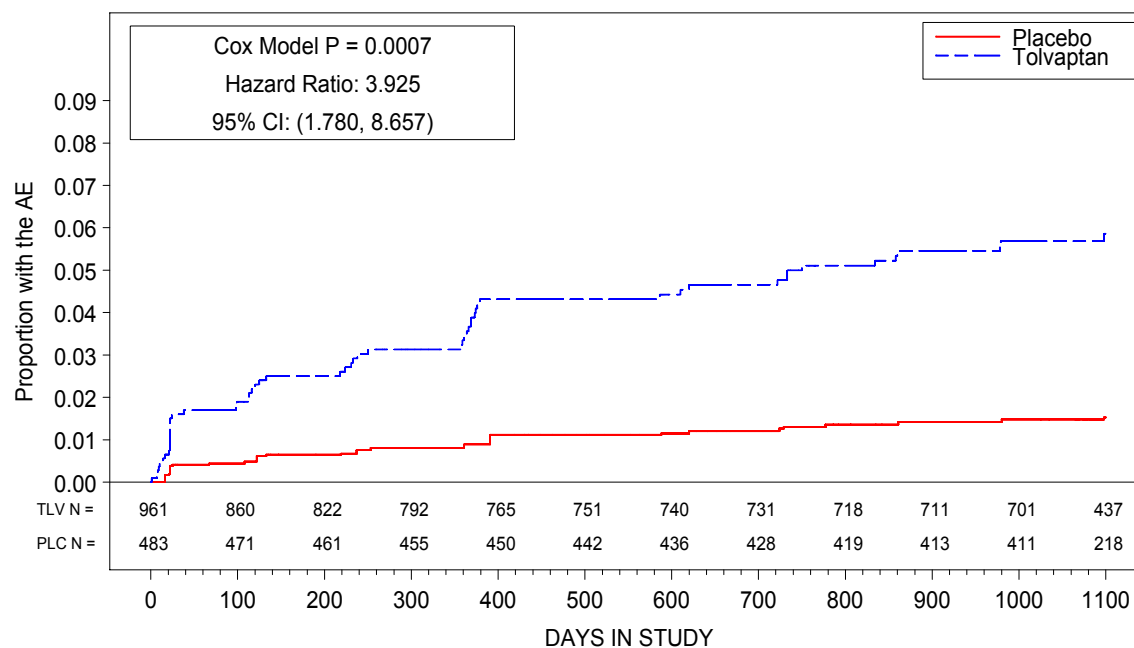


図 2.7.4.7-5 Kaplan-Meier Curves of Time to First Treatment-emergent Adverse Events in the Hypernatremia CMQ

PLC = placebo, TLV = tolvaptan.

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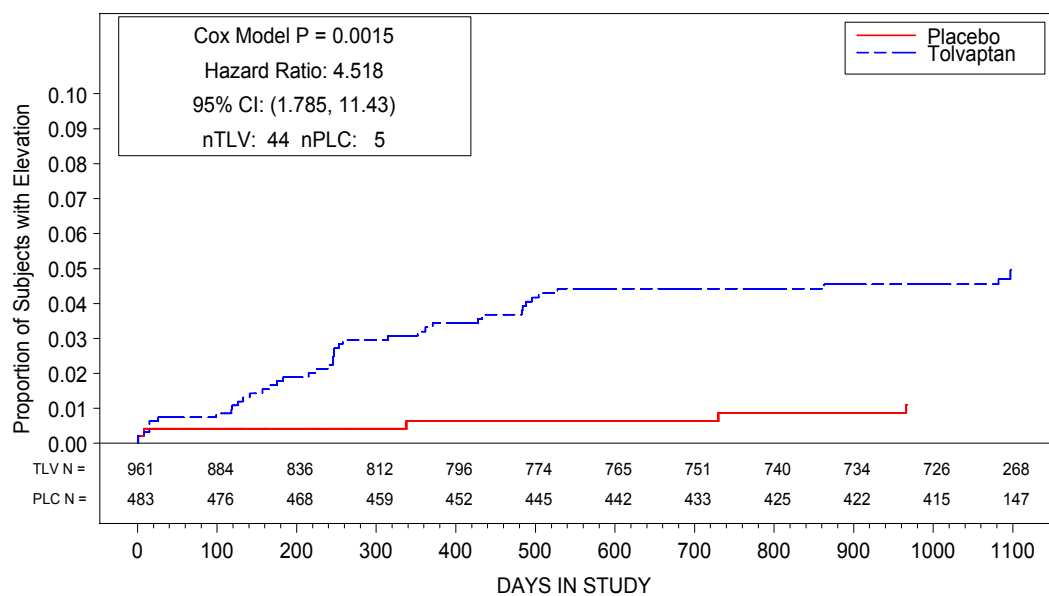


図 2.7.4.7-6 Kaplan-Meier Curves for Time to First Elevation in ALT of Greater Than 3 Times ULN, Safety Population

PLC = placebo; TLV = tolvaptan.

Note: Included central and local laboratory data.

<資料番号 5.3.5.1-01 : Figure11.8.1.6.5.3-1>

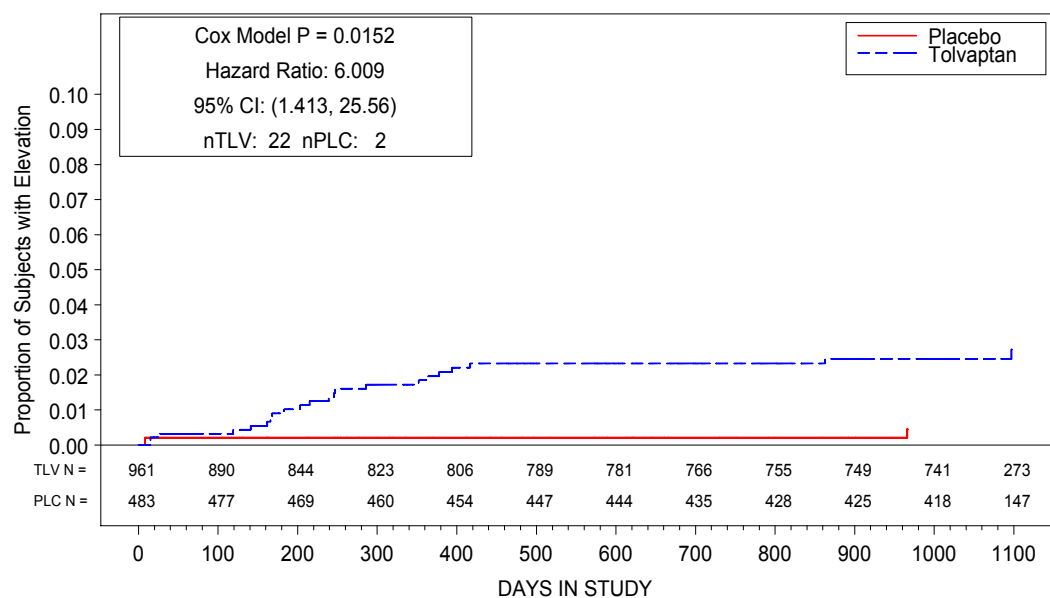


図 2.7.4.7-7 Kaplan-Meier Curves for Time to First Elevation in ALT of Greater Than 5 Times ULN, Safety Population

PLC = placebo; TLV = tolvaptan.

Note: Includes central and local laboratory data.

<資料番号 5.3.5.1-01 : Figure11.8.1.6.5.3-2>

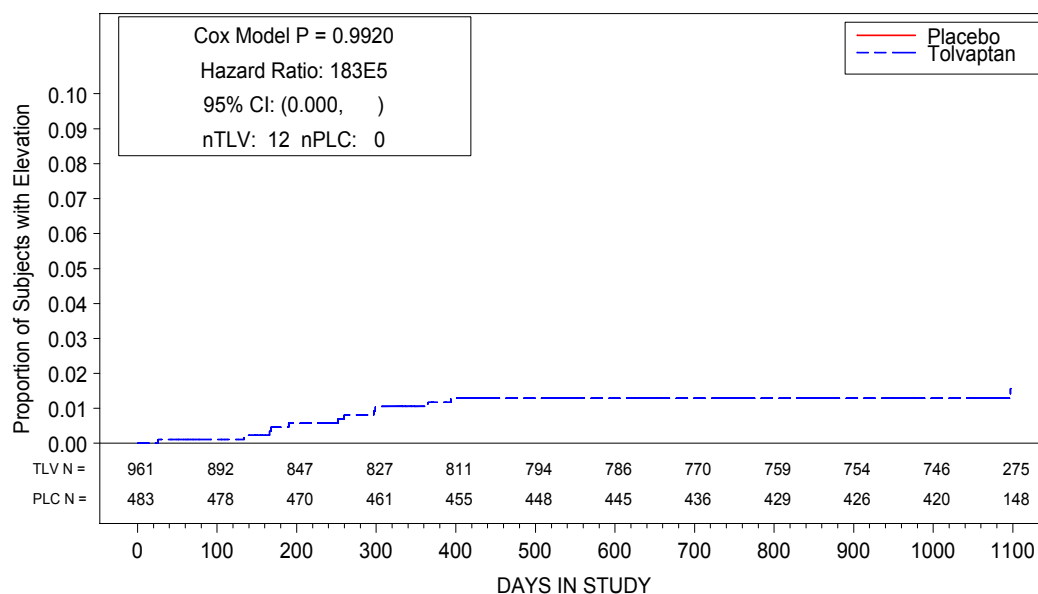


図 2.7.4.7-8 Kaplan-Meier Curve for Time to First Elevation in ALT of Greater Than 10 Times ULN, Safety Population

PLC = placebo; TLV = tolvaptan.

Note: Includes central and local laboratory data.

<資料番号 5.3.5.1-01 : Figure11.8.1.6.5.3-3>

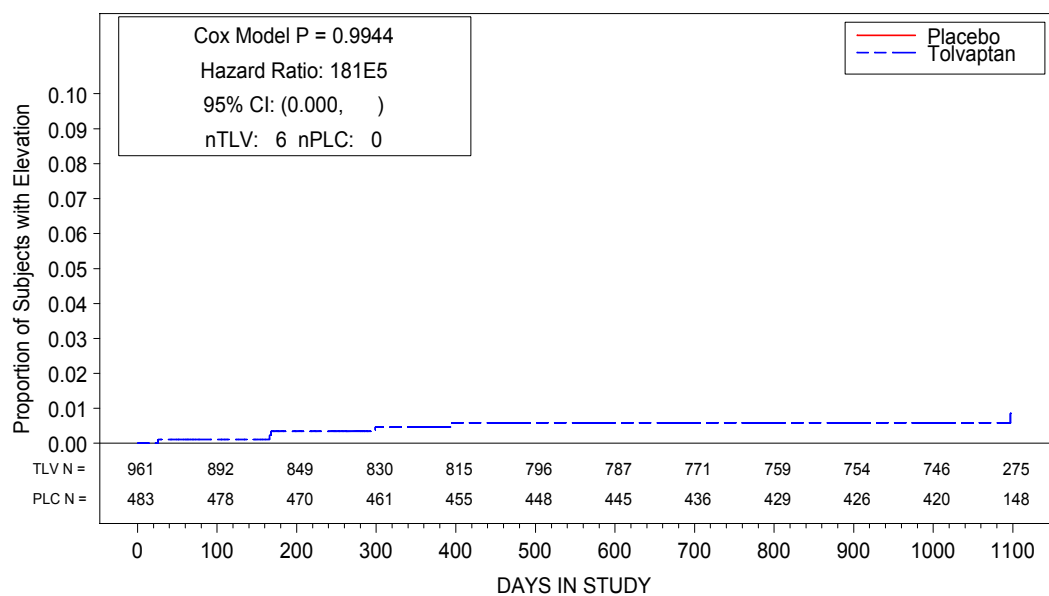


図 2.7.4.7-9 Kaplan-Meier Curve for Time to First Elevation in ALT of Greater Than 20 Times ULN, Safety Population

PLC = placebo; TLV = tolvaptan.

Note: Includes central and local laboratory data.

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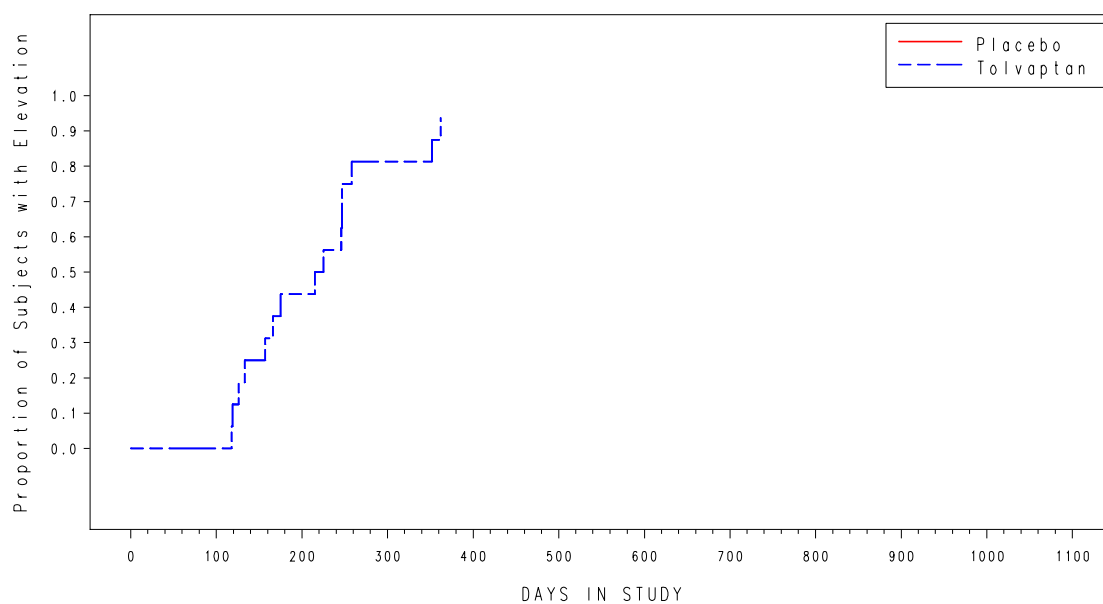


図 2.7.4.7-10 Kaplan-Meier Curves for Time to First Elevation in ALT of Greater Than 3 Times ULN, Subset of “Highly Likely” and “Probable”

Note: Includes central and local laboratory data.

<資料番号 5.3.5.1-01 : Figure11.8.1.6.8.2.1.3-1>

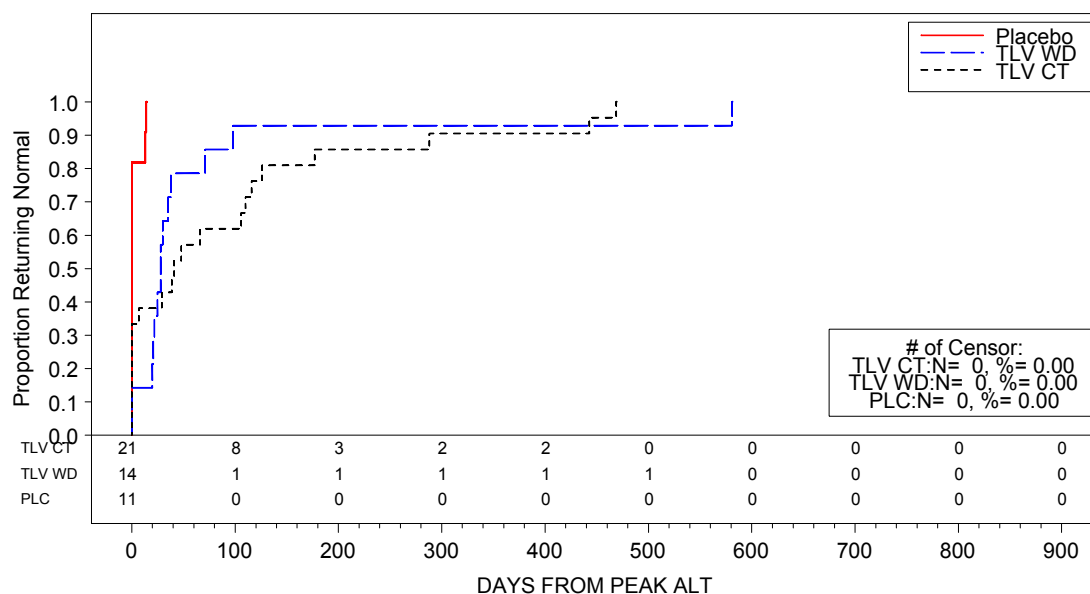


図 2.7.4.7-11 Kaplan-Meier Curves of Time From Peak ALT to Less Than or Equal to 3 Times ULN, Adjudicated Subjects

CT = continued IMP after peak ALT was measured; WD = discontinued IMP before peak ALT was measured or within 2 days of peak measurement.

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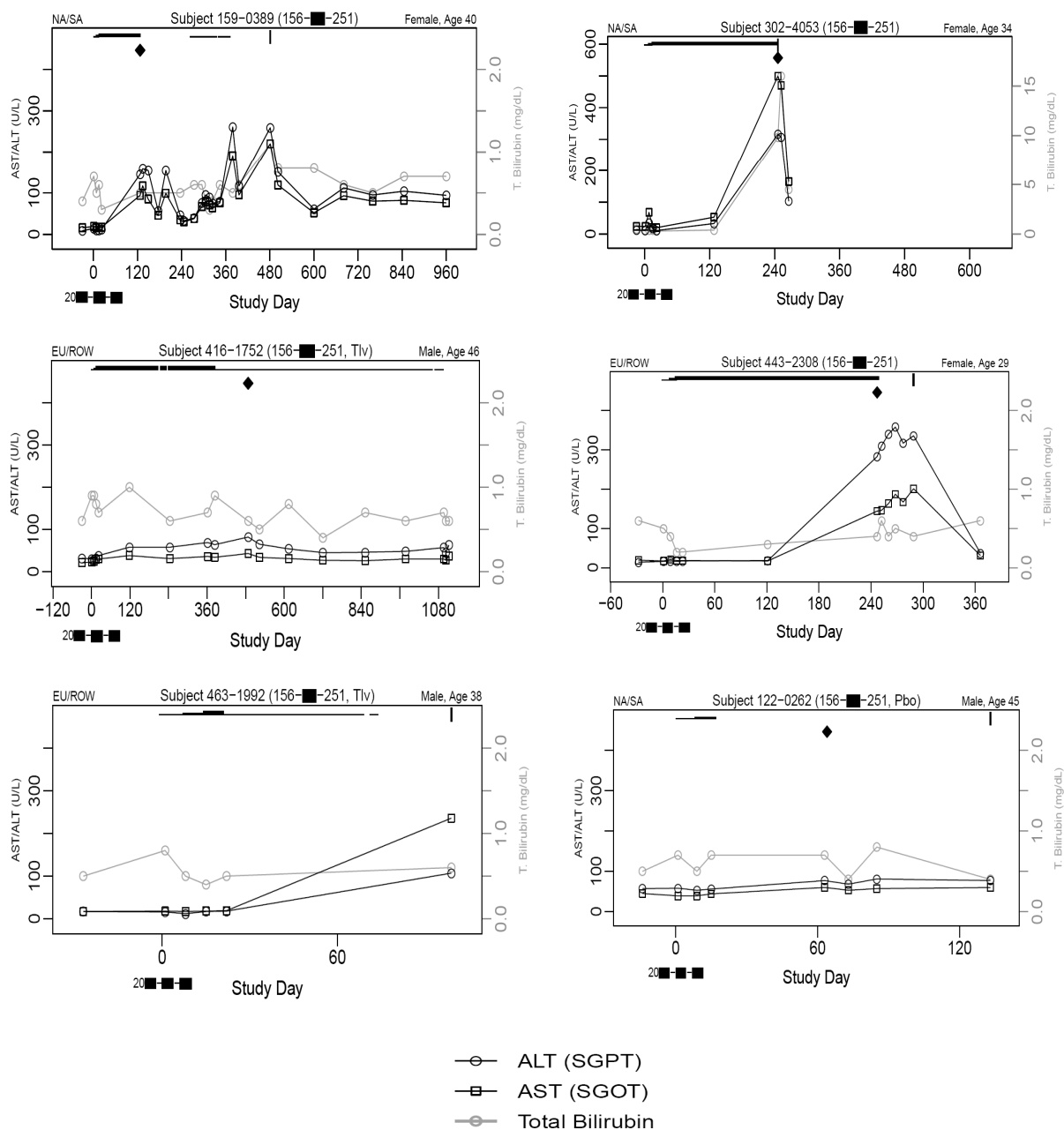


図 2.7.4.7-12 Liver Function Test Values Over Time for Subjects Censored From the Analysis of Time From Peak ALT to the ULN or Lower

NA = North America; Pbo = placebo; SA = South America; T = total.

Note: The subject's IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15, 60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an IRE).

<資料番号 5.3.5.1-01 : Figure11.8.1.6.7.3.2-2>

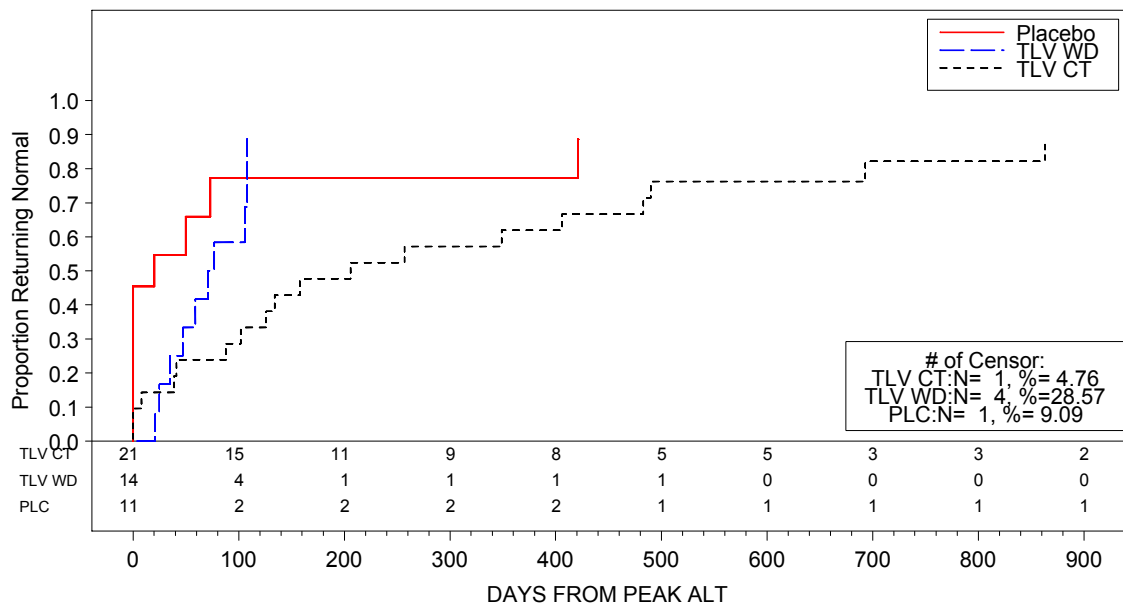


図 2.7.4.7-13 Kaplan-Meier Curves of Time From Peak ALT to the ULN or Below, Adjudicated Subjects

CT = continued IMP after peak ALT was measured; WD = discontinued IMP before peak ALT was measured or within 2 days of peak measurement.

Note: Five tolavaptan subjects and one placebo subjects were censored from this analysis because the ALT had not returned to $\leq 1 \times \text{ULN}$ as of the last recorded measurement.

<資料番号 5.3.5.1-01 : Figure11.8.1.6.7.3.2-1>

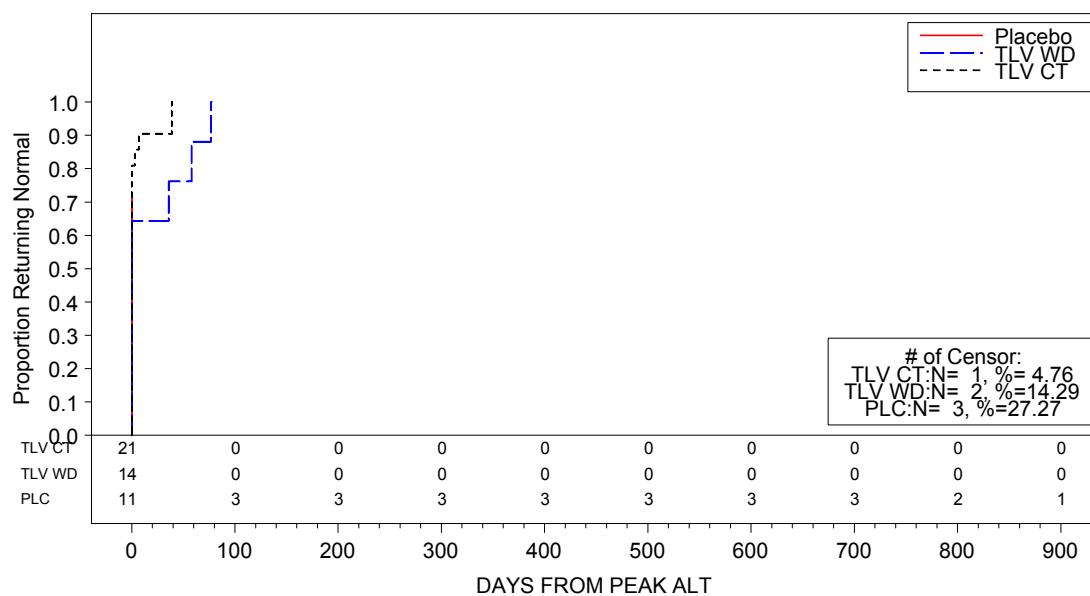
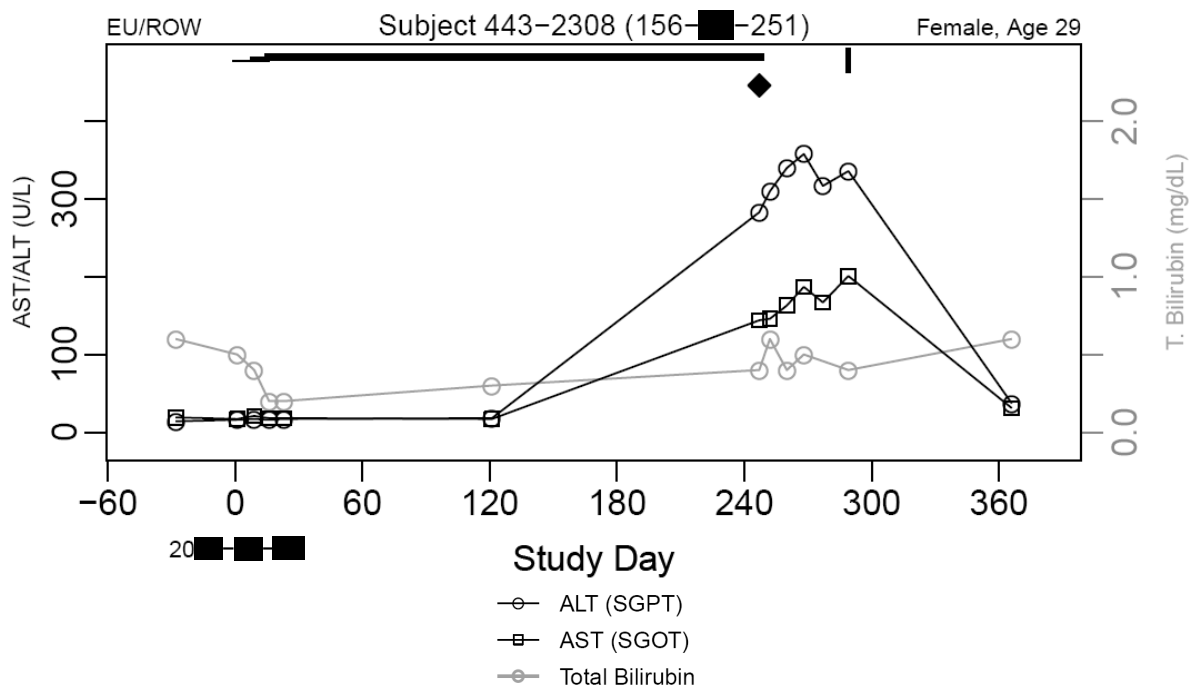


図 2.7.4.7-14 Kaplan-Meier Curves of Time From Peak BT to the ULN or Lower, Adjudicated Subjects

CT = continued IMP after peak ALT was measured; WD = discontinued IMP before peak ALT was measured or within 2 days of peak measurement.

<資料番号 5.3.5.1-01 : Figure11.8.1.6.7.3.3-1>



2.7.4.7-15 Liver Function Test Values Over Time for Subject 251-443-2308

T = total.

Note: The subject's IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15, 60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an IRE).

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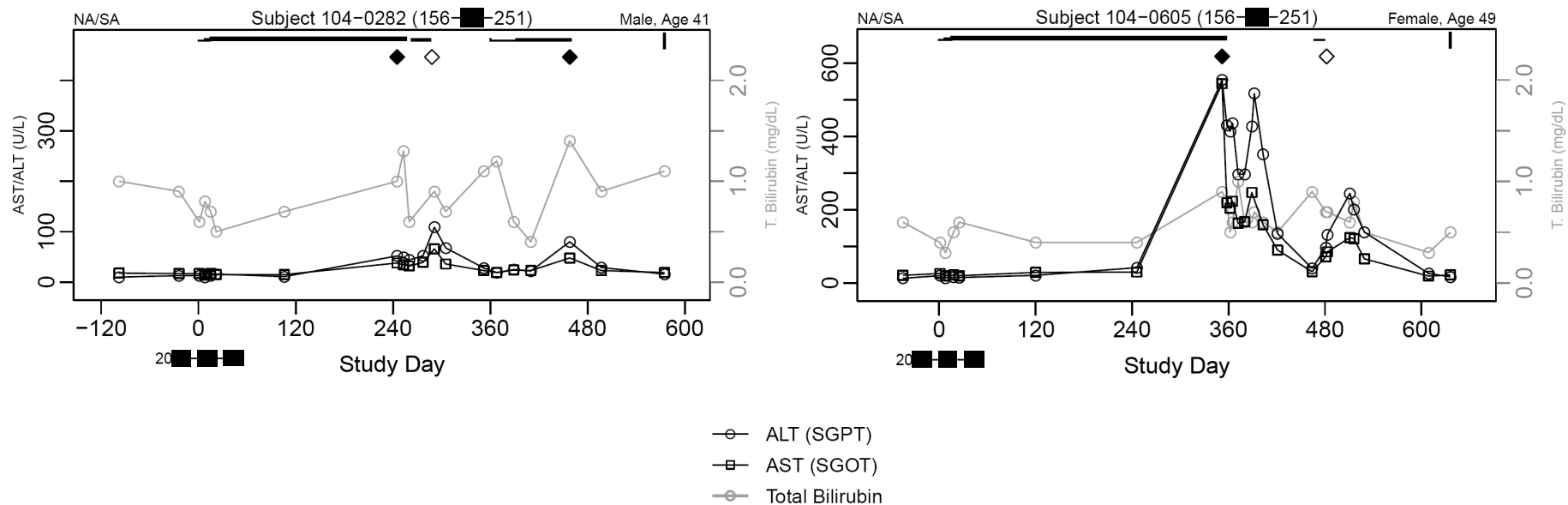
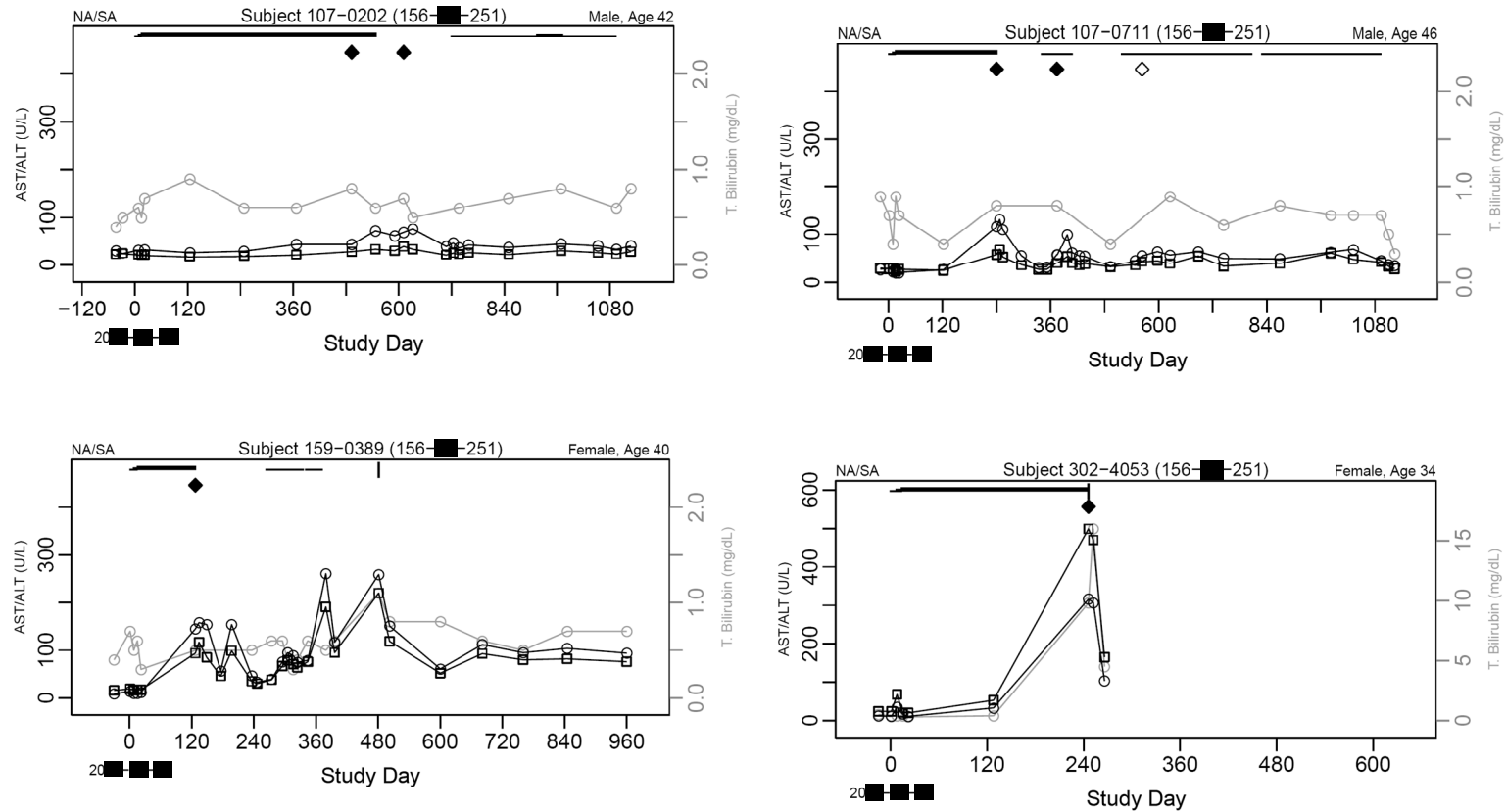


图 2.7.4.7-16 Liver Function Test Values Over Time for Subjects With Events Having a "Probable" Causal Relationship to IMP

NA = North America; SA = South America; T = total.

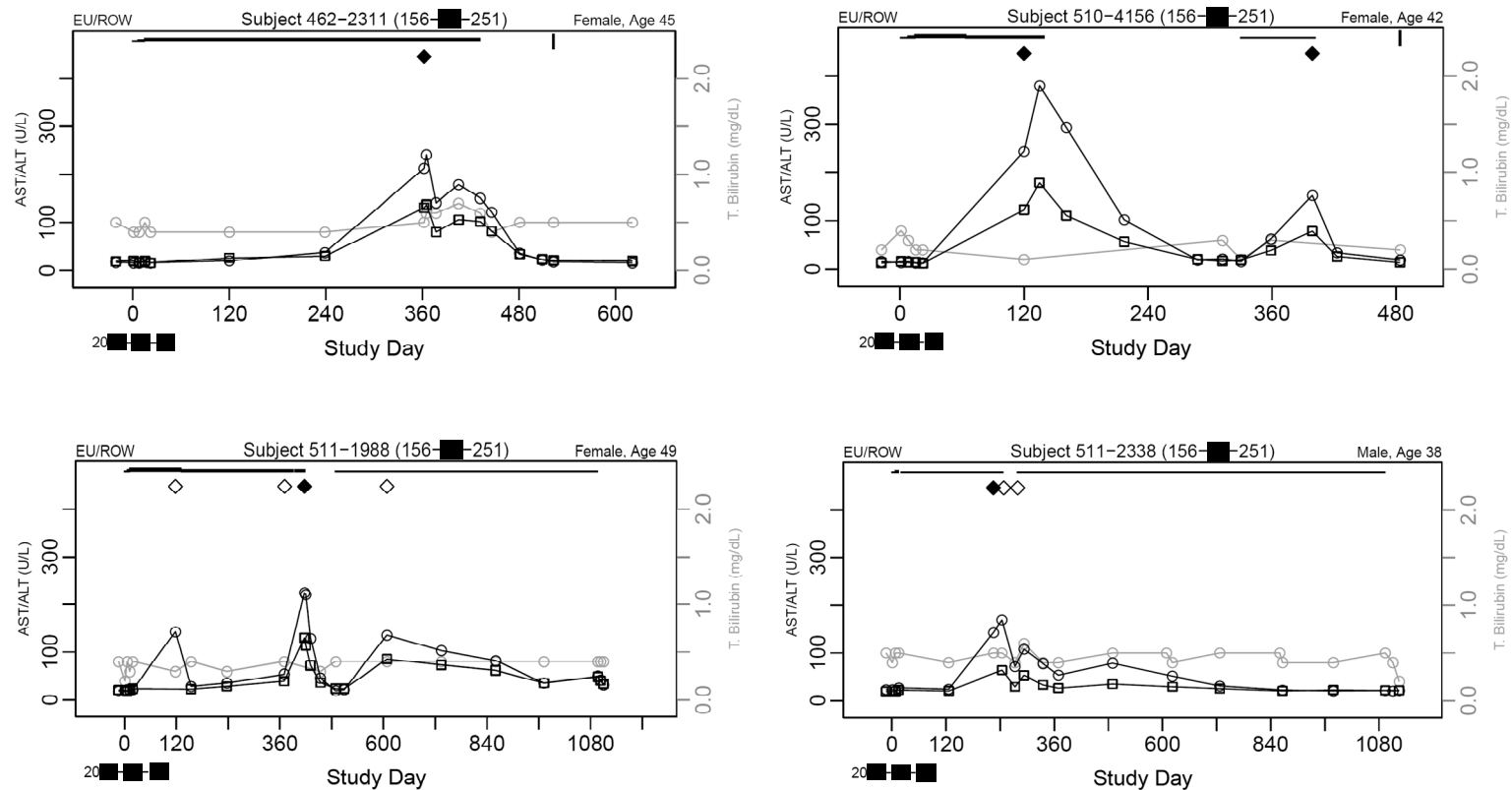
Note: The subject's IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15,60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an IRE).



2.7.4.7-16 Liver Function Test Values Over Time for Subjects With Events Having a “Probable” Causal Relationship to IMP, Continued

NA = North America; SA = South America; T = total.

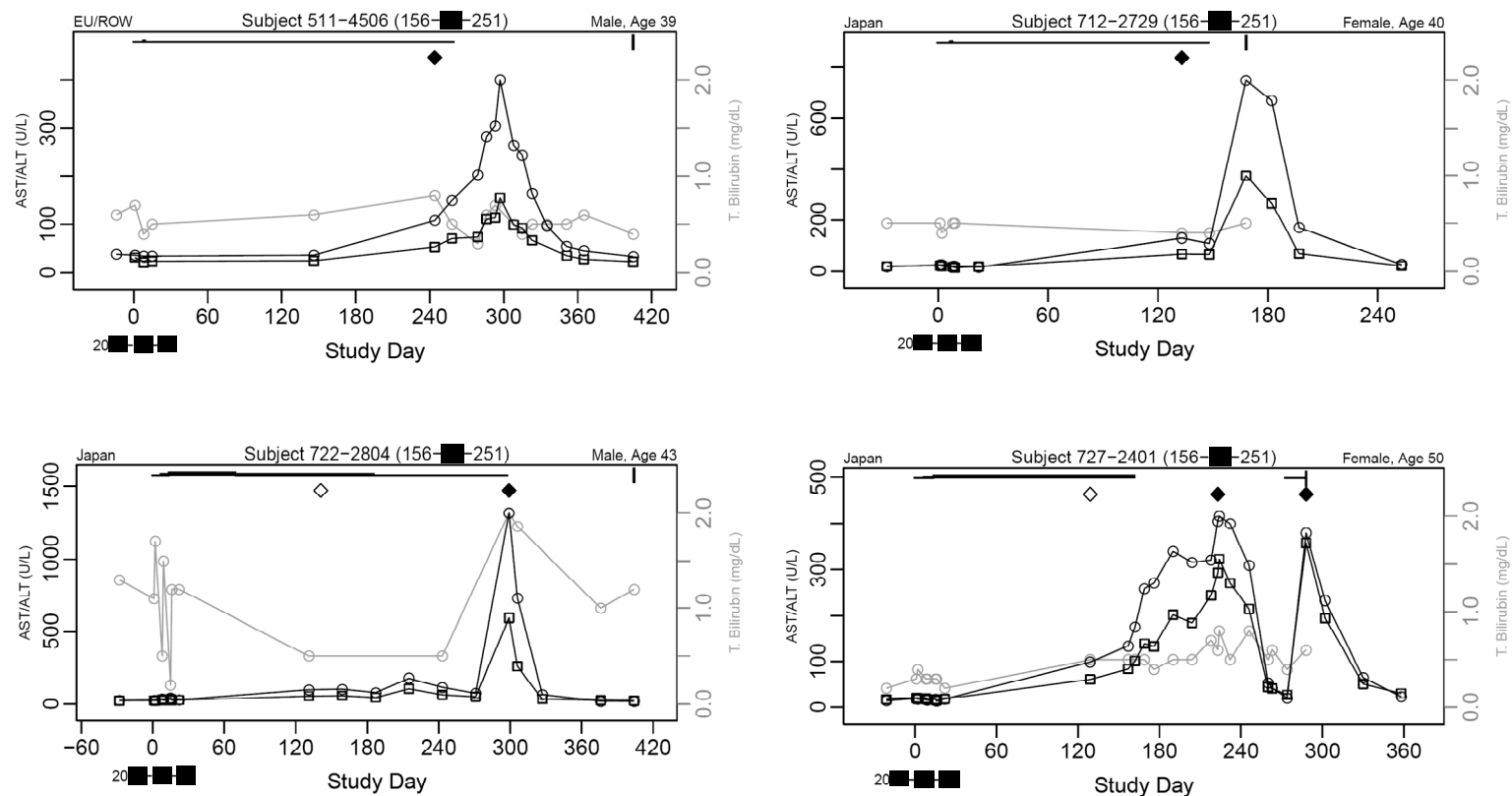
Note: The subject’s IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15,60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an IRE).



2.7.4.7-16 Liver Function Test Values Over Time for Subjects With Events Having a “Probable” Causal Relationship to IMP, Continued

NA = North America; SA = South America; T = total.

Note: The subject’s IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15,60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an IRE).



2.7.4.7-16 Liver Function Test Values Over Time for Subjects With Events Having a “Probable” Causal Relationship to IMP, Continued

NA = North America; SA = South America; T = total.

Note: The subject’s IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15, 60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an IRE).

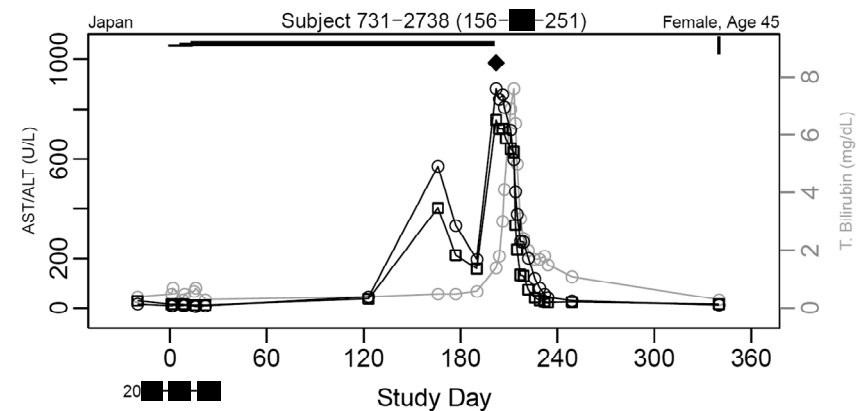
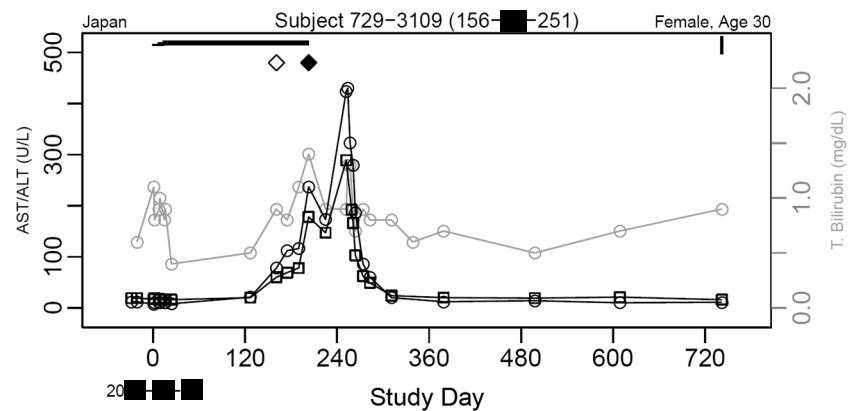


図 2.7.4.7-16 Liver Function Test Values Over Time for Subjects With Events Having a “Probable” Causal Relationship to IMP, Continued

NA = North America; SA = South America; T = total.

Note: The subject’s IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15,60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an IRE).

<資料番号 5.3.5.1-01 : Figure11.8.1.6.8.2.1.4-2>

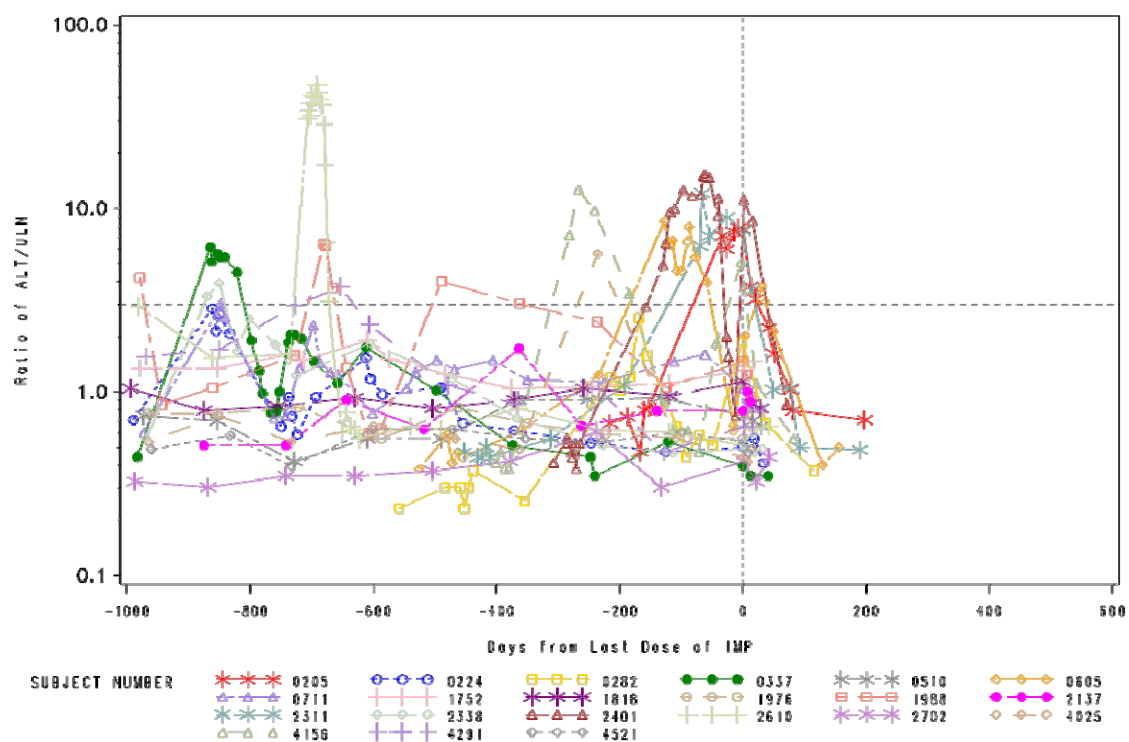


図 2.7.4.7-17 Longitudinal Time Course (Spaghetti Plot) of Ratio of ALT/ULN Over Time for Tolvaptan Adjudicated Subjects Who Continued/Resumed IMP After Highest Peak (21 of 35 Tolvaptan Subjects), Trial 156-251.

IMP = investigational medicinal product; ULN = upper limit of normal.

<資料番号 5.3.5.3-02 : SCS CF-1>

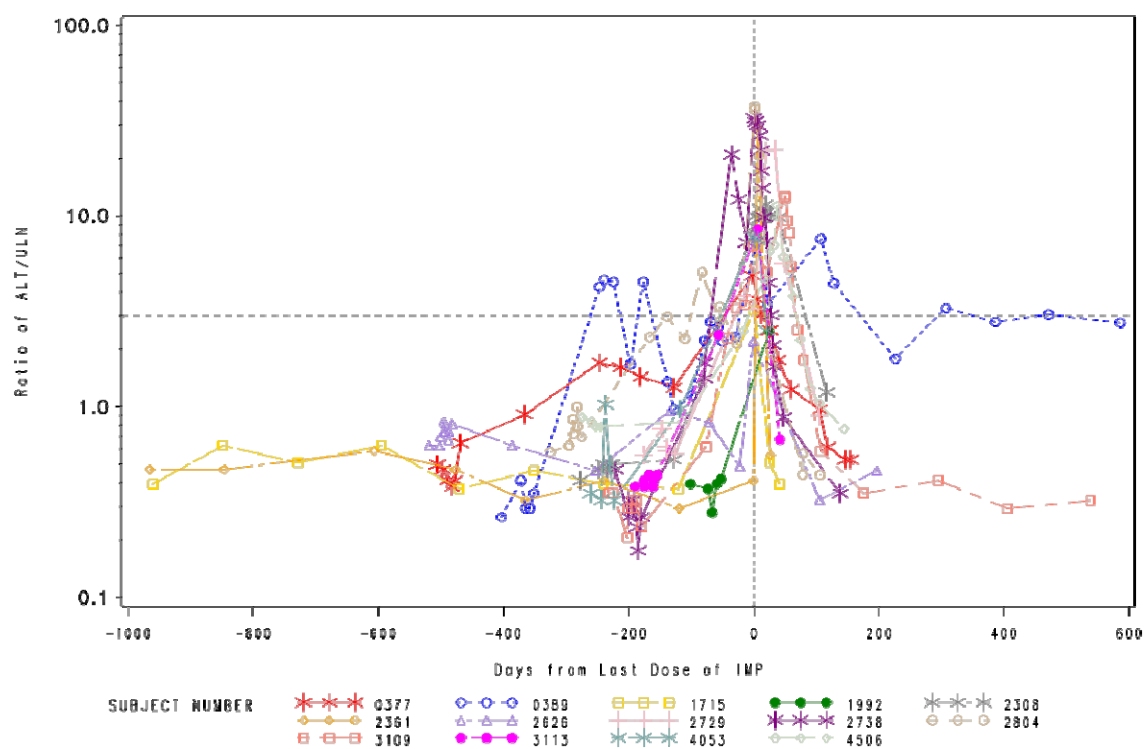


図 2.7.4.7-18 Longitudinal Time Course (Spaghetti Plot) of Ratio of ALT/ULN Over Time for Tolvaptan Adjudicated Subjects Who Discontinued IMP Before or Within Two Days of Peak (14 of 35 Tolvaptan Subjects), Trial 156-251

IMP = investigational medicinal product; ULN = upper limit of normal.

<資料番号 5.3.5.3-02 : SCS CF-2>

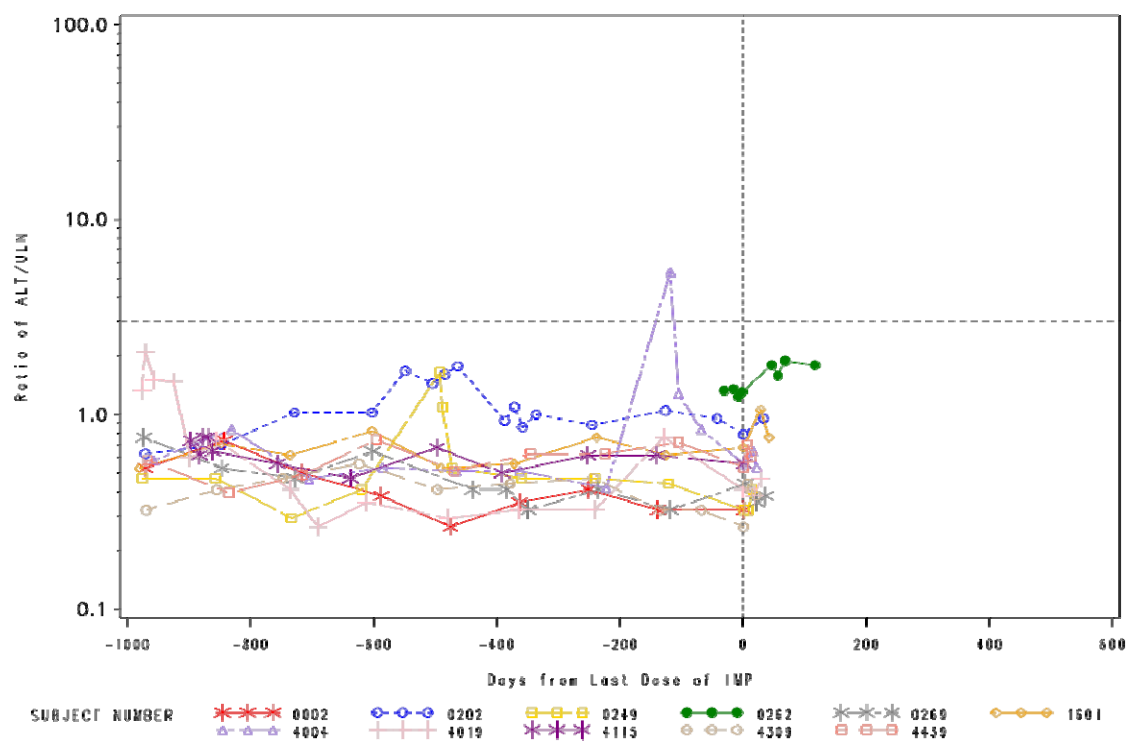


図 2.7.4.7-19 Longitudinal Time Course (Spaghetti Plot) of Ratio of ALT/ULN Over Time for Placebo Adjudicated Subjects (N = 11), Trial 156-251

IMP = investigational medicinal product; ULN = upper limit of normal.

<資料番号 5.3.5.3-02 : SCS CF-3>

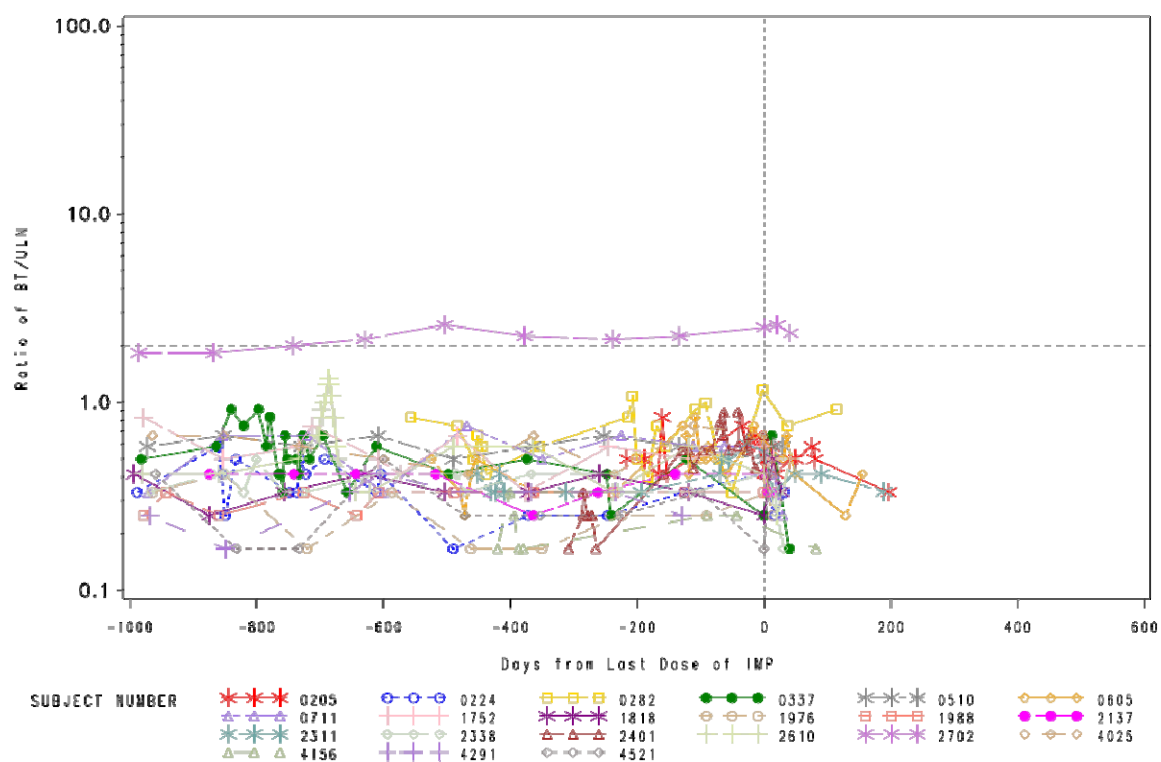


図 2.7.4.7-20 Longitudinal Time Course (Spaghetti Plot) of Ratio of BT/ULN Over Time for Tolvaptan Adjudicated Subjects Who Continued/Resumed IMP After Highest Peak (21 of 35 Tolvaptan Subjects), Trial 156-251

BT = total bilirubin; IMP = investigational medicinal product; ULN = upper limit of normal.

<資料番号 5.3.5.3-02 : SCS CF-4>

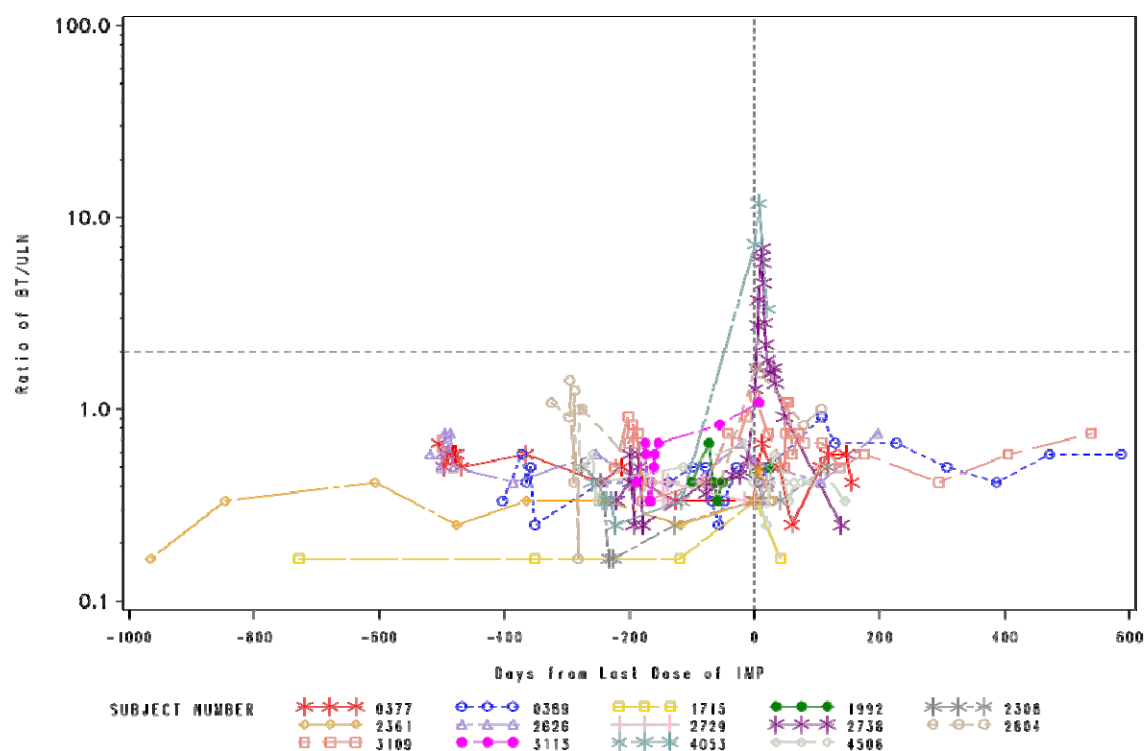


図 2.7.4.7-21 Longitudinal Time Course (Spaghetti Plot) of Ratio of BT/ULN Over Time for Tolvaptan Adjudicated Subjects Who Discontinued IMP Before or Within Two Days of Peak (14 of 35 Tolvaptan Subjects), Trial 156-XXXX-251

BT = total bilirubin; IMP = investigational medicinal product; ULN = upper limit of normal.

<資料番号 5.3.5.3-02 : SCS CF-5>

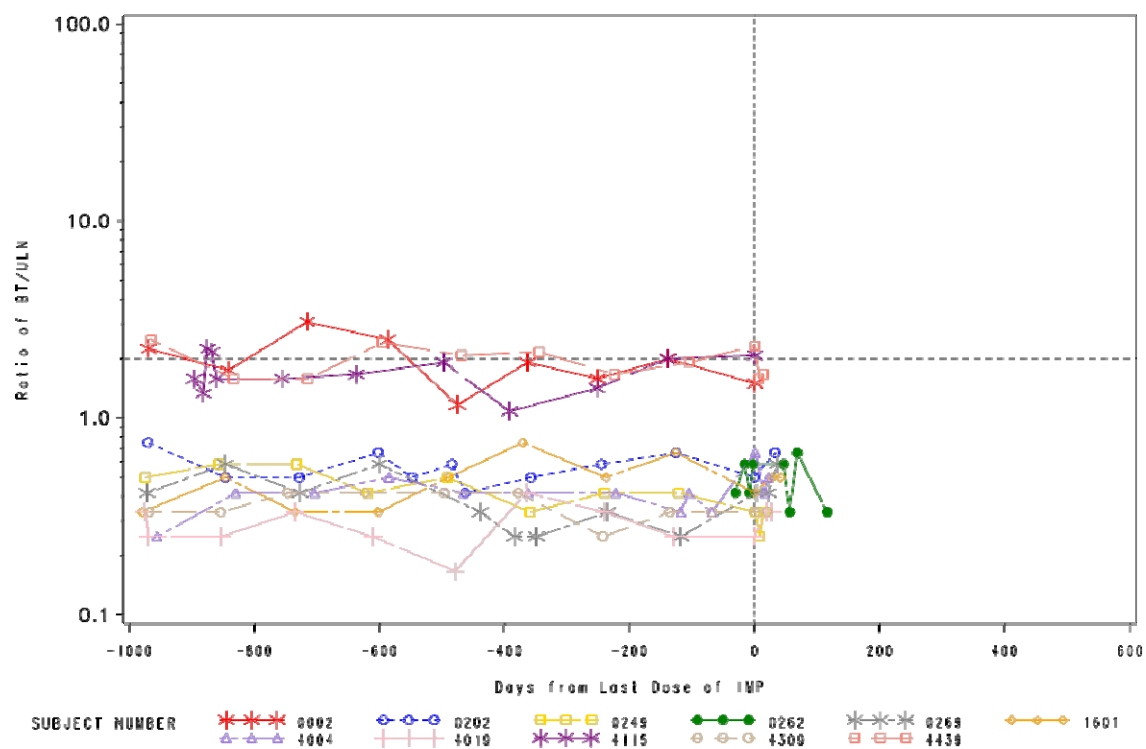
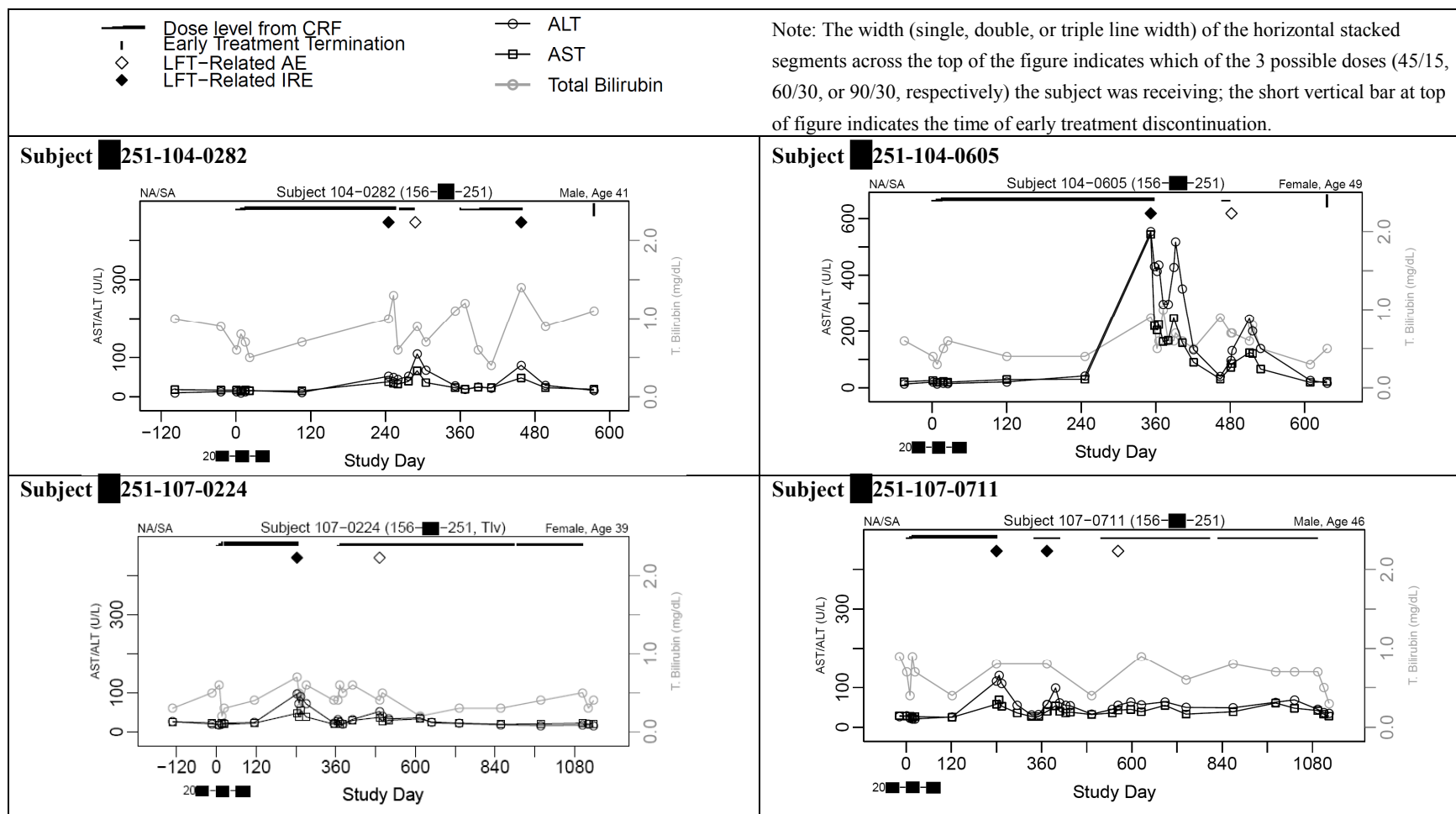


図 2.7.4.7-22 Longitudinal Time Course (Spaghetti Plot) of Ratio of BT/ULN Over Time for Placebo Adjudicated Subjects (N = 11), Trial 156-251

BT = total bilirubin; IMP = investigational medicinal product; ULN = upper limit of normal

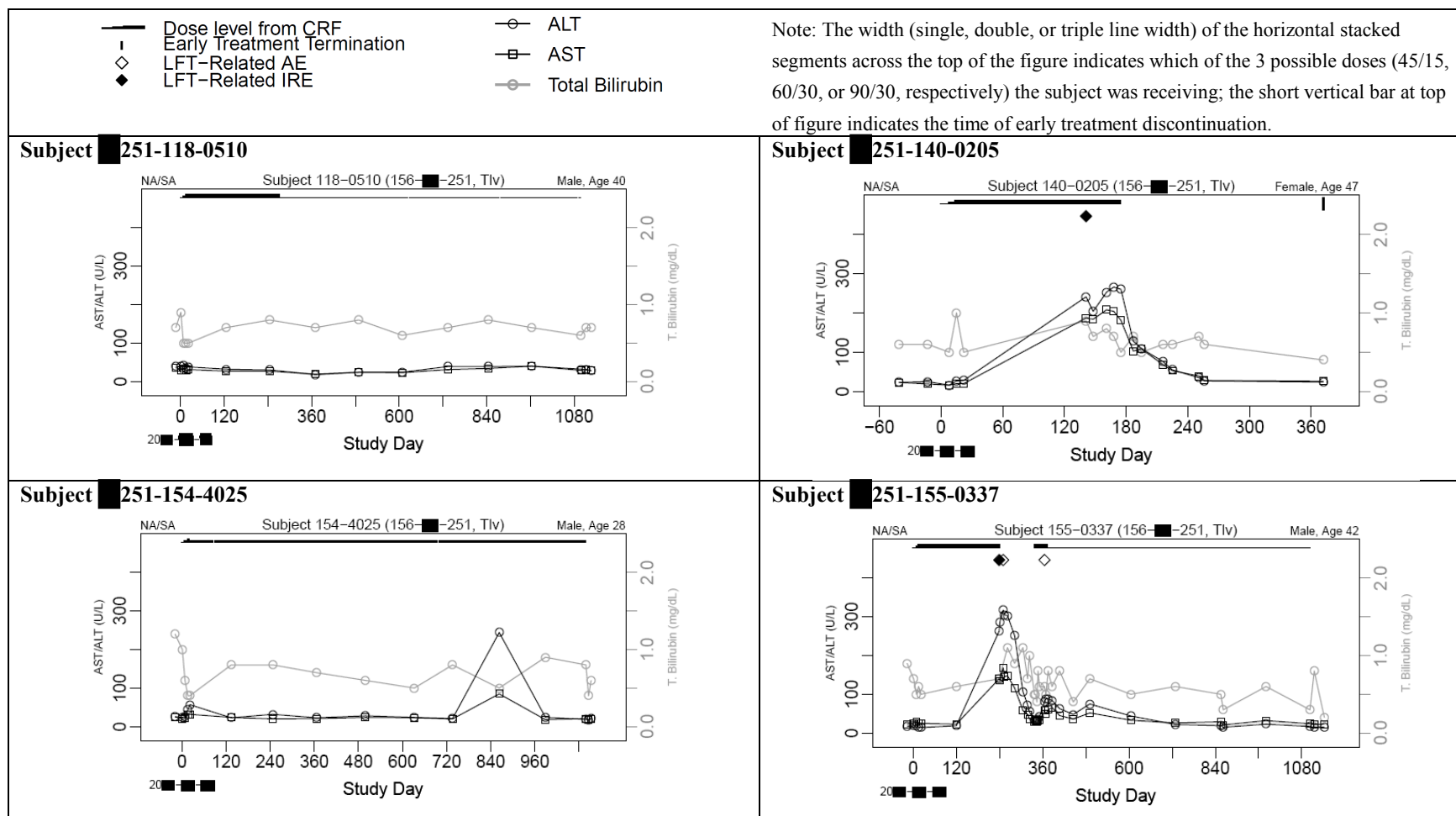
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2.7.4.7-23 Time Course Plots for Adjudicated Tolvaptan Subjects Who Continued/Resumed IMP After Highest Peak (N = 21), Trial 156-251

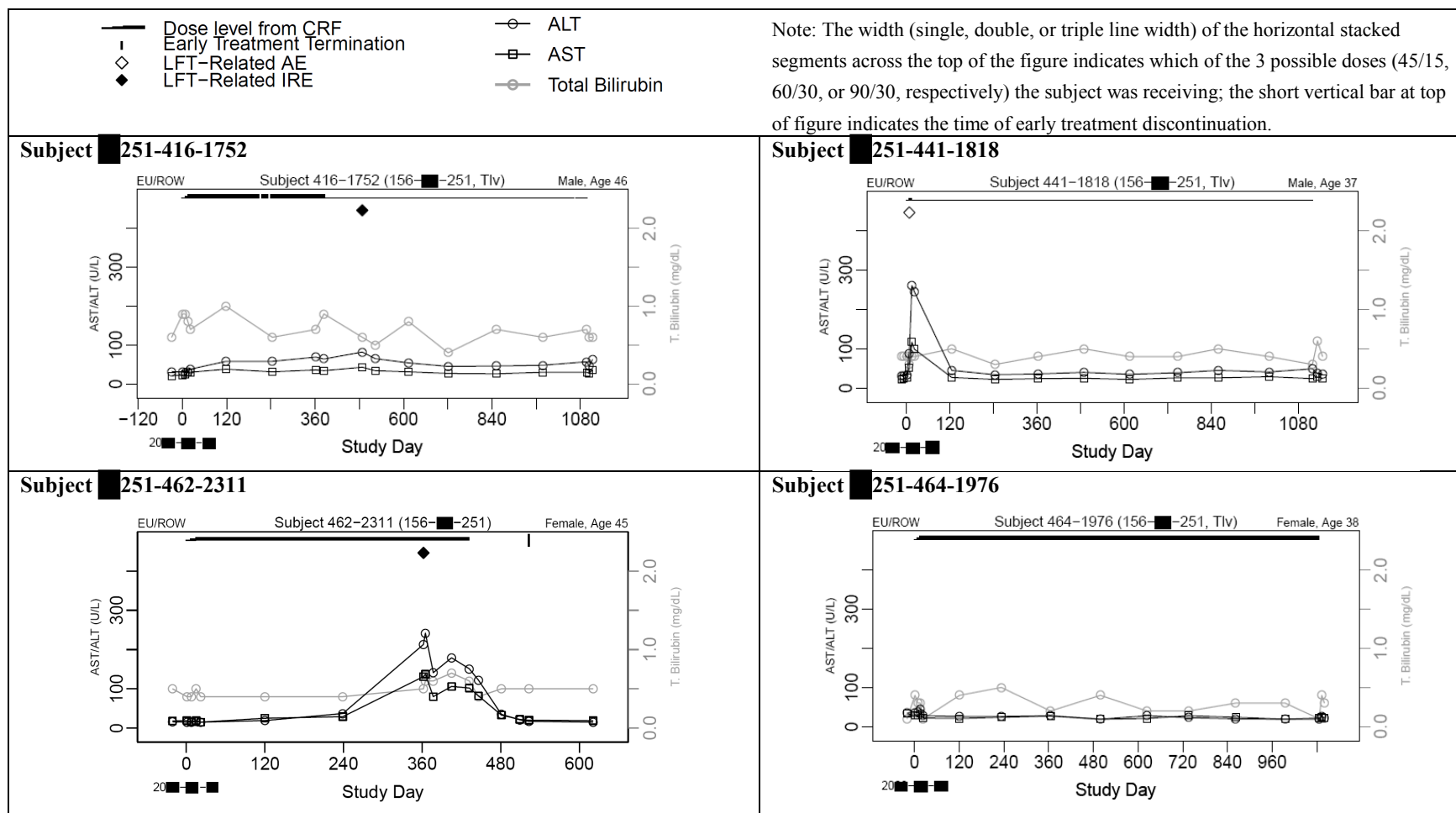
AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.



2.7.4.7-23 Time Course Plots for Adjudicated Tolvaptan Subjects Who Continued/Resumed IMP After Highest Peak (N = 21), Trial 156--251 (continued)

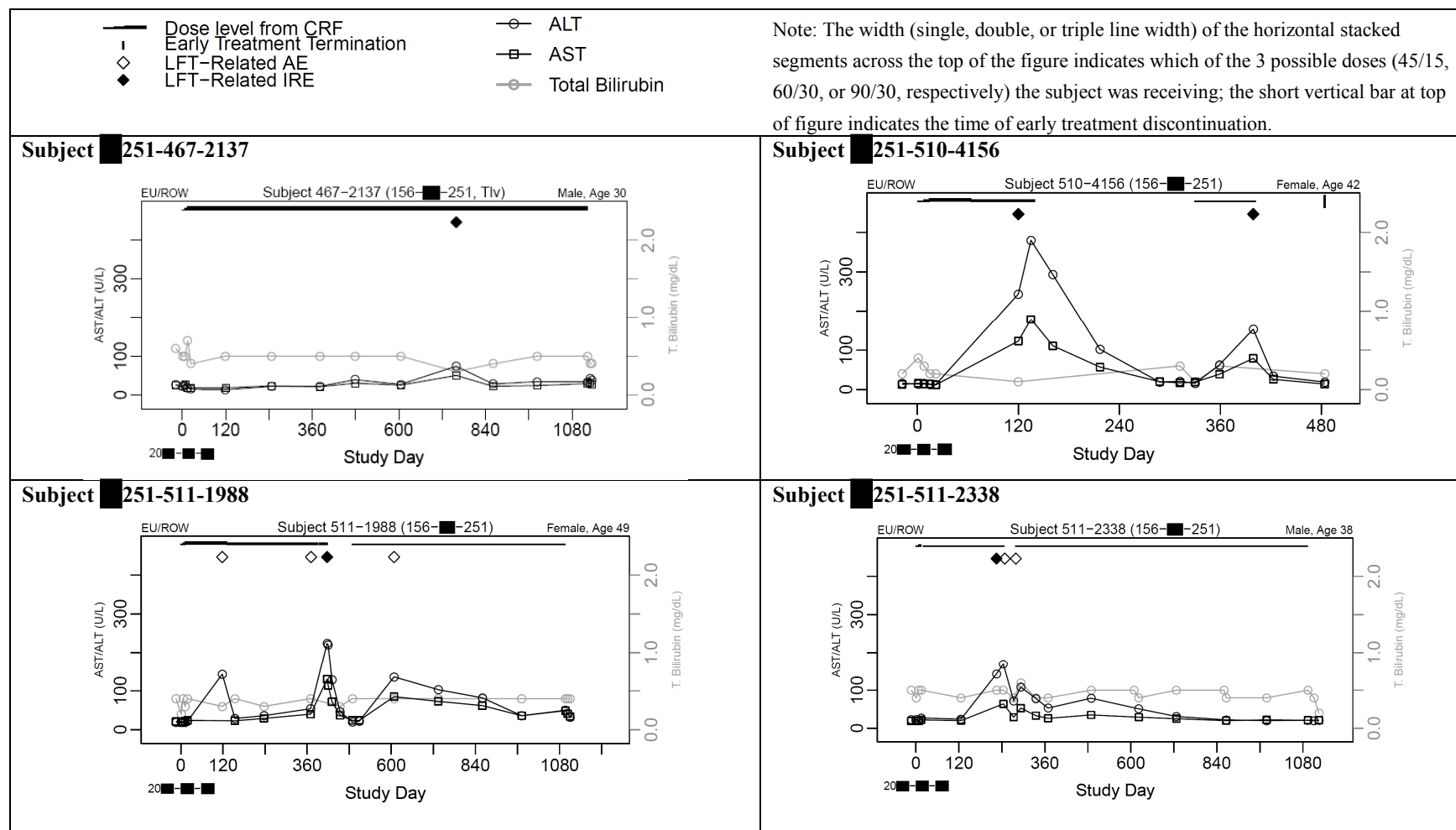
AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.
 Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.



2.7.4.7-23 Time Course Plots for Adjudicated Tolvaptan Subjects Who Continued/Resumed IMP After Highest Peak (N = 21), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.



2.7.4.7-23 Time Course Plots for Adjudicated Tolvaptan Subjects Who Continued/Resumed IMP After Highest Peak (N = 21), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

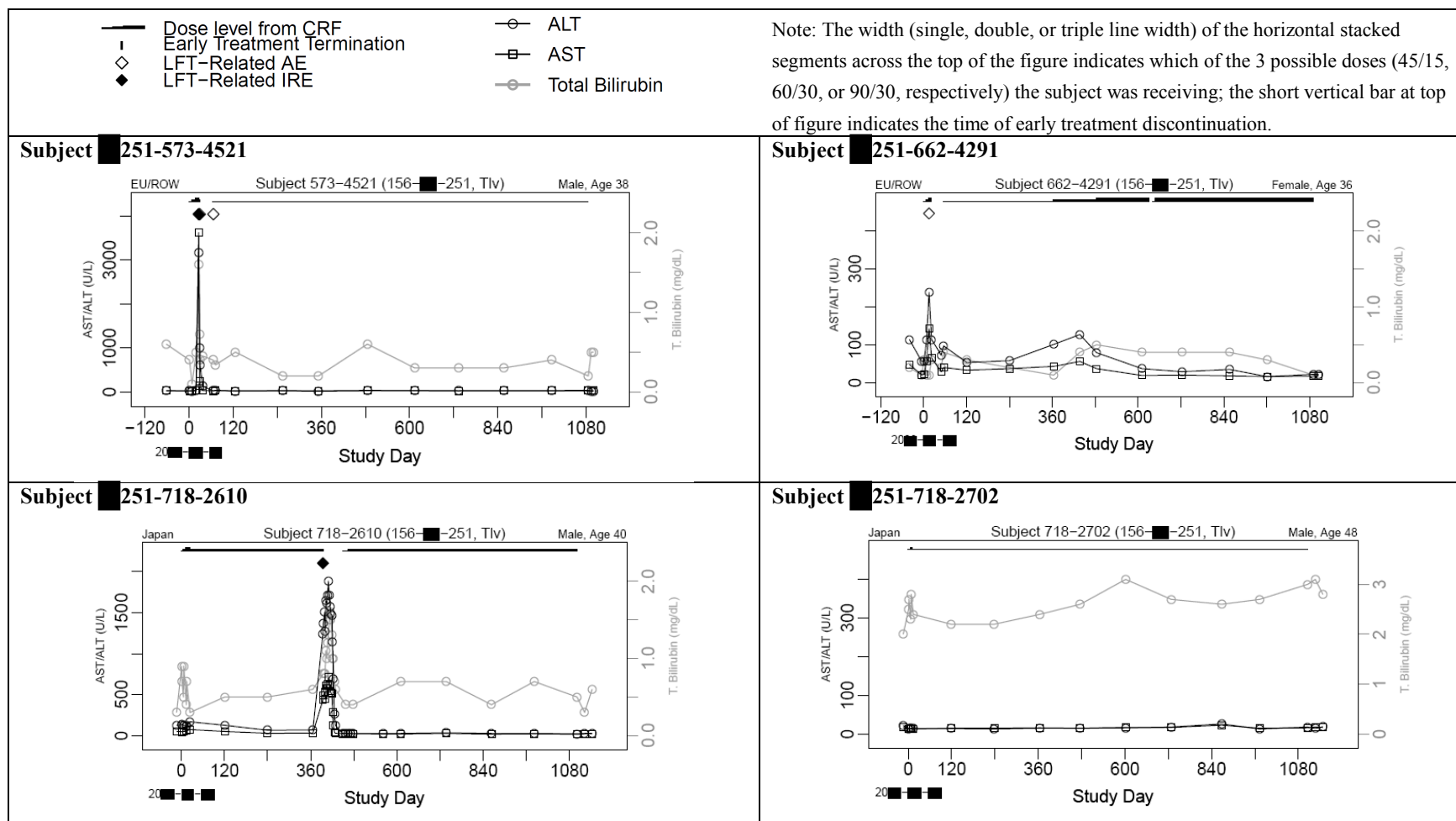
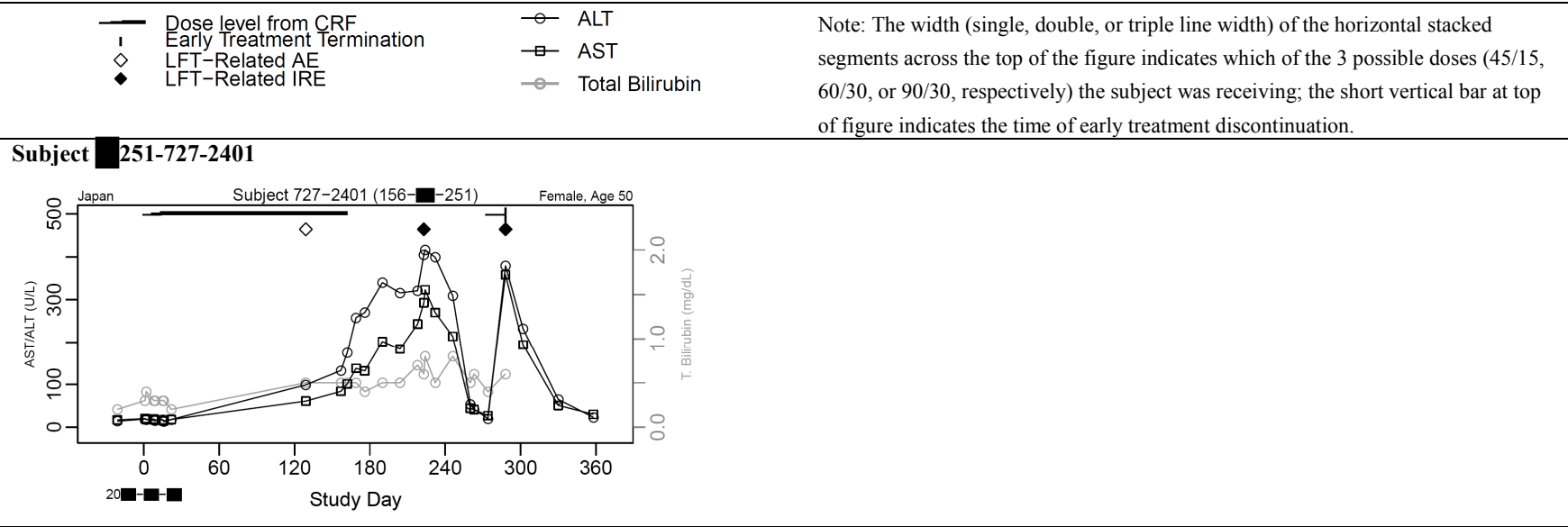


図 2.7.4.7-23 Time Course Plots for Adjudicated Tolvaptan Subjects Who Continued/Resumed IMP After Highest Peak (N = 21), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

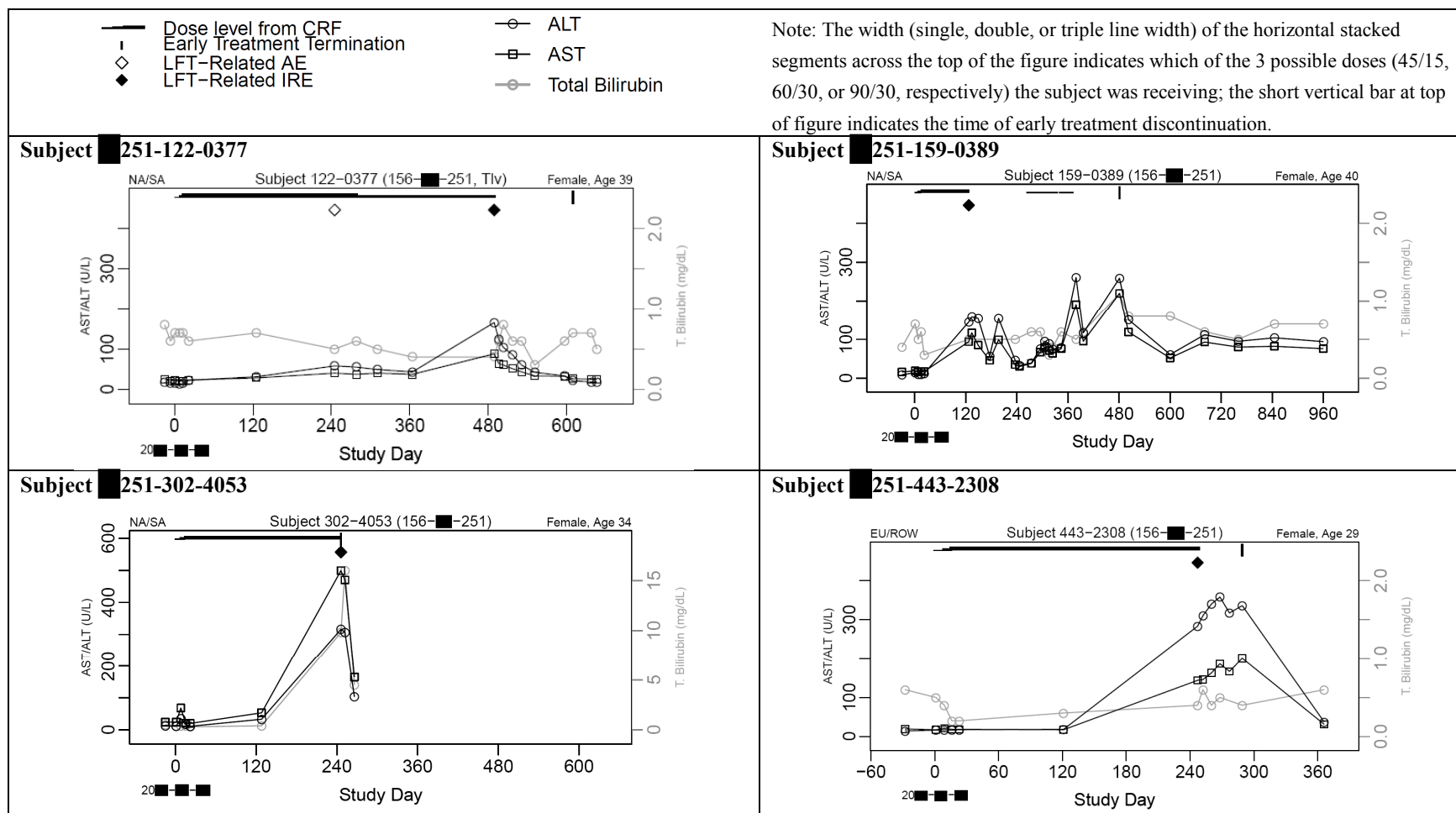


2.7.4.7-23 Time Course Plots for Adjudicated Tolvaptan Subjects Who Continued/Resumed IMP After Highest Peak (N = 21), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

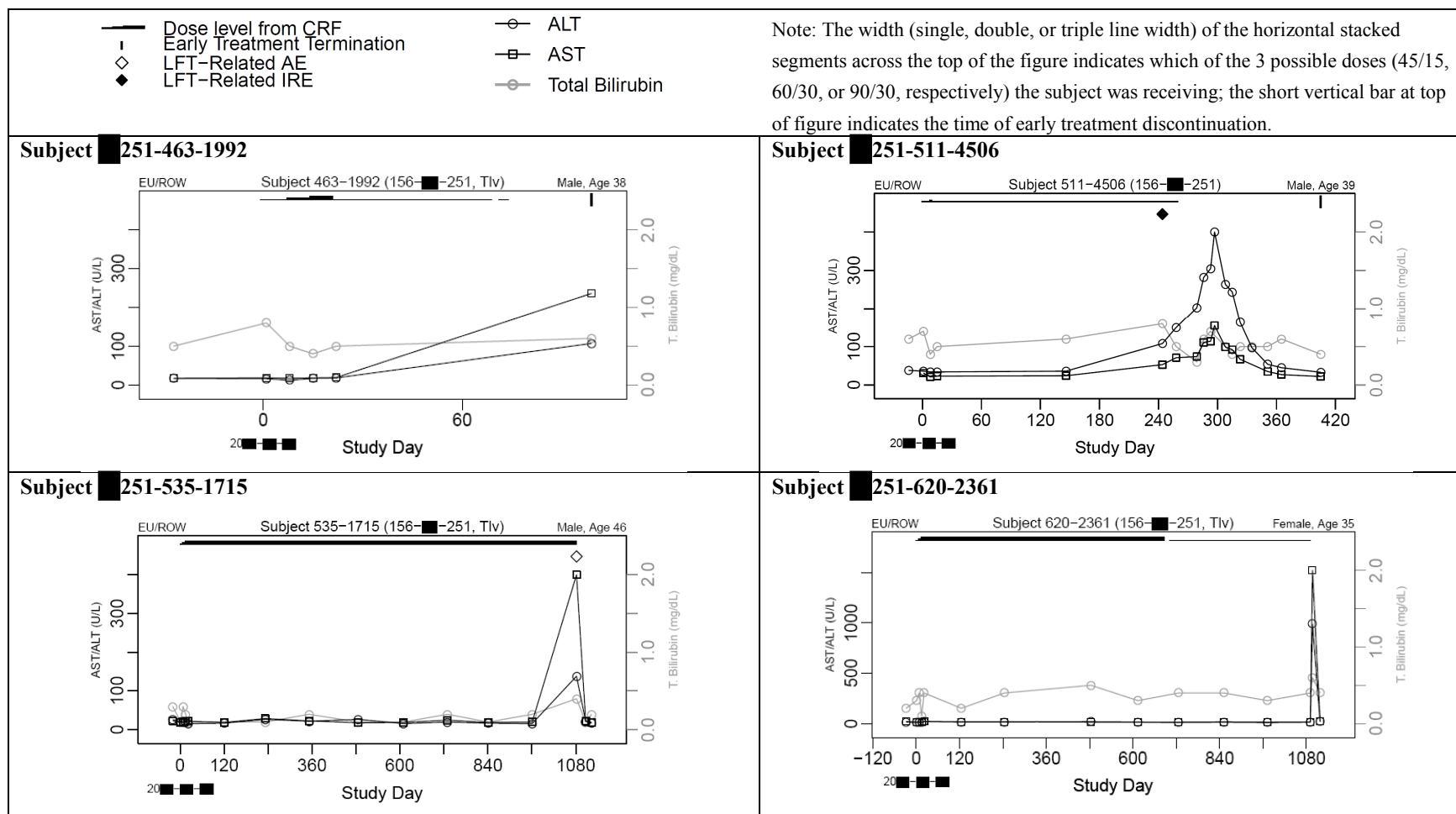
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<資料番号 5.3.5.3-02 : SCS CF-7>



2.7.4.7-24 Time Course Plots for Adjudicated Tolvaptan Subjects Who Discontinued IMP Before or Within Two Days of Peak (N = 14), Trial 156-251

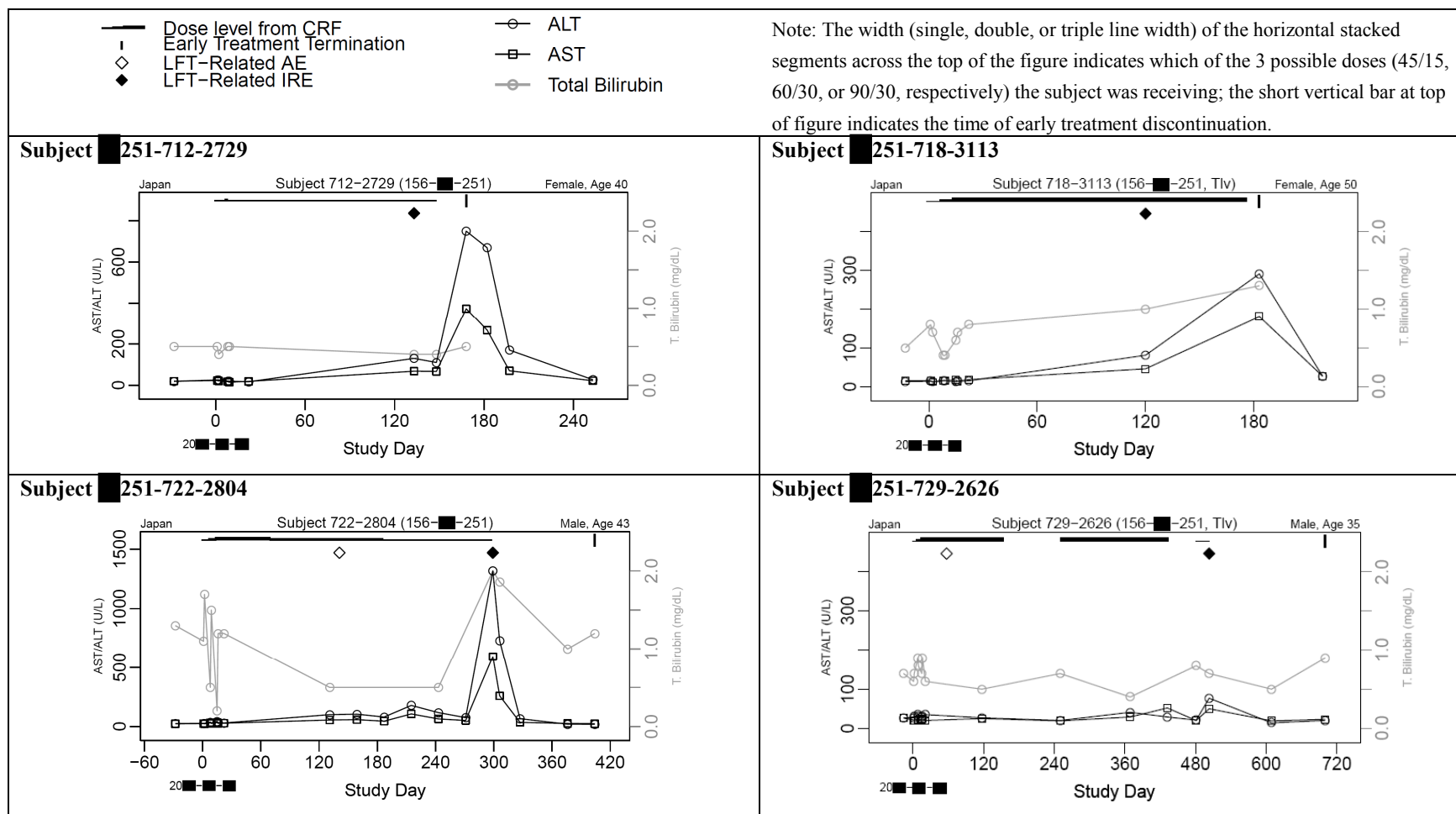
AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.
 Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.



☒ 2.7.4.7-24 Time Course Plots for Adjudicated Tolvaptan Subjects Who Discontinued IMP Before or Within Two Days of Peak (N = 14), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.



☒ 2.7.4.7-24 Time Course Plots for Adjudicated Tolvaptan Subjects Who Discontinued IMP Before or Within Two Days of Peak (N = 14), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

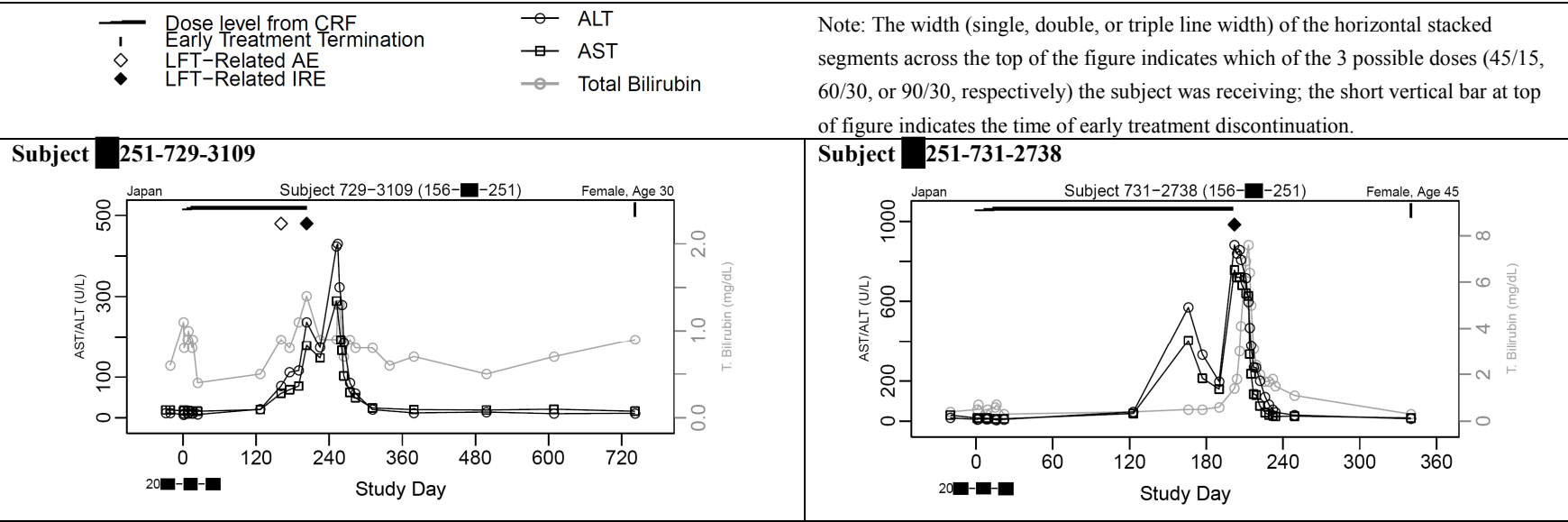
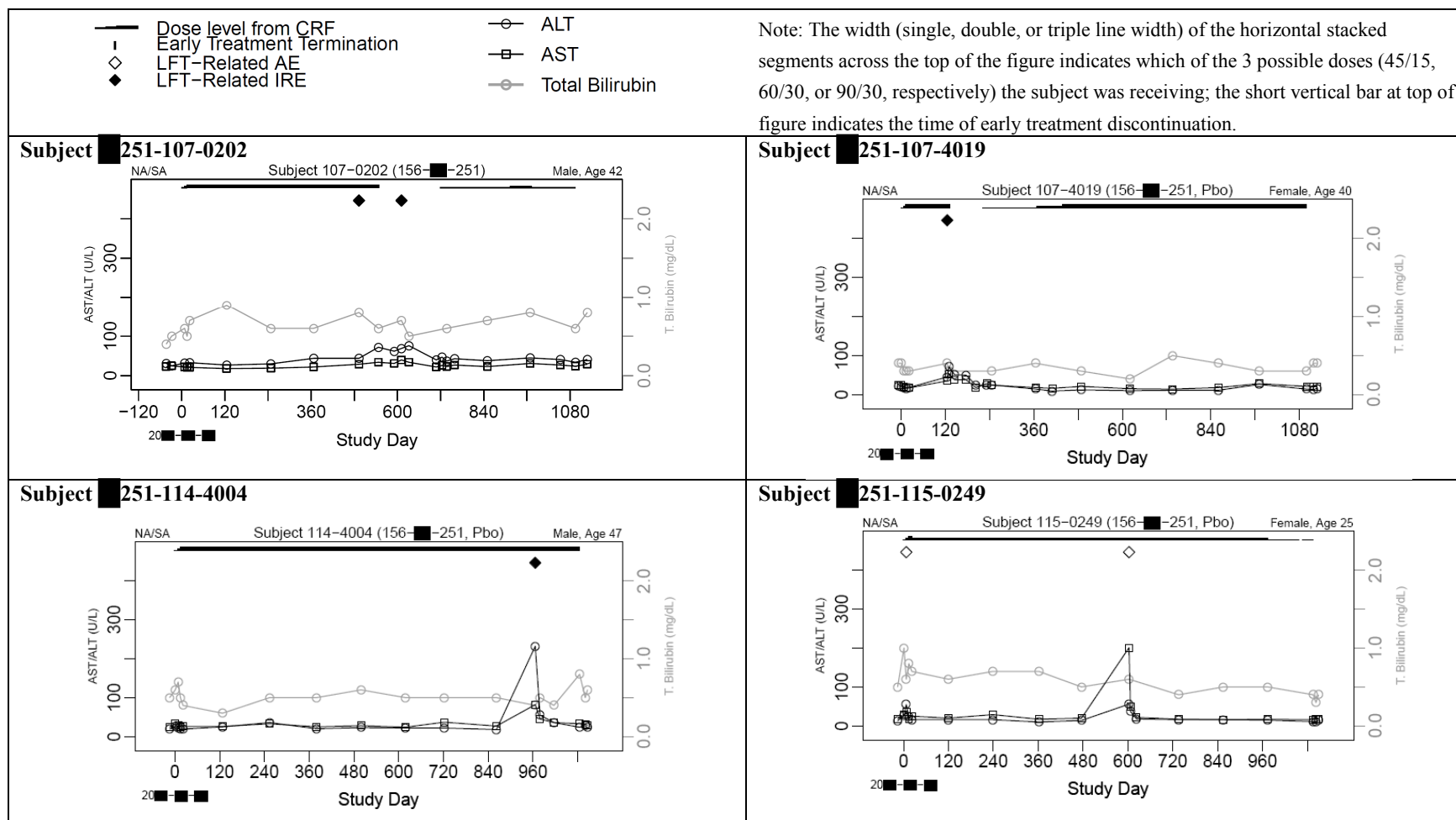


図 2.7.4.7-24 Time Course Plots for Adjudicated Tolvaptan Subjects Who Discontinued IMP Before or Within Two Days of Peak (N = 14), 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

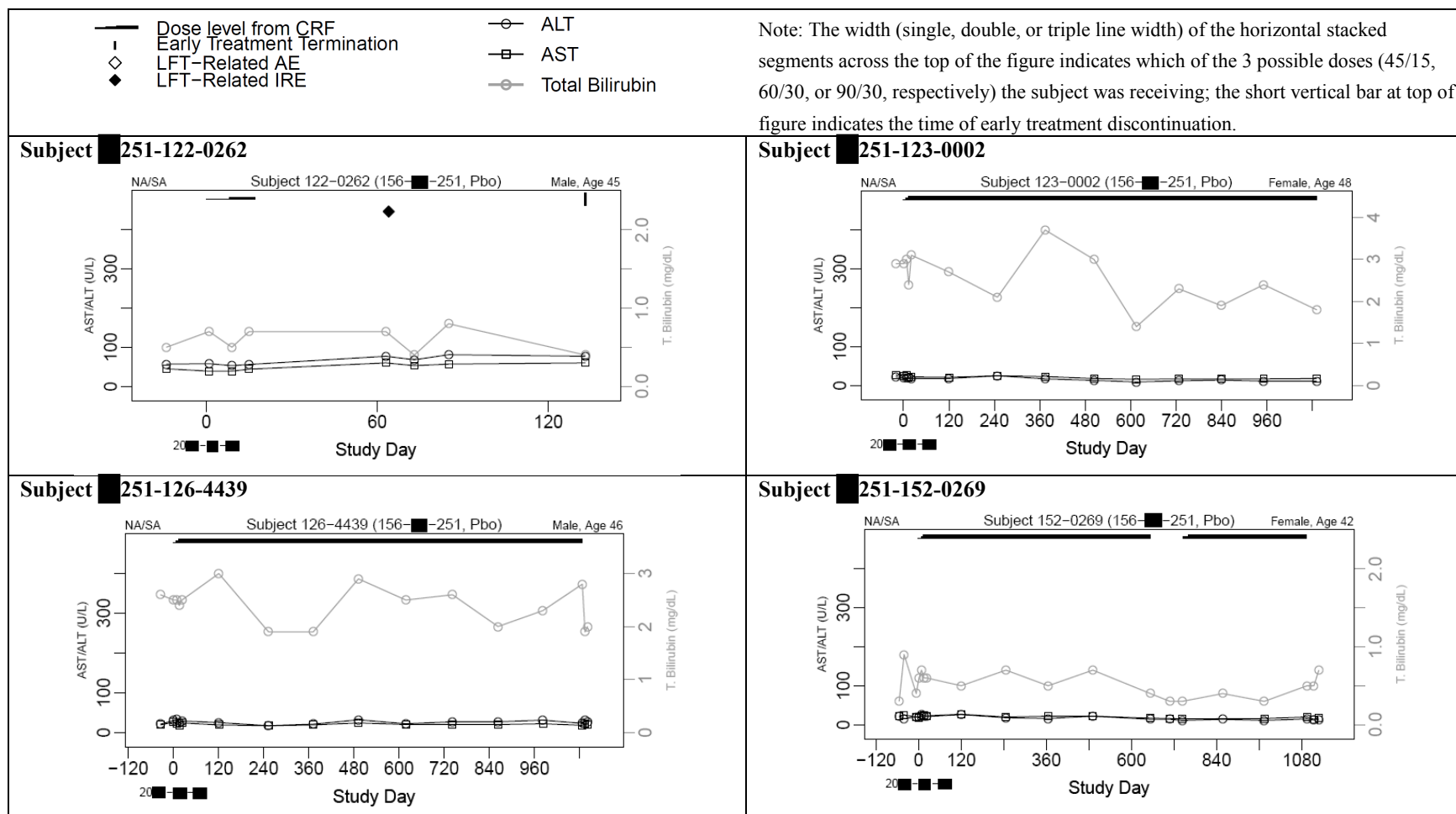
Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

<資料番号 5.3.5.3-02 : SCS CF-8>



2.7.4.7-25 Time Course Plots for Adjudicated Placebo Subjects (N = 11), Trial 156-251

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; Pbo = placebo; ROW = rest of world; SA = South America; T = total.
 Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.



2.7.4.7-25 Time Course Plots for Adjudicated Placebo Subjects (N = 11), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; Pbo = placebo; ROW = rest of world; SA = South America; T = total.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin

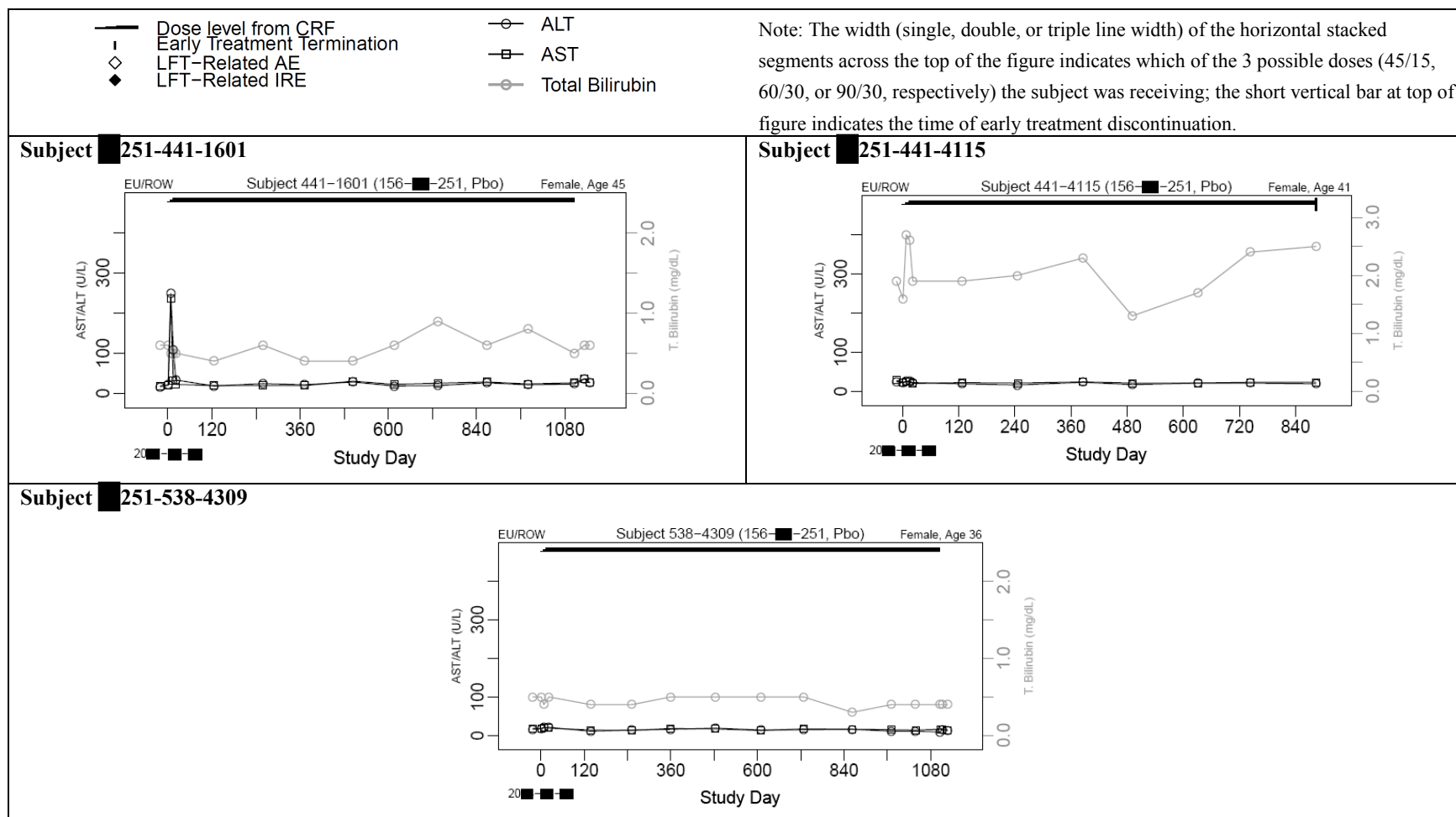


図 2.7.4.7-25 Time Course Plots for Adjudicated Placebo Subjects (N = 11), Trial 156-251 (continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test; NA = North America; Pbo = placebo; ROW = rest of world; SA = South America; T = total.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

<資料番号 5.3.5.3-02 : SCS CF-9>

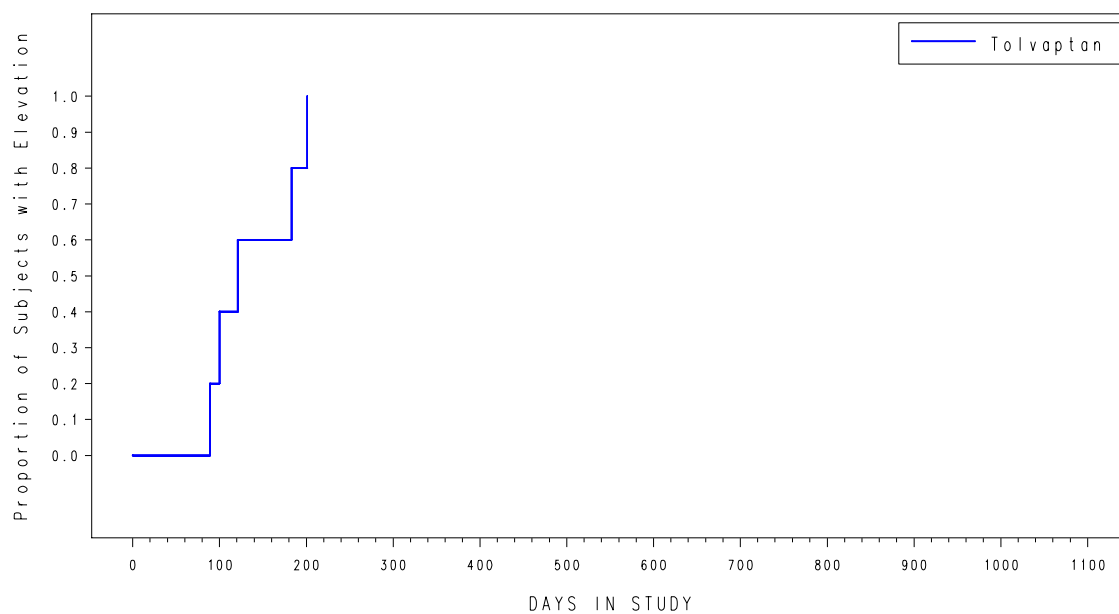


図 2.7.4.7-26 Kaplan-Meier Curve for Time to First Elevation in ALT of Greater Than 3 Times ULN, Subset of “Highly Likely” and “Probable” (156-271)

Note: Includes central and local laboratory data

<資料番号 5.3.5.2-05 : Figure10.8.7.4.2.3.2-1>

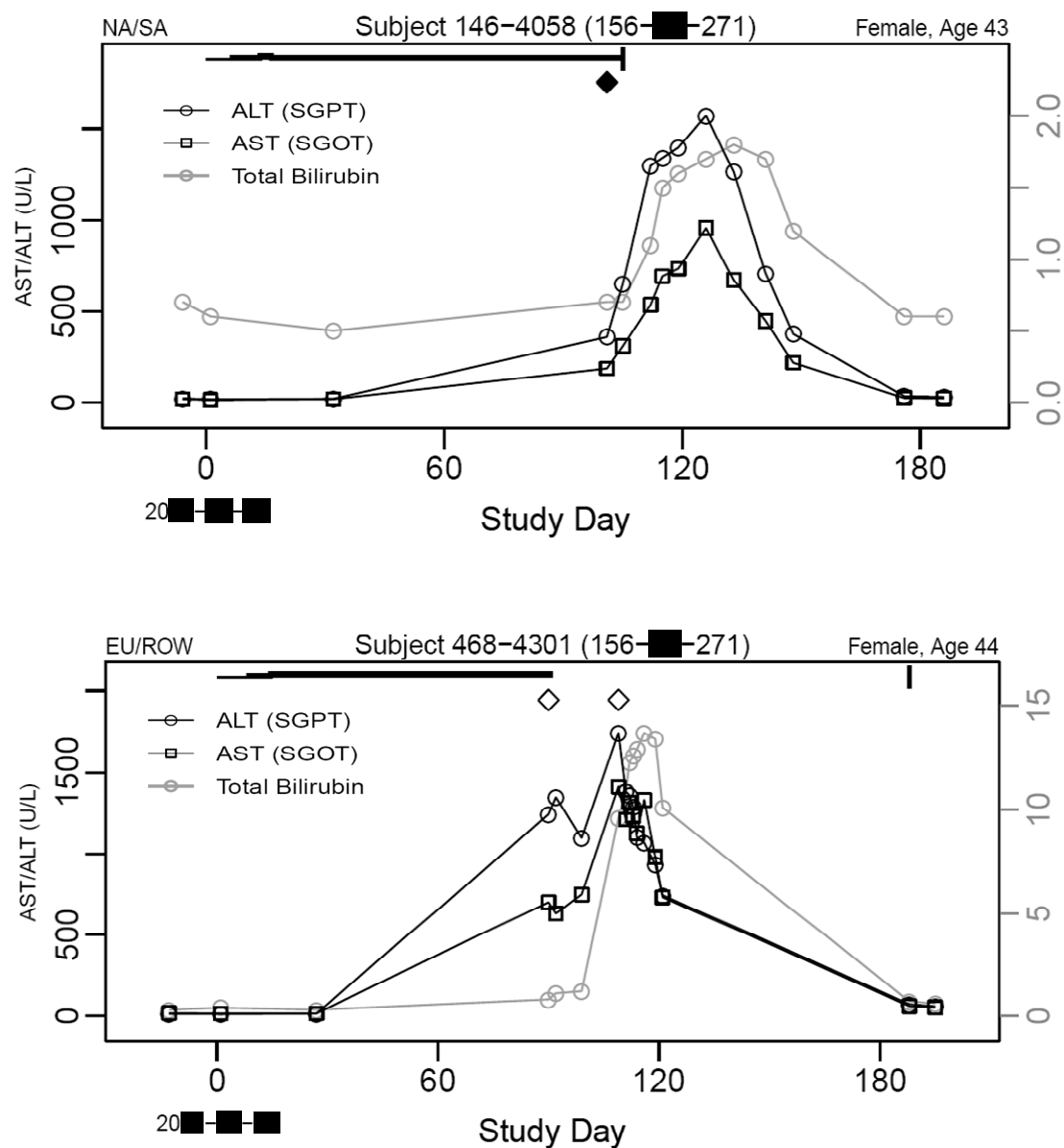


図 2.7.4.7-27 Liver Function Test Values Over Time for Subjects Adjudicated as “Highly Likely” (156-271)

NA = North America; ROW = rest of world; SA = South America; T = total.

Note: The subject’s IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15, 60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an immediately reportable event).

<資料番号 5.3.5.2-05 : Figure10.8.7.4.2.3.3-1>

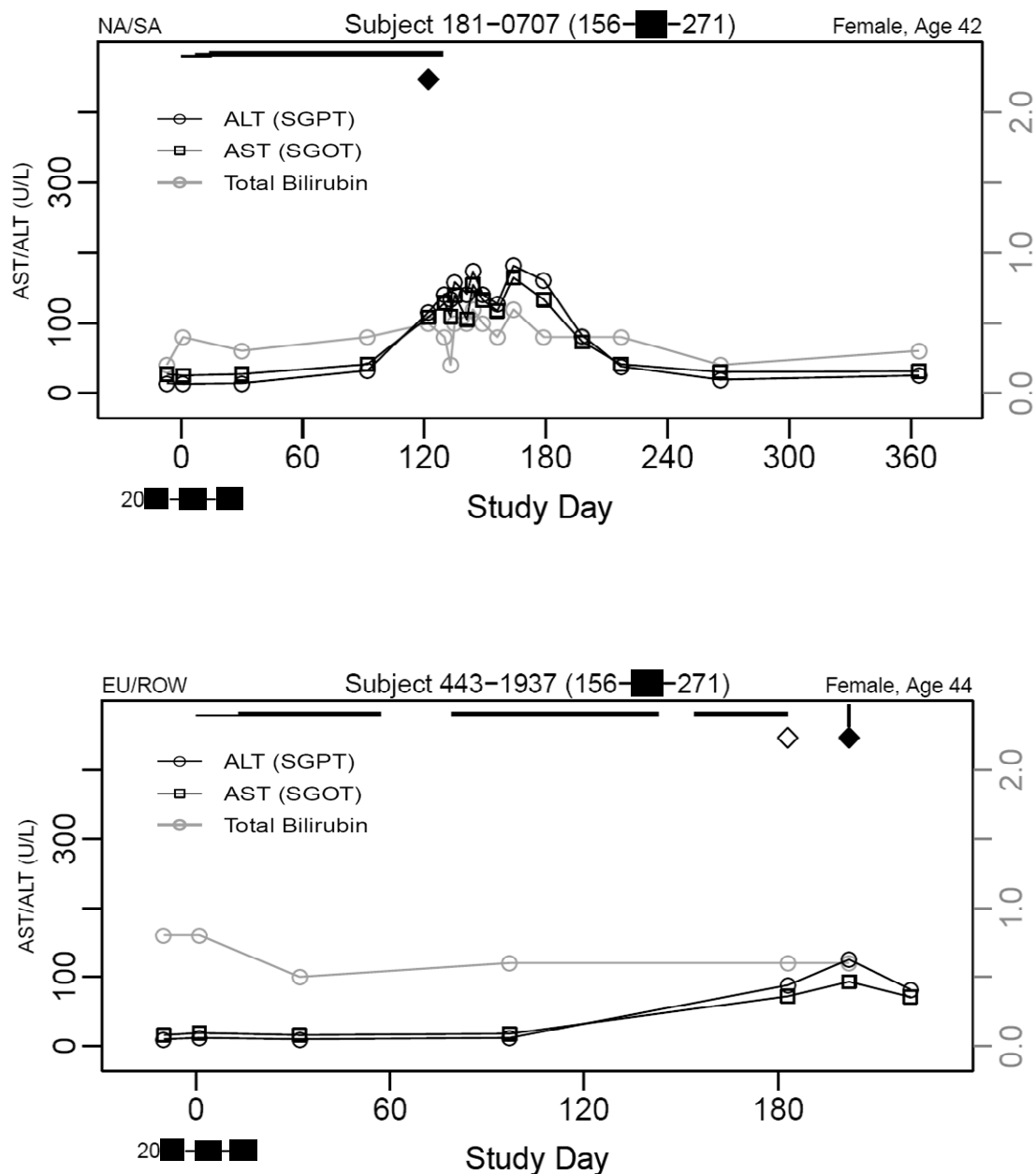


図 2.7.4.7-28 Liver Function Test Values Over Time for Subjects With Events Having a “Probable” Causal Relationship to IMP (156-271)

NA = North America; ROW = rest of world; SA = South America; T = total.

Note: The subject’s IMP history is shown along the top of the panel (solid bar). The width of the solid bar indicates which of the three possible doses (45/15, 60/30, or 90/30 mg) the subject was receiving. A vertical bar indicates the time of early termination from the trial. The diamond indicates the time of hepatic AE report (solid diamond indicates the event was an immediately reportable event).

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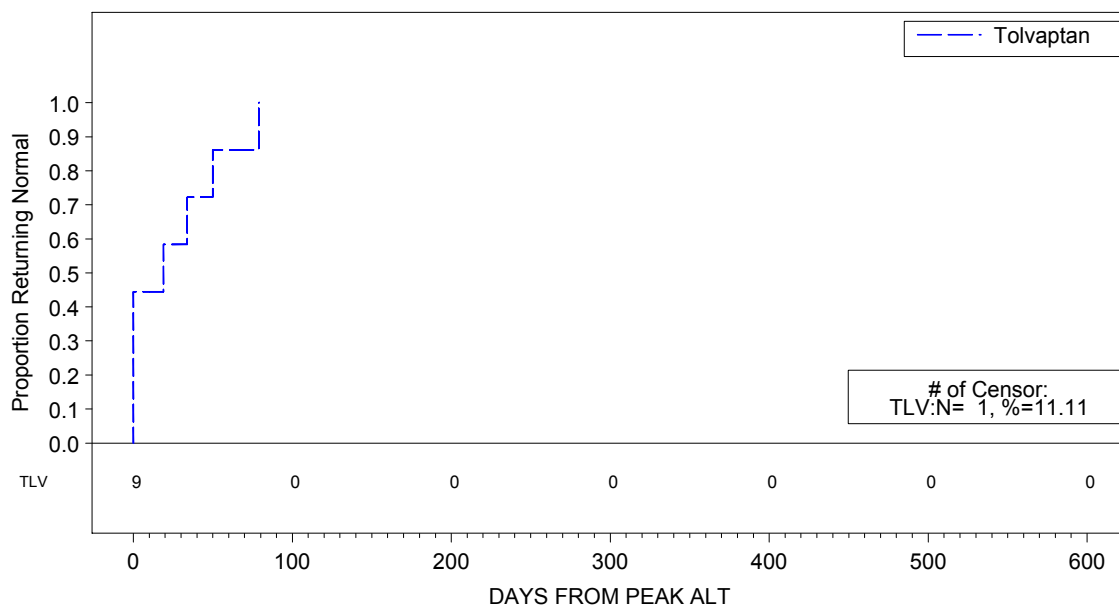


図 2.7.4.7-29 Kaplan-Meier Curves of Time From Peak ALT to Less Than or Equal to 3 Times ULN, Adjudicated Subjects (N = 9), Trial 156-[REDACTED]-271

ALT = alanine aminotransferase; TLV = tolvaptan; ULN = upper limit of normal.

Note: The censored subject (Subject [REDACTED]271-552-4349, delayed-treated tolvaptan) was identified for adjudication using data obtained after the [REDACTED] 20[REDACTED] cutoff date and was included in the adjudication for completeness (further details are provided in SCS CT-8). The subject was censored from this analysis because the ALT had not returned to $\leq 3 \times \text{ULN}$ as of the last recorded measurement in the dataset (CSR 156-[REDACTED]-271 ST-1.2). Tolvaptan treatment for this subject was discontinued due to a serious TEAE of Transaminases Increased (post cutoff data on file). The ALT was $5.5 \times \text{ULN}$ around the time of treatment discontinuation (CSR 156-[REDACTED]-271 ST-1.2). However, further follow up showed that the ALT had resolved to $\leq 3 \times \text{ULN}$ by approximately 70 days after peaking (the last reported ALT measurement was 53 U/L [reference range 6 to 43 U/L]) and the serious TEAE was reported as resolved 73 days after discontinuation of tolvaptan (post cutoff data on file).

<資料番号 5.3.5.3-02 : SCS CF-10>

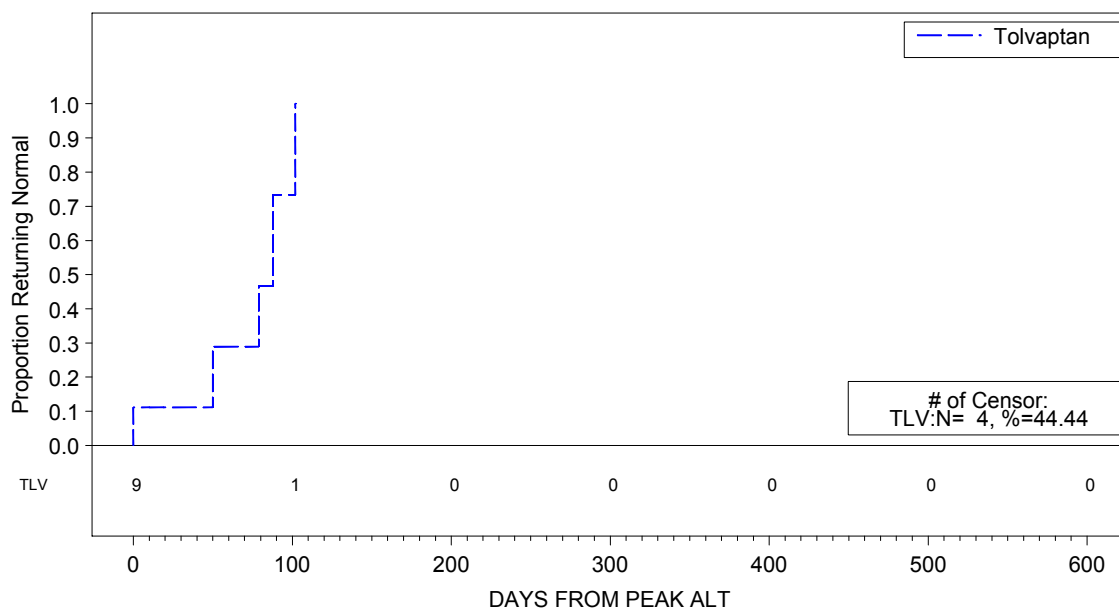


図 2.7.4.7-30 Kaplan-Meier Curves of Time From Peak ALT to the ULN or Below, Adjudicated Subjects (N = 9), Trial 156-271

ALT = alanine aminotransferase; TLV = tolvaptan; ULN = upper limit of normal.

Note: Four tolvaptan subjects were censored from this analysis because the ALT had not returned to $\leq 1 \times \text{ULN}$ as of the last recorded measurement in the dataset:

- Subject 271-552-4349 (delayed-treated tolvaptan) was identified for adjudication using data obtained after the 20 cutoff date and was included in the adjudication for completeness (further details are provided in SCS CT-8). Tolvaptan treatment for this subject was discontinued due to a serious TEAE of Transaminases Increased (post cutoff data on file). The ALT was $5.5 \times \text{ULN}$ around the time of treatment discontinuation (CSR 156-271 ST-1.2). Based on further follow up, the last reported ALT measurement approximately 70 days after peaking was 53 U/L (reference range 6-43 U/L) and the serious TEAE was reported as resolved 73 days after discontinuation of tolvaptan (post cutoff data on file).
- Subject 271-443-1937 (delayed-treated tolvaptan) discontinued tolvaptan treatment due to a serious TEAE of Transaminases Increased (ALT was $3.7 \times \text{ULN}$); after discontinuation of tolvaptan the ALT decreased, and was $1.6 \times \text{ULN}$ as of the last measurement on record as of the cutoff date of 20 (CSR 156-271 ST-1.2).
- Subject 271-468-4301 (delayed-treated tolvaptan) had transaminase elevations on Day 89 (ALT $36.6 \times \text{ULN}$ and AST $20.7 \times \text{ULN}$) and relatively concurrent elevation of BT ($9.7 \times \text{ULN}$ on Day 108). Serious TEAEs of Cytolytic Hepatitis and Hepatitis Cholestatic were reported for this subject, which led to the discontinuation of IMP; both events are reported as resolving. The ALT decreased to $1.7 \times \text{ULN}$ (CSR 156-271 ST-1.2) by 104 days after the last dose of tolvaptan.
- Subject 271-514-4360 (early-treated tolvaptan) had ALT of $1.6 \times \text{ULN}$ and AST of $5.4 \times \text{ULN}$ 90 days after initiation of tolvaptan. Tolvaptan treatment was ongoing at this time and these are the last measurements on record as of the cutoff date of 20 (CSR 156-271 ST-1.2).

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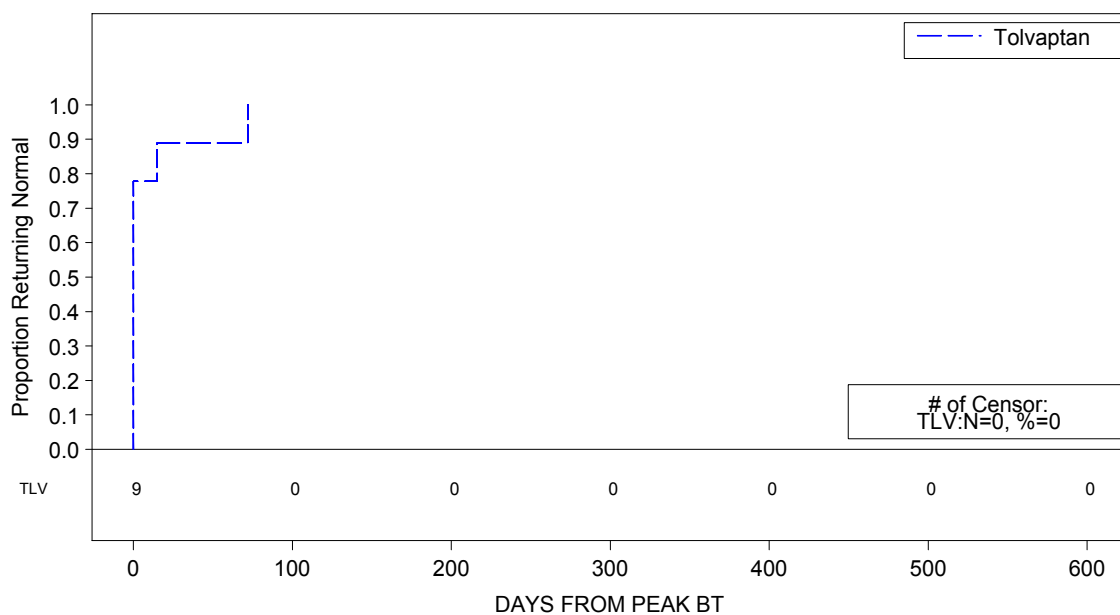
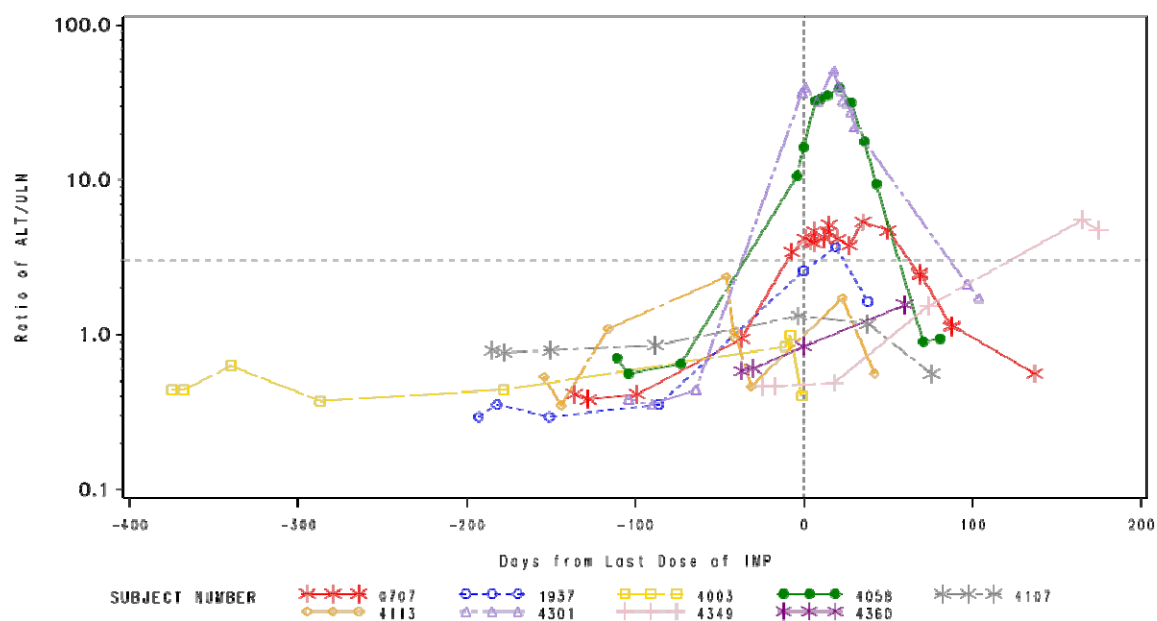


図 2.7.4.7-31 Kaplan-Meier Curves of Time From Peak BT to the ULN or Below, Adjudicated Subjects (N = 9), Trial 156-271

BT = total bilirubin; TLV = tolvaptan; ULN = upper limit of normal.

<資料番号 5.3.5.3-02 : SCS CF-12>



NOTE: Subjects 0707, 4003, 4058, 4113, 4301, 4360 and 4349 were not discontinued and their last dose were imputed as the last day of IMP based on the data cutoff.
 Subject 4058 has Liver Function Test Abnormal AE on [REDACTED] 20 with ACTION: Drug Withdrawn.
 Subject 0707 has Liver Function Test Abnormal AE on [REDACTED] 20 with ACTION: Drug Withdrawn.
 Subject 4301 has Liver Function Test Abnormal AE on [REDACTED] 20 with ACTION: Drug Withdrawn.

☒ 2.7.4.7-32 Longitudinal Time Course (Spaghetti Plot) of Ratio of ALT/ULN Over Time for Tolvaptan Adjudicated Subjects (N = 9), Trial 156-271

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase;

IMP = investigational medicinal product; ULN = upper limit of normal.

Note: Subject [REDACTED] 271-552-4349 (delayed-treated tolvaptan) was identified for adjudication using data obtained after the [REDACTED] 20 [REDACTED] cutoff date and was included in the adjudication for completeness (further details are in SCS CT-8). Further follow up information was obtained after this figure was prepared. Tolvaptan treatment for this subject was discontinued due to a serious TEAE of Transaminases Increased (post cutoff data on file). The ALT was $5.5 \times$ ULN around the time of treatment discontinuation (CSR 156-[REDACTED]-271 ST-1.2). Based on further follow up, the last reported ALT measurement approximately 70 days after peaking was 53 U/L (reference range 6-43 U/L) and the serious TEAE was reported as resolved 73 days after discontinuation of tolvaptan (post cutoff data on file).

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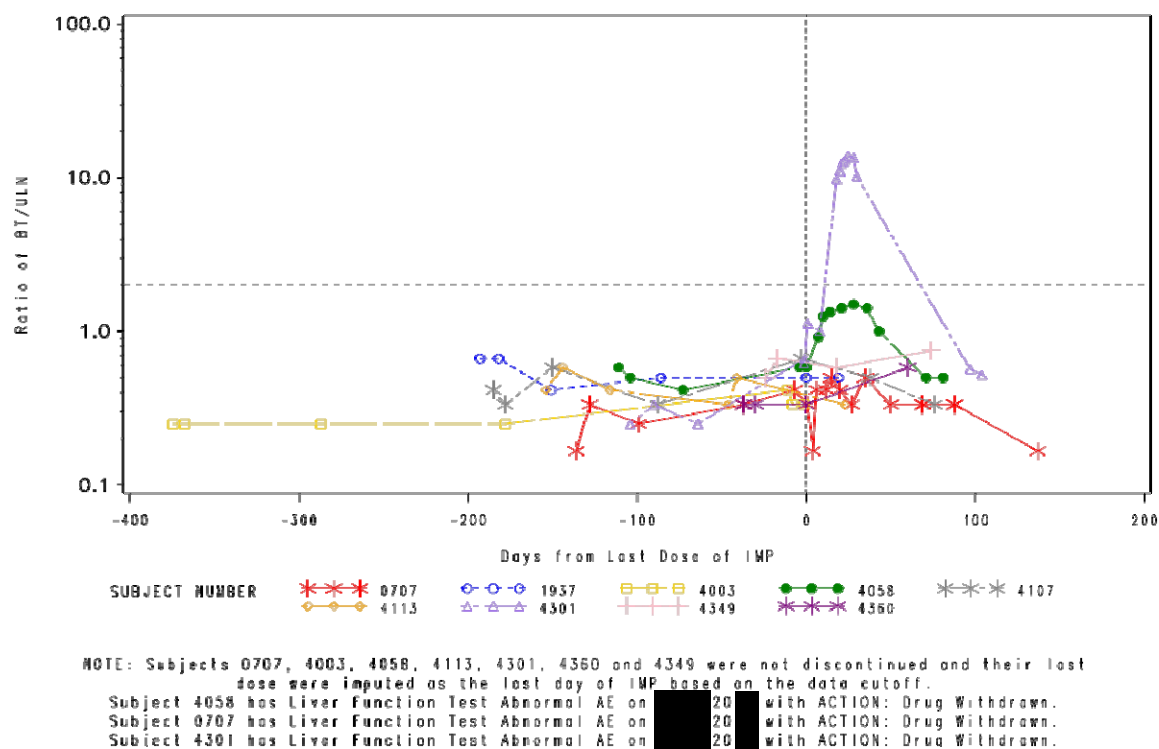


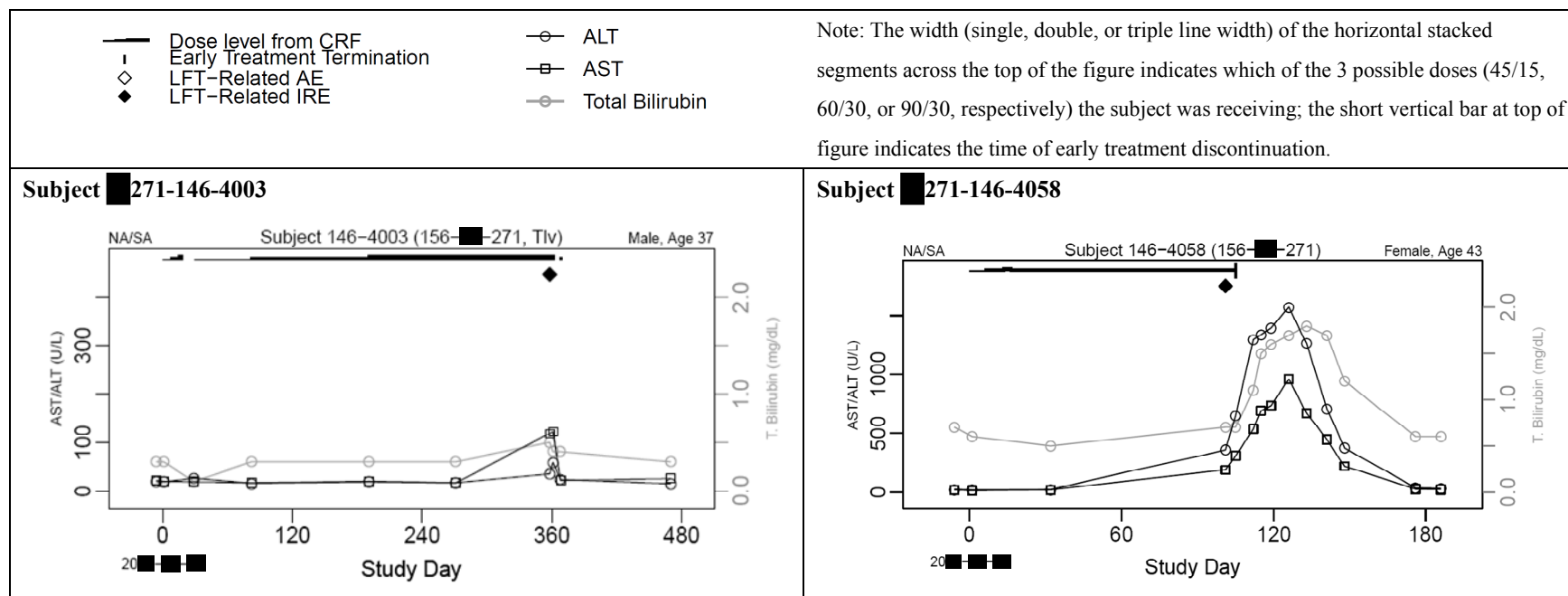
図 2.7.4.7-33 Longitudinal Time Course (Spaghetti Plot) of Ratio of BT/ULN Over Time for Tolvaptan Adjudicated Subjects (N = 9), Trial 156-[REDACTED]-271

AE = adverse event; BT = total bilirubin; IMP = investigational medicinal product; ULN = upper limit of normal.

Subject [REDACTED]271-552-4349 (delayed-treated tolvaptan) was identified for adjudication using data obtained after the [REDACTED] 20 [REDACTED] cutoff date and was included in the adjudication for completeness (further details are in SCS CT-8). Further follow up information was obtained after this figure was prepared.

Tolvaptan treatment for this subject was discontinued due to a serious TEAE of Transaminases Increased (post cutoff data on file). The ALT was $5.5 \times \text{ULN}$ around the time of treatment discontinuation (CSR 156-[REDACTED]-271 ST-1.2). Based on further follow up, the last reported ALT measurement approximately 70 days after peaking was 53 U/L (reference range 6-43 U/L) and the serious TEAE was reported as resolved 73 days after discontinuation of tolvaptan (post cutoff data on file).

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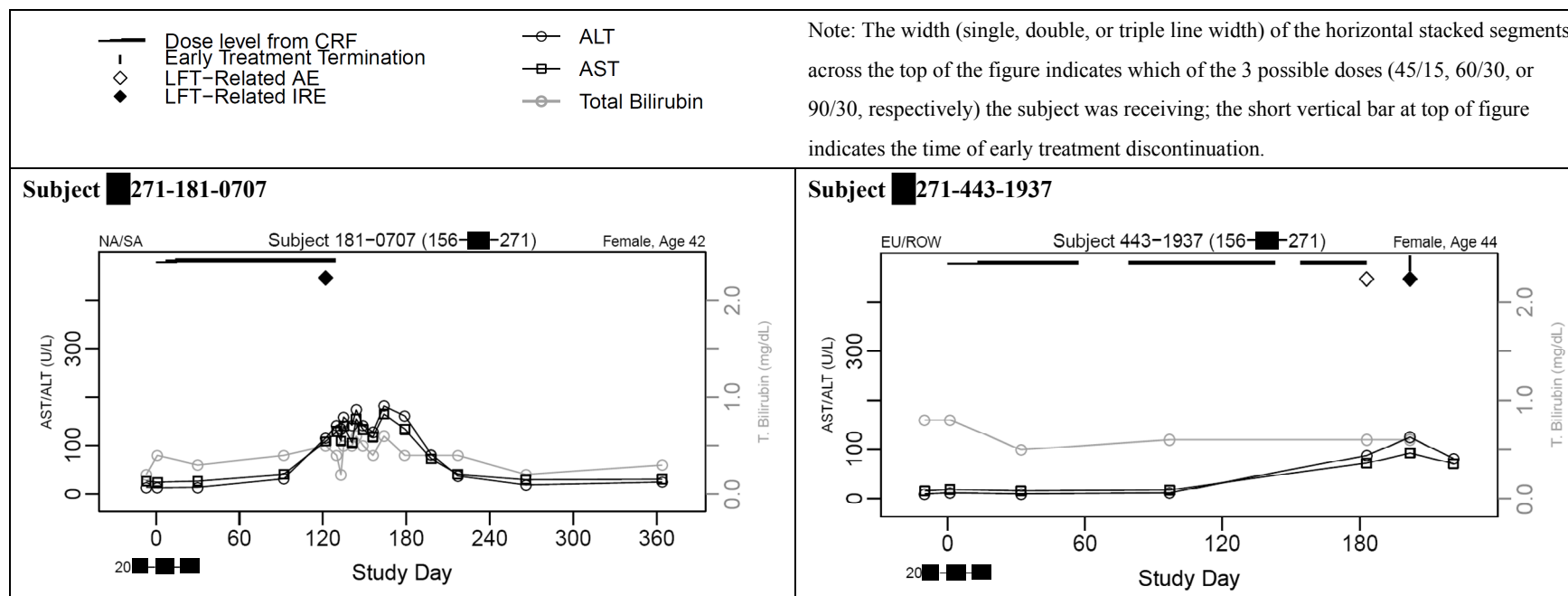
2.7.4.7-34 Time Course Plots for Adjudicated Subjects in Trial 156-271 (N = 9)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test;

NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolcaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

Note: For ongoing Trial 156-271, these figures may contain additional post cutoff laboratory data as compared with the CSR 156-271 Supplemental Tables (STs).



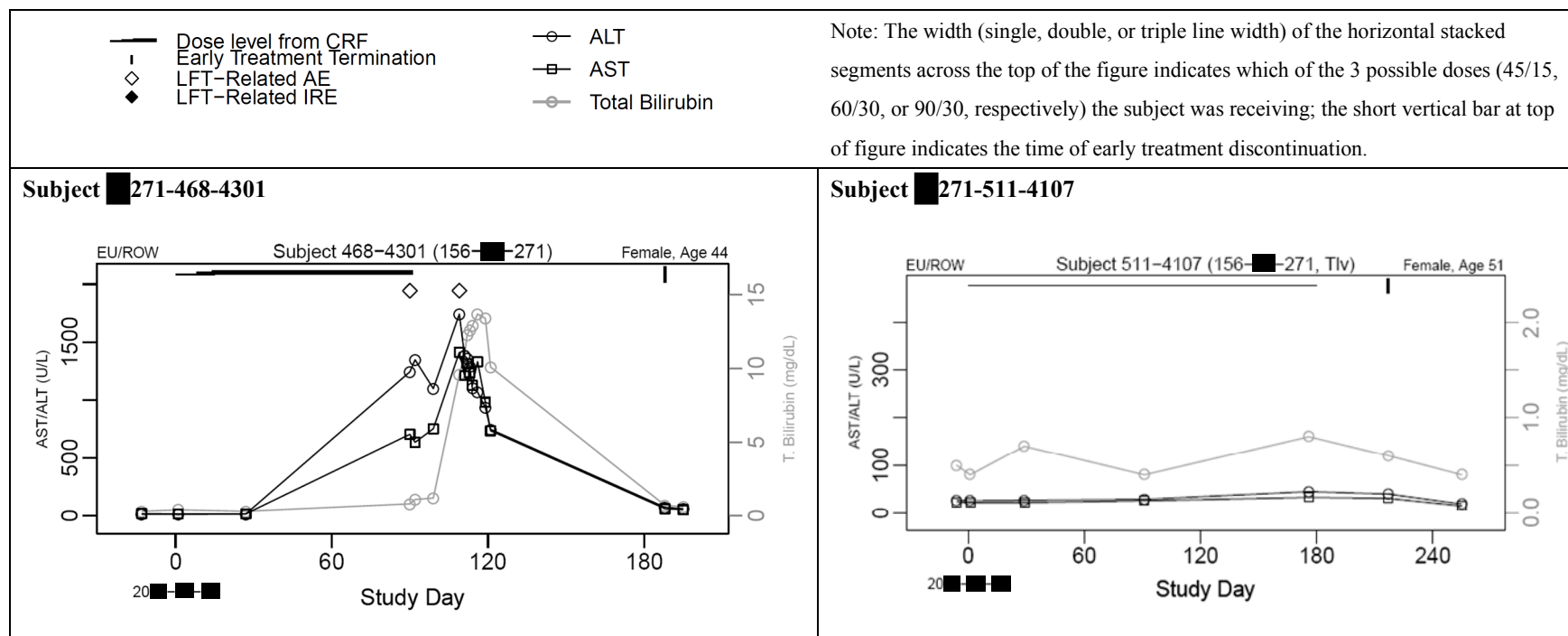
2.7.4.7-34 Time Course Plots for Adjudicated Subjects in Trial 156-271 (N = 9) (Continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test;

NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

Note: For ongoing Trial 156-271, these figures may contain additional post cutoff laboratory data as compared with the CSR 156-271 Supplemental Tables (STs).



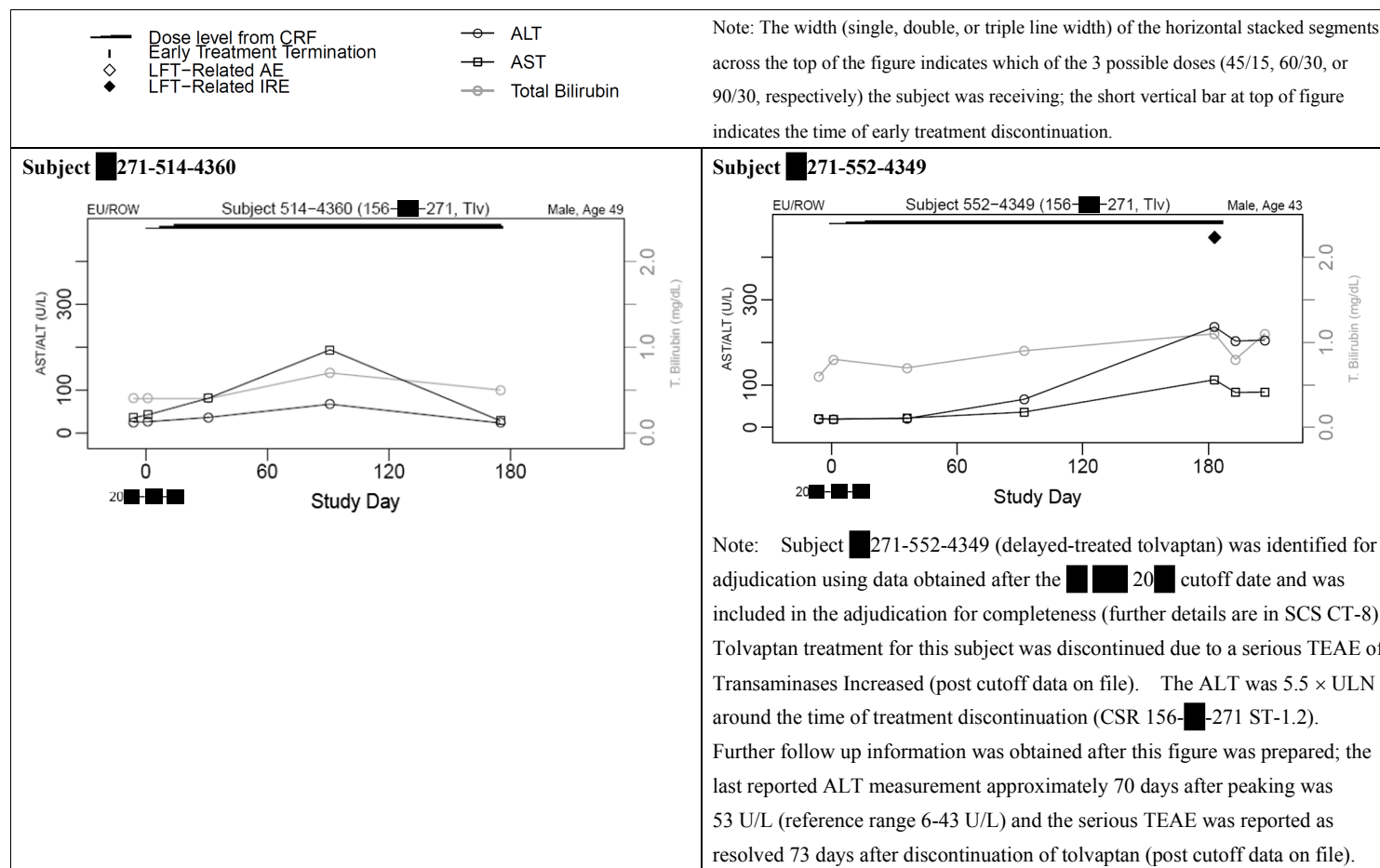
2.7.4.7-34 Time Course Plots for Adjudicated Subjects in Trial 156-271 (N = 9) (Continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test;

NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolcapant.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

Note: For ongoing Trial 156-271, these figures may contain additional post cutoff laboratory data as compared with the CSR 156-271 Supplemental Tables (STs).



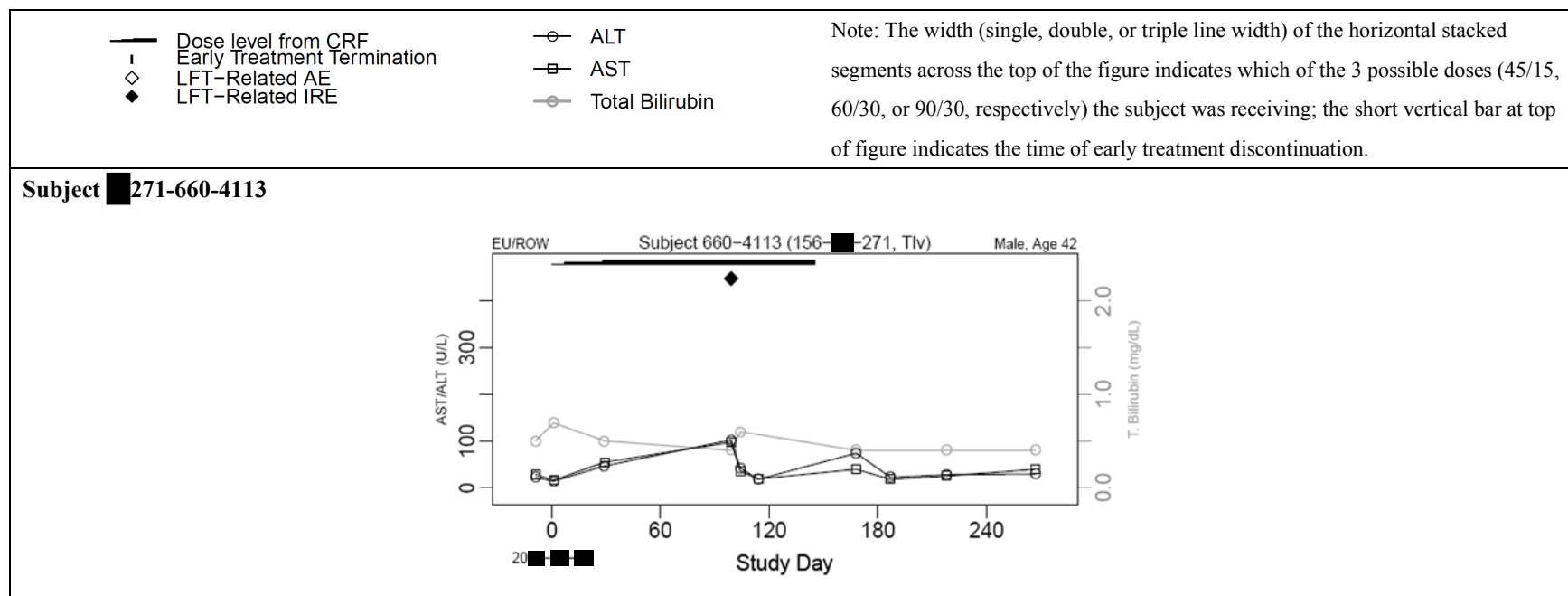
2.7.4.7-34 Time Course Plots for Adjudicated Subjects in Trial 156-271 (N = 9) (Continued)

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRF = case report form; EU = Europe; IRE = immediately reportable event; LFT = liver function test;

NA = North America; ROW = rest of world; SA = South America; T = total; Tlv = tolvaptan.

Note: Figures produced by the Statistical Data Analysis Center of the University of Wisconsin.

Note: For ongoing Trial 156-271, these figures may contain additional post cutoff laboratory data as compared with the CSR 156-271 Supplemental Tables (STs).



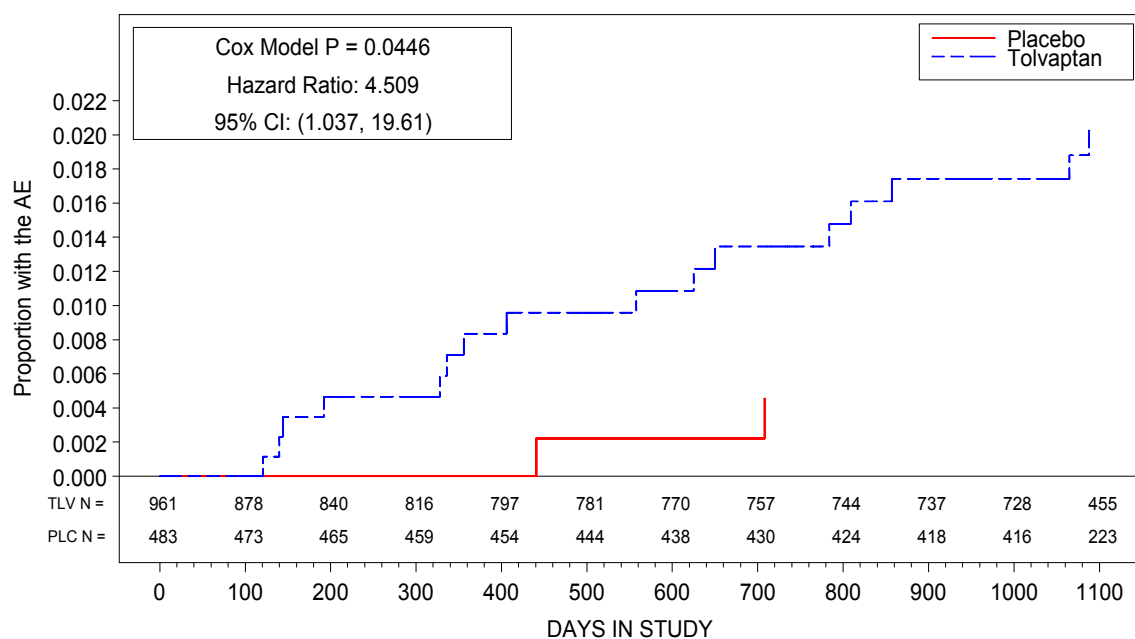
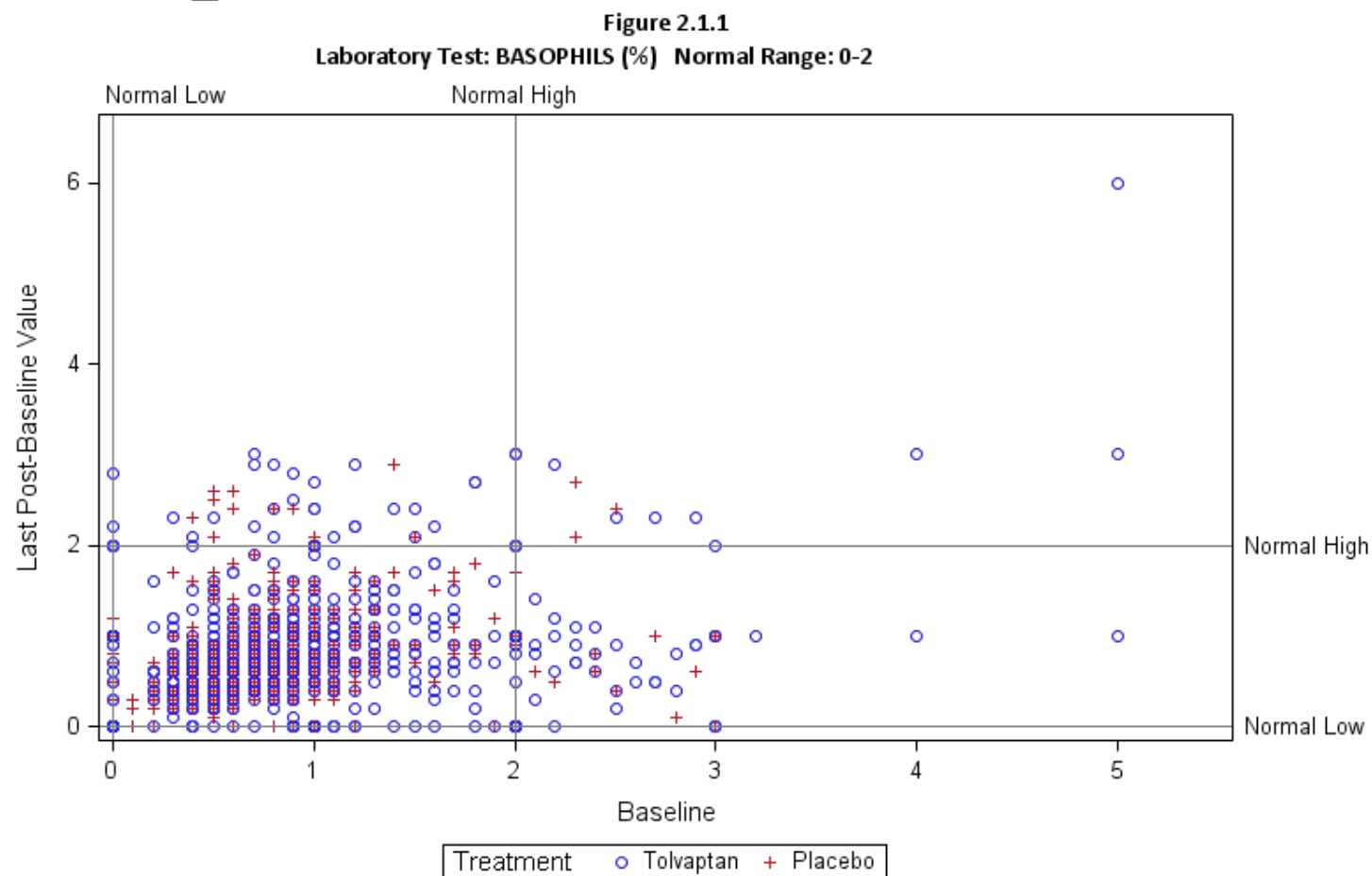


図 2.7.4.7-35 Kaplan-Meier Curves of Time to First Treatment-emergent Adverse Events in the Malignant Tumor SMQ

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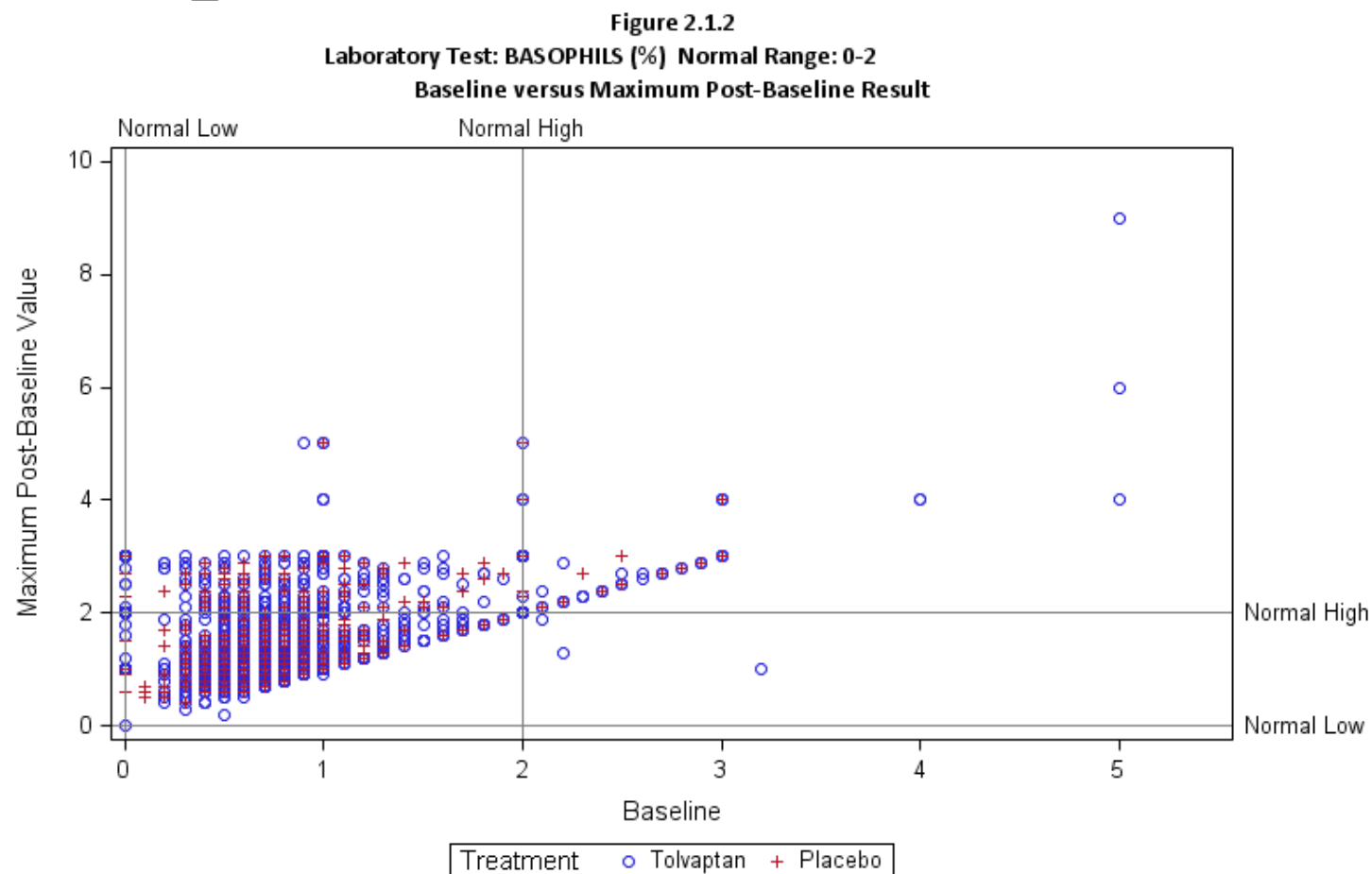
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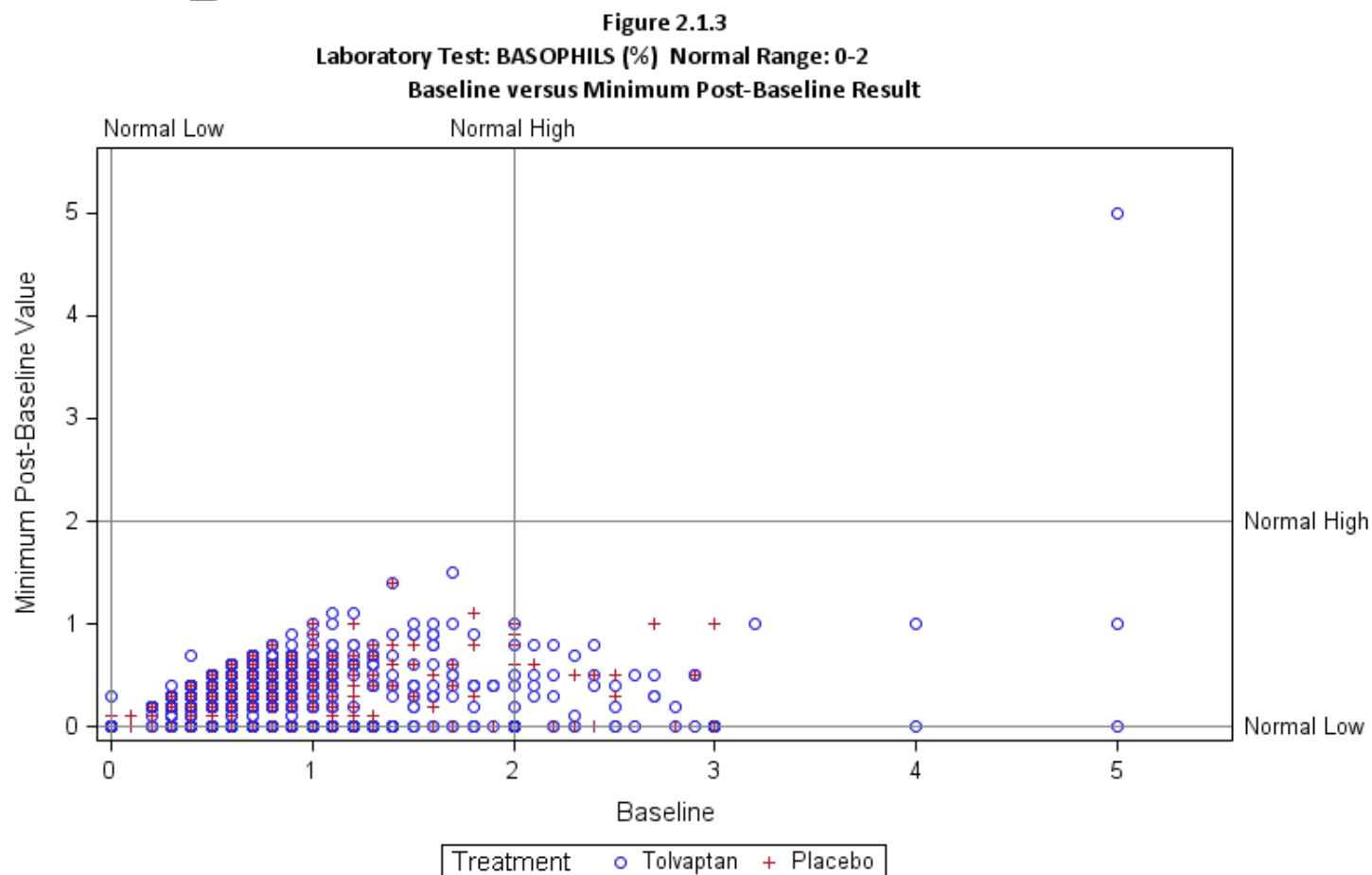
图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)



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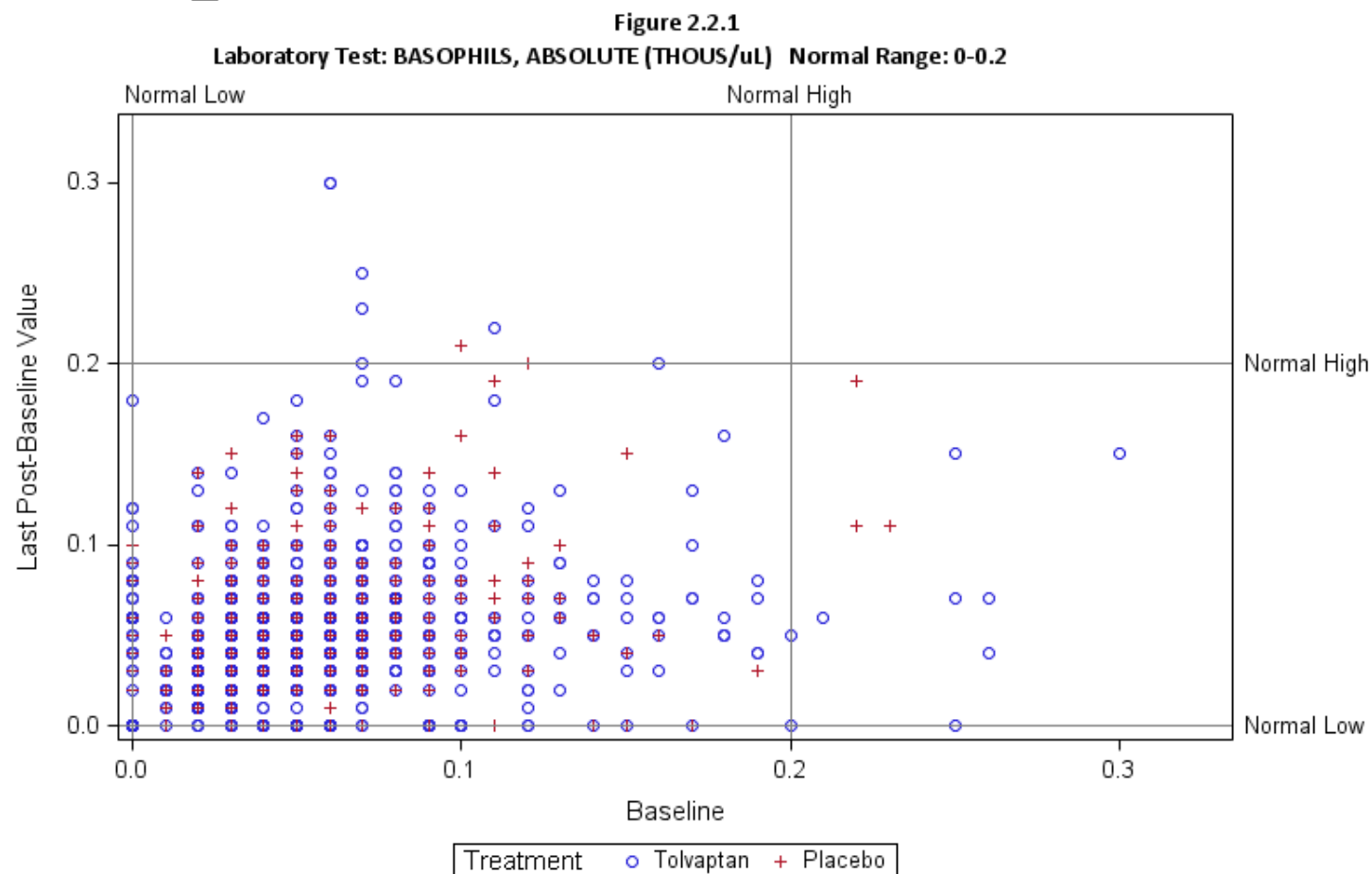
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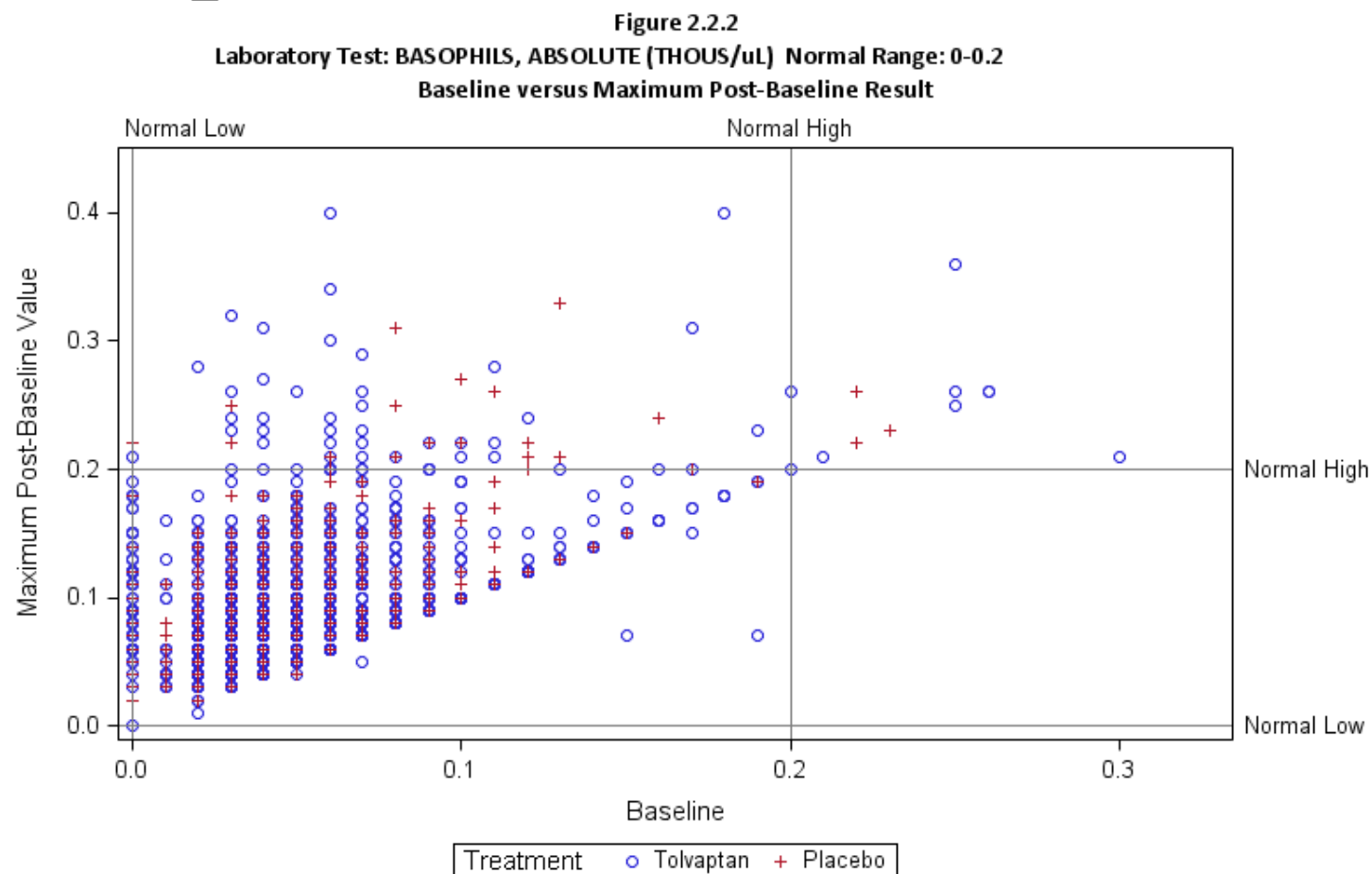
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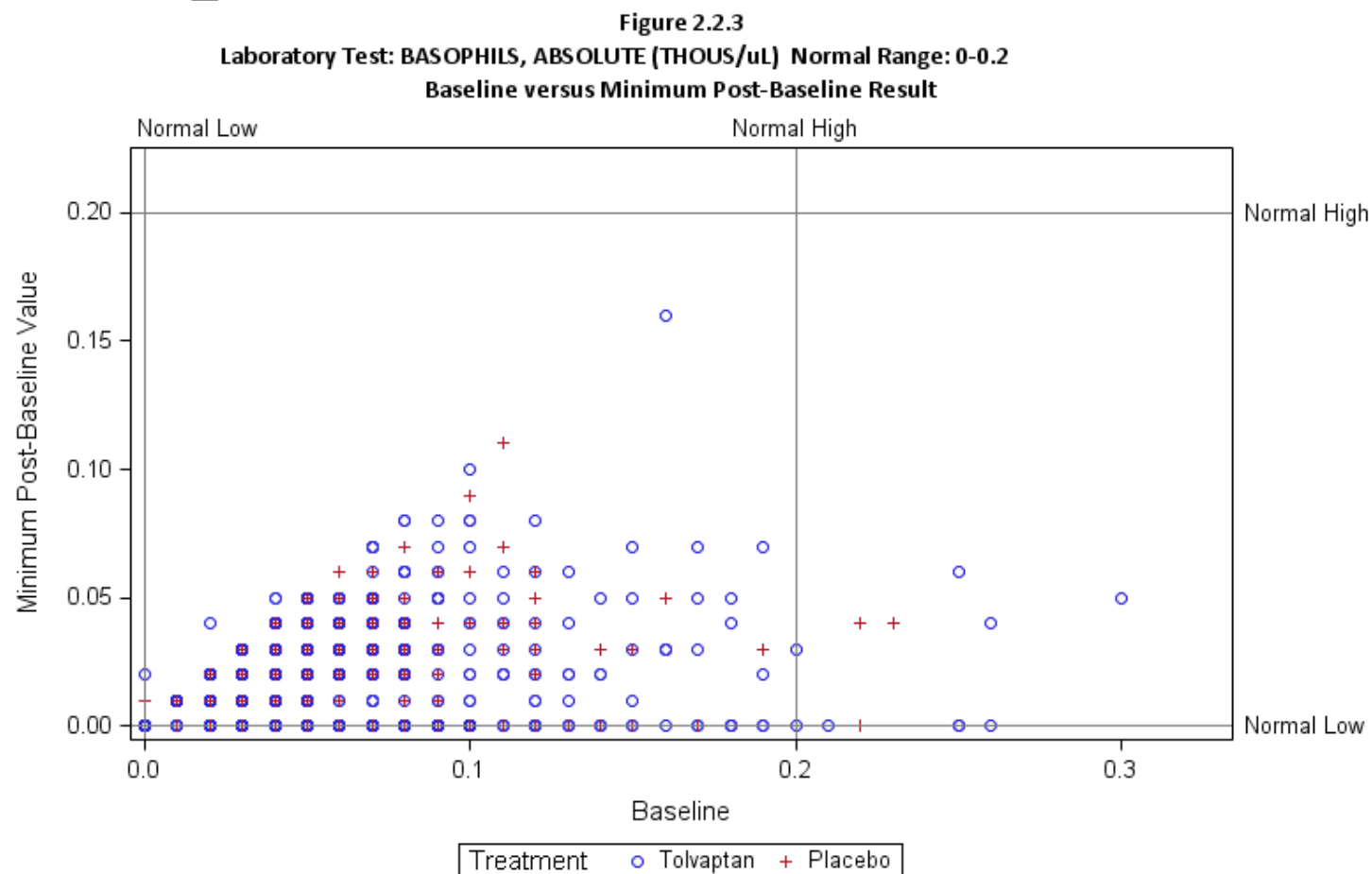
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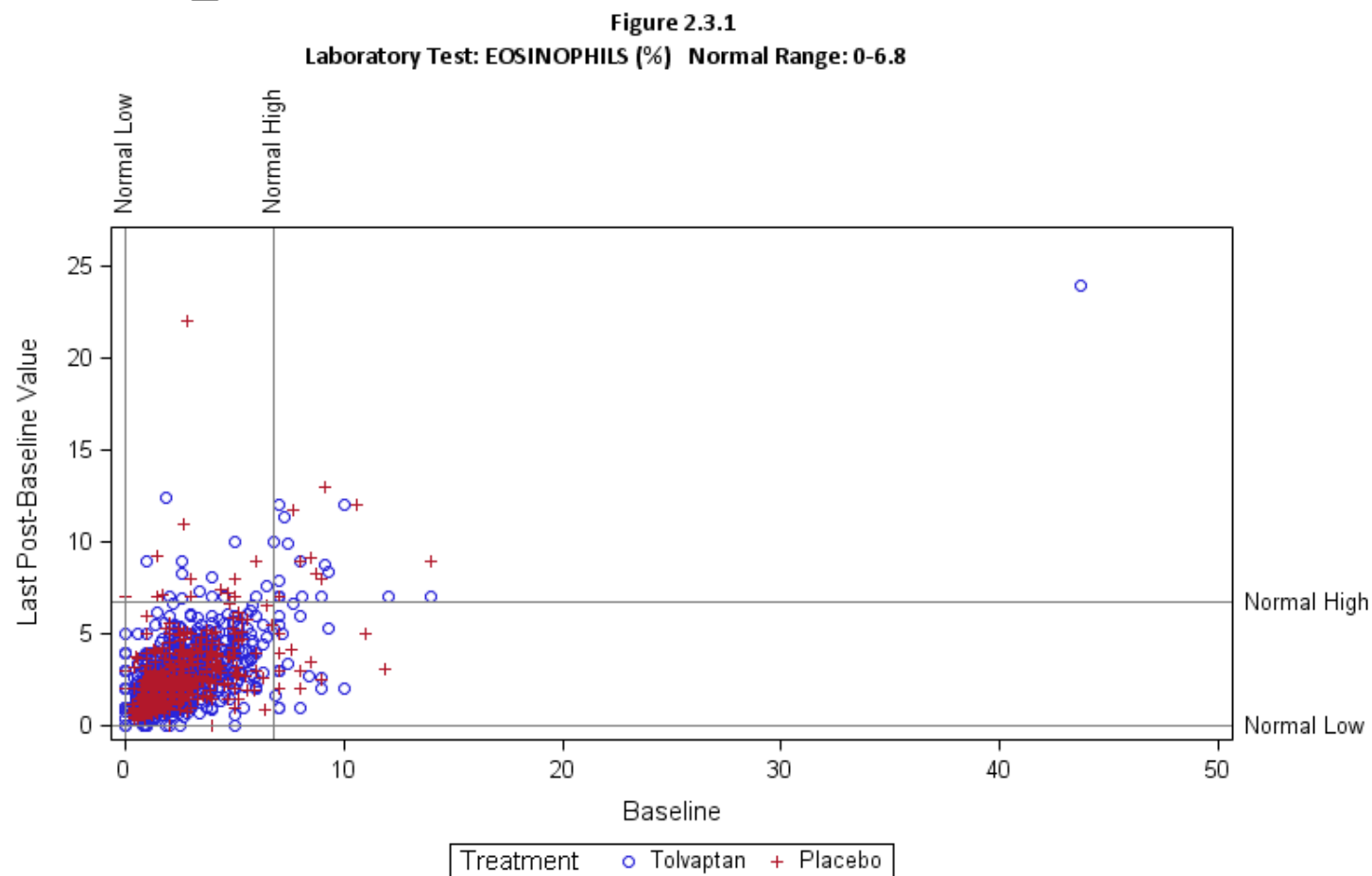


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

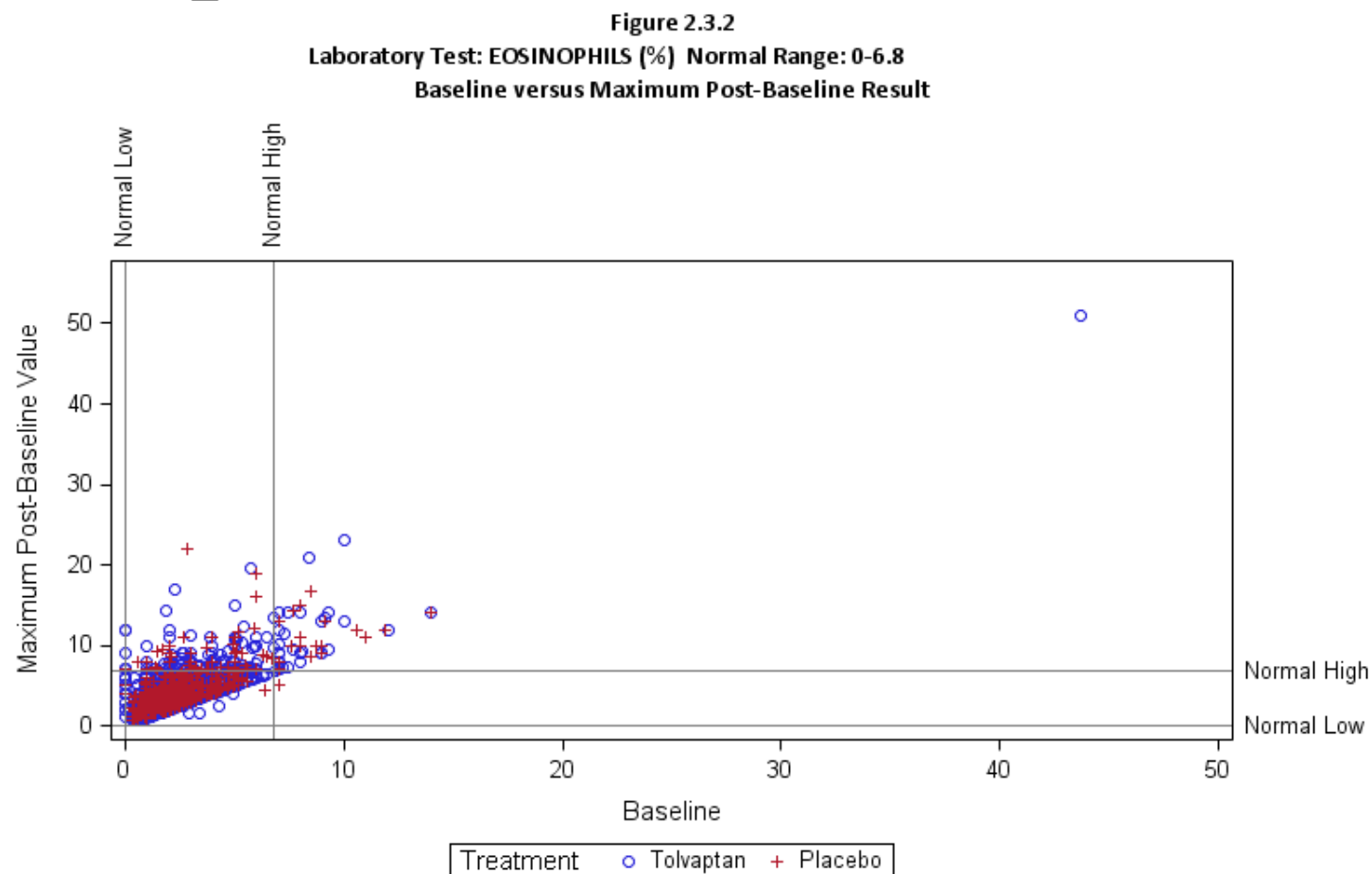
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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

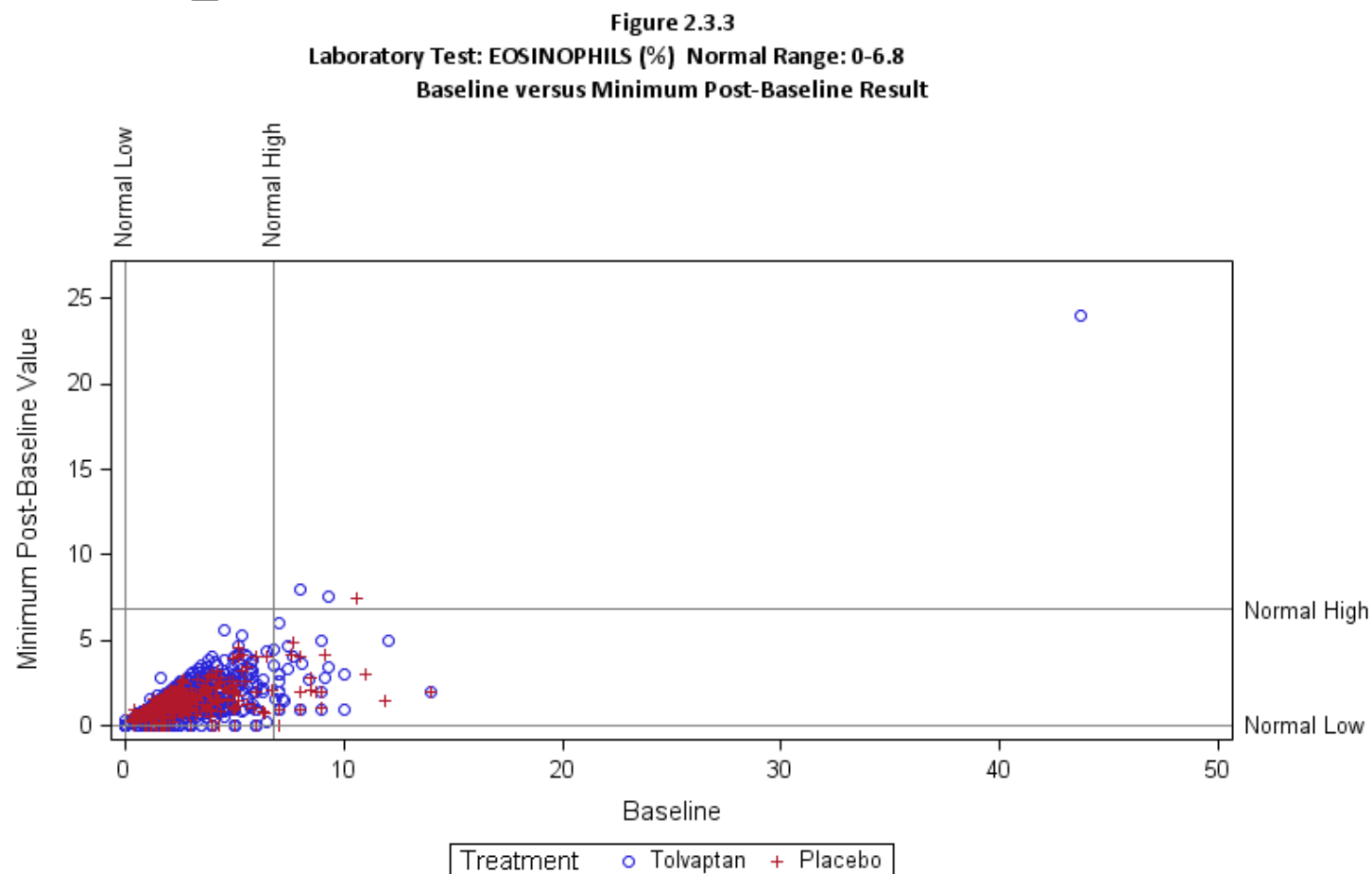


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

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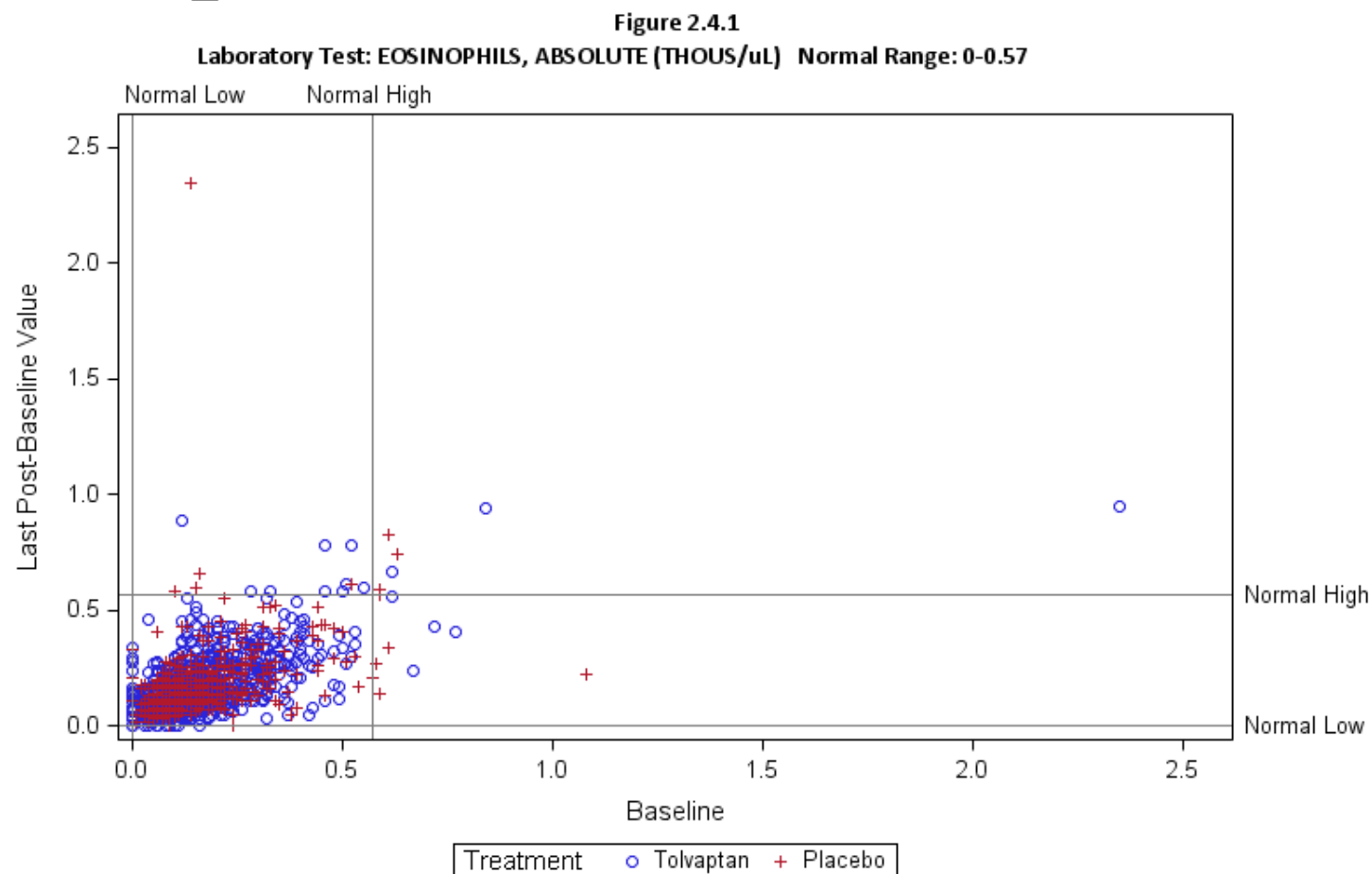


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

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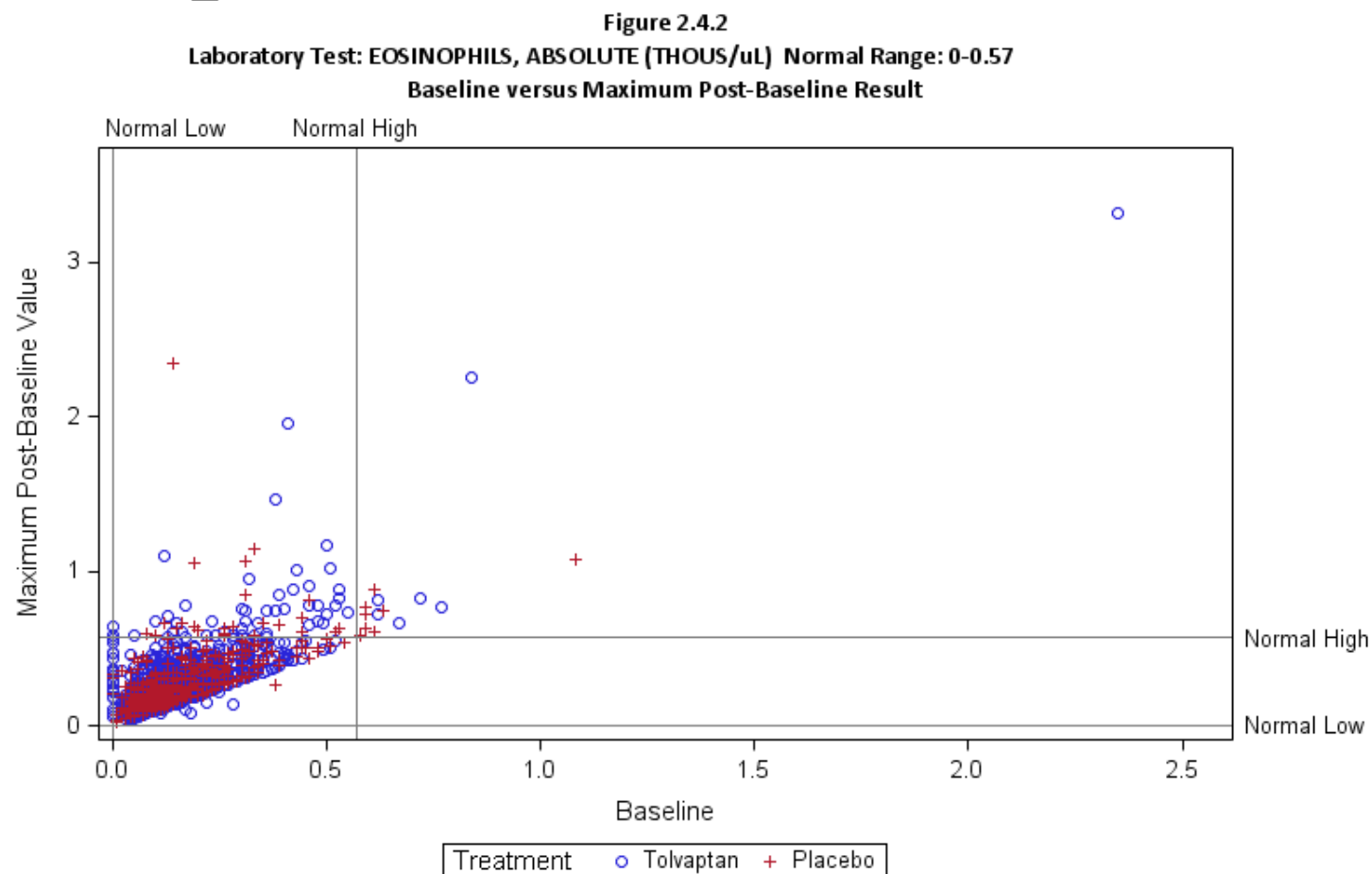


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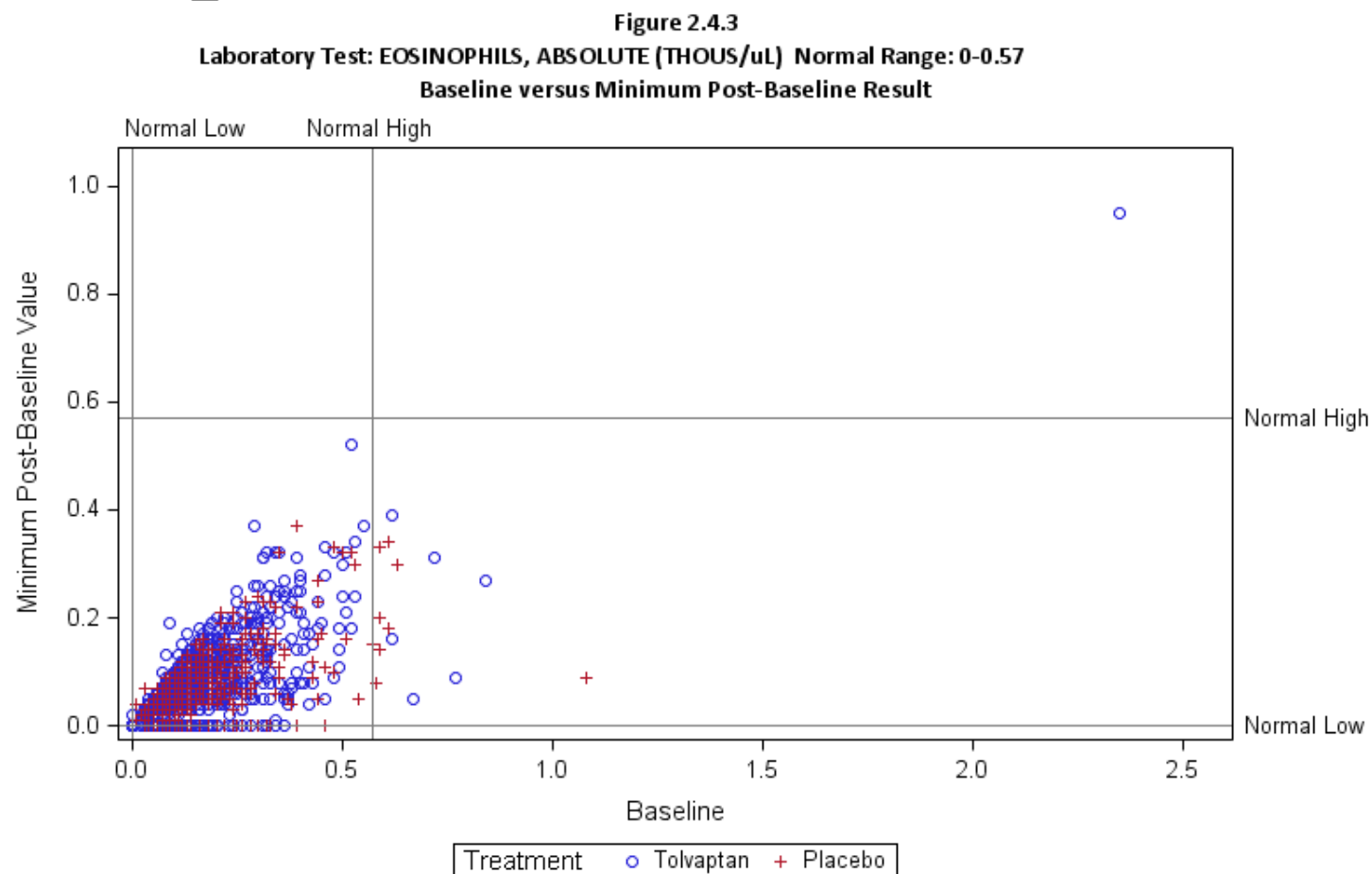


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

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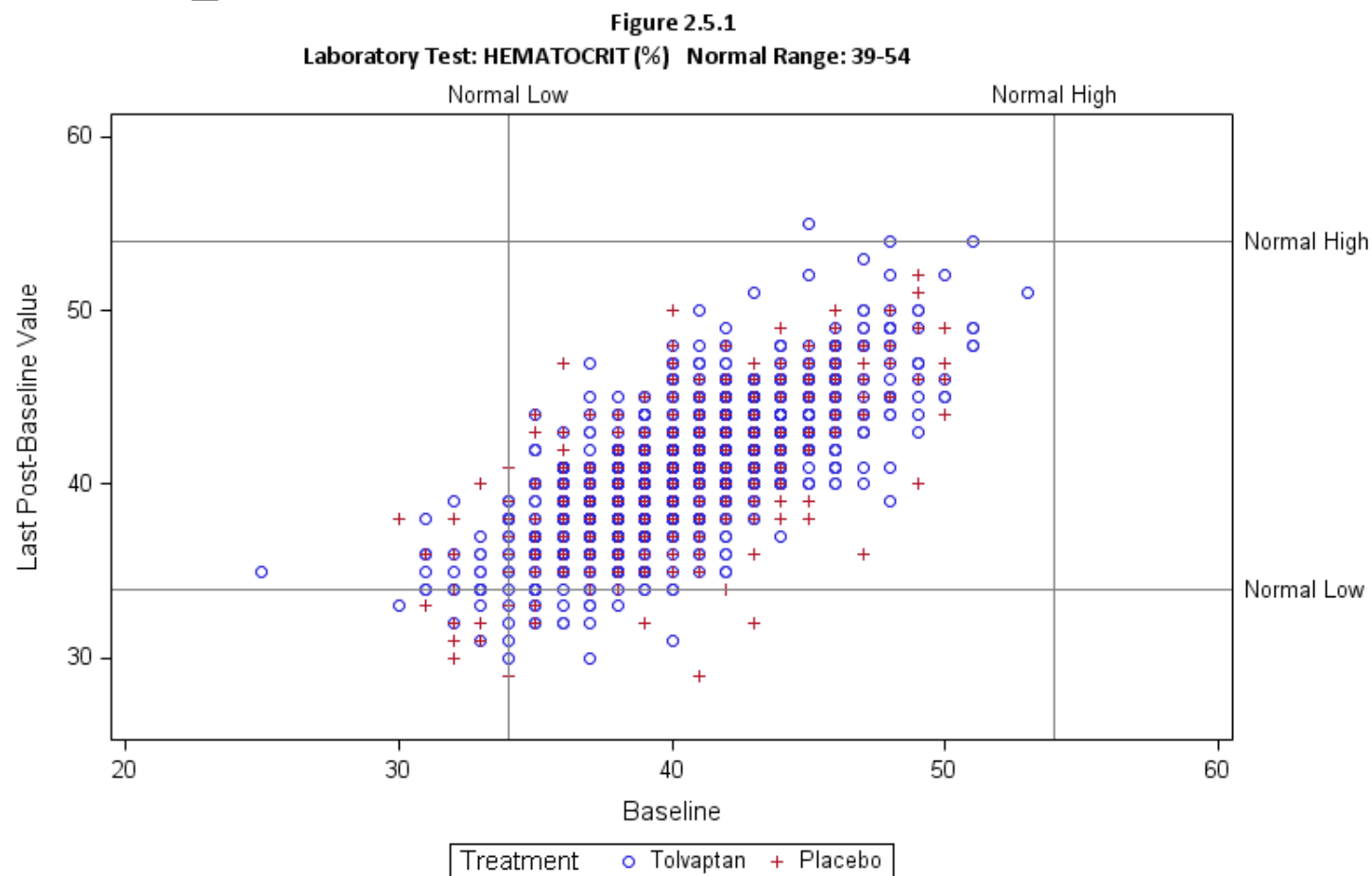


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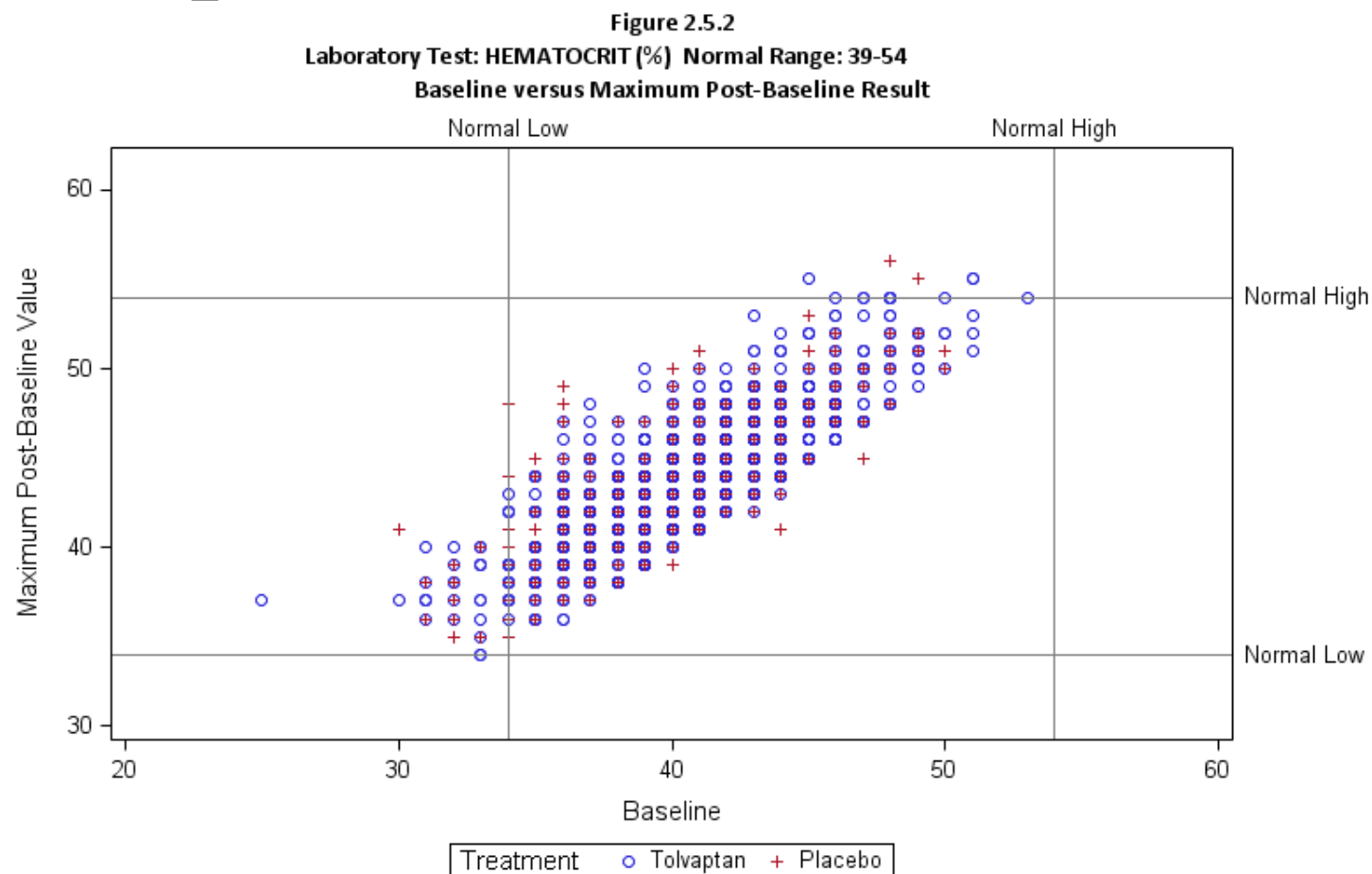
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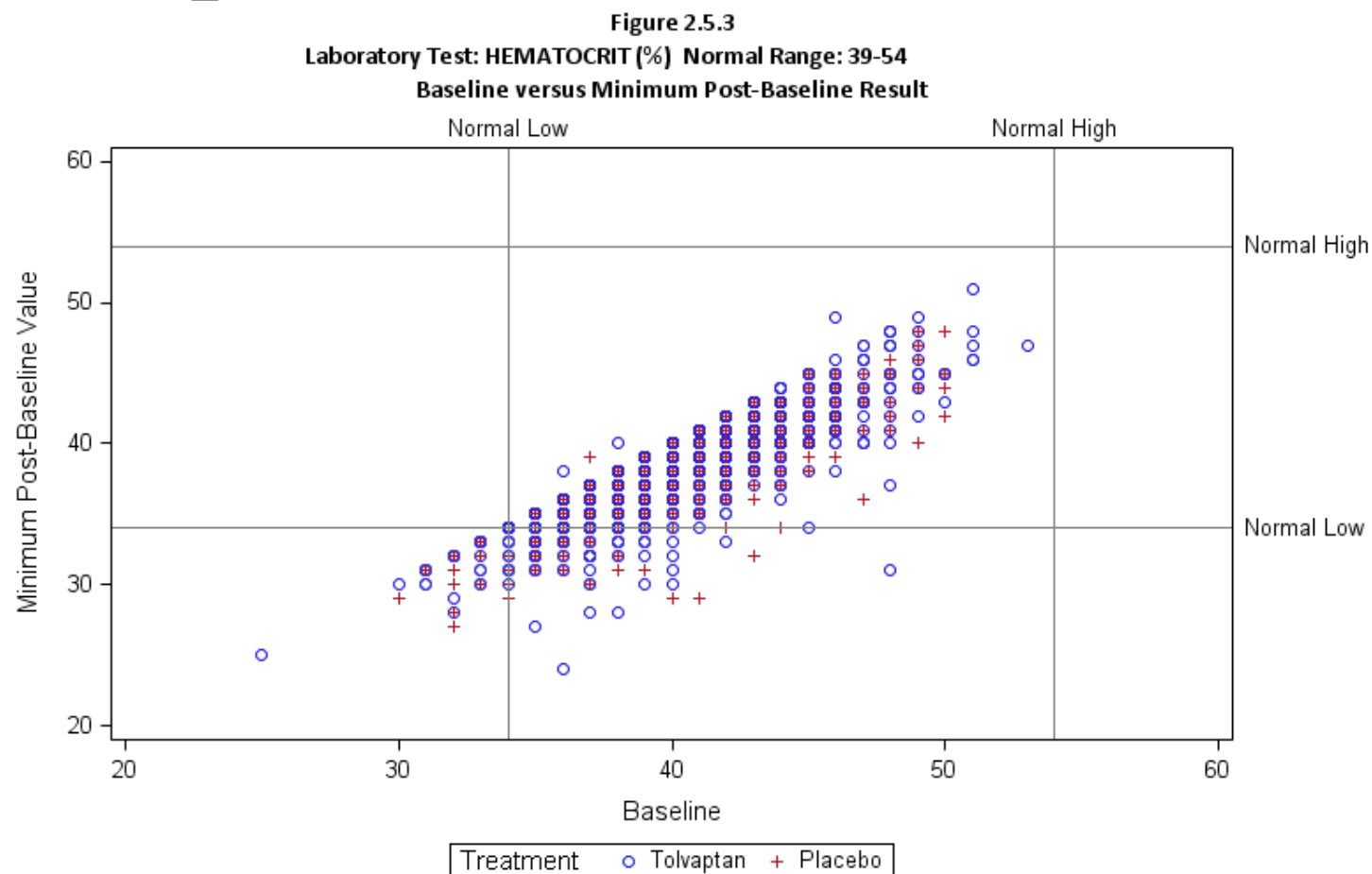


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

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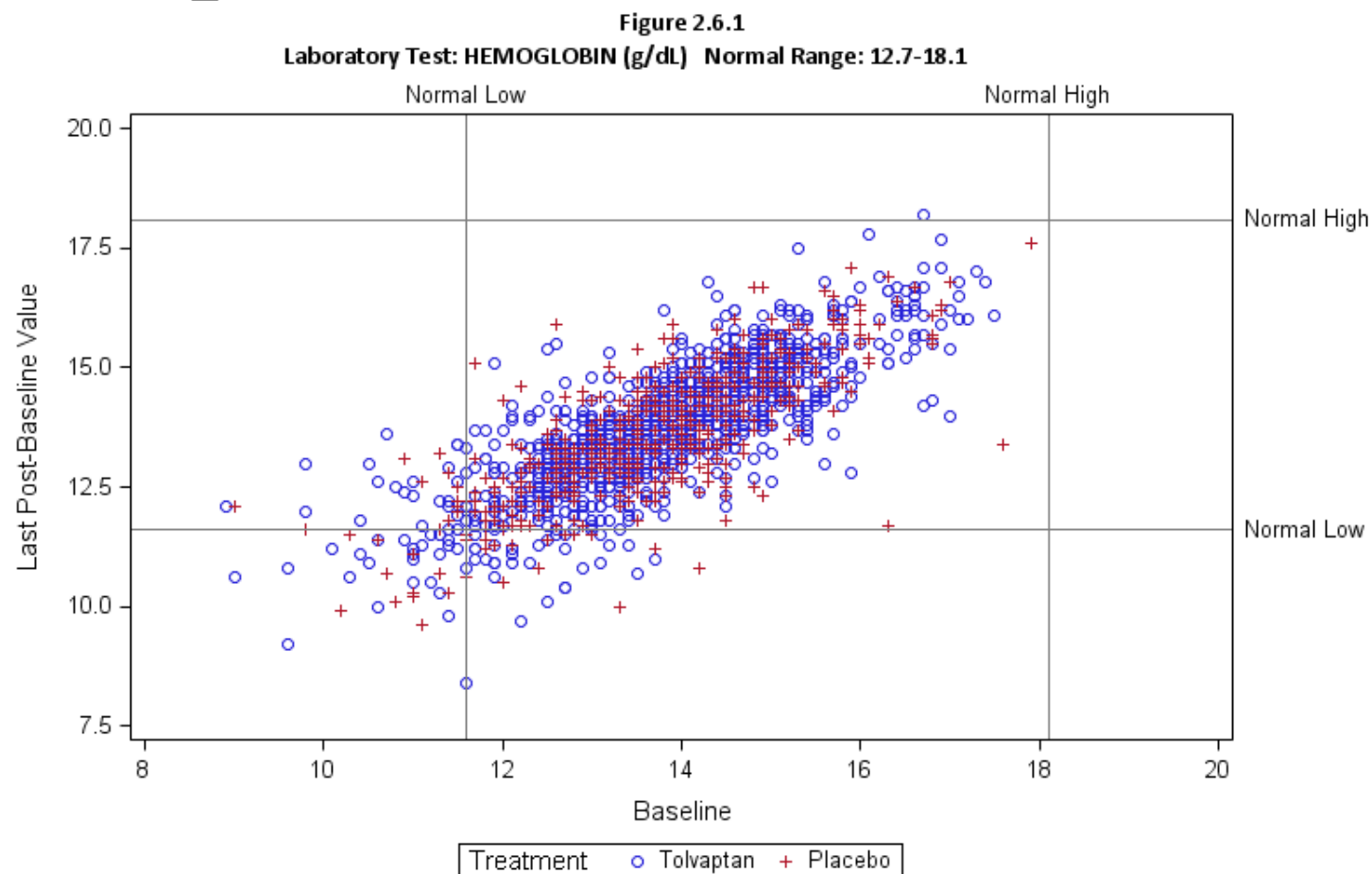


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

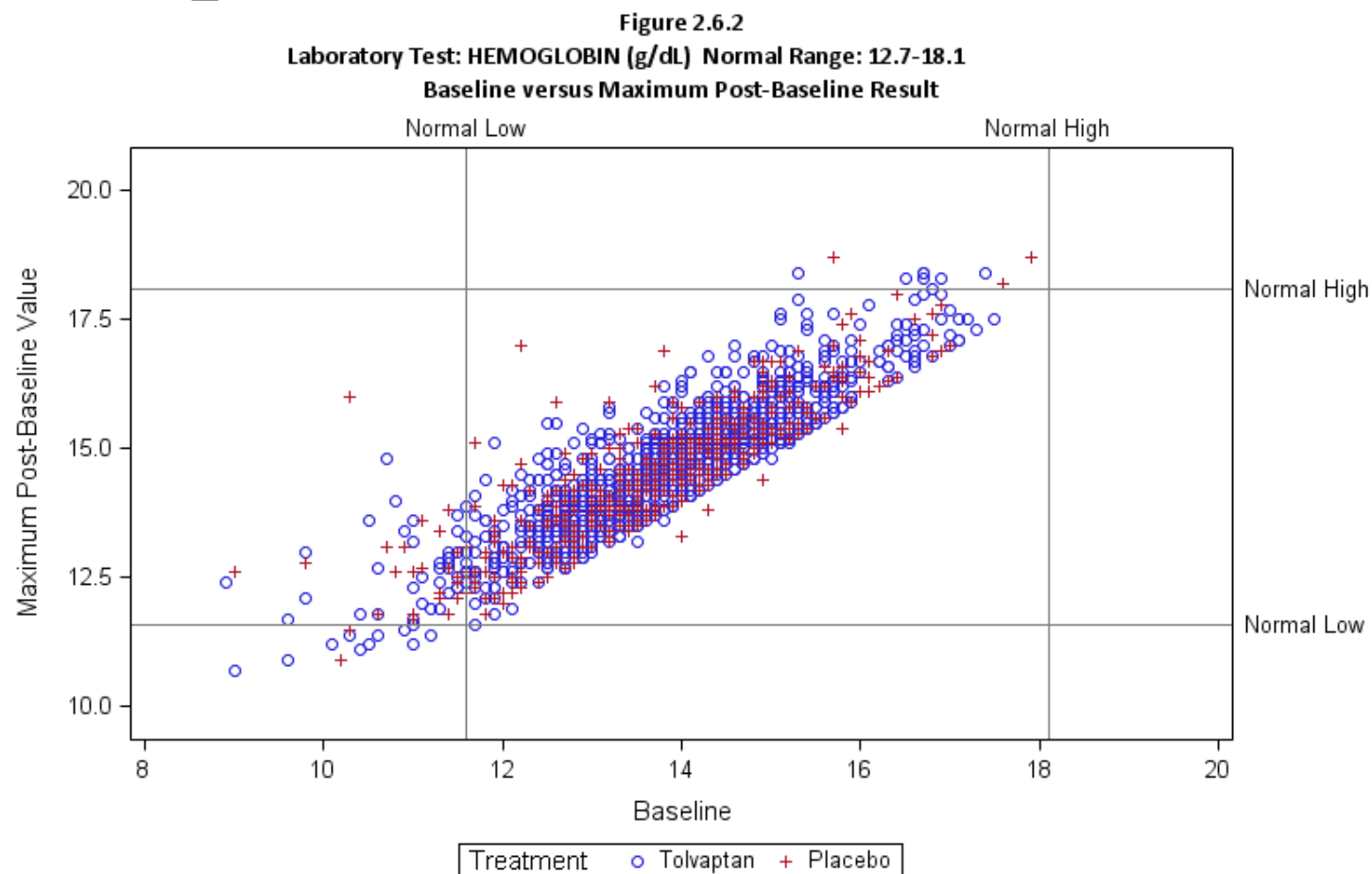
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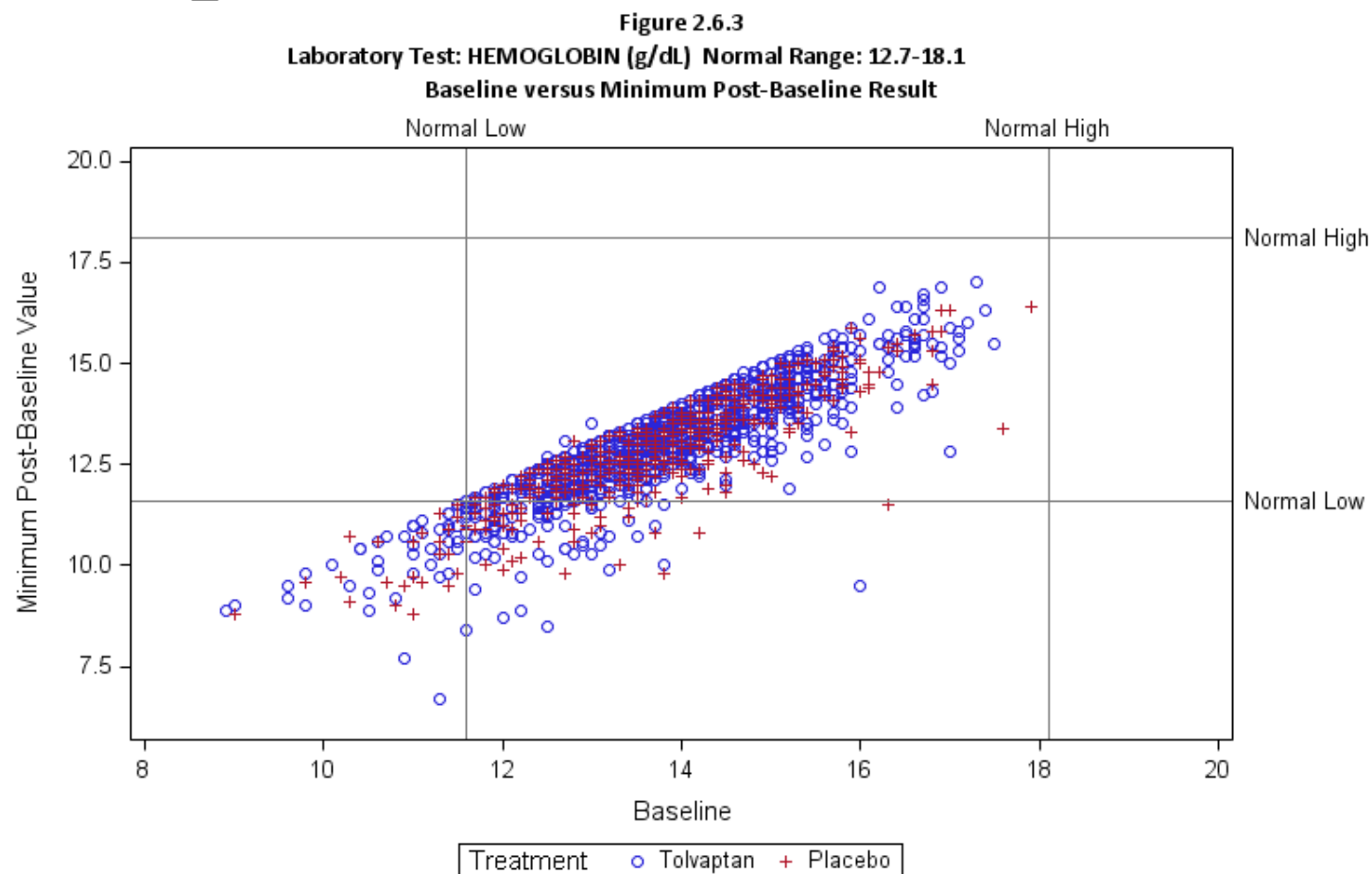
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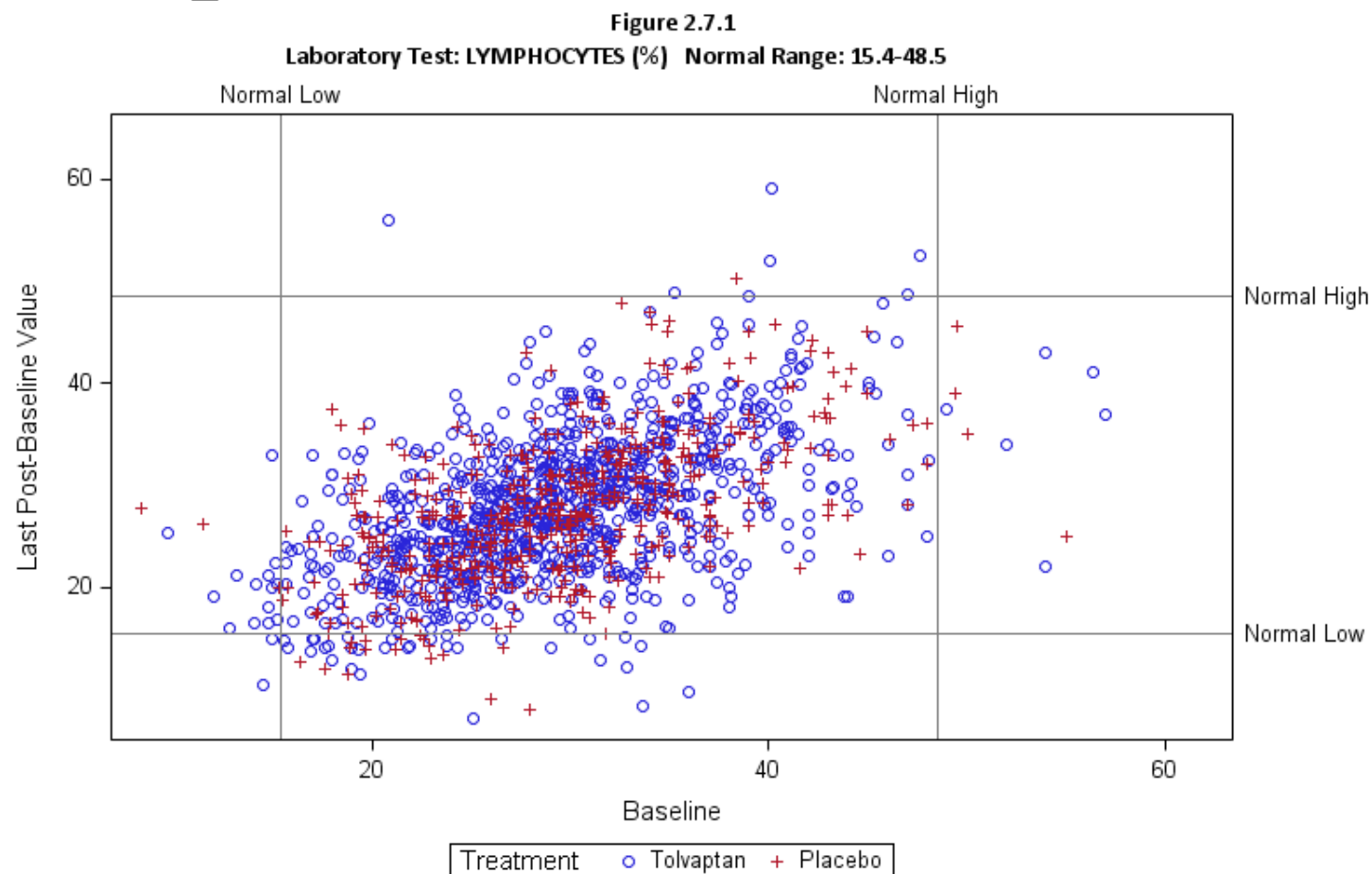


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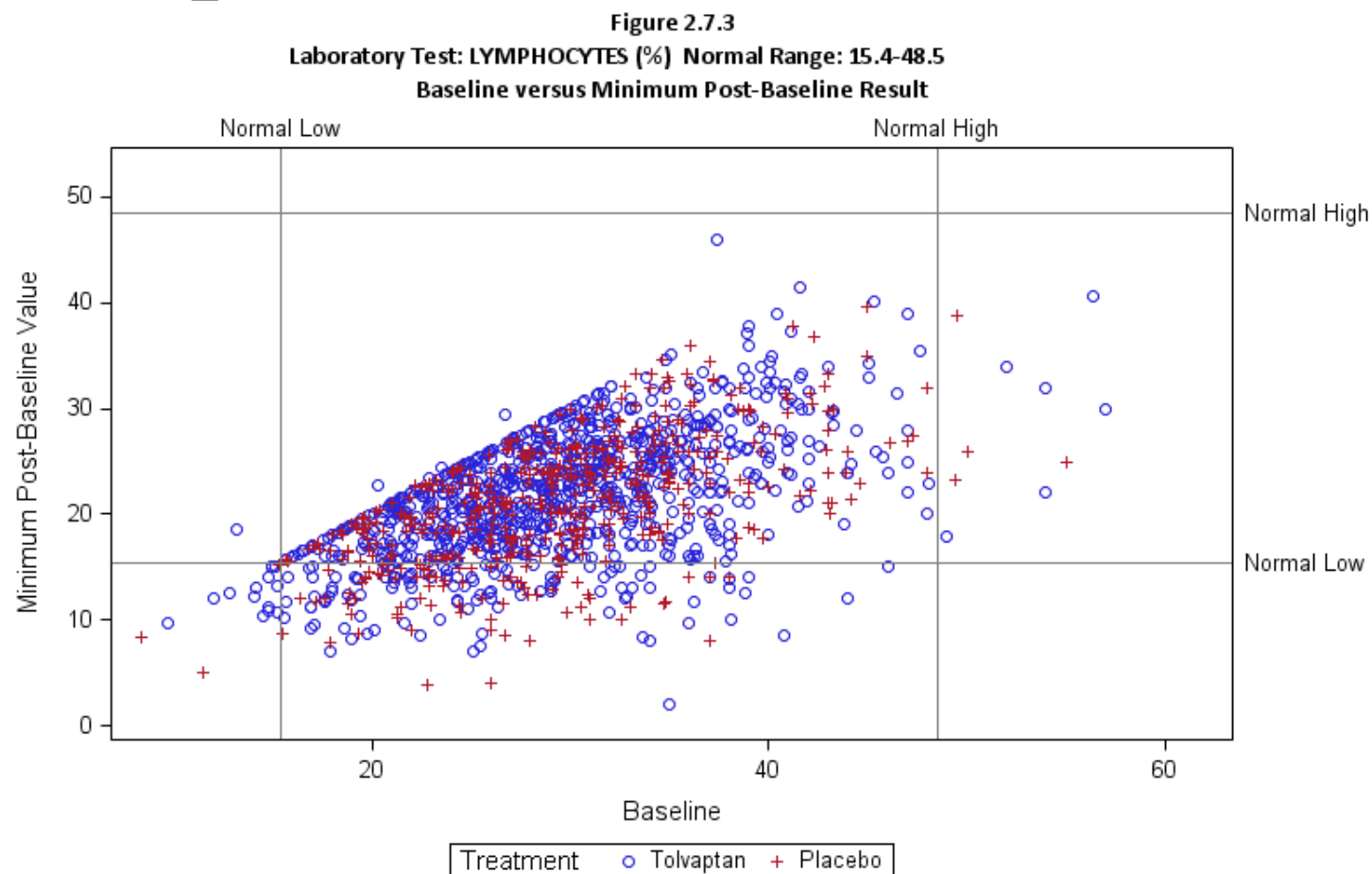
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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

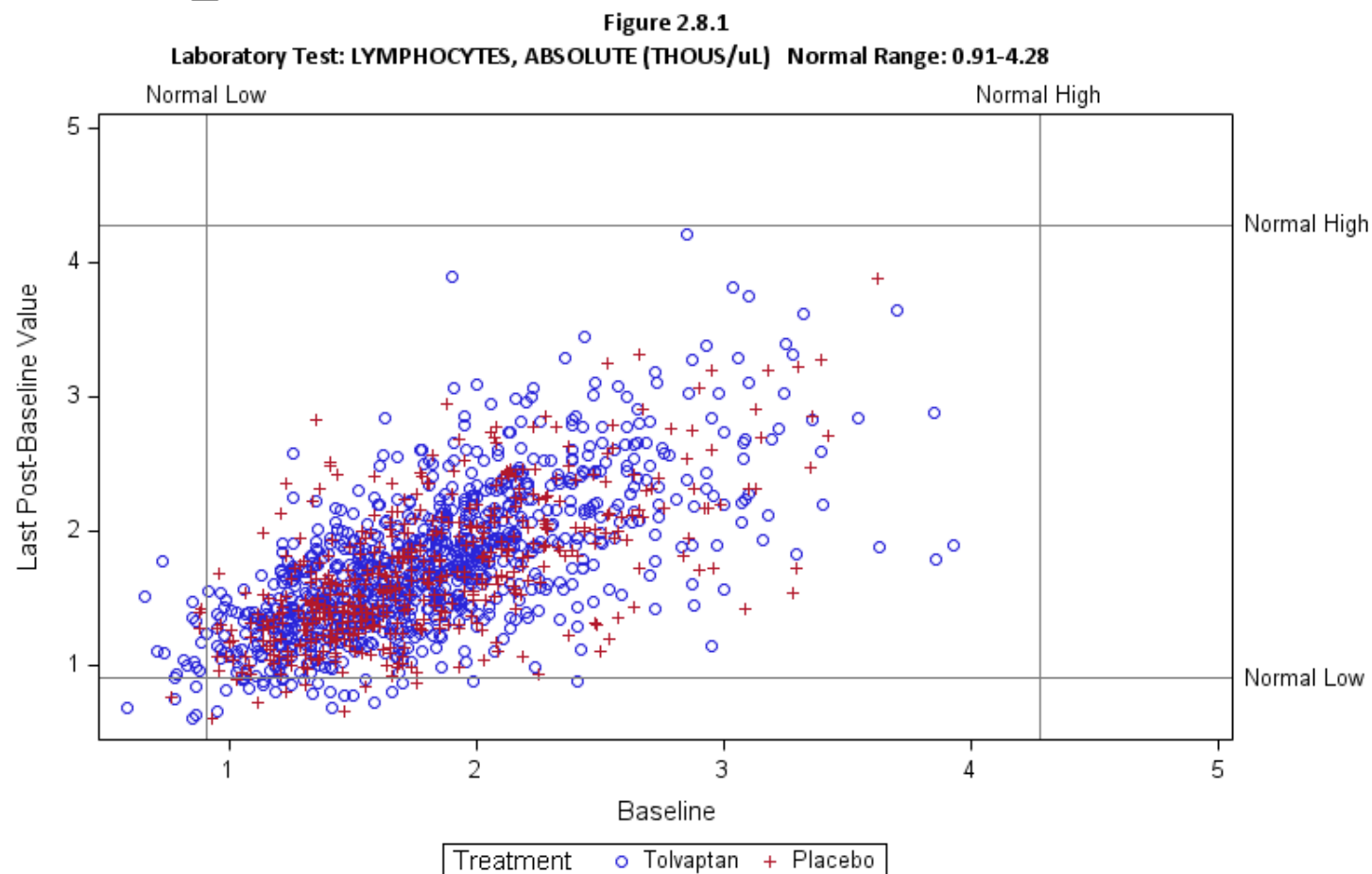


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

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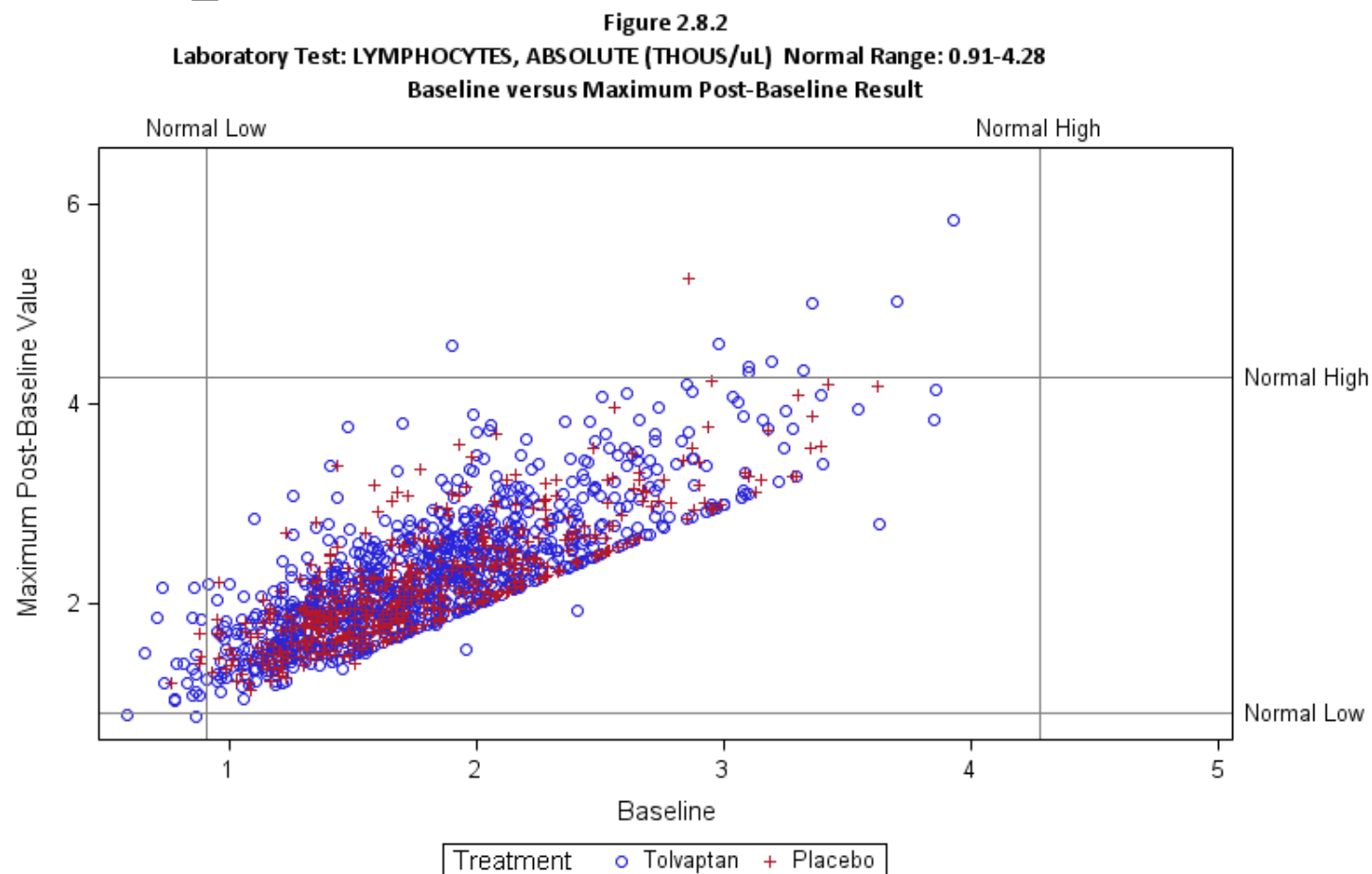


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

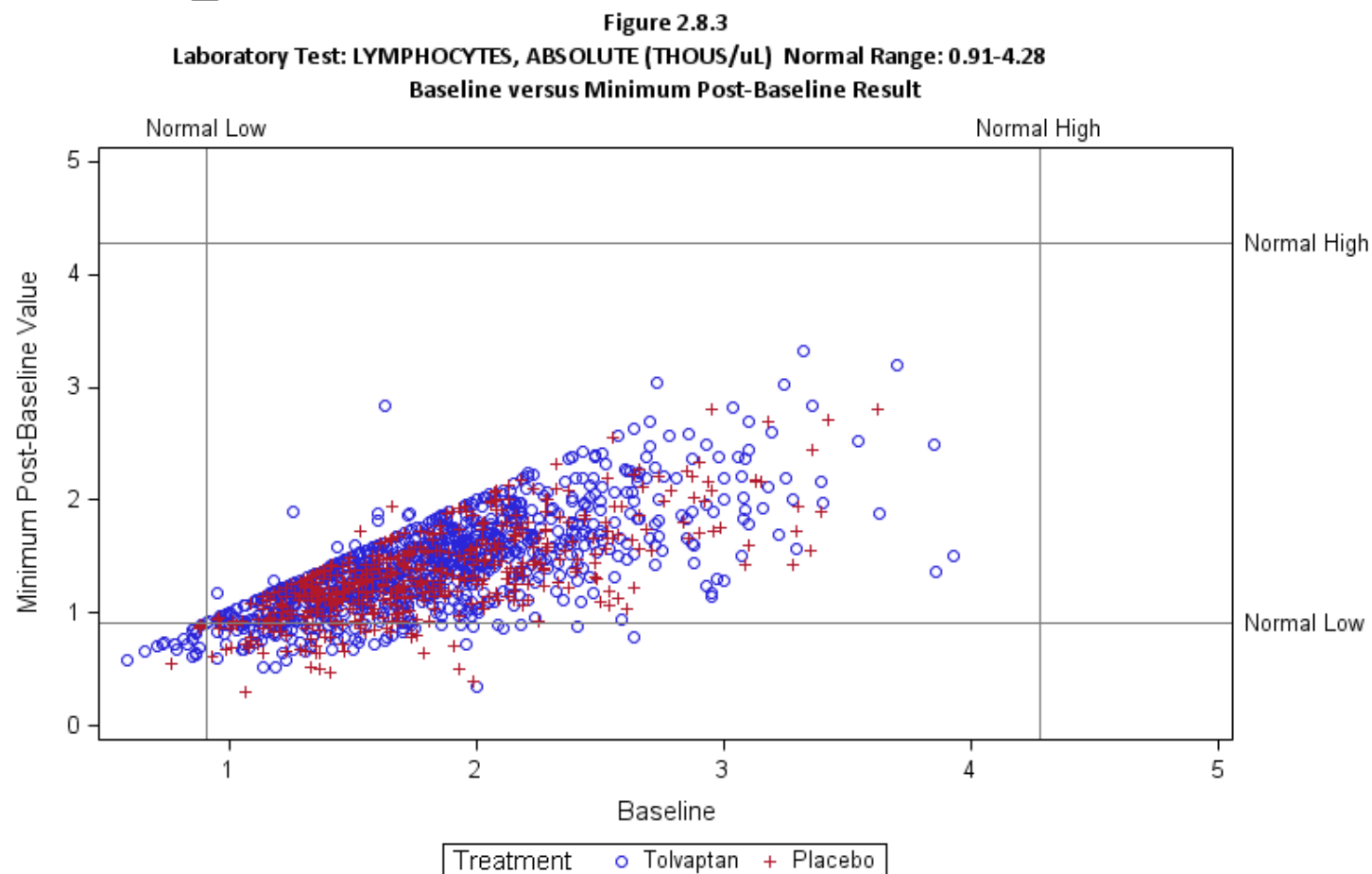
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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

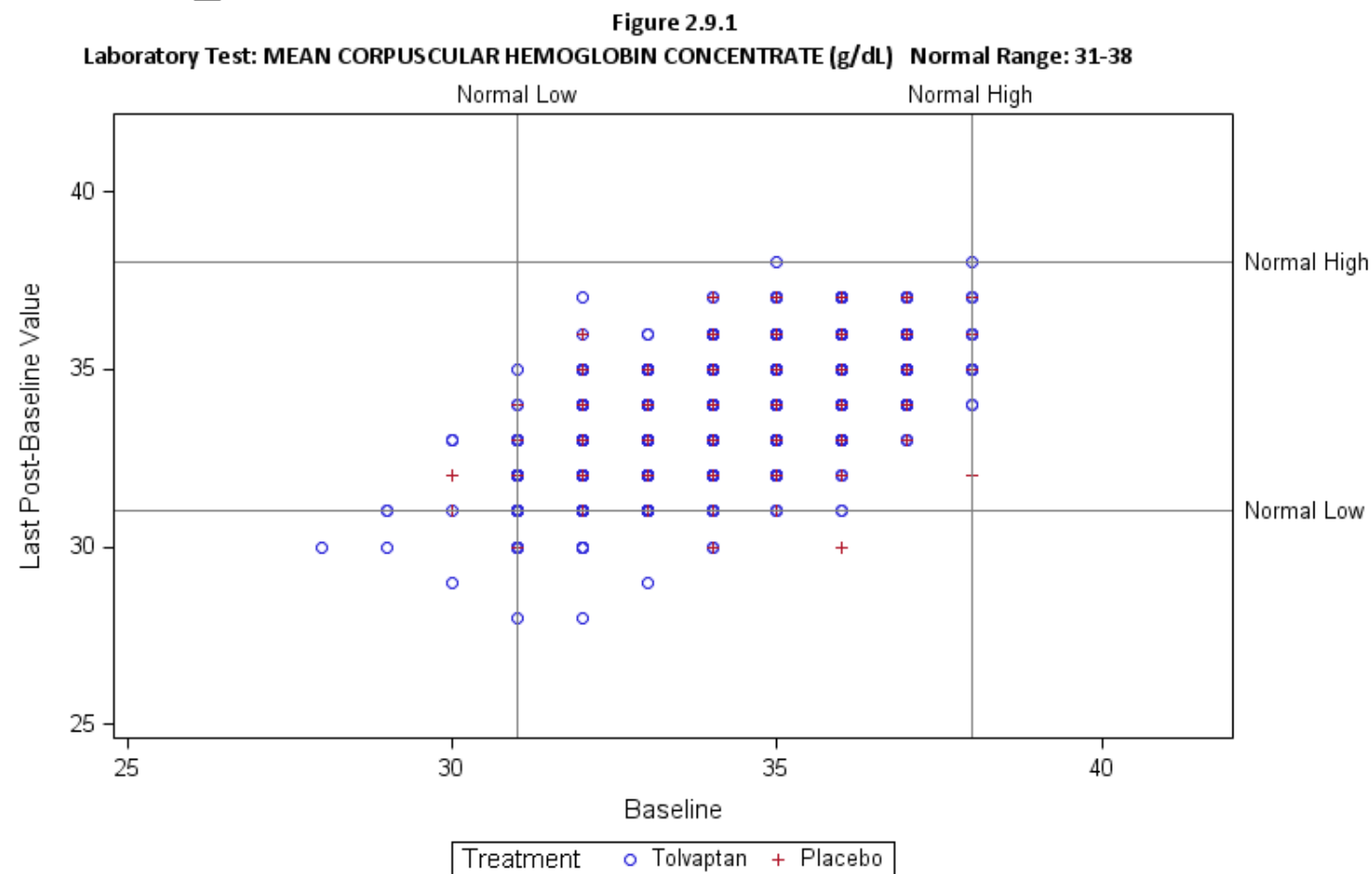
OPC41061
 PROTOCOL P156-251



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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

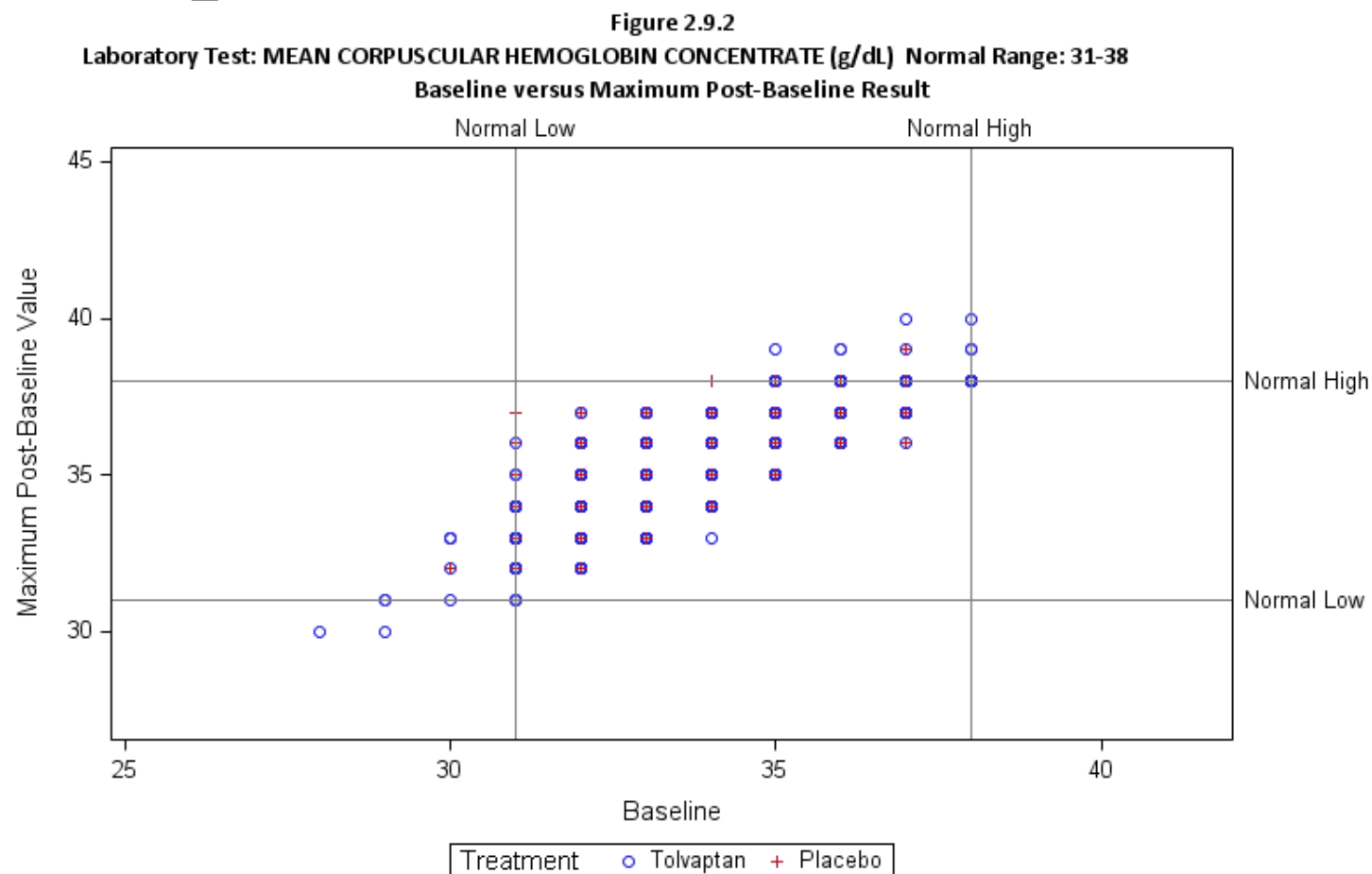


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

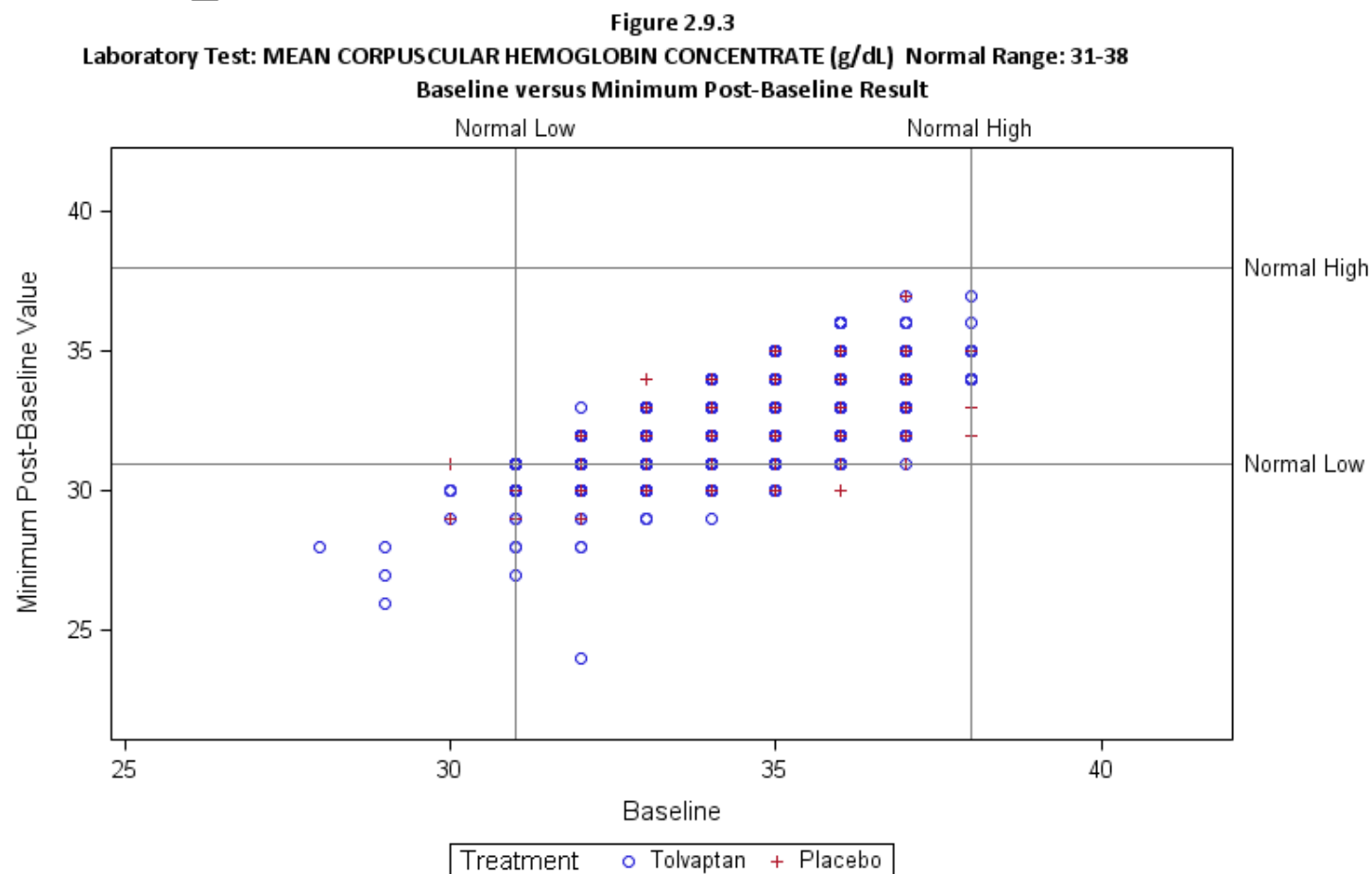


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

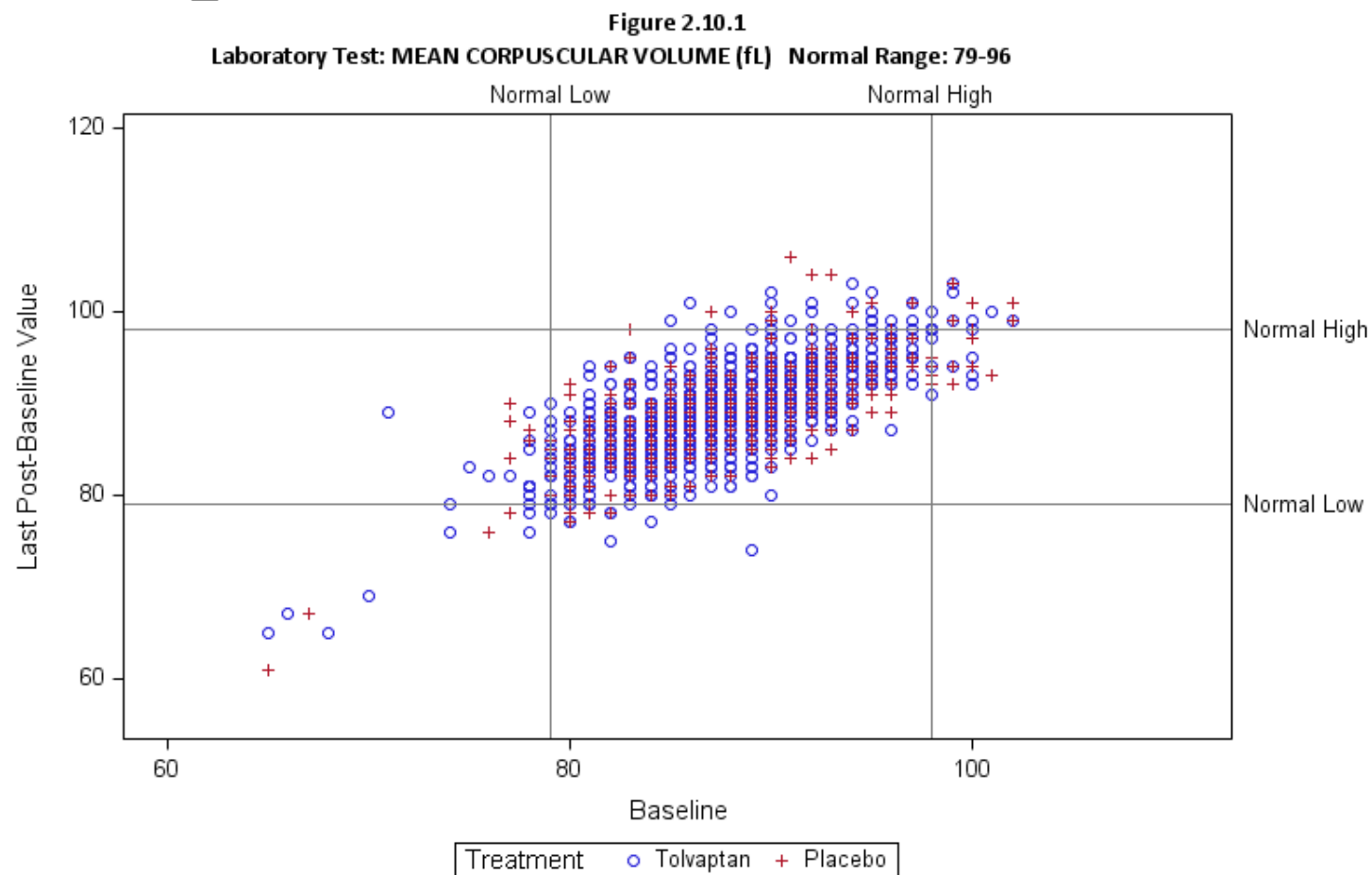


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

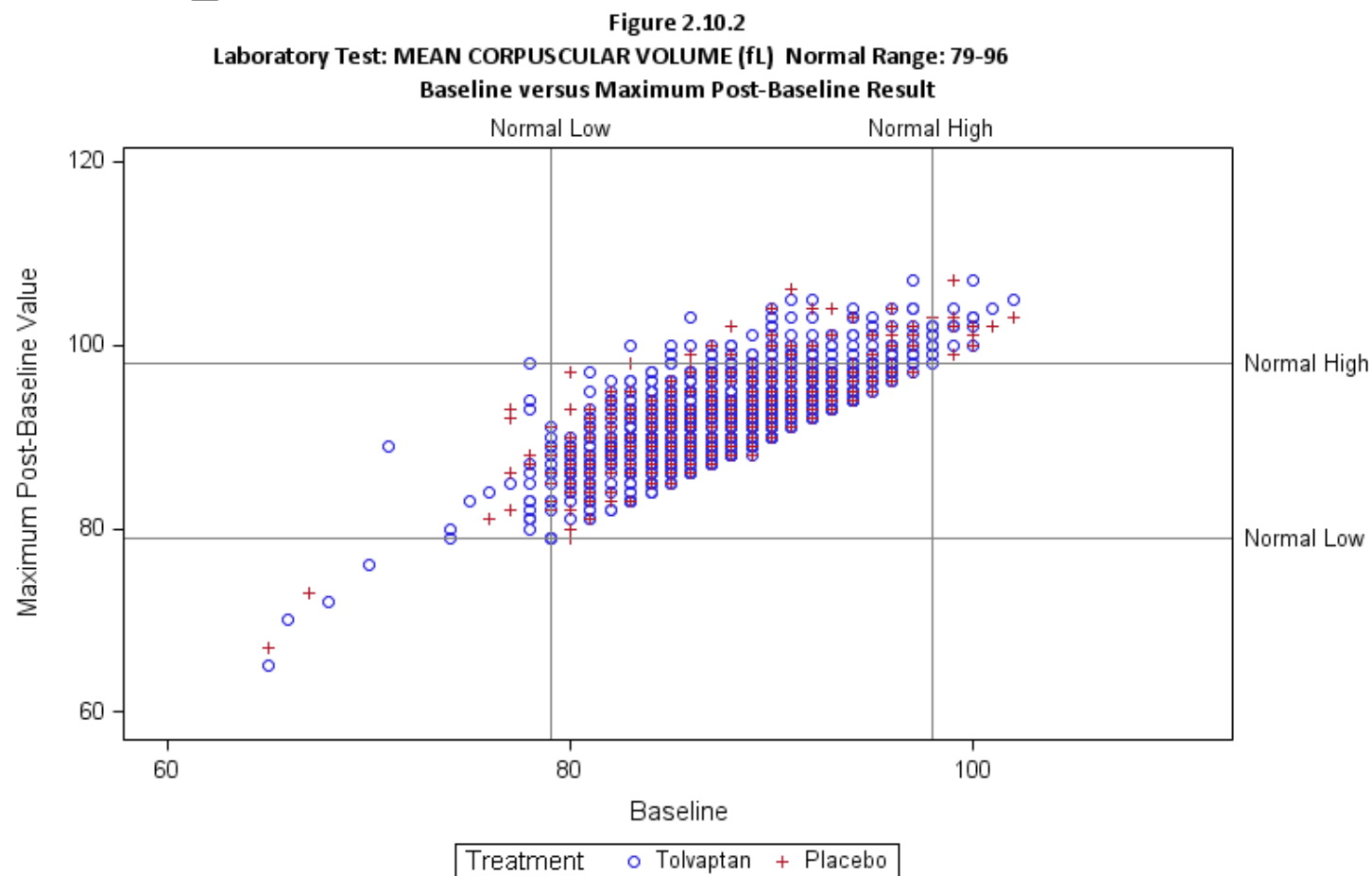


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

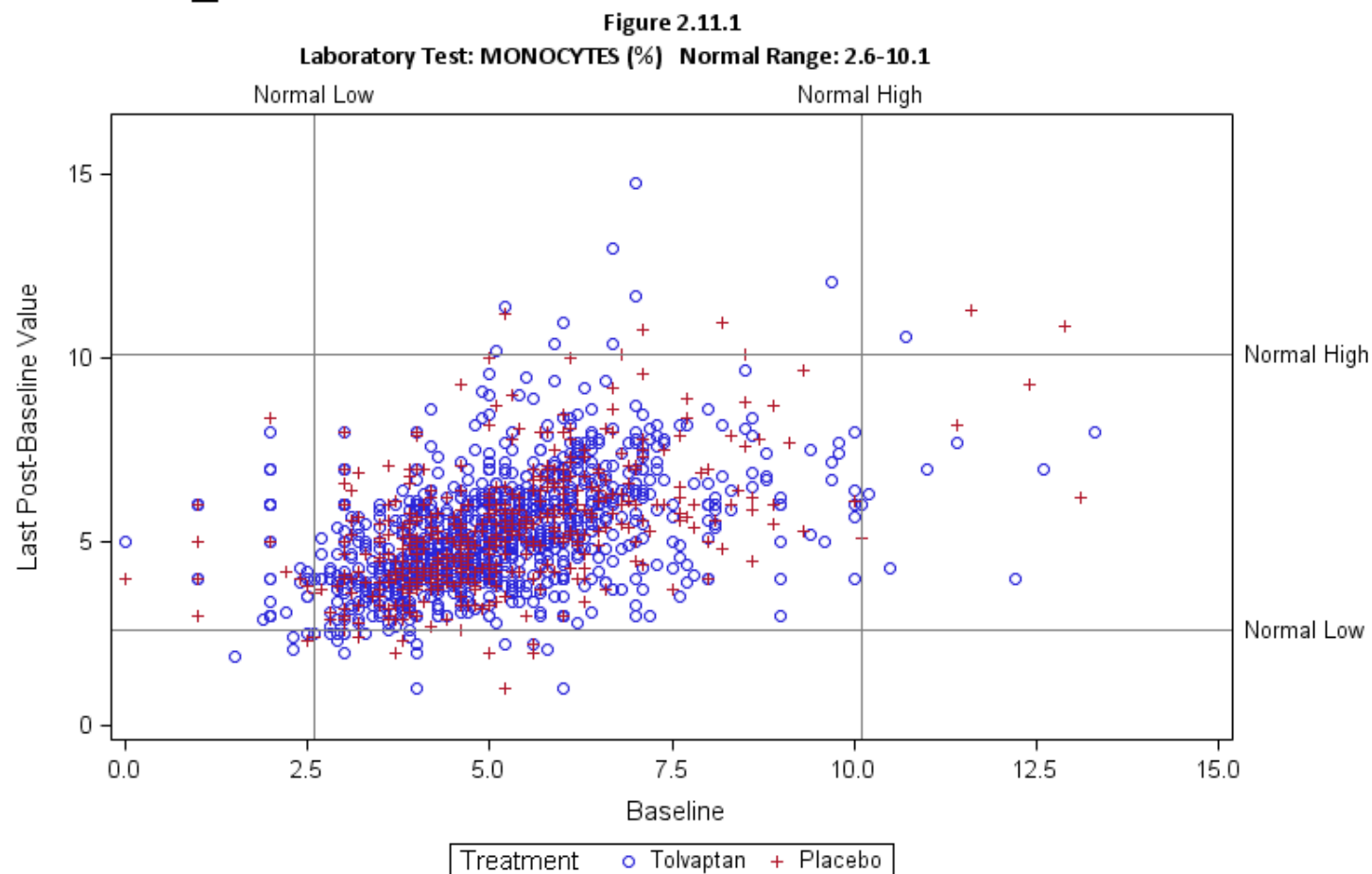


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

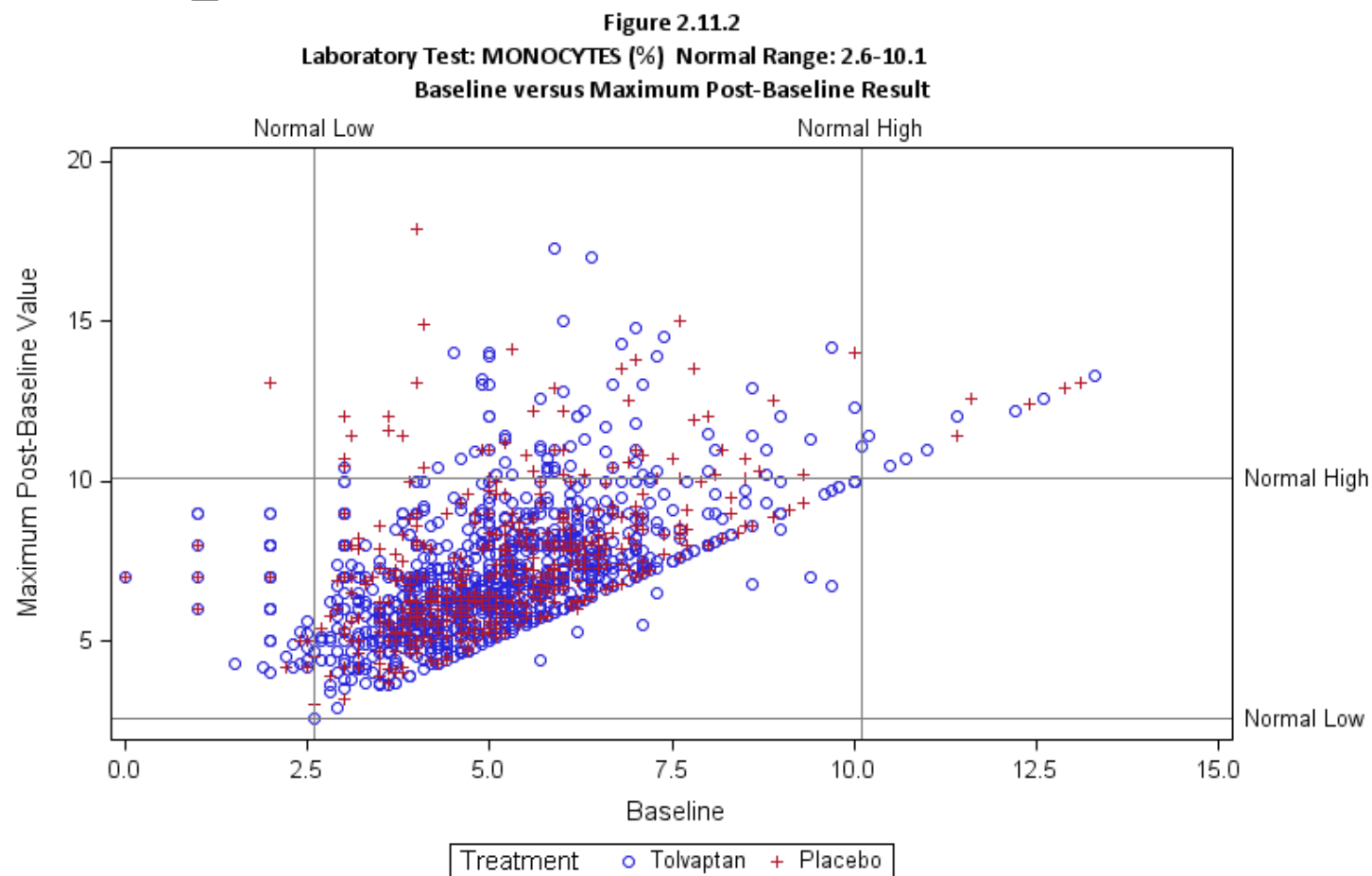


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

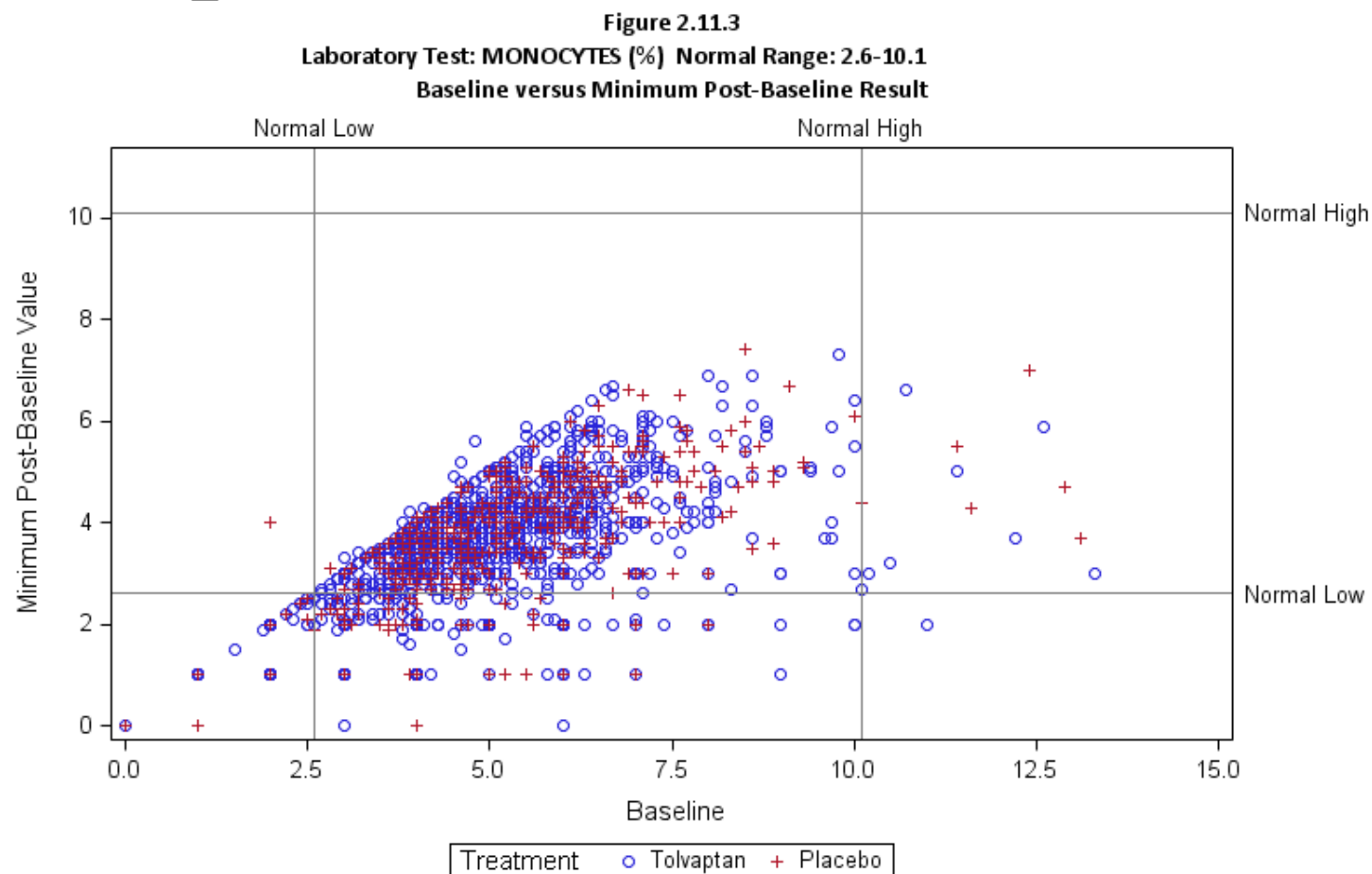


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

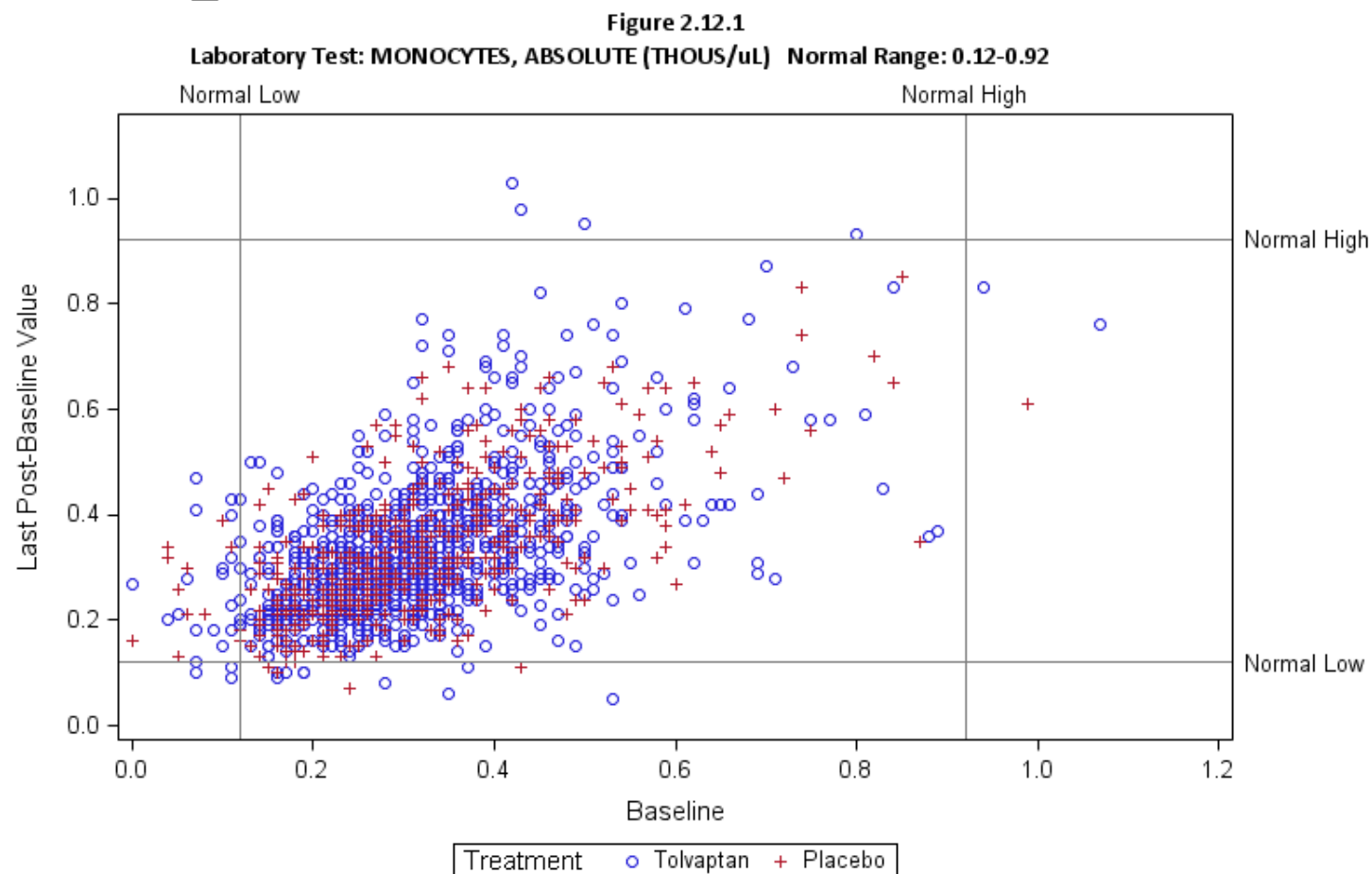


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

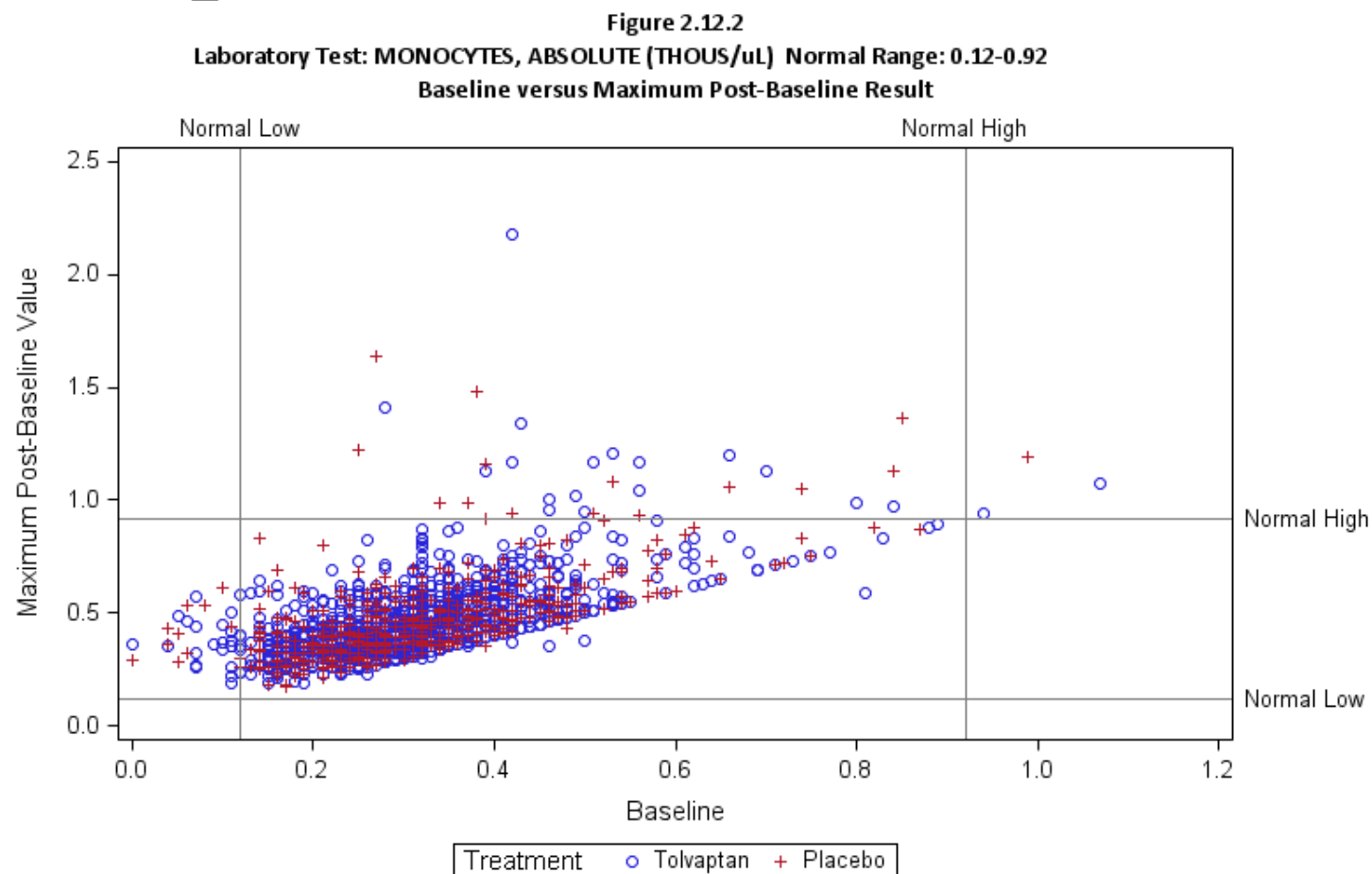


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251



Source: K:\OPC41061\P156-251\dataset\analysis\HEMO

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

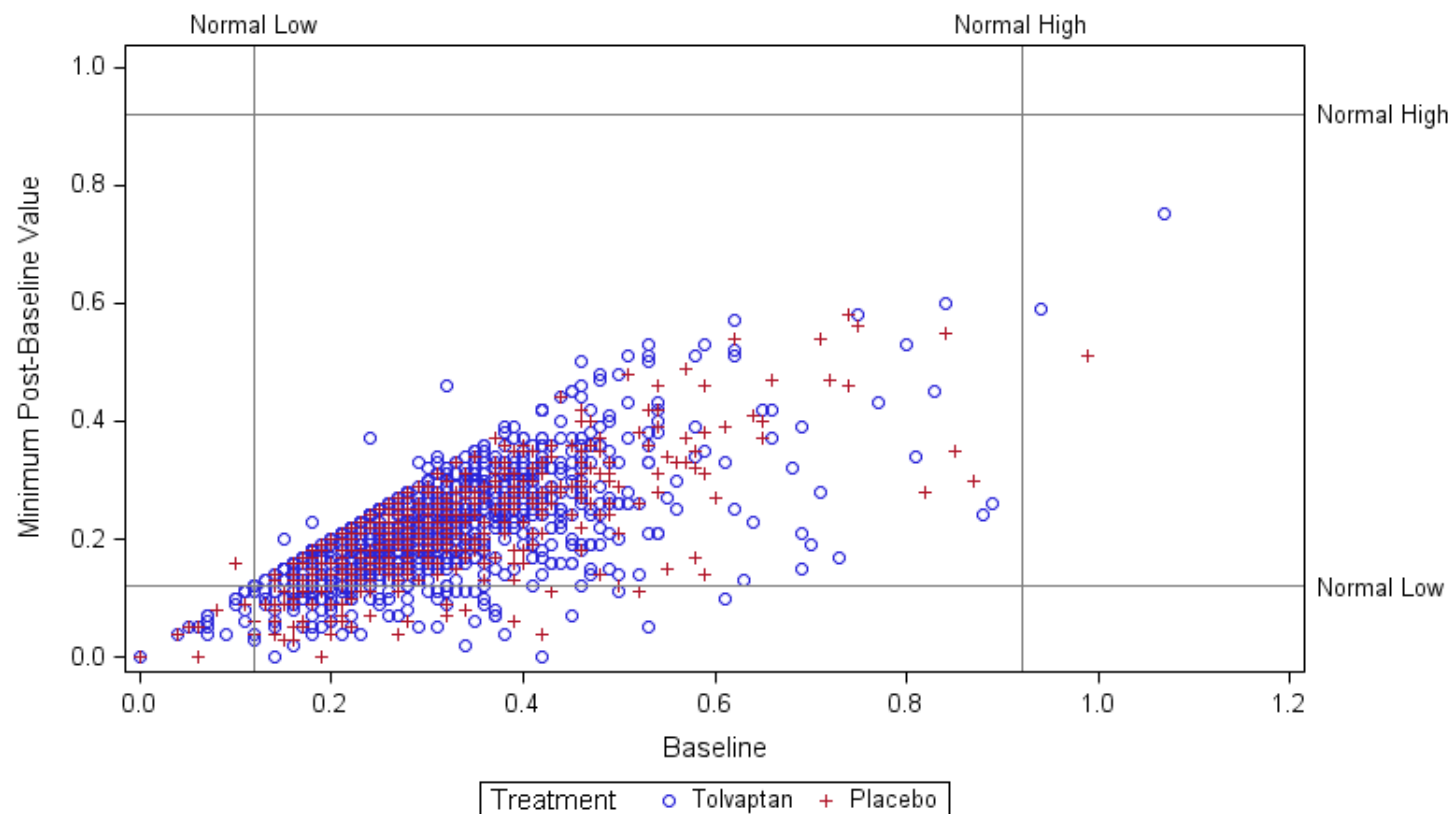
OPC41061

PROTOCOL P156-251

Figure 2.12.3

Laboratory Test: MONOCYTES, ABSOLUTE (THOUS/uL) Normal Range: 0.12-0.92

Baseline versus Minimum Post-Baseline Result

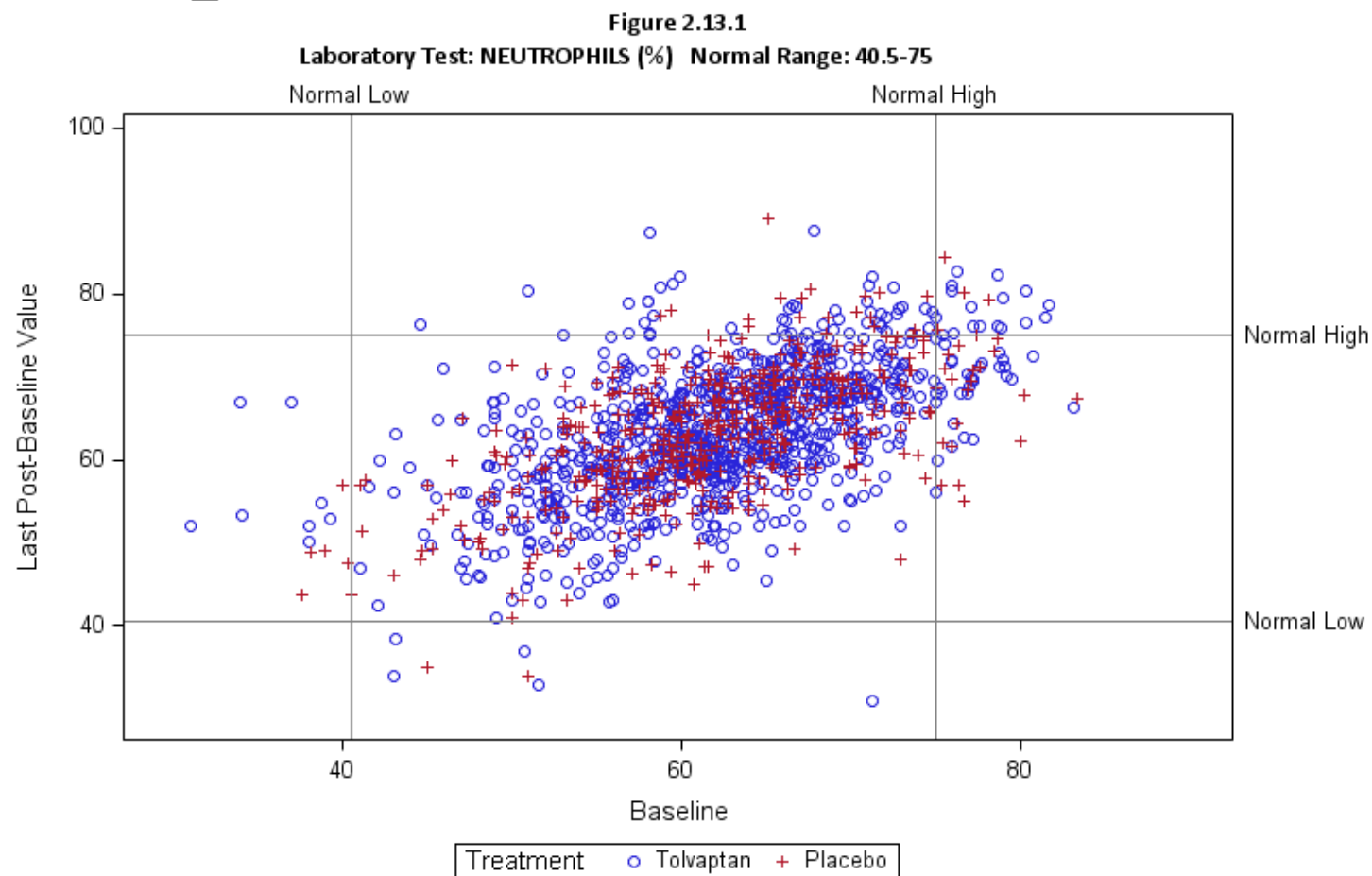


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

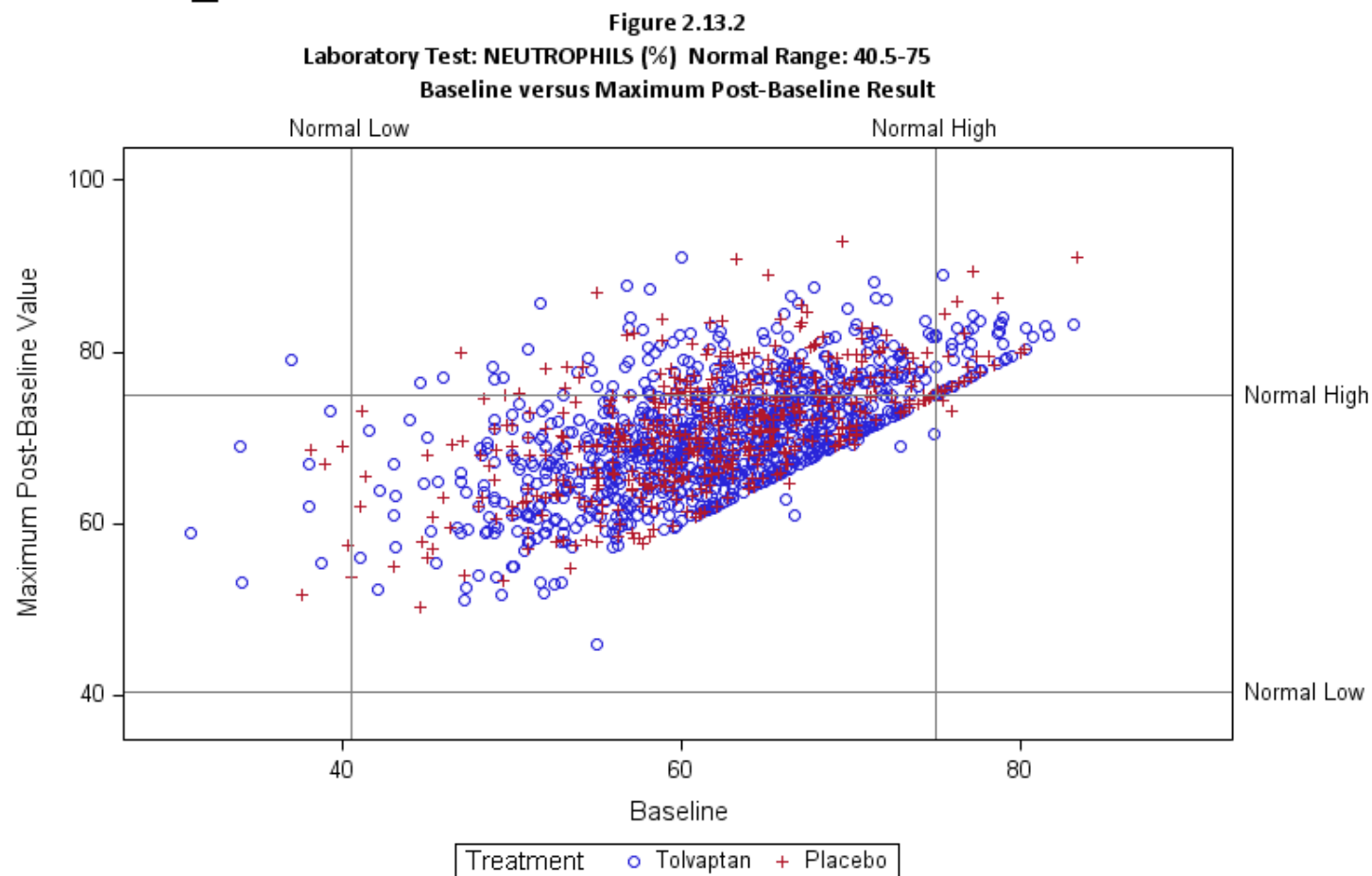


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

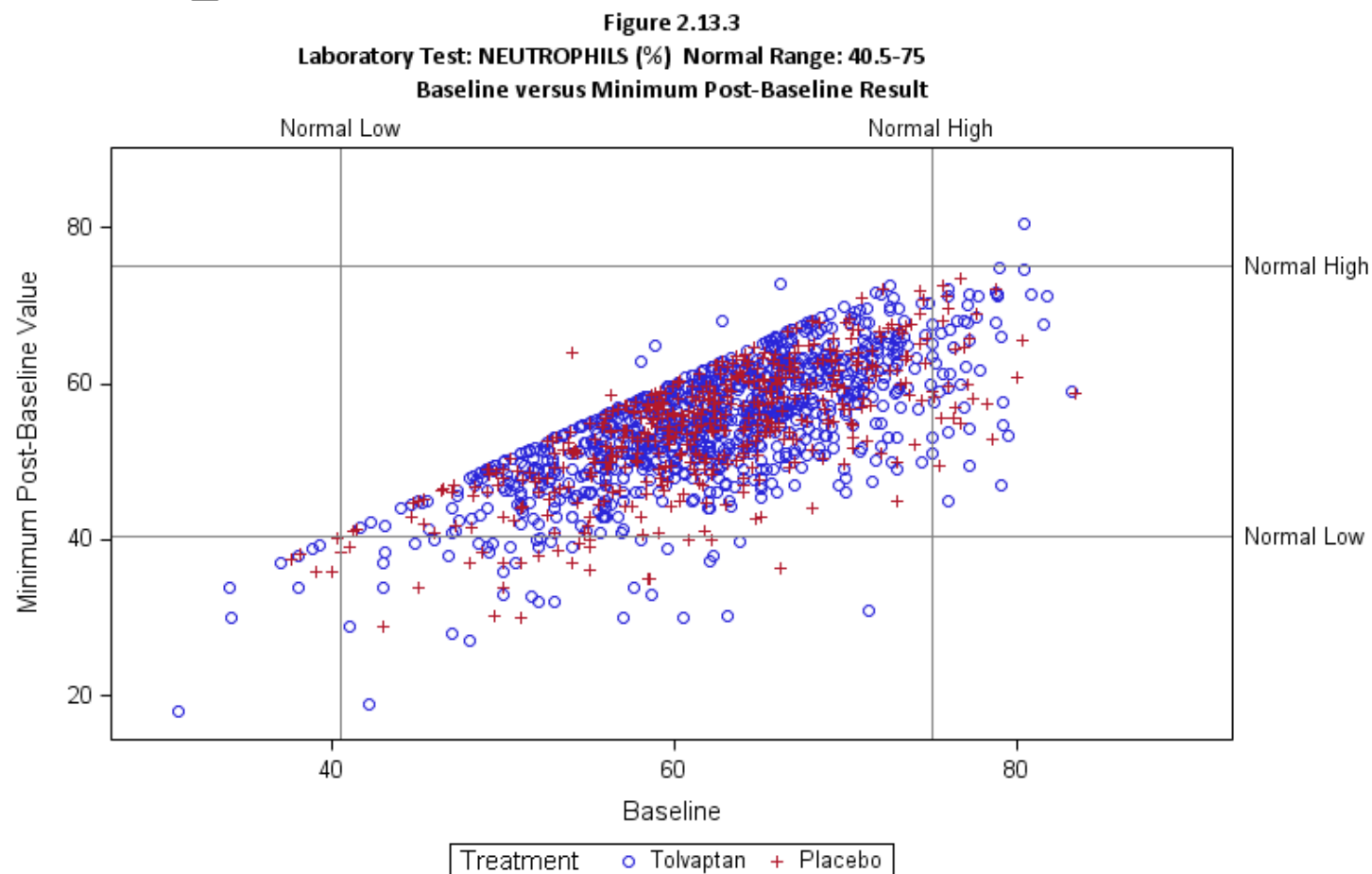


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251



Source: K:\OPC41061\P156-251\data set\analysis\HEM0

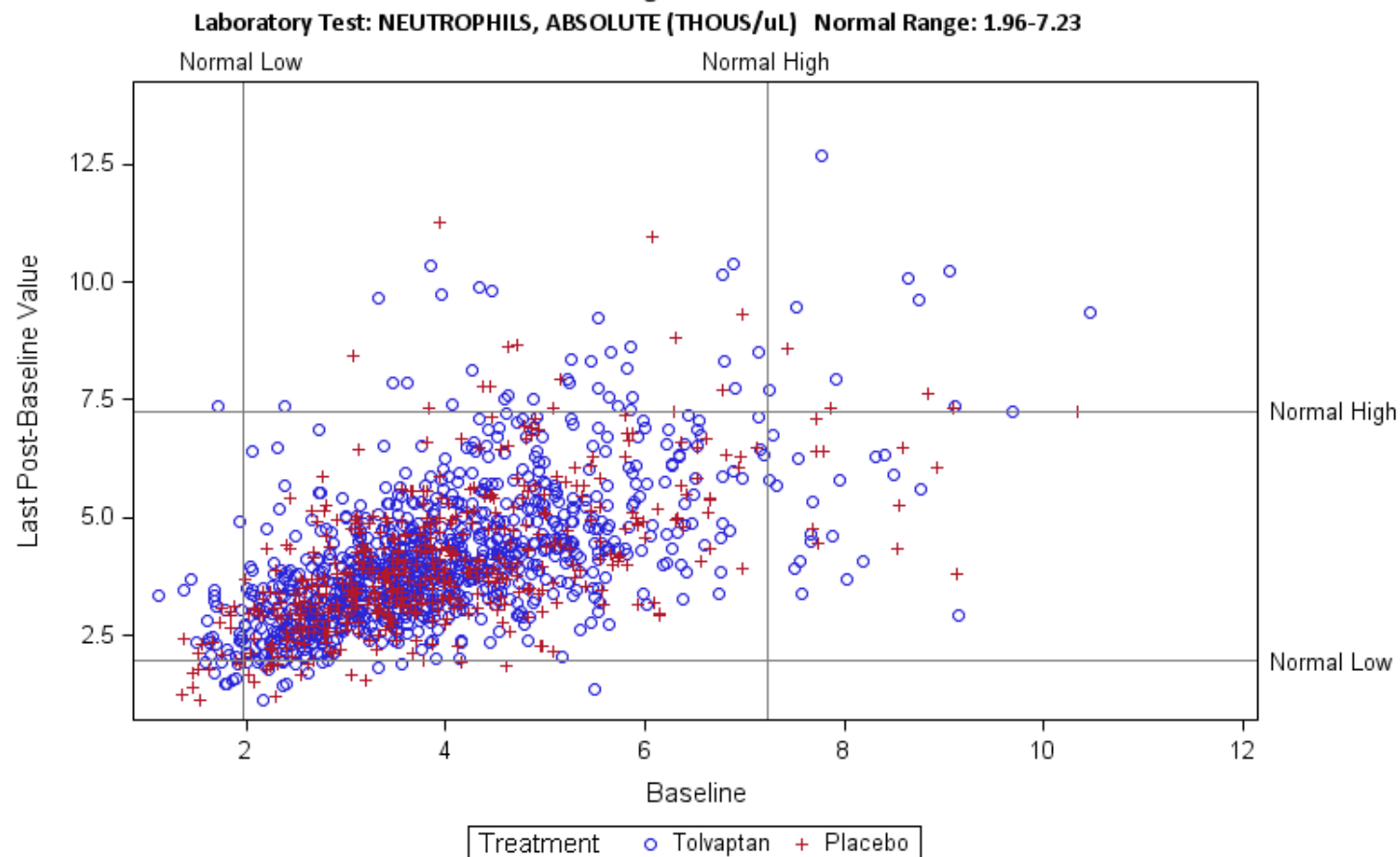
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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061

PROTOCOL P156-251

Figure 2.14.1

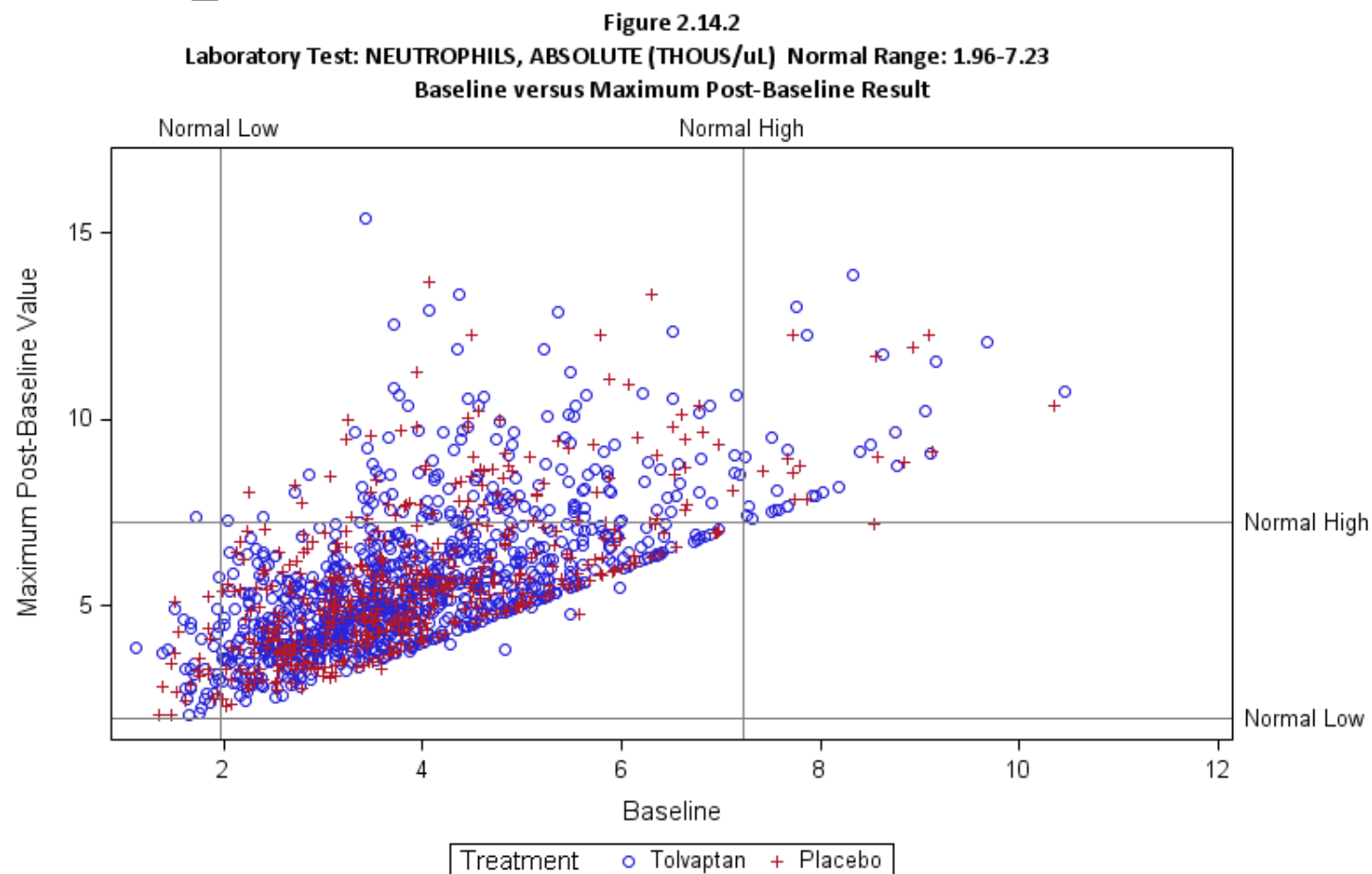


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

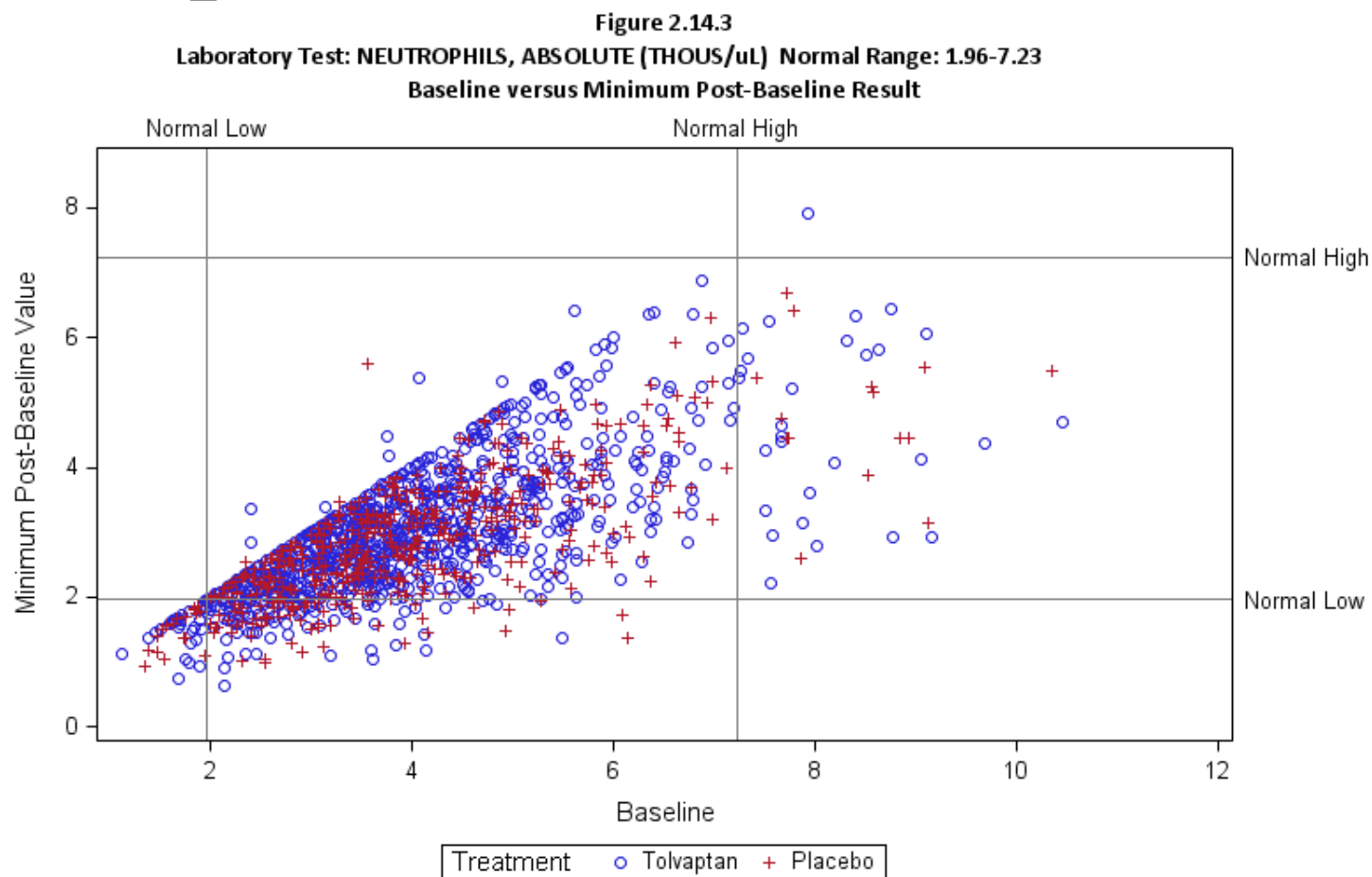


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

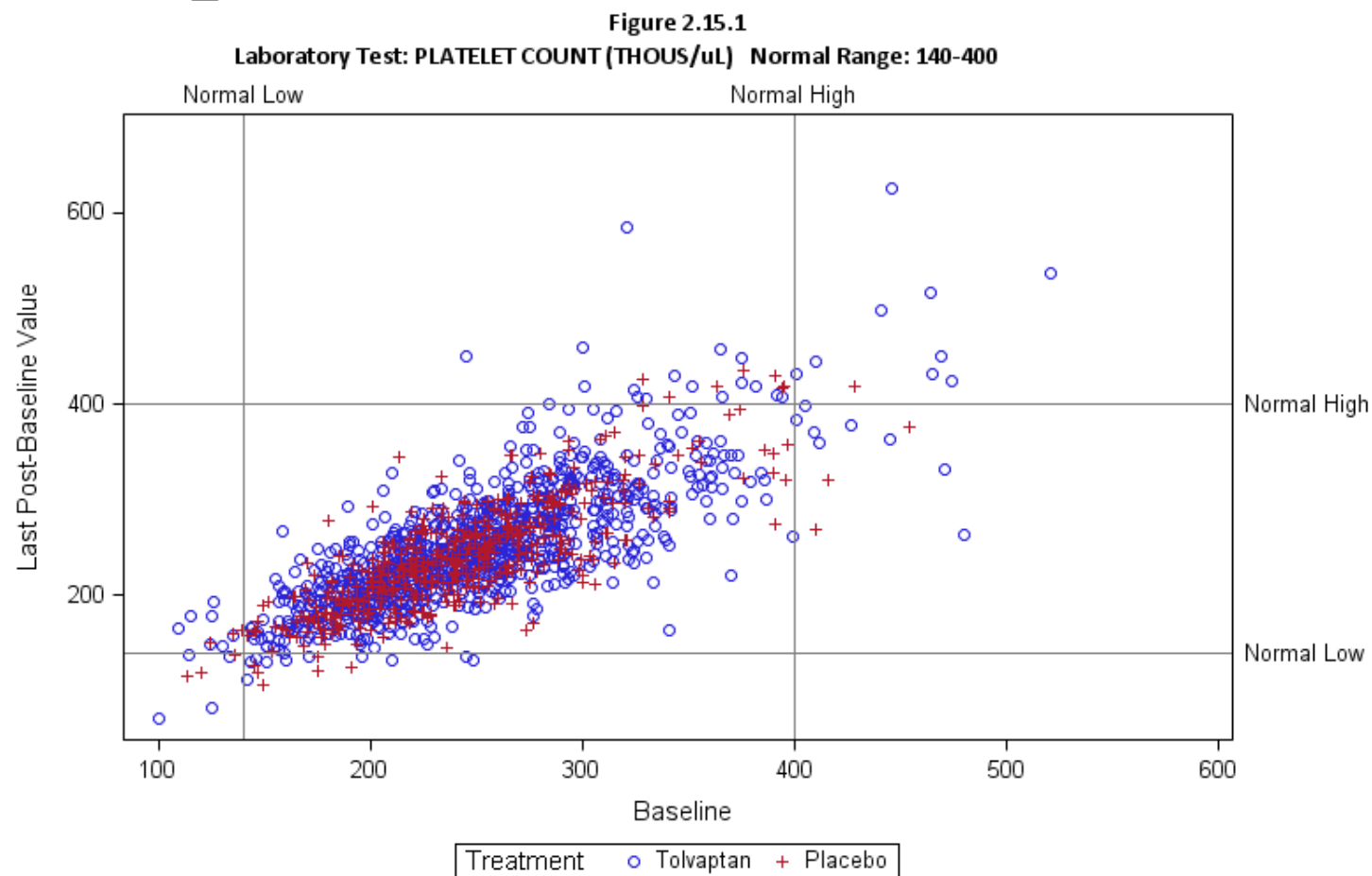


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

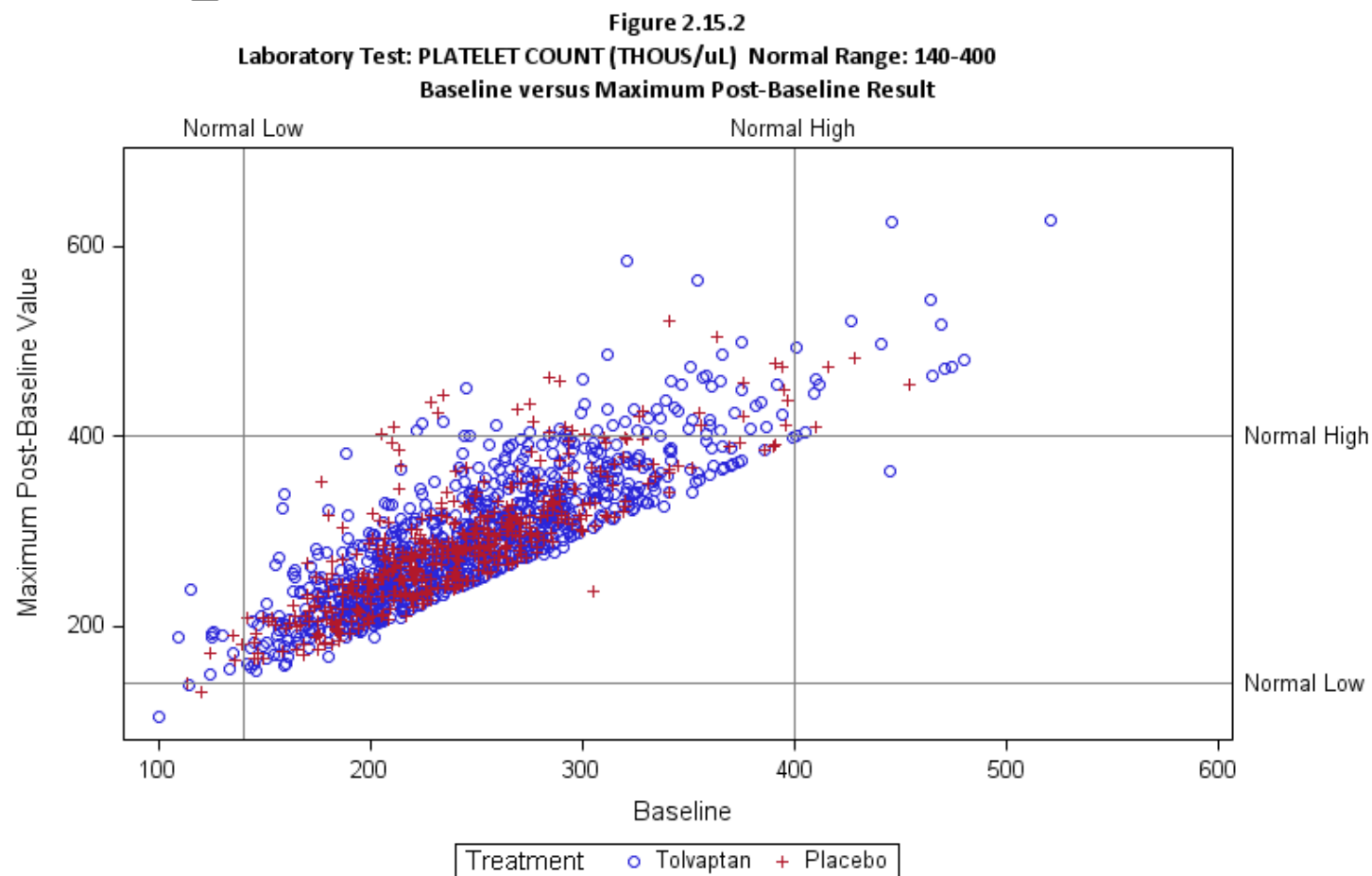


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

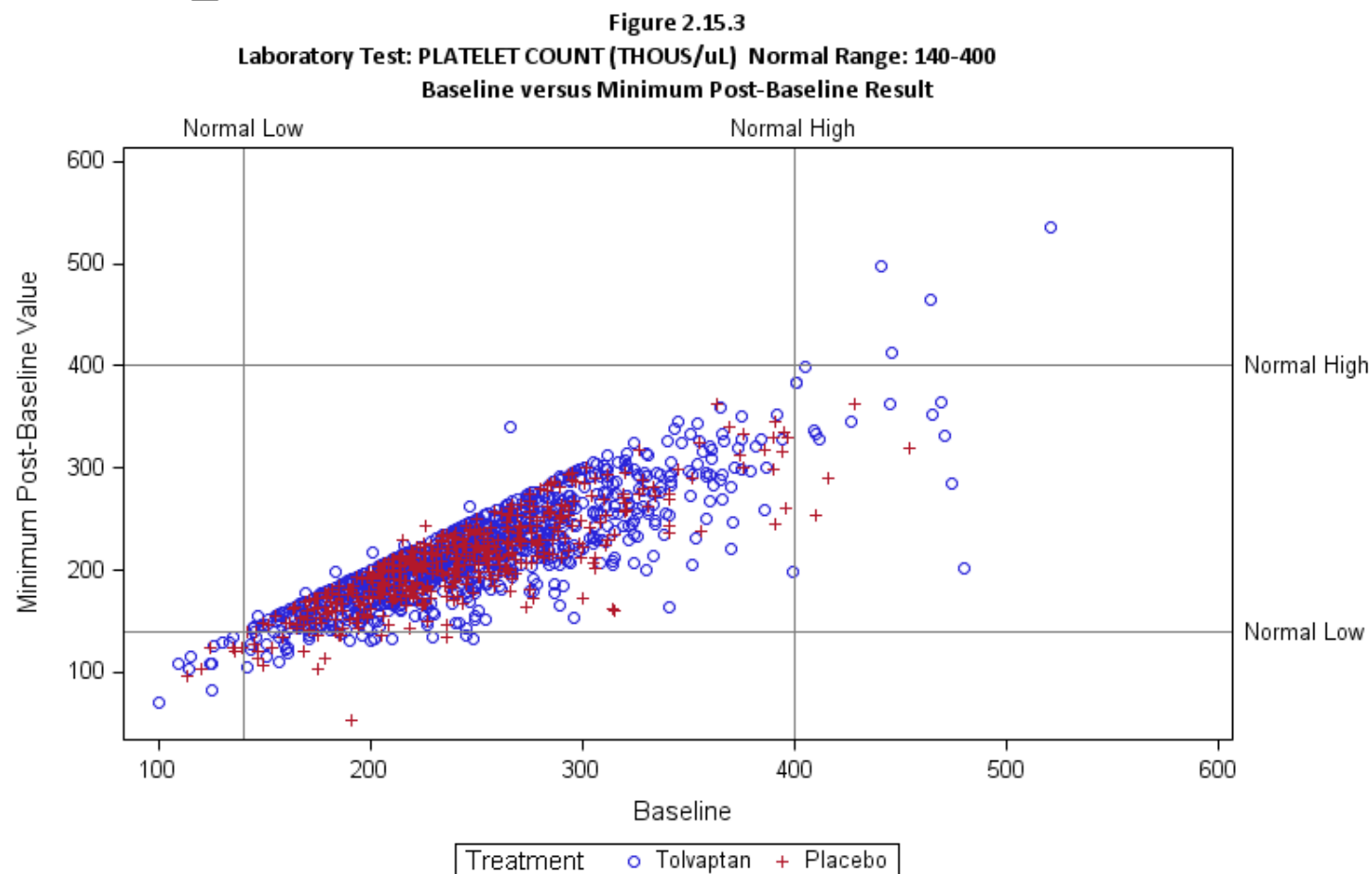


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

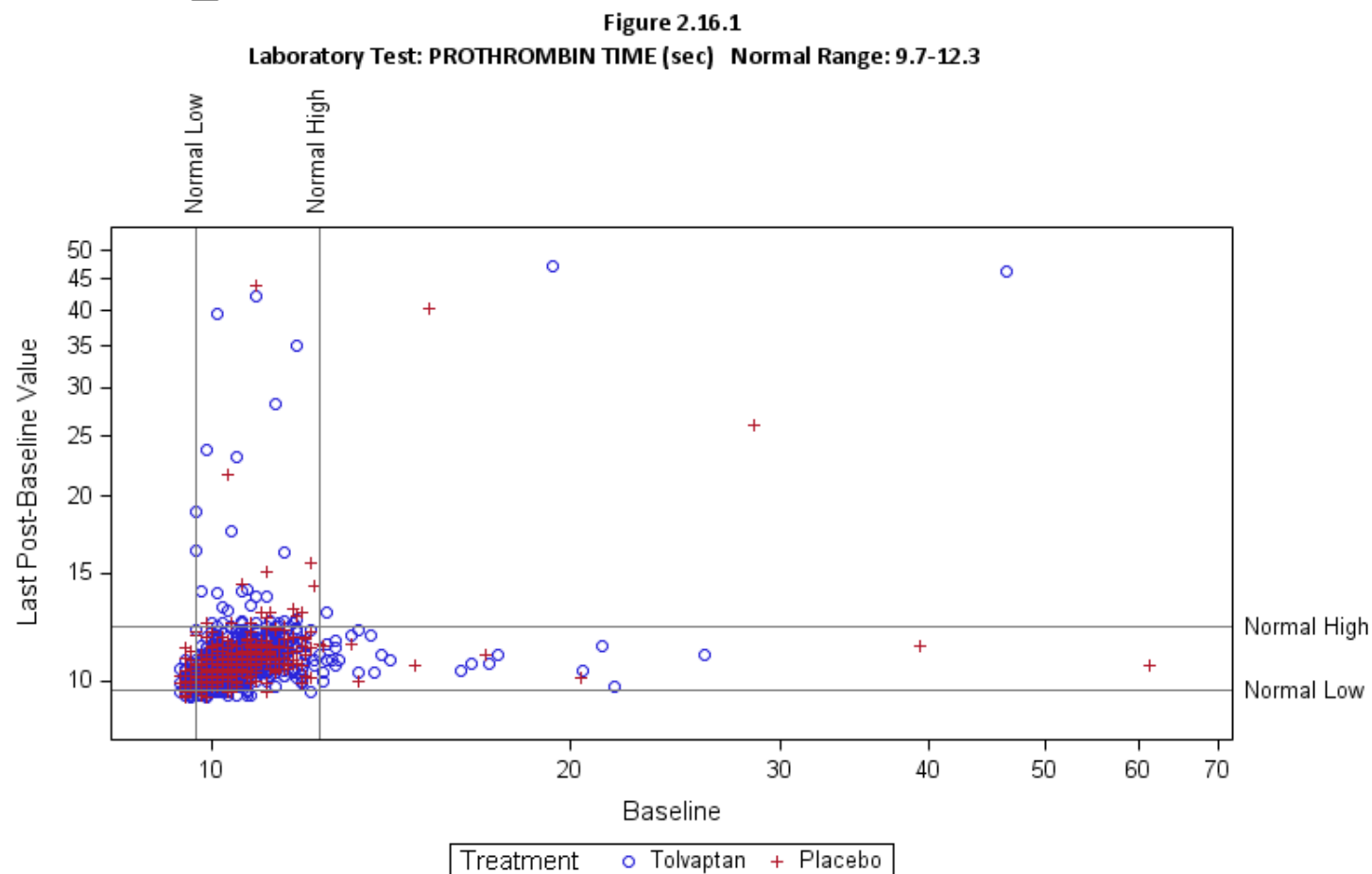


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

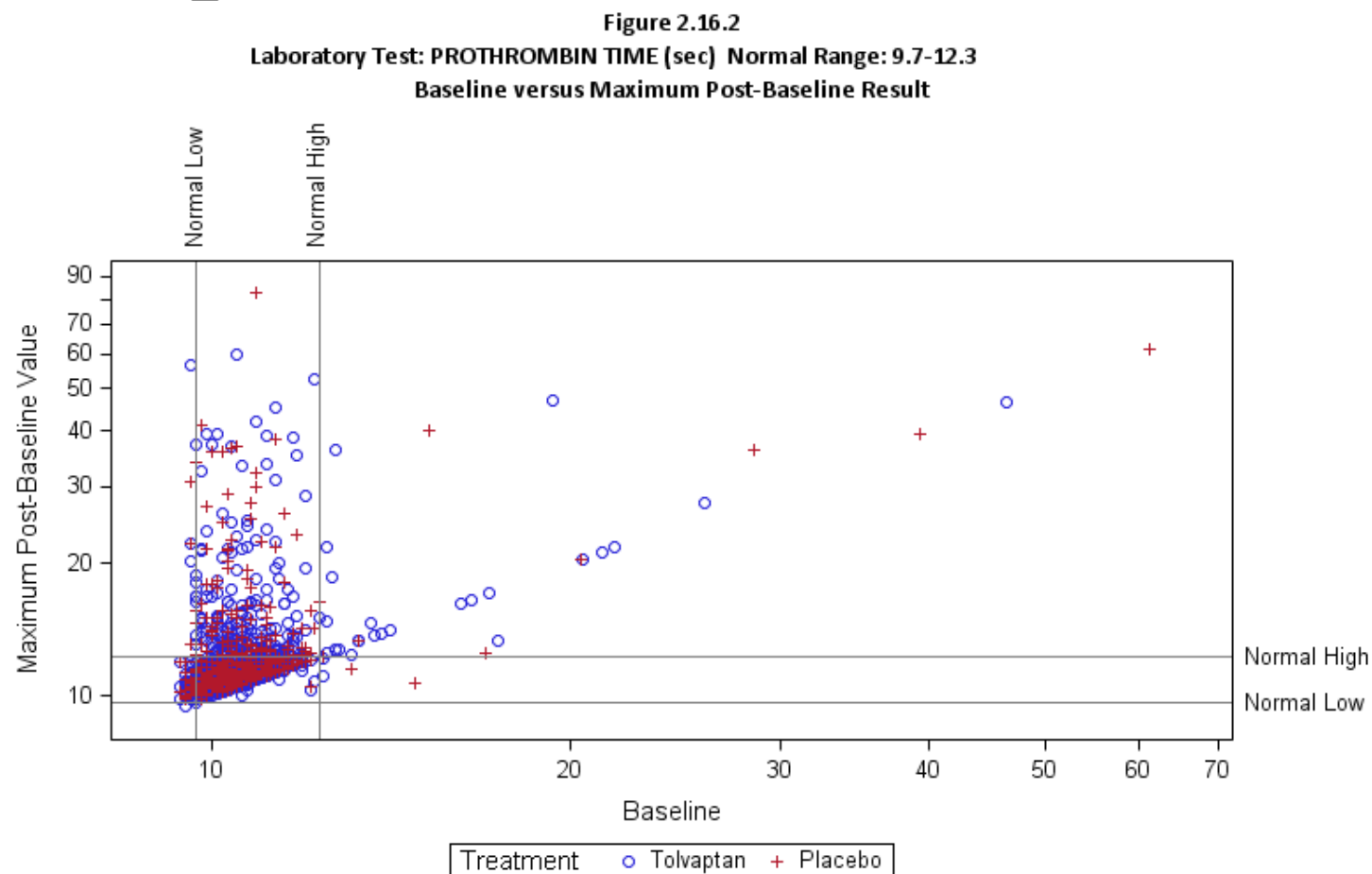


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

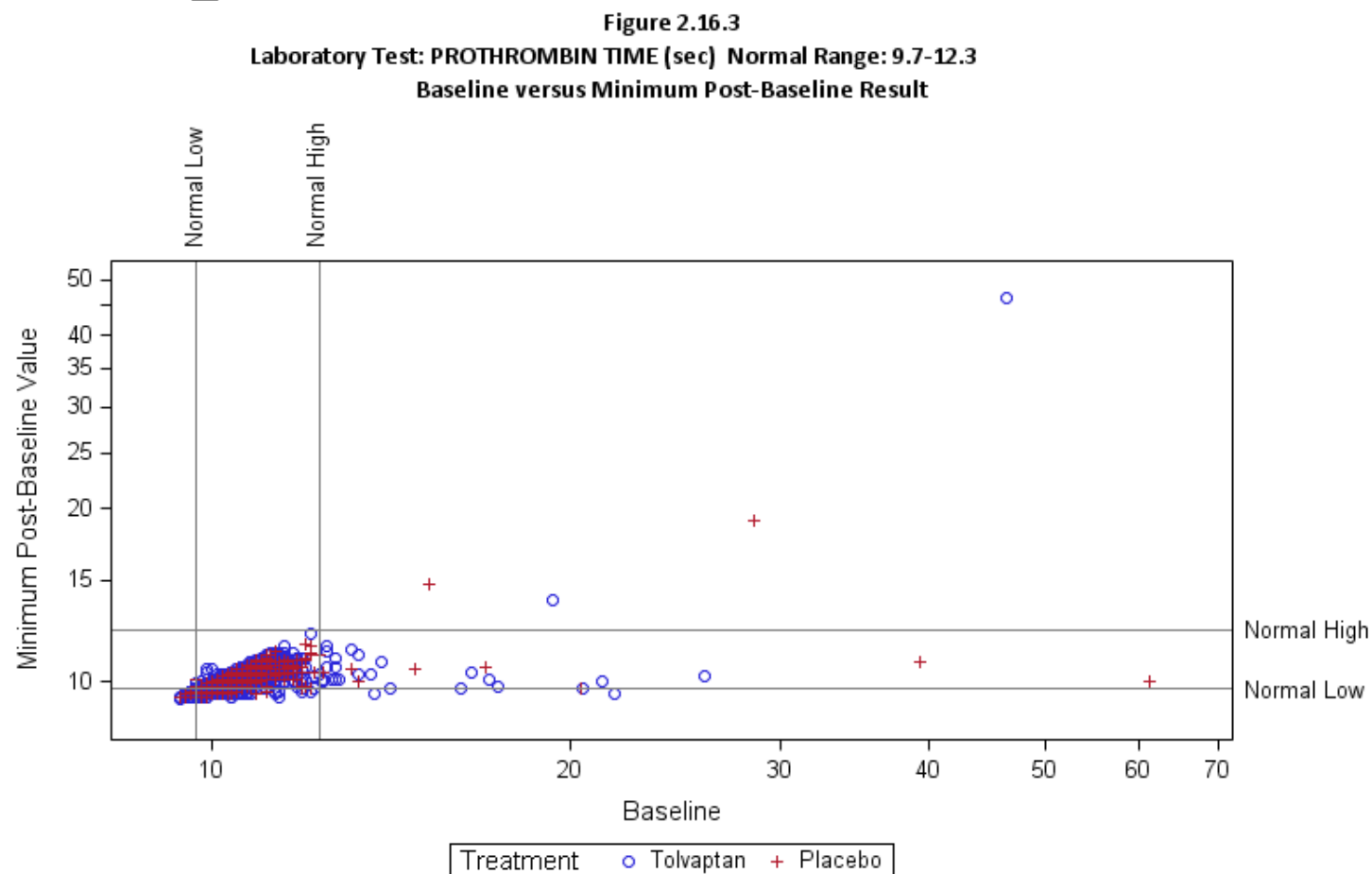


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

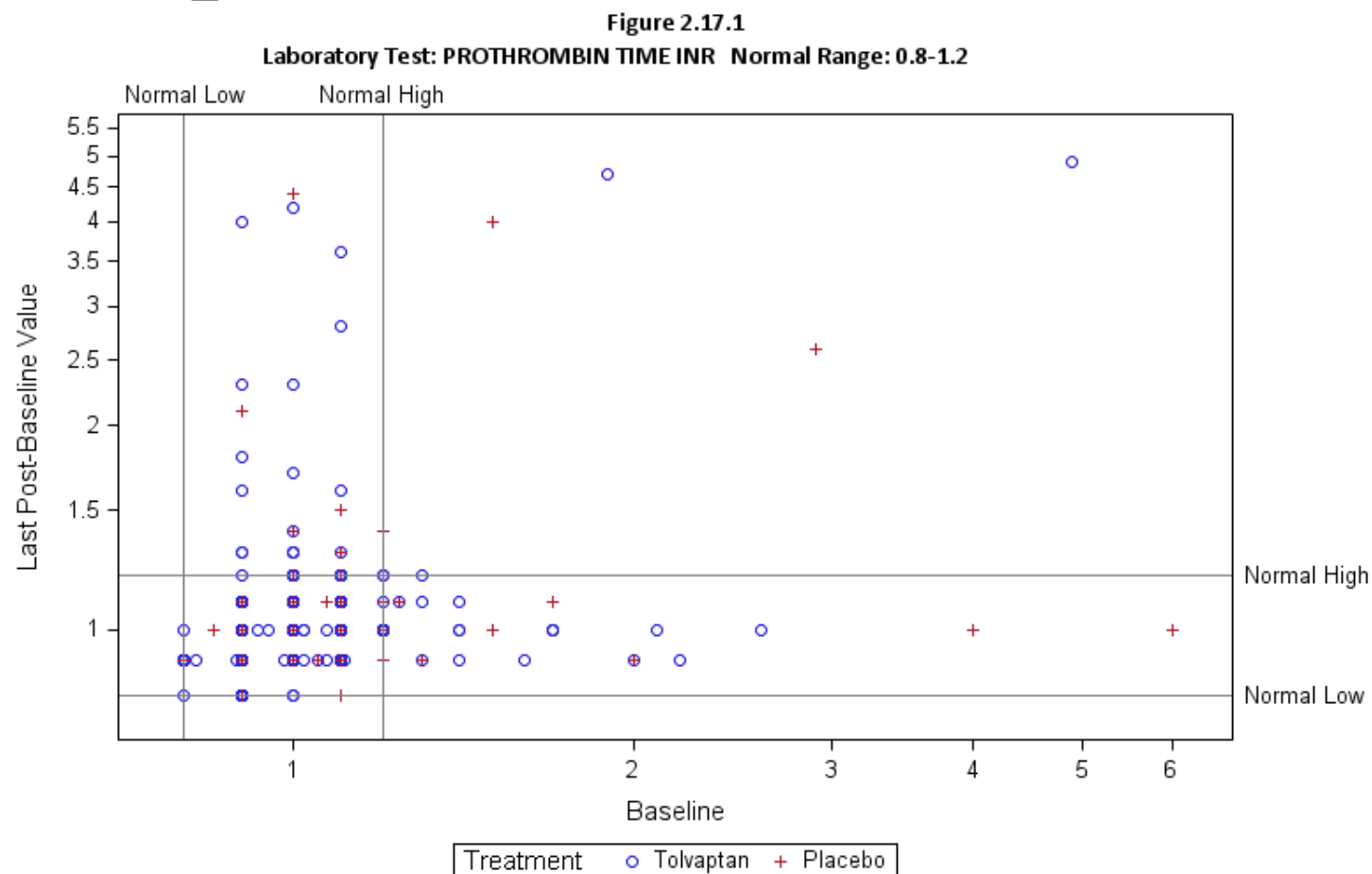
OPC41061
 PROTOCOL P156-251



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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

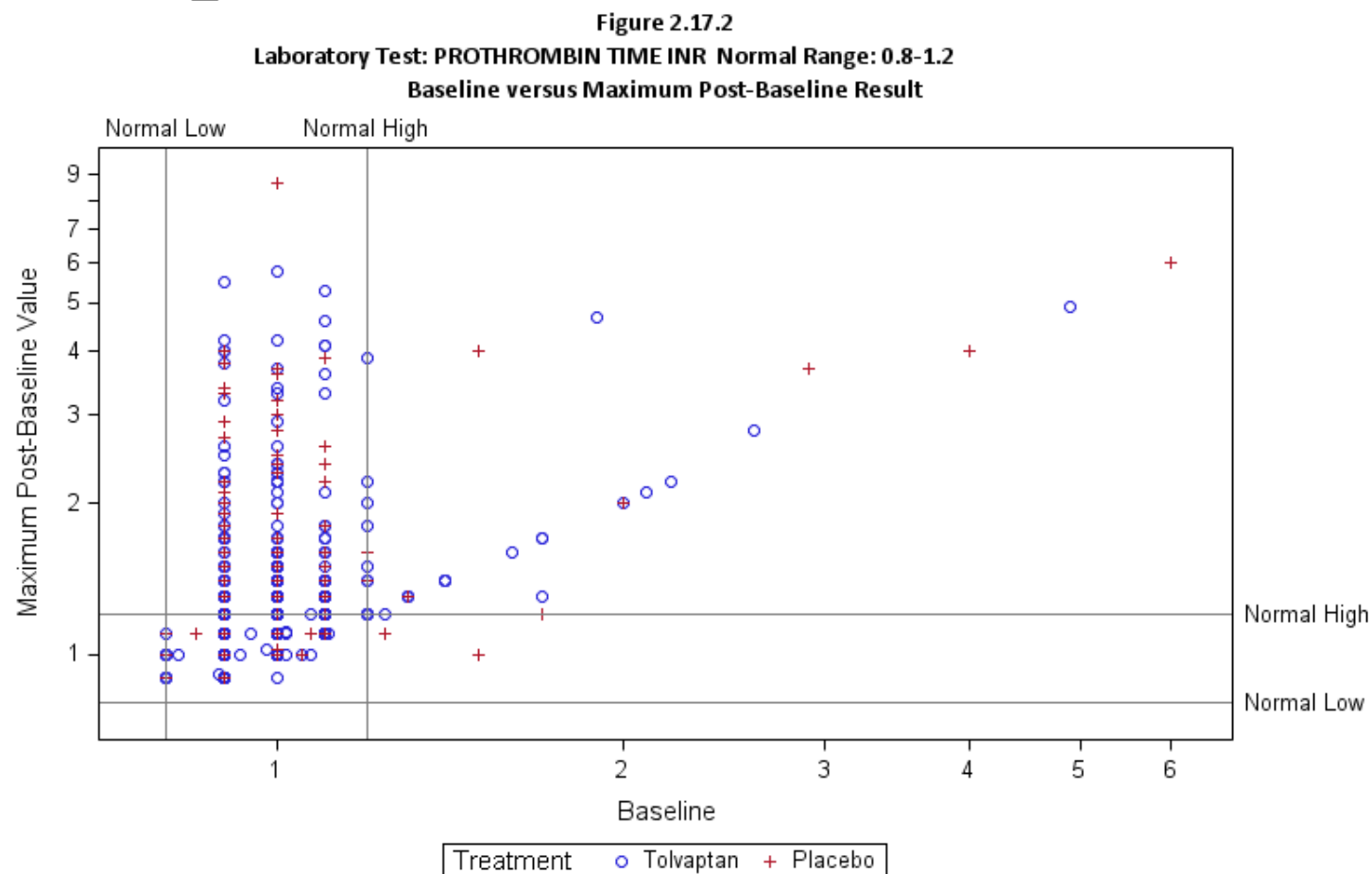
OPC41061
 PROTOCOL P156-251



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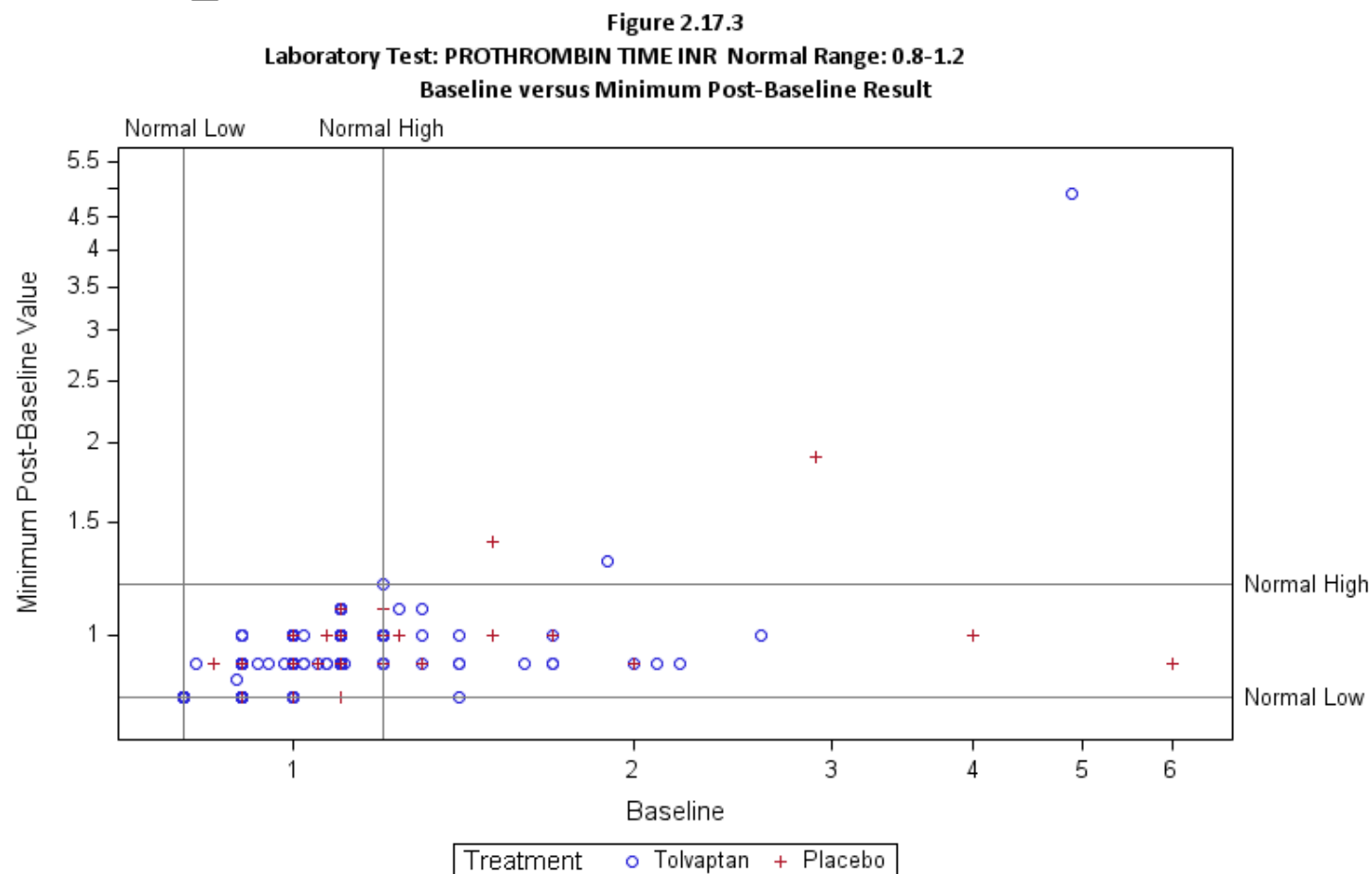
图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)



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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

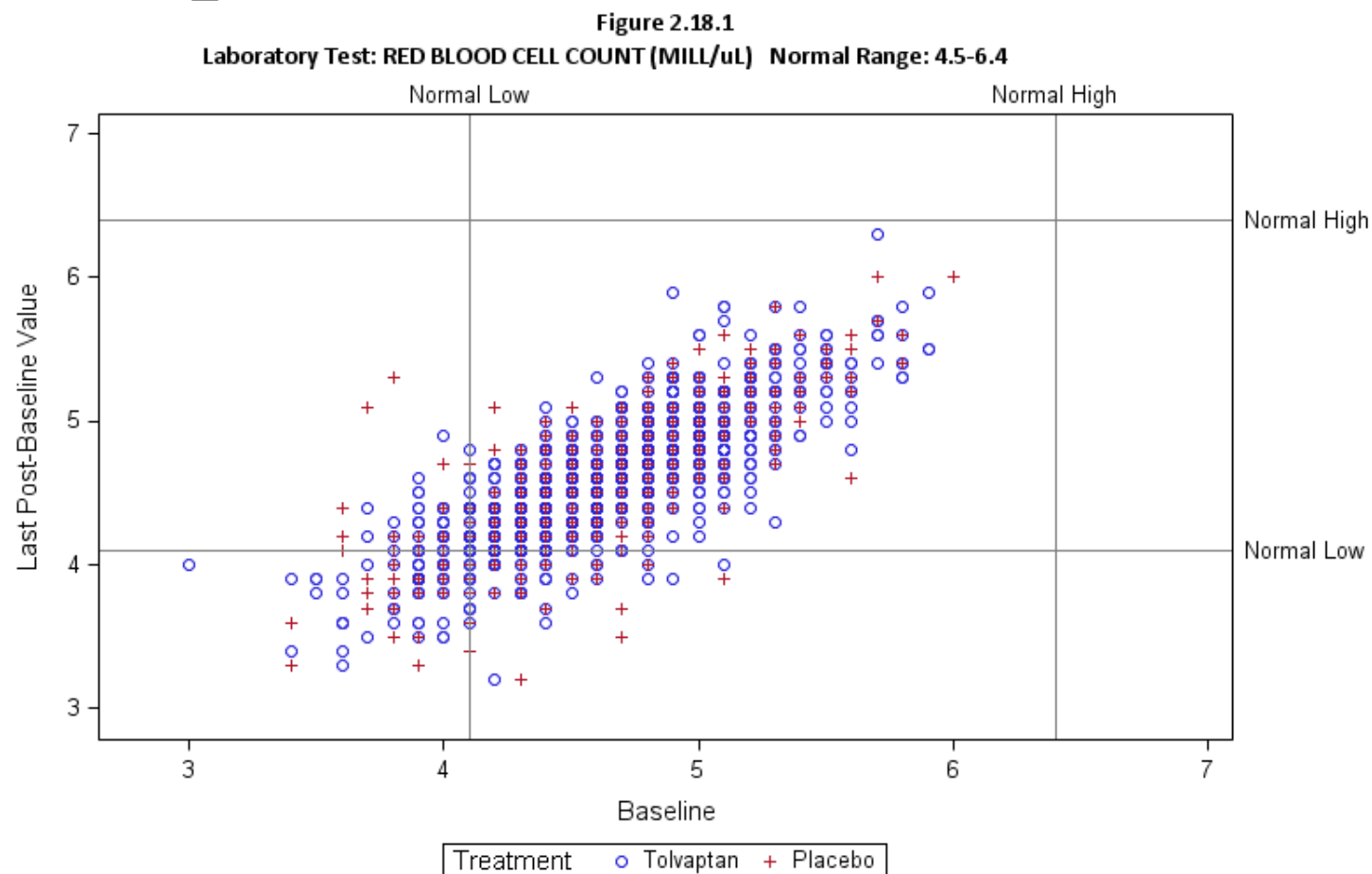


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

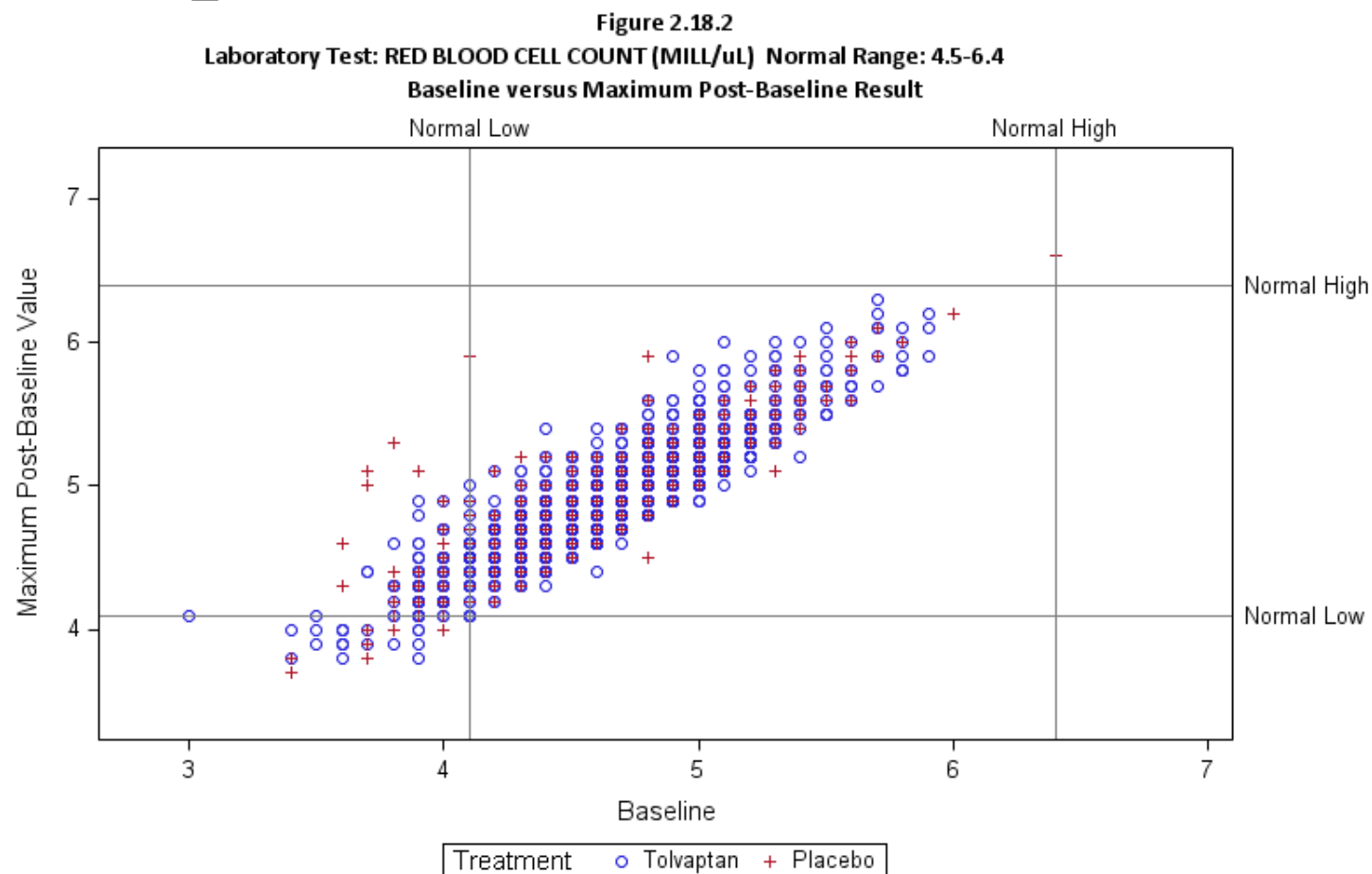
OPC41061
 PROTOCOL P156-251



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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

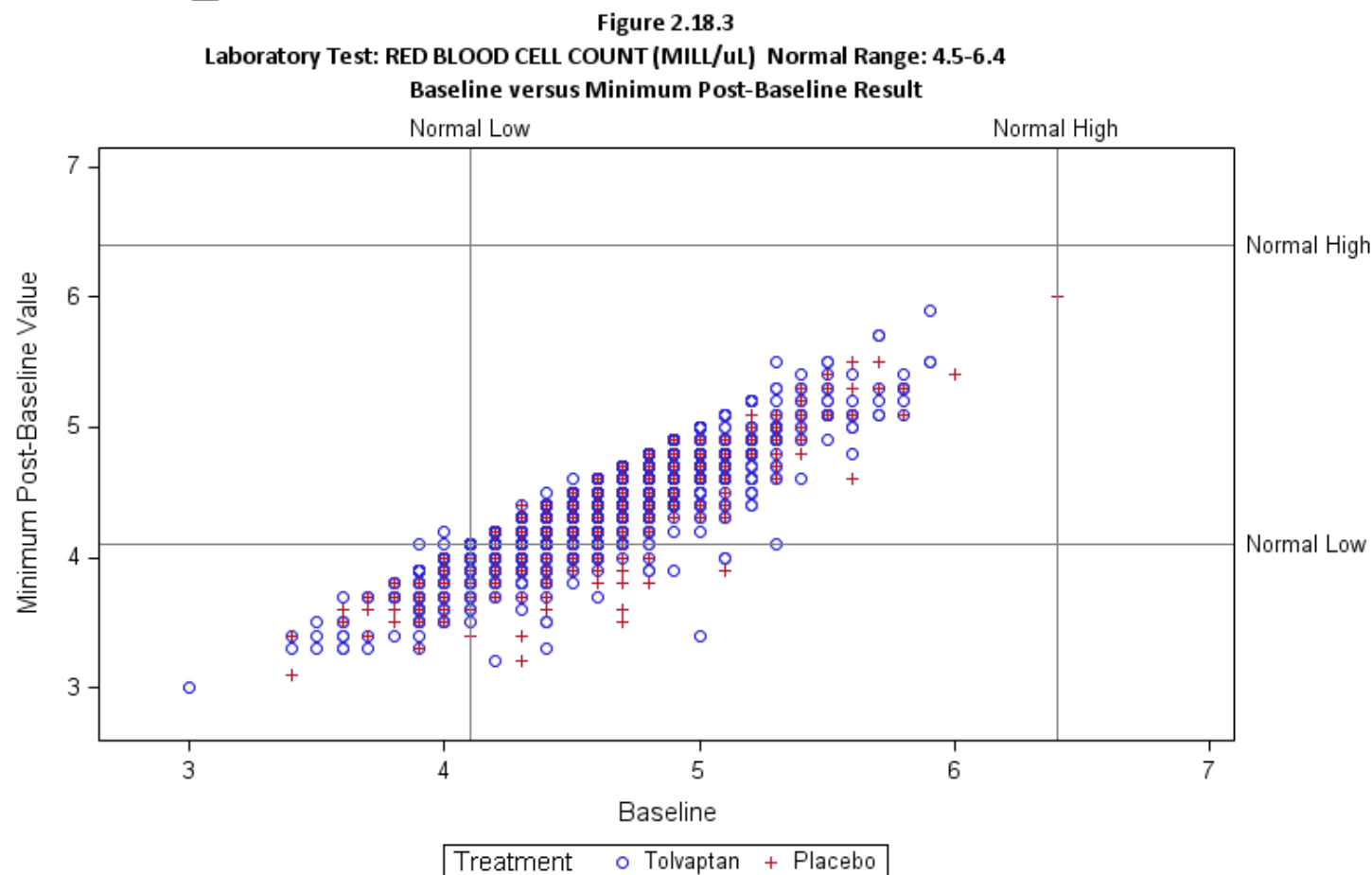


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

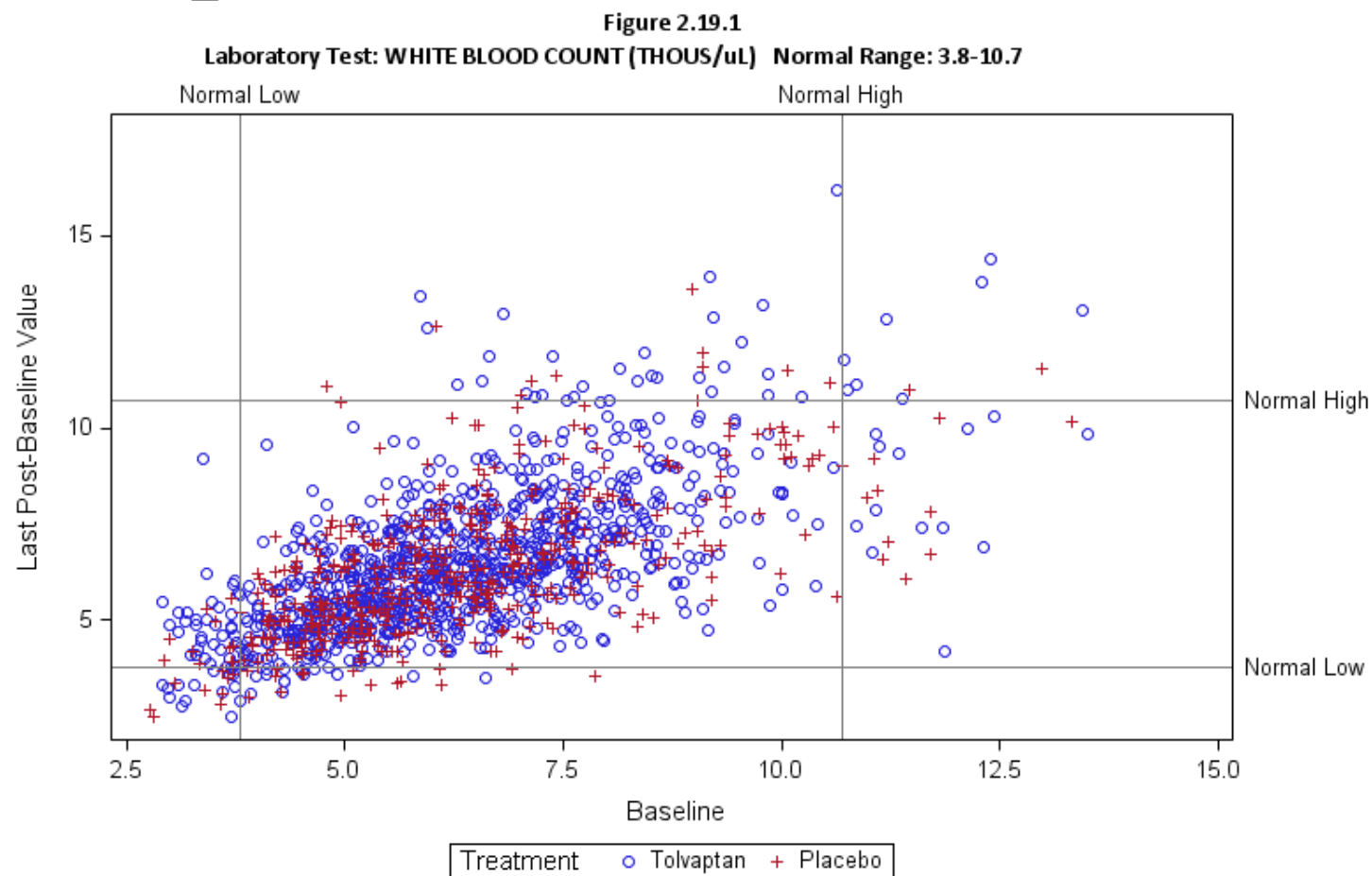


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

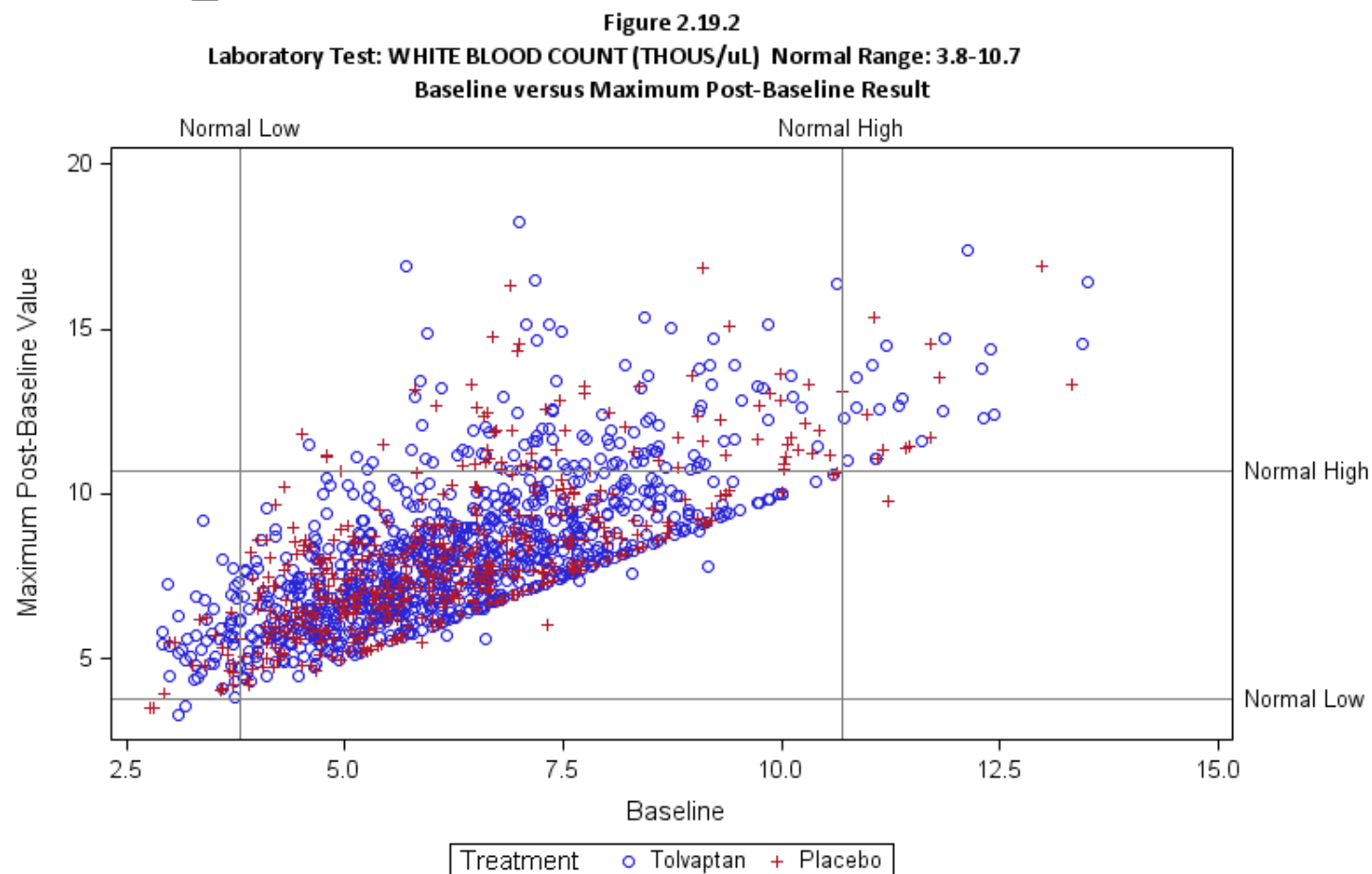


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图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
 PROTOCOL P156-251



Source: K:\OPC41061\P156-251\data set\analysis\HEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

图 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

OPC41061
PROTOCOL P156-251

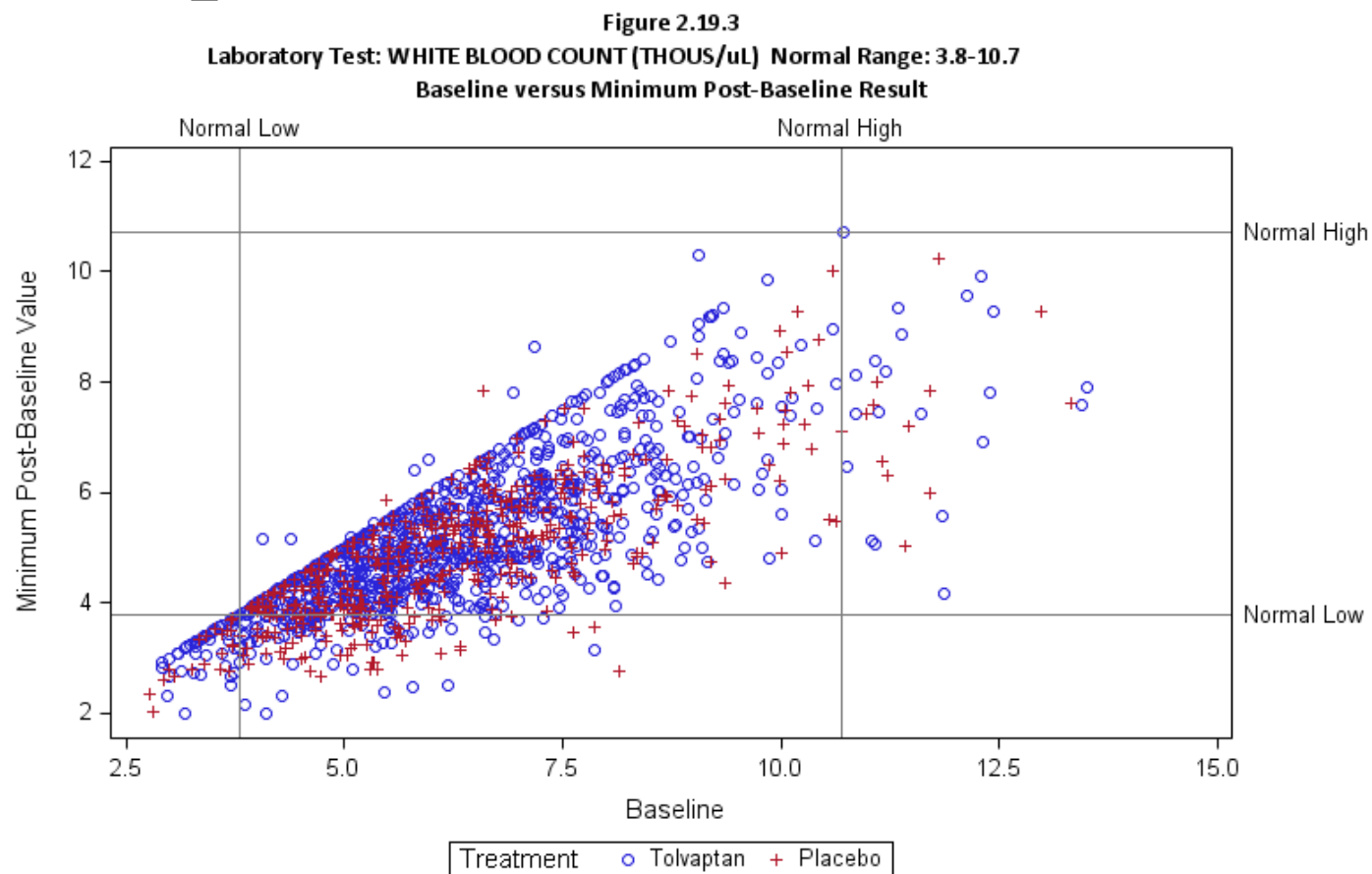
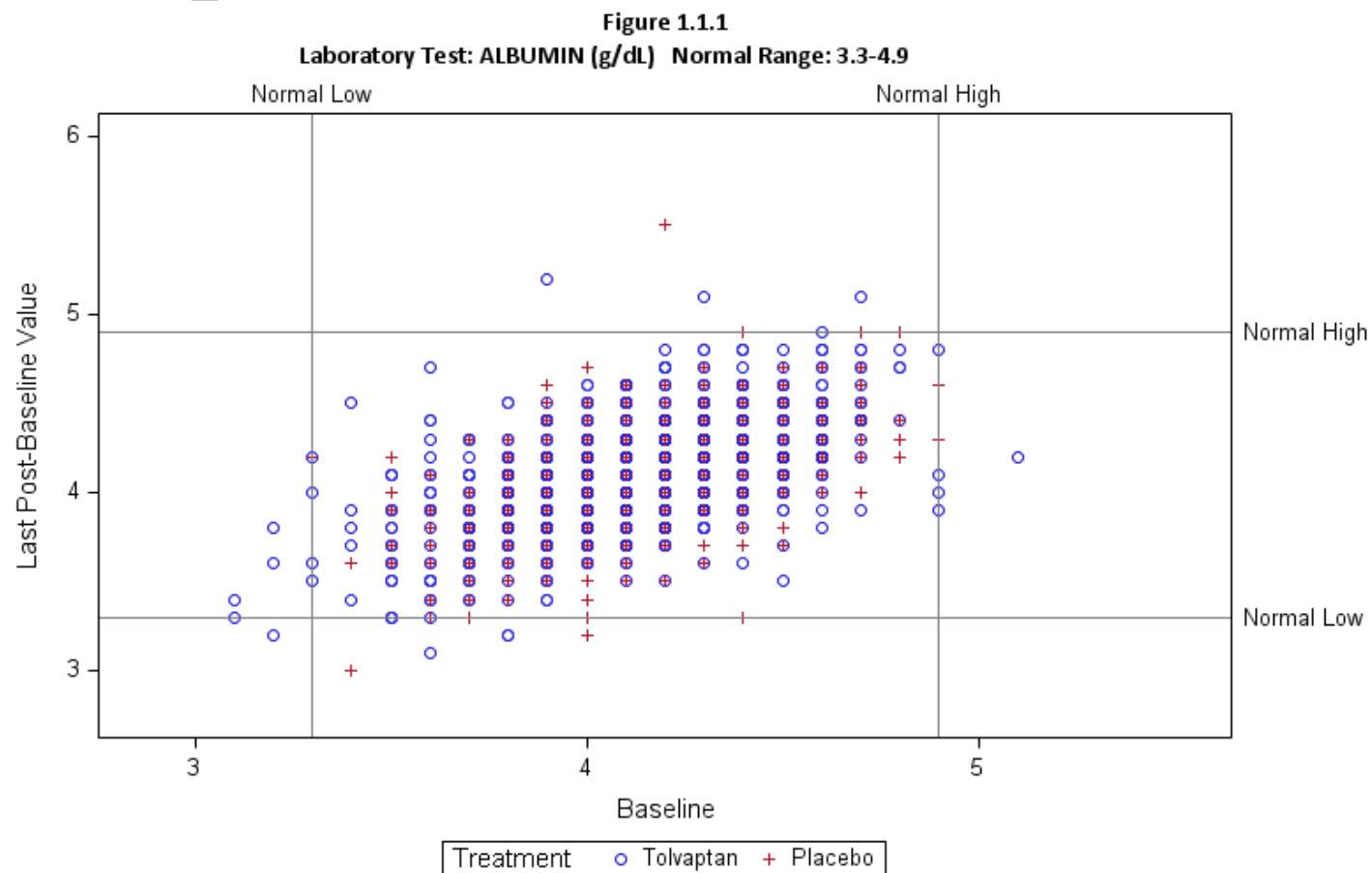


図 2.7.4.7-36 X-Y Plots (Hematology Parameters) (156-251)

<資料番号 5.3.5.3-02 : Figure 2.1.1~2.19.3>

OPC41061
 PROTOCOL P156-251

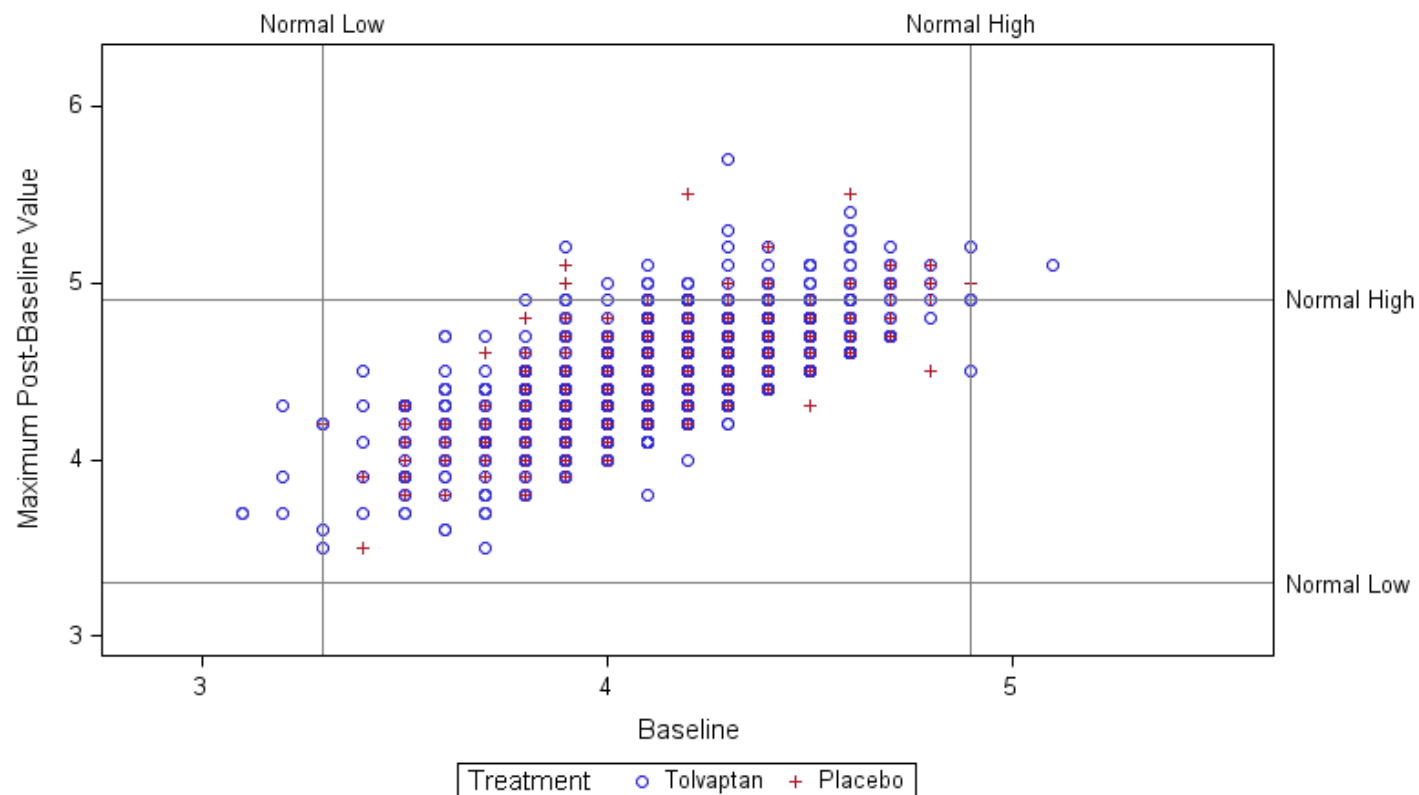


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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.1.2
 Laboratory Test: ALBUMIN (g/dL) Normal Range: 3.3-4.9
 Baseline versus Maximum Post-Baseline Result



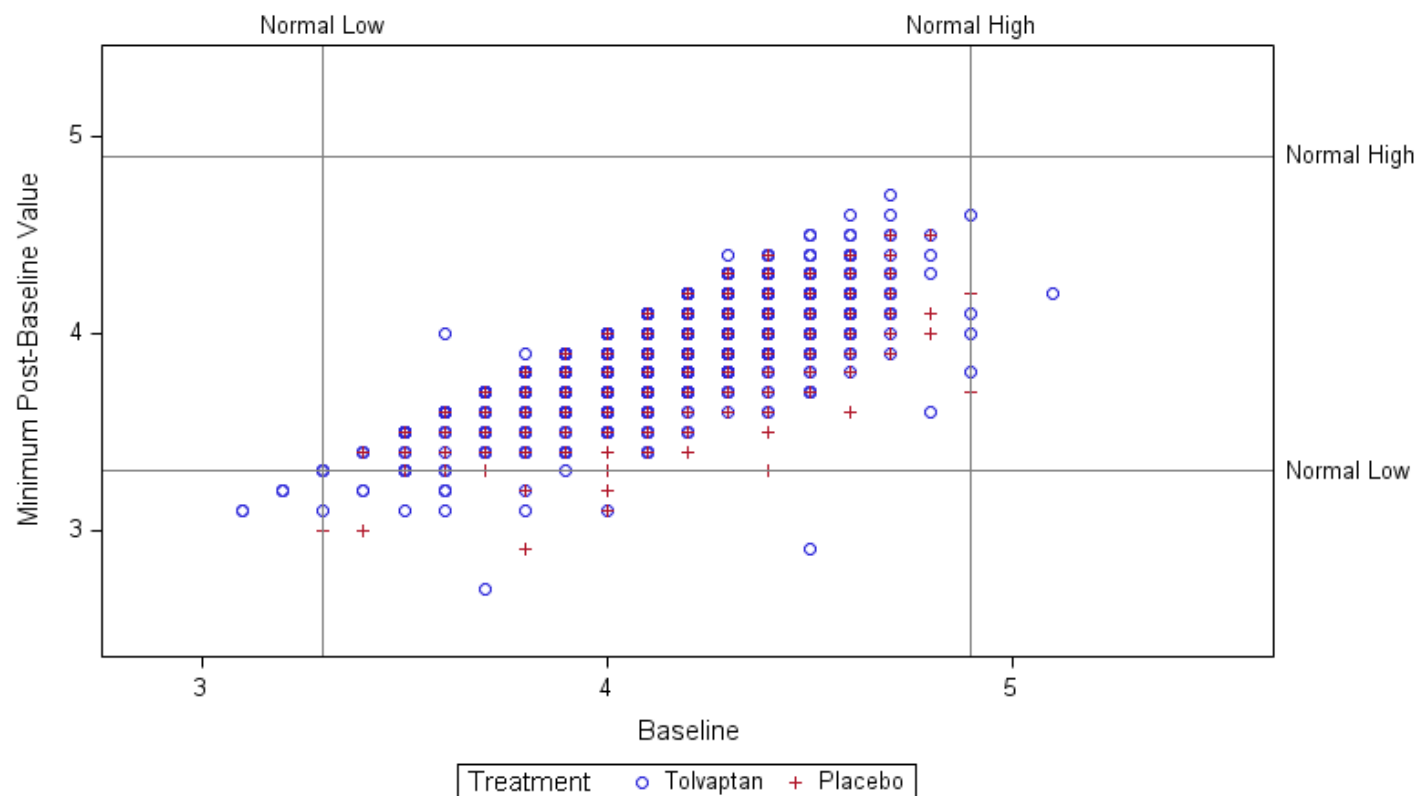
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.1.3
 Laboratory Test: ALBUMIN (g/dL) Normal Range: 3.3-4.9
 Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0
 Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

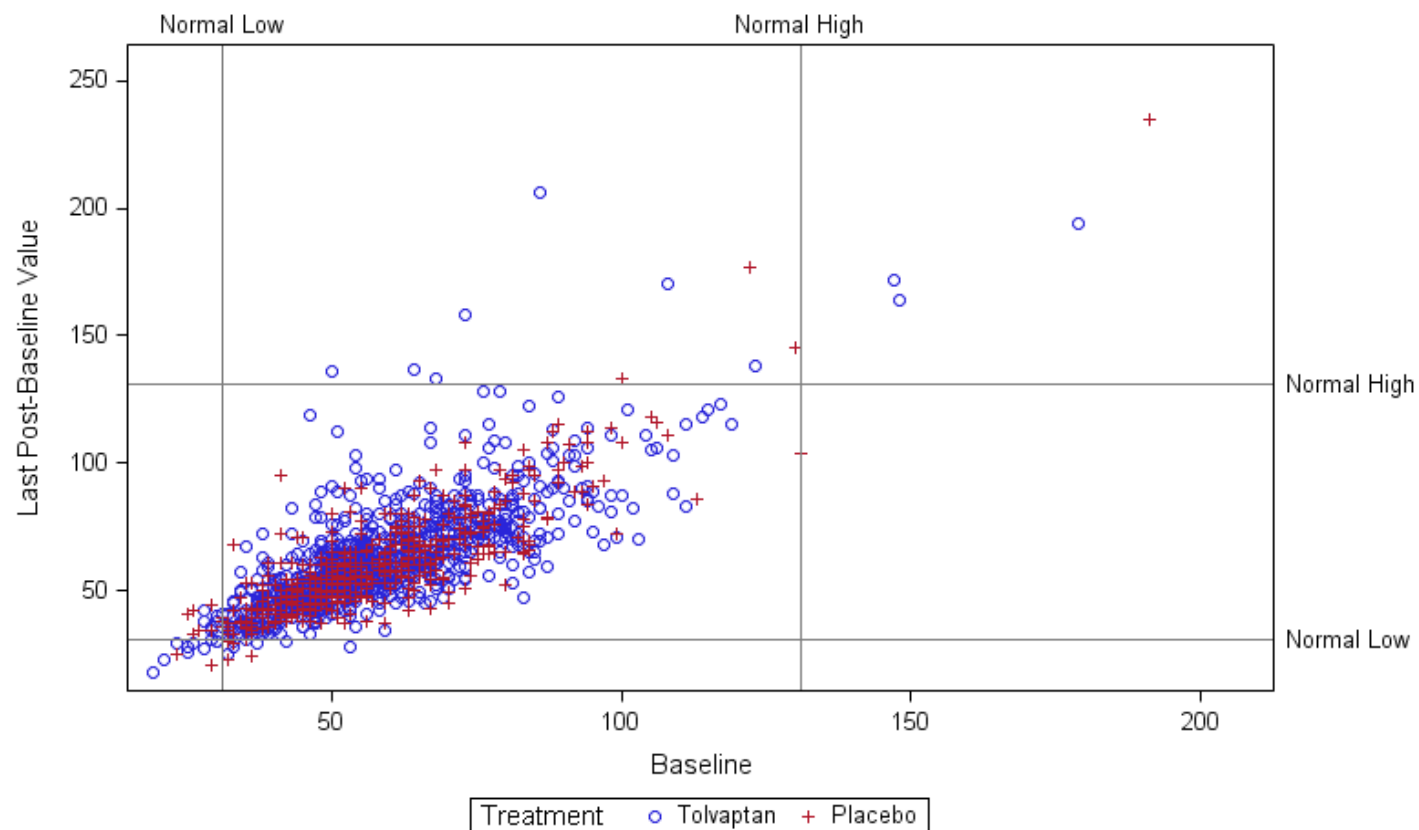
2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061

PROTOCOL P156-251

Figure 1.2.1

Laboratory Test: ALKALINE PHOSPHATASE (IU/L) Normal Range: 31-129



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

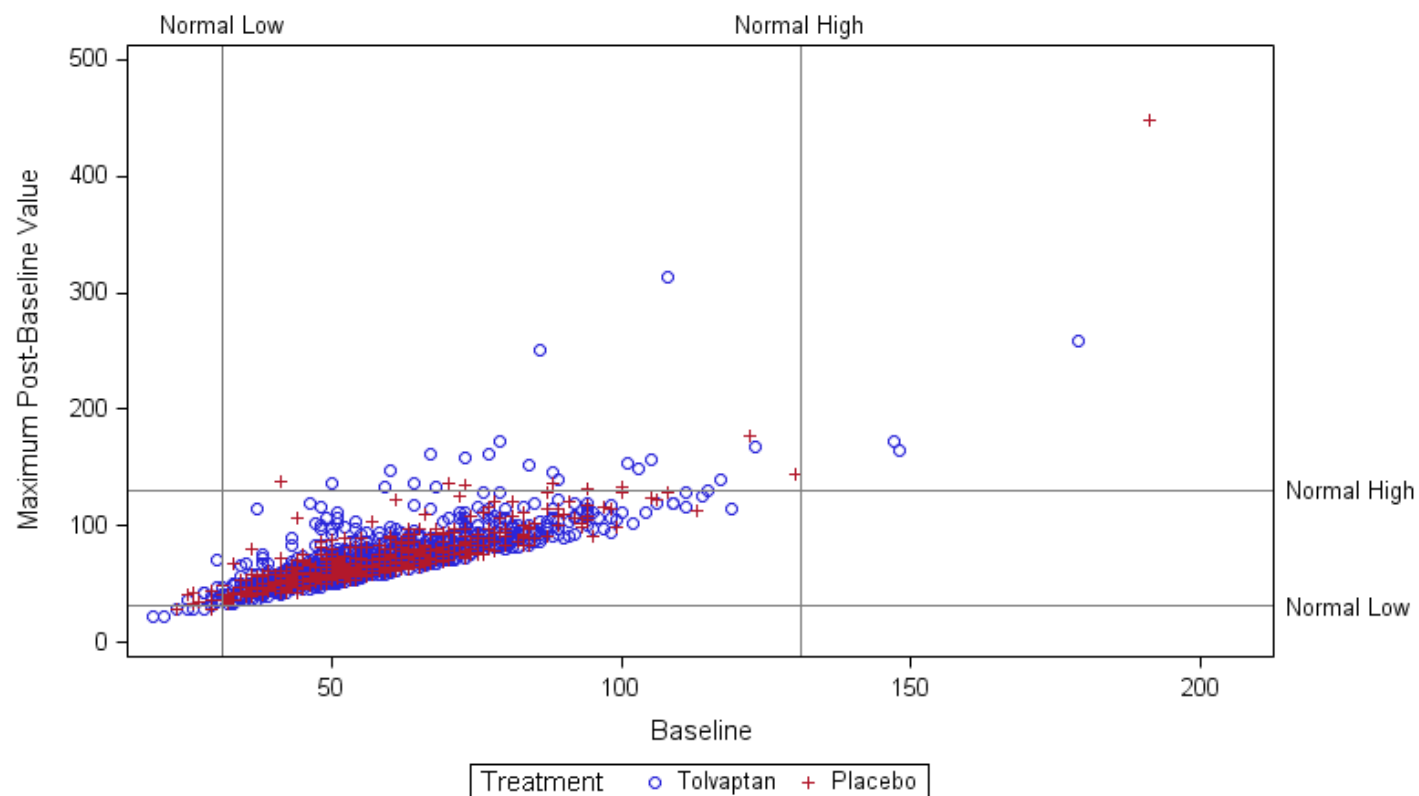
OPC41061

PROTOCOL P156-251

Figure 1.2.2

Laboratory Test: ALKALINE PHOSPHATASE (IU/L) Normal Range: 31-129

Baseline versus Maximum Post-Baseline Result

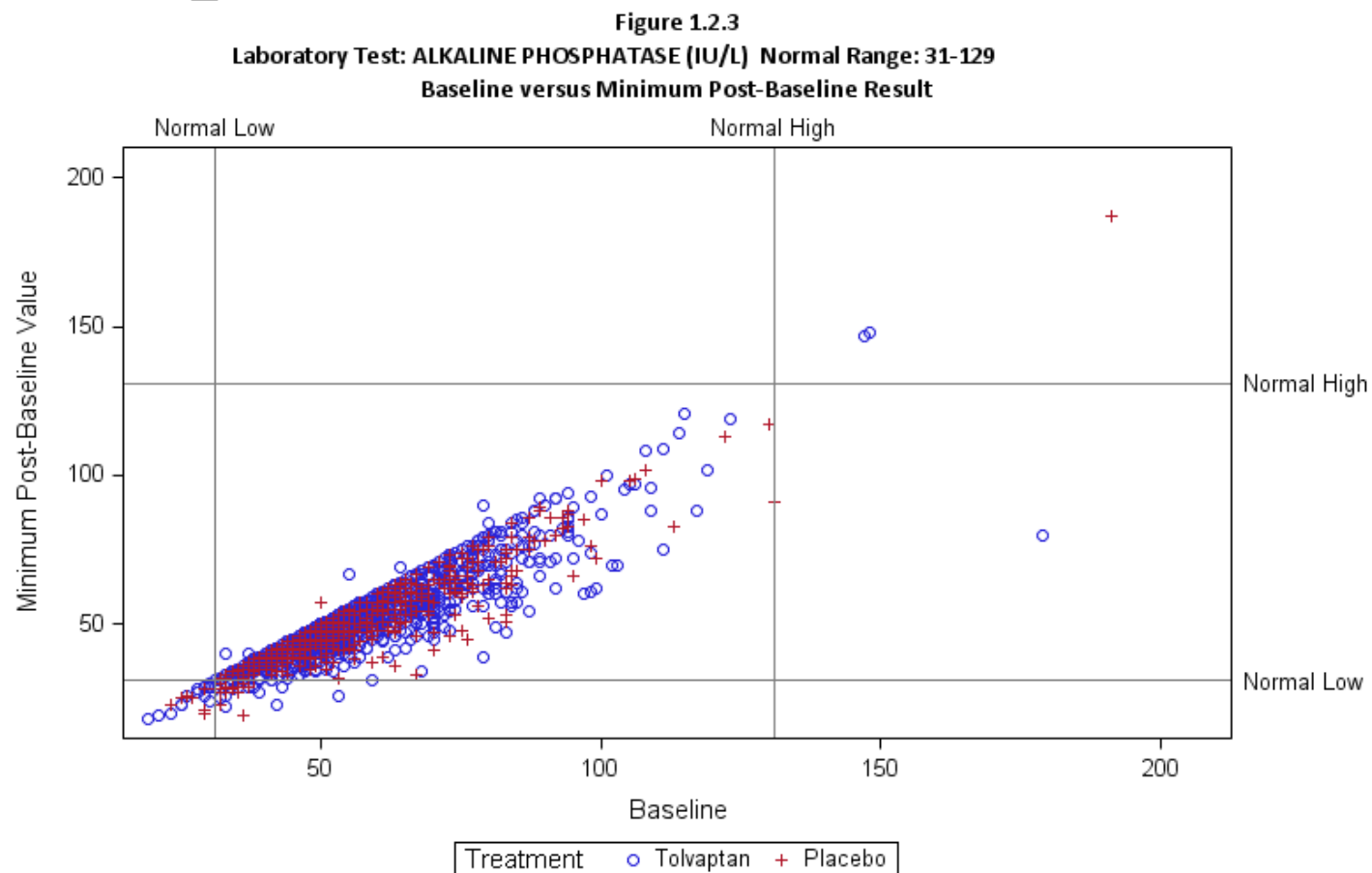


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

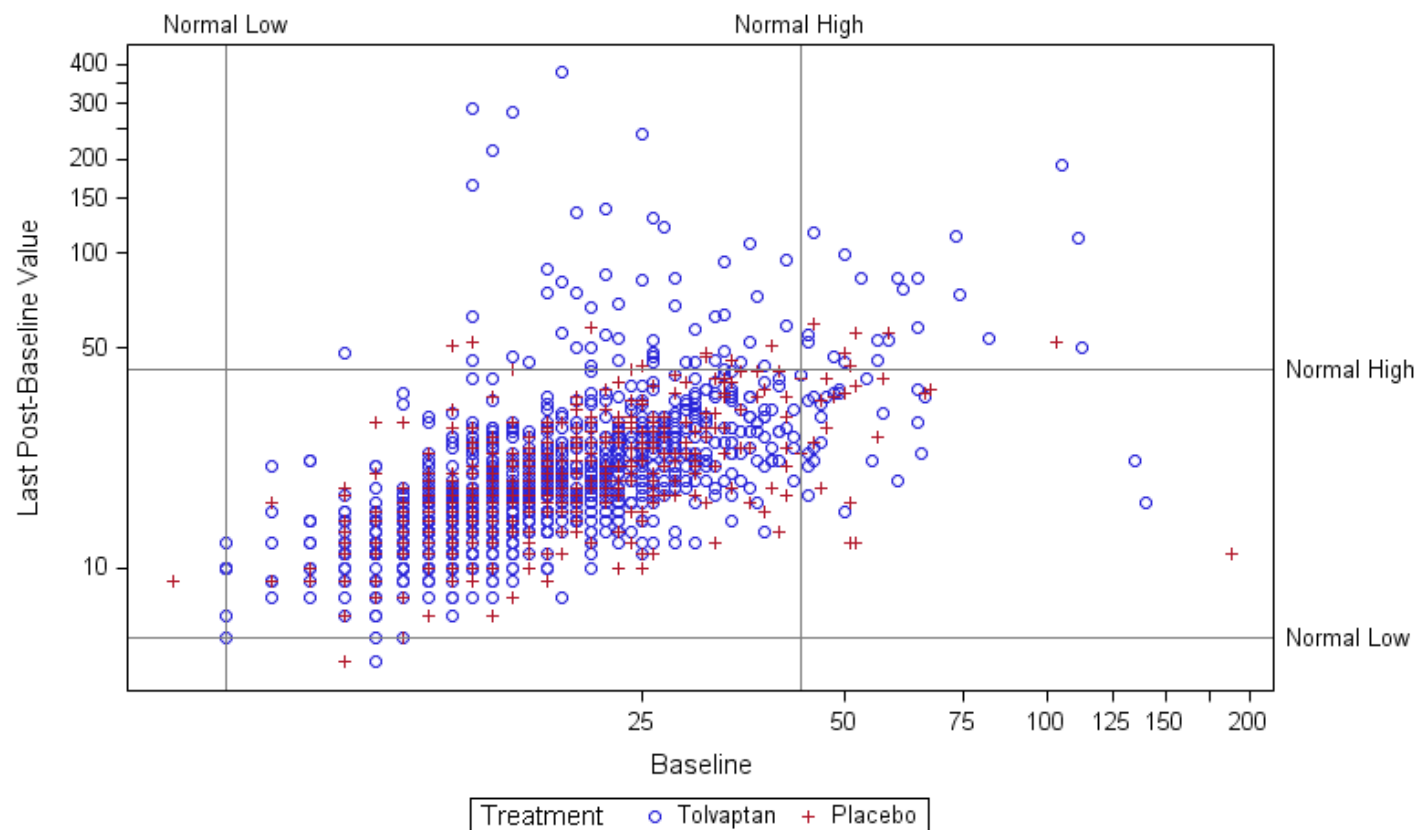


Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0
 Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.3.1
 Laboratory Test: ALT (SGPT) (IU/L) Normal Range: 6-43



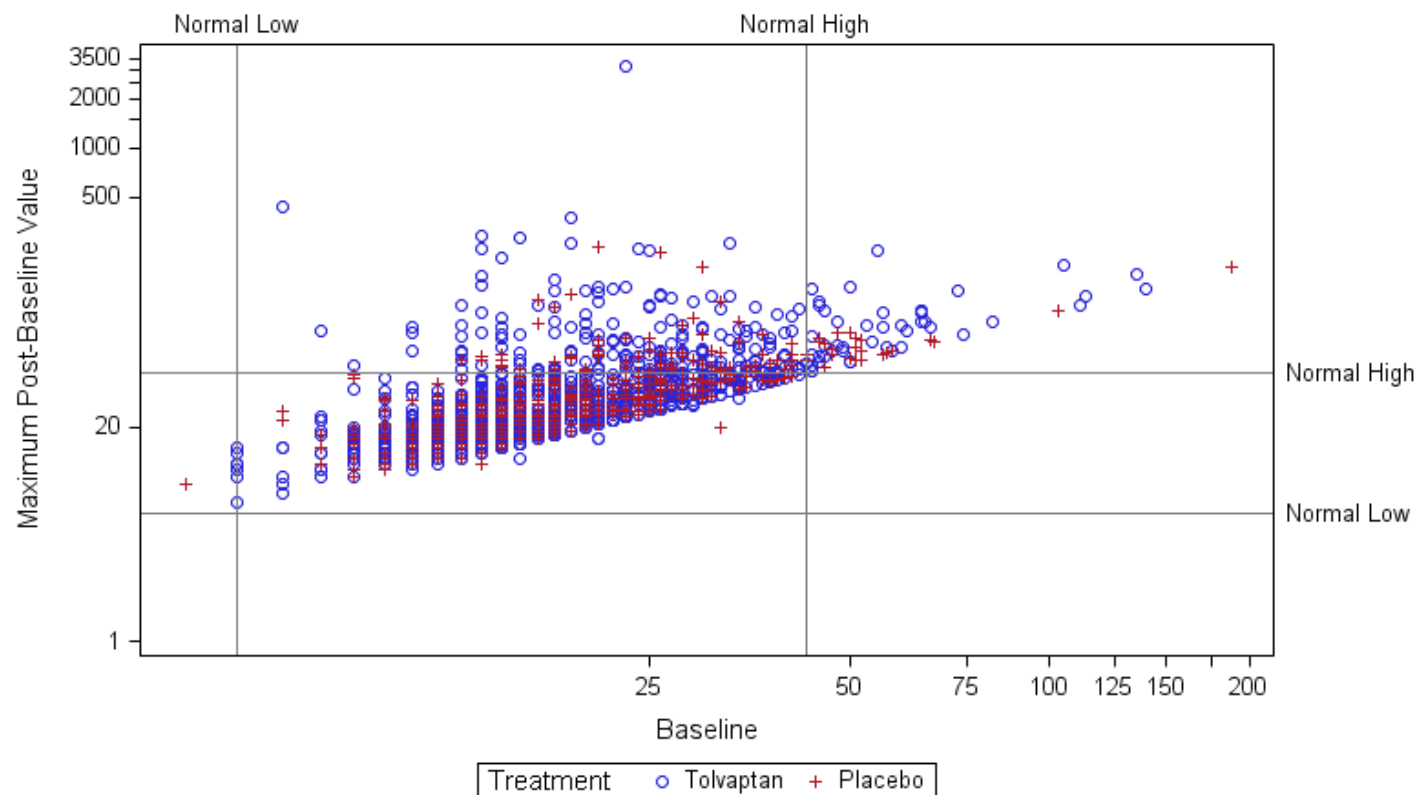
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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.3.2
 Laboratory Test: ALT (SGPT) (IU/L) Normal Range: 6-43
 Baseline versus Maximum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0
 Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

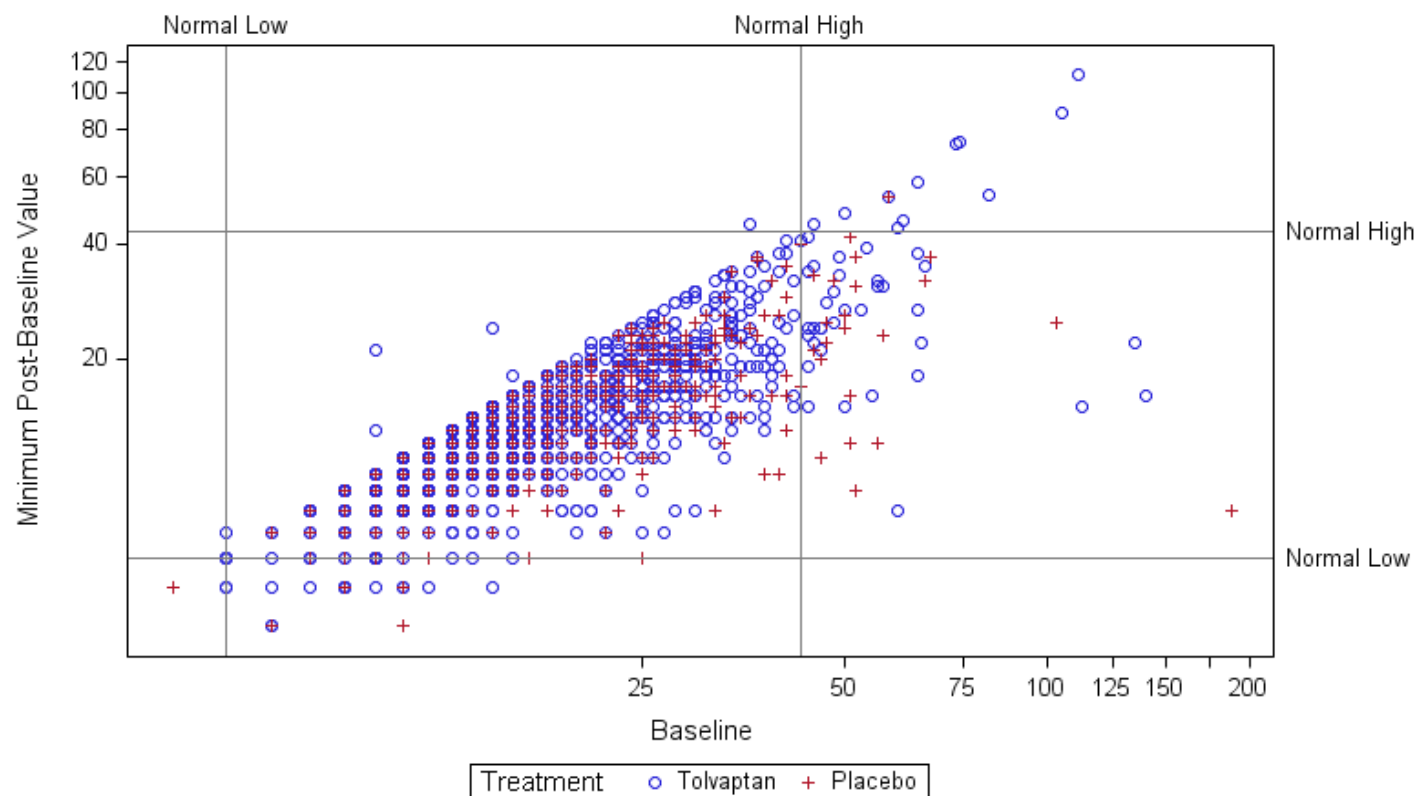
OPC41061

PROTOCOL P156-251

Figure 1.3.3

Laboratory Test: ALT (SGPT) (IU/L) Normal Range: 6-43

Baseline versus Minimum Post-Baseline Result



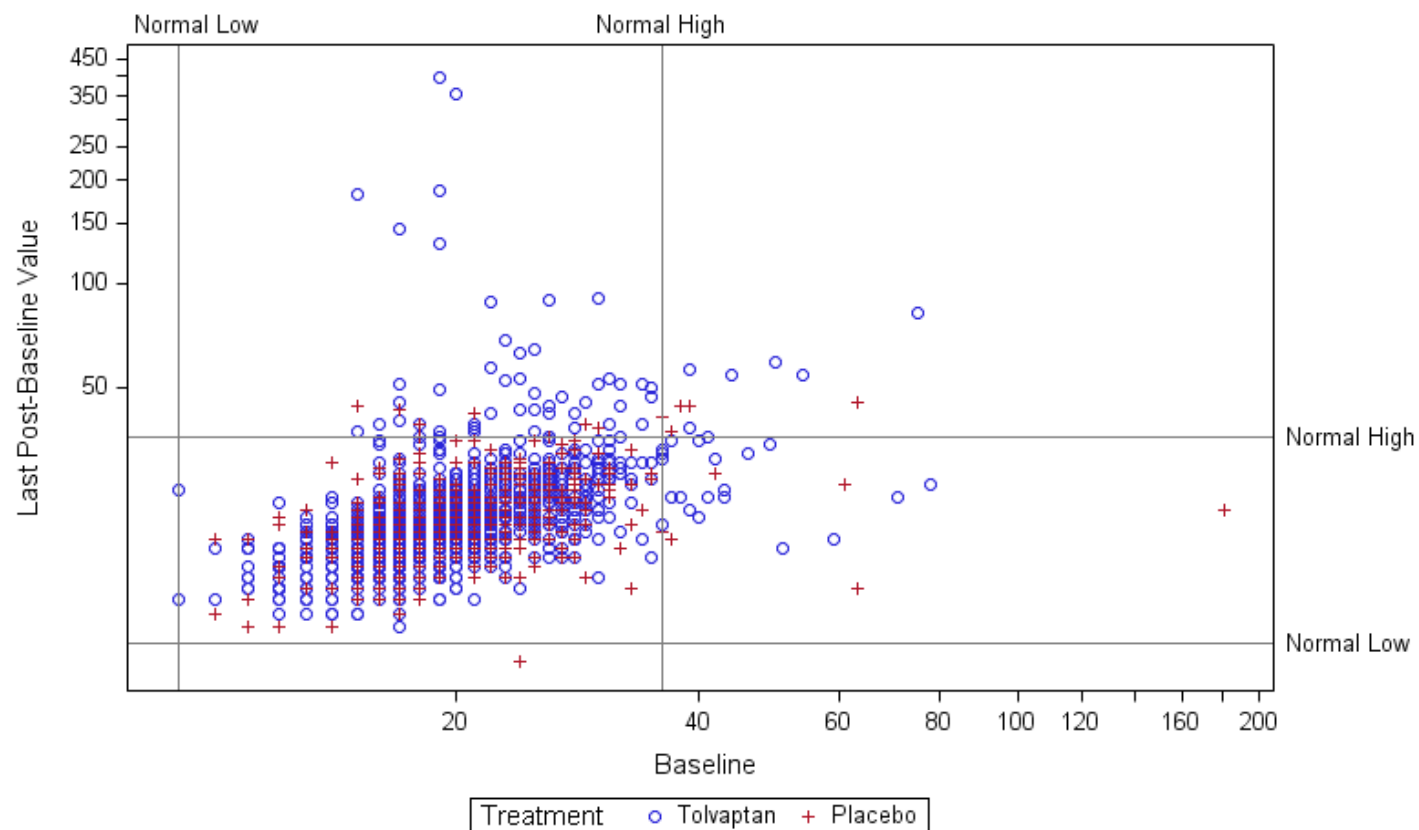
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
PROTOCOL P156-251

Figure 1.4.1
Laboratory Test: AST (SGOT) (IU/L) Normal Range: 11-36



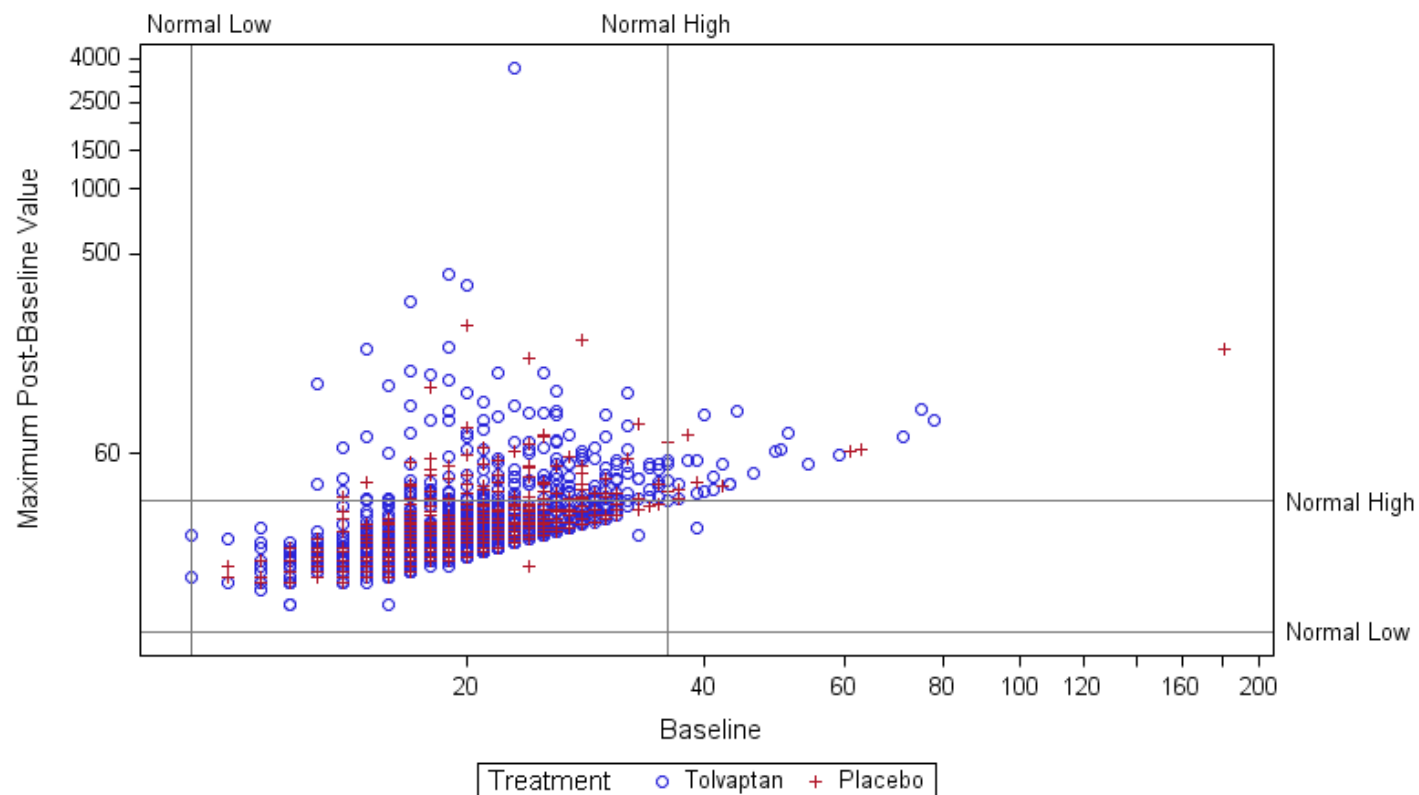
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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.4.2
 Laboratory Test: AST (SGOT) (IU/L) Normal Range: 11-36
 Baseline versus Maximum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

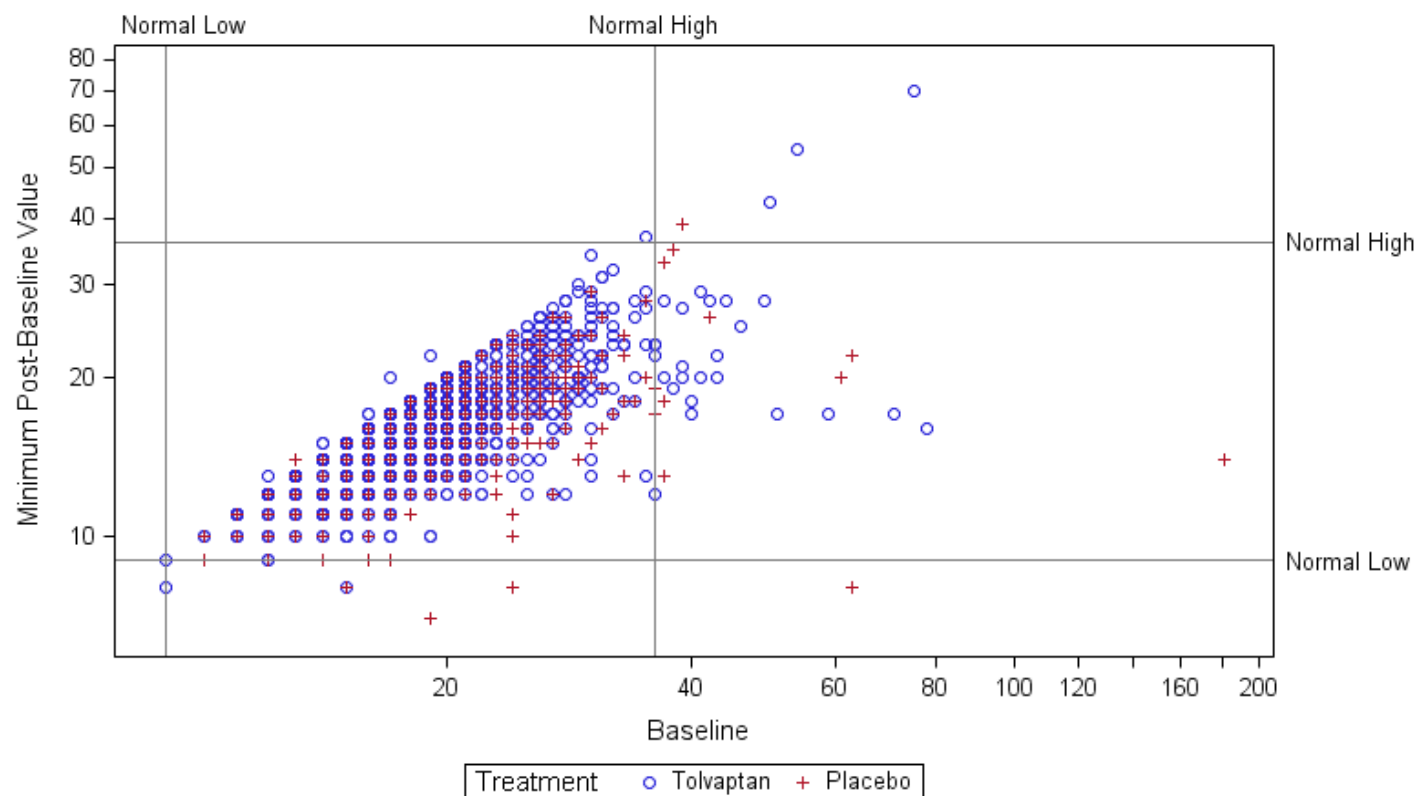
OPC41061

PROTOCOL P156-251

Figure 1.4.3

Laboratory Test: AST (SGOT) (IU/L) Normal Range: 11-36

Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEND

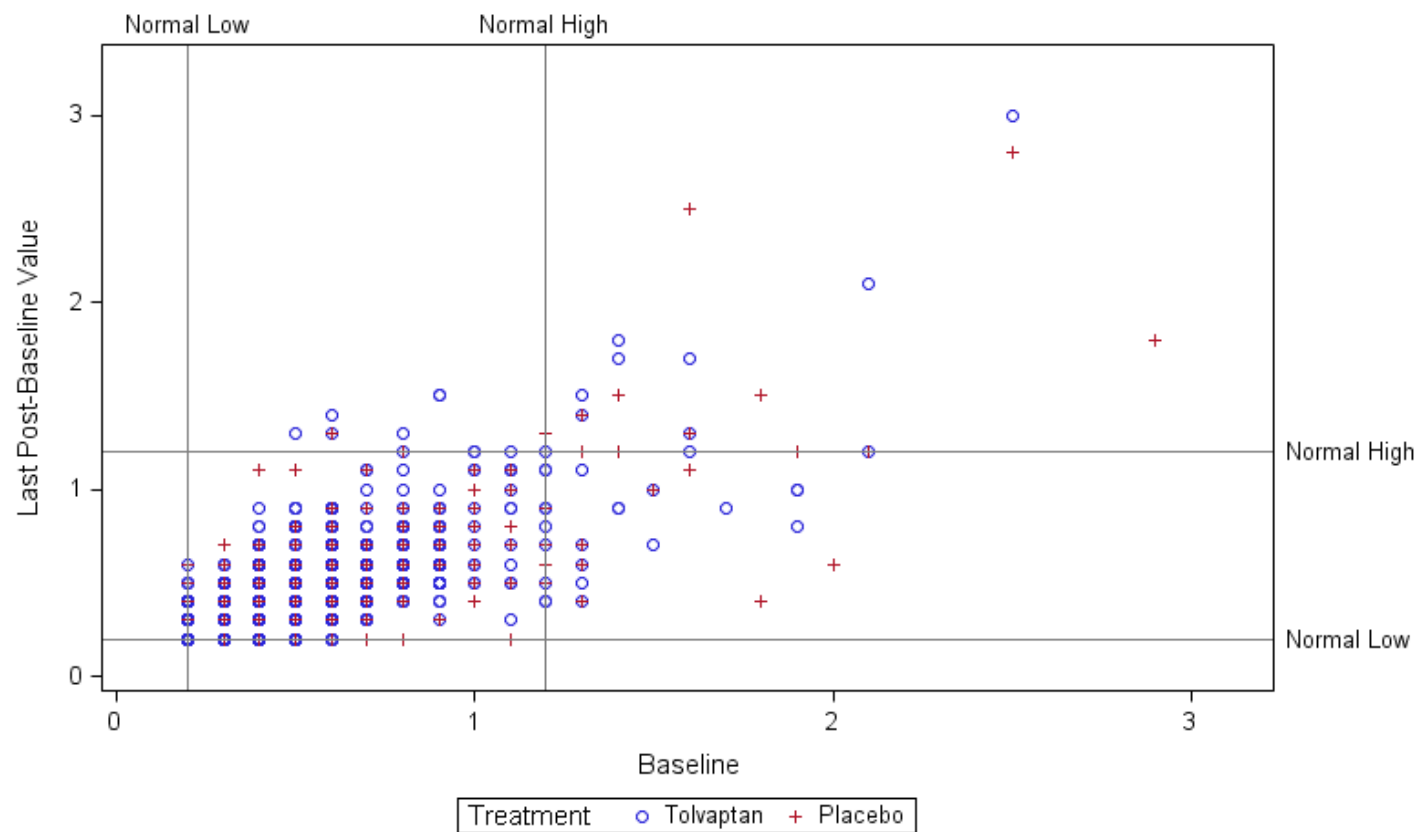
Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.5.1

Laboratory Test: BILIRUBIN, TOTAL (mg/dL) Normal Range: 0.2-1.2



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

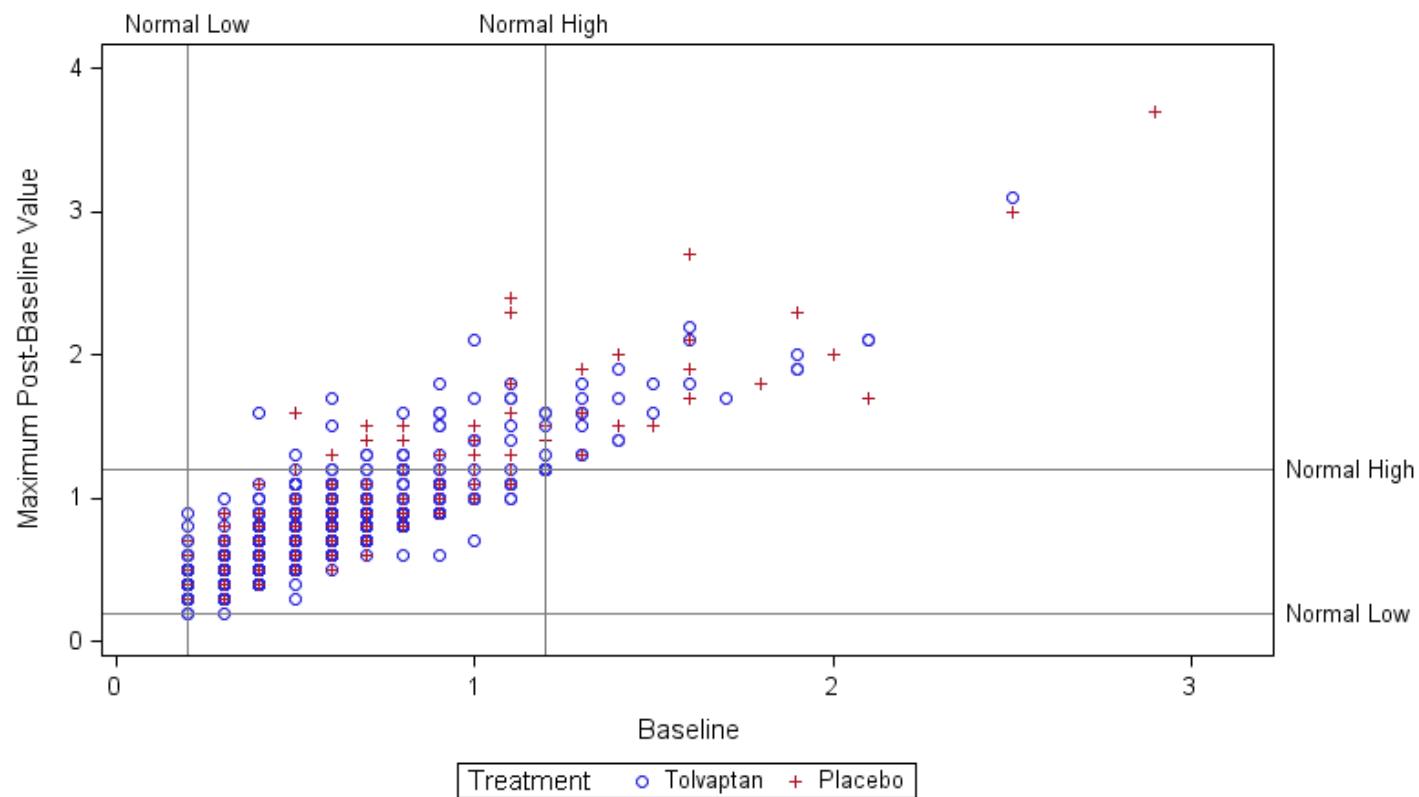
Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.5.2

Laboratory Test: BILIRUBIN, TOTAL (mg/dL) Normal Range: 0.2-1.2
 Baseline versus Maximum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

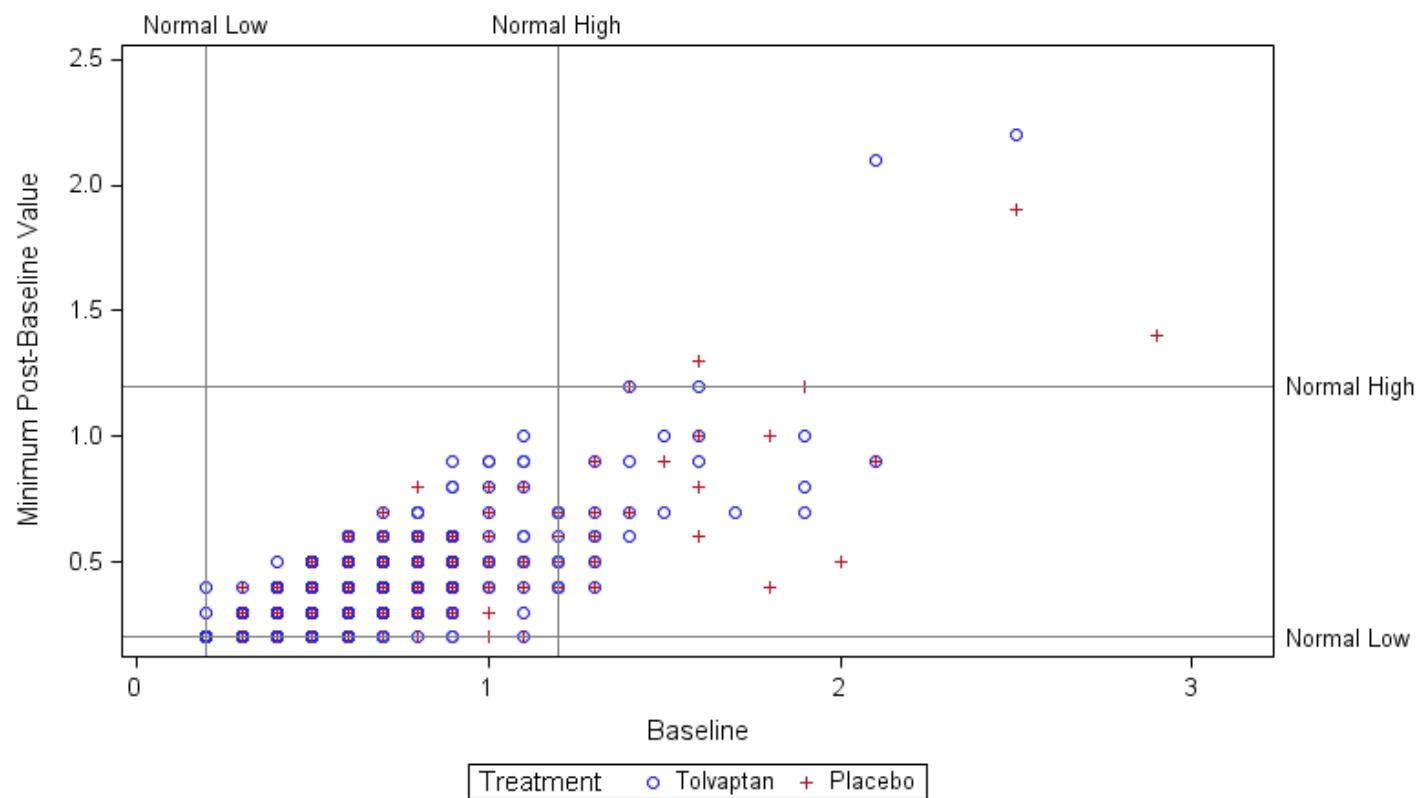
OPC41061

PROTOCOL P156-251

Figure 1.5.3

Laboratory Test: BILIRUBIN, TOTAL (mg/dL) Normal Range: 0.2-1.2

Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

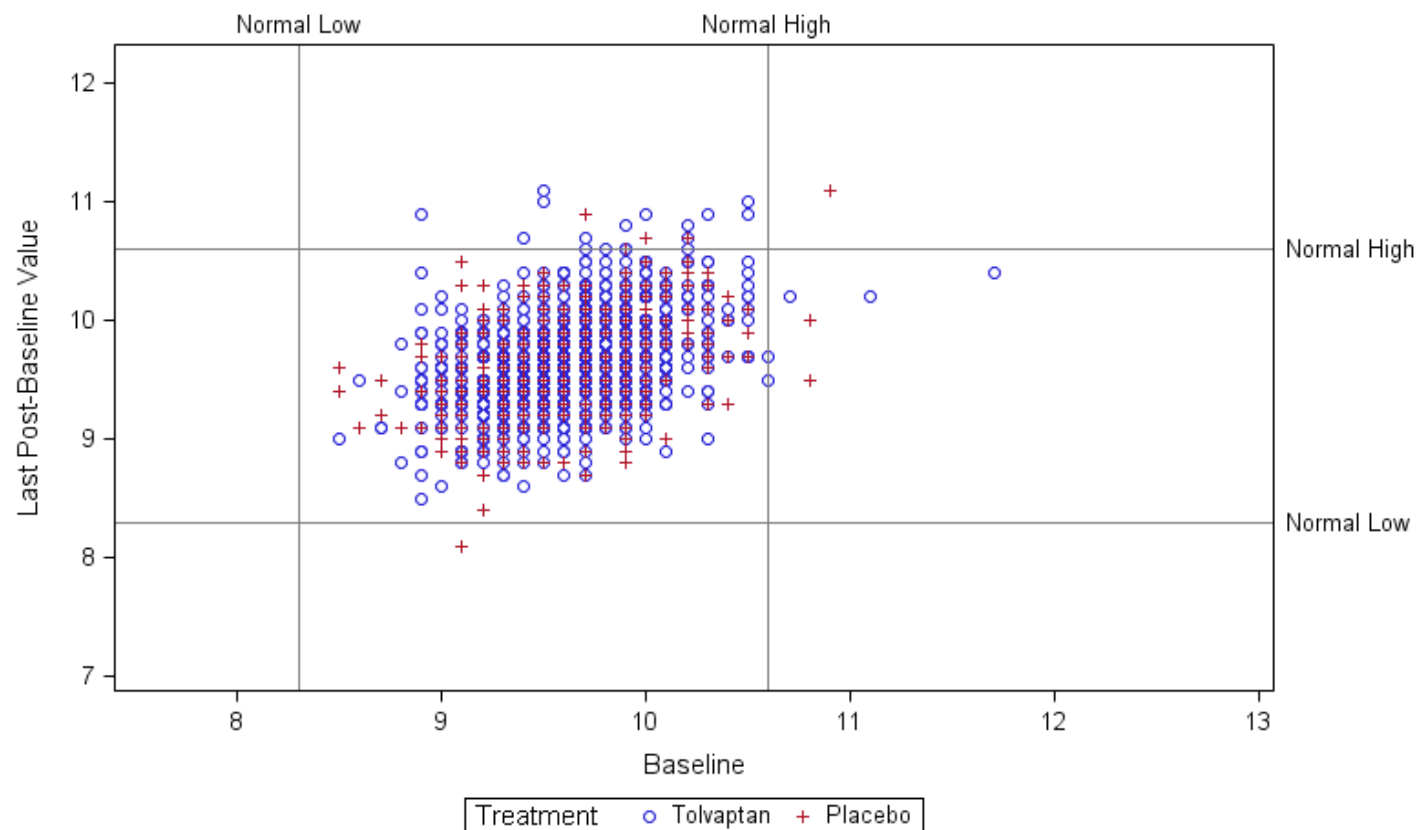
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
PROTOCOL P156-251

Figure 1.6.1

Laboratory Test: CALCIUM (mg/dL) Normal Range: 8.3-10.6



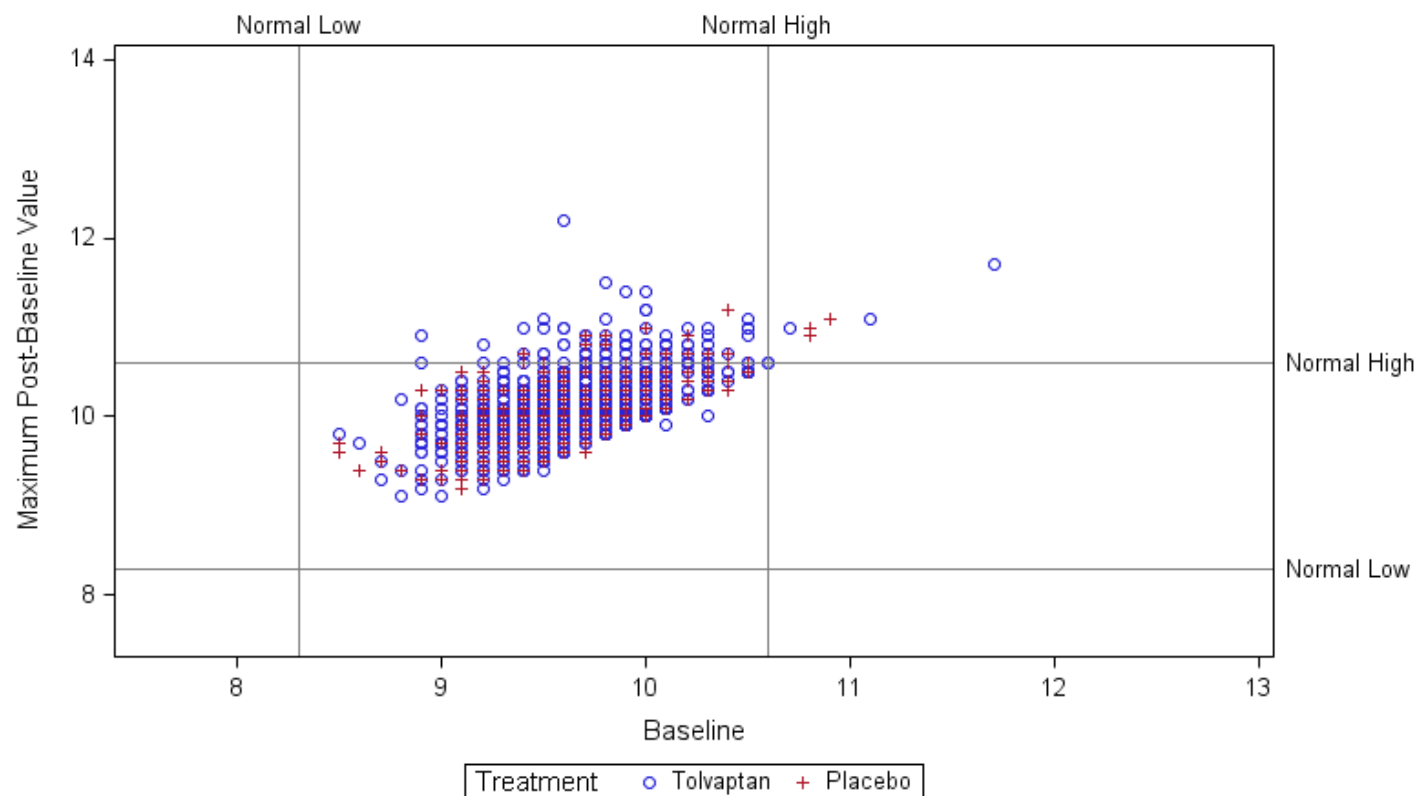
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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
PROTOCOL P156-251

Figure 1.6.2
Laboratory Test: CALCIUM (mg/dL) Normal Range: 8.3-10.6
Baseline versus Maximum Post-Baseline Result



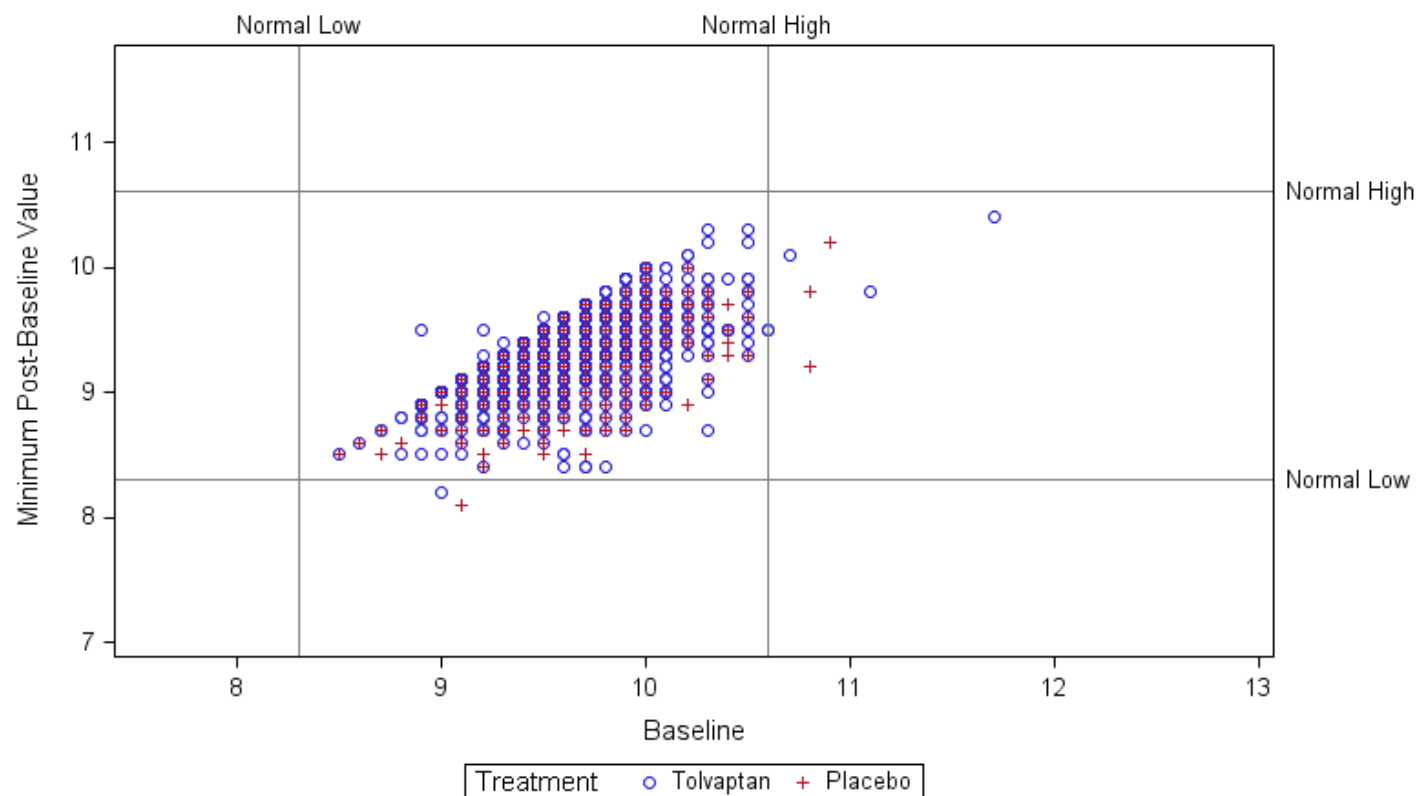
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.6.3
 Laboratory Test: CALCIUM (mg/dL) Normal Range: 8.3-10.6
 Baseline versus Minimum Post-Baseline Result



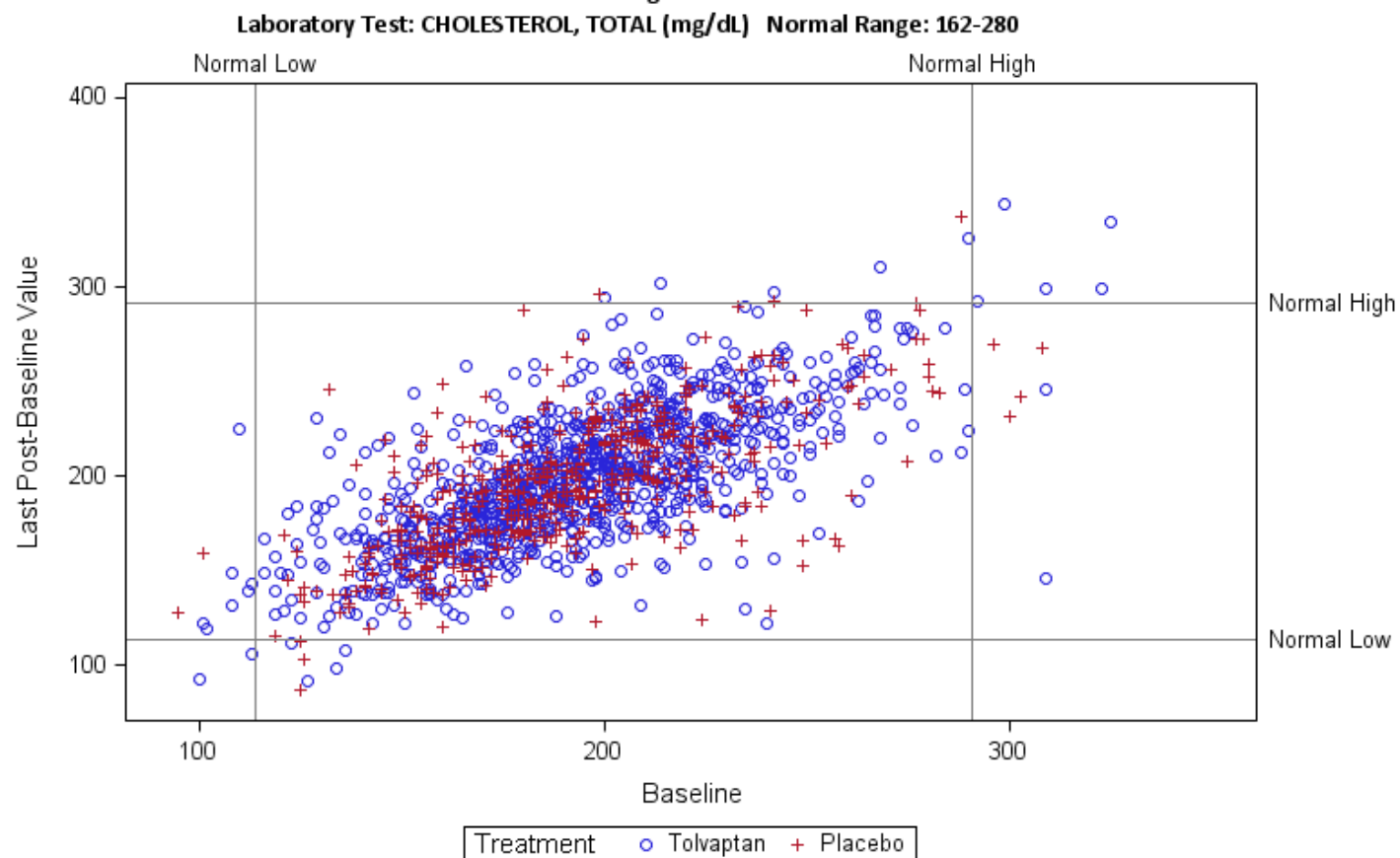
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.7.1

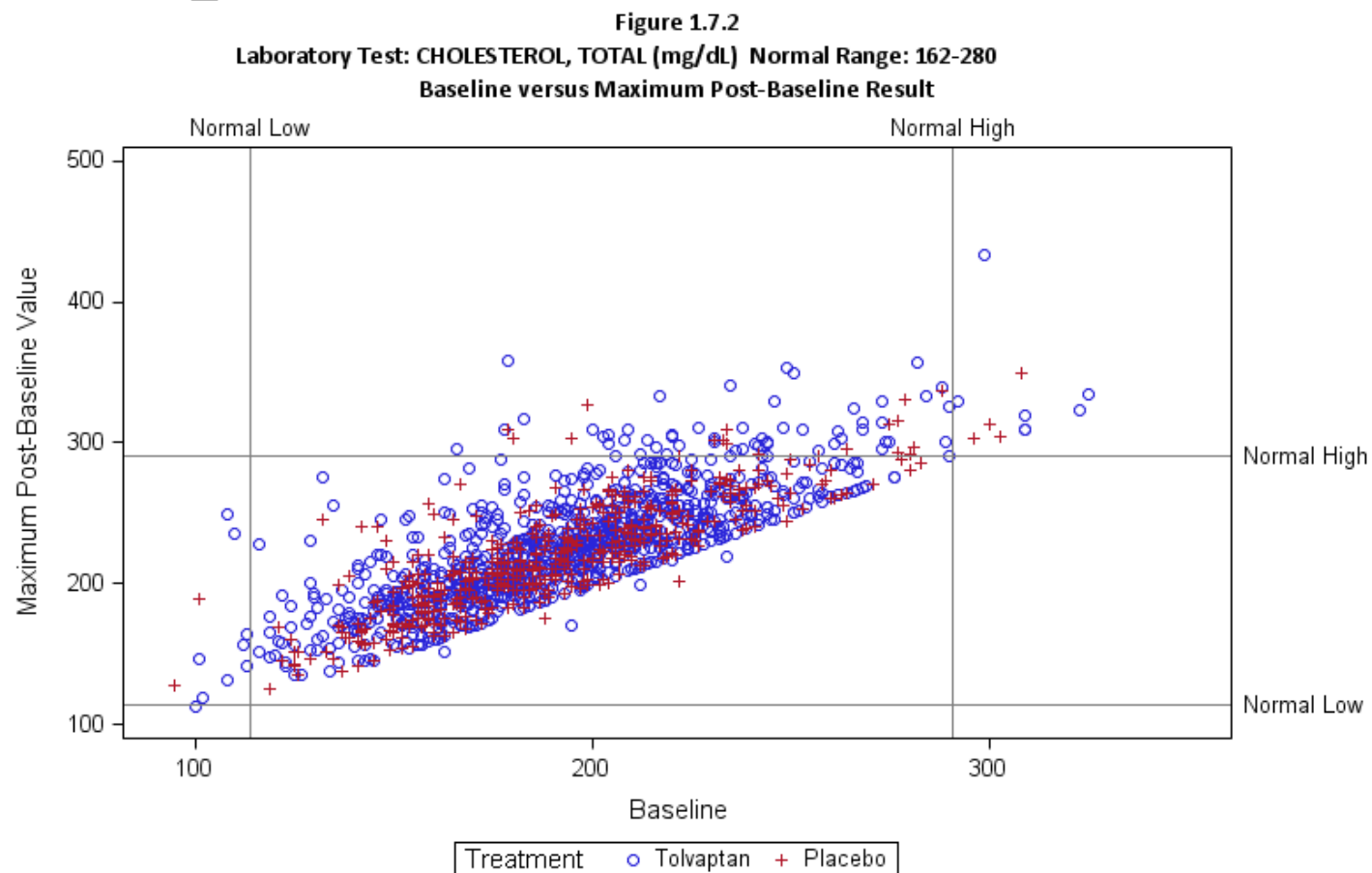


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图 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

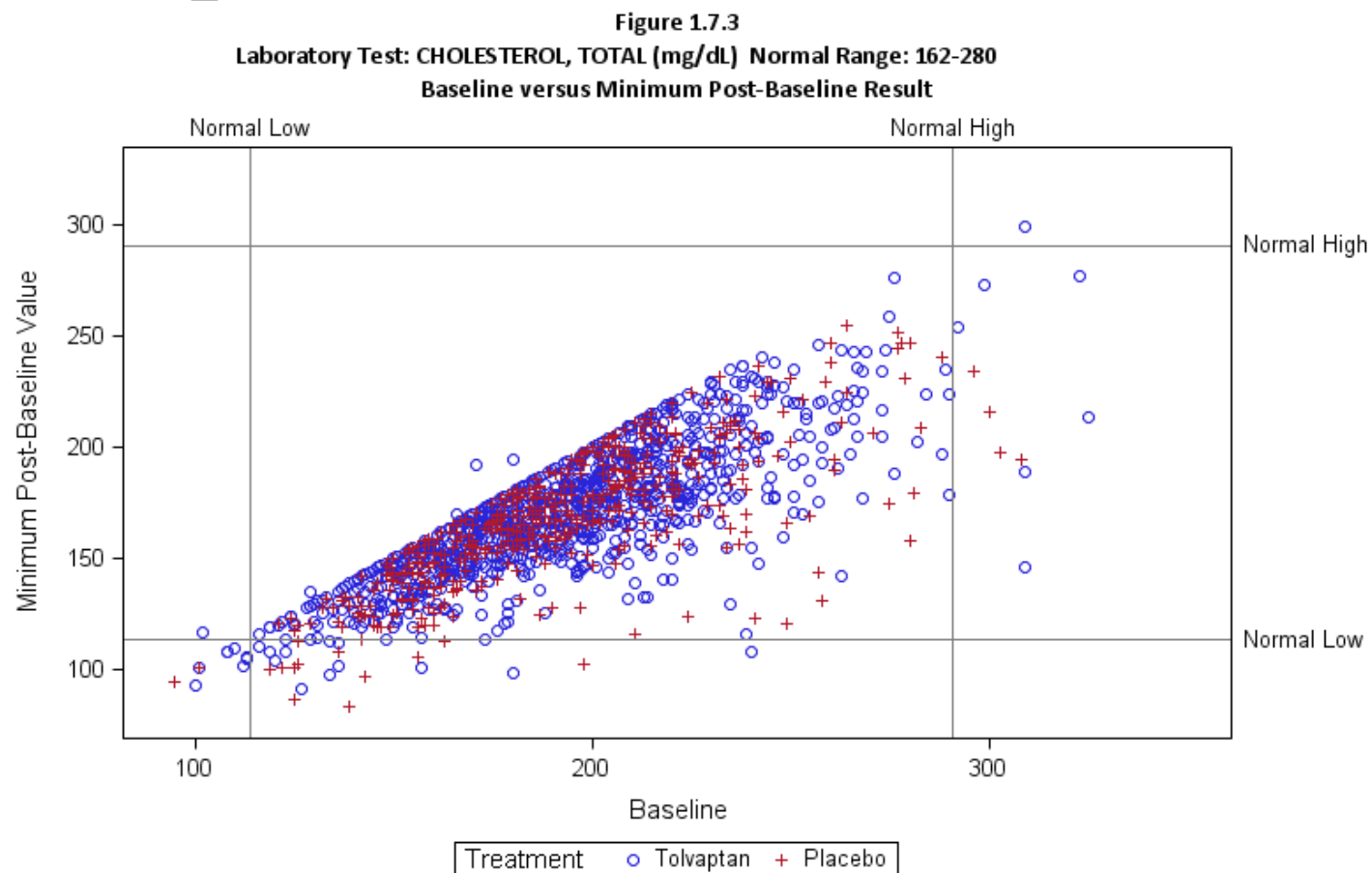
OPC41061
 PROTOCOL P156-251



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0
 Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

图 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251



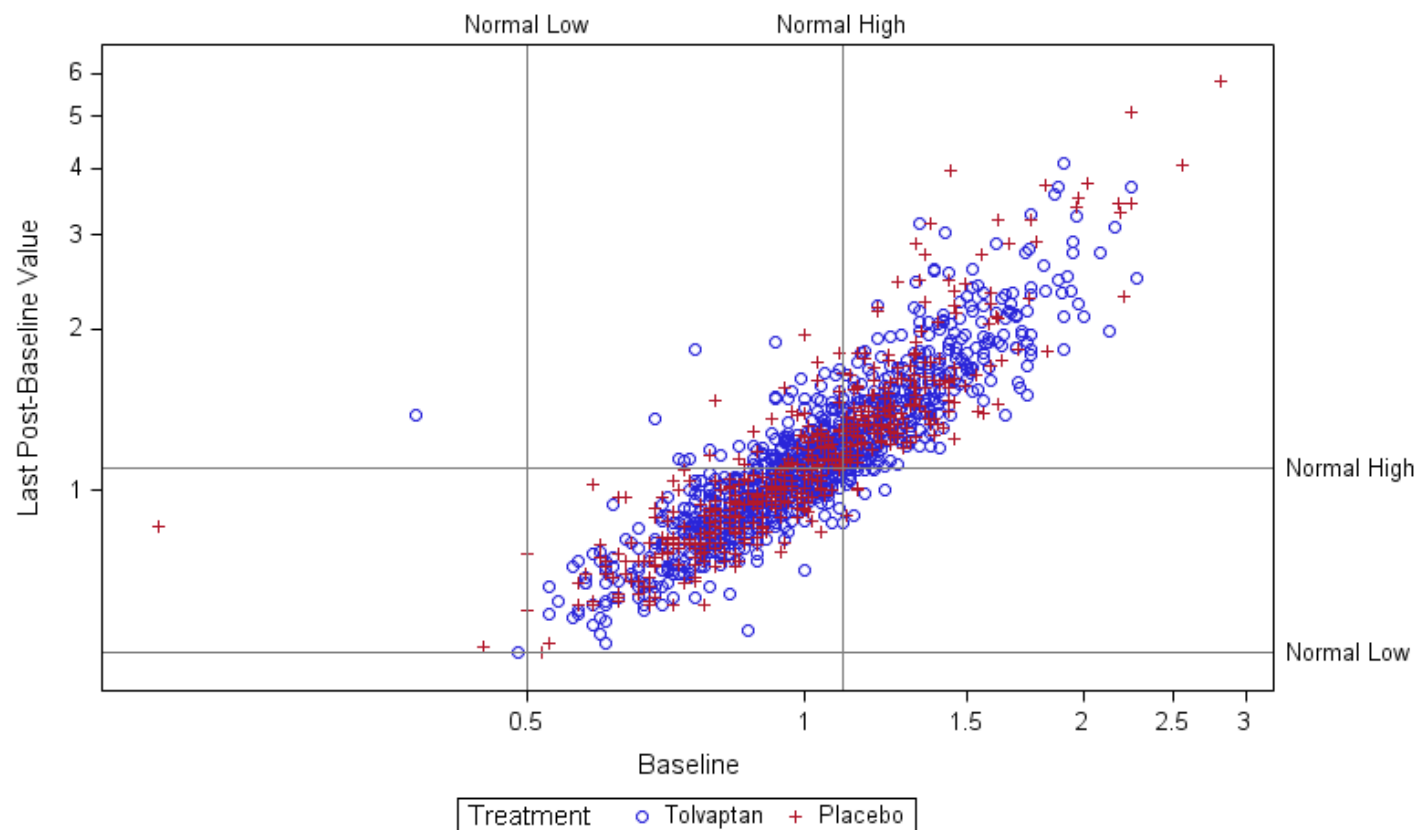
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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.8.1
 Laboratory Test: CREATININE (mg/dL) Normal Range: 0.5-1.1

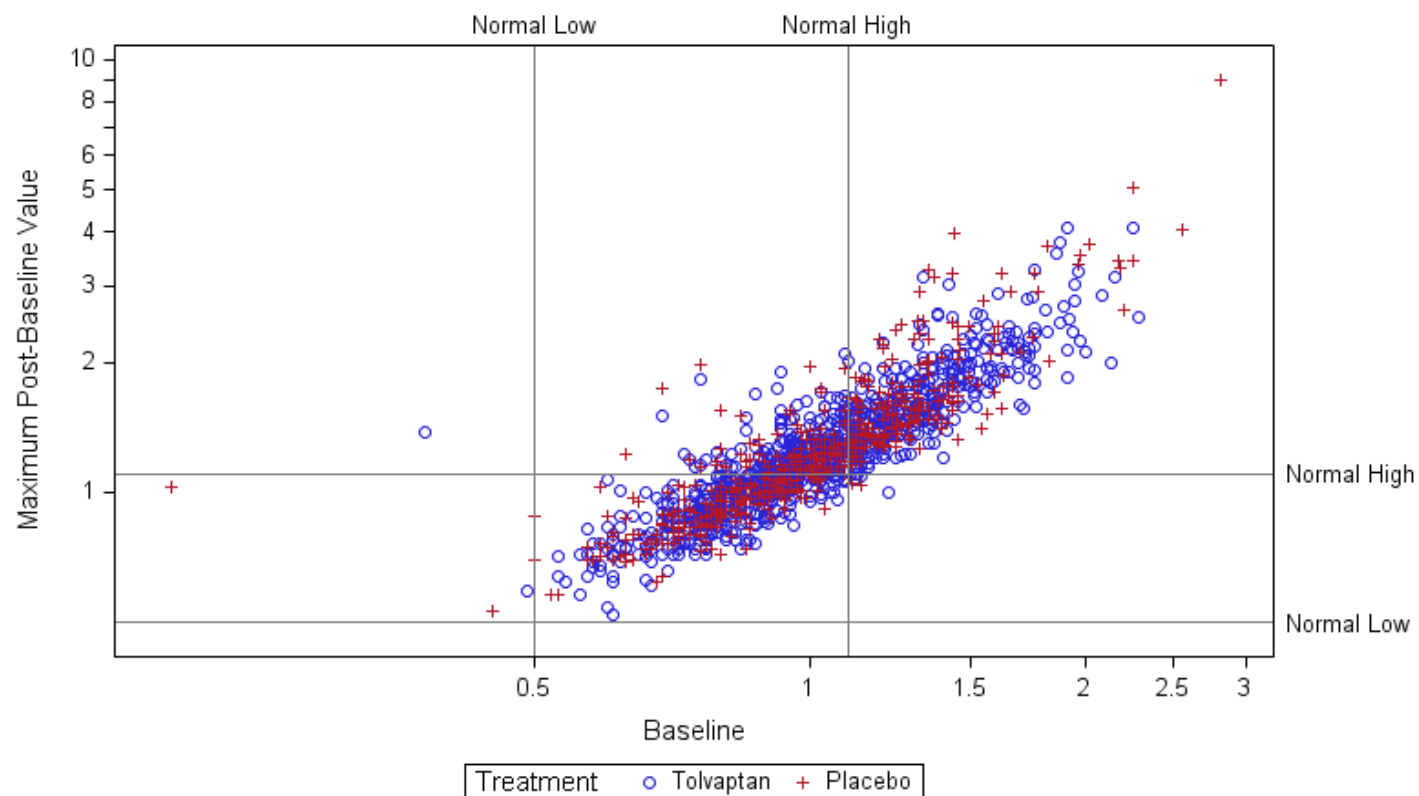


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 Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.8.2
 Laboratory Test: CREATININE (mg/dL) Normal Range: 0.5-1.1
 Baseline versus Maximum Post-Baseline Result

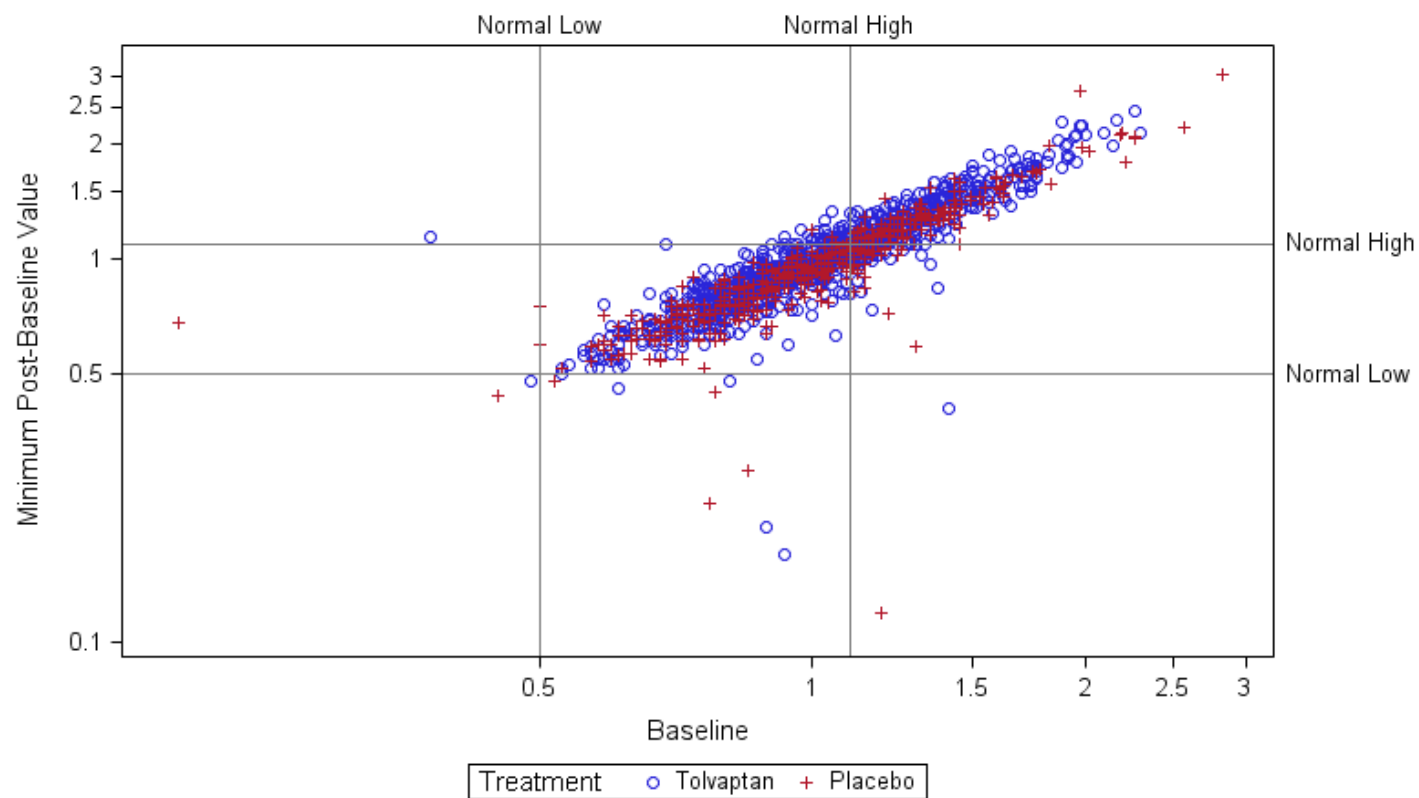


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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
PROTOCOL P156-251

Figure 1.8.3
Laboratory Test: CREATININE (mg/dL) Normal Range: 0.5-1.1
Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

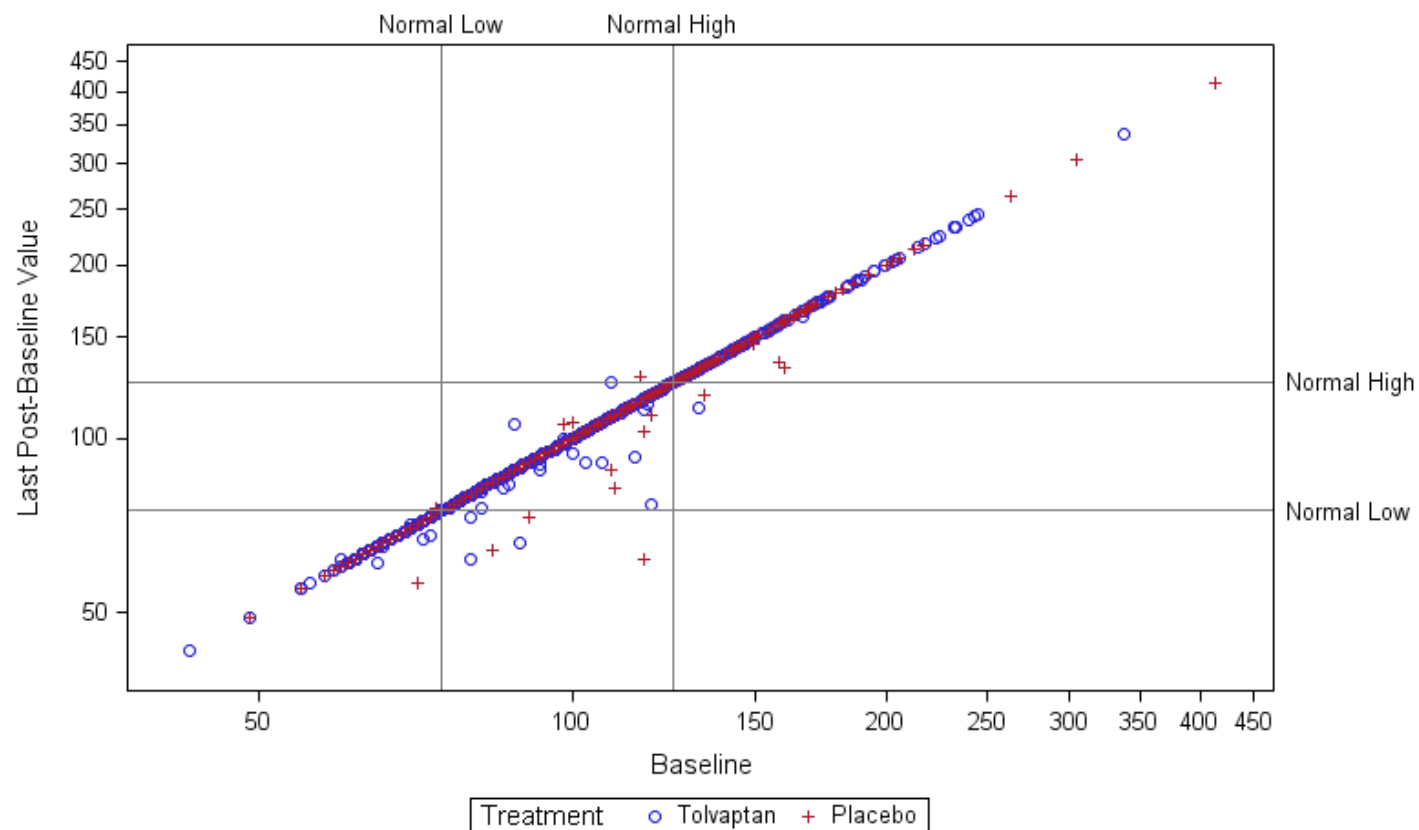
2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061

PROTOCOL P156-251

Figure 1.9.1

Laboratory Test: CREATININE CLEARANCE (ml/min) Normal Range: 85-125



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

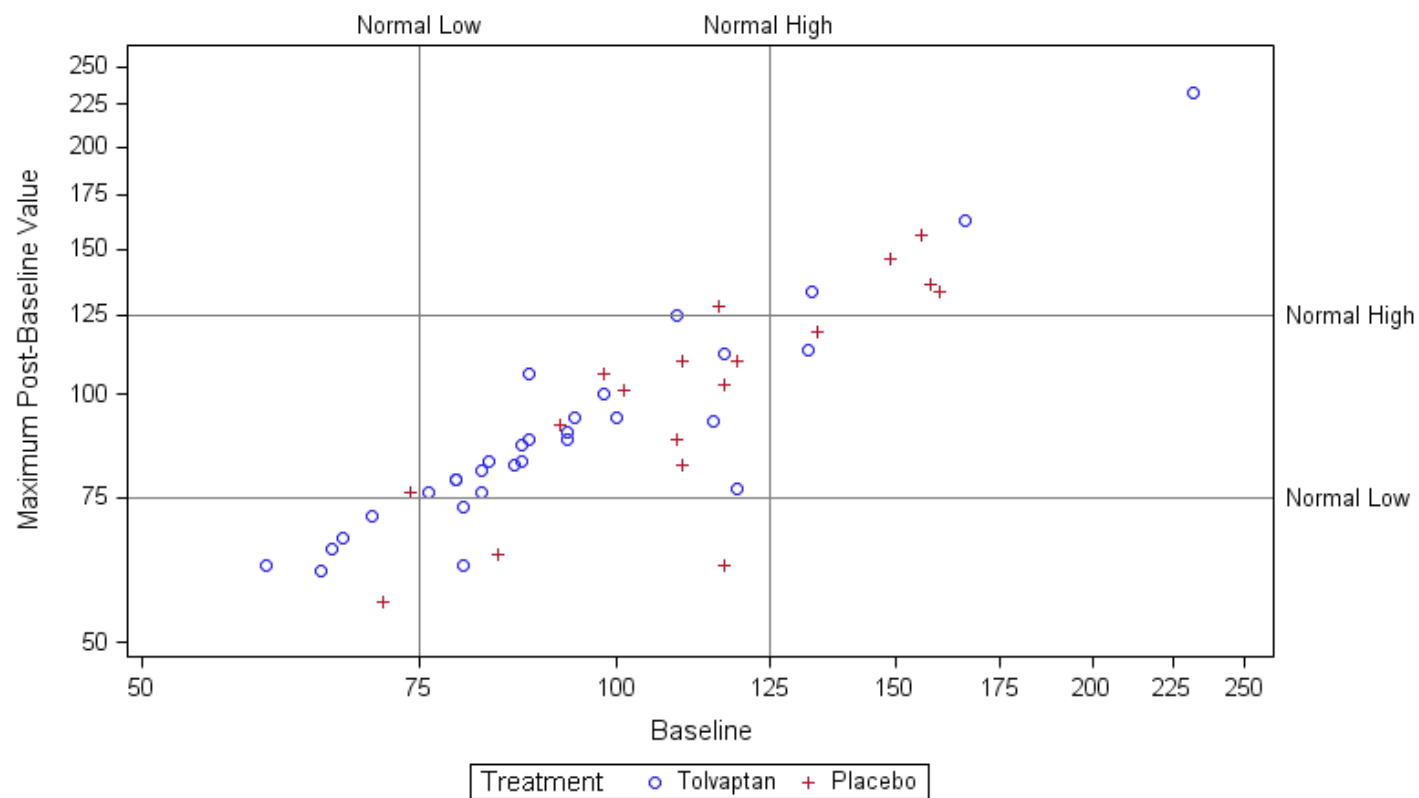
OPC41061

PROTOCOL P156-251

Figure 1.9.2

Laboratory Test: CREATININE CLEARANCE (ml/min) Normal Range: 75-115

Baseline versus Maximum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

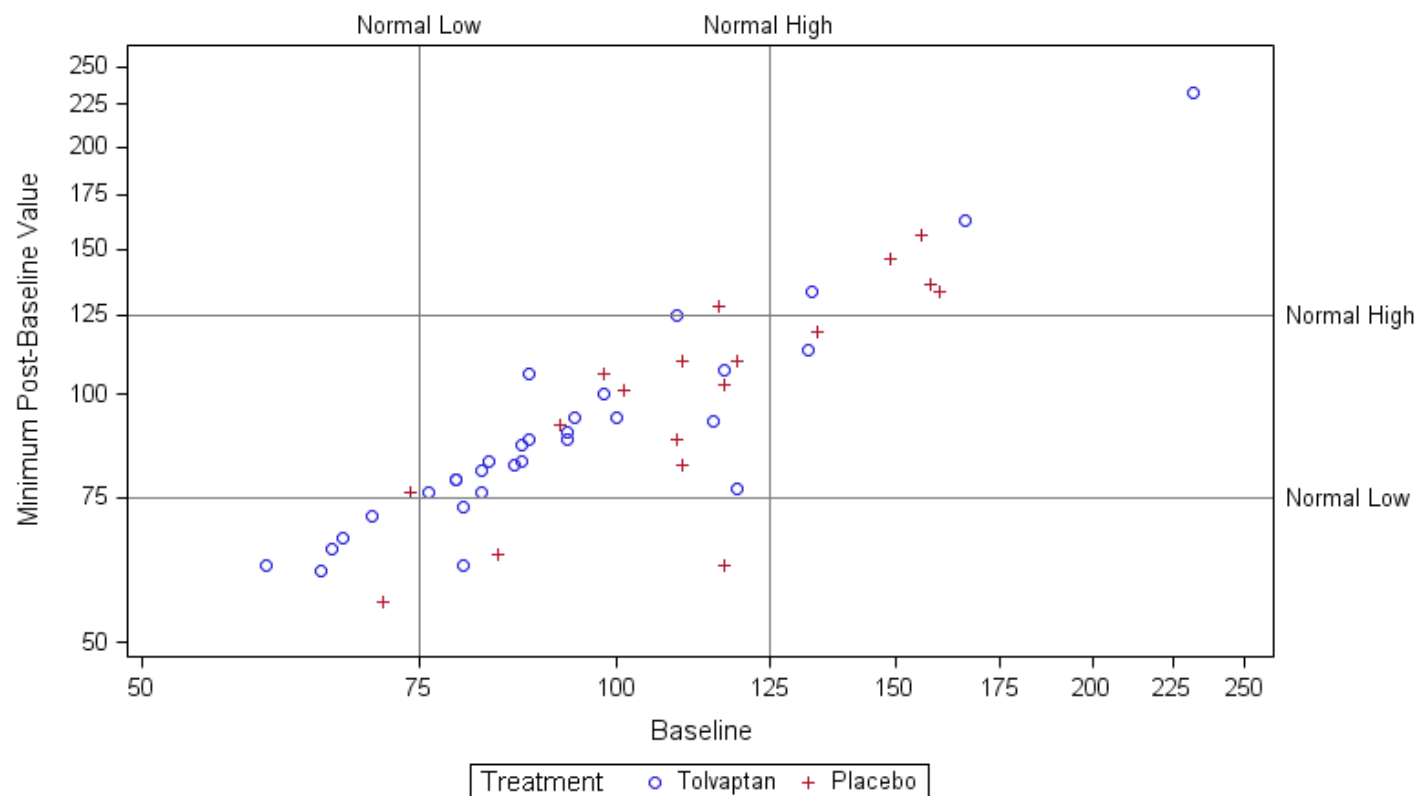
OPC41061

PROTOCOL P156-251

Figure 1.9.3

Laboratory Test: CREATININE CLEARANCE (ml/min) Normal Range: 75-115

Baseline versus Minimum Post-Baseline Result

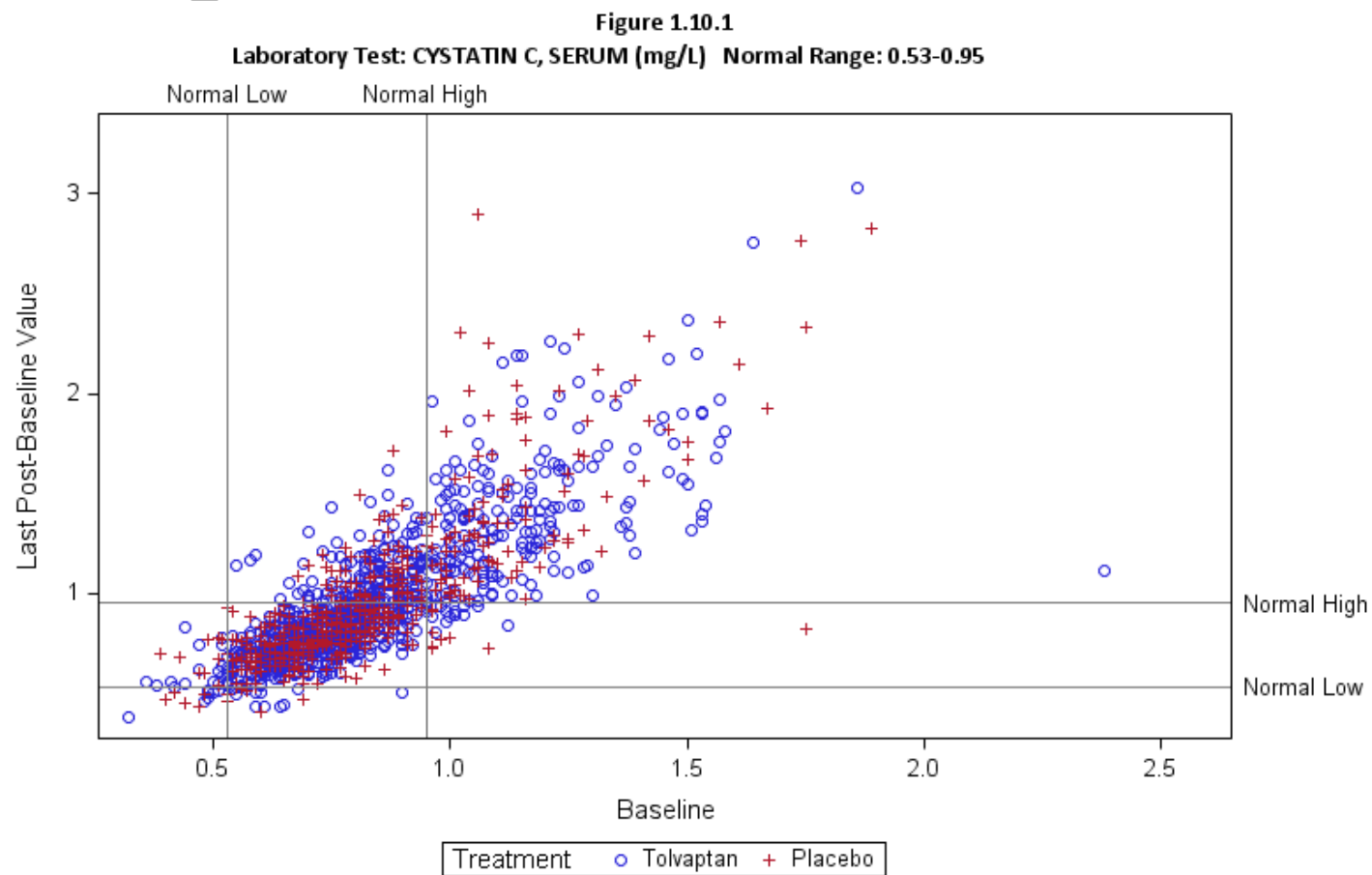


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

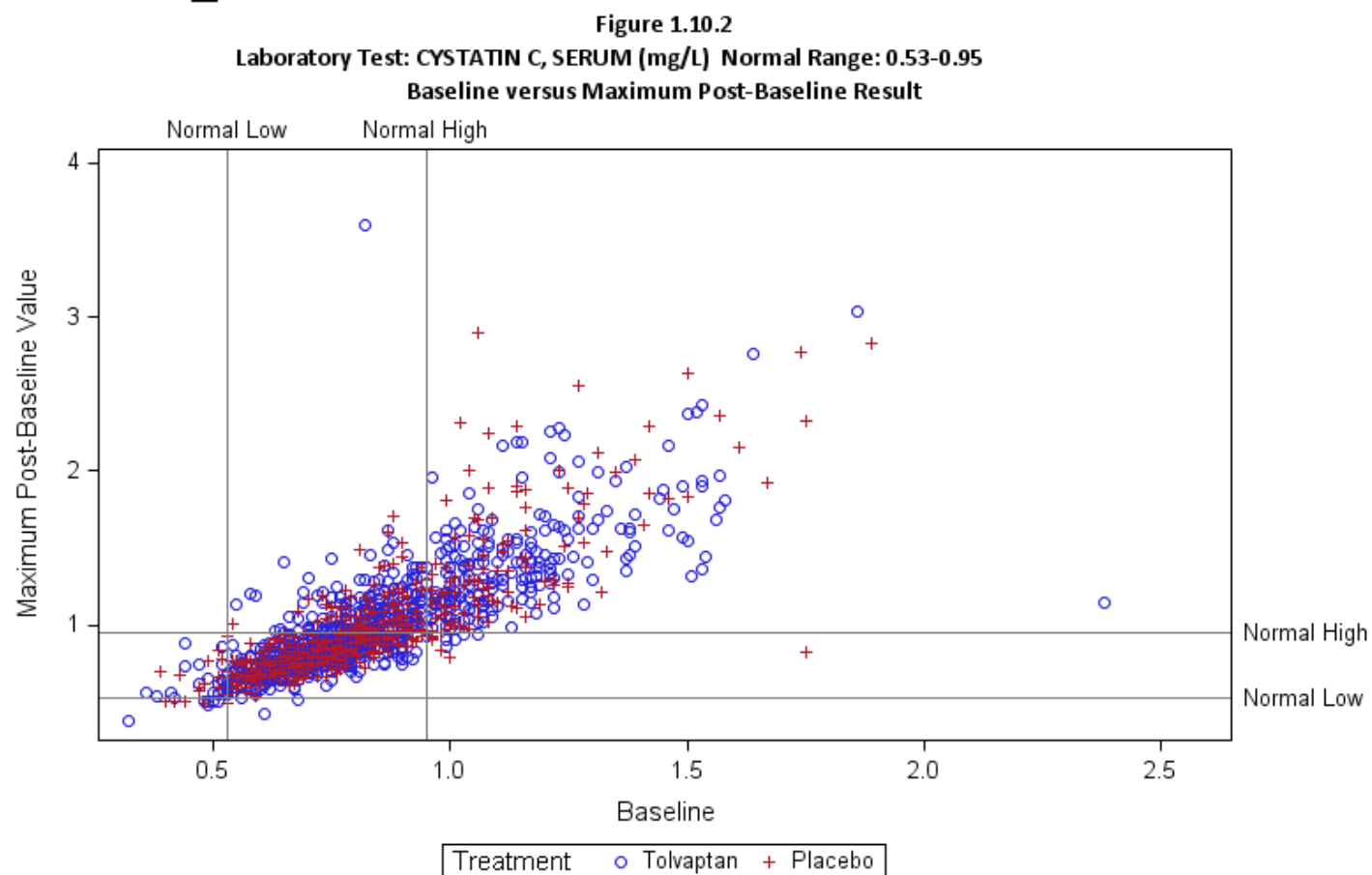


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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

☒ 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

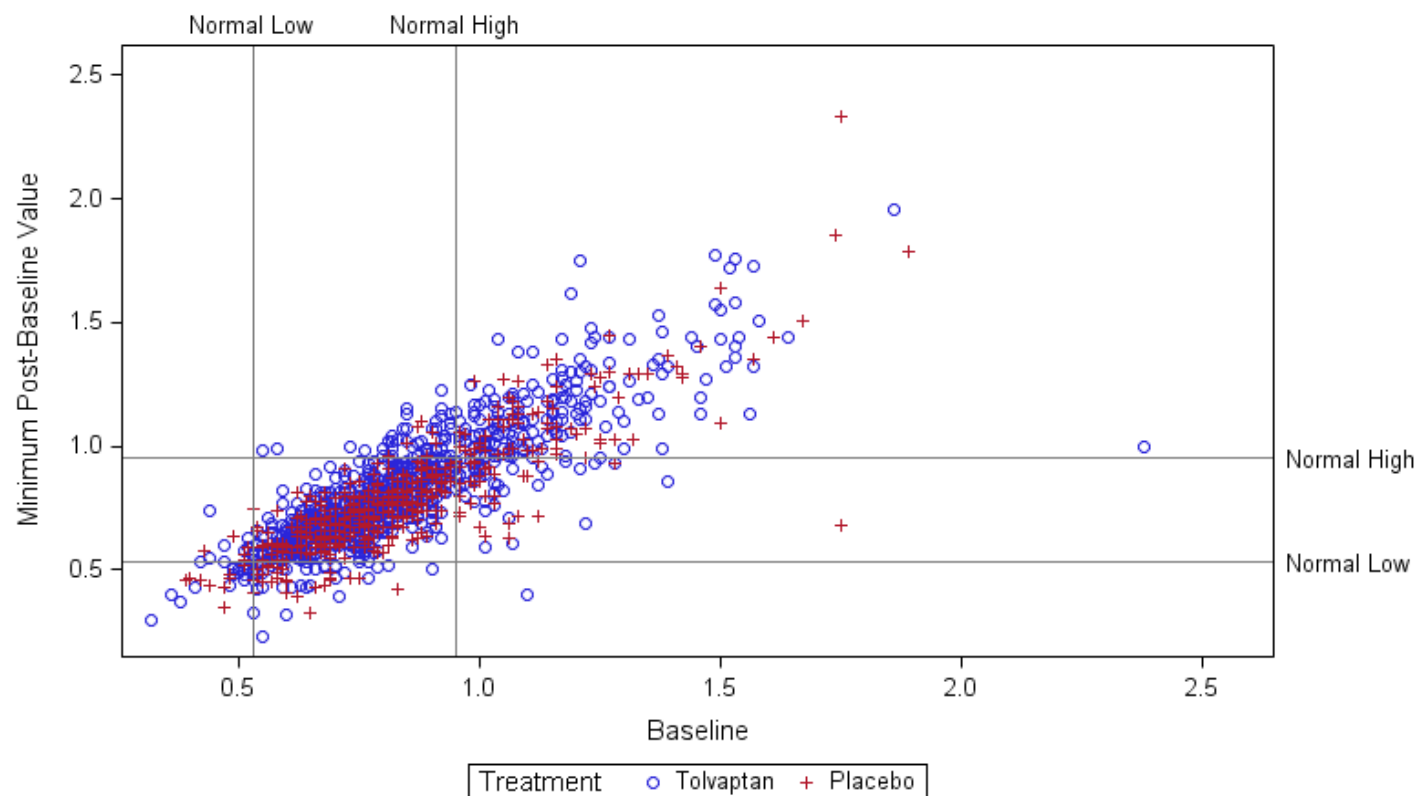
OPC41061

PROTOCOL P156-251

Figure 1.10.3

Laboratory Test: CYSTATIN C, SERUM (mg/L) Normal Range: 0.53-0.95

Baseline versus Minimum Post-Baseline Result

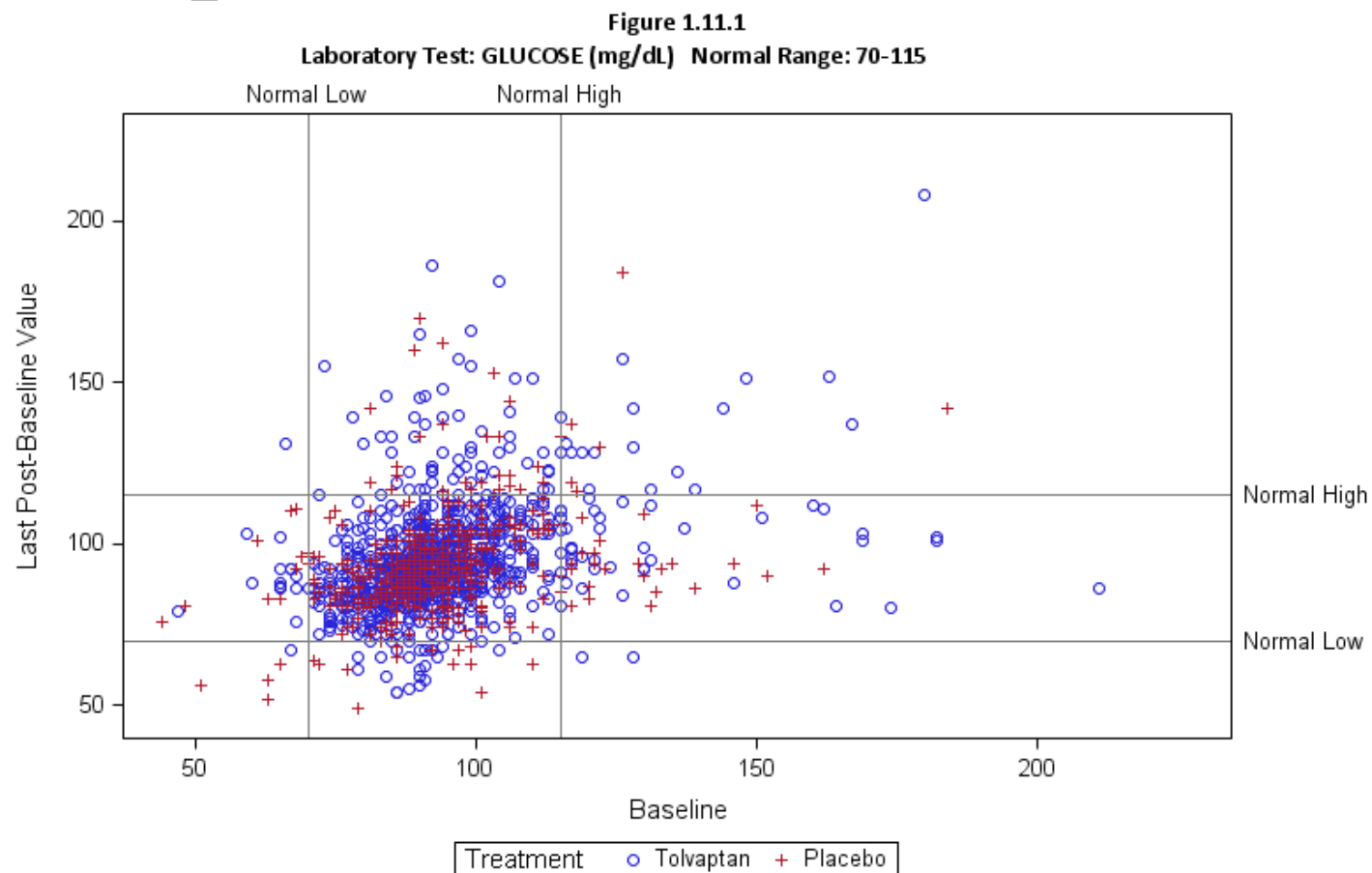


Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251



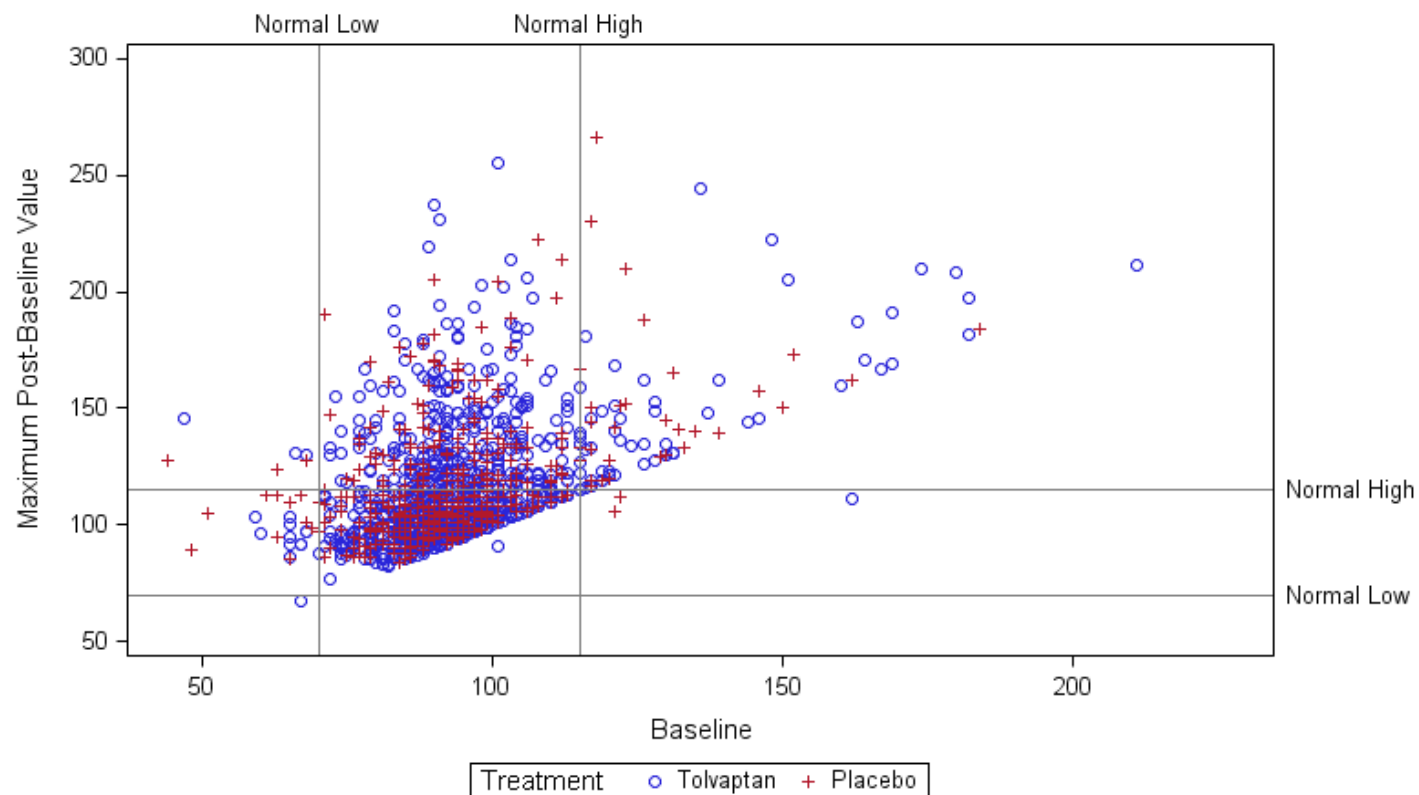
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.11.2
 Laboratory Test: GLUCOSE (mg/dL) Normal Range: 70-115
 Baseline versus Maximum Post-Baseline Result



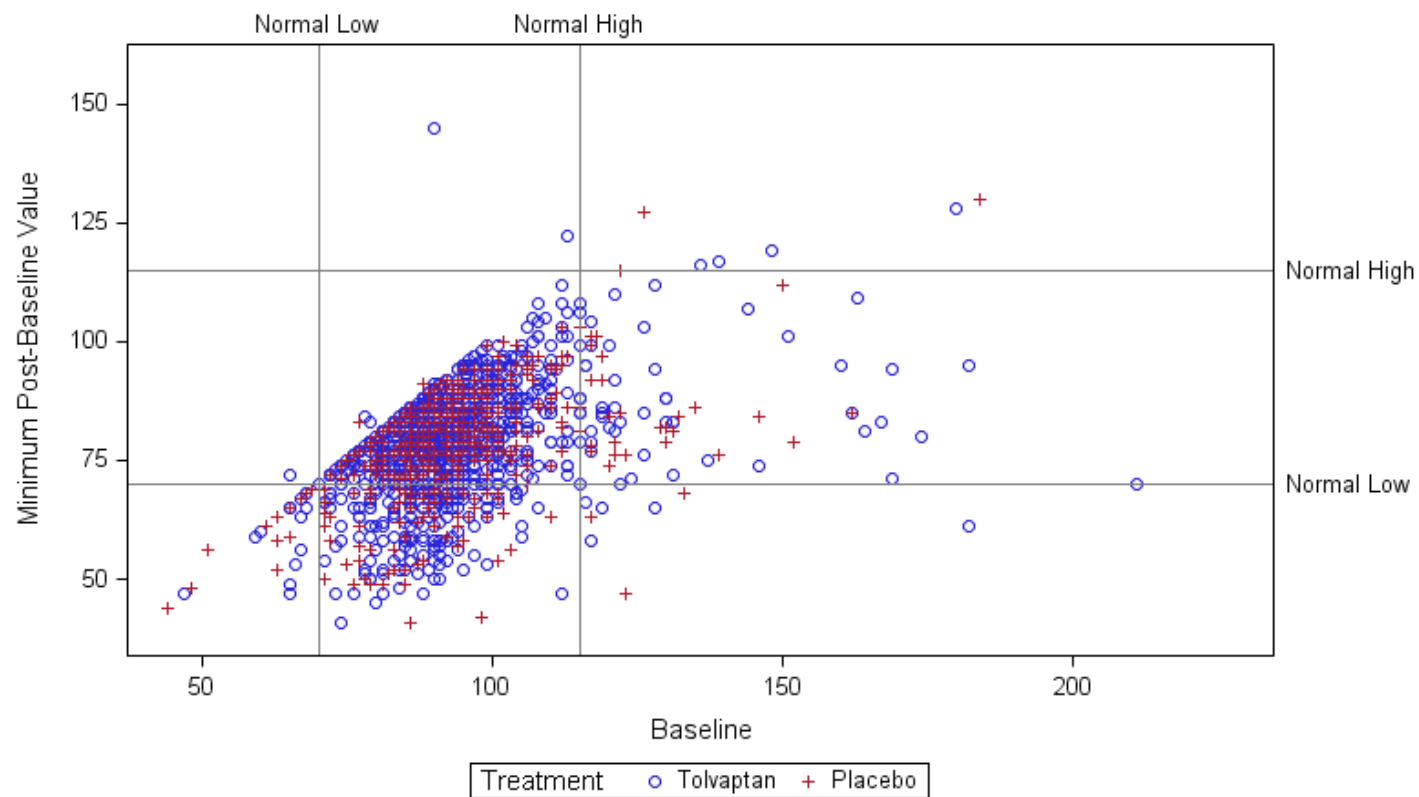
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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.11.3
 Laboratory Test: GLUCOSE (mg/dL) Normal Range: 70-115
 Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

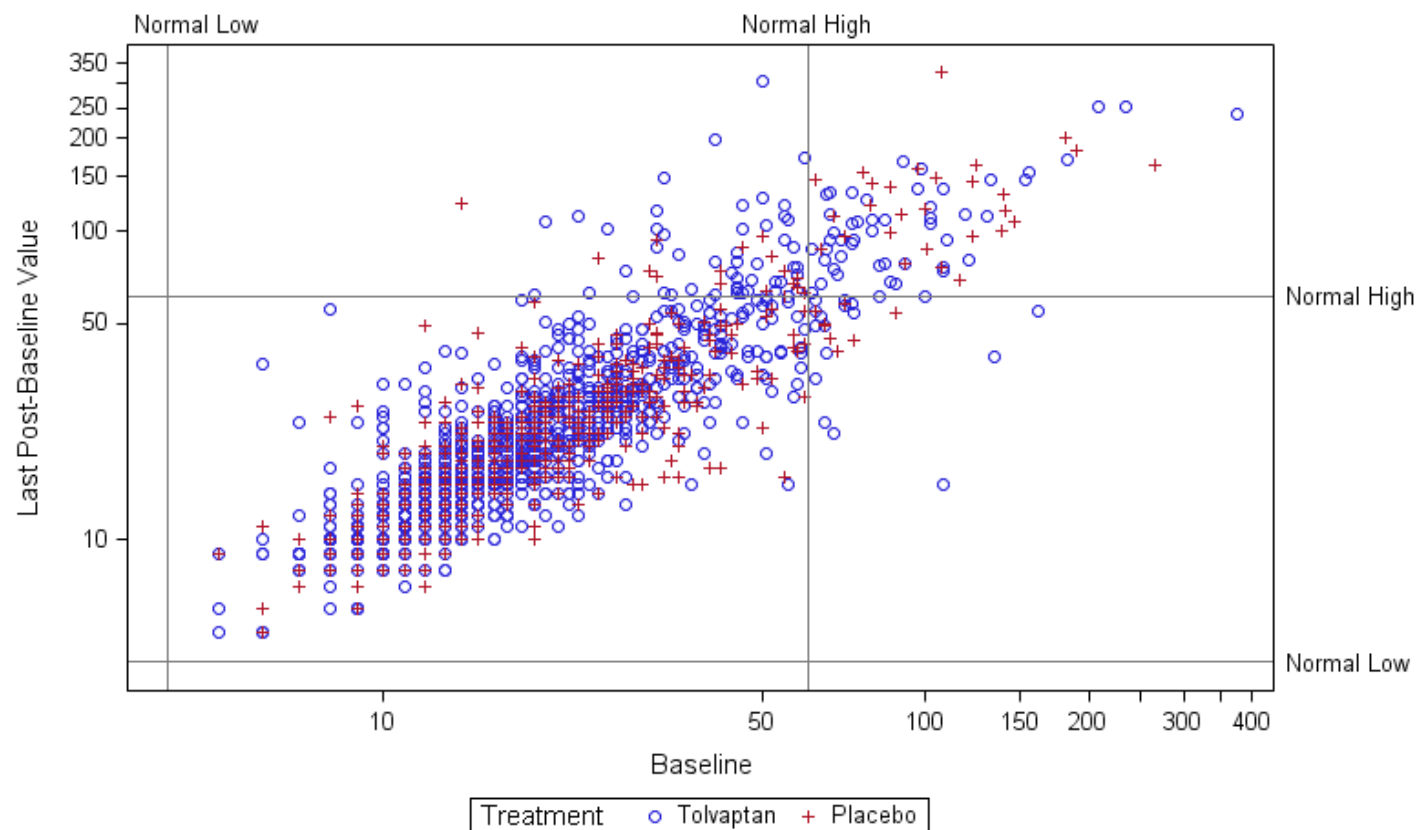
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.12.1

Laboratory Test: GLUTAMYL TRANSFERASE (IU/L) Normal Range: 10-61



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

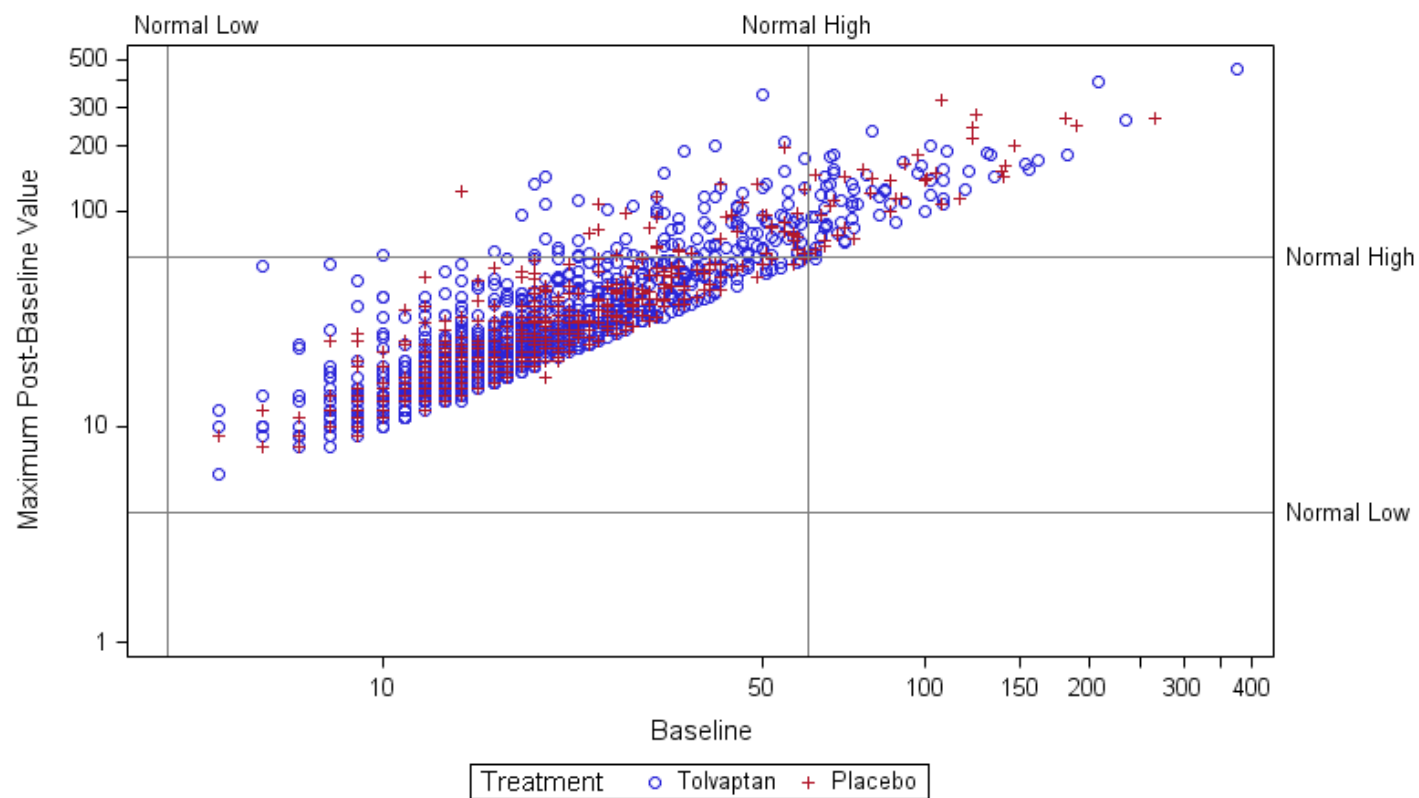
OPC41061

PROTOCOL P156-251

Figure 1.12.2

Laboratory Test: GLUTAMYL TRANSFERASE (IU/L) Normal Range: 10-61

Baseline versus Maximum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

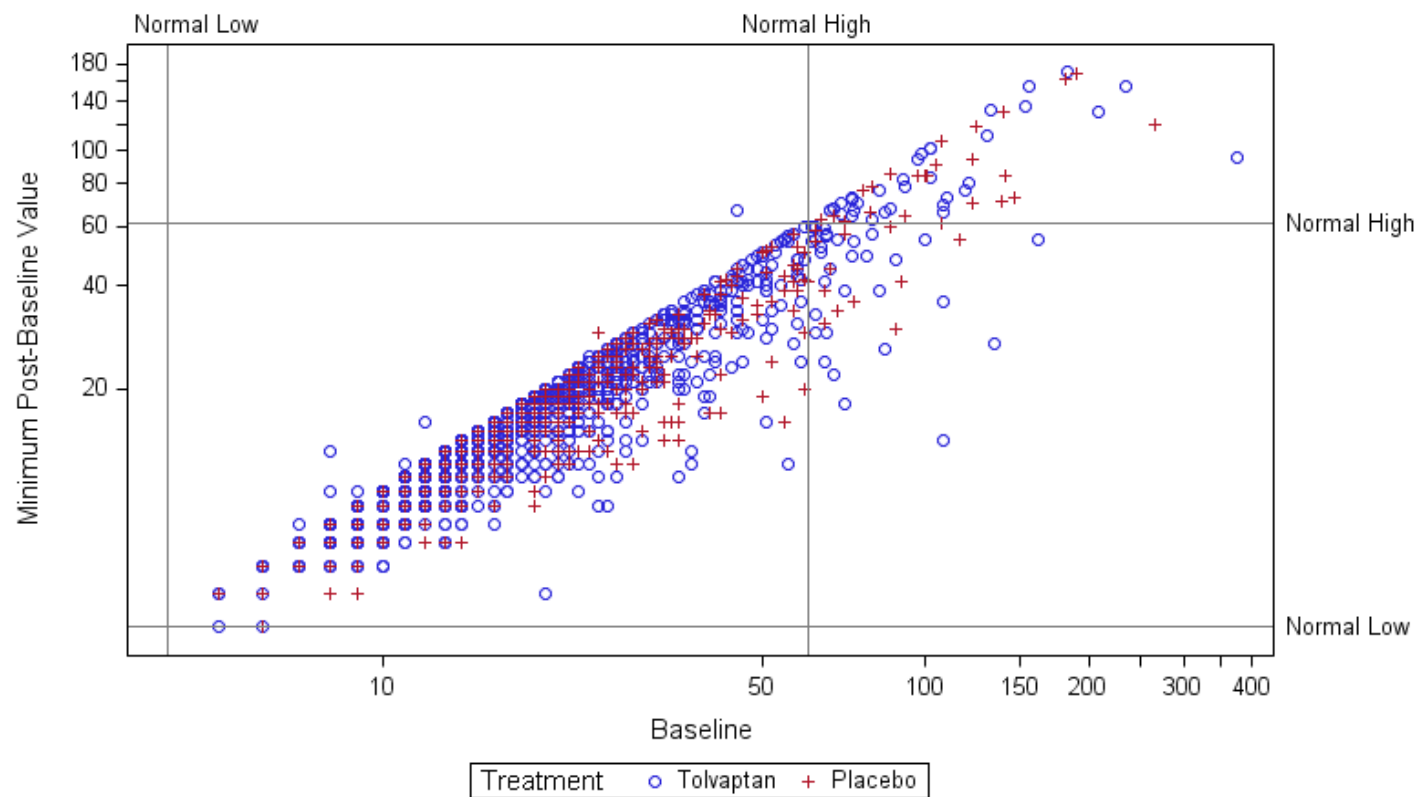
OPC41061

PROTOCOL P156-251

Figure 1.12.3

Laboratory Test: GLUTAMYL TRANSFERASE (IU/L) Normal Range: 10-61

Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

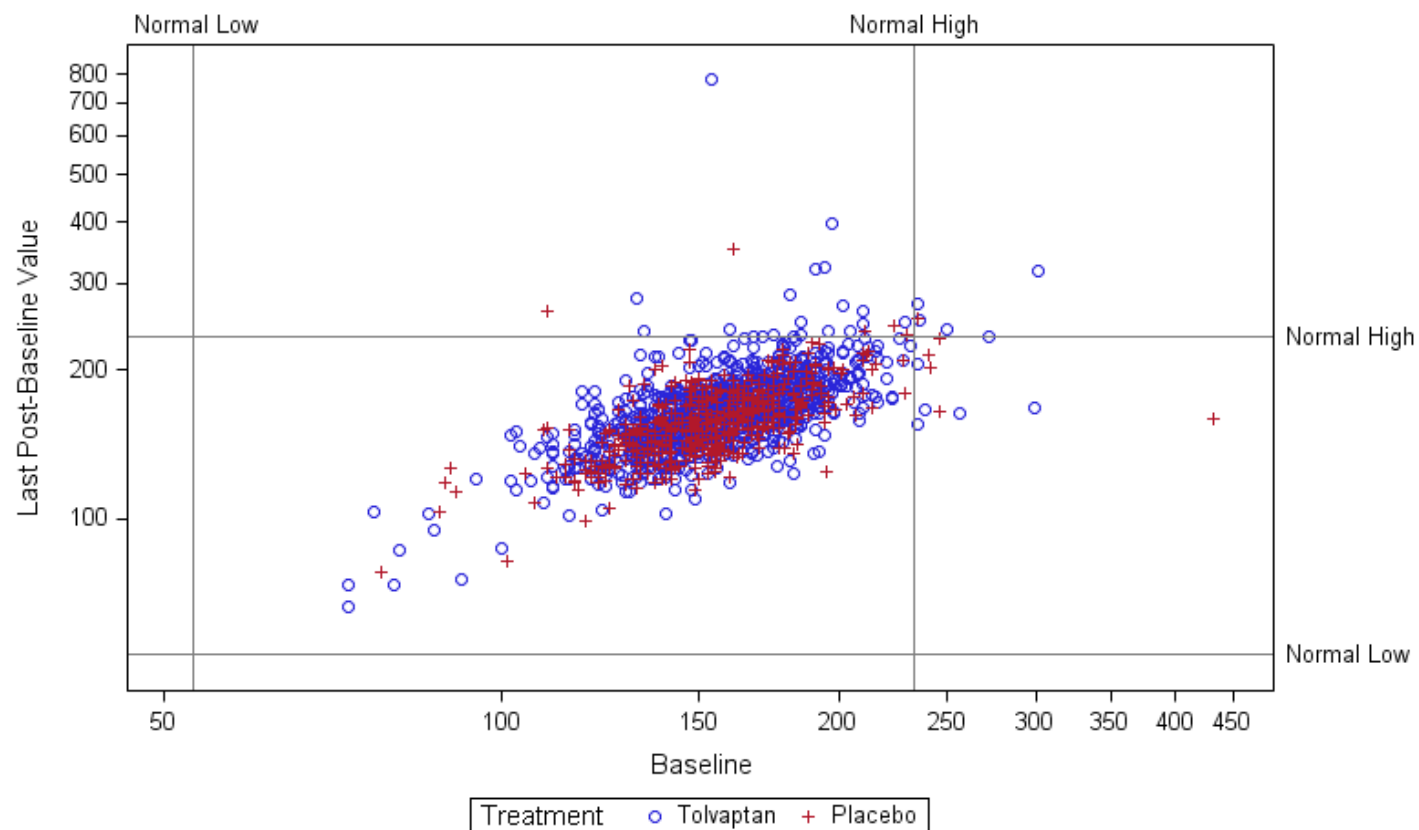
2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061

PROTOCOL P156-251

Figure 1.13.1

Laboratory Test: LACTIC DEHYDROGENASE (IU/L) Normal Range: 53-234



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

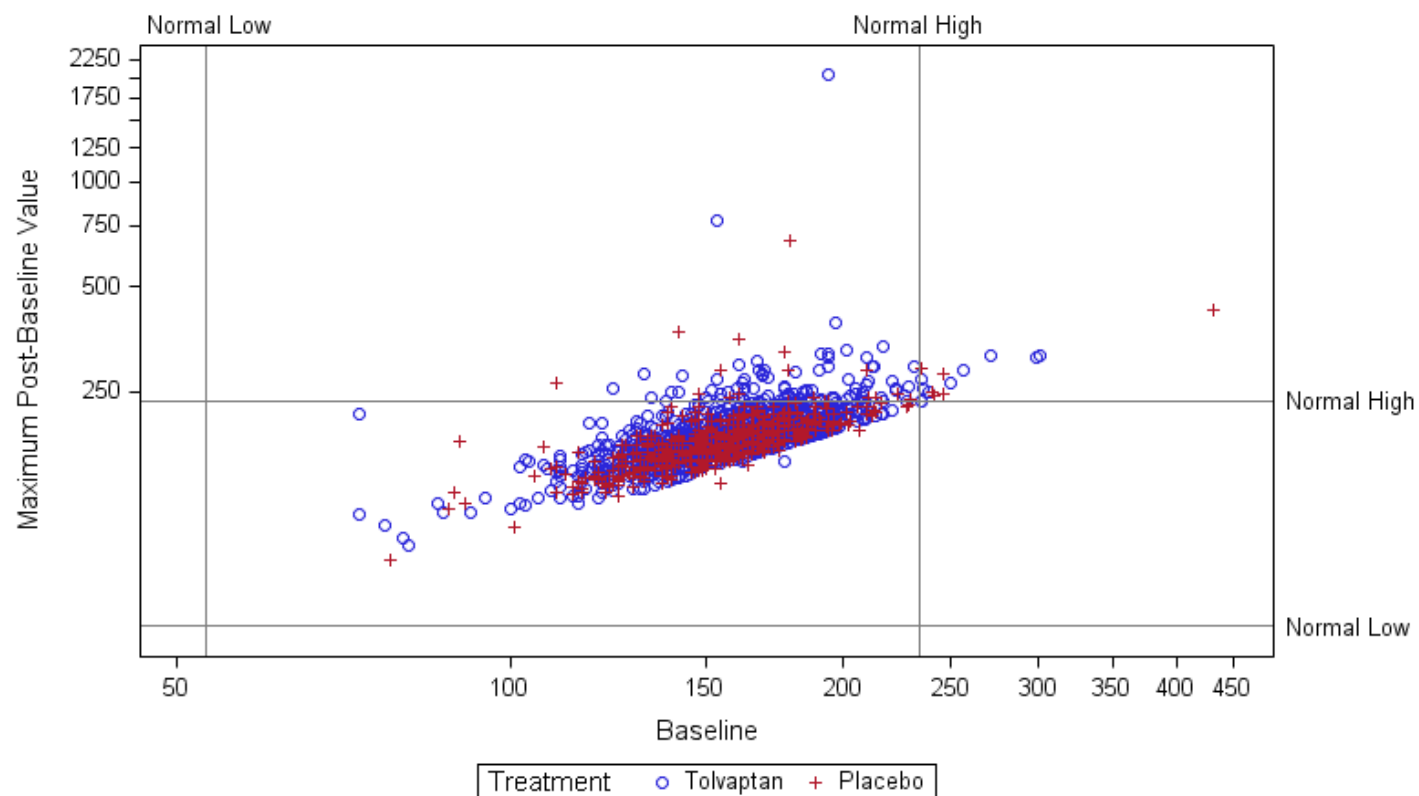
OPC41061

PROTOCOL P156-251

Figure 1.13.2

Laboratory Test: LACTIC DEHYDROGENASE (IU/L) Normal Range: 53-234

Baseline versus Maximum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

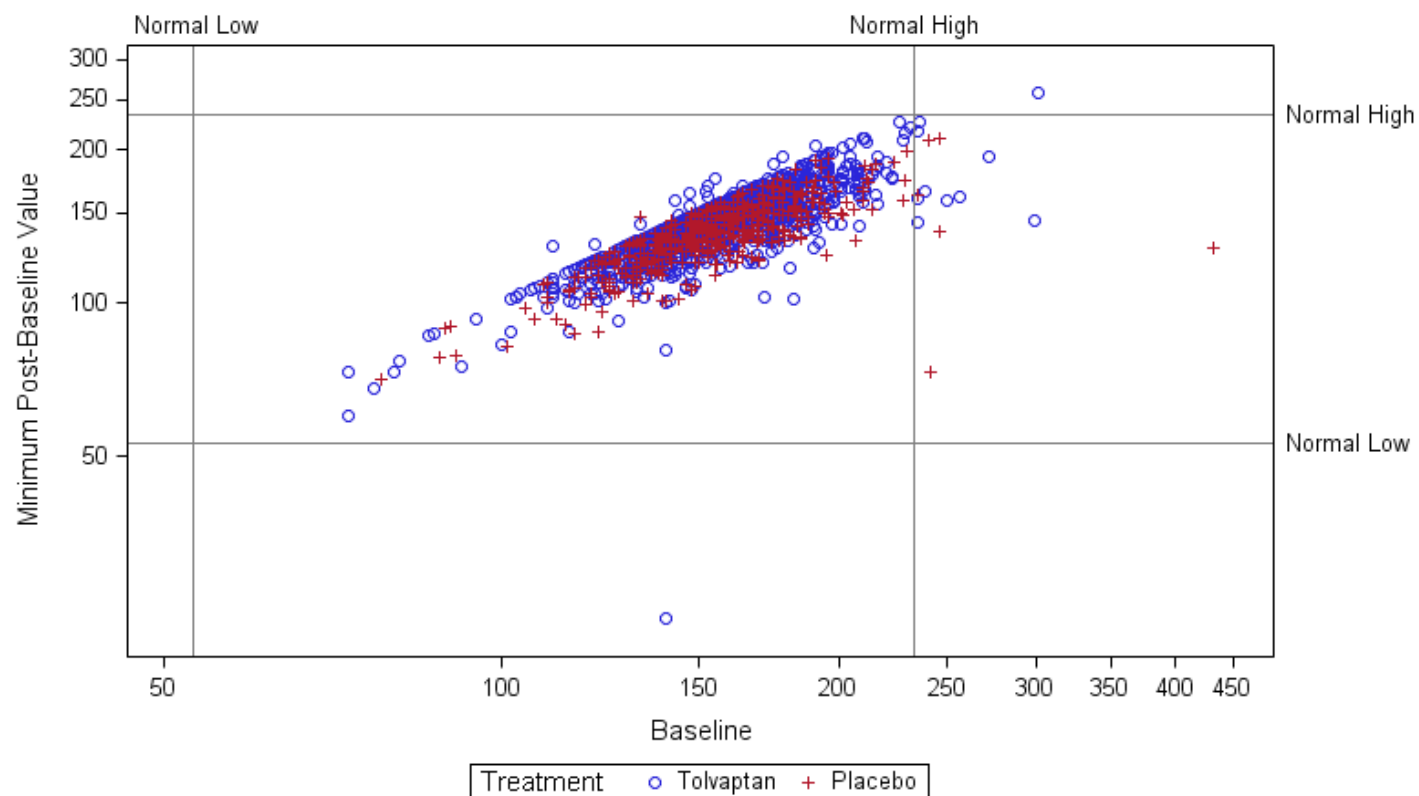
OPC41061

PROTOCOL P156-251

Figure 1.13.3

Laboratory Test: LACTIC DEHYDROGENASE (IU/L) Normal Range: 53-234

Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEND

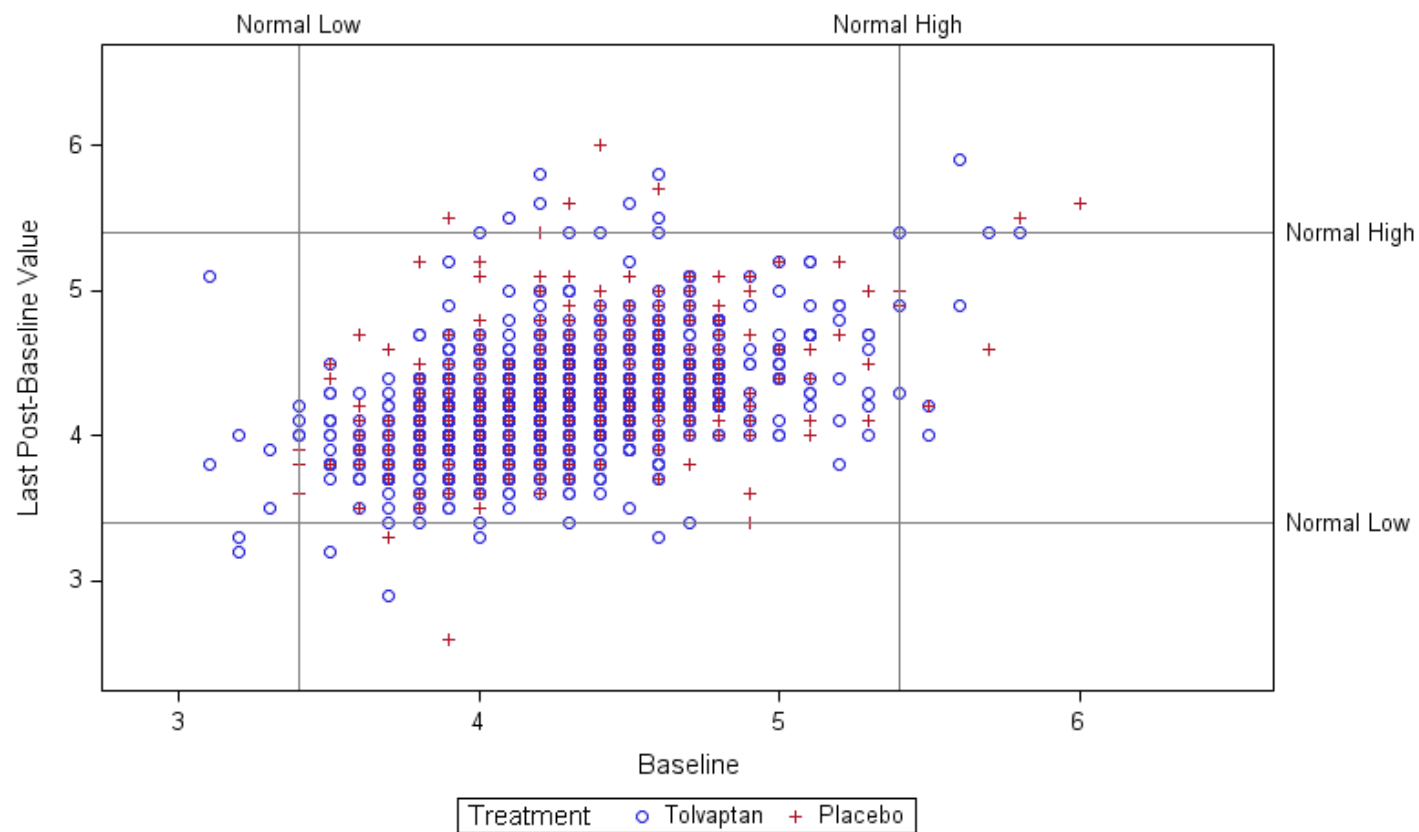
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.14.1

Laboratory Test: POTASSIUM (mEq/L) Normal Range: 3.4-5.4



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

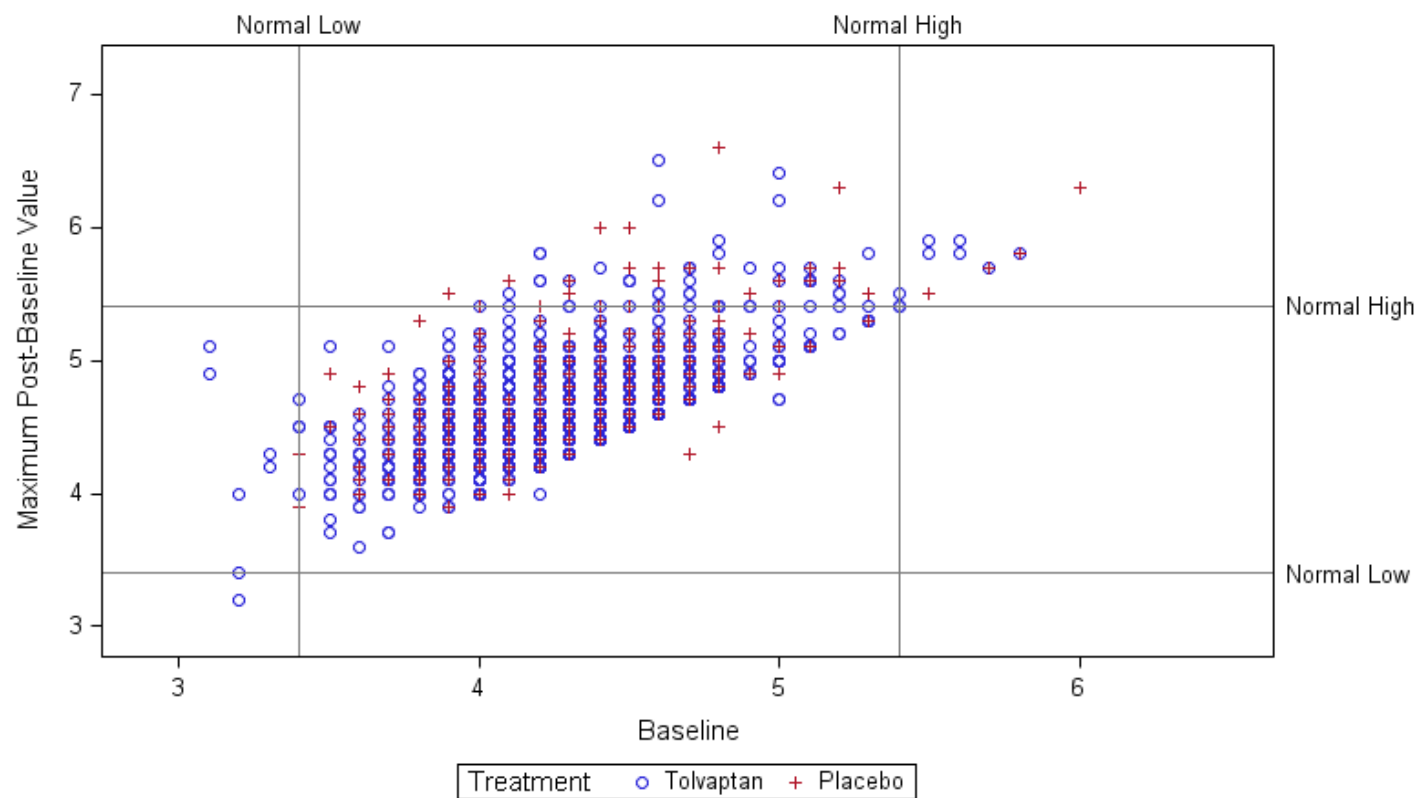
OPC41061

PROTOCOL P156-251

Figure 1.14.2

Laboratory Test: POTASSIUM (mEq/L) Normal Range: 3.4-5.4

Baseline versus Maximum Post-Baseline Result



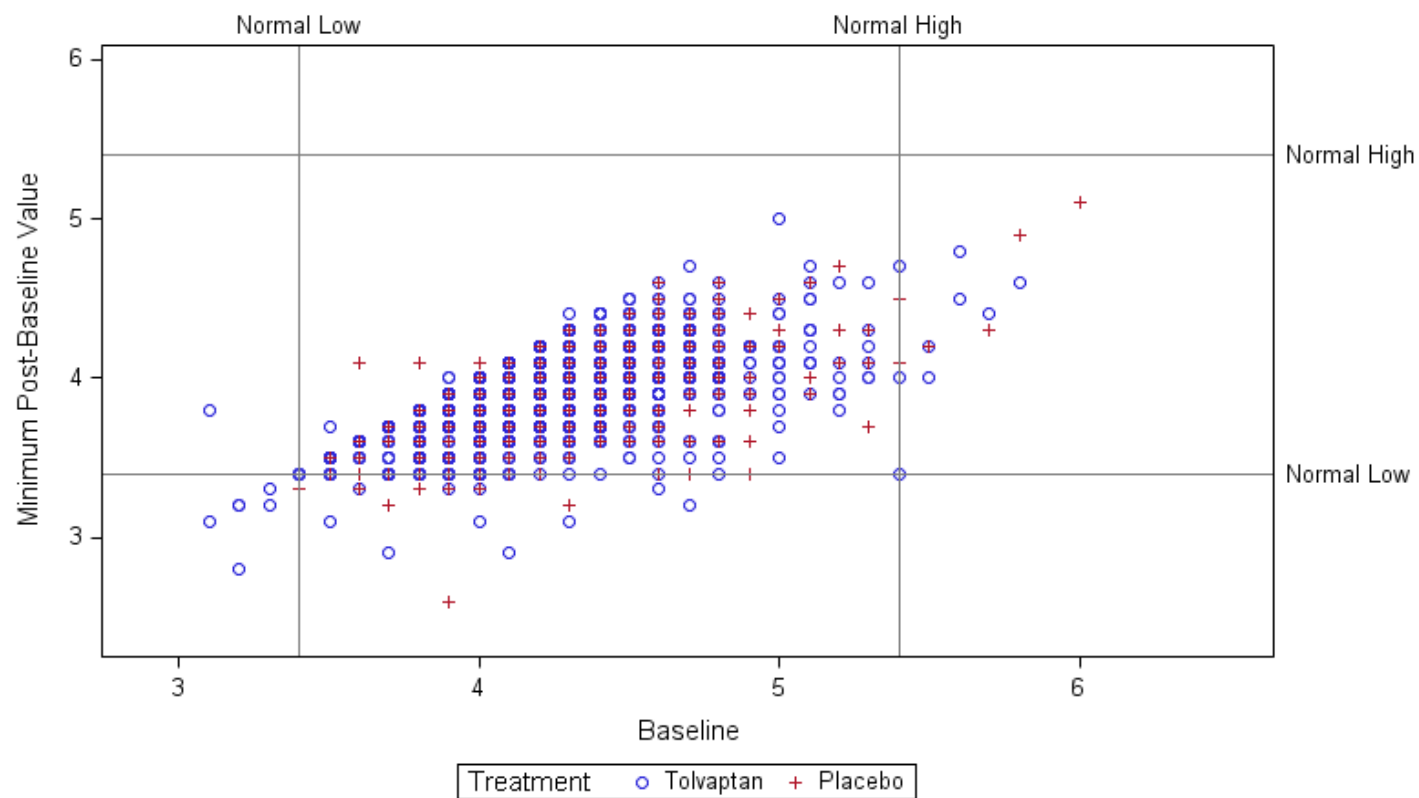
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.14.3
 Laboratory Test: POTASSIUM (mEq/L) Normal Range: 3.4-5.4
 Baseline versus Minimum Post-Baseline Result

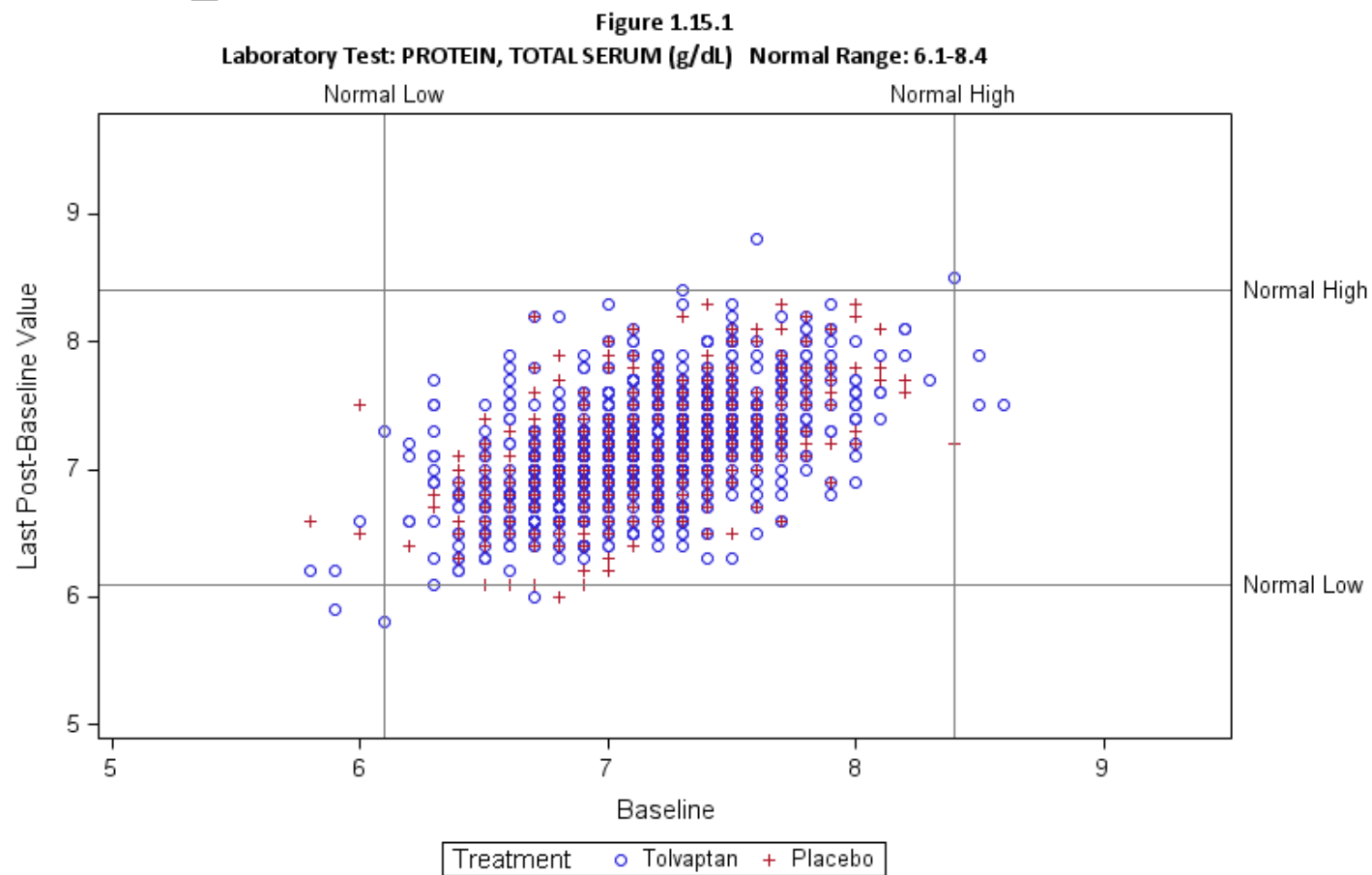


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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

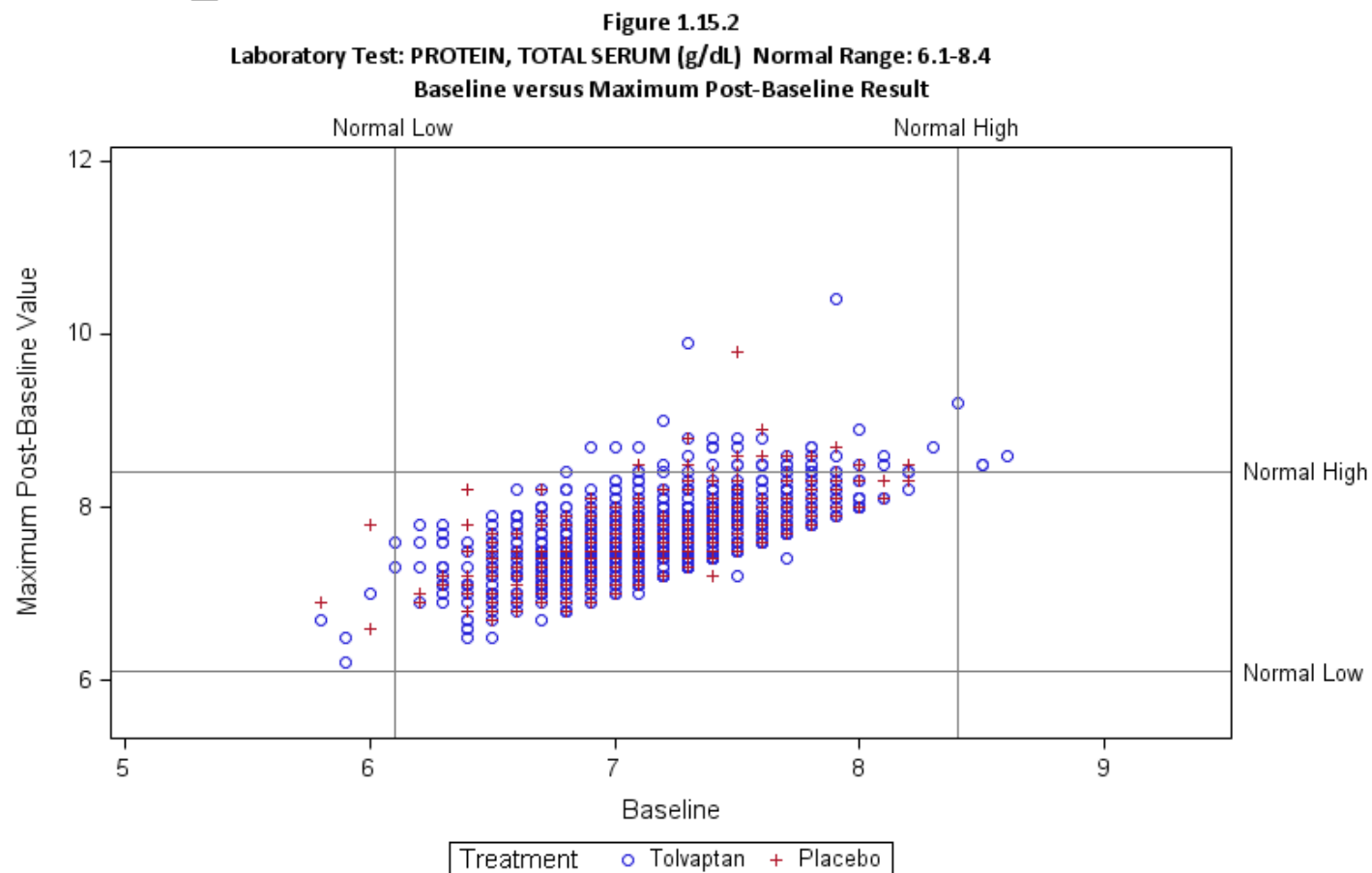


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☒ 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

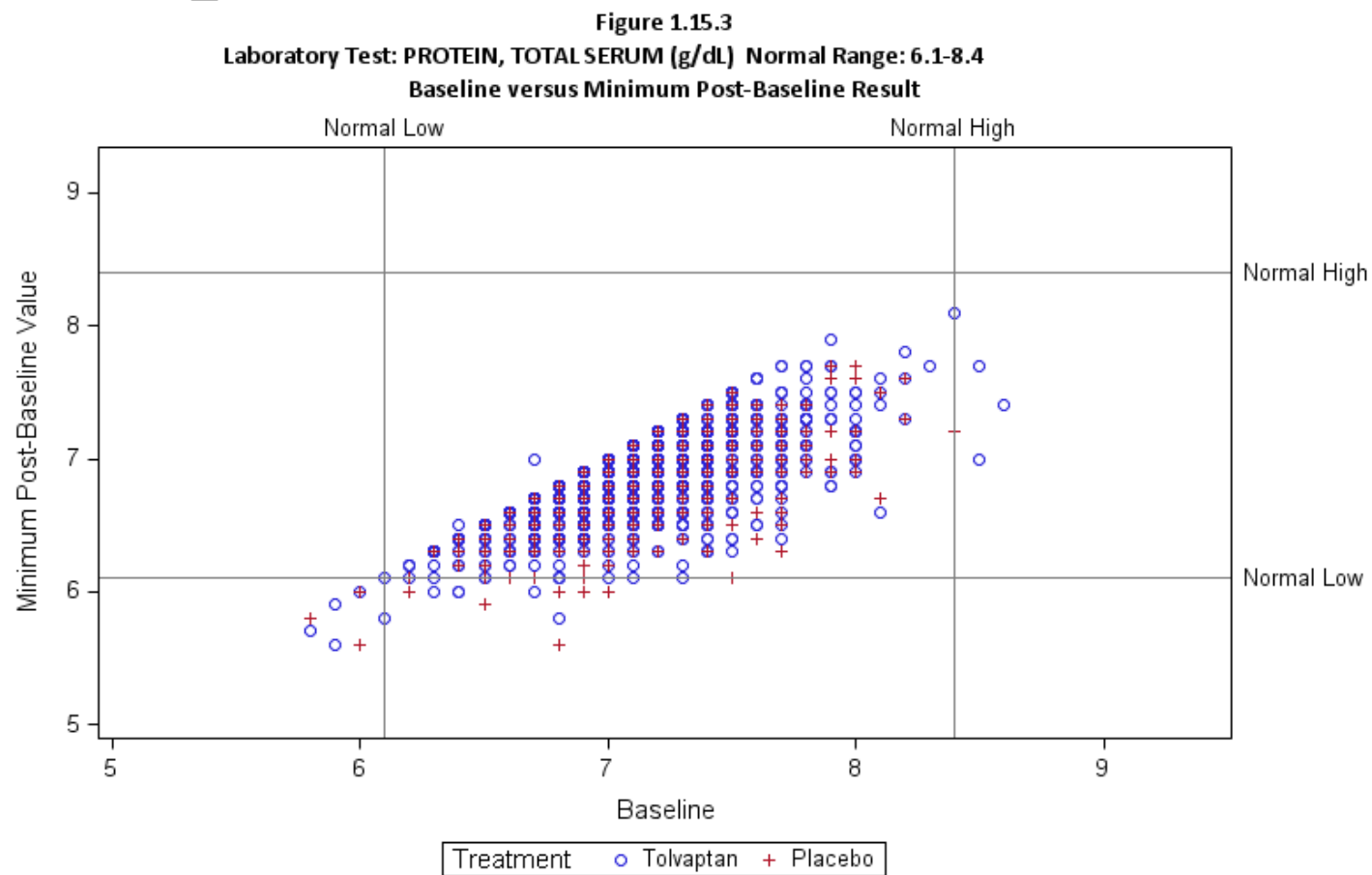


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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251



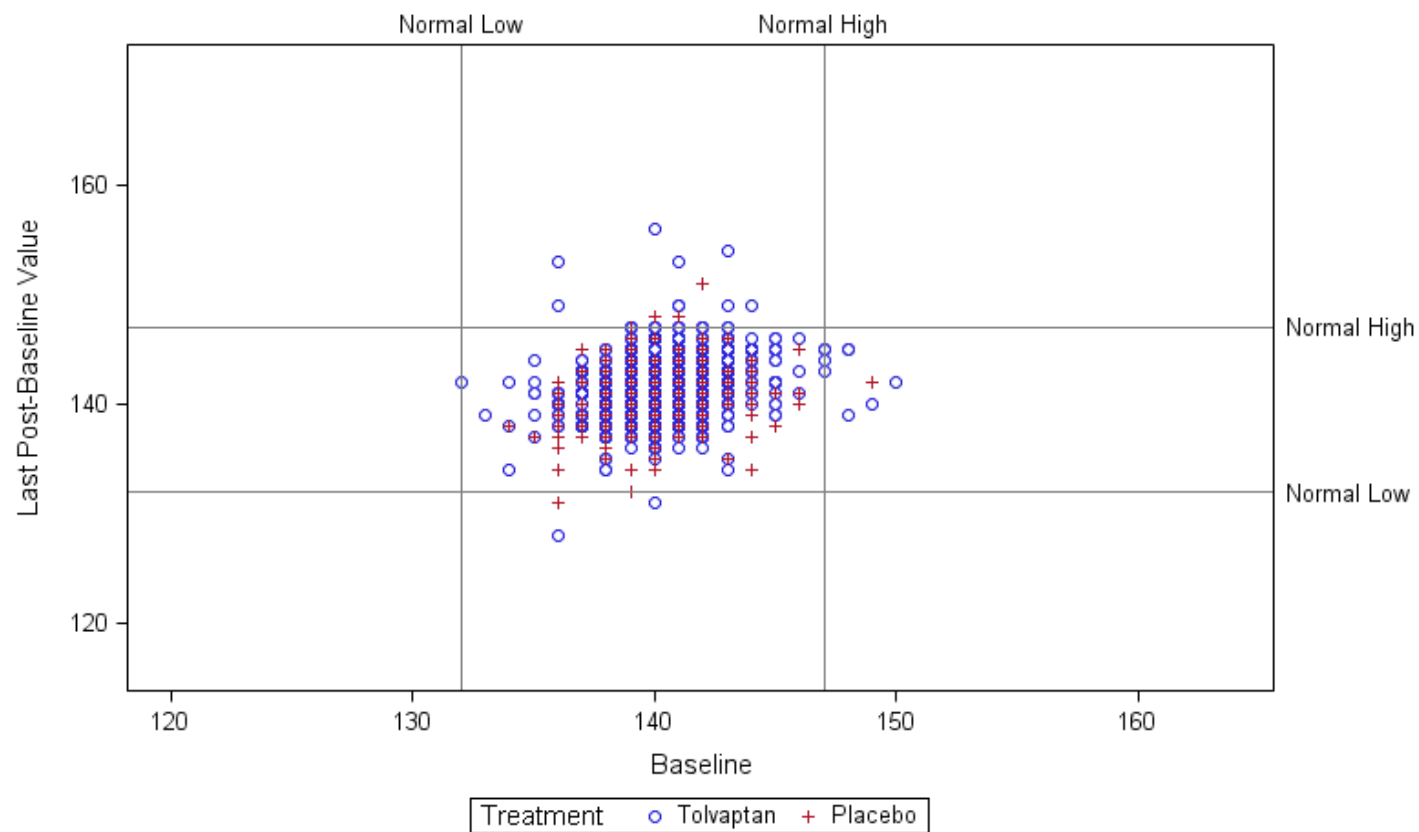
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.16.1
 Laboratory Test: SODIUM (mEq/L) Normal Range: 132-147



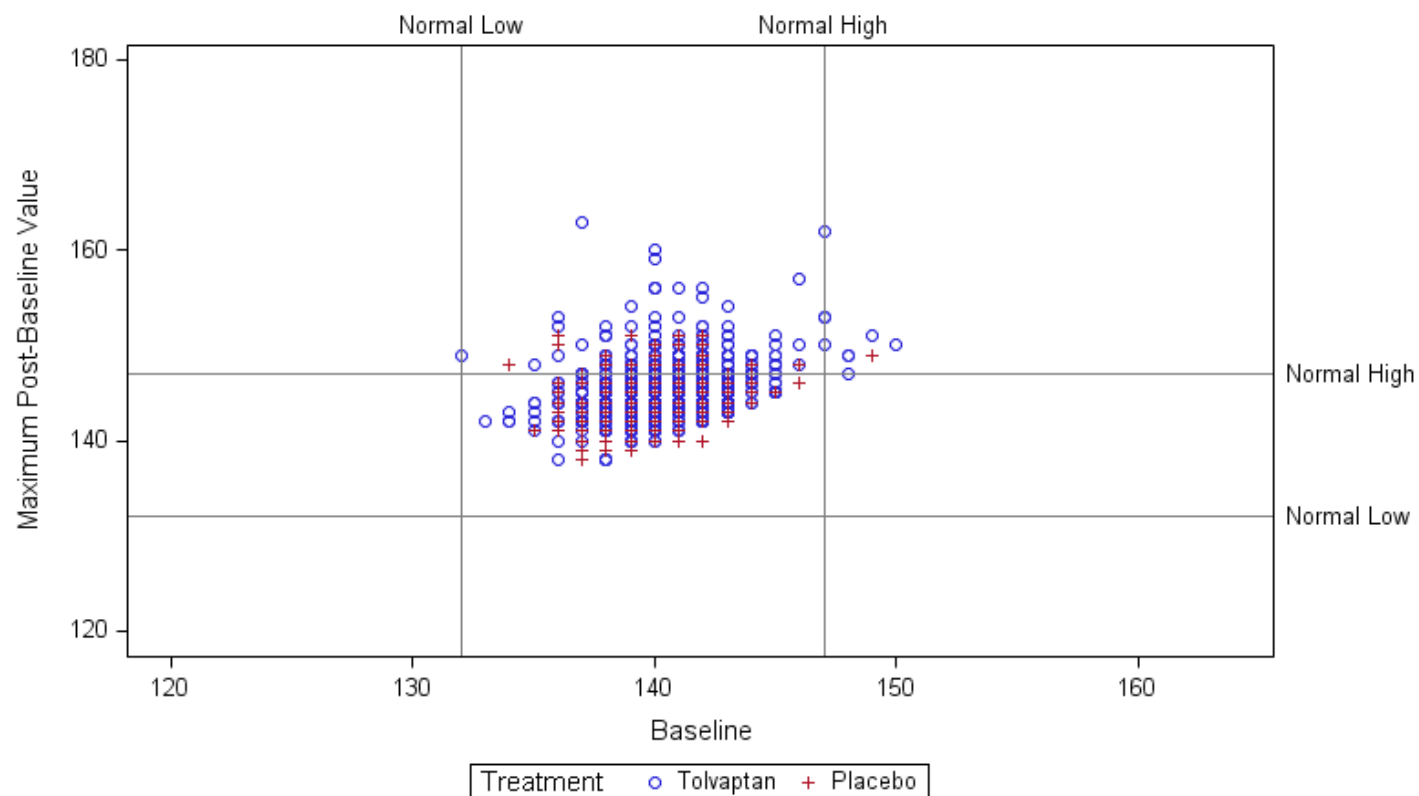
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.16.2
 Laboratory Test: SODIUM (mEq/L) Normal Range: 132-147
 Baseline versus Maximum Post-Baseline Result

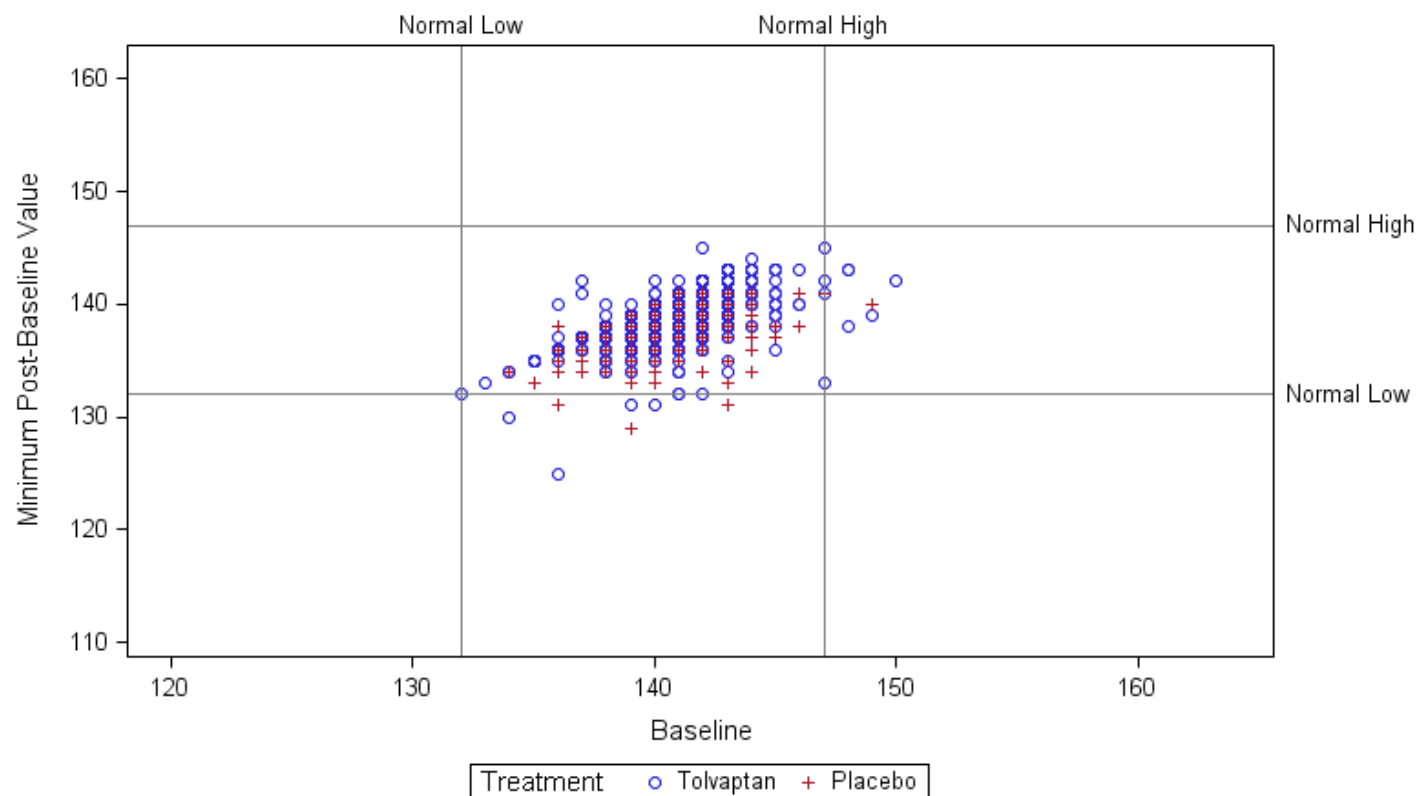


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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.16.3
 Laboratory Test: SODIUM (mEq/L) Normal Range: 132-147
 Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0
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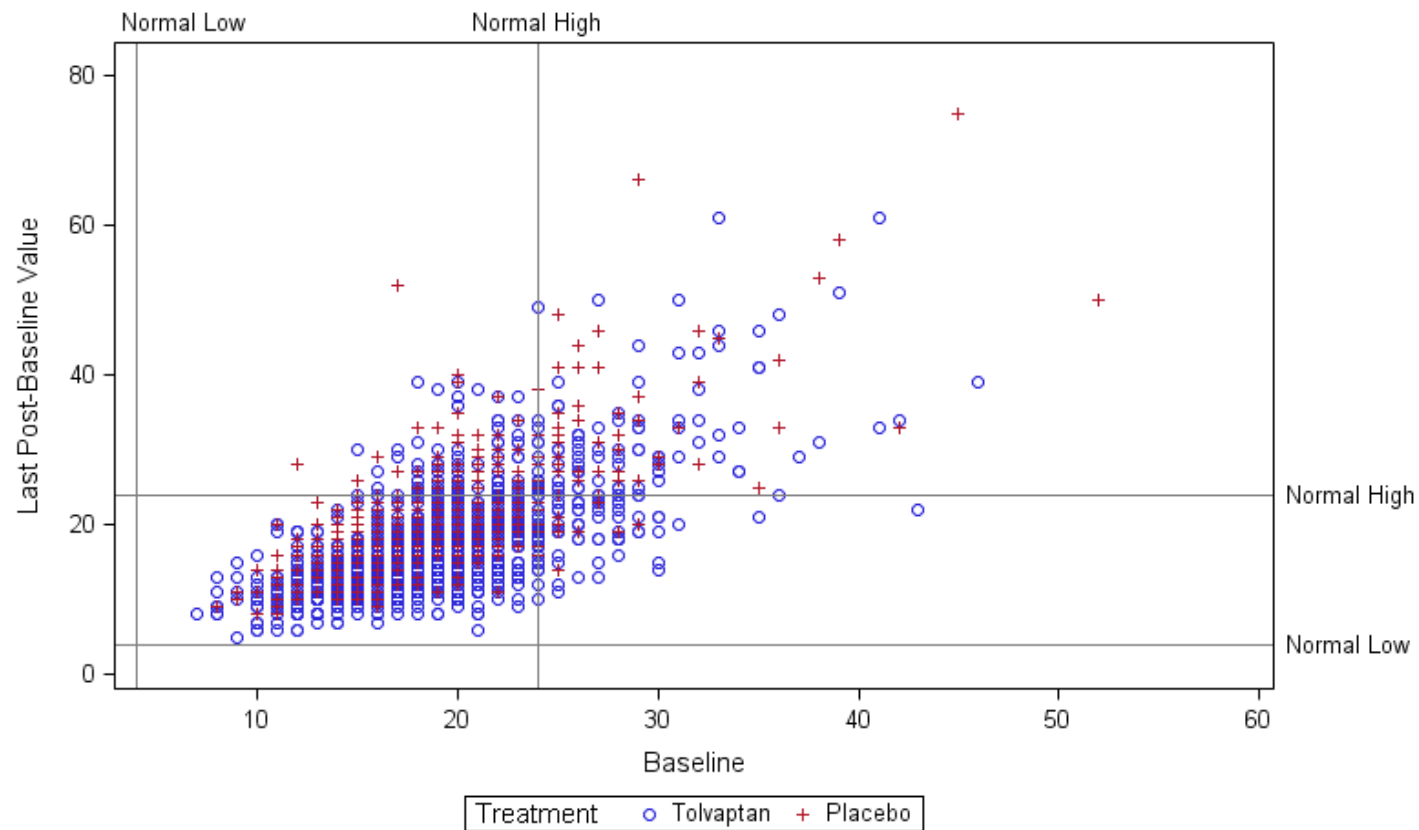
2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

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PROTOCOL P156-251

Figure 1.17.1

Laboratory Test: UREA NITROGEN (mg/dL) Normal Range: 4-24



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

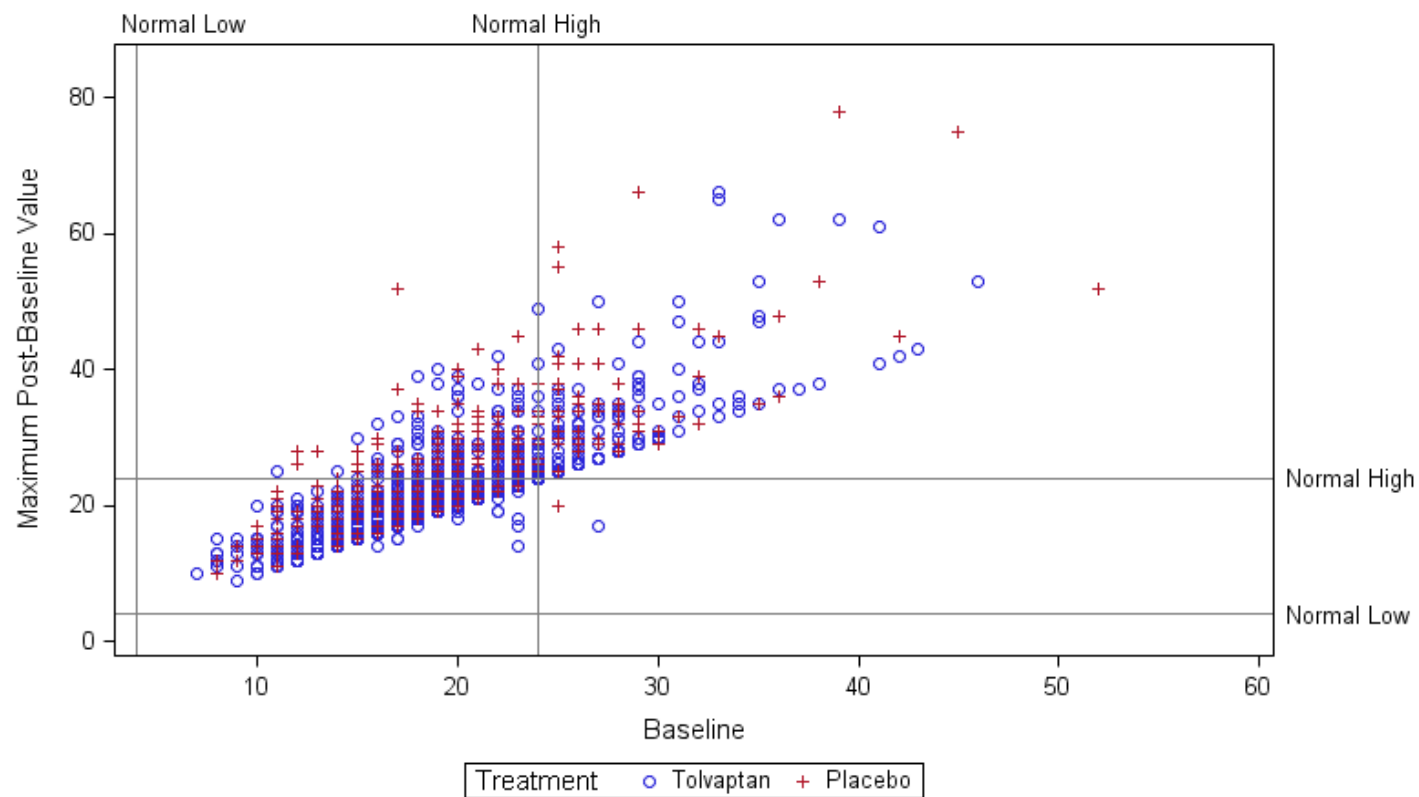
OPC41061

PROTOCOL P156-251

Figure 1.17.2

Laboratory Test: UREA NITROGEN (mg/dL) Normal Range: 4-24

Baseline versus Maximum Post-Baseline Result



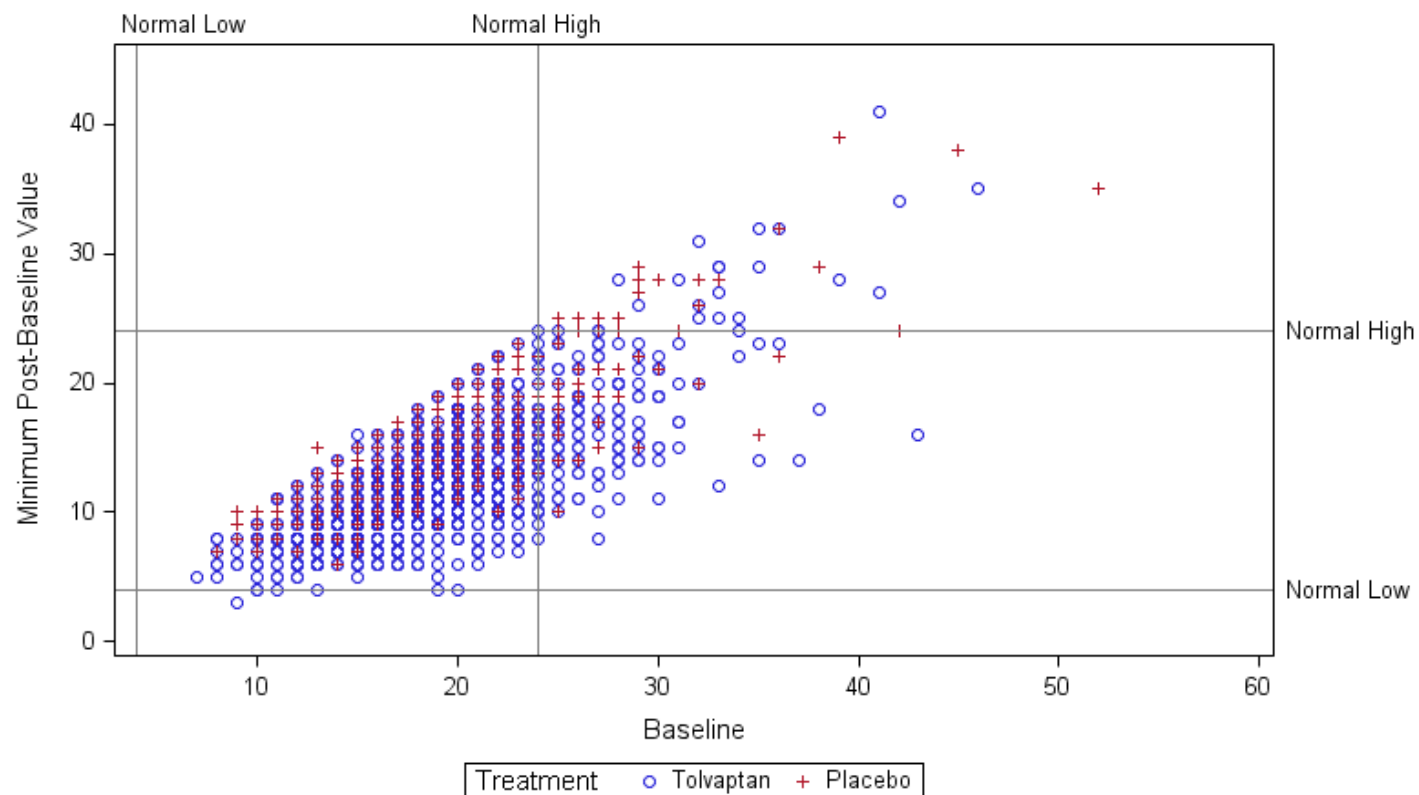
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2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.17.3
 Laboratory Test: UREA NITROGEN (mg/dL) Normal Range: 4-24
 Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEMD

Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

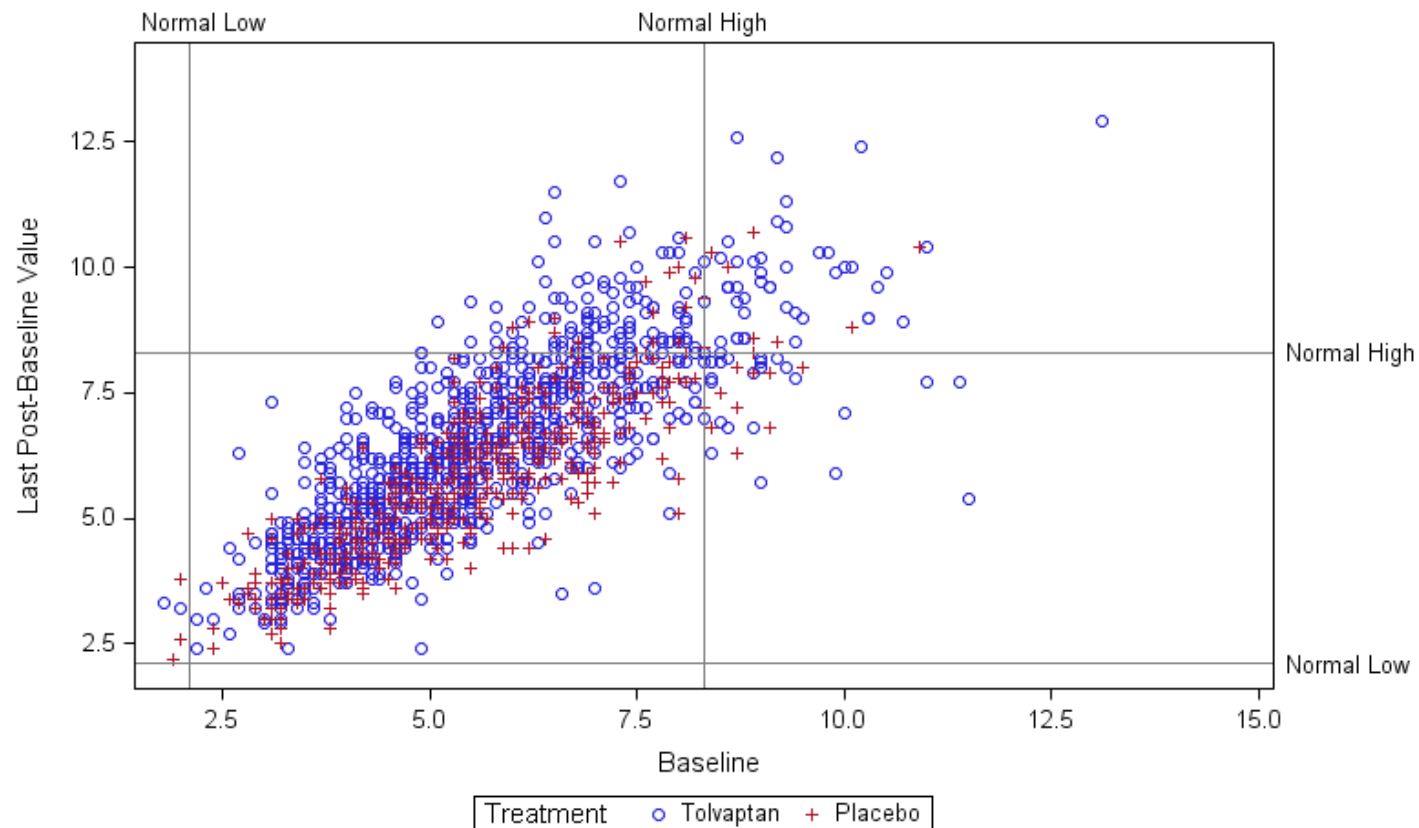
2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061

PROTOCOL P156-251

Figure 1.18.1

Laboratory Test: URIC ACID (mg/dL) Normal Range: 2.1-8.2



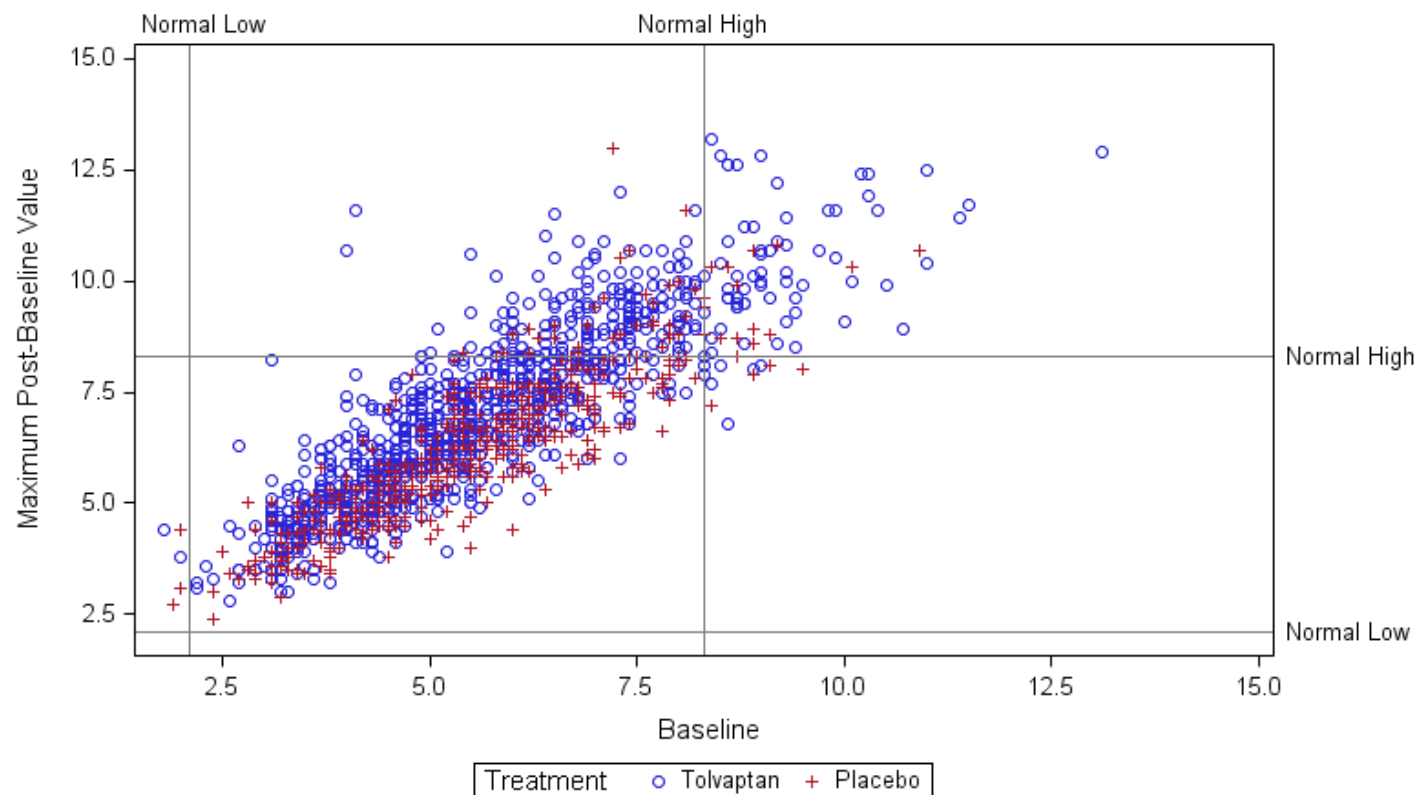
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Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
 PROTOCOL P156-251

Figure 1.18.2
 Laboratory Test: URIC ACID (mg/dL) Normal Range: 2.1-8.2
 Baseline versus Maximum Post-Baseline Result

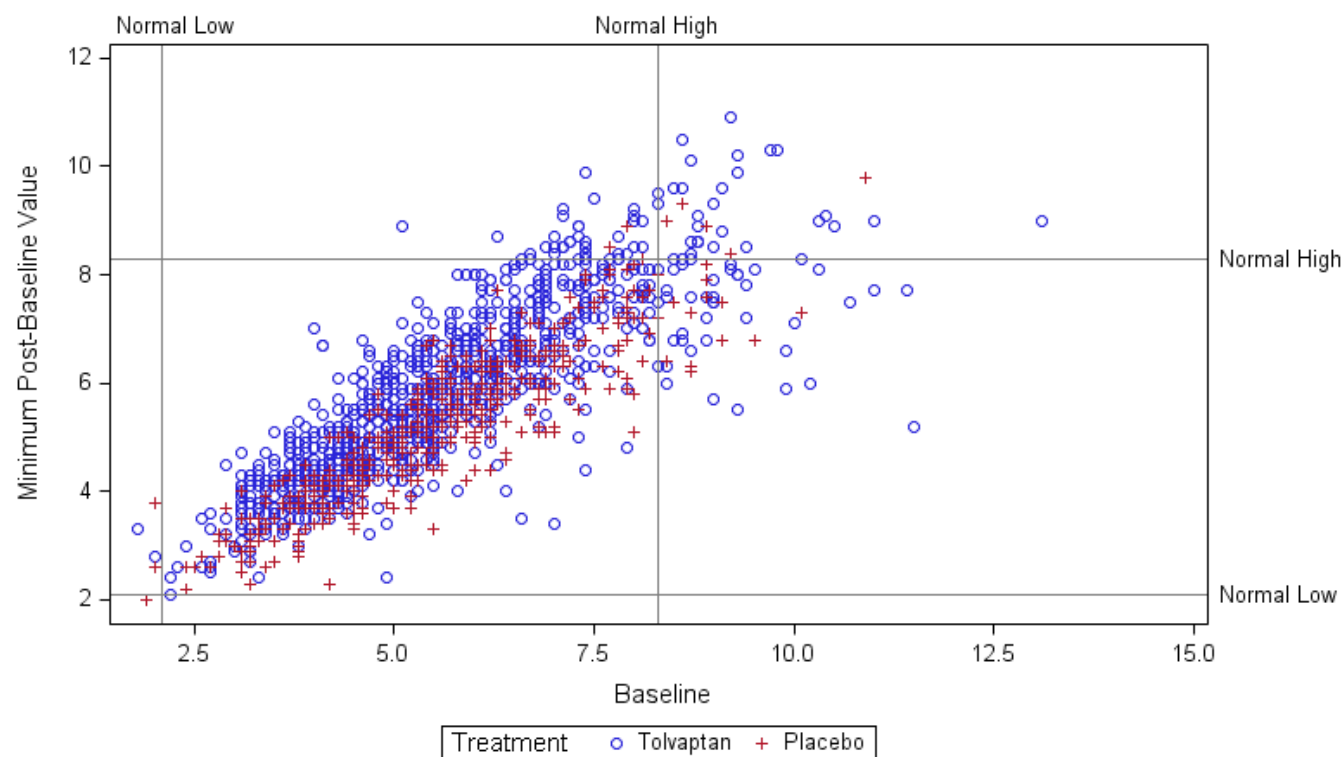


Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0
 Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: :10:26:28

2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

OPC41061
PROTOCOL P156-251

Figure 1.18.3
Laboratory Test: URIC ACID (mg/dL) Normal Range: 2.1-8.2
Baseline versus Minimum Post-Baseline Result



Source: K:\OPC41061\P156-251\dataset\analysis\CHEM0
Program: K:\OPC41061\P156-251\STAT\Figure\Pat\lab.sas Execution: 10:26:28

図 2.7.4.7-37 X-Y Plots (Serum Chemistry Parameters) (156-251)

<資料番号 5.3.5.3-02 : Figure 1.1.1~1.18.3>

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
Thirst/Dry Mouth	CMQ	口内乾燥, 咽喉乾燥, 口唇乾燥, 粘膜乾燥, 多飲症, 口渴, 舌乾燥
Dehydration	CMQ	無尿, 高窒素血症, 血中クレアチニン増加, 血圧低下, 起立血圧, 起立血圧低下, 収縮期血圧低下, 便秘, 腎クレアチニン・クリアランス減少, 脱水, 糖尿病性高浸透圧性昏睡, 浮動性めまい, 体位性めまい, 皮膚乾燥, 血行動態不安定, 高クレアチニン血症, 低血圧, 血液量減少症, 血液量減少性ショック, 乏尿, 起立性低血圧, 腎不全, 急性腎不全, 腎機能障害, ショック, 皮膚ツルゴール低下, 失神, 血管迷走神経性失神, 口渴, 舌乾燥, 尿流量減少, 尿量減少, 尿中ナトリウム減少, 体重減少
	血液量減少性ショック状態 SMQ	循環虚脱, 血液量減少性ショック, ショック, 出血性ショック, 急性腎前性腎不全, 急性呼吸不全, 無尿, 血圧測定不能, 脳低灌流, 肝臓うっ血, 肝腎不全, 低灌流, 多臓器不全, 心筋抑制, 臓器不全, 腎不全, 急性腎不全
Urination	CMQ	膀胱不快感, 排尿困難, 遺尿, 水腎症, 失禁, 排尿異常, 尿意切迫, 神経因性膀胱, 夜間頻尿, 頻尿, 多尿, 尿失禁, 尿閉, 尿量増加
Effects on Sodium, Potassium, and Calcium	低ナトリウム血症 CMQ	抗利尿ホルモン異常, 血中抗利尿ホルモン検査異常, 血中抗利尿ホルモン増加, 血中ナトリウム異常, 血中ナトリウム減少, 異所性抗利尿ホルモン分泌, 低ナトリウム血症, 低ナトリウム血性脳症, 低ナトリウム血症候群, 抗利尿ホルモン不適合分泌, 新生児低ナトリウム血症, 浸透圧性脱髄症候群, 低ナトリウム血症の急速補正, 血中電解質異常, 血中電解質減少, 血液浸透圧異常, 血液浸透圧低下, 脳浮腫, 細胞毒性浮腫, 尿浸透圧低下, 尿浸透圧上昇, 尿中ナトリウム異常, 尿中ナトリウム減少, 尿中ナトリウム増加, 血管原性脳浮腫, 水中毒
	高ナトリウム血症 CMQ	血中クロール増加, 血液浸透圧上昇, 血中ナトリウム増加, 昏睡, 脱髄性多発ニューロパチー, 電解質失調, 高クロール血症, 高ナトリウム血症, 高浸透圧状態, 脳室周囲白質軟化症, 尿比重減少, 尿浸透圧低下, 血中ナトリウム異常, 血中電解質異常, 血中電解質増加, 血液浸透圧異常, 尿中ナトリウム異常, 尿中ナトリウム減少, 尿中ナトリウム増加, 尿浸透圧上昇
	低カリウム血症 CMQ	無力症, 血中カリウム減少, 心停止, 心臓死, 慢性疲労症候群, 伝導障害, 心電図異常, 心電図異常T波, 心電図T波振幅減少, 疲労, 線維筋痛, 心拍数不整, 低カリウム血症, 反射減弱, 筋緊張低下, 企図振戦, 嗜眠, 倦怠感, 筋肉疲労, 筋力低下, 筋無力症候群, 動悸, 不全麻痺, 心突然死, 突然死, 頻脈性不整脈, トルサーード ポアント, 心室性不整脈, 心室性頻脈性不整脈, 心室性頻脈

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
	高カリウム血症 CMQ	血中カリウム異常, 血中カリウム増加, 電解質失調, 高カリウム血症, 反射亢進, 易刺激性, 不随意性筋収縮, 筋拘縮, 筋固縮, 筋痙縮, 筋攣縮
	低カルシウム血症 CMQ	血中カルシウム減少, 血中リン増加, カルシウムイオン減少, 痙攣, 高リン酸塩血症, 低アルブミン血症, 低カルシウム血症, 低蛋白血症, 反射減弱, 反射亢進, 筋痙縮, 筋攣縮, 筋無力症候群, てんかん重積状態
	高カルシウム血症 CMQ	無力症, 血中カルシウム増加, 血中副甲状腺ホルモン増加, 血中リン減少, 認知衰退, 錯乱状態, 譫妄, 失見当識, 電解質失調, 高カルシウム血症, 副甲状腺機能亢進症, 続発性副甲状腺機能亢進症, 低リン酸血症, 意識消失, 精神状態変化, 代謝性脳症, 無機質代謝障害, 悪心, 人格変化, 昏眠
Renal Function	急性腎不全 SMQ	急性リン酸腎症, 急性腎前性腎不全, 無尿, 高窒素血症, 持続的血液透析濾過, 透析, 血液透析, 新生児無尿, 中毒性ネフロパシー, 乏尿, 腹膜透析, 腎不全, 急性腎不全, 新生児腎不全, 腎機能障害, 新生児腎障害, アルブミン尿, 血中クレアチニン異常, 血中クレアチニン増加, 血中尿素異常, 血中尿素増加, 血中尿素窒素/クレアチニン比増加, 腎クレアチニン・クリアランス異常, 腎クレアチニン・クリアランス減少, 尿中クレアチニン異常, 尿中クレアチニン減少, クリスタル腎症, 糸球体濾過率異常, 糸球体濾過率減少, 高クレアチニン血症, 腎炎, 腎疾患による浮腫, 尿中蛋白陽性, 蛋白尿, 腎機能検査異常, 腎移植, 腎尿細管障害, 腎尿細管壊死, 尿細管間質性腎炎, 腎尿素クリアランス減少, 尿量減少
Effect on Creatinine	血中クレアチニン増加 CMQ	血中クレアチニン, 血中クレアチニン異常, 血中クレアチニン増加, 血中尿素窒素/クレアチニン比, 血中尿素窒素/クレアチニン比減少, 血中尿素窒素/クレアチニン比増加, 腎クレアチニン・クリアランス, 腎クレアチニン・クリアランス異常, 腎クレアチニン・クリアランス減少, 腎クレアチニン・クリアランス増加, 高クレアチニン血症, 腎機能検査異常
Effect on Blood Urea Nitrogen	血中尿素増加 CMQ	血中尿素, 血中尿素異常, 血中尿素増加, 血中尿素窒素/クレアチニン比, 血中尿素窒素/クレアチニン比増加, 腎機能検査異常
Effect on Cystatin C	シスタチンC増加	シスタチンC, シスタチンC異常, シスタチンC増加
Effect on Uric Acid	血中尿酸増加 CMQ	血中尿酸, 血中尿酸異常, 血中尿酸増加, 痛風, 痛風性関節炎, 痛風結節
Blood Pressure	高血圧 SMQ	進行性高血圧, 外来血圧上昇, 拡張期血圧上昇, コントロール不良の血圧, 血圧上昇, 血圧管理, 起立血圧上昇, 収縮期血圧上昇, 拡張期高血圧, 子癇, 内分泌性高血圧, 本態性高血圧症, 妊娠高血圧, HELLP症候群, 高アルドステロン症, 高血圧, 新生児高血圧, 高血圧性血管障害, 高血圧

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		性心拡大, 高血圧性心筋症, 高血圧クリーゼ, 高血圧緊急症, 高血圧性脳症, 高血圧性心疾患, 高血圧性腎症, 不安定高血圧, 悪性高血圧, 悪性高血圧性心疾患, 悪性腎性高血圧, 胎児に影響する母体の高血圧症, 平均動脈圧上昇, 代謝症候群, 神経性高血圧, 起立性高血圧, 子癇前症, 高血圧前症, 処置による高血圧, 腎性高血圧, 腎血管性高血圧, 高血圧性網膜症, 続発性アルドステロン症, 二次性高血圧, 収縮期高血圧, 断薬性高血圧, 尿中アルドステロン異常, 尿中アルドステロン増加, アンギオテンシン変換酵素増加, アンギオテンシン 1 増加, アンギオテンシン 2 増加, 血中アルドステロン異常, 血中アルドステロン増加, 血中カテコールアミン異常, 血中カテコールアミン増加, 血圧異常, 外来血圧異常, 拡張期血圧異常, 血圧変動, 起立血圧異常, 収縮期血圧異常, 尿中カテコールアミン異常, 尿中カテコールアミン増加, 利尿療法, 異所性アルドステロン分泌, 異所性レニン分泌, エピネフリン異常, エピネフリン増加, 不安定血圧, 尿中メタネフリン異常, 尿中メタネフリン増加, ノンディッピング, ノルエピネフリン異常, ノルエピネフリン増加, 尿中ノルメタネフリン増加, 偽アルドステロン症, レニン異常, レニン増加, レニン・アンギオテンシン系阻害, チラミン反応
Thrombosis/ Hypercoagulable State	動脈の塞栓および血栓 SMQ	急性心筋梗塞, 黒内障, 一過性黒内障, 大動脈バイパス, 大動脈塞栓, 大動脈手術, 大動脈血栓症, 大動脈造影異常, 動脈切除, 動脈置換, 動脈バイパス手術, 動脈グラフト, 動脈閉塞性疾患, 動脈ステント挿入, 動脈治療手技, 動脈血栓症, 四肢動脈血栓症, 動脈造影異常, 頸動脈血管造影異常, アテレクトミー, 大脳基底核梗塞, 脳底動脈閉塞, 脳底動脈血栓症, 一過性失明, 腕頭動脈閉塞, 内包性前兆症候群, 頸動脈形成, 頸動脈塞栓, 頸動脈バイパス, 頸動脈閉塞, 頸動脈ステント挿入, 頸動脈血栓症, 頸動脈内膜摘除, 小脳動脈閉塞, 小脳動脈血栓症, 小脳塞栓症, 大脳動脈塞栓症, 大脳動脈閉塞, 大脳動脈血栓症, 脳低灌流, 脳血管不全, 脳血管狭窄, 腹腔動脈閉塞, 冠動脈ステント挿入, 冠動脈バイパス, 冠動脈塞栓症, 冠動脈閉塞, 冠動脈再閉塞, 冠動脈内膜摘除, 冠動脈再建, 薬剤性塞栓性皮膚症, 動脈塞栓症, 動脈内膜摘除, 大腿動脈塞栓症, 大腿動脈閉塞, 肝動脈塞栓症, 肝動脈閉塞, 肝動脈血栓症, 小指球ハンマー症候群, 腸骨動脈塞栓症, 腸骨動脈閉塞, 腸骨動脈血栓症, 大動脈内バルーン挿入, 術中大脳動脈閉塞, 虚血性脳梗塞, 虚血性脳卒中, ラクナ梗塞, ルリーシュ症候

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		群, 腸間膜動脈硬化症, 腸間膜動脈塞栓, 腸間膜動脈狭窄, 腸間膜動脈ステント挿入, 腸間膜動脈血栓症, 心筋梗塞, 乳頭筋梗塞, 陰茎動脈閉塞, 経皮的冠インターベンション, 末梢動脈閉塞性疾患, 末梢動脈再閉塞, 末梢動脈形成, 末梢血管塞栓症, 膝窩動脈捕捉症候群, 処置後心筋梗塞, 梗塞後狭心症, 脳実質外動脈閉塞, 肺動脈治療手技, 肺動脈血栓症, 腎動脈閉塞, 腎動脈血栓症, 腎塞栓, 網膜動脈塞栓症, 網膜動脈閉塞, 網膜動脈血栓症, 無症候性心筋梗塞, 脊髄動脈塞栓症, 脊髄動脈血栓症, 脾臓塞栓症, ストレス心筋症, 進行性脳卒中, 鎖骨下動脈塞栓症, 鎖骨下動脈閉塞, 鎖骨下動脈血栓症, 上腸間膜動脈症候群, 血栓塞栓除去, 血栓性微小血管症, 血栓性血小板減少性紫斑病, 一過性脳虚血発作, 腹腔動脈血栓, 椎骨動脈閉塞, 椎骨動脈血栓症, 一過性視力低下, 腋窩静脈血栓症, バッドキアリ症候群, 静脈カテーテル留置, 海綿静脈洞血栓症, 中心静脈カテーテル留置, 大脳静脈血栓症, 圧迫ストッキング使用, 深部静脈血栓症, 術後深部静脈血栓症, 静脈塞栓症, 肝静脈閉塞, 肝静脈血栓症, ホーマンズ徴候陽性, 腸骨静脈閉塞, 下大静脈症候群, 下大静脈閉塞, 頭蓋内静脈洞血栓症, 静脈内カテーテル管理, 頸静脈血栓症, マイ・トゥルナー症候群, 腸間膜静脈血栓症, 産科的肺塞栓症, パジエット・シュレッター症候群, 骨盤静脈血栓症, 陰茎静脈血栓症, 静脈切除術, 静脈形成, 門脈閉塞, 門脈血栓症, 処置後肺塞栓症, 血栓後症候群, 術後血栓症, 分娩後静脈血栓症, 肺塞栓症, 肺梗塞, 肺微小塞栓, 肺血栓症, 肺静脈閉塞, 肺静脈閉塞性疾患, 肺静脈血栓症, 腎静脈塞栓症, 腎静脈閉塞, 腎静脈血栓症, 網膜静脈閉塞, 網膜静脈血栓症, S I Q I I I T I I I パターン, 脾静脈閉塞, 脾静脈血栓症, 鎖骨下静脈血栓症, 上矢状洞血栓症, 上大静脈症候群, 血栓性静脈炎, 遊走性血栓性静脈炎, 新生児血栓性静脈炎, 表在性血栓性静脈炎, 血栓性静脈瘤, 陰茎海綿体血栓症, 横静脈洞血栓症, 血管グラフト, 大静脈塞栓症, 大静脈フィルター挿入, 大静脈血栓症, 静脈造影異常, 静脈閉塞性疾患, 静脈閉塞性肝疾患, 静脈閉塞, 静脈手術, 静脈再疎通, 静脈ステント挿入, 静脈血栓症, 妊娠中の静脈血栓症, 四肢静脈血栓症, 新生児静脈血栓症

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
Thrombosis/ Hypercoagulable State	血管タイプ不明あるいは混合型の塞栓 および血栓 SMQ	血管造影異常, 脳血管造影異常, 末梢血管造影異常, 血管形成, 動静脈瘻閉塞, 動静脈瘻血栓症, 心房血栓症, 大脳基底核卒中, 骨梗塞, 脳幹梗塞, 脳幹卒中, 脳幹血栓症, 小脳梗塞, 脳梗塞, 胎児脳梗塞, 脳虚血, 敗血症性脳梗塞, 脳血栓症, 脳脊髄血栓性タンポナーデ, 脳血管発作, 脳血管発作予防, 脳血管障害, 脳血管手術, 脈絡膜梗塞, 側副血行, 冠動脈形成, 冠動脈血栓症, 冠動脈バイパス血栓症, 医療機器閉塞, 両麻痺, 方向性ドップラー法血流量試験異常, 播種性血管内凝固, 新生児の播種性血管内凝固, 塞栓性脳梗塞, 塞栓性肺炎, 塞栓性脳卒中, 塞栓症, 胎児脳血管障害, 移植片血栓症, 出血性脳梗塞, 出血性梗塞, 出血性卒中, 卒中の出血性変化, 不全片麻痺, 片麻痺, 肝梗塞, 埋込み部位血栓, 梗塞, 注入部位血栓, 注射部位血栓, 内耳梗塞, 腸梗塞, 心臓内腫瘍, 心臓内血栓, 腸間膜閉塞, 腸間膜血行不全, 不全単麻痺, 単麻痺, 視神経梗塞, 膝梗塞, 奇異性塞栓症, 不全対麻痺, 対麻痺, 不全麻痺, 末梢血行再建, 下垂体梗塞, 胎盤梗塞, 空気圧迫療法, 門脈シャント, 処置後脳卒中, 人工血管移植, 四肢不全麻痺, 四肢麻痺, 腎梗塞, 網膜梗塞, 網膜血管血栓症, シャント閉塞, シャント血栓症, 脊髄梗塞, 脾臓梗塞, ステンント塞栓形成, 外科的血管シャント, 精巣梗塞, 視床梗塞, 血栓除去, 血栓性閉塞性血管炎, 血栓溶解, 血栓症, 医療機器内血栓, 腸間膜血栓症, 血栓症予防, 血栓性脳梗塞, 血栓性脳卒中, 甲状腺梗塞, 腫瘍性塞栓症, 腫瘍性血栓症, 超音波血管造影異常, ドップラー超音波異常, 臍帯血栓症, 血管グラフト血栓症, 血管手術, 血管ステント挿入, 血管拡張術, 血管穿刺部位血栓, 視覚正中線偏位症候群, ホワイト・クロット症候群
Coagulation/ Hemostatic Disorders/Increased Bleeding	出血関連臨床検査用語 SMQ	尿中血, 尿中血陽性, 胃内容物潜血陽性, 便潜血陽性, 活性化部分トロンボプラスチン時間異常, 活性化部分トロンボプラスチン時間延長, 抗第 I X 因子抗体陽性, 抗第 V 因子抗体陽性, 抗第 V I I 因子抗体陽性, 抗第 V I I I 因子抗体陽性, 抗第 X 因子抗体陽性, 抗第 X I 因子抗体陽性, 抗第 X I I 因子抗体陽性, アンチトロンビン I I I 増加, 出血時間異常, 出血時間延長, 血中フィブリノゲン異常, 血中フィブリノゲン減少, 血中トロンビン異常, 血中トロンビン減少, 血中トロンボプラスチン異常, 血中トロンボプラスチン減少, 毛細血管脆弱性異常, 毛細血管脆弱性試験値増加, 毛細血管透過性増加, 循環抗凝血素, 血餅退縮異常, 血餅退縮時間延長, 凝固因子減少, 凝固因子欠乏症, 凝固第 I X 因子量異常, 凝固第 I X

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		因子量減少, 凝固第Ⅴ因子量異常, 凝固第Ⅴ因子量減少, 凝固第ⅤⅠⅠ因子量異常, 凝固第ⅤⅠⅠ因子量減少, 凝固第ⅤⅠⅠⅠ因子量異常, 凝固第ⅤⅠⅠⅠ因子量減少, 凝固第Ⅹ因子量異常, 凝固第Ⅹ因子量減少, 凝固第ⅩⅠ因子量異常, 凝固第ⅩⅠ因子量減少, 凝固第ⅩⅠⅠ因子量異常, 凝固第ⅩⅠⅠ因子量減少, 凝固第ⅩⅠⅠⅠ因子量異常, 凝固第ⅩⅠⅠⅠ因子量減少, 凝固時間異常, 凝固時間延長, エタノールゲル化試験陽性, フィブリン異常, フィブリンDダイマー減少, フィブリンDダイマー増加, フィブリン減少, フィブリン分解産物, フィブリン分解産物増加, 線維素溶解異常, 線維素溶解亢進, ヘマトクリット異常, ヘマトクリット減少, ヘモグロビン異常, ヘモグロビン減少, I NR異常, I NR増加, カオリンセファリン凝固時間異常, カオリンセファリン凝固時間延長, プラスミン減少, プラスミン・インヒビター増加, プラスミノーゲン活性化因子インヒビター, プラスミノーゲン活性化因子インヒビター減少, プラスミノーゲン減少, プラスミノーゲン増加, 血小板第4因子減少, プロテインC減少, プロテインC増加, プロテインS異常, プロテインS増加, プロトロンビン量異常, プロトロンビン量減少, プロトロンビン時間異常, プロトロンビン時間延長, プロトロンビン時間比異常, プロトロンビン時間比増加, 赤血球数減少, 網状赤血球数増加, 網状赤血球百分率異常, 網状赤血球百分率増加, ラッセルクサリヘビ毒時間異常, トロンビン時間異常, トロンビン時間延長, トロンビン・アンチトロンビンⅠⅠⅠ複合体異常, トロンビン・アンチトロンビンⅠⅠⅠ複合体増加, フォンウィルブランド因子抗体陽性, フォンウィルブランド因子多量体異常
	出血関連用語（臨床検査用語を除く） SMQ	腹壁血腫, 腹壁出血, 異常消退出血, 急性出血性白質脳炎, 副腎血腫, 副腎出血, 肛門出血, 出血性肛門潰瘍, 吻合部出血, 出血性吻合部潰瘍, 動脈瘤破裂, 肛門直腸静脈瘤出血, 分娩前出血, 大動脈瘤破裂, 大動脈解離破裂, 大動脈壁内血腫, 大動脈破裂, 適用部位出血, 適用部位血腫, 動脈出血, 動静脈瘻部位血腫, 動静脈瘻部位出血, 動静脈グラフト部位血腫, 動静脈グラフト部位出血, 収れん薬療法, 心房破裂, 耳介血腫, 大脳基底核出血, 膀胱タンポナーデ, 分娩前後出血, 出血性静脈瘤, 血性水疱, 尿中血, 尿中血陽性, 血性分泌物, 血性腹膜透析排液, 脳幹出血, 乳房血腫, 乳房出血, 子宮広間膜血腫, 気管支出血, 頸動脈瘤破裂, カテーテル留置部位血腫, カテーテル留置部位出血, 頭血腫, 小脳血腫, 小脳出血, 梅毒

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		性脳動脈瘤破裂, 出血性脳動静脈奇形, 脳血腫, 脳出血, 胎児脳出血, 新生児脳出血, 外傷性脳出血, 脳微小出血, 子宮頸部血腫, 子宮頸部出血, 脈絡膜血腫, 脈絡膜出血, 慢性胃腸出血, 毛様体出血, 性交出血, 結腸血腫, 結膜出血, 挫傷, 角膜出血, カレン徴候, 出血性膀胱炎, 血性下痢, 播種性血管内凝固, 出血性腸憩室炎, 出血性腸憩室, 出血性十二指腸潰瘍, 出血性十二指腸炎, 機能障害性子宮出血, 耳出血, 斑状出血, 出血性脳炎, 出血性腸炎, 鼻出血, 失血, 硬膜外血腫, 血液溢出, 眼出血, 眼瞼出血, 胎児・母体間出血, 胃出血, 出血性胃潰瘍, 閉塞性出血性胃潰瘍, 穿孔性胃潰瘍, 胃静脈瘤出血, 出血性アルコール胃炎, 出血性胃炎, 胃十二指腸出血, 出血性胃十二指腸炎, 出血性胃腸管血管異形成, 胃腸出血, 出血性胃腸潰瘍, 性器出血, 歯肉出血, 移植部位出血, 出血性関節症, 吐血, 血便排泄, 血腫, 血腫除去, 血腫感染, 卵管留血症, 血精液症, 鼓室内出血, 血尿, 外傷性血尿, 血性胆汁, 血友病性関節症, 咯血, 出血, 冠動脈出血, 胎児出血, 頭蓋内出血, 新生児出血, 皮下出血, 表皮下出血, 尿路出血, 出血性貧血, 出血性動静脈奇形, 血性腹水, 出血性脳梗塞, 出血性素因, 新生児出血性疾患, 出血性障害, 出血性びらん性胃炎, 出血性肝嚢胞, 出血性梗塞, 出血性卵嚢胞, 出血性卒中, 卒中の出血性変化, 出血性腫瘍壊死, 出血性蕁麻疹, 出血性血管炎, 痔出血, 止血, 血胸, ヘノッホ・シェーンライン紫斑病, 肝臓血管腫破裂, 肝血腫, 肝出血, 遺伝性出血性毛細血管拡張症, 前房出血, 埋込み部位血腫, 埋込み部位出血, 切開部位血腫, 切開部位出血, 内出血発生の増加傾向, 人工流産による出血, 注入部位血腫, 注入部位出血, 注射部位血腫, 注射部位出血, 腸出血, 腹腔内血腫, 腹腔内出血, 脳内血腫除去術, 頭蓋内血腫, 頭蓋内腫瘍出血, 分娩時出血, 脳室内出血, 新生児脳室内出血, 虹彩出血, 涙器出血, 大腸出血, 出血性大腸潰瘍, 喉頭血腫, 喉頭出血, 口唇血腫, 口唇出血, 下部消化管出血, マヨッキ紫斑病, マロリー・ワイス症候群, 縦隔血腫, 縦隔出血, メレナ, 新生児メレナ, 髄膜出血, 機能性子宮出血, 月経過多, 腸間膜血腫, 腸間膜出血, 不正子宮出血, 口腔内出血, 粘膜出血, 筋肉内出血, 心筋出血, 心筋断裂, 母斑出血, 爪床出血, 出血性腎炎, 血性乳頭滲出液, 眼球後出血, 食道出血, 食道潰瘍出血, 食道静脈瘤出血, 出血性食道炎, 術中出血, 視神経乳頭出血, 視神経鞘出血, 骨出血, 卵嚢血腫, 卵嚢出血, 脾臓出血, 出血性脾炎, 乳頭筋出血, 副鼻腔血腫, 副甲状腺出血, 耳下腺出血, 骨盤血腫, 産科的骨盤

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		血腫, 骨盤内出血, 陰茎血腫, 陰茎出血, 出血性消化性潰瘍, 心嚢内出血, 会陰血腫, 眼窩周囲血腫, 腎周囲血腫, 腹膜血腫, 腹膜出血, 点状出血, 咽頭血腫, 咽頭出血, 下垂体出血, 前置胎盤による出血, 胸腔内出血, 頻発過多月経, 流産後の出血, 処置後血腫, 処置後血尿, 処置後出血, 閉経後出血, 分娩後出血, 胎盤早期剥離, 処置による出血, 出血性直腸炎, 前立腺出血, 肺胞出血, 肺血腫, 肺出血, 穿刺部位出血, 紫斑, 新生児紫斑, 老人性紫斑, 被殻出血, 直腸出血, 出血性直腸潰瘍, 腎嚢胞出血, 腎血腫, 腎出血, 気道出血, 新生児気道出血, 網膜出血, 出血性網膜症, 後腹膜血腫, 後腹膜出血, 胎盤後血腫, 破裂性脳動脈瘤, 強膜出血, 陰嚢血腫, 陰嚢血腫, 出血性ショック, 皮膚出血, 出血性皮膚潰瘍, 小腸出血, 出血性小腸潰瘍, 軟部組織出血, 精索出血, 脊髓出血, 脊髓硬膜外出血, 脊髓血腫, 脾血腫, 脾臓出血, 脾静脈瘤出血, 線状出血, 特発性血腫, 出血性口内炎, くも膜下出血, 新生児くも膜下出血, 皮下血腫, 硬膜下血腫, 硬膜下血腫除去, 硬膜下出血, 新生児硬膜下出血, 帽状腱膜下血腫, 精巣出血, 視床出血, 分娩第3期出血, 胸部出血, 血小板減少性紫斑病, 血栓性血小板減少性紫斑病, 甲状腺出血, 舌血腫, 舌出血, 扁桃出血, 齒槽出血, 気管出血, 外傷性血腫, 外傷性出血, 外傷性頭蓋内出血, 腫瘍出血, 潰瘍性出血, 臍帯出血, 臍血腫, 臍出血, 上部消化管出血, 尿管出血, 尿道出血, 膀胱出血, 尿生殖器出血, 子宮血腫, 子宮出血, ワクチン接種部位血腫, ワクチン接種部位出血, 腔血腫, 腔出血, 静脈瘤破裂, 血管偽動脈瘤破裂, 血管性紫斑病, 血管破裂, 静脈出血, 心室破裂, 血管穿刺部位血腫, 血管穿刺部位出血, 硝子体出血, 外陰血腫, 外陰部血腫除去, 外陰部出血, 創傷出血
	消化管の出血 SMQ	肛門出血, 出血性肛門潰瘍, 吻合部出血, 出血性吻合部潰瘍, 慢性胃腸出血, 結腸血腫, 血性下痢, 出血性腸憩室炎, 十二指腸手術, 出血性十二指腸潰瘍, 出血性十二指腸炎, 出血性腸炎, 胃出血, 胃内容物潜血陽性, 出血性胃潰瘍, 閉塞性出血性胃潰瘍, 胃静脈瘤出血, 出血性アルコール胃炎, 出血性胃炎, 胃十二指腸出血, 出血性胃十二指腸炎, 胃腸吻合部漏出, 胃腸出血, 出血性胃腸潰瘍, 吐血, 血便排泄, 出血性びらん性胃炎, 痔出血, 腸血腫, 腸出血, 腸管ポリープ出血, 大腸出血, 出血性大腸潰瘍, 下部消化管出血, マロリー・ワイス症候群, メレナ, 新生児メレナ, 便潜血陽性, 食道出血, 食道潰瘍出血, 食道静脈瘤出血, 出血性食道炎, 出血性消化性潰瘍, 出血性直腸炎, 直腸出血, 出血性直腸潰

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		瘍, 小腸出血, 出血性小腸潰瘍, 潰瘍性出血, 上部消化管出血
Effects on Glucose	高血糖／糖尿病の発症 SMQ	血中1, 5-アンヒドログルシトール減少, 血中ブドウ糖増加, 糖尿病を合併する妊娠, 糖尿病, コントロール不良の糖尿病, 高浸透圧をとまう糖尿病, 糖尿病性昏睡, 糖尿病性肝障害, 糖尿病性高血糖昏睡, 糖尿病性高浸透圧性昏睡, 糖尿病性ケトアシドーシス, 糖尿病性ケトアシドーシス性高血糖昏睡, フルクトサミン増加, 妊娠糖尿病, 耐糖能障害, 妊娠時の耐糖能障害, 尿中ブドウ糖陽性, 糖尿, 妊娠糖尿, グリコヘモグロビン増加, 高血糖, 高血糖性高浸透圧性非ケトン性症候群, 高血糖性痙攣, 高血糖性意識消失, 空腹時血中ブドウ糖不良, インスリン抵抗性, インスリン抵抗性症候群, インスリン抵抗性糖尿病, インスリン必要2型糖尿病, ケトアシドーシス, ケトン尿, ケトーシス, 成人潜在性自己免疫性糖尿病, 代謝症候群, 新生児糖尿病, 膵性糖尿病, 1型糖尿病, 2型糖尿病, 尿中ケトン体陽性, 異常体重減少, 異常体重増加, アシドーシス, 意識変容状態, 抗GAD抗体陽性, 抗インスリン抗体増加, 抗インスリン抗体陽性, 抗インスリン受容体抗体増加, 抗インスリン受容体抗体陽性, 抗膵島細胞抗体陽性, 血中コレステロール増加, 血中ブドウ糖異常, 血中ブドウ糖変動, 血中インスリン異常, 血中インスリン減少, 血中乳酸増加, 血液浸透圧上昇, 血中トリグリセリド増加, ボディ・マス・インデックス減少, ボディ・マス・インデックス増加, 中心性肥満, 昏睡, 脱水, 意識レベルの低下, 耐糖能低下, ブドウ糖負荷試験異常, 空腹, 高コレステロール血症, 高乳酸血症, 高脂血症, 高浸透圧状態, 過食, 高トリグリセリド血症, 低血糖症, 低インスリン血症, インスリン分泌障害, 食欲亢進, インスリン必要量の増加, インスリン自己免疫症候群, インスリン耐性試験異常, 乳酸アシドーシス, 脂質増加, 意識消失, 代謝性アシドーシス, 肥満, 過体重, 多飲症, 多尿, 刺激反応遅滞, 口渇, 過少体重, 刺激無反応, 体重減少, 体重増加
	高血糖／糖尿病の発症 CMQ	血中1, 5-アンヒドログルシトール減少, 血中ブドウ糖増加, 糖尿病を合併する妊娠, 糖尿病, コントロール不良の糖尿病, 高浸透圧をとまう糖尿病, 糖尿病性昏睡, 糖尿病性肝障害, 糖尿病性高血糖昏睡, 糖尿病性高浸透圧性昏睡, 糖尿病性ケトアシドーシス, 糖尿病性ケトアシドーシス性高血糖昏睡, フルクトサミン増加, 妊娠糖尿病, 耐糖能障害, 妊娠時の耐糖能障害, 尿中ブドウ糖陽性, 糖尿, 妊娠糖尿, グリコヘモ

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		グロビン増加, 高血糖, 高血糖性高浸透圧性非ケトン性症候群, 高血糖性痙攣, 高血糖性意識消失, 空腹時血中ブドウ糖不良, インスリン抵抗性, インスリン抵抗性症候群, インスリン抵抗性糖尿病, インスリン必要 2 型糖尿病, ケトアシドーシス, ケトン尿, ケトーシス, 成人潜在性自己免疫性糖尿病, 代謝症候群, 新生児糖尿病, 膵性糖尿病, 1 型糖尿病, 2 型糖尿病, 尿中ケトン体陽性, 異常体重減少, 異常体重増加, アシドーシス, 意識変容状態, 抗 G A D 抗体陽性, 抗インスリン抗体増加, 抗インスリン抗体陽性, 抗インスリン受容体抗体増加, 抗インスリン受容体抗体陽性, 抗膵島細胞抗体陽性, 血中コレステロール増加, 血中ブドウ糖異常, 血中ブドウ糖変動, 血中インスリン異常, 血中インスリン減少, 血中乳酸増加, 血液浸透圧上昇, 血中トリグリセリド増加, ボディ・マス・インデックス減少, ボディ・マス・インデックス増加, 中心性肥満, 昏睡, 脱水, 意識レベルの低下, 耐糖能低下, ブドウ糖負荷試験異常, 空腹, 高コレステロール血症, 高乳酸血症, 高脂血症, 高浸透圧状態, 過食, 高トリグリセリド血症, 低血糖症, 低インスリン血症, インスリン分泌障害, 食欲亢進, インスリン必要量の増加, インスリン自己免疫症候群, インスリン耐性試験異常, 乳酸アシドーシス, 脂質増加, 意識消失, 代謝性アシドーシス, 肥満, 過体重, 刺激反応遅滞, 過少体重, 刺激無反応, 体重減少, 体重増加
ADPKD-related Conditions	腎臓痛 CMQ	腎臓痛, 側腹部痛, 腰痛血尿症候群
	腎結石症 CMQ	腎結石症, 腎結石除去, 腎結石症予防
	血尿 CMQ	血尿, 腰痛血尿症候群, 外傷性血尿, 処置後血尿
	アルブミン尿 CMQ	アルブミン尿, ミクロアルブミン尿
	尿路感染 CMQ	サイトメガロウイルス性尿路感染, 大腸菌性尿路感染, 泌尿生殖器感染, 尿路感染予防, レンサ球菌性尿路感染, 尿路感染, 細菌性尿路感染, 腸球菌性尿路感染, 真菌性尿路感染, シュードモナス性尿路感染, ブドウ球菌性尿路感染, ウイルス性尿路感染
	貧血 CMQ	貧血, 葉酸欠乏性貧血, 自己免疫性溶血性貧血, ハインツ小体貧血, 大球性貧血, 巨赤芽球性貧血, 慢性疾患の貧血, 悪性疾患下の貧血, 妊娠貧血, 術後貧血, 貧血予防, 脾性貧血, ビタミン B 1 2 欠乏性貧血, ビタミン B 6 欠乏性貧血, 再生不良性貧血, 自己免疫性再生不良性貧血, Cardiac haemolytic anaemia, 冷式溶血性貧血, 先天性貧血, 先天性再生不良性貧血,

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		クームス試験陰性溶血性貧血, クームス試験陽性溶血性貧血, 欠乏性貧血, 溶血性貧血, 酵素特異性溶血性貧血, 溶血性黄疸性貧血, 出血性貧血, 遺伝性鉄芽球性貧血, ヘキソキナーゼ欠乏性貧血, 高色素性貧血, 低色素性貧血, 低形成性貧血, 鉄欠乏性貧血, 白赤芽球性貧血, 黒血症, 微小血管症性溶血性貧血, 小球性貧血, 腎性貧血, 正色素性正球性貧血, 悪性貧血, 蛋白欠乏性貧血, ビルビン酸キナーゼ欠乏性貧血, 不応性貧血, 芽球増加を伴う不応性貧血, 環状鉄芽球を伴う不応性貧血, 鎌状赤血球貧血, 鎌状赤血球貧血クリーゼ, 鉄芽球性貧血, 球状赤血球性貧血, 棘細胞性貧血, 温式溶血性貧血
	結腸憩室炎 CMQ	憩室炎, 出血性腸憩室炎, メッケル憩室炎, 食道憩室炎, 憩室周囲炎, 憩室穿孔, 憩室切除, 憩室, 胃憩室, 腸憩室, 出血性腸憩室, 食道憩室, 憩室周膿瘍, 憩室周囲炎
	血管異常 CMQ	動脈瘤, 動静脈瘤, 血管瘤修復, 動脈瘤破裂, 動脈瘤切除, 大動脈瘤, 大動脈瘤修復, 大動脈瘤破裂, 梅毒性大動脈瘤, 動脈瘤修復, 心臓瘤, 心臓瘤修復, 心偽動脈瘤, 頸動脈瘤破裂, 頸動脈瘤, 梅毒性脳動脈瘤破裂, シャルコ・ブシャー微小動脈瘤, 冠動脈瘤, 解離性冠動脈瘤, 大腿動脈瘤, 肝動脈瘤, 感染性動脈瘤, 脳内動脈瘤手術, 胸部大動脈瘤修復, 頭蓋内動脈瘤, 末梢動脈瘤, 肺動脈瘤, 腎動脈瘤, 網膜血管瘤, 破裂性脳動脈瘤, 脾臓動脈瘤, 鎖骨下動脈瘤, 血管偽動脈瘤, 血管偽動脈瘤破裂, 静脈性血管瘤
	腹部および単径ヘルニア CMQ	腹部ヘルニア, 壊疽性腹部ヘルニア, 閉塞を伴う腹部ヘルニア, 腹部ヘルニア修復, 腹部絞扼性ヘルニア, 壊疽性ヘルニア, 閉塞性ヘルニア, ヘルニア痛, ヘルニア修復, 内臓ヘルニア, 単径ヘルニア, 壊疽性単径ヘルニア, 単径部ヘルニア修復, 絞扼性単径ヘルニア, 閉塞性単径ヘルニア, 絞扼性ヘルニア修復, 臍ヘルニア, 壊疽性臍ヘルニア, 臍ヘルニア穿孔, 臍帯ヘルニア修復, 閉塞性臍ヘルニア
	肝嚢胞 CMQ	肝嚢胞, 肝嚢胞感染, 肝嚢胞破裂, 出血性肝嚢胞
	その他嚢胞 CMQ	脳嚢胞, 肝嚢胞, 卵巣嚢胞, 脾嚢胞, 腎嚢胞, 腎嚢胞感染, 脾嚢胞, 精巣嚢胞, 甲状腺嚢腫, 子宮嚢胞
Arrhythmia-related Disorders	不整脈に関連する臨床検査、徴候および症状 SMQ	変時性応答不全, 心電図再分極異常, 心電図RR間隔延長, 心電図U波異常, 心電図2相性U波, ギャロップ・リズム陽性, 心突然死, 徐脈, 心停止, 心臓死, 心電図テレメトリー異常, 心肺停止, 心電図異常, 外来心電図異常, 心電図変化, 心拍数異常, 心拍数減少, 心拍数増加, 意識消失, 動悸,

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TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		リバウンド頻脈, 突然死, 失神, 頻脈, 発作性頻脈
	非特異的不整脈用語 SMQ	不整脈, 交互脈, 心拍数不整, ペースメーカー原性不整脈, ペースメーカー症候群, 発作性不整脈, 無脈性電気活動, 再灌流性不整脈, 離脱性不整脈
Bradyarrhythmias	SMQ	徐脈性不整脈, 心室無収縮
Tachyarrhythmias	上室性頻脈性不整脈 SMQ	上室性不整脈, 心房細動, 心房粗動, 心房副収縮, 心房頻脈, 上室性期外収縮, 上室性頻脈性不整脈, 心電図P波逆転, 心電図異常P波, 逆行性P波, 洞性頻脈, 上室性頻脈
	非特異的頻脈性不整脈用語 SMQ	房室興奮の異常, 房室性期外収縮, 心粗動, 期外収縮, 頻脈性不整脈
	心室性頻脈性不整脈 SMQ	頻脈性固有心室調律, 心細動, 副収縮, 固有心室調律, トルサーードポアント, 心室性不整脈, 心室性期外収縮, 心室細動, 心室粗動, 心室性副収縮, 心室早期興奮, 心室性頻脈性不整脈, 心室性頻脈
Conduction Disorders	伝導障害 SMQ	心臓副伝導路, アダムス・ストークス症候群, 死戦調律, 心房内伝導時間遅延, 房室ブロック, 完全房室ブロック, 第一度房室ブロック, 第二度房室ブロック, 房室伝導時間短縮, 房室解離, 二束ブロック, ブルガダ症候群, 脚ブロック, 両側性脚ブロック, 左脚ブロック, 右脚ブロック, 伝導障害, 心電図δ波異常, 心電図PQ間隔延長, 心電図PR延長, 心電図PR短縮, 心電図QRS群延長, 心電図QT延長, 心電図再分極異常, ルネーグル病, QT延長症候群, 洞房ブロック, 三束ブロック, 心室同期不全, ウォルフ・パーキンソン・ホワイト症候群
	洞結節機能障害 SMQ	結節性不整脈, 結節性調律, 洞不全症候群, 洞停止, 洞性不整脈, 洞性徐脈, 移動性ペースメーカー
Myocardial Infarction/Ischemic Heart Disease	心筋梗塞 SMQ	急性冠動脈症候群, 急性心筋梗塞, 血中クレアチンホスホキナーゼMB異常, 血中クレアチンホスホキナーゼMB増加, 冠動脈塞栓症, 冠動脈閉塞, 冠動脈再閉塞, 冠動脈血栓症, 冠動脈バイパス血栓症, コーニス症候群, 心筋梗塞, 心筋再灌流障害, 乳頭筋梗塞, 処置後心筋梗塞, 梗塞後狭心症, 無症候性心筋梗塞, トロポニンI増加, トロポニン増加, トロポニンT増加, 血中クレアチンホスホキナーゼ異常, 血中クレアチンホスホキナーゼ増加, 心筋酵素増加, 心電図異常Q波, 心電図ST部分異常, 心電図ST部分上昇, 心電図ST-T部分上昇, 梗塞, 心筋血流スキャン異常, 移植血管閉塞
	その他の虚血性心疾患 SMQ	狭心症, 不安定狭心症, 冠動脈硬化症, 冠動脈攣縮, 冠動脈形成, 冠動脈

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		ステント挿入, 冠動脈バイパス, 冠動脈疾患, 冠動脈解離, 冠動脈不全, 冠動脈再狭窄, 冠動脈狭窄, 冠動脈内膜摘除, 冠動脈ノーリフロー現象, 冠動脈入口部狭窄, 冠動脈再建, 解離性冠動脈瘤, 心筋虚血の心電図所見, 体外カウターパルスーション, 冠動脈出血, ステント内冠動脈再狭窄, 虚血性心筋症, 微小血管性狭心症, 心筋虚血, 経皮的冠インターベンション, プリンツメタル狭心症, ストレス心筋症, 鎖骨下冠動脈スチール症候群, 心内膜下虚血, 冠血管造影異常, 心臓負荷試験異常, 冠動脈コンピュータ断層撮影異常, 心電図S T部分下降, 心電図S T-T部分異常, 心電図S T-T部分下降, 心電図異常T波, 心電図T波逆転, 運動負荷心電図異常, 運動試験異常, 負荷心エコー像異常
Hepatic Disorders	非感染性肝炎 SMQ	急性肝移植片対宿主病, アレルギー性肝炎, 自己免疫性肝炎, 慢性肝炎, 肝細胞融解性肝炎, 肝移植片対宿主病, 肝炎, 急性肝炎, 胆汁うっ滞性肝炎, 慢性活動性肝炎, 慢性持続性肝炎, 劇症肝炎, 中毒性肝炎, 虚血性肝炎, ループス肝炎, 放射線肝炎, 肉芽腫性肝疾患, 肝サルコイドーシス
	肝臓に起因する胆汁うっ滞および黄疸 SMQ	ビリルビン排泄障害, 胆血症, 胆汁うっ滞, 胆汁うっ滞性肝損傷, 胆汁うっ滞性そう痒症, 胆汁うっ滞性肝炎, 高ビリルビン血症, 黄疸指数上昇, 黄疸, 胆汁うっ滞性黄疸, 肝細胞性黄疸, 混合型肝損傷, 黄疸眼, 胆汁分泌不全, 黄色皮膚
	肝臓関連臨床検査、徴候および症状 SMQ	アラニン・アミノトランスフェラーゼ異常, アラニン・アミノトランスフェラーゼ増加, アンモニア異常, アンモニア増加, 腹水, アスパラギン酸アミノトランスフェラーゼ異常, アスパラギン酸アミノトランスフェラーゼ増加, 細菌感染腹水, 胆汁量異常, 胆汁量減少, 抱合ビリルビン異常, 抱合ビリルビン増加, 肝生検異常, 血中ビリルビン異常, 血中ビリルビン増加, 血中非抱合ビリルビン増加, プロモスルフォフタレイン検査異常, メズサ頭, チャイルド・ピュー・ターコットスコア増加, 肝性口臭, ガラクトース排泄能検査異常, ガラクトース排泄能検査値減少, ユーグルタミルトランスフェラーゼ異常, ユーグルタミルトランスフェラーゼ増加, グアナーゼ増加, ヘパプラスチン異常, ヘパプラスチン減少, 肝動脈血流減少, 肝臓うっ血, 肝酵素異常, 肝酵素低下, 肝酵素上昇, 肝機能異常, 肝性胸水, 肝腫瘍, 肝臓痛, 肝分離, 肝血管抵抗増加, 肝胆道スキャン異常, 肝腫大, 肝脾腫大, 高アンモニア血症, 高ビリルビン血症, 胆汁過多, 高トランスアミナーゼ血症, ハイの法則例, カイザー・フライシャー輪, 肝機

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		能検査異常, 肝硬結, 季肋下肝触知, 肝スキャン異常, 肝圧痛, m-A S T増加, 総分岐鎖アミノ酸/チロシンモル比, 肝疾患による浮腫, 肝周囲不快感, 門脈逆流, 総胆汁酸増加, トランスアミナーゼ異常, トランスアミナーゼ上昇, 肝超音波検査異常, 尿中ビリルビン増加, 肝胆道X線異常, 5-ヌクレオチダーゼ上昇, 血中アルカリホスファターゼ異常, 血中アルカリホスファターゼ増加, 血中コリンエステラーゼ異常, 血中コリンエステラーゼ減少, 胆汁分泌不全, グルタミン酸脱水素酵素増加, 血性腹水, 低アルブミン血症, ロイシンアミノペプチダーゼ上昇, 門脈周囲浮腫, 腹腔液蛋白異常, 腹腔液蛋白減少, 腹腔液蛋白増加, 胆道気腫, 門脈血流減少, 門脈圧上昇, レチノール結合蛋白減少, 尿中ウロビリノーゲン減少, 尿中ウロビリノーゲン増加
	肝臓に関連する凝固および出血障害 SMQ	アンチトロンビン I I I 減少, 血中フィブリノゲン異常, 血中フィブリノゲン減少, 血中トロンビン異常, 血中トロンビン減少, 血中トロンボプラスチン異常, 血中トロンボプラスチン減少, 凝固因子減少, 凝固第 I X 因子量異常, 凝固第 I X 因子量減少, 凝固第 V 因子量異常, 凝固第 V 因子量減少, 凝固第 V I I 因子量異常, 凝固第 V I I 因子量減少, 凝固第 X 因子量異常, 凝固第 X 因子量減少, 凝固低下状態, 低フィブリノゲン血症, 低プロトロンビン血症, 低トロンビン血症, 低トロンボプラスチン血症, I N R 異常, I N R 増加, プロテイン C 減少, プロテイン S 異常, プロテイン S 減少, プロトロンビン量異常, プロトロンビン量減少, プロトロンビン時間異常, プロトロンビン時間延長, プロトロンビン時間比異常, プロトロンビン時間比増加, トロンビン時間異常, トロンビン時間延長
	肝不全、肝線維症、肝硬変およびその他の肝細胞障害 SMQ	急性肝不全, 急性黄色肝萎縮, 腹水, 固定姿勢保持困難, 細菌感染腹水, 胆汁性肝硬変, 原発性胆汁性肝硬変, 胆管線維症, 胆汁うっ滞性肝損傷, 慢性肝不全, 肝性昏睡, 特発性肝硬変, 糖尿病性肝障害, 十二指腸静脈瘤, 胃静脈瘤, 胃静脈瘤出血, 肝切除, 肝萎縮, 肝石灰化, 肝硬変, 肝性脳症, 肝性脳症予防, 肝不全, 肝線維症, 肝性胸水, 肝好酸球浸潤, 肝病変, 肝壊死, 脂肪肝, 劇症肝炎, 肝胆道系疾患, 肝細胞泡沫細胞症候群, 肝細胞損傷, 肝肺症候群, 肝腎不全, 肝腎症候群, 肝毒性, 腸静脈瘤, 肝小腸移植, 肝障害, 肝損傷, 肝臓手術, 肝移植, ルポイド肝硬変症, 混合型肝損傷, 結節性再生性過形成, 肝疾患による浮腫, 食道静脈瘤出血, 門脈圧亢進症, 門脈圧亢進性腸症, 門脈圧亢進性胃障害, 門脈三分岐炎, 門脈肺高血圧症,

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TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		肝腎移植, 門脈逆流, ライ症候群, レイノルズ症候群, 脾静脈瘤, 脾静脈瘤出血, 亜急性肝不全, 食道静脈瘤, 肛門直腸静脈瘤, 肛門直腸静脈瘤出血, 腹腔静脈シャント, 門脈シャント, 肝過小グラフト症候群, くも状母斑
Glaucoma	SMQ	閉塞隅角緑内障, 境界域緑内障, 発達緑内障, 糖尿病性緑内障, 眼底検査異常, 緑内障, 緑内障薬物療法, 緑内障手術, 外傷性緑内障, 緑内障性毛様体炎発症, 緑内障性視神経乳頭萎縮, 隅角鏡検査異常, 光輪視, 眼圧変動, 眼圧上昇, 眼圧検査異常, 虹彩切開, 視覚コントラスト感度低下, 正常眼圧緑内障, 高眼圧症, 開放隅角緑内障, 眼部液ドレナージ, 視神経乳頭辺縁不鮮明, 視神経乳頭陥凹／乳頭比増加, 視神経乳頭陥凹, 水晶体融解性緑内障, 水晶体線維柱帯切除, 色素性緑内障, 瞳孔対光反射試験異常, 細隙灯試験異常, 線維柱帯切除, 線維柱帯形成, 視野検査異常, 黒内障, 一過性黒内障, 前房隅角血管新生, 濾過胞炎, 失明, 昼盲, 一過性失明, 片側失明, 白内障, 結膜濾過胞漏出, 眼電図異常, 眼レーザー手術, 眼痛, 顔面痛, グレア, 虹彩分離, 虹彩萎縮, 虹彩手術, 前房狭隅角, 夜盲, 眼充血, 眼底血圧検査異常, 視神経乳頭障害, 羞明, 瞳孔ブロック, 網膜図異常, ザイデル試験陽性, テノン嚢胞, 霧視, 視力低下, 一過性視力低下, 視覚誘発電位異常
Potential Immune- mediated Reactions	アナフィラキシー反応 SMQ	アナフィラキシー反応, アナフィラキシーショック, アナフィラキシー性輸血反応, アナフィラキシー様反応, アナフィラキシー様ショック, 循環虚脱, 初回透析症候群, コーニス症候群, ショック, 1型過敏症, 急性呼吸不全, 喘息, 気管支浮腫, 気管支痙攣, 心肺機能窮迫, 胸部不快感, 息詰まり, 息詰まり感, 口周囲浮腫, 咳嗽, 呼吸困難, 過換気, 喉頭障害による呼吸困難, 喉頭浮腫, 喉頭痙攣, 喉頭気管浮腫, 鼻閉塞, 口腔浮腫, 口腔咽頭痙攣, 口腔咽頭腫脹, 呼吸停止, 呼吸窮迫, 呼吸不全, 可逆性気道閉塞, 異物感, くしゃみ, 上気道性喘鳴, 舌腫脹, 頻呼吸, 咽喉絞扼感, 舌浮腫, 気管閉塞, 気管浮腫, 上気道閉塞, 喘鳴, アレルギー性浮腫, 血管浮腫, チアノーゼ, 紅斑, 眼球浮腫, 眼そう痒症, 眼部腫脹, 眼瞼浮腫, 顔面浮腫, 固定疹, 潮紅, 全身紅斑, 注射部位蕁麻疹, 口唇浮腫, 口唇腫脹, 眼充血, 浮腫, 眼窩周囲浮腫, そう痒症, アレルギー性そう痒症, 全身性そう痒症, 発疹, 紅斑性皮疹, 全身性皮疹, そう痒性皮疹, 皮膚腫脹, 腫脹, 顔面腫脹, 蕁麻疹, 丘疹状蕁麻疹, 血圧低下, 拡張期血圧低下, 収縮期血圧低下,

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		心停止, 心肺停止, 心血管不全, 拡張期低血圧, 低血圧
	血管浮腫 SMQ	アレルギー性浮腫, 血管浮腫, 口周囲浮腫, 結膜浮腫, 角膜浮腫, 喉頭蓋浮腫, 眼球浮腫, 眼部腫脹, 眼瞼浮腫, 顔面浮腫, 歯肉浮腫, 歯肉腫脹, グライヒ症候群, 遺伝性血管浮腫, 特発性蕁麻疹, 喉頭浮腫, 喉頭気管浮腫, 輪部腫脹, 口唇浮腫, 口唇腫脹, 眼呼吸器症候群, 口腔浮腫, 口腔咽頭腫脹, 口蓋浮腫, 眼窩周囲浮腫, 咽頭浮腫, 強膜浮腫, 小腸血管浮腫, 顔面腫脹, 舌腫脹, 舌浮腫, 気管浮腫, 蕁麻疹, コリン性蕁麻疹, 慢性蕁麻疹, 丘疹状蕁麻疹, 耳介腫脹, 乳房浮腫, 乳房腫脹, 息詰まり, 息詰まり感, 薬物過敏症, 気管内挿管, 消化管浮腫, 全身性浮腫, 性器腫脹, 過敏症, 喉頭障害による呼吸困難, 喉頭閉塞, 局所腫脹, 限局性浮腫, 鼻閉塞, 鼻浮腫, 乳頭浮腫, 乳頭腫脹, 閉塞性気道障害, 浮腫, 性器浮腫, 粘膜浮腫, 新生児浮腫, 末梢性浮腫, 眼窩浮腫, 陰茎浮腫, 陰茎腫脹, 新生児末梢性浮腫, 可逆性気道閉塞, 陰嚢浮腫, 陰嚢腫脹, 皮膚浮腫, 皮膚腫脹, 上気道性喘鳴, 窒息感, 腫脹, 咽喉絞扼感, 気管閉塞, 気管切開, 1 型過敏症, 上気道閉塞, 腔浮腫, 内臓浮腫, 外陰浮腫, 外陰腔腫脹, 喘鳴
	アナフィラキシーショック SMQ	アナフィラキシー反応, アナフィラキシーショック, アナフィラキシー性輸血反応, アナフィラキシー様反応, アナフィラキシー様ショック, 循環虚脱, 血液分布異常性ショック, ショック, 急性腎前性腎不全, 急性呼吸不全, 無尿, 血圧測定不能, 脳低灌流, 新生児灰白症候群, 肝臓うっ血, 肝頸静脈逆流, 肝腎不全, 低灌流, 頸静脈拡張, 多臓器不全, 心筋抑制, 新生児無尿, 新生児多臓器不全, 新生児呼吸不全, 臓器不全, プロポフォール注入症候群, 腎不全, 急性腎不全, 新生児腎不全, 呼吸不全
Neoplasms	悪性腫瘍 SMQ	5 q マイナス症候群, 腹壁の悪性新生物, 末端部黒子様黒色腫第 1 期, 末端部黒子様黒色腫第 2 期, 末端部黒子様黒色腫第 3 期, 末端部黒子様黒色腫第 4 期, 末端部黒子様黒色腫, 病期不明, 急性混合性白血病, 急性白血病, 急性白血病、寛解期, 急性リンパ性白血病, 急性リンパ性白血病（寛解期）, 再発急性リンパ性白血病, 急性巨核芽球性白血病, 急性巨核芽球性白血病（寛解期）, 急性単球性白血病, 急性単球性白血病（寛解期）, 急性骨髄性白血病, 急性骨髄性白血病（寛解期）, 再発急性骨髄性白血病, 急性骨髄単球性白血病, 急性前骨髄球性白血病, 腺癌, 子宮頸部腺癌, 膵腺癌, 腺様嚢胞癌, 子宮頸部腺扁平上皮癌, 腺扁平上皮癌, 肺腺扁平上皮癌, 再発肺腺扁平上皮癌, 肺腺扁平上皮癌第 0 期, 肺腺扁平上皮癌第 1 期, 肺

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		腺扁平上皮癌第2期, 肺腺扁平上皮癌第3期, 肺腺扁平上皮癌第4期, 副腎癌, 転移性副腎癌, 副腎皮質癌, 成人T細胞リンパ腫・白血病, 再発成人T細胞リンパ腫・白血病, 治療抵抗性成人T細胞リンパ腫・白血病, 成人T細胞リンパ腫・白血病第1期, 成人T細胞リンパ腫・白血病第2期, 成人T細胞リンパ腫・白血病第3期, 成人T細胞リンパ腫・白血病第4期, 感覚神経芽腫, 無白血病性白血病, 胞巣状軟部肉腫, 転移性胞巣状軟部肉腫, 限局性胞巣状軟部肉腫, 再発胞巣状軟部肉腫, 肛門癌, 転移性肛門癌, 再発肛門癌, 肛門癌第0期, 肛門癌第1期, 肛門癌第2期, 肛門癌第3期, 肛門癌第4期, 退形成星細胞腫, 未分化大細胞型リンパ腫、T細胞およびヌル細胞型, 再発未分化大細胞型リンパ腫、T細胞およびヌル細胞型, 治療抵抗性未分化大細胞型リンパ腫、T細胞およびヌル細胞型, 未分化大細胞型リンパ腫、T細胞およびヌル細胞型第1期, 未分化大細胞型リンパ腫、T細胞およびヌル細胞型第2期, 未分化大細胞型リンパ腫、T細胞およびヌル細胞型第3期, 未分化大細胞型リンパ腫、T細胞およびヌル細胞型第4期, 血管中心性リンパ腫, 再発血管中心性リンパ腫, 治療抵抗性血管中心性リンパ腫, 血管中心性リンパ腫第1期, 血管中心性リンパ腫第2期, 血管中心性リンパ腫第3期, 血管中心性リンパ腫第4期, 血管免疫芽球性T細胞性リンパ腫, 再発血管免疫芽球性T細胞性リンパ腫, 治療抵抗性血管免疫芽球性T細胞性リンパ腫, 血管免疫芽球性T細胞性リンパ腫第1期, 血管免疫芽球性T細胞性リンパ腫第2期, 血管免疫芽球性T細胞性リンパ腫第3期, 血管免疫芽球性T細胞性リンパ腫第4期, 血管肉腫, 転移性血管肉腫, 限局性血管肉腫, 再発血管肉腫, 星細胞腫, 悪性星細胞腫, 前駆B細胞型急性白血病, 基底細胞癌, 基底扁平上皮癌, 皮膚基底有棘細胞癌, B細胞性リンパ腫, 再発B細胞性リンパ腫, 治療抵抗性B細胞性リンパ腫, B細胞性リンパ腫第1期, B細胞性リンパ腫第2期, B細胞性リンパ腫第3期, B細胞性リンパ腫第4期, B細胞性小リンパ球性リンパ腫, 再発B細胞性小リンパ球性リンパ腫, 治療抵抗性B細胞性小リンパ球性リンパ腫, B細胞性小リンパ球性リンパ腫第1期, B細胞性小リンパ球性リンパ腫第2期, B細胞性小リンパ球性リンパ腫第3期, B細胞性小リンパ球性リンパ腫第4期, B細胞型急性白血病, 分類不能なB細胞性リンパ腫ハイグレード, 分類不能なB細胞性リンパ腫ローグレード, 胆管癌, 切除不能な胆管癌, 再発胆管癌, 切除可能な胆管癌, 胆管癌第0期,

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		胆管癌第1期, 胆管癌第2期, 胆管癌第3期, 胆管癌第4期, 転移性胆道癌, 再発膀胱腺癌, 膀胱腺癌第0期, 膀胱腺癌第1期, 膀胱腺癌第2期, 膀胱腺癌第3期, 膀胱腺癌第4期, 膀胱腺癌、病期不明, 膀胱癌, 再発膀胱癌, 膀胱癌第0期、上皮内癌を伴う, 膀胱癌第0期、上皮内癌を除く, 膀胱癌第1期、上皮内癌を伴う, 膀胱癌第1期、上皮内癌を除く, 膀胱癌第2期, 膀胱癌第3期, 膀胱癌第4期, 再発膀胱扁平上皮癌, 膀胱扁平上皮癌第0期, 膀胱扁平上皮癌第1期, 膀胱扁平上皮癌第2期, 膀胱扁平上皮癌第3期, 膀胱扁平上皮癌第4期, 膀胱扁平上皮癌、病期不明, 膀胱移行上皮癌, 転移性膀胱移行上皮癌, 再発膀胱移行上皮癌, 膀胱移行上皮癌第0期, 膀胱移行上皮癌第1期, 膀胱移行上皮癌第2期, 膀胱移行上皮癌第3期, 膀胱移行上皮癌第4期, 芽球発症, 骨髄性白血病の芽球発症, 転移性骨癌, 白血病細胞の骨髄浸潤, 腫瘍細胞の骨髄浸潤, 骨の悪性新生物, 骨肉腫, ボーエン病, 転移性脳悪性腫瘍, 脳の悪性新生物, 脳幹神経膠腫, 乳癌, 女性乳癌, 乳房の上皮内癌, 男性乳癌, 転移性乳癌, 再発乳癌, 乳癌第1期, 乳癌第2期, 乳癌第3期, 乳癌第4期, 乳房肉腫, 転移性乳房肉腫, 再発乳房肉腫, 気管支癌, 細気管支肺胞上皮癌, バーキット白血病, バーキットリンパ腫, 再発バーキットリンパ腫, 治療抵抗性バーキットリンパ腫, バーキットリンパ腫第1期, バーキットリンパ腫第2期, バーキットリンパ腫第3期, バーキットリンパ腫第4期, ブシュケ・レーベンシユタイン腫瘍, 癌、寛解期, カルチノイド腫瘍, 虫垂のカルチノイド腫瘍, 盲腸のカルチノイド腫瘍, 十二指腸のカルチノイド腫瘍, 消化管のカルチノイド腫瘍, 膵のカルチノイド腫瘍, 前立腺のカルチノイド腫瘍, 小腸のカルチノイド腫瘍, 胃のカルチノイド腫瘍, 肺カルチノイド腫瘍, 上皮内癌, 眼の上皮内癌, 陰茎上皮内癌, 皮膚上皮内癌, 気管の上皮内癌, 心臓の悪性新生物, 中枢神経系リンパ腫, 大脳神経芽腫, 転移性子宮頸部癌, 子宮頸部癌, 子宮頸部癌第0期, 子宮頸部癌第1期, 子宮頸部癌第2期, 子宮頸部癌第3期, 子宮頸部癌第4期, 緑色腫, 緑色腫（寛解期）, 軟骨肉腫, 転移性軟骨肉腫, 再発軟骨肉腫, 脊索腫, 絨毛癌, 脈絡膜黒色腫, 脈絡叢癌, 慢性好酸球性白血病, 慢性白血病, 慢性白血病、寛解期, 慢性リンパ性白血病, 慢性リンパ性白血病（寛解期）, 再発慢性リンパ性白血病, 治療抵抗性慢性リンパ性白血病, 慢性リンパ性白血病第0期, 慢性リンパ性白血病第1期, 慢性リンパ性白血病第2期, 慢性リンパ性白血病第3期,

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		慢性リンパ性白血病第4期, 慢性リンパ性白血病急性転化, 慢性骨髄性白血病, 慢性骨髄性白血病（寛解期）, 慢性骨髄性白血病急性転化, 慢性骨髄単球性白血病, 慢性骨髄単球性白血病（寛解期）, 子宮内膜明細胞癌, 腎臓明細胞肉腫, 中枢神経系胚腫, 結腸癌, 転移性結腸癌, 再発結腸癌, 結腸癌第0期, 結腸癌第1期, 結腸癌第2期, 結腸癌第3期, 結腸癌第4期, 結腸直腸癌, 転移性結腸直腸癌, 再発結腸直腸癌, 結腸直腸癌第1期, 結腸直腸癌第2期, 結腸直腸癌第3期, 結腸直腸癌第4期, 結腸直腸癌第0期, 先天性線維肉腫, 結膜黒色腫, 対側乳癌, 皮膚線維肉腫, 線維形成性小円形細胞腫瘍, びまん性大細胞型B細胞性リンパ腫, 再発びまん性大細胞型B細胞性リンパ腫, 治療抵抗性びまん性大細胞型B細胞性リンパ腫, びまん性大細胞型B細胞性リンパ腫第1期, びまん性大細胞型B細胞性リンパ腫第2期, びまん性大細胞型B細胞性リンパ腫第3期, びまん性大細胞型B細胞性リンパ腫第4期, 播種性大細胞型リンパ腫, 耳の悪性新生物, エクリン腺癌, 内分泌腺の悪性新生物, 子宮内膜癌, 転移性子宮内膜癌, 再発子宮内膜癌, 子宮内膜癌第0期, 子宮内膜癌第1期, 子宮内膜癌第2期, 子宮内膜癌第3期, 子宮内膜癌第4期, 子宮内膜肉腫, 転移性子宮内膜肉腫, 子宮内膜肉腫再発, 好酸球性白血病, 悪性上衣細胞腫, 喉頭蓋癌, 類上皮肉腫, 転移性類上皮肉腫, 限局性類上皮肉腫, 再発類上皮肉腫, エプスタイン・バーウイルス関連リンパ腫, 赤血病性骨髄症（寛解期）, 赤白血病, ユーイング肉腫, 転移性ユーイング肉腫, 再発ユーイング肉腫, 性腺外原発性胎児性癌, 性腺外原発性胚細胞癌, 性腺外原発性混合胚細胞腫瘍第1期, 性腺外原発性混合胚細胞腫瘍第2期, 性腺外原発性混合胚細胞腫瘍第3期, 性腺外原発性悪性奇形腫, 性腺外原発性非セミノーマ, 性腺外原発性非セミノーマ第1期, 性腺外原発性非セミノーマ第2期, 性腺外原発性非セミノーマ第3期, 性腺外原発性非セミノーマ第4期, 性腺外原発性（純）セミノーマ第1期, 性腺外原発性（純）セミノーマ第2期, 性腺外原発性（純）セミノーマ第3期, 性腺外原発性（純）セミノーマ第4期, 乳房外パジェット病, 節外周辺帯B細胞リンパ腫（MAL T型）, 再発性節外性周辺帯B細胞リンパ腫（MAL T型）, 治療抵抗性節外性周辺帯B細胞リンパ腫（MAL T型）, 節外性周辺帯B細胞リンパ腫（MAL T型）第1期, 節外性周辺帯B細胞リンパ腫（MAL T型）第2期, 節外性周辺帯B細胞リンパ腫（MAL T型）第3期, 節外性周辺帯B細胞リン

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		パ腫（MAL T型）第4期，節外性NK・T細胞性リンパ腫、鼻型，眼球外網膜芽細胞腫，骨外性ユーイング肉腫，転移性骨外性ユーイング肉腫，限局性骨外性ユーイング肉腫，再発骨外性ユーイング肉腫，骨外性軟骨肉腫，転移性骨外性軟骨肉腫，限局性骨外性軟骨肉腫，再発骨外性軟骨肉腫，骨外性骨肉腫，転移性骨外性骨肉腫，限局性骨外性骨肉腫，再発骨外性骨肉腫，卵管癌，転移性卵管癌，卵管癌第1期，卵管癌第2期，卵管癌第3期，卵管癌第4期，女性生殖器上皮内癌，線維肉腫，転移性線維肉腫，限局性線維肉腫，小細胞型濾胞中心リンパ腫びまん性，再発性小細胞型濾胞中心リンパ腫びまん性，治療抵抗性小細胞型濾胞中心リンパ腫びまん性，小細胞型濾胞中心リンパ腫びまん性第1期，小細胞型濾胞中心リンパ腫びまん性第2期，小細胞型濾胞中心リンパ腫びまん性第3期，小細胞型濾胞中心リンパ腫びまん性第4期，濾胞中心リンパ腫、濾胞グレード1、2、3，再発濾胞中心リンパ腫、濾胞グレード1、2、3，治療抵抗性濾胞中心リンパ腫、濾胞グレード1、2、3，濾胞中心リンパ腫、濾胞グレード1、2、3第1期，濾胞中心リンパ腫、濾胞グレード1、2、3第2期，濾胞中心リンパ腫、濾胞グレード1、2、3第3期，濾胞中心リンパ腫、濾胞グレード1、2、3第4期，胆嚢癌，転移性胆嚢癌，切除不能な胆嚢癌，再発胆嚢癌，胆嚢癌第0期，胆嚢癌第1期，胆嚢癌第2期，胆嚢癌第3期，胆嚢癌第4期，神経節細胞芽腫，胃癌，再発胃癌，胃癌第0期，胃癌第1期，胃癌第2期，胃癌第3期，胃癌第4期，胃肉腫，悪性ガストリノーマ，転移性消化器癌，消化器癌，消化器上皮内癌，消化管間質性癌，消化管間質性腫瘍，胃食道癌，女性生殖器の悪性新生物，男性生殖器の悪性新生物，胚細胞癌，転移性胚細胞癌，妊娠性絨毛性腫瘍，歯肉癌，神経膠芽細胞腫，多形性神経膠芽細胞腫，神経膠腫，大脳神経膠腫症，膠細胞神経細胞腫瘍，神経膠肉腫，声門癌，グルカゴン産生腫瘍，血管周囲細胞腫，髄膜血管外皮腫，血液学的悪性疾患，毛様細胞白血病，頭頸部癌，転移性頭頸部癌，頭頸部癌第1期，頭頸部癌第2期，頭頸部癌第3期，頭頸部癌第4期，肝血管肉腫，転移性肝癌，肝癌第1期，肝癌第2期，肝癌第3期，肝癌第4期，肝の悪性新生物，切除不能な肝臓悪性新生物，再発肝臓悪性新生物，切除可能な肝臓悪性新生物，肝胆道系上皮内癌，肝芽腫，再発肝芽腫，肝脾T細胞リンパ腫，遺伝性平滑筋腫様腎細胞癌，遺伝性乳頭状腎癌，ハイグレードB細胞性バーキット様リンパ腫，再発ハイグレードB細胞性バ

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		一キット様リンパ腫, 治療抵抗性ハイグレードB細胞性バーキット様リンパ腫, ハイグレードB細胞性バーキット様リンパ腫第1期, ハイグレードB細胞性バーキット様リンパ腫第2期, ハイグレードB細胞性バーキット様リンパ腫第3期, ハイグレードB細胞性バーキット様リンパ腫第4期, 組織球性髄様細網症, ホジキン病, リンパ球減少型ホジキン病第1期、部位不明, 横隔膜下リンパ球減少型ホジキン病第1期, 横隔膜上リンパ球減少型ホジキン病第1期, リンパ球減少型ホジキン病第2期、部位不明, 横隔膜下リンパ球減少型ホジキン病第2期, 横隔膜上リンパ球減少型ホジキン病第2期, 再発リンパ球減少型ホジキン病, 治療抵抗性リンパ球減少型ホジキン病, リンパ球減少型ホジキン病第3期, リンパ球減少型ホジキン病第4期, リンパ球減少型ホジキン病、病期不明, リンパ球優位型ホジキン病第1期、部位不明, 横隔膜下リンパ球優位型ホジキン病第1期, 横隔膜上リンパ球優位型ホジキン病第1期, リンパ球優位型ホジキン病第2期、部位不明, 横隔膜下リンパ球優位型ホジキン病第2期, 横隔膜上リンパ球優位型ホジキン病第2期, 再発リンパ球優位型ホジキン病, 治療抵抗性リンパ球優位型ホジキン病, リンパ球優位型ホジキン病第3期, リンパ球優位型ホジキン病第4期, リンパ球優位型ホジキン病、病期不明, 再発混合細胞型ホジキン病, 治療抵抗性混合細胞型ホジキン病, 混合細胞型ホジキン病第1期、部位不明, 横隔膜下混合細胞型ホジキン病第1期, 横隔膜上混合細胞型ホジキン病第1期, 横隔膜下混合細胞型ホジキン病第2期, 横隔膜上混合細胞型ホジキン病第2期, 混合細胞型ホジキン病第3期, 混合細胞型ホジキン病第4期, 混合細胞型ホジキン病、病期不明, 再発結節性硬化症型ホジキン病, 治療抵抗性結節性硬化症型ホジキン病, 結節性硬化症型ホジキン病第1期、部位不明, 横隔膜下結節硬化型ホジキン病第1期, 横隔膜上結節硬化型ホジキン病第1期, 横隔膜下結節硬化型ホジキン病第2期, 横隔膜上結節硬化型ホジキン病第2期, 結節性硬化症型ホジキン病第3期, 結節性硬化症型ホジキン病第4期, 結節性硬化症型ホジキン病、病期不明, 再発ホジキン病, 治療抵抗性ホジキン病, ホジキン病第1期, ホジキン病第2期, ホジキン病第3期, ホジキン病第4期, 分類不能のホジキン病, 下咽頭癌, 再発下咽頭癌, 下咽頭癌第0期, 下咽頭癌第1期, 下咽頭癌第2期, 下咽頭癌第3期, 下咽頭癌第4期, 免疫芽球性リンパ腫, 再発炎症性乳癌, 炎症性乳癌第3期, 炎症性乳癌第4期,

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		炎症性乳癌, 炎症性筋線維芽細胞性腫瘍, 腸管腺癌, 腸管T細胞性リンパ腫, 再発腸管T細胞性リンパ腫, 治療抵抗性腸管T細胞性リンパ腫, 腸管T細胞性リンパ腫第1期, 腸管T細胞性リンパ腫第2期, 腸管T細胞性リンパ腫第3期, 腸管T細胞性リンパ腫第4期, 頭蓋内悪性髄膜腫, 眼球内黒色腫, 眼球内網膜芽細胞腫, 虹彩黒色腫, 若年性慢性骨髓単球性白血病, カポジ肉腫, エイズ関連カポジ肉腫, 古典的カポジ肉腫, ケラトアカントーマ, 呼吸器大細胞癌、病期不明, 転移性肺大細胞癌, 再発肺大細胞癌, 肺大細胞癌第0期, 肺大細胞癌第1期, 肺大細胞癌第2期, 肺大細胞癌第3期, 肺大細胞癌第4期, 大腸癌, 喉頭癌, 転移性喉頭癌, 再発喉頭癌, 喉頭癌第0期, 喉頭癌第1期, 喉頭癌第2期, 喉頭癌第3期, 喉頭癌第4期, 平滑筋肉腫, 転移性平滑筋肉腫, 限局性平滑筋肉腫, 再発平滑筋肉腫, 再発悪性黒子, 悪性黒子第1期, 悪性黒子第2期, 悪性黒子第3期, 悪性黒子第4期, 悪性黒子、病期不明, 白血病, 好塩基球性白血病, 皮膚白血病, 顆粒球白血病, 白血病、寛解期, 単球性白血病, 形質細胞性白血病, 形質細胞性白血病（寛解期）, 白血病再発, 白血病浸潤, 白血病脳浸潤, 白血病髄外浸潤, 白血病歯肉浸潤, 白血病肝浸潤, 白血病肺浸潤, 白血病腎浸潤, 白血性リンパ腫, 白血病性網膜症, 形成性胃組織炎, 口唇および口腔内癌, 再発口唇および口腔内癌, 口唇および口腔内癌第0期, 口唇および口腔内癌第1期, 口唇および口腔内癌第2期, 口唇および口腔内癌第3期, 口唇および口腔内癌第4期, 口唇の悪性新生物、病期不明, 脂肪肉腫, 転移性脂肪肉腫, 限局性脂肪肉腫, 再発脂肪肉腫, 肝癌破裂, 肺腺癌, 転移性肺腺癌, 再発肺腺癌, 肺腺癌第0期, 肺腺癌第1期, 肺腺癌第2期, 肺腺癌第3期, 肺腺癌第4期, 転移性肺癌, 再発肺癌、細胞タイプ不明, 肺癌第0期、細胞タイプ不明, 肺癌第1期、細胞タイプ不明, 肺癌第2期、細胞タイプ不明, 肺癌第3期、細胞タイプ不明, 肺癌第4期、細胞タイプ不明, 悪性肺浸潤, 肺の悪性新生物, 転移性肺扁平上皮癌, 再発肺扁平上皮癌, 肺扁平上皮癌第0期, 肺扁平上皮癌第1期, 肺扁平上皮癌第2期, 肺扁平上皮癌第3期, 肺扁平上皮癌第4期, 肺扁平上皮癌、病期不明, リンパ管肉腫, 癌性リンパ管症, リンパ性白血病, リンパ球性リンパ腫, リンパ性白血病（寛解期）, リンパ腫, エイズ関連リンパ腫, 皮膚型リンパ腫, リンパ腫の転化, リンパ形質細胞様リンパ腫・免疫細胞腫, 再発リンパ形質細胞様リンパ腫・免疫細胞腫, 治療抵抗性リンパ形質細胞様リンパ腫・免疫細胞腫

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		胞腫, リンパ形質細胞様リンパ腫・免疫細胞腫第1期, リンパ形質細胞様リンパ腫・免疫細胞腫第2期, リンパ形質細胞様リンパ腫・免疫細胞腫第3期, リンパ形質細胞様リンパ腫・免疫細胞腫第4期, 男性生殖器上皮内癌, 肛門直腸の悪性新生物, 脳神経の悪性新生物, 悪性線維性組織球腫, 転移性悪性線維性組織球腫, 限局性悪性線維性組織球腫, 再発悪性線維性組織球腫, 悪性神経膠腫, 悪性血管周囲細胞腫, 転移性悪性血管周囲細胞腫, 限局性悪性血管周囲細胞腫, 再発悪性血管周囲細胞腫, 肝胆道系の悪性新生物, 悪性組織球増殖症, 悪性胞状奇胎, 悪性リンパ様新生物, 分類不能なハイグレードの悪性リンパ腫, 分類不能なローグレードの悪性リンパ腫, 肥満細胞の悪性新生物, 縦隔の悪性新生物, 悪性黒色腫, 表皮内悪性黒色腫, 眼瞼の悪性黒色腫, 皮膚以外の悪性黒色腫, 悪性黒色腫第1期, 悪性黒色腫第2期, 悪性黒色腫第3期, 悪性黒色腫第4期, 悪性間葉腫, 転移性悪性間葉腫, 限局性悪性間葉腫, 再発悪性間葉腫, 腸間膜の悪性新生物, 中耳の悪性新生物, 筋の悪性新生物, フェーター膨大部の悪性新生物, 耳介軟骨の悪性新生物, 脈絡膜の悪性新生物, 結膜の悪性新生物, 角膜の悪性新生物, 精巣上体の悪性新生物, 眼の悪性新生物, 眼瞼の悪性新生物, ランゲルハンス島の悪性新生物, 涙管の悪性新生物, 涙腺の悪性新生物, 眼窩の悪性新生物, 尿道傍腺の悪性新生物, 胎盤の悪性新生物, 胸膜の悪性新生物, 腎盂の悪性新生物, 網膜の悪性新生物, 精嚢の悪性新生物, 精索の悪性新生物, 脊髄の悪性新生物, 胸部の悪性新生物, 子宮付属器の悪性新生物, 神経系の悪性新生物, 乳頭の悪性新生物, 女性乳頭の悪性新生物, 男性乳頭の悪性新生物, 悪性乏突起神経膠腫, 悪性卵巣嚢腫, 口蓋の悪性新生物, 心膜の悪性新生物, 腹膜の悪性新生物, 下垂体の悪性腫瘍, 気道の悪性新生物, 軟部組織の悪性新生物, 脾臓の悪性新生物, 悪性転換, 尿路の悪性新生物, マントル細胞リンパ腫, 再発マントル細胞リンパ腫, 治療抵抗性マントル細胞リンパ腫, マントル細胞リンパ腫第1期, マントル細胞リンパ腫第2期, マントル細胞リンパ腫第3期, マントル細胞リンパ腫第4期, 肥満細胞性白血病, 成熟B細胞型急性白血病, 髄芽腫, 再発髄芽腫, 再発黒色腫, 黒色腫性髄膜炎, 悪性髄膜腫, 悪性中皮腫, 進行した悪性中皮腫, 再発悪性中皮腫, 腹腔内転移, 腹壁転移, 副腎転移, 胆道転移, 膀胱転移, 骨転移, 骨髄転移, 乳房転移, 中枢神経系転移, 胸壁転移, 横隔膜転移, 耳管転移, 眼転移, 卵管転移, 胆嚢転移, 胃腸

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		管転移, 心転移, 腎転移, 大腸転移, 喉頭転移, 肝転移, 肺転移, リンパ節転移, 髄膜転移, 口腔転移, 筋転移, 副鼻腔転移, 頸部転移, 神経系転移, 食道転移, 卵巣転移, 脾転移, 骨盤転移, 陰茎転移, 会陰転移, 末梢神経系転移, 末梢血管系転移, 腹膜転移, 咽頭転移, 下垂体転移, 胎盤転移, 胸膜転移, 前立腺転移, 直腸転移, 生殖器転移, 後腹膜転移, 唾液腺転移, 皮膚転移, 小腸転移, 軟部組織転移, 脊椎転移, 脾臓転移, 胃転移, 精巣転移, 縦隔転移, 呼吸器系転移, 胸部転移, 甲状腺転移, 気管転移, 尿路転移, 子宮転移, 転移, 転移性気管支癌, 転移性カルチノイド腫瘍, 膀胱の転移性癌, 転移性絨毛癌, 転移性胃癌, 転移性神経膠腫, 転移性リンパ腫, 転移性悪性黒色腫, 転移性新生物, 転移性眼球黒色腫, 転移性腎細胞癌, 転移性唾液腺癌, 転移性扁平上皮癌, 転移性子宮癌, 混合星状・上衣細胞腫, 肝細胞癌・胆管細胞癌の混合型, 混合乏突起星細胞腫, 単球性白血病、寛解期, 粘液性子宮内膜癌, 粘液性類表皮癌, 多発性骨髄腫, 菌状息肉症, 再発菌状息肉症, 治療抵抗性菌状息肉症, 菌状息肉症第1期, 菌状息肉症第2期, 菌状息肉症第3期, 菌状息肉症第4期, 骨髄芽球腫, 骨髄性白血病, 骨髄性白血病、寛解期, 再発ミエローマ, 鼻腔癌, 副鼻腔癌, 上咽頭癌, 再発上咽頭癌, 上咽頭癌第0期, 上咽頭癌第1期, 上咽頭癌第2期, 上咽頭癌第3期, 上咽頭癌第4期, ナチュラルキラー細胞白血病, ナチュラルキラー細胞リンパ芽球性リンパ腫, 新生児白血病, 新生児神経芽腫, 悪性新生物, 腎芽細胞腫, 悪性神経線維鞘腫, 神経芽腫, 再発神経芽腫, 神経内分泌癌, 転移性神経内分泌癌, 皮膚神経内分泌癌, 神経内分泌腫瘍, 神経線維肉腫, 転移性神経線維肉腫, 限局性神経線維肉腫, 再発神経線維肉腫, リンパ節周辺帯B細胞性リンパ腫, 再発リンパ節周辺帯B細胞性リンパ腫, 治療抵抗性リンパ節周辺帯B細胞性リンパ腫, リンパ節周辺帯B細胞性リンパ腫第1期, リンパ節周辺帯B細胞性リンパ腫第2期, リンパ節周辺帯B細胞性リンパ腫第3期, リンパ節周辺帯B細胞性リンパ腫第4期, 中枢神経系非胚腫性胚細胞腫瘍, 非ホジキンリンパ腫, 転移性非ホジキンリンパ腫, 再発非ホジキンリンパ腫, 治療抵抗性非ホジキンリンパ腫, 非ホジキンリンパ腫第1期, 非ホジキンリンパ腫第2期, 非ホジキンリンパ腫第3期, 非ホジキンリンパ腫第4期, トランスフォームした再発非ホジキンリンパ腫, 組織型不明の侵襲性非ホジキンリンパ腫, 組織型不明の侵襲性再発非ホジキンリンパ腫, 組織型不明の侵襲性治療抵抗性非ホジキ

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		ンリンパ腫, 組織型不明の侵襲性非ホジキンリンパ腫第 1 期, 組織型不明の侵襲性非ホジキンリンパ腫第 2 期, 組織型不明の侵襲性非ホジキンリンパ腫第 3 期, 組織型不明の侵襲性非ホジキンリンパ腫第 4 期, 組織型不明の無症候性非ホジキンリンパ腫, 組織型不明の無症候性非ホジキンリンパ腫第 1 期, 組織型不明の無症候性非ホジキンリンパ腫第 2 期, 組織型不明の無症候性非ホジキンリンパ腫第 3 期, 組織型不明の無症候性非ホジキンリンパ腫第 4 期, 非腎細胞性腎癌, 非小細胞肺癌, 転移性非小細胞肺癌, 再発非小細胞肺癌, 非小細胞肺癌第 0 期, 非小細胞肺癌第 1 期, 非小細胞肺癌第 2 期, 非小細胞肺癌第 3 期, 非小細胞肺癌第 3 A 期, 非小細胞肺癌第 3 B 期, 非小細胞肺癌第 4 期, 転移性眼悪性腫瘍, 眼部血管外皮腫, 食道腺癌, 転移性食道腺癌, 再発食道腺癌, 食道腺癌第 0 期, 食道腺癌第 1 期, 食道腺癌第 2 期, 食道腺癌第 3 期, 食道腺癌第 4 期, 転移性食道癌, 食道癌, 再発食道癌, 食道癌第 0 期, 食道扁平上皮癌, 転移性食道扁平上皮癌, 再発食道扁平上皮癌, 食道扁平上皮癌第 0 期, 食道扁平上皮癌第 1 期, 食道扁平上皮癌第 2 期, 食道扁平上皮癌第 3 期, 食道扁平上皮癌第 4 期, 希突起神経膠腫, 視神経膠腫, 視索神経膠腫, 転移性口腔内癌, 再発中咽頭癌, 中咽頭癌第 0 期, 中咽頭癌第 1 期, 中咽頭癌第 2 期, 中咽頭癌第 3 期, 中咽頭癌第 4 期, 中咽頭癌、病期不明, 限局性骨肉腫, 転移性骨肉腫, 再発骨肉腫, 転移性耳悪性腫瘍, 卵巣癌, 転移性卵巣癌, 再発卵巣癌, 卵巣癌第 1 期, 卵巣癌第 2 期, 卵巣癌第 3 期, 卵巣癌第 4 期, 卵巣未分化胚細胞腫第 1 期, 卵巣未分化胚細胞腫第 2 期, 卵巣未分化胚細胞腫第 3 期, 卵巣未分化胚細胞腫第 4 期, 卵巣未分化胚細胞腫、病期不明, 卵巣胎芽性癌, 卵巣上皮癌, 転移性卵巣上皮癌, 再発卵巣上皮癌, 卵巣上皮癌第 1 期, 卵巣上皮癌第 2 期, 卵巣上皮癌第 3 期, 卵巣上皮癌第 4 期, 卵巣胚細胞癌, 卵巣胚細胞癌第 1 期, 卵巣胚細胞癌第 2 期, 卵巣胚細胞癌第 3 期, 卵巣胚細胞癌第 4 期, 卵巣胚細胞絨毛癌第 1 期, 卵巣胚細胞絨毛癌第 2 期, 卵巣胚細胞絨毛癌第 3 期, 卵巣胚細胞絨毛癌第 4 期, 卵巣胚細胞胎芽性癌第 1 期, 卵巣胚細胞胎芽性癌第 2 期, 卵巣胚細胞胎芽性癌第 3 期, 卵巣胚細胞胎芽性癌第 4 期, 卵巣胚細胞内胚葉洞腫瘍第 1 期, 卵巣胚細胞内胚葉洞腫瘍第 2 期, 卵巣胚細胞内胚葉洞腫瘍第 3 期, 卵巣胚細胞内胚葉洞腫瘍第 4 期, 卵巣胚細胞多胎芽腫第 1 期, 卵巣胚細胞多胎芽腫第 2 期, 卵巣胚細胞多胎芽腫第 3 期, 卵巣胚細胞多胎芽腫第 4 期, 卵巣胚細胞

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		奇形腫第1期, 卵巣胚細胞奇形腫第2期, 卵巣胚細胞奇形腫第3期, 卵巣胚細胞奇形腫第4期, 卵巣顆粒卵胞膜細胞腫, 低悪性度卵巣腫瘍, 間質性卵巣癌, 陰茎パジェット病, 皮膚パジェット病, 乳房パジェット病, 外陰部パジェット病, パンコースト腫瘍, 膵癌, 転移性膵癌, 切除不能な膵癌, 再発膵癌, 切除可能な膵癌, 膵癌第0期, 膵癌第1期, 膵癌第2期, 膵癌第3期, 膵癌第4期, 膵神経内分泌腫瘍, 転移性膵神経内分泌腫瘍, 膵肉腫, 乳頭状漿液性子宮内膜癌, 傍神経節の悪性新生物, 副鼻腔および鼻腔の悪性新生物, 再発副鼻腔および鼻腔悪性新生物, 副鼻腔および鼻腔悪性新生物第0期, 副鼻腔および鼻腔悪性新生物第1期, 副鼻腔および鼻腔悪性新生物第2期, 副鼻腔および鼻腔悪性新生物第3期, 副鼻腔および鼻腔悪性新生物第4期, 悪性副甲状腺腫瘍, 陰茎の悪性新生物, 陰茎癌, 転移性陰茎癌, 再発陰茎癌, 陰茎癌第1期, 陰茎癌第2期, 陰茎癌第3期, 陰茎癌第4期, 進行した心膜悪性中皮腫, 限局性心膜悪性中皮腫, 再発心膜悪性中皮腫, 末梢性神経上皮腫, 骨末梢神経上皮腫, 転移性骨末梢神経上皮腫, 再発骨末梢神経上皮腫, 軟部組織末梢神経上皮腫, 末梢性T細胞性リンパ腫, 組織型不明, 再発組織型不明の末梢性T細胞性リンパ腫, 治療抵抗性組織型不明の末梢性T細胞性リンパ腫, 組織型不明の末梢性T細胞性リンパ腫第1期, 組織型不明の末梢性T細胞性リンパ腫第2期, 組織型不明の末梢性T細胞性リンパ腫第3期, 組織型不明の末梢性T細胞性リンパ腫第4期, 転移性腹膜癌, 腹膜悪性中皮腫, 進行した腹膜悪性中皮腫, 再発腹膜悪性中皮腫, 腹膜肉腫, 悪性褐色細胞腫, 転移性咽頭癌, 再発咽頭癌, 咽頭癌第0期, 咽頭癌第1期, 咽頭癌第2期, 咽頭癌第3期, 咽頭癌第4期, 咽頭癌、病期不明, 松果体胚腫, 松果体実質部の悪性新生物, 松果体芽腫, 転移性下垂体癌, 再発悪性下垂体新生物, 形質芽球性リンパ腫, 形質細胞腫, 胸膜中皮腫, 胸膜悪性中皮腫, 進行した胸膜悪性中皮腫, 再発胸膜悪性中皮腫, 胸膜肉腫, 汗孔癌, 輪状後部癌, 前駆Bリンパ芽球性リンパ腫, 再発前駆Bリンパ芽球性リンパ腫, 治療抵抗性前駆Bリンパ芽球性リンパ腫, 前駆Bリンパ芽球性リンパ腫第1期, 前駆Bリンパ芽球性リンパ腫第2期, 前駆Bリンパ芽球性リンパ腫第3期, 前駆Bリンパ芽球性リンパ腫第4期, 前駆Tリンパ芽球性リンパ腫・白血病, 再発前駆Tリンパ芽球性リンパ腫・白血病, 治療抵抗性前駆Tリンパ芽球性リンパ腫・白血病, 前駆Tリンパ芽球性リンパ腫・白血病第1期, 前駆Tリ

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		ンパ芽球性リンパ腫・白血病第2期, 前駆Tリンパ芽球性リンパ腫・白血病第3期, 前駆Tリンパ芽球性リンパ腫・白血病第4期, 原発性体腔性リンパ腫, 縦隔原発B細胞性大細胞型リンパ腫, 再発縦隔原発B細胞性大細胞型リンパ腫, 治療抵抗性縦隔原発B細胞性大細胞型リンパ腫, 縦隔原発B細胞性大細胞型リンパ腫第1期, 縦隔原発B細胞性大細胞型リンパ腫第2期, 縦隔原発B細胞性大細胞型リンパ腫第3期, 縦隔原発B細胞性大細胞型リンパ腫第4期, 未分化神経外胚葉性腫瘍, 転移性未分化神経外胚葉性腫瘍, 前リンパ性白血病, 前立腺癌, 転移性前立腺癌, 再発前立腺癌, 前立腺癌第0期, 前立腺癌第1期, 前立腺癌第2期, 前立腺癌第3期, 前立腺癌第4期, 偽肉腫, 直腸癌, 転移性直腸癌, 再発直腸癌, 直腸癌第0期, 直腸癌第1期, 直腸癌第2期, 直腸癌第3期, 直腸癌第4期, 直腸S状結腸癌, 転移性直腸S状結腸癌, 再発直腸S状結腸癌, 直腸S状結腸癌第0期, 直腸S状結腸癌第1期, 直腸S状結腸癌第2期, 直腸S状結腸癌第3期, 直腸S状結腸癌第4期, 再発癌, 難治性癌, 腎癌, 転移性腎癌, 再発腎癌, 腎癌第1期, 腎癌第2期, 腎癌第3期, 腎癌第4期, 腎細胞癌, 再発腎細胞癌, 腎細胞癌第1期, 腎細胞癌第2期, 腎細胞癌第3期, 腎細胞癌第4期, 気道の上皮内癌, 網膜メラノーマ, 網膜芽腫, 両側性網膜芽細胞腫, 片側性網膜芽細胞腫, 後腹膜癌, 転移性後腹膜新生物, 腎臓杆状細胞腫, 横紋筋肉腫, 再発横紋筋肉腫, リクター症候群, 唾液腺癌, 再発唾液腺癌, 唾液腺癌第0期, 唾液腺癌第1期, 唾液腺癌第2期, 唾液腺癌第3期, 唾液腺癌第4期, 肉腫, 転移性肉腫, 皮膚の肉腫, 子宮肉腫, 肉腫症, 陰囊癌, 脂腺癌, セミノーマ, 印環細胞癌, 転移性副鼻腔癌, 皮膚癌, 転移性皮膚癌, 小細胞癌, 子宮頸部小細胞癌, 進展型小細胞肺癌, 限局型小細胞肺癌, 転移性小細胞肺癌, 再発小細胞肺癌, 小細胞肺癌, 病期不明, 小腸癌, 転移性小腸癌, 切除不能な小腸癌, 再発小腸癌, 切除可能な小腸癌, 小腸癌第0期, 小腸癌第1期, 小腸癌第2期, 小腸癌第3期, 小腸癌第4期, 小腸平滑筋肉腫, 脾の充実性偽乳頭状腫瘍, 悪性脊髄髄膜腫, 紡錘細胞肉腫, 脾臓周辺帯リンパ腫, 再発性脾臓周辺帯リンパ腫, 治療抵抗性脾臓周辺帯リンパ腫, 脾臓周辺帯リンパ腫第1期, 脾臓周辺帯リンパ腫第2期, 脾臓周辺帯リンパ腫第3期, 脾臓周辺帯リンパ腫第4期, 扁平上皮癌, 皮膚有棘細胞癌, 子宮頸部扁平上皮癌, 子宮内膜扁平上皮癌, スチュアート・トリーヴェス症候群, 表在拡大型黒色腫第1期, 表在拡大型黒

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		色腫第2期, 表在拡大型黒色腫第3期, 表在拡大型黒色腫第4期, 表在拡大型黒色腫、病期不明, 滑膜肉腫, 転移性滑膜肉腫, 限局性滑膜肉腫, 再発滑膜肉腫, T細胞性慢性リンパ性白血病, T細胞性リンパ腫, 再発T細胞性リンパ腫, 治療抵抗性T細胞性リンパ腫, T細胞性リンパ腫第1期, T細胞性リンパ腫第2期, T細胞性リンパ腫第3期, T細胞性リンパ腫第4期, T細胞性前リンパ性白血病, T細胞型急性白血病, 分類不能なT細胞性リンパ腫、ハイグレード, 分類不能なT細胞性リンパ腫、ローグレード, 転移性精巣癌, 精巣絨毛癌, 再発精巣絨毛癌, 精巣絨毛癌第1期, 精巣絨毛癌第2期, 精巣絨毛癌第3期, 精巣胎芽性癌, 精巣胎芽性癌第1期, 精巣胎芽性癌第2期, 精巣胎芽性癌第3期, 精巣胚細胞性癌, 転移性精巣胚細胞性癌, 精巣胚細胞性混合腫瘍第1期, 精巣胚細胞性混合腫瘍第2期, 精巣胚細胞性混合腫瘍第3期, 精巣平滑筋肉腫, 精巣悪性奇形腫第1期, 精巣悪性奇形腫第2期, 精巣悪性奇形腫第3期, 精巣（純粋）セミノーマ, 精巣（純粋）セミノーマ第1期, 精巣（純粋）セミノーマ第2期, 精巣（純粋）セミノーマ第3期, 精巣卵黄囊腫瘍第1期, 精巣卵黄囊腫瘍第2期, 精巣卵黄囊腫瘍第3期, 精巣癌, 再発精巣癌, 咽喉癌, 転移性胸腺癌, 悪性胸腺腫, 再発悪性胸腺腫, 甲状腺癌, 転移性甲状腺癌, 甲状腺癌第0期, 甲状腺癌第1期, 甲状腺癌第2期, 甲状腺癌第3期, 甲状腺癌第4期, 転移性舌癌, 再発舌癌, 舌癌第0期, 舌癌第1期, 舌癌第2期, 舌癌第3期, 舌癌第4期, 舌の悪性新生物、病期不明, 扁桃癌, 気管癌, 腎盂および尿管の転移性移行上皮癌, 腎盂および尿管移行上皮癌, 腎盂および尿管の限局性移行上皮癌, 腎盂および尿管の再発移行上皮癌, 腎盂および尿管の局所性移行上皮癌, 移行上皮癌, 転移性移行上皮癌, 未分化型肉腫, 尿管癌, 限局性尿管癌, 転移性尿管癌, 再発尿管癌, 局所性尿管癌, 尿道癌, 限局性尿道癌, 転移性尿道癌, 再発尿道癌, 局所性尿道癌, 膀胱肉腫, 尿路上皮内癌, 子宮癌, 子宮上皮内癌, 子宮平滑筋肉腫, 陰癌, 転移性陰癌, 再発陰癌, 陰癌第0期, 陰癌第1期, 陰癌第2期, 陰癌第3期, 陰癌第4A期, 陰癌第4B期, 外陰部癌, 転移性外陰部癌, 再発外陰部癌, 外陰部癌第0期, 外陰部癌第1期, 外陰部癌第2期, 外陰部癌第3期, 外陰部癌第4期, ワルデンストローム・マクログロブリン血症, 再発ワルデンストローム・マクログロブリン血症, 治療抵抗性ワルデンストローム・マクログロブリン血症, ワルデンストローム・マクログロブリン血症第1期, ワルデンス

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		トローム・マクログロブリン血症第2期, ワルデンストローム・マクログロブリン血症第3期, ワルデンストローム・マクログロブリン血症第4期
	詳細不明の腫瘍 SMQ	腹部新生物, 腹壁新生物, A C T H産生性下垂体腫瘍, 副腎新生物, 肛門新生物, アプドーマ, 異型線維黄色腫, 胆道新生物, 膀胱新生物, 骨巨細胞腫瘍, 骨新生物, 境界悪性卵巣腫瘍, 脳新生物, 脳奇形腫, 乳房新生物, 気管支新生物, 詳細不明の心臓新生物, 心奇形腫, 頸動脈球腫瘍, 軟骨新生物, 中枢神経系新生物, 小脳腫瘍, 小脳橋角部腫瘍, 子宮頸部新生物, 脈絡膜新生物, 結腸新生物, 先天性奇形腫, 結膜新生物, 原発性後天性結膜メラノーシス, 葉状肉腫, 横隔膜新生物, 十二指腸新生物, 異形成母斑症候群, 耳新生物, 内分泌腺新生物, 子宮内膜新生物, 脳室上衣細胞腫, 精巣上体新生物, エプスタイン・バーウイルス関連リンパ増殖性障害, 眼瞼腫瘍, 卵管新生物, 女性生殖器新生物, 胃新生物, ガストリノーマ, 消化器新生物, 泌尿生殖器新生物, 顆粒細胞腫, 成長ホルモン産生性下垂体腫瘍, 造血器新生物, 肝新生物, 肝胆道系新生物, ホルモン産生卵巣腫瘍, 下咽頭新生物, インスリノーマ, 虹彩新生物, 涙管新生物, ランゲルハンス細胞組織球症, 大顆粒性リンパ球増多症, 喉頭新生物, 口唇新生物, 肺新生物, リンパ系新生物, リンパ増殖性障害, リンパ増殖性障害、寛解期, 男性生殖器新生物, 上顎顔面洞新生物, 縦隔新生物, 髄膜新生物, 中皮腫, 中皮腫、悪性度不明, 唾液腺混合腫瘍, ミュラー管混合腫瘍, 筋新生物, 鼻新生物, 新生物, 虫垂新生物, 角膜新生物、悪性度不明, 眼窩新生物, 胸腺新生物, 新生物進行, 前立腺新生物, 新生物再発, 皮膚の新生物, 神経系新生物, 神経外胚葉新生物, ニューロテンシノーマ, 乳頭新生物, 非分泌型下垂体腺腫, 眼部新生物, 食道新生物, 大網新生物, 視神経新生物, 口腔新生物, 中咽頭新生物, 卵巣新生物, 膣新生物, 傍神経節新生物, 副鼻腔新生物, 副甲状腺腫瘍, 骨盤新生物, 陰茎新生物, 心膜新生物, 末梢神経系新生物, 腹膜新生物, 褐色細胞腫, 咽頭新生物, 松果体新生物, 松果体腫, 下垂体腫瘍, 再発下垂体腫瘍, 胎盤新生物, 胸膜新生物, プロラクチン産生性下垂体腫瘍, 直腸新生物, 腎新生物, 気道新生物, 網膜新生物, 後眼窩新生物, 後腹膜新生物, 唾液腺新生物, 分泌型下垂体腺腫, 皮膚新生物出血, 平滑筋細胞新生物, 軟部組織新生物, ソマトスタチノーマ, 脊髄新生物, 悪性度不明の脾臓新生物, 腱新生物, 奇形腫, 精巣奇形腫, 精巣新生物, 胸腺腫, 甲状腺新生物, 甲状腺刺激ホルモン産生性下垂体腫瘍,

表 2.7.4.7-1 Table of MedDRA Preferred Terms That Comprised Each SMQ/CMQ Used to Evaluate Adverse Events of Special Interest

TEAE Category of Special Interest	Query Type	MedDRA PTs Included in Query
		舌新生物, 扁桃新生物, 気管新生物, 尿管新生物, 尿道新生物, 尿路新生物, 子宮新生物, 腔新生物, 血管新生物, ビポーマ, 声帯新生物, 外陰新生物, 卵黄囊腫瘍、部位不明
Agranulocytosis	SMQ	無顆粒球症, 再生不良性貧血, 自己免疫性再生不良性貧血, 骨髓機能不全, 有熱性骨髓無形成, 発熱性好中球減少症, 好中球減少性大腸炎, 好中球減少性感染, 好中球減少性敗血症, 汎血球減少症, 汎骨髓障害, 真性白血球系無形成, 腹部敗血症, 急性扁桃炎, 細菌性敗血症, 胆道性敗血症, ブルセラ性敗血症, カンピロバクター性敗血症, 敗血症性脳梗塞, シトロバクター性敗血症, クロストリジウム・ディフィシレ性敗血症, コリネバクテリウム性敗血症, 医療機器関連敗血症, エンテロバクター性敗血症, 腸球菌性敗血症, 大腸菌性敗血症, B群レンサ球菌性新生児敗血症, ヘモフィルス性敗血症, ヘリコバクター性敗血症, クレブシエラ性敗血症, リステリア性敗血症, 髄膜炎菌性敗血症, 小球菌性敗血症, 粘膜潰瘍, 敗血症性心筋炎, ノカルジア性敗血症, 骨盤内敗血症, 扁桃周囲膿瘍, 扁桃周囲炎, 咽頭膿瘍, 咽頭潰瘍, 咽頭炎, 細菌性咽頭炎, マイコプラズマ咽頭炎, レンサ球菌性咽頭炎, 咽頭扁桃炎, 敗血症性ペスト, 肺炎球菌性敗血症, 処置後敗血症, 産褥敗血症, シュードアレシエリア性敗血症, シュードモナス性敗血症, 肺敗血症, サルモネラ性敗血症, 敗血症, 新生児敗血症, パスツレラ菌性敗血症, 敗血症症候群, 敗血症性塞栓, 敗血症性脳症, 敗血症性壊死, 敗血症性静脈炎, 敗血疹, 敗血症性ショック, セラチア性敗血症, ブドウ球菌性敗血症, ステノトロフォモナス性敗血症, 壊死性口内炎, レンサ球菌性敗血症, 化膿性血栓静脈炎, 扁桃潰瘍, 扁桃炎, 臍帯敗血症, 尿路性敗血症, ウイルス性敗血症, 膿創
Drug Abuse/Overdose	薬物乱用 CMQ	依存, 薬物乱用, 薬物依存, 薬物依存、分娩前, 薬物依存、分娩後, 薬剤離脱症候群, 企図的薬剤誤用, 企図的過量投与, 企図的多剤過量投与, ニコチン依存, 多物質依存, 物質乱用, タバコ乱用, タバコ離脱症状, 離脱症候群
	薬剤関連過量投与の疑い CMQ	偶発的過量投与, 企図的過量投与, 多剤過量投与, 偶発的多剤過量投与, 企図的多剤過量投与, 過量投与

<資料番号 5.3.5.1-01 : 17.9>

MedDRA preferred term

腹壁新生物, 腹壁の悪性新生物, 末端部黒子様黒色腫第1期, 末端部黒子様黒色腫第2期, 末端部黒子様黒色腫第3期, 末端部黒子様黒色腫第4期, 末端部黒子様黒色腫、病期不明, 肛門癌, 転移性肛門癌, 再発肛門癌, 肛門癌第0期, 肛門癌第1期, 肛門癌第2期, 肛門癌第3期, 肛門癌第4期, 肛門新生物, 基底細胞癌, 基底扁平上皮癌, 皮膚基底有棘細胞癌, ボーエン病, 乳房新生物, プシケ・レーベンシュタイン腫瘍, 上皮内癌, 陰茎上皮内癌, 皮膚上皮内癌, 結膜黒色腫, 皮膚線維肉腫, 異形成母斑症候群, 耳の悪性新生物, 眼瞼腫瘍, 女性生殖器の悪性新生物, 男性生殖器の悪性新生物, 再発炎症性乳癌, 炎症性乳癌第3期, 炎症性乳癌第4期, 炎症性乳癌, 炎症性筋線維芽細胞性腫瘍, 眼球内黒色腫, 虹彩黒色腫, ケラトアカントーマ, 涙管新生物, 再発悪性黒子, 悪性黒子第1期, 悪性黒子第2期, 悪性黒子第3期, 悪性黒子第4期, 悪性黒子、病期不明, 皮膚白血病, 白血病浸潤, 口唇および口腔内癌, 再発口唇および口腔内癌, 口唇および口腔内癌第0期, 口唇および口腔内癌第1期, 口唇および口腔内癌第2期, 口唇および口腔内癌第3期, 口唇および口腔内癌第4期, 口唇新生物, 口唇の悪性新生物、病期不明, 皮膚型リンパ腫, 肛門直腸の悪性新生物, 悪性線維性組織球腫, 転移性悪性線維性組織球腫, 限局性悪性線維性組織球腫, 再発悪性線維性組織球腫, 悪性組織球増殖症, 悪性胞状奇胎, 肥満細胞の悪性新生物, 悪性黒色腫, 表皮内悪性黒色腫, 眼瞼の悪性黒色腫, 皮膚以外の悪性黒色腫, 悪性黒色腫第1期, 悪性黒色腫第2期, 悪性黒色腫第3期, 悪性黒色腫第4期, 眼瞼の悪性新生物, 乳頭の悪性新生物, 女性乳頭の悪性新生物, 男性乳頭の悪性新生物, 再発黒色腫, 乳房転移, 胸壁転移, 陰茎転移, 皮膚転移, 転移性悪性黒色腫, 転移性眼球黒色腫, 転移性扁平上皮癌, 鼻腔癌, 鼻新生物, 新生物, 皮膚の新生物, 乳頭新生物, 転移性口腔内癌, 転移性耳悪性腫瘍, 陰茎パジェット病, 皮膚パジェット病, 乳房パジェット病, 外陰部パジェット病, 陰茎の悪性新生物, 陰茎新生物, 陰茎癌, 転移性陰茎癌, 再発陰茎癌, 陰茎癌第1期, 陰茎癌第2期, 陰茎癌第3期, 陰茎癌第4期, 陰囊癌, 皮膚癌, 転移性皮膚癌, 皮膚新生物出血, 扁平上皮癌, 皮膚有棘細胞癌, 表在拡大黒色腫第1期, 表在拡大黒色腫第2期, 表在拡大黒色腫第3期, 表在拡大黒色腫第4期, 表在拡大黒色腫、病期不明, 外陰部癌, 転移性外陰部癌, 再発外陰部癌, 外陰部癌第0期, 外陰部癌第1期, 外陰部癌第2期, 外陰部癌第3期, 外陰部癌第4期, 外陰新生物

MedDRA Version14.1

<資料番号5.3.5.3-02 : CT-13.6>

表2.7.4.7-3

156-PKD-CSS

CT-11 Numbers of Subjects Exposed to Immediate-release Tolvaptan Tablets in Completed or Ongoing Trials in the ADPKD Program

Clinical Trials ^a	Subjects Exposed, N, to Oral Tolvaptan IR
Phase 3 Pivotal (Multinational)	
156-████-251	961
Phase 2 and 3 Supportive (Multinational, US, Japan)	
Phase 2 or 3 open-label extension:	
-156-████-250	46 (43)
-156-████-002	17 (17)
-[156-████-271]	904 (601) ^b
-[156-████-003]	13 (13)
-[156-████-003]	108 (67)
Phase 1 and 2 Clinical Pharmacology Trials in ADPKD or Renally Impaired Subjects (US, Japan)	
Single-dose trials:	
-156-████-248	8
-156-████-282	37 ^c
Single- and multiple-dose or multiple-dose trials:	
-156-████-001	18
-156-████-249	37
-156-████-260	20
-156-████-284	29
-156-████-285	12 ^d
Phase 1 Clinical Pharmacology Trials in Healthy Subjects (US, Japan, Korea)	
Single-dose trials:	
-156-████-256	14
-156-████-295	44
TOTAL, All Trials	1581
- ADPKD subjects	1432
- Healthy subjects	112

[] Indicates ongoing trial.

() Indicates subjects who were exposed to tolvaptan IR tablets in more than one trial.

Note: Only exposure to IR tolvaptan tablets is counted. Subjects are counted only once in totals where exposed to tolvaptan IR tablets in more than one trial.

Exposure from ongoing, double-blind Trial 156-████-290 is excluded.

^a Data cut-off date for ongoing trials: █████ 20██ for Asian trials; █████ 20██ for all others.^b Ten rollover subjects from Trial 156-████-285 exposed previously to tolvaptan MR capsules and 293 placebo subjects from Trial 156-████-251 are counted as unique tolvaptan IR tablet exposures.^c Included healthy and renally impaired subjects. Though ADPKD subjects were allowed, none enrolled.^d Only includes exposures to IR oral tolvaptan tablets (MR oral tolvaptan capsules were also studied).

<資料番号 5.3.5.3-02:SCS CT-1.1 to SCS CT-1.3, SCS CT-2.1.1, SCS CT-2.2.1, SCS CT-2.3.1, SCS CT-2.4.1, SCS CT-2.8.1, SCS CT-2.9.1, SCS CT-2.10.1.1.1, SCS CT-2.11.1, SCS CT-2.13.1, SCS CT-2.14.1.1, 5.3.5.1-01:CT-1.1, 5.3.5.2-05:CT-1.1, 5.3.4.2-06:CT-1, 5.3.1.1-01:CT-1, 5.3.1.2-01:CT-1.1, CT-2.1>

表2.7.4.7-4

156-PKD-CSS

JCT-1.3 Extent of Exposure to Study Medication: All Studies

Duration of exposure	15-45 mg (N=53)		60-120 mg (N=1521)		Total (N=1541)	
	Last dose	Cumulative ^a	Last dose	Cumulative ^a	Last dose	Cumulative ^a
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1 DAY	0 (0.0)	53 (100.0)	60 (3.9)	1521 (100.0)	60 (3.9)	1541 (100.0)
1 WEEK	36 (67.9)	53 (100.0)	95 (6.2)	1461 (96.1)	98 (6.4)	1481 (96.1)
2 WEEK	0 (0.0)	17 (32.1)	44 (2.9)	1366 (89.8)	44 (2.9)	1383 (89.7)
3 WEEK	0 (0.0)	17 (32.1)	47 (3.1)	1322 (86.9)	47 (3.0)	1339 (86.9)
6 MONTHS	2 (3.8)	17 (32.1)	273 (17.9)	1275 (83.8)	275 (17.8)	1292 (83.8)
12 MONTHS	1 (1.9)	15 (28.3)	130 (8.5)	1002 (65.9)	131 (8.5)	1017 (66.0)
18 MONTHS	0 (0.0)	14 (26.4)	47 (3.1)	872 (57.3)	47 (3.0)	886 (57.5)
24 MONTHS	1 (1.9)	14 (26.4)	24 (1.6)	825 (54.2)	25 (1.6)	839 (54.4)
30 MONTHS	0 (0.0)	13 (24.5)	13 (0.9)	801 (52.7)	13 (0.8)	814 (52.8)
36 MONTHS	0 (0.0)	13 (24.5)	125 (8.2)	788 (51.8)	125 (8.1)	801 (52.0)
42 MONTHS	0 (0.0)	13 (24.5)	449 (29.5)	663 (43.6)	449 (29.1)	676 (43.9)
48 MONTHS	2 (3.8)	13 (24.5)	147 (9.7)	214 (14.1)	149 (9.7)	227 (14.7)
54 MONTHS	0 (0.0)	11 (20.8)	41 (2.7)	67 (4.4)	40 (2.6)	78 (5.1)
60 MONTHS	11 (20.8)	11 (20.8)	13 (0.9)	26 (1.7)	25 (1.6)	38 (2.5)
66 MONTHS	0 (0.0)	0 (0.0)	11 (0.7)	13 (0.9)	11 (0.7)	13 (0.8)
> 66 MONTHS	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.1)	2 (0.1)	2 (0.1)

Protocols: 04-001, 04-248, 04-249, 04-250, 04-251, 05-002, 06-260, 05-256, 08-271, 09-282, 09-284, 09-285, 09-003, 10-003 and 11-295.

^a Cumulative includes all subjects exposed for the specific time period.

<資料番号5.3.5.3-02 : JCT-1.3>

表2.7.4.7-5

156-PKD-CSS

JCT-1.1 Extent of Exposure to Study Medication: All PKD Studies

Duration of exposure	15-45 mg (N=53)		60-120 mg (N=1412)		Total (N=1432)	
	Last dose	Cumulative ^a	Last dose	Cumulative ^a	Last dose	Cumulative ^a
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1 DAY	0 (0.0)	53 (100.0)	23 (1.6)	1412 (100.0)	23 (1.6)	1432 (100.0)
1 WEEK	36 (67.9)	53 (100.0)	23 (1.6)	1389 (98.4)	26 (1.8)	1409 (98.4)
2 WEEK	0 (0.0)	17 (32.1)	44 (3.1)	1366 (96.7)	44 (3.1)	1383 (96.6)
3 WEEK	0 (0.0)	17 (32.1)	47 (3.3)	1322 (93.6)	47 (3.3)	1339 (93.5)
6 MONTHS	2 (3.8)	17 (32.1)	273 (19.3)	1275 (90.3)	275 (19.2)	1292 (90.2)
12 MONTHS	1 (1.9)	15 (28.3)	130 (9.2)	1002 (71.0)	131 (9.1)	1017 (71.0)
18 MONTHS	0 (0.0)	14 (26.4)	47 (3.3)	872 (61.8)	47 (3.3)	886 (61.9)
24 MONTHS	1 (1.9)	14 (26.4)	24 (1.7)	825 (58.4)	25 (1.7)	839 (58.6)
30 MONTHS	0 (0.0)	13 (24.5)	13 (0.9)	801 (56.7)	13 (0.9)	814 (56.8)
36 MONTHS	0 (0.0)	13 (24.5)	125 (8.9)	788 (55.8)	125 (8.7)	801 (55.9)
42 MONTHS	0 (0.0)	13 (24.5)	449 (31.8)	663 (47.0)	449 (31.4)	676 (47.2)
48 MONTHS	2 (3.8)	13 (24.5)	147 (10.4)	214 (15.2)	149 (10.4)	227 (15.9)
54 MONTHS	0 (0.0)	11 (20.8)	41 (2.9)	67 (4.7)	40 (2.8)	78 (5.4)
60 MONTHS	11 (20.8)	11 (20.8)	13 (0.8)	26 (1.8)	25 (1.7)	38 (2.7)
66 MONTHS	0 (0.0)	0 (0.0)	11 (0.8)	13 (0.9)	11 (0.8)	13 (0.9)
> 66 MONTHS	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.1)	2 (0.1)	2 (0.1)

Protocols: 04-001, 04-248, 04-249, 04-250, 04-251, 05-002, 06-260, 08-271, 09-284, 09-285, 09-003, 10-003.

^a Cumulative includes all subjects exposed for the specific time period.

<資料番号5.3.5.3-02 : JCT-1.1>

表2.7.4.7-6
 156-251
 CT-7.1 Extent of Exposure to Study Medication (全体)

Duration of exposure	Tolvaptan (N=961)			Placebo (N=483)		
	Last dose n (%)	Cumulative ^a n (%)	Average daily Dose ^b	Last dose n (%)	Cumulative ^a n (%)	Average daily Dose ^b
1 WEEK	18 (1.9)	961 (100.0)	58.92	0 (0.0)	483 (100.0)	58.66
2 WEEKS	13 (1.4)	943 (98.1)	85.27	3 (0.6)	483 (100.0)	86.37
3 WEEKS	14 (1.5)	929 (96.7)	107.70	3 (0.6)	480 (99.4)	113.70
4 MONTHS	51 (5.3)	915 (95.2)	104.29	6 (1.2)	476 (98.6)	114.30
8 MONTHS	29 (3.0)	864 (89.9)	101.53	9 (1.9)	470 (97.3)	112.51
12 MONTHS	27 (2.8)	836 (87.0)	99.60	7 (1.4)	462 (95.7)	112.36
16 MONTHS	18 (1.9)	809 (84.2)	98.34	9 (1.9)	455 (94.2)	111.85
20 MONTHS	17 (1.8)	791 (82.3)	97.38	8 (1.7)	446 (92.3)	110.72
24 MONTHS	12 (1.2)	774 (80.5)	97.04	11 (2.3)	437 (90.5)	110.76
28 MONTHS	10 (1.0)	762 (79.3)	96.51	5 (1.0)	427 (88.4)	111.30
32 MONTHS	10 (1.0)	752 (78.3)	96.28	4 (0.8)	422 (87.4)	110.48
36 MONTHS	377 (39.2)	742 (77.2)	96.45	241 (49.9)	418 (86.5)	110.55
> 36 MONTHS	365 (38.0)	365 (38.0)	96.70	177 (36.6)	177 (36.6)	108.35
ANY EXPOSURE	961 (100.0)	961 (100.0)	95.29	483 (100.0)	483 (100.0)	110.02

^a Cumulative includes all subjects exposed for the specific time period.

^b Represents average daily dose from day 1 through indicated visit.

<資料番号5.3.5.1-01 : CT-7.1>

表2.7.4.7-7

156-251

CT-7.2 Exposure to Study Medication by Dose (全体)

Visit ^a	Tolvaptan (N=961)						Placebo (N=483)					
	N	Missing n (%)	0mg n (%)	60mg n (%)	90mg n (%)	120mg n (%)	N	Missing n (%)	0mg n (%)	60mg n (%)	90mg n (%)	120mg n (%)
1 WEEK	961	0 (0.0)	1 (0.1)	958 (99.7)	2 (0.2)	0 (0.0)	483	0 (0.0)	1 (0.2)	482 (99.8)	0 (0.0)	0 (0.0)
2 WEEKS	943	0 (0.0)	5 (0.5)	51 (5.4)	885 (93.8)	2 (0.2)	483	0 (0.0)	2 (0.4)	3 (0.6)	478 (99.0)	0 (0.0)
3 WEEKS	929	0 (0.0)	4 (0.4)	88 (9.5)	85 (9.1)	752 (80.9)	480	0 (0.0)	1 (0.2)	8 (1.7)	21 (4.4)	450 (93.8)
4 MONTHS	915	0 (0.0)	6 (0.7)	122 (13.3)	142 (15.5)	645 (70.5)	476	0 (0.0)	2 (0.4)	12 (2.5)	29 (6.1)	433 (91.0)
8 MONTHS	864	0 (0.0)	10 (1.2)	132 (15.3)	162 (18.8)	560 (64.8)	470	0 (0.0)	5 (1.1)	16 (3.4)	37 (7.9)	412 (87.7)
12 MONTHS	836	1 (0.1)	12 (1.4)	146 (17.5)	162 (19.4)	515 (61.6)	462	0 (0.0)	3 (0.6)	20 (4.3)	36 (7.8)	403 (87.2)
16 MONTHS	809	0 (0.0)	9 (1.1)	164 (20.3)	154 (19.0)	482 (59.6)	455	0 (0.0)	3 (0.7)	24 (5.3)	36 (7.9)	392 (86.2)
20 MONTHS	791	0 (0.0)	12 (1.5)	167 (21.1)	153 (19.3)	459 (58.0)	446	0 (0.0)	3 (0.7)	25 (5.6)	37 (8.3)	381 (85.4)
24 MONTHS	774	0 (0.0)	6 (0.8)	169 (21.8)	166 (21.4)	433 (55.9)	437	0 (0.0)	3 (0.7)	25 (5.7)	37 (8.5)	372 (85.1)
28 MONTHS	762	0 (0.0)	5 (0.7)	173 (22.7)	167 (21.9)	417 (54.7)	427	0 (0.0)	1 (0.2)	24 (5.6)	39 (9.1)	363 (85.0)
32 MONTHS	752	0 (0.0)	4 (0.5)	175 (23.3)	166 (22.1)	407 (54.1)	422	0 (0.0)	2 (0.5)	30 (7.1)	37 (8.8)	353 (83.6)
36 MONTHS	742	0 (0.0)	2 (0.3)	179 (24.1)	157 (21.2)	404 (54.4)	418	0 (0.0)	0 (0.0)	32 (7.7)	38 (9.1)	348 (83.3)
> 36 MONTHS	365	0 (0.0)	2 (0.5)	81 (22.2)	71 (19.5)	211 (57.8)	177	0 (0.0)	0 (0.0)	13 (7.3)	23 (13.0)	141 (79.7)

^a Represents modal dose since prior visit.

<資料番号5.3.5.1-01 : CT-7.2>

表2.7.4.7-8
 156-251
 CT-8.1 Adverse Events (All Causalities) - Within Treatment Period (全体)

	Tolvaptan	Placebo	Total
Number of:	N %	N %	N %
SUBJECTS TREATED	961	483	1444
SUBJECT YEARS OF DRUG EXPOSURE	2334.5	1305.5	3640
SUBJECTS WITH ADVERSE EVENTS	941 (97.9)	469 (97.1)	1410 (97.6)
ADVERSE EVENTS	10909	4968	15877
SUBJECTS WITH TREATMENT-EMERGENT ADVERSE EVENTS	941 (97.9)	469 (97.1)	1410 (97.6)
TREATMENT-EMERGENT ADVERSE EVENTS	8544	3775	12319
SUBJECTS WITH SERIOUS TREATMENT-EMERGENT ADVERSE EVENTS	177 (18.4)	95 (19.7)	272 (18.8)
SUBJECTS WITH SEVERE TREATMENT-EMERGENT ADVERSE EVENTS	203 (21.1)	88 (18.2)	291 (20.2)
SUBJECTS DISCONTINUED STUDY MEDICATION DUE TO ADVERSE EVENTS	144 (15.0)	21 (4.3)	165 (11.4)
SUBJECTS WHO DIED	0 (0.0)	0 (0.0)	0 (0.0)

<資料番号5.3.5.1-01 : CT-8.1>

表2.7.4.7-9

156-XXXX-251

JT-7.1 Extent of Exposure to Study Medication (日本の被験者)

Duration of exposure	Tolvaptan (N=118)			Placebo (N=59)		
	Last dose n (%)	Cumulative ^a n (%)	Average daily Dose ^b	Last dose n (%)	Cumulative ^a n (%)	Average daily Dose ^b
1 WEEK	1 (0.8)	118 (100.0)	60.20	0 (0.0)	59 (100.0)	60.29
2 WEEKS	1 (0.8)	117 (99.2)	87.40	0 (0.0)	59 (100.0)	89.16
3 WEEKS	2 (1.7)	116 (98.3)	108.65	1 (1.7)	59 (100.0)	117.17
4 MONTHS	2 (1.7)	114 (96.6)	101.19	0 (0.0)	58 (98.3)	116.44
8 MONTHS	8 (6.8)	112 (94.9)	94.41	0 (0.0)	58 (98.3)	115.86
12 MONTHS	2 (1.7)	104 (88.1)	93.90	0 (0.0)	58 (98.3)	114.52
16 MONTHS	4 (3.4)	102 (86.4)	92.78	2 (3.4)	58 (98.3)	113.61
20 MONTHS	2 (1.7)	98 (83.1)	93.89	0 (0.0)	56 (94.9)	114.22
24 MONTHS	1 (0.8)	96 (81.4)	92.66	1 (1.7)	56 (94.9)	112.55
28 MONTHS	1 (0.8)	95 (80.5)	92.60	0 (0.0)	55 (93.2)	113.66
32 MONTHS	1 (0.8)	94 (79.7)	93.02	0 (0.0)	55 (93.2)	112.10
36 MONTHS	39 (33.1)	93 (78.8)	93.09	22 (37.3)	55 (93.2)	112.87
> 36 MONTHS	54 (45.8)	54 (45.8)	92.40	33 (55.9)	33 (55.9)	108.93
ANY EXPOSURE	118 (100.0)	118 (100.0)	92.62	59 (100.0)	59 (100.0)	113.17

^a Cumulative includes all subjects exposed for the specific time period.^b Represents average daily dose from day 1 through indicated visit.

<資料番号5.3.5.3-02 : JT-7.1>

表2.7.4.7-10

156-XXXX-251

JT-7.2 Exposure to Study Medication by Dose (日本の被験者)

Visit ^a	Tolvaptan (N=118)						Placebo (N=59)					
	N	Missing n (%)	0 mg n (%)	60 mg n (%)	90 mg n (%)	120 mg n (%)	N	Missing n (%)	0 mg n (%)	60 mg n (%)	90 mg n (%)	120 mg n (%)
1 WEEK	118	0 (0.0)	0 (0.0)	118 (100.0)	0 (0.0)	0 (0.0)	59	0 (0.0)	0 (0.0)	59 (100.0)	0 (0.0)	0 (0.0)
2 WEEKS	117	0 (0.0)	1 (0.9)	5 (4.3)	111 (94.9)	0 (0.0)	59	0 (0.0)	0 (0.0)	0 (0.0)	59 (100.0)	0 (0.0)
3 WEEKS	116	0 (0.0)	0 (0.0)	13 (11.2)	5 (4.3)	98 (84.5)	59	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	57 (96.6)
4 MONTHS	114	0 (0.0)	0 (0.0)	16 (14.0)	22 (19.3)	76 (66.7)	58	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.2)	55 (94.8)
8 MONTHS	112	0 (0.0)	2 (1.8)	19 (17.0)	32 (28.6)	59 (52.7)	58	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.2)	55 (94.8)
12 MONTHS	104	0 (0.0)	1 (1.0)	21 (20.2)	28 (26.9)	54 (51.9)	58	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.2)	55 (94.8)
16 MONTHS	102	0 (0.0)	1 (1.0)	21 (20.6)	27 (26.5)	53 (52.0)	58	0 (0.0)	1 (1.7)	0 (0.0)	3 (5.2)	54 (93.1)
20 MONTHS	98	0 (0.0)	0 (0.0)	21 (21.4)	27 (27.6)	50 (51.0)	56	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.4)	53 (94.6)
24 MONTHS	96	0 (0.0)	1 (1.0)	21 (21.9)	27 (28.1)	47 (49.0)	56	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.4)	53 (94.6)
28 MONTHS	95	0 (0.0)	0 (0.0)	22 (23.2)	27 (28.4)	46 (48.4)	55	0 (0.0)	0 (0.0)	0 (0.0)	4 (7.3)	51 (92.7)
32 MONTHS	94	0 (0.0)	0 (0.0)	22 (23.4)	26 (27.7)	46 (48.9)	55	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.5)	52 (94.5)
36 MONTHS	93	0 (0.0)	0 (0.0)	22 (23.7)	25 (26.9)	46 (49.5)	55	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.5)	52 (94.5)
> 36 MONTHS	54	0 (0.0)	0 (0.0)	11 (20.4)	13 (24.1)	30 (55.6)	33	0 (0.0)	0 (0.0)	0 (0.0)	5 (15.2)	28 (84.8)

^a Represents modal dose since prior visit.

<資料番号5.3.5.3-02 : JT-7.2>

表2.7.4.7-11

156-XXXX-251

NT-7.1 Extent of Exposure to Study Medication (海外の被験者)

Duration of exposure	Tolvaptan (N=843)			Placebo (N=424)		
	Last dose n (%)	Cumulative ^a n (%)	Average daily Dose ^b	Last dose n (%)	Cumulative ^a n (%)	Average daily Dose ^b
1 WEEK	17 (2.0)	843 (100.0)	58.75	0 (0.0)	424 (100.0)	58.43
2 WEEKS	12 (1.4)	826 (98.0)	84.96	3 (0.7)	424 (100.0)	85.98
3 WEEKS	12 (1.4)	813 (96.4)	107.57	2 (0.5)	421 (99.3)	113.22
4 MONTHS	49 (5.8)	801 (95.0)	104.74	6 (1.4)	418 (98.6)	114.00
8 MONTHS	21 (2.5)	752 (89.2)	102.59	9 (2.1)	412 (97.2)	112.04
12 MONTHS	25 (3.0)	732 (86.8)	100.41	7 (1.7)	404 (95.3)	112.05
16 MONTHS	14 (1.7)	707 (83.9)	99.14	7 (1.7)	397 (93.6)	111.59
20 MONTHS	15 (1.8)	693 (82.2)	97.87	8 (1.9)	390 (92.0)	110.22
24 MONTHS	11 (1.3)	678 (80.4)	97.66	10 (2.4)	381 (89.9)	110.49
28 MONTHS	9 (1.1)	667 (79.1)	97.07	5 (1.2)	372 (87.7)	110.95
32 MONTHS	9 (1.1)	658 (78.1)	96.74	4 (0.9)	367 (86.6)	110.23
36 MONTHS	338 (40.1)	649 (77.0)	96.93	219 (51.7)	363 (85.6)	110.19
> 36 MONTHS	311 (36.9)	311 (36.9)	97.45	144 (34.0)	144 (34.0)	108.22
ANY EXPOSURE	843 (100.0)	843 (100.0)	95.67	424 (100.0)	424 (100.0)	109.58

^a Cumulative includes all subjects exposed for the specific time period.

^b Represents average daily dose from day 1 through indicated visit.

< 資料番号5.3.5.3-02 : NT-7.1 >

表2.7.4.7-12
156-251
NT-7.2 Exposure to Study Medication by Dose (海外の被験者)

Visit ^a	Tolvaptan (N=843)						Placebo (N=424)					
	N	Missing n (%)	0 mg n (%)	60 mg n (%)	90 mg n (%)	120 mg n (%)	N	Missing n (%)	0 mg n (%)	60 mg n (%)	90 mg n (%)	120 mg n (%)
1 WEEK	843	0 (0.0)	1 (0.1)	840 (99.6)	2 (0.2)	0 (0.0)	424	0 (0.0)	1 (0.2)	423 (99.8)	0 (0.0)	0 (0.0)
2 WEEKS	826	0 (0.0)	4 (0.5)	46 (5.6)	774 (93.7)	2 (0.2)	424	0 (0.0)	2 (0.5)	3 (0.7)	419 (98.8)	0 (0.0)
3 WEEKS	813	0 (0.0)	4 (0.5)	75 (9.2)	80 (9.8)	654 (80.4)	421	0 (0.0)	1 (0.2)	8 (1.9)	19 (4.5)	393 (93.3)
4 MONTHS	801	0 (0.0)	6 (0.7)	106 (13.2)	120 (15.0)	569 (71.0)	418	0 (0.0)	2 (0.5)	12 (2.9)	26 (6.2)	378 (90.4)
8 MONTHS	752	0 (0.0)	8 (1.1)	113 (15.0)	130 (17.3)	501 (66.6)	412	0 (0.0)	5 (1.2)	16 (3.9)	34 (8.3)	357 (86.7)
12 MONTHS	732	1 (0.1)	11 (1.5)	125 (17.1)	134 (18.3)	461 (63.0)	404	0 (0.0)	3 (0.7)	20 (5.0)	33 (8.2)	348 (86.1)
16 MONTHS	707	0 (0.0)	8 (1.1)	143 (20.2)	127 (18.0)	429 (60.7)	397	0 (0.0)	2 (0.5)	24 (6.0)	33 (8.3)	338 (85.1)
20 MONTHS	693	0 (0.0)	12 (1.7)	146 (21.1)	126 (18.2)	409 (59.0)	390	0 (0.0)	3 (0.8)	25 (6.4)	34 (8.7)	328 (84.1)
24 MONTHS	678	0 (0.0)	5 (0.7)	148 (21.8)	139 (20.5)	386 (56.9)	381	0 (0.0)	3 (0.8)	25 (6.6)	34 (8.9)	319 (83.7)
28 MONTHS	667	0 (0.0)	5 (0.7)	151 (22.6)	140 (21.0)	371 (55.6)	372	0 (0.0)	1 (0.3)	24 (6.5)	35 (9.4)	312 (83.9)
32 MONTHS	658	0 (0.0)	4 (0.6)	153 (23.3)	140 (21.3)	361 (54.9)	367	0 (0.0)	2 (0.5)	30 (8.2)	34 (9.3)	301 (82.0)
36 MONTHS	649	0 (0.0)	2 (0.3)	157 (24.2)	132 (20.3)	358 (55.2)	363	0 (0.0)	0 (0.0)	32 (8.8)	35 (9.6)	296 (81.5)
> 36 MONTHS	311	0 (0.0)	2 (0.6)	70 (22.5)	58 (18.6)	181 (58.2)	144	0 (0.0)	0 (0.0)	13 (9.0)	18 (12.5)	113 (78.5)

^aRepresents modal dose since prior visit.

<資料番号5.3.5.3-02 : NT-7.2>

表2.7.4.7-13
156-PKD-CSS
JCT-1.2 Extent of Exposure to Study Medication: All Healthy Subjects Studies

Duration of exposure	60 mg (N=14)		90 mg (N=58)		Total (N=72)	
	Last dose	Cumulative ^a	Last dose	Cumulative ^a	Last dose	Cumulative ^a
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1 DAY	0 (0.0)	14 (100.0)	0 (0.0)	58 (100.0)	0 (0.0)	72 (100.0)
2 DAYS	14 (100.0)	14 (100.0)	58 (100.0)	58 (100.0)	72 (100.0)	72 (100.0)

Protocols: 05-256 and 11-295.
^a Cumulative includes all subjects exposed for the specific time period.
< 資料番号5.3.5.3-02 : JCT-1.2 >

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
血液およびリンパ系障害			
貧血	27 (2.8)	24 (5.0)	51 (3.5)
凝血異常	1 (0.1)	1 (0.2)	2 (0.1)
好酸球増加症	2 (0.2)	2 (0.4)	4 (0.3)
低色素性貧血	1 (0.1)	0 (0.0)	1 (0.1)
鉄欠乏性貧血	6 (0.6)	4 (0.8)	10 (0.7)
白血球増加症	3 (0.3)	2 (0.4)	5 (0.3)
白血球減少症	1 (0.1)	4 (0.8)	5 (0.3)
リンパ節症	5 (0.5)	2 (0.4)	7 (0.5)
腎性貧血	0 (0.0)	1 (0.2)	1 (0.1)
好中球増加症	3 (0.3)	1 (0.2)	4 (0.3)
正色素性正球性貧血	1 (0.1)	0 (0.0)	1 (0.1)
汎血球減少症	2 (0.2)	0 (0.0)	2 (0.1)
赤血球増加症	1 (0.1)	0 (0.0)	1 (0.1)
脾臓障害	1 (0.1)	0 (0.0)	1 (0.1)
血小板減少症	1 (0.1)	1 (0.2)	2 (0.1)
血小板増加症	1 (0.1)	0 (0.0)	1 (0.1)
心臓障害			
急性心筋梗塞	0 (0.0)	2 (0.4)	2 (0.1)
狭心症	10 (1.0)	3 (0.6)	13 (0.9)
大動脈弁閉鎖不全症	0 (0.0)	1 (0.2)	1 (0.1)
不整脈	7 (0.7)	2 (0.4)	9 (0.6)
心房細動	5 (0.5)	3 (0.6)	8 (0.6)
房室ブロック	1 (0.1)	0 (0.0)	1 (0.1)
第一度房室ブロック	1 (0.1)	0 (0.0)	1 (0.1)
徐脈	12 (1.2)	6 (1.2)	18 (1.2)
右脚ブロック	1 (0.1)	0 (0.0)	1 (0.1)
心臓瘤	0 (0.0)	2 (0.4)	2 (0.1)
心不全	0 (0.0)	1 (0.2)	1 (0.1)
心臓弁膜疾患	1 (0.1)	0 (0.0)	1 (0.1)
心拡大	1 (0.1)	0 (0.0)	1 (0.1)
心筋症	1 (0.1)	0 (0.0)	1 (0.1)
伝導障害	1 (0.1)	0 (0.0)	1 (0.1)
冠動脈疾患	1 (0.1)	0 (0.0)	1 (0.1)
チアノーゼ	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
心臓障害			
期外収縮	1 (0.1)	1 (0.2)	2 (0.1)
左房肥大	0 (0.0)	1 (0.2)	1 (0.1)
左室機能不全	1 (0.1)	0 (0.0)	1 (0.1)
左室不全	1 (0.1)	0 (0.0)	1 (0.1)
左室肥大	5 (0.5)	1 (0.2)	6 (0.4)
僧帽弁疾患	1 (0.1)	0 (0.0)	1 (0.1)
僧帽弁閉鎖不全症	1 (0.1)	2 (0.4)	3 (0.2)
僧帽弁逸脱	2 (0.2)	1 (0.2)	3 (0.2)
心筋梗塞	1 (0.1)	0 (0.0)	1 (0.1)
心筋虚血	1 (0.1)	0 (0.0)	1 (0.1)
動悸	34 (3.5)	6 (1.2)	40 (2.8)
心嚢液貯留	2 (0.2)	0 (0.0)	2 (0.1)
心膜炎	2 (0.2)	0 (0.0)	2 (0.1)
洞不全症候群	1 (0.1)	0 (0.0)	1 (0.1)
洞性不整脈	1 (0.1)	0 (0.0)	1 (0.1)
洞性徐脈	2 (0.2)	1 (0.2)	3 (0.2)
上室性期外収縮	1 (0.1)	0 (0.0)	1 (0.1)
上室性頻脈	4 (0.4)	0 (0.0)	4 (0.3)
頻脈	13 (1.4)	5 (1.0)	18 (1.2)
三尖弁閉鎖不全症	0 (0.0)	1 (0.2)	1 (0.1)
心室性期外収縮	9 (0.9)	0 (0.0)	9 (0.6)
ウォルフ・パーキンソン・ホワイ ト症候群	0 (0.0)	1 (0.2)	1 (0.1)
先天性、家族性および遺伝性障害			
心房中隔欠損症	0 (0.0)	2 (0.4)	2 (0.1)
第Ⅴ因子ライデン変異	0 (0.0)	1 (0.2)	1 (0.1)
多発性内分泌腺腫症	0 (0.0)	1 (0.2)	1 (0.1)
多嚢胞性肝疾患	3 (0.3)	2 (0.4)	5 (0.3)
脊椎奇形	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺管嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
耳および迷路障害			
耳垢栓塞	2 (0.2)	0 (0.0)	2 (0.1)
難聴	1 (0.1)	2 (0.4)	3 (0.2)
耳閉	3 (0.3)	1 (0.2)	4 (0.3)
耳不快感	2 (0.2)	1 (0.2)	3 (0.2)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
耳および迷路障害			
耳痛	7 (0.7)	3 (0.6)	10 (0.7)
耳そう痒症	0 (0.0)	1 (0.2)	1 (0.1)
内リンパ水腫	0 (0.0)	1 (0.2)	1 (0.1)
耳管障害	1 (0.1)	0 (0.0)	1 (0.1)
聴覚障害	1 (0.1)	0 (0.0)	1 (0.1)
聴力低下	1 (0.1)	0 (0.0)	1 (0.1)
内耳障害	0 (0.0)	1 (0.2)	1 (0.1)
メニエール病	0 (0.0)	1 (0.2)	1 (0.1)
中耳滲出液	0 (0.0)	1 (0.2)	1 (0.1)
乗物酔い	3 (0.3)	1 (0.2)	4 (0.3)
耳鳴	11 (1.1)	2 (0.4)	13 (0.9)
回転性めまい	24 (2.5)	18 (3.7)	42 (2.9)
頭位性回転性めまい	2 (0.2)	1 (0.2)	3 (0.2)
内分泌障害			
アンドロゲン欠乏症	1 (0.1)	0 (0.0)	1 (0.1)
自己免疫性甲状腺炎	1 (0.1)	1 (0.2)	2 (0.1)
バセドウ病	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺腫	1 (0.1)	1 (0.2)	2 (0.1)
副甲状腺機能亢進症	1 (0.1)	0 (0.0)	1 (0.1)
続発性副甲状腺機能亢進症	0 (0.0)	1 (0.2)	1 (0.1)
続発性副甲状腺機能低下症	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺機能低下症	6 (0.6)	2 (0.4)	8 (0.6)
エストロゲン欠乏症	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺炎	1 (0.1)	1 (0.2)	2 (0.1)
眼障害			
調節障害	1 (0.1)	0 (0.0)	1 (0.1)
眼瞼炎	3 (0.3)	1 (0.2)	4 (0.3)
白内障	1 (0.1)	0 (0.0)	1 (0.1)
霰粒腫	1 (0.1)	0 (0.0)	1 (0.1)
結膜出血	7 (0.7)	2 (0.4)	9 (0.6)
結膜充血	0 (0.0)	1 (0.2)	1 (0.1)
結膜炎	14 (1.5)	7 (1.4)	21 (1.5)
アレルギー性結膜炎	3 (0.3)	2 (0.4)	5 (0.3)
角膜障害	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
眼障害			
眼の隈	0 (0.0)	1 (0.2)	1 (0.1)
眼乾燥	15 (1.6)	7 (1.4)	22 (1.5)
外眼筋不全麻痺	0 (0.0)	1 (0.2)	1 (0.1)
眼の障害	1 (0.1)	1 (0.2)	2 (0.1)
眼出血	1 (0.1)	1 (0.2)	2 (0.1)
眼の炎症	0 (0.0)	1 (0.2)	1 (0.1)
眼痛	5 (0.5)	1 (0.2)	6 (0.4)
眼部腫脹	1 (0.1)	2 (0.4)	3 (0.2)
眼瞼浮腫	4 (0.4)	1 (0.2)	5 (0.3)
眼瞼下垂	2 (0.2)	0 (0.0)	2 (0.1)
眼瞼皮膚乾燥	1 (0.1)	0 (0.0)	1 (0.1)
眼瞼そう痒症	0 (0.0)	1 (0.2)	1 (0.1)
緑内障	5 (0.5)	1 (0.2)	6 (0.4)
遠視	1 (0.1)	0 (0.0)	1 (0.1)
虹彩炎	1 (0.1)	1 (0.2)	2 (0.1)
流涙増加	0 (0.0)	1 (0.2)	1 (0.1)
眼充血	2 (0.2)	1 (0.2)	3 (0.2)
開放隅角緑内障	0 (0.0)	1 (0.2)	1 (0.1)
眼窩周囲浮腫	0 (0.0)	1 (0.2)	1 (0.1)
羞明	1 (0.1)	0 (0.0)	1 (0.1)
光視症	1 (0.1)	0 (0.0)	1 (0.1)
老視	1 (0.1)	0 (0.0)	1 (0.1)
翼状片	1 (0.1)	0 (0.0)	1 (0.1)
網膜剥離	2 (0.2)	1 (0.2)	3 (0.2)
強膜出血	0 (0.0)	1 (0.2)	1 (0.1)
強膜炎	1 (0.1)	1 (0.2)	2 (0.1)
暗点	1 (0.1)	0 (0.0)	1 (0.1)
ブドウ膜炎	0 (0.0)	1 (0.2)	1 (0.1)
霧視	3 (0.3)	2 (0.4)	5 (0.3)
視力低下	2 (0.2)	0 (0.0)	2 (0.1)
視力障害	2 (0.2)	3 (0.6)	5 (0.3)
硝子体剥離	3 (0.3)	0 (0.0)	3 (0.2)
硝子体浮遊物	2 (0.2)	0 (0.0)	2 (0.1)
眼球乾燥	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
腹部癒着	0 (0.0)	1 (0.2)	1 (0.1)
腹部不快感	29 (3.0)	10 (2.1)	39 (2.7)
腹部膨満	47 (4.9)	16 (3.3)	63 (4.4)
腹部ヘルニア	5 (0.5)	6 (1.2)	11 (0.8)
閉塞を伴う腹部ヘルニア	0 (0.0)	1 (0.2)	1 (0.1)
腹部腫瘍	1 (0.1)	1 (0.2)	2 (0.1)
腹痛	62 (6.5)	32 (6.6)	94 (6.5)
下腹部痛	7 (0.7)	4 (0.8)	11 (0.8)
上腹部痛	63 (6.6)	42 (8.7)	105 (7.3)
腹部硬直	1 (0.1)	0 (0.0)	1 (0.1)
腹部圧痛	8 (0.8)	2 (0.4)	10 (0.7)
裂肛	4 (0.4)	1 (0.2)	5 (0.3)
痔瘻	1 (0.1)	0 (0.0)	1 (0.1)
肛門そう痒症	1 (0.1)	0 (0.0)	1 (0.1)
アフタ性口内炎	7 (0.7)	1 (0.2)	8 (0.6)
腹水	0 (0.0)	1 (0.2)	1 (0.1)
便通不規則	1 (0.1)	0 (0.0)	1 (0.1)
呼気臭	2 (0.2)	0 (0.0)	2 (0.1)
口唇のひび割れ	1 (0.1)	0 (0.0)	1 (0.1)
口唇炎	5 (0.5)	0 (0.0)	5 (0.3)
大腸炎	1 (0.1)	4 (0.8)	5 (0.3)
結腸ポリープ	4 (0.4)	2 (0.4)	6 (0.4)
便秘	81 (8.4)	12 (2.5)	93 (6.4)
クローン病	1 (0.1)	0 (0.0)	1 (0.1)
齲歯	8 (0.8)	5 (1.0)	13 (0.9)
歯不快感	4 (0.4)	1 (0.2)	5 (0.3)
下痢	128 (13.3)	53 (11.0)	181 (12.5)
憩室	1 (0.1)	0 (0.0)	1 (0.1)
腸憩室	4 (0.4)	2 (0.4)	6 (0.4)
口内乾燥	154 (16.0)	60 (12.4)	214 (14.8)
十二指腸潰瘍	1 (0.1)	1 (0.2)	2 (0.1)
十二指腸炎	3 (0.3)	0 (0.0)	3 (0.2)
消化不良	76 (7.9)	16 (3.3)	92 (6.4)
嚥下障害	6 (0.6)	1 (0.2)	7 (0.5)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
小腸炎	8 (0.8)	2 (0.4)	10 (0.7)
腸炎	0 (0.0)	2 (0.4)	2 (0.1)
心窩部不快感	4 (0.4)	2 (0.4)	6 (0.4)
びらん性十二指腸炎	1 (0.1)	0 (0.0)	1 (0.1)
おくび	1 (0.1)	0 (0.0)	1 (0.1)
糞塊	0 (0.0)	1 (0.2)	1 (0.1)
大腿ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
鼓腸	8 (0.8)	1 (0.2)	9 (0.6)
食中毒	4 (0.4)	2 (0.4)	6 (0.4)
機能的胃腸障害	1 (0.1)	0 (0.0)	1 (0.1)
胃障害	2 (0.2)	1 (0.2)	3 (0.2)
胃ポリープ	2 (0.2)	2 (0.4)	4 (0.3)
胃潰瘍	0 (0.0)	1 (0.2)	1 (0.1)
胃炎	14 (1.5)	6 (1.2)	20 (1.4)
びらん性胃炎	1 (0.1)	0 (0.0)	1 (0.1)
胃腸障害	5 (0.5)	2 (0.4)	7 (0.5)
消化管運動過剰	1 (0.1)	0 (0.0)	1 (0.1)
胃腸の炎症	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動障害	1 (0.1)	0 (0.0)	1 (0.1)
消化器痛	1 (0.1)	1 (0.2)	2 (0.1)
胃腸音異常	1 (0.1)	1 (0.2)	2 (0.1)
胃食道逆流性疾患	43 (4.5)	16 (3.3)	59 (4.1)
歯肉障害	0 (0.0)	1 (0.2)	1 (0.1)
歯肉痛	0 (0.0)	2 (0.4)	2 (0.1)
歯肉退縮	1 (0.1)	2 (0.4)	3 (0.2)
歯肉炎	4 (0.4)	4 (0.8)	8 (0.6)
舌炎	0 (0.0)	1 (0.2)	1 (0.1)
舌痛	3 (0.3)	0 (0.0)	3 (0.2)
血便排泄	3 (0.3)	4 (0.8)	7 (0.5)
痔出血	1 (0.1)	0 (0.0)	1 (0.1)
痔核	14 (1.5)	9 (1.9)	23 (1.6)
裂孔ヘルニア	8 (0.8)	4 (0.8)	12 (0.8)
胃酸過多	1 (0.1)	2 (0.4)	3 (0.2)
口の感覚鈍麻	1 (0.1)	1 (0.2)	2 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
回腸炎	1 (0.1)	0 (0.0)	1 (0.1)
イレウス	1 (0.1)	0 (0.0)	1 (0.1)
臍径ヘルニア	7 (0.7)	6 (1.2)	13 (0.9)
内ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
腸出血	0 (0.0)	1 (0.2)	1 (0.1)
過敏性腸症候群	1 (0.1)	5 (1.0)	6 (0.4)
口唇乾燥	6 (0.6)	2 (0.4)	8 (0.6)
口唇腫脹	1 (0.1)	0 (0.0)	1 (0.1)
弛緩歯	1 (0.1)	0 (0.0)	1 (0.1)
下部消化管出血	1 (0.1)	0 (0.0)	1 (0.1)
吸収不良	1 (0.1)	1 (0.2)	2 (0.1)
メレナ	0 (0.0)	2 (0.4)	2 (0.1)
口腔嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
口腔内出血	0 (0.0)	1 (0.2)	1 (0.1)
口腔内潰瘍形成	0 (0.0)	1 (0.2)	1 (0.1)
悪心	98 (10.2)	57 (11.8)	155 (10.7)
嚥下痛	0 (0.0)	1 (0.2)	1 (0.1)
食道炎	5 (0.5)	2 (0.4)	7 (0.5)
口腔障害	1 (0.1)	0 (0.0)	1 (0.1)
口腔扁平苔癬	1 (0.1)	0 (0.0)	1 (0.1)
口腔内痛	1 (0.1)	0 (0.0)	1 (0.1)
膵嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
急性膵炎	0 (0.0)	1 (0.2)	1 (0.1)
再発性膵炎	0 (0.0)	1 (0.2)	1 (0.1)
口の錯感覚	1 (0.1)	0 (0.0)	1 (0.1)
歯周病	1 (0.1)	0 (0.0)	1 (0.1)
歯周炎	2 (0.2)	1 (0.2)	3 (0.2)
腹膜出血	0 (0.0)	1 (0.2)	1 (0.1)
結腸直腸ポリープ	1 (0.1)	0 (0.0)	1 (0.1)
肛門周囲痛	1 (0.1)	0 (0.0)	1 (0.1)
歯根嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
直腸出血	5 (0.5)	0 (0.0)	5 (0.3)
直腸脱	0 (0.0)	1 (0.2)	1 (0.1)
吐き戻し	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
レッチング	1 (0.1)	1 (0.2)	2 (0.1)
唾液管の炎症	0 (0.0)	1 (0.2)	1 (0.1)
S 状結腸炎	0 (0.0)	1 (0.2)	1 (0.1)
口内炎	6 (0.6)	1 (0.2)	7 (0.5)
舌苔	2 (0.2)	0 (0.0)	2 (0.1)
舌変色	3 (0.3)	0 (0.0)	3 (0.2)
舌障害	1 (0.1)	1 (0.2)	2 (0.1)
舌乾燥	1 (0.1)	2 (0.4)	3 (0.2)
舌粘膜剥脱	1 (0.1)	0 (0.0)	1 (0.1)
変色歯	0 (0.0)	1 (0.2)	1 (0.1)
歯の障害	3 (0.3)	3 (0.6)	6 (0.4)
歯痛	10 (1.0)	12 (2.5)	22 (1.5)
臍ヘルニア	21 (2.2)	7 (1.4)	28 (1.9)
閉塞性臍ヘルニア	0 (0.0)	1 (0.2)	1 (0.1)
嘔吐	79 (8.2)	40 (8.3)	119 (8.2)
一般・全身障害および投与部位の状態			
無力症	57 (5.9)	27 (5.6)	84 (5.8)
腋窩痛	1 (0.1)	1 (0.2)	2 (0.1)
胸部不快感	13 (1.4)	4 (0.8)	17 (1.2)
胸痛	42 (4.4)	12 (2.5)	54 (3.7)
悪寒	12 (1.2)	2 (0.4)	14 (1.0)
嚢胞	6 (0.6)	5 (1.0)	11 (0.8)
医療機器位置異常	0 (0.0)	1 (0.2)	1 (0.1)
異形成	0 (0.0)	1 (0.2)	1 (0.1)
早期満腹	1 (0.1)	2 (0.4)	3 (0.2)
運動耐性低下	3 (0.3)	0 (0.0)	3 (0.2)
顔面浮腫	2 (0.2)	0 (0.0)	2 (0.1)
脂肪組織増加	1 (0.1)	0 (0.0)	1 (0.1)
疲労	131 (13.6)	47 (9.7)	178 (12.3)
異常感	1 (0.1)	1 (0.2)	2 (0.1)
冷感	9 (0.9)	0 (0.0)	9 (0.6)
酩酊感	1 (0.1)	0 (0.0)	1 (0.1)
熱感	3 (0.3)	2 (0.4)	5 (0.3)
びくびく感	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態			
ヘルニア	2 (0.2)	1 (0.2)	3 (0.2)
高熱	0 (0.0)	1 (0.2)	1 (0.1)
治癒不良	1 (0.1)	0 (0.0)	1 (0.1)
炎症	1 (0.1)	0 (0.0)	1 (0.1)
インフルエンザ様疾患	7 (0.7)	5 (1.0)	12 (0.8)
易刺激性	5 (0.5)	1 (0.2)	6 (0.4)
局所腫脹	1 (0.1)	1 (0.2)	2 (0.1)
倦怠感	24 (2.5)	10 (2.1)	34 (2.4)
粘膜乾燥	8 (0.8)	2 (0.4)	10 (0.7)
小結節	2 (0.2)	0 (0.0)	2 (0.1)
非心臓性胸痛	0 (0.0)	2 (0.4)	2 (0.1)
浮腫	16 (1.7)	9 (1.9)	25 (1.7)
末梢性浮腫	81 (8.4)	46 (9.5)	127 (8.8)
疼痛	16 (1.7)	4 (0.8)	20 (1.4)
発熱	45 (4.7)	42 (8.7)	87 (6.0)
不活発	1 (0.1)	1 (0.2)	2 (0.1)
恥骨上痛	1 (0.1)	1 (0.2)	2 (0.1)
腫脹	1 (0.1)	0 (0.0)	1 (0.1)
温度変化不耐症	7 (0.7)	1 (0.2)	8 (0.6)
口渇	531 (55.3)	99 (20.5)	630 (43.6)
ワクチン接種部位反応	0 (0.0)	1 (0.2)	1 (0.1)
血管穿刺部位血腫	1 (0.1)	0 (0.0)	1 (0.1)
肝胆道系障害			
胆道ジスキネジー	1 (0.1)	0 (0.0)	1 (0.1)
細胆管炎	0 (0.0)	1 (0.2)	1 (0.1)
胆管炎	2 (0.2)	0 (0.0)	2 (0.1)
胆嚢炎	1 (0.1)	0 (0.0)	1 (0.1)
胆石症	3 (0.3)	1 (0.2)	4 (0.3)
胆嚢痛	1 (0.1)	0 (0.0)	1 (0.1)
胆嚢ポリープ	4 (0.4)	2 (0.4)	6 (0.4)
肝嚢胞	13 (1.4)	10 (2.1)	23 (1.6)
肝嚢胞破裂	1 (0.1)	0 (0.0)	1 (0.1)
肝機能異常	12 (1.2)	2 (0.4)	14 (1.0)
肝臓痛	7 (0.7)	3 (0.6)	10 (0.7)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
肝胆道系障害			
脂肪肝	3 (0.3)	0 (0.0)	3 (0.2)
肝炎	1 (0.1)	0 (0.0)	1 (0.1)
肝腫大	9 (0.9)	3 (0.6)	12 (0.8)
高ビリルビン血症	1 (0.1)	1 (0.2)	2 (0.1)
肝障害	5 (0.5)	1 (0.2)	6 (0.4)
肝圧痛	3 (0.3)	0 (0.0)	3 (0.2)
門脈圧亢進症	0 (0.0)	1 (0.2)	1 (0.1)
免疫系障害			
アレルギー性浮腫	1 (0.1)	0 (0.0)	1 (0.1)
節足動物咬傷アレルギー	4 (0.4)	0 (0.0)	4 (0.3)
節足動物刺傷アレルギー	2 (0.2)	0 (0.0)	2 (0.1)
アナフィラキシーショック	1 (0.1)	0 (0.0)	1 (0.1)
アナフィラキシー様反応	1 (0.1)	0 (0.0)	1 (0.1)
造影剤アレルギー	0 (0.0)	1 (0.2)	1 (0.1)
薬物過敏症	3 (0.3)	2 (0.4)	5 (0.3)
食物アレルギー	3 (0.3)	0 (0.0)	3 (0.2)
家塵アレルギー	1 (0.1)	0 (0.0)	1 (0.1)
過敏症	7 (0.7)	2 (0.4)	9 (0.6)
複合アレルギー	2 (0.2)	0 (0.0)	2 (0.1)
季節性アレルギー	26 (2.7)	10 (2.1)	36 (2.5)
感染症および寄生虫症			
膿瘍	1 (0.1)	2 (0.4)	3 (0.2)
四肢膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
急性副鼻腔炎	3 (0.3)	2 (0.4)	5 (0.3)
急性扁桃炎	6 (0.6)	4 (0.8)	10 (0.7)
アデノイド咽頭炎	1 (0.1)	0 (0.0)	1 (0.1)
真菌性肛門感染	1 (0.1)	0 (0.0)	1 (0.1)
肛門感染	1 (0.1)	0 (0.0)	1 (0.1)
虫垂炎	2 (0.2)	4 (0.8)	6 (0.4)
細菌性関節炎	1 (0.1)	1 (0.2)	2 (0.1)
感染性関節炎	1 (0.1)	0 (0.0)	1 (0.1)
回虫症	0 (0.0)	1 (0.2)	1 (0.1)
細菌尿	3 (0.3)	1 (0.2)	4 (0.3)
バルトリン腺膿瘍	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
感染症および寄生虫症			
β溶血性レンサ球菌感染	0 (0.0)	1 (0.2)	1 (0.1)
乳房感染	0 (0.0)	2 (0.4)	2 (0.1)
気管支炎	58 (6.0)	33 (6.8)	91 (6.3)
ウイルス性気管支炎	2 (0.2)	1 (0.2)	3 (0.2)
気管支肺炎	0 (0.0)	1 (0.2)	1 (0.1)
カンジダ症	2 (0.2)	3 (0.6)	5 (0.3)
蜂巣炎	6 (0.6)	1 (0.2)	7 (0.5)
眼窩蜂巣炎	0 (0.0)	1 (0.2)	1 (0.1)
子宮頸管炎	1 (0.1)	0 (0.0)	1 (0.1)
慢性副鼻腔炎	0 (0.0)	1 (0.2)	1 (0.1)
クロストリジウム性大腸炎	1 (0.1)	0 (0.0)	1 (0.1)
感染性結膜炎	1 (0.1)	0 (0.0)	1 (0.1)
膀胱炎	11 (1.1)	12 (2.5)	23 (1.6)
サイトメガロウイルス感染	1 (0.1)	0 (0.0)	1 (0.1)
憩室炎	4 (0.4)	1 (0.2)	5 (0.3)
耳感染	22 (2.3)	7 (1.4)	29 (2.0)
耳垂感染	1 (0.1)	0 (0.0)	1 (0.1)
感染性腸炎	1 (0.1)	1 (0.2)	2 (0.1)
感染性小腸結腸炎	1 (0.1)	0 (0.0)	1 (0.1)
伝染性紅斑	0 (0.0)	1 (0.2)	1 (0.1)
遊走性紅斑	1 (0.1)	0 (0.0)	1 (0.1)
眼感染	1 (0.1)	3 (0.6)	4 (0.3)
眼瞼感染	0 (0.0)	1 (0.2)	1 (0.1)
熱性感染症	0 (0.0)	1 (0.2)	1 (0.1)
毛包炎	1 (0.1)	0 (0.0)	1 (0.1)
真菌感染	5 (0.5)	4 (0.8)	9 (0.6)
皮膚真菌感染	2 (0.2)	1 (0.2)	3 (0.2)
せつ	1 (0.1)	0 (0.0)	1 (0.1)
胃感染	1 (0.1)	0 (0.0)	1 (0.1)
胃腸炎	54 (5.6)	21 (4.3)	75 (5.2)
ノロウイルス性胃腸炎	2 (0.2)	0 (0.0)	2 (0.1)
ウイルス性胃腸炎	20 (2.1)	6 (1.2)	26 (1.8)
細菌性消化管感染	1 (0.1)	0 (0.0)	1 (0.1)
真菌性消化管感染	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
消化管感染	4 (0.4)	2 (0.4)	6 (0.4)
ウイルス性消化管感染	3 (0.3)	2 (0.4)	5 (0.3)
陰部ヘルペス	1 (0.1)	0 (0.0)	1 (0.1)
泌尿生殖器感染	1 (0.1)	0 (0.0)	1 (0.1)
ジアルジア症	1 (0.1)	1 (0.2)	2 (0.1)
歯肉膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
H1N1インフルエンザ	0 (0.0)	4 (0.8)	4 (0.3)
ヘリコバクター性胃炎	0 (0.0)	1 (0.2)	1 (0.1)
ヘリコバクター感染	2 (0.2)	1 (0.2)	3 (0.2)
肝嚢胞感染	0 (0.0)	2 (0.4)	2 (0.1)
B型肝炎	2 (0.2)	0 (0.0)	2 (0.1)
C型肝炎	1 (0.1)	0 (0.0)	1 (0.1)
単純ヘルペス	4 (0.4)	2 (0.4)	6 (0.4)
ヘルペスウイルス感染	3 (0.3)	1 (0.2)	4 (0.3)
带状疱疹	7 (0.7)	7 (1.4)	14 (1.0)
麦粒腫	7 (0.7)	5 (1.0)	12 (0.8)
切開部位膿瘍	0 (0.0)	1 (0.2)	1 (0.1)
感染性嚢腫	1 (0.1)	0 (0.0)	1 (0.1)
感染	1 (0.1)	2 (0.4)	3 (0.2)
伝染性単核症	1 (0.1)	1 (0.2)	2 (0.1)
インフルエンザ	75 (7.8)	38 (7.9)	113 (7.8)
腎感染	5 (0.5)	2 (0.4)	7 (0.5)
迷路炎	2 (0.2)	1 (0.2)	3 (0.2)
喉頭炎	4 (0.4)	4 (0.8)	8 (0.6)
肝膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
限局性感染	4 (0.4)	1 (0.2)	5 (0.3)
下気道感染	7 (0.7)	3 (0.6)	10 (0.7)
ライム病	2 (0.2)	0 (0.0)	2 (0.1)
リンパ節感染	0 (0.0)	1 (0.2)	1 (0.1)
リンパ管炎	2 (0.2)	0 (0.0)	2 (0.1)
マラリア	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス性髄膜炎	0 (0.0)	1 (0.2)	1 (0.1)
マイコプラズマ感染	1 (0.1)	0 (0.0)	1 (0.1)
鼓膜炎	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
感染症および寄生虫症			
爪感染	0 (0.0)	1 (0.2)	1 (0.1)
鼻咽頭炎	211 (22.0)	111 (23.0)	322 (22.3)
線虫症	1 (0.1)	0 (0.0)	1 (0.1)
オンコセルカ症	1 (0.1)	0 (0.0)	1 (0.1)
爪真菌症	3 (0.3)	3 (0.6)	6 (0.4)
口腔カンジダ症	6 (0.6)	0 (0.0)	6 (0.4)
口腔真菌感染	3 (0.3)	0 (0.0)	3 (0.2)
口腔ヘルペス	8 (0.8)	5 (1.0)	13 (0.9)
口腔感染	0 (0.0)	1 (0.2)	1 (0.1)
精巣炎	0 (0.0)	1 (0.2)	1 (0.1)
外耳炎	1 (0.1)	2 (0.4)	3 (0.2)
中耳炎	5 (0.5)	3 (0.6)	8 (0.6)
急性中耳炎	1 (0.1)	0 (0.0)	1 (0.1)
乳頭腫ウイルス感染	1 (0.1)	1 (0.2)	2 (0.1)
爪囲炎	1 (0.1)	0 (0.0)	1 (0.1)
耳下腺炎	2 (0.2)	2 (0.4)	4 (0.3)
骨盤内感染	0 (0.0)	1 (0.2)	1 (0.1)
歯冠周囲炎	0 (0.0)	1 (0.2)	1 (0.1)
会陰膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
扁桃周囲炎	1 (0.1)	0 (0.0)	1 (0.1)
百日咳	1 (0.1)	1 (0.2)	2 (0.1)
咽頭炎	16 (1.7)	16 (3.3)	32 (2.2)
レンサ球菌性咽頭炎	7 (0.7)	4 (0.8)	11 (0.8)
肺炎	11 (1.1)	5 (1.0)	16 (1.1)
前立腺感染	1 (0.1)	0 (0.0)	1 (0.1)
歯髄炎	0 (0.0)	1 (0.2)	1 (0.1)
腎盂腎炎	8 (0.8)	9 (1.9)	17 (1.2)
腎嚢胞感染	9 (0.9)	13 (2.7)	22 (1.5)
気道感染	6 (0.6)	4 (0.8)	10 (0.7)
ウイルス性気道感染	5 (0.5)	0 (0.0)	5 (0.3)
鼻炎	14 (1.5)	11 (2.3)	25 (1.7)
卵管卵巣炎	1 (0.1)	0 (0.0)	1 (0.1)
敗血症	0 (0.0)	2 (0.4)	2 (0.1)
副鼻腔炎	53 (5.5)	23 (4.8)	76 (5.3)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
皮膚感染	3 (0.3)	0 (0.0)	3 (0.2)
軟部組織感染	1 (0.1)	0 (0.0)	1 (0.1)
ブドウ球菌感染	1 (0.1)	1 (0.2)	2 (0.1)
ブドウ球菌性咽頭炎	1 (0.1)	0 (0.0)	1 (0.1)
ブドウ球菌皮膚感染	0 (0.0)	1 (0.2)	1 (0.1)
糞線虫症	1 (0.1)	0 (0.0)	1 (0.1)
皮下組織膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
梅毒	1 (0.1)	0 (0.0)	1 (0.1)
足部白癬	2 (0.2)	0 (0.0)	2 (0.1)
癬風	0 (0.0)	1 (0.2)	1 (0.1)
扁桃炎	13 (1.4)	6 (1.2)	19 (1.3)
歯膿瘍	7 (0.7)	5 (1.0)	12 (0.8)
歯感染	8 (0.8)	5 (1.0)	13 (0.9)
気管炎	2 (0.2)	1 (0.2)	3 (0.2)
気管気管支炎	1 (0.1)	0 (0.0)	1 (0.1)
トリコモナス症	1 (0.1)	0 (0.0)	1 (0.1)
上気道感染	82 (8.5)	42 (8.7)	124 (8.6)
尿路感染	81 (8.4)	61 (12.6)	142 (9.8)
泌尿生殖器細菌感染	1 (0.1)	0 (0.0)	1 (0.1)
膣感染	1 (0.1)	2 (0.4)	3 (0.2)
細菌性膣炎	1 (0.1)	0 (0.0)	1 (0.1)
水痘	0 (0.0)	1 (0.2)	1 (0.1)
ウイルス感染	21 (2.2)	13 (2.7)	34 (2.4)
ウイルス性鼻炎	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス性上気道感染	4 (0.4)	1 (0.2)	5 (0.3)
外陰部膣カンジダ症	5 (0.5)	3 (0.6)	8 (0.6)
外陰膣真菌感染	4 (0.4)	4 (0.8)	8 (0.6)
創傷感染	2 (0.2)	1 (0.2)	3 (0.2)
膿創	1 (0.1)	0 (0.0)	1 (0.1)
傷害、中毒および処置合併症			
腹部損傷	1 (0.1)	0 (0.0)	1 (0.1)
動物咬傷	2 (0.2)	0 (0.0)	2 (0.1)
足関節部骨折	2 (0.2)	1 (0.2)	3 (0.2)
節足動物咬傷	8 (0.8)	3 (0.6)	11 (0.8)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症			
節足動物刺傷	1 (0.1)	2 (0.4)	3 (0.2)
剥離骨折	1 (0.1)	0 (0.0)	1 (0.1)
背部損傷	2 (0.2)	0 (0.0)	2 (0.1)
咬刺傷	1 (0.1)	0 (0.0)	1 (0.1)
滑液包損傷	1 (0.1)	0 (0.0)	1 (0.1)
軟骨損傷	4 (0.4)	0 (0.0)	4 (0.3)
胸部損傷	0 (0.0)	1 (0.2)	1 (0.1)
凍瘡	1 (0.1)	0 (0.0)	1 (0.1)
鎖骨骨折	1 (0.1)	0 (0.0)	1 (0.1)
挫傷	18 (1.9)	6 (1.2)	24 (1.7)
角膜擦過傷	2 (0.2)	0 (0.0)	2 (0.1)
上顎炎	2 (0.2)	0 (0.0)	2 (0.1)
擦過傷	5 (0.5)	0 (0.0)	5 (0.3)
眼外傷	2 (0.2)	0 (0.0)	2 (0.1)
眼の貫通性外傷	1 (0.1)	0 (0.0)	1 (0.1)
転倒	5 (0.5)	6 (1.2)	11 (0.8)
足骨折	6 (0.6)	3 (0.6)	9 (0.6)
眼内異物	1 (0.1)	0 (0.0)	1 (0.1)
骨折	0 (0.0)	1 (0.2)	1 (0.1)
外傷性血尿	0 (0.0)	1 (0.2)	1 (0.1)
手骨折	1 (0.1)	1 (0.2)	2 (0.1)
頭部損傷	1 (0.1)	1 (0.2)	2 (0.1)
熱疲労	1 (0.1)	0 (0.0)	1 (0.1)
熱射病	3 (0.3)	0 (0.0)	3 (0.2)
腸脛靱帯症候群	1 (0.1)	0 (0.0)	1 (0.1)
ステント内動脈再狭窄	0 (0.0)	1 (0.2)	1 (0.1)
切開部位痛	1 (0.1)	0 (0.0)	1 (0.1)
人工流産による出血	1 (0.1)	0 (0.0)	1 (0.1)
損傷	0 (0.0)	1 (0.2)	1 (0.1)
顎の骨折	0 (0.0)	1 (0.2)	1 (0.1)
関節脱臼	3 (0.3)	3 (0.6)	6 (0.4)
関節損傷	9 (0.9)	7 (1.4)	16 (1.1)
裂傷	6 (0.6)	4 (0.8)	10 (0.7)
靱帯損傷	1 (0.1)	1 (0.2)	2 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症			
靱帯断裂	2 (0.2)	4 (0.8)	6 (0.4)
靱帯捻挫	14 (1.5)	11 (2.3)	25 (1.7)
四肢損傷	3 (0.3)	5 (1.0)	8 (0.6)
口唇損傷	1 (0.1)	0 (0.0)	1 (0.1)
下肢骨折	0 (0.0)	1 (0.2)	1 (0.1)
腰椎骨折	1 (0.1)	0 (0.0)	1 (0.1)
半月板障害	5 (0.5)	7 (1.4)	12 (0.8)
多発骨折	2 (0.2)	1 (0.2)	3 (0.2)
筋断裂	2 (0.2)	1 (0.2)	3 (0.2)
肉離れ	9 (0.9)	6 (1.2)	15 (1.0)
頸部損傷	1 (0.1)	0 (0.0)	1 (0.1)
眼窩周囲血腫	2 (0.2)	1 (0.2)	3 (0.2)
処置後合併症	0 (0.0)	1 (0.2)	1 (0.1)
処置後血尿	0 (0.0)	1 (0.2)	1 (0.1)
処置後出血	1 (0.1)	0 (0.0)	1 (0.1)
外傷後疼痛	2 (0.2)	3 (0.6)	5 (0.3)
処置による疼痛	9 (0.9)	6 (1.2)	15 (1.0)
処置による嘔吐	1 (0.1)	0 (0.0)	1 (0.1)
恥骨骨折	0 (0.0)	1 (0.2)	1 (0.1)
橈骨骨折	1 (0.1)	0 (0.0)	1 (0.1)
肋骨骨折	4 (0.4)	1 (0.2)	5 (0.3)
骨格損傷	3 (0.3)	1 (0.2)	4 (0.3)
軟部組織損傷	1 (0.1)	0 (0.0)	1 (0.1)
脊椎圧迫骨折	1 (0.1)	0 (0.0)	1 (0.1)
脊椎骨折	1 (0.1)	0 (0.0)	1 (0.1)
刺創	1 (0.1)	0 (0.0)	1 (0.1)
ストレス骨折	2 (0.2)	0 (0.0)	2 (0.1)
サンバーン	3 (0.3)	1 (0.2)	4 (0.3)
眼の擦過傷	1 (0.1)	0 (0.0)	1 (0.1)
腱損傷	1 (0.1)	1 (0.2)	2 (0.1)
腱断裂	1 (0.1)	0 (0.0)	1 (0.1)
熱傷	4 (0.4)	2 (0.4)	6 (0.4)
脛骨骨折	1 (0.1)	3 (0.6)	4 (0.3)
歯牙破折	2 (0.2)	0 (0.0)	2 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症			
外傷性血腫	1 (0.1)	0 (0.0)	1 (0.1)
尺骨骨折	1 (0.1)	0 (0.0)	1 (0.1)
上肢骨折	0 (0.0)	1 (0.2)	1 (0.1)
創傷	2 (0.2)	2 (0.4)	4 (0.3)
手首関節骨折	1 (0.1)	2 (0.4)	3 (0.2)
臨床検査			
活性化部分トロンボプラスチン時間延長	2 (0.2)	2 (0.4)	4 (0.3)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	1 (0.2)	1 (0.1)
アラニン・アミノトランスフェラーゼ増加	39 (4.1)	17 (3.5)	56 (3.9)
アスパラギン酸アミノトランスフェラーゼ増加	36 (3.7)	16 (3.3)	52 (3.6)
細菌検査陽性	2 (0.2)	3 (0.6)	5 (0.3)
血中アルカリホスファターゼ増加	3 (0.3)	1 (0.2)	4 (0.3)
血中ビリルビン増加	2 (0.2)	2 (0.4)	4 (0.3)
血中カルシウム増加	6 (0.6)	0 (0.0)	6 (0.4)
血中コレステロール増加	14 (1.5)	7 (1.4)	21 (1.5)
血中クレアチンホスホキナーゼ増加	6 (0.6)	1 (0.2)	7 (0.5)
血中クレアチニン増加	135 (14.0)	71 (14.7)	206 (14.3)
血中ブドウ糖減少	0 (0.0)	2 (0.4)	2 (0.1)
血中ブドウ糖増加	7 (0.7)	1 (0.2)	8 (0.6)
血中乳酸脱水素酵素増加	5 (0.5)	1 (0.2)	6 (0.4)
血中エストロゲン減少	0 (0.0)	1 (0.2)	1 (0.1)
血中副甲状腺ホルモン増加	1 (0.1)	0 (0.0)	1 (0.1)
血中カリウム減少	4 (0.4)	0 (0.0)	4 (0.3)
血中カリウム増加	6 (0.6)	3 (0.6)	9 (0.6)
血圧低下	1 (0.1)	1 (0.2)	2 (0.1)
拡張期血圧上昇	1 (0.1)	1 (0.2)	2 (0.1)
血圧上昇	10 (1.0)	7 (1.4)	17 (1.2)
血中ナトリウム減少	1 (0.1)	0 (0.0)	1 (0.1)
血中ナトリウム増加	14 (1.5)	1 (0.2)	15 (1.0)
血中テストステロン減少	1 (0.1)	0 (0.0)	1 (0.1)
血中甲状腺刺激ホルモン増加	3 (0.3)	0 (0.0)	3 (0.2)
血中トリグリセリド増加	0 (0.0)	2 (0.4)	2 (0.1)
血中尿素増加	10 (1.0)	12 (2.5)	22 (1.5)
血中尿酸増加	24 (2.5)	6 (1.2)	30 (2.1)

2.7.4 臨床的安全性

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
臨床検査			
尿中血陽性	1 (0.1)	0 (0.0)	1 (0.1)
体温上昇	1 (0.1)	0 (0.0)	1 (0.1)
C-反応性蛋白増加	1 (0.1)	0 (0.0)	1 (0.1)
癌胎児性抗原増加	0 (0.0)	1 (0.2)	1 (0.1)
心雑音	5 (0.5)	3 (0.6)	8 (0.6)
腎クレアチニン・クリアランス増加	1 (0.1)	0 (0.0)	1 (0.1)
尿中クレアチニン増加	0 (0.0)	1 (0.2)	1 (0.1)
シスタチンC増加	6 (0.6)	7 (1.4)	13 (0.9)
心電図QT間隔	1 (0.1)	0 (0.0)	1 (0.1)
心電図再分極異常	1 (0.1)	1 (0.2)	2 (0.1)
心電図異常T波	1 (0.1)	0 (0.0)	1 (0.1)
心電図T波逆転	1 (0.1)	1 (0.2)	2 (0.1)
好酸球数増加	3 (0.3)	2 (0.4)	5 (0.3)
大腸菌検査陽性	1 (0.1)	1 (0.2)	2 (0.1)
γ-グルタミルトランスフェラーゼ増加	23 (2.4)	11 (2.3)	34 (2.4)
胃内pH低下	1 (0.1)	0 (0.0)	1 (0.1)
尿中ブドウ糖	1 (0.1)	0 (0.0)	1 (0.1)
ヘマトクリット減少	1 (0.1)	2 (0.4)	3 (0.2)
ヘマトクリット増加	1 (0.1)	0 (0.0)	1 (0.1)
ヘモグロビン減少	2 (0.2)	3 (0.6)	5 (0.3)
心拍数増加	0 (0.0)	1 (0.2)	1 (0.1)
心拍数不整	1 (0.1)	0 (0.0)	1 (0.1)
心音異常	0 (0.0)	1 (0.2)	1 (0.1)
肝酵素異常	1 (0.1)	0 (0.0)	1 (0.1)
肝酵素上昇	17 (1.8)	1 (0.2)	18 (1.2)
ヒト乳頭腫ウイルス検査陽性	1 (0.1)	0 (0.0)	1 (0.1)
炎症マーカー上昇	0 (0.0)	1 (0.2)	1 (0.1)
INR増加	7 (0.7)	0 (0.0)	7 (0.5)
眼圧上昇	2 (0.2)	0 (0.0)	2 (0.1)
腎触知	3 (0.3)	2 (0.4)	5 (0.3)
リパーゼ増加	0 (0.0)	1 (0.2)	1 (0.1)
肝機能検査異常	6 (0.6)	3 (0.6)	9 (0.6)
季肋下肝触知	1 (0.1)	0 (0.0)	1 (0.1)
低比重リポ蛋白減少	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
臨床検査			
リンパ球数増加	0 (0.0)	1 (0.2)	1 (0.1)
リンパ球形態異常	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球容積減少	1 (0.1)	2 (0.4)	3 (0.2)
平均赤血球容積増加	4 (0.4)	1 (0.2)	5 (0.3)
好中球数減少	1 (0.1)	3 (0.6)	4 (0.3)
好中球数増加	1 (0.1)	2 (0.4)	3 (0.2)
便潜血	1 (0.1)	0 (0.0)	1 (0.1)
便潜血陽性	1 (0.1)	0 (0.0)	1 (0.1)
血小板数減少	1 (0.1)	2 (0.4)	3 (0.2)
血小板数増加	1 (0.1)	0 (0.0)	1 (0.1)
尿蛋白	1 (0.1)	1 (0.2)	2 (0.1)
プロトロンビン時間異常	1 (0.1)	0 (0.0)	1 (0.1)
プロトロンビン時間延長	5 (0.5)	0 (0.0)	5 (0.3)
QOL低下	1 (0.1)	0 (0.0)	1 (0.1)
赤血球数減少	1 (0.1)	4 (0.8)	5 (0.3)
尿中赤血球陽性	0 (0.0)	1 (0.2)	1 (0.1)
子宮頸部スミア異常	0 (0.0)	1 (0.2)	1 (0.1)
トランスアミナーゼ上昇	11 (1.1)	2 (0.4)	13 (0.9)
卵巣超音波検査異常	1 (0.1)	0 (0.0)	1 (0.1)
尿検査異常	0 (0.0)	2 (0.4)	2 (0.1)
尿浸透圧低下	9 (0.9)	1 (0.2)	10 (0.7)
尿浸透圧上昇	1 (0.1)	0 (0.0)	1 (0.1)
尿量増加	15 (1.6)	2 (0.4)	17 (1.2)
ビタミンD減少	0 (0.0)	3 (0.6)	3 (0.2)
ウエスト周囲径増加	1 (0.1)	0 (0.0)	1 (0.1)
体重減少	46 (4.8)	16 (3.3)	62 (4.3)
体重増加	46 (4.8)	19 (3.9)	65 (4.5)
白血球数減少	1 (0.1)	2 (0.4)	3 (0.2)
白血球数増加	3 (0.3)	4 (0.8)	7 (0.5)
尿中白血球	1 (0.1)	1 (0.2)	2 (0.1)
尿中白血球陽性	1 (0.1)	1 (0.2)	2 (0.1)
代謝および栄養障害			
アシドーシス	0 (0.0)	2 (0.4)	2 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
代謝および栄養障害			
食欲減退	69 (7.2)	5 (1.0)	74 (5.1)
脱水	18 (1.9)	11 (2.3)	29 (2.0)
糖尿病	7 (0.7)	0 (0.0)	7 (0.5)
コントロール不良の糖尿病	1 (0.1)	0 (0.0)	1 (0.1)
脂質異常症	4 (0.4)	0 (0.0)	4 (0.3)
体液貯留	1 (0.1)	1 (0.2)	2 (0.1)
食物渴望	2 (0.2)	0 (0.0)	2 (0.1)
食物不耐性	1 (0.1)	0 (0.0)	1 (0.1)
耐糖能障害	1 (0.1)	1 (0.2)	2 (0.1)
痛風	28 (2.9)	7 (1.4)	35 (2.4)
高アミラーゼ血症	0 (0.0)	1 (0.2)	1 (0.1)
高カルシウム血症	5 (0.5)	2 (0.4)	7 (0.5)
高コレステロール血症	26 (2.7)	12 (2.5)	38 (2.6)
高クレアチニン血症	0 (0.0)	1 (0.2)	1 (0.1)
高血糖	6 (0.6)	10 (2.1)	16 (1.1)
高カリウム血症	7 (0.7)	3 (0.6)	10 (0.7)
高脂血症	12 (1.2)	3 (0.6)	15 (1.0)
高ナトリウム血症	27 (2.8)	5 (1.0)	32 (2.2)
高リン酸塩血症	2 (0.2)	0 (0.0)	2 (0.1)
高トリグリセリド血症	2 (0.2)	1 (0.2)	3 (0.2)
高尿酸血症	37 (3.9)	9 (1.9)	46 (3.2)
低アルブミン血症	1 (0.1)	1 (0.2)	2 (0.1)
低カルシウム血症	1 (0.1)	2 (0.4)	3 (0.2)
低血糖症	6 (0.6)	0 (0.0)	6 (0.4)
低カリウム血症	6 (0.6)	2 (0.4)	8 (0.6)
低マグネシウム血症	1 (0.1)	0 (0.0)	1 (0.1)
低ナトリウム血症	5 (0.5)	2 (0.4)	7 (0.5)
低リン酸血症	2 (0.2)	0 (0.0)	2 (0.1)
血液量減少症	2 (0.2)	0 (0.0)	2 (0.1)
食欲亢進	1 (0.1)	1 (0.2)	2 (0.1)
鉄欠乏	4 (0.4)	0 (0.0)	4 (0.3)
ラクトース不耐性	1 (0.1)	0 (0.0)	1 (0.1)
代謝性アシドーシス	1 (0.1)	0 (0.0)	1 (0.1)
肥満	0 (0.0)	2 (0.4)	2 (0.1)

表2.7.4.7-14

156-251

CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
代謝および栄養障害			
過体重	3 (0.3)	0 (0.0)	3 (0.2)
多飲症	100 (10.4)	17 (3.5)	117 (8.1)
2 型糖尿病	2 (0.2)	0 (0.0)	2 (0.1)
ビタミンB 1 2 欠乏	1 (0.1)	0 (0.0)	1 (0.1)
ビタミンD 欠乏	9 (0.9)	5 (1.0)	14 (1.0)
体重変動	2 (0.2)	0 (0.0)	2 (0.1)
筋骨格系および結合組織障害			
関節痛	69 (7.2)	28 (5.8)	97 (6.7)
関節炎	6 (0.6)	1 (0.2)	7 (0.5)
反応性関節炎	1 (0.1)	0 (0.0)	1 (0.1)
関節障害	1 (0.1)	0 (0.0)	1 (0.1)
背部痛	133 (13.8)	88 (18.2)	221 (15.3)
骨痛	3 (0.3)	4 (0.8)	7 (0.5)
滑液包石灰化	1 (0.1)	0 (0.0)	1 (0.1)
滑液包炎	5 (0.5)	1 (0.2)	6 (0.4)
軟骨肥厚	1 (0.1)	0 (0.0)	1 (0.1)
頸部脊柱管狭窄症	1 (0.1)	0 (0.0)	1 (0.1)
ピロリン酸カルシウム結晶性軟骨石灰化症	2 (0.2)	0 (0.0)	2 (0.1)
軟骨軟化症	0 (0.0)	1 (0.2)	1 (0.1)
軟骨疾患	0 (0.0)	1 (0.2)	1 (0.1)
尾骨痛	0 (0.0)	2 (0.4)	2 (0.1)
肋軟骨炎	2 (0.2)	0 (0.0)	2 (0.1)
歯槽異常	1 (0.1)	0 (0.0)	1 (0.1)
外骨腫	2 (0.2)	1 (0.2)	3 (0.2)
筋膜炎	1 (0.1)	0 (0.0)	1 (0.1)
線維筋痛	2 (0.2)	1 (0.2)	3 (0.2)
瘻孔	1 (0.1)	0 (0.0)	1 (0.1)
側腹部痛	11 (1.1)	10 (2.1)	21 (1.5)
足変形	2 (0.2)	2 (0.4)	4 (0.3)
痛風性関節炎	1 (0.1)	0 (0.0)	1 (0.1)
腓径部痛	2 (0.2)	1 (0.2)	3 (0.2)
椎間板変性症	3 (0.3)	0 (0.0)	3 (0.2)
椎間板障害	1 (0.1)	0 (0.0)	1 (0.1)
椎間板突出	13 (1.4)	7 (1.4)	20 (1.4)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
筋骨格系および結合組織障害			
関節滲出液	4 (0.4)	0 (0.0)	4 (0.3)
関節可動域低下	1 (0.1)	0 (0.0)	1 (0.1)
関節硬直	0 (0.0)	1 (0.2)	1 (0.1)
関節腫脹	9 (0.9)	5 (1.0)	14 (1.0)
靱帯障害	0 (0.0)	1 (0.2)	1 (0.1)
靱帯痛	2 (0.2)	0 (0.0)	2 (0.1)
四肢非対称	1 (0.1)	0 (0.0)	1 (0.1)
四肢不快感	2 (0.2)	0 (0.0)	2 (0.1)
筋肉疲労	1 (0.1)	0 (0.0)	1 (0.1)
筋痙縮	35 (3.6)	17 (3.5)	52 (3.6)
筋緊張	2 (0.2)	2 (0.4)	4 (0.3)
筋攣縮	2 (0.2)	1 (0.2)	3 (0.2)
筋力低下	1 (0.1)	4 (0.8)	5 (0.3)
筋骨格系胸痛	9 (0.9)	3 (0.6)	12 (0.8)
筋骨格不快感	6 (0.6)	0 (0.0)	6 (0.4)
筋骨格痛	37 (3.9)	17 (3.5)	54 (3.7)
筋骨格硬直	11 (1.1)	2 (0.4)	13 (0.9)
筋肉痛	50 (5.2)	16 (3.3)	66 (4.6)
筋炎	1 (0.1)	0 (0.0)	1 (0.1)
頸部腫瘍	1 (0.1)	0 (0.0)	1 (0.1)
頸部痛	25 (2.6)	12 (2.5)	37 (2.6)
変形性関節症	7 (0.7)	6 (1.2)	13 (0.9)
骨関節障害	1 (0.1)	0 (0.0)	1 (0.1)
骨端症	1 (0.1)	0 (0.0)	1 (0.1)
骨壊死	0 (0.0)	1 (0.2)	1 (0.1)
骨減少症	3 (0.3)	2 (0.4)	5 (0.3)
骨粗鬆症	1 (0.1)	0 (0.0)	1 (0.1)
四肢痛	42 (4.4)	27 (5.6)	69 (4.8)
顎痛	3 (0.3)	2 (0.4)	5 (0.3)
膝蓋大腿関節痛症候群	0 (0.0)	1 (0.2)	1 (0.1)
関節周囲炎	4 (0.4)	4 (0.8)	8 (0.6)
足底筋膜炎	7 (0.7)	1 (0.2)	8 (0.6)
恥骨痛	1 (0.1)	2 (0.4)	3 (0.2)
関節リウマチ	3 (0.3)	0 (0.0)	3 (0.2)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
筋骨格系および結合組織障害			
肩回旋筋腱板症候群	3 (0.3)	0 (0.0)	3 (0.2)
仙腸骨炎	3 (0.3)	0 (0.0)	3 (0.2)
側弯症	1 (0.1)	1 (0.2)	2 (0.1)
重感	1 (0.1)	4 (0.8)	5 (0.3)
脊椎障害	1 (0.1)	0 (0.0)	1 (0.1)
変形性脊椎症	1 (0.1)	4 (0.8)	5 (0.3)
脊椎炎	0 (0.0)	1 (0.2)	1 (0.1)
脊椎すべり症	0 (0.0)	1 (0.2)	1 (0.1)
滑液嚢腫	3 (0.3)	1 (0.2)	4 (0.3)
滑膜炎	0 (0.0)	1 (0.2)	1 (0.1)
腱障害	2 (0.2)	1 (0.2)	3 (0.2)
腱痛	3 (0.3)	1 (0.2)	4 (0.3)
腱炎	16 (1.7)	10 (2.1)	26 (1.8)
腱鞘炎	2 (0.2)	1 (0.2)	3 (0.2)
斜頸	5 (0.5)	0 (0.0)	5 (0.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）			
アクロコルドン	1 (0.1)	0 (0.0)	1 (0.1)
基底細胞癌	8 (0.8)	1 (0.2)	9 (0.6)
乳房の良性新生物	2 (0.2)	2 (0.4)	4 (0.3)
甲状腺の良性新生物	1 (0.1)	0 (0.0)	1 (0.1)
乳癌	3 (0.3)	1 (0.2)	4 (0.3)
子宮頸部癌第0期	1 (0.1)	0 (0.0)	1 (0.1)
真珠腫	0 (0.0)	1 (0.2)	1 (0.1)
慢性骨髄性白血病	1 (0.1)	0 (0.0)	1 (0.1)
異形成母斑	0 (0.0)	1 (0.2)	1 (0.1)
血管腫	1 (0.1)	0 (0.0)	1 (0.1)
肝臓血管腫	0 (0.0)	1 (0.2)	1 (0.1)
カボジ肉腫	1 (0.1)	0 (0.0)	1 (0.1)
脂肪腫	4 (0.4)	2 (0.4)	6 (0.4)
悪性黒色腫	2 (0.2)	0 (0.0)	2 (0.1)
表皮内悪性黒色腫	1 (0.1)	0 (0.0)	1 (0.1)
メラノサイト性母斑	3 (0.3)	2 (0.4)	5 (0.3)
下垂体の良性腫瘍	1 (0.1)	0 (0.0)	1 (0.1)
脂漏性角化症	2 (0.2)	2 (0.4)	4 (0.3)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）			
皮膚乳頭腫	5 (0.5)	3 (0.6)	8 (0.6)
扁平上皮癌	0 (0.0)	1 (0.2)	1 (0.1)
汗腺腫瘍	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺新生物	0 (0.0)	1 (0.2)	1 (0.1)
子宮平滑筋腫	10 (1.0)	5 (1.0)	15 (1.0)
神経系障害			
味覚消失	1 (0.1)	1 (0.2)	2 (0.1)
健忘	2 (0.2)	1 (0.2)	3 (0.2)
失声症	1 (0.1)	1 (0.2)	2 (0.1)
くも膜嚢胞	2 (0.2)	3 (0.6)	5 (0.3)
平衡障害	1 (0.1)	2 (0.4)	3 (0.2)
灼熱感	1 (0.1)	1 (0.2)	2 (0.1)
頸動脈瘤	1 (0.1)	1 (0.2)	2 (0.1)
手根管症候群	2 (0.2)	0 (0.0)	2 (0.1)
脳出血	1 (0.1)	0 (0.0)	1 (0.1)
脳梗塞	1 (0.1)	0 (0.0)	1 (0.1)
脳虚血	1 (0.1)	0 (0.0)	1 (0.1)
群発頭痛	1 (0.1)	0 (0.0)	1 (0.1)
痙攣	0 (0.0)	1 (0.2)	1 (0.1)
協調運動異常	1 (0.1)	0 (0.0)	1 (0.1)
脳神経障害	0 (0.0)	1 (0.2)	1 (0.1)
意識レベルの低下	1 (0.1)	0 (0.0)	1 (0.1)
注意力障害	8 (0.8)	1 (0.2)	9 (0.6)
浮動性めまい	109 (11.3)	42 (8.7)	151 (10.5)
労作性めまい	1 (0.1)	0 (0.0)	1 (0.1)
体位性めまい	6 (0.6)	0 (0.0)	6 (0.4)
異常感覚	2 (0.2)	0 (0.0)	2 (0.1)
味覚異常	21 (2.2)	7 (1.4)	28 (1.9)
脳症	1 (0.1)	0 (0.0)	1 (0.1)
頭部不快感	1 (0.1)	0 (0.0)	1 (0.1)
頭痛	241 (25.1)	121 (25.1)	362 (25.1)
味覚過敏	1 (0.1)	0 (0.0)	1 (0.1)
感覚鈍麻	15 (1.6)	12 (2.5)	27 (1.9)
反射減弱	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
筋緊張低下	2 (0.2)	0 (0.0)	2 (0.1)
頭蓋内動脈瘤	7 (0.7)	3 (0.6)	10 (0.7)
虚血性脳卒中	0 (0.0)	1 (0.2)	1 (0.1)
嗜眠	5 (0.5)	3 (0.6)	8 (0.6)
意識消失	4 (0.4)	0 (0.0)	4 (0.3)
記憶障害	2 (0.2)	2 (0.4)	4 (0.3)
精神的機能障害	1 (0.1)	1 (0.2)	2 (0.1)
片頭痛	22 (2.3)	10 (2.1)	32 (2.2)
前兆を伴う片頭痛	1 (0.1)	0 (0.0)	1 (0.1)
単麻痺	1 (0.1)	0 (0.0)	1 (0.1)
不随意性筋収縮	3 (0.3)	0 (0.0)	3 (0.2)
ナルコレプシー	3 (0.3)	0 (0.0)	3 (0.2)
神経圧迫	1 (0.1)	0 (0.0)	1 (0.1)
神経根圧迫	1 (0.1)	0 (0.0)	1 (0.1)
神経痛	3 (0.3)	1 (0.2)	4 (0.3)
末梢性ニューロパチー	1 (0.1)	2 (0.4)	3 (0.2)
起立不耐性	1 (0.1)	0 (0.0)	1 (0.1)
錯感覚	19 (2.0)	13 (2.7)	32 (2.2)
パーキンソン病	1 (0.1)	0 (0.0)	1 (0.1)
パーキンソニズム	1 (0.1)	0 (0.0)	1 (0.1)
嗅覚錯誤	1 (0.1)	1 (0.2)	2 (0.1)
気脳体	1 (0.1)	0 (0.0)	1 (0.1)
多発ニューロパチー	0 (0.0)	1 (0.2)	1 (0.1)
失神寸前の状態	3 (0.3)	0 (0.0)	3 (0.2)
根症候群	0 (0.0)	1 (0.2)	1 (0.1)
下肢静止不能症候群	2 (0.2)	3 (0.6)	5 (0.3)
坐骨神経痛	9 (0.9)	6 (1.2)	15 (1.0)
感覚障害	2 (0.2)	0 (0.0)	2 (0.1)
副鼻腔炎に伴う頭痛	1 (0.1)	1 (0.2)	2 (0.1)
傾眠	3 (0.3)	3 (0.6)	6 (0.4)
くも膜下出血	1 (0.1)	2 (0.4)	3 (0.2)
失神	16 (1.7)	3 (0.6)	19 (1.3)
緊張性頭痛	3 (0.3)	3 (0.6)	6 (0.4)
一過性脳虚血発作	0 (0.0)	2 (0.4)	2 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
振戦	2 (0.2)	1 (0.2)	3 (0.2)
トンネル状視野	1 (0.1)	0 (0.0)	1 (0.1)
椎骨動脈解離	1 (0.1)	0 (0.0)	1 (0.1)
第7脳神経麻痺	1 (0.1)	2 (0.4)	3 (0.2)
精神障害			
異常行動	0 (0.0)	1 (0.2)	1 (0.1)
異常な夢	2 (0.2)	2 (0.4)	4 (0.3)
激越	2 (0.2)	0 (0.0)	2 (0.1)
怒り	0 (0.0)	1 (0.2)	1 (0.1)
不安	30 (3.1)	8 (1.7)	38 (2.6)
不安障害	2 (0.2)	0 (0.0)	2 (0.1)
注意欠陥多動性障害	1 (0.1)	0 (0.0)	1 (0.1)
自閉症スペクトラム障害	1 (0.1)	0 (0.0)	1 (0.1)
精神緩慢	1 (0.1)	0 (0.0)	1 (0.1)
燃え尽き症候群	1 (0.1)	0 (0.0)	1 (0.1)
閉所恐怖症	1 (0.1)	0 (0.0)	1 (0.1)
抑うつ気分	2 (0.2)	2 (0.4)	4 (0.3)
うつ病	42 (4.4)	21 (4.3)	63 (4.4)
睡眠異常	1 (0.1)	0 (0.0)	1 (0.1)
初期不眠症	1 (0.1)	0 (0.0)	1 (0.1)
不眠症	55 (5.7)	21 (4.3)	76 (5.3)
リビドー減退	5 (0.5)	1 (0.2)	6 (0.4)
性欲障害	1 (0.1)	1 (0.2)	2 (0.1)
リビド消失	1 (0.1)	0 (0.0)	1 (0.1)
大うつ病	2 (0.2)	0 (0.0)	2 (0.1)
精神障害	0 (0.0)	1 (0.2)	1 (0.1)
中期不眠症	1 (0.1)	0 (0.0)	1 (0.1)
気分変化	1 (0.1)	0 (0.0)	1 (0.1)
気分動揺	1 (0.1)	1 (0.2)	2 (0.1)
神経過敏	5 (0.5)	1 (0.2)	6 (0.4)
ニコチン依存	1 (0.1)	2 (0.4)	3 (0.2)
悪夢	1 (0.1)	0 (0.0)	1 (0.1)
パニック発作	5 (0.5)	2 (0.4)	7 (0.5)
パニック反応	2 (0.2)	0 (0.0)	2 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
精神障害			
外傷後ストレス障害	0 (0.0)	1 (0.2)	1 (0.1)
心身症	0 (0.0)	1 (0.2)	1 (0.1)
落ち着きのなさ	1 (0.1)	0 (0.0)	1 (0.1)
統合失調感情障害	0 (0.0)	1 (0.2)	1 (0.1)
統合失調症	1 (0.1)	0 (0.0)	1 (0.1)
睡眠障害	6 (0.6)	3 (0.6)	9 (0.6)
夢遊症	1 (0.1)	0 (0.0)	1 (0.1)
ストレス	9 (0.9)	10 (2.1)	19 (1.3)
自殺企図	1 (0.1)	1 (0.2)	2 (0.1)
腎および尿路障害			
アルブミン尿	1 (0.1)	0 (0.0)	1 (0.1)
高窒素血症	0 (0.0)	1 (0.2)	1 (0.1)
膀胱不快感	0 (0.0)	1 (0.2)	1 (0.1)
膀胱刺激症状	1 (0.1)	0 (0.0)	1 (0.1)
膀胱痛	2 (0.2)	0 (0.0)	2 (0.1)
膀胱脱	2 (0.2)	1 (0.2)	3 (0.2)
膀胱痙縮	1 (0.1)	0 (0.0)	1 (0.1)
尿路結石	1 (0.1)	3 (0.6)	4 (0.3)
着色尿	1 (0.1)	1 (0.2)	2 (0.1)
非感染性膀胱炎	1 (0.1)	0 (0.0)	1 (0.1)
排尿困難	17 (1.8)	9 (1.9)	26 (1.8)
遺尿	2 (0.2)	0 (0.0)	2 (0.1)
糖尿	0 (0.0)	1 (0.2)	1 (0.1)
血尿	75 (7.8)	68 (14.1)	143 (9.9)
水腎症	1 (0.1)	0 (0.0)	1 (0.1)
緊張性膀胱	1 (0.1)	0 (0.0)	1 (0.1)
失禁	2 (0.2)	0 (0.0)	2 (0.1)
腎腫大	3 (0.3)	3 (0.6)	6 (0.4)
白血球尿	2 (0.2)	4 (0.8)	6 (0.4)
尿意切迫	8 (0.8)	2 (0.4)	10 (0.7)
腎炎	0 (0.0)	1 (0.2)	1 (0.1)
腎結石症	15 (1.6)	14 (2.9)	29 (2.0)
夜間頻尿	280 (29.1)	63 (13.0)	343 (23.8)
乏尿	2 (0.2)	0 (0.0)	2 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
腎および尿路障害			
頻尿	223 (23.2)	26 (5.4)	249 (17.2)
多尿	368 (38.3)	83 (17.2)	451 (31.2)
蛋白尿	4 (0.4)	8 (1.7)	12 (0.8)
腎仙痛	3 (0.3)	5 (1.0)	8 (0.6)
腎嚢胞	1 (0.1)	1 (0.2)	2 (0.1)
腎嚢胞出血	6 (0.6)	9 (1.9)	15 (1.0)
腎嚢胞破裂	7 (0.7)	5 (1.0)	12 (0.8)
腎障害	0 (0.0)	1 (0.2)	1 (0.1)
腎不全	0 (0.0)	1 (0.2)	1 (0.1)
急性腎不全	2 (0.2)	2 (0.4)	4 (0.3)
慢性腎不全	2 (0.2)	0 (0.0)	2 (0.1)
腎機能障害	13 (1.4)	8 (1.7)	21 (1.5)
腎臓痛	260 (27.1)	171 (35.4)	431 (29.8)
有痛性排尿困難	1 (0.1)	0 (0.0)	1 (0.1)
腹圧性尿失禁	0 (0.0)	1 (0.2)	1 (0.1)
終末尿滴下	1 (0.1)	0 (0.0)	1 (0.1)
尿道狭窄	1 (0.1)	0 (0.0)	1 (0.1)
切迫性尿失禁	1 (0.1)	1 (0.2)	2 (0.1)
排尿躊躇	1 (0.1)	0 (0.0)	1 (0.1)
尿失禁	9 (0.9)	2 (0.4)	11 (0.8)
尿閉	1 (0.1)	2 (0.4)	3 (0.2)
尿路障害	0 (0.0)	2 (0.4)	2 (0.1)
尿流量減少	2 (0.2)	0 (0.0)	2 (0.1)
尿臭異常	0 (0.0)	1 (0.2)	1 (0.1)
生殖系および乳房障害			
子宮付属器痛	1 (0.1)	0 (0.0)	1 (0.1)
無月経	4 (0.4)	5 (1.0)	9 (0.6)
精子無力症	0 (0.0)	1 (0.2)	1 (0.1)
萎縮性外陰陰炎	1 (0.1)	0 (0.0)	1 (0.1)
無精子症	0 (0.0)	1 (0.2)	1 (0.1)
バルトリン腺炎	0 (0.0)	1 (0.2)	1 (0.1)
良性前立腺肥大症	0 (0.0)	1 (0.2)	1 (0.1)
乳房嚢胞	2 (0.2)	1 (0.2)	3 (0.2)
乳房不快感	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
生殖系および乳房障害			
乳房腫瘍	2 (0.2)	1 (0.2)	3 (0.2)
乳房痛	1 (0.1)	0 (0.0)	1 (0.1)
子宮頸部上皮異形成	2 (0.2)	1 (0.2)	3 (0.2)
子宮頸管ポリープ	2 (0.2)	0 (0.0)	2 (0.1)
性交出血	1 (0.1)	0 (0.0)	1 (0.1)
膀胱瘤	1 (0.1)	0 (0.0)	1 (0.1)
月経困難症	3 (0.3)	4 (0.8)	7 (0.5)
性交困難	1 (0.1)	1 (0.2)	2 (0.1)
射精障害	1 (0.1)	0 (0.0)	1 (0.1)
子宮内膜症	0 (0.0)	2 (0.4)	2 (0.1)
精巣上体嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
精巣上体炎	2 (0.2)	1 (0.2)	3 (0.2)
勃起不全	10 (1.0)	2 (0.4)	12 (0.8)
線維嚢胞性乳腺疾患	0 (0.0)	1 (0.2)	1 (0.1)
乳汁漏出症	2 (0.2)	0 (0.0)	2 (0.1)
性器出血	3 (0.3)	2 (0.4)	5 (0.3)
血精液症	4 (0.4)	0 (0.0)	4 (0.3)
出血性卵巣嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
過少月経	1 (0.1)	0 (0.0)	1 (0.1)
子宮瘤	0 (0.0)	1 (0.2)	1 (0.1)
不妊症	0 (0.0)	2 (0.4)	2 (0.1)
機能性子宮出血	1 (0.1)	0 (0.0)	1 (0.1)
閉経期症状	0 (0.0)	1 (0.2)	1 (0.1)
月経過多	14 (1.5)	9 (1.9)	23 (1.6)
月経障害	3 (0.3)	0 (0.0)	3 (0.2)
月経遅延	0 (0.0)	2 (0.4)	2 (0.1)
不規則月経	8 (0.8)	4 (0.8)	12 (0.8)
不正子宮出血	2 (0.2)	4 (0.8)	6 (0.4)
卵巣嚢胞	6 (0.6)	6 (1.2)	12 (0.8)
卵巣障害	0 (0.0)	1 (0.2)	1 (0.1)
卵巣捻転	2 (0.2)	0 (0.0)	2 (0.1)
排卵痛	1 (0.1)	0 (0.0)	1 (0.1)
骨盤不快感	1 (0.1)	0 (0.0)	1 (0.1)
骨盤痛	2 (0.2)	0 (0.0)	2 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
生殖系および乳房障害			
骨盤脱	1 (0.1)	0 (0.0)	1 (0.1)
会陰痛	1 (0.1)	0 (0.0)	1 (0.1)
ペイロニー病	2 (0.2)	0 (0.0)	2 (0.1)
閉経後出血	1 (0.1)	0 (0.0)	1 (0.1)
月経前症候群	1 (0.1)	0 (0.0)	1 (0.1)
前立腺炎	4 (0.4)	3 (0.6)	7 (0.5)
前立腺腫大	1 (0.1)	0 (0.0)	1 (0.1)
精嚢嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
性功能不全	2 (0.2)	1 (0.2)	3 (0.2)
精嚢嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
精嚢腫瘍	1 (0.1)	1 (0.2)	2 (0.1)
精嚢痛	2 (0.2)	3 (0.6)	5 (0.3)
子宮ポリープ	0 (0.0)	4 (0.8)	4 (0.3)
子宮脱	3 (0.3)	1 (0.2)	4 (0.3)
子宮腔脱	1 (0.1)	0 (0.0)	1 (0.1)
嚢嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
嚢分泌物	1 (0.1)	2 (0.4)	3 (0.2)
嚢出血	6 (0.6)	1 (0.2)	7 (0.5)
精索静脈瘤	1 (0.1)	1 (0.2)	2 (0.1)
外陰嚢乾燥	3 (0.3)	3 (0.6)	6 (0.4)
呼吸器、胸郭および縦隔障害			
喘息	11 (1.1)	4 (0.8)	15 (1.0)
運動誘発喘息	0 (0.0)	1 (0.2)	1 (0.1)
慢性気管支炎	1 (0.1)	0 (0.0)	1 (0.1)
気管支痙攣	1 (0.1)	1 (0.2)	2 (0.1)
咳嗽	77 (8.0)	38 (7.9)	115 (8.0)
咽喉乾燥	6 (0.6)	2 (0.4)	8 (0.6)
発声障害	3 (0.3)	0 (0.0)	3 (0.2)
呼吸困難	22 (2.3)	6 (1.2)	28 (1.9)
安静時呼吸困難	1 (0.1)	0 (0.0)	1 (0.1)
労作性呼吸困難	4 (0.4)	1 (0.2)	5 (0.3)
鼻出血	7 (0.7)	5 (1.0)	12 (0.8)
過換気	1 (0.1)	0 (0.0)	1 (0.1)
喉頭嚢腫	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害			
喉頭浮腫	2 (0.2)	1 (0.2)	3 (0.2)
肺障害	2 (0.2)	0 (0.0)	2 (0.1)
鼻閉	7 (0.7)	5 (1.0)	12 (0.8)
鼻乾燥	2 (0.2)	2 (0.4)	4 (0.3)
鼻の炎症	0 (0.0)	1 (0.2)	1 (0.1)
鼻閉塞	2 (0.2)	1 (0.2)	3 (0.2)
鼻中隔弯曲	2 (0.2)	0 (0.0)	2 (0.1)
夜間呼吸困難	0 (0.0)	1 (0.2)	1 (0.1)
口腔咽頭痛	46 (4.8)	18 (3.7)	64 (4.4)
咽頭紅斑	1 (0.1)	1 (0.2)	2 (0.1)
咽頭の炎症	1 (0.1)	0 (0.0)	1 (0.1)
咽頭浮腫	0 (0.0)	1 (0.2)	1 (0.1)
胸水	1 (0.1)	0 (0.0)	1 (0.1)
胸膜痛	1 (0.1)	0 (0.0)	1 (0.1)
肺臓炎	1 (0.1)	0 (0.0)	1 (0.1)
湿性咳嗽	2 (0.2)	0 (0.0)	2 (0.1)
肺塞栓症	1 (0.1)	0 (0.0)	1 (0.1)
肺線維症	1 (0.1)	0 (0.0)	1 (0.1)
呼吸不全	1 (0.1)	0 (0.0)	1 (0.1)
気道うっ血	2 (0.2)	0 (0.0)	2 (0.1)
鼻痛	2 (0.2)	0 (0.0)	2 (0.1)
アレルギー性鼻炎	9 (0.9)	4 (0.8)	13 (0.9)
鼻漏	10 (1.0)	3 (0.6)	13 (0.9)
低音性連続性ラ音	1 (0.1)	0 (0.0)	1 (0.1)
副鼻腔うっ血	6 (0.6)	2 (0.4)	8 (0.6)
睡眠時無呼吸症候群	5 (0.5)	0 (0.0)	5 (0.3)
くしゃみ	1 (0.1)	1 (0.2)	2 (0.1)
いびき	2 (0.2)	1 (0.2)	3 (0.2)
咽喉絞扼感	0 (0.0)	1 (0.2)	1 (0.1)
扁桃肥大	1 (0.1)	0 (0.0)	1 (0.1)
扁桃の炎症	0 (0.0)	1 (0.2)	1 (0.1)
扁桃結石	1 (0.1)	0 (0.0)	1 (0.1)
上気道の炎症	3 (0.3)	1 (0.2)	4 (0.3)
上気道咳症候群	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
呼吸器、胸郭および縦隔障害			
喘鳴	2 (0.2)	5 (1.0)	7 (0.5)
皮膚および皮下組織障害			
ざ瘡	14 (1.5)	8 (1.7)	22 (1.5)
日光性角化症	1 (0.1)	0 (0.0)	1 (0.1)
脱毛症	15 (1.6)	7 (1.4)	22 (1.5)
円形脱毛症	0 (0.0)	1 (0.2)	1 (0.1)
アンドロゲン性脱毛症	1 (0.1)	0 (0.0)	1 (0.1)
血管浮腫	2 (0.2)	0 (0.0)	2 (0.1)
水疱	2 (0.2)	0 (0.0)	2 (0.1)
血性水疱	1 (0.1)	0 (0.0)	1 (0.1)
冷汗	1 (0.1)	0 (0.0)	1 (0.1)
皮膚嚢腫	0 (0.0)	1 (0.2)	1 (0.1)
皮膚炎	4 (0.4)	1 (0.2)	5 (0.3)
アレルギー性皮膚炎	5 (0.5)	4 (0.8)	9 (0.6)
アトピー性皮膚炎	1 (0.1)	1 (0.2)	2 (0.1)
接触性皮膚炎	9 (0.9)	4 (0.8)	13 (0.9)
皮膚症	1 (0.1)	0 (0.0)	1 (0.1)
薬疹	0 (0.0)	1 (0.2)	1 (0.1)
皮膚乾燥	47 (4.9)	8 (1.7)	55 (3.8)
斑状出血	1 (0.1)	1 (0.2)	2 (0.1)
湿疹	19 (2.0)	3 (0.6)	22 (1.5)
湿潤性湿疹	0 (0.0)	1 (0.2)	1 (0.1)
紅斑	9 (0.9)	2 (0.4)	11 (0.8)
多形紅斑	1 (0.1)	1 (0.2)	2 (0.1)
過剰皮膚	1 (0.1)	0 (0.0)	1 (0.1)
毛髪成長異常	0 (0.0)	1 (0.2)	1 (0.1)
紅色汗疹	2 (0.2)	0 (0.0)	2 (0.1)
汗腺炎	1 (0.1)	0 (0.0)	1 (0.1)
多汗症	5 (0.5)	4 (0.8)	9 (0.6)
過角化	1 (0.1)	2 (0.4)	3 (0.2)
乏汗症	2 (0.2)	0 (0.0)	2 (0.1)
内出血発生の増加傾向	2 (0.2)	0 (0.0)	2 (0.1)
嵌入爪	1 (0.1)	0 (0.0)	1 (0.1)
間擦疹	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
皮膚および皮下組織障害			
網状皮斑	1 (0.1)	0 (0.0)	1 (0.1)
斑	0 (0.0)	1 (0.2)	1 (0.1)
機械性蕁麻疹	2 (0.2)	0 (0.0)	2 (0.1)
爪の障害	5 (0.5)	0 (0.0)	5 (0.3)
爪成長異常	0 (0.0)	1 (0.2)	1 (0.1)
神経皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
寝汗	5 (0.5)	2 (0.4)	7 (0.5)
爪破損	1 (0.1)	0 (0.0)	1 (0.1)
皮膚疼痛	1 (0.1)	0 (0.0)	1 (0.1)
丘疹	1 (0.1)	1 (0.2)	2 (0.1)
点状出血	1 (0.1)	0 (0.0)	1 (0.1)
光線過敏性反応	1 (0.1)	0 (0.0)	1 (0.1)
色素沈着障害	3 (0.3)	1 (0.2)	4 (0.3)
皰疹	0 (0.0)	1 (0.2)	1 (0.1)
ばら色皰疹	1 (0.1)	2 (0.4)	3 (0.2)
そう痒症	33 (3.4)	13 (2.7)	46 (3.2)
全身性そう痒症	1 (0.1)	0 (0.0)	1 (0.1)
乾癬	1 (0.1)	0 (0.0)	1 (0.1)
発疹	40 (4.2)	9 (1.9)	49 (3.4)
紅斑性皮疹	3 (0.3)	2 (0.4)	5 (0.3)
斑状丘疹状皮疹	0 (0.0)	1 (0.2)	1 (0.1)
そう痒性皮疹	3 (0.3)	0 (0.0)	3 (0.2)
酒さ	5 (0.5)	0 (0.0)	5 (0.3)
脂腺障害	1 (0.1)	0 (0.0)	1 (0.1)
脂漏性皮膚炎	2 (0.2)	1 (0.2)	3 (0.2)
皮膚色素脱失	1 (0.1)	0 (0.0)	1 (0.1)
皮膚変色	4 (0.4)	0 (0.0)	4 (0.3)
皮膚色素過剰	1 (0.1)	0 (0.0)	1 (0.1)
皮膚刺激	2 (0.2)	2 (0.4)	4 (0.3)
皮膚病変	4 (0.4)	2 (0.4)	6 (0.4)
皮膚反応	0 (0.0)	1 (0.2)	1 (0.1)
皮膚潰瘍	1 (0.1)	1 (0.2)	2 (0.1)
うつ滞性皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
顔面腫脹	1 (0.1)	1 (0.2)	2 (0.1)

表2.7.4.7-14

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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
皮膚および皮下組織障害			
蕁麻疹	14 (1.5)	4 (0.8)	18 (1.2)
慢性蕁麻疹	2 (0.2)	0 (0.0)	2 (0.1)
尋常性白斑	1 (0.1)	0 (0.0)	1 (0.1)
乾皮症	1 (0.1)	0 (0.0)	1 (0.1)
社会環境			
閉経	2 (0.2)	1 (0.2)	3 (0.2)
外科および内科処置			
収れん薬療法	1 (0.1)	0 (0.0)	1 (0.1)
ジフテリア免疫	1 (0.1)	0 (0.0)	1 (0.1)
子宮頚管拡張および子宮内搔爬	0 (0.0)	1 (0.2)	1 (0.1)
ビタミン補給	1 (0.1)	0 (0.0)	1 (0.1)
血管障害			
血管障害	1 (0.1)	0 (0.0)	1 (0.1)
大動脈拡張	1 (0.1)	2 (0.4)	3 (0.2)
動脈硬化症	3 (0.3)	0 (0.0)	3 (0.2)
コントロール不良の血圧	2 (0.2)	1 (0.2)	3 (0.2)
循環虚脱	0 (0.0)	1 (0.2)	1 (0.1)
深部静脈血栓症	1 (0.1)	1 (0.2)	2 (0.1)
潮紅	1 (0.1)	0 (0.0)	1 (0.1)
血腫	6 (0.6)	4 (0.8)	10 (0.7)
出血	1 (0.1)	0 (0.0)	1 (0.1)
ほてり	8 (0.8)	3 (0.6)	11 (0.8)
高血圧	310 (32.3)	174 (36.0)	484 (33.5)
高血圧クリーゼ	2 (0.2)	0 (0.0)	2 (0.1)
低血圧	30 (3.1)	15 (3.1)	45 (3.1)
腸骨動脈狭窄	0 (0.0)	1 (0.2)	1 (0.1)
不安定血圧	1 (0.1)	0 (0.0)	1 (0.1)
微小血管症	1 (0.1)	0 (0.0)	1 (0.1)
起立性低血圧	5 (0.5)	5 (1.0)	10 (0.7)
末梢冷感	11 (1.1)	3 (0.6)	14 (1.0)
静脈炎	1 (0.1)	0 (0.0)	1 (0.1)
レイノー現象	3 (0.3)	1 (0.2)	4 (0.3)
血栓性静脈炎	1 (0.1)	1 (0.2)	2 (0.1)
表在性血栓性静脈炎	3 (0.3)	0 (0.0)	3 (0.2)

表2.7.4.7-14
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CT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term（全体）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
血管障害			
血栓性静脈瘤	1 (0.1)	0 (0.0)	1 (0.1)
血栓症	2 (0.2)	0 (0.0)	2 (0.1)
静脈瘤	7 (0.7)	1 (0.2)	8 (0.6)
血管压迫	0 (0.0)	1 (0.2)	1 (0.1)
静脈不全	1 (0.1)	0 (0.0)	1 (0.1)
TOTAL	941 (97.9)	469 (97.1)	1410 (97.6)

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表2.7.4.7-15
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 JT-8.1 Adverse Events (All Causalities)- Within Treatment Period（日本の被験者）

	Tolvaptan	Placebo	Total
Number of:	N %	N %	N %
SUBJECTS TREATED	118	59	177
SUBJECT YEARS OF DRUG EXPOSURE	292.6	167.1	459.7
SUBJECTS WITH ADVERSE EVENTS	117 (99.2)	59 (100.0)	176 (99.4)
ADVERSE EVENTS	1540	739	2279
SUBJECTS WITH TREATMENT-EMERGENT ADVERSE EVENTS	117 (99.2)	59 (100.0)	176 (99.4)
TREATMENT-EMERGENT ADVERSE EVENTS ^a	1159	504	1663
SUBJECTS WITH SERIOUS TREATMENT-EMERGENT ADVERSE EVENTS	23 (19.5)	10 (16.9)	33 (18.6)
SUBJECTS WITH SEVERE TREATMENT-EMERGENT ADVERSE EVENTS	13 (11.0)	6 (10.2)	19 (10.7)
SUBJECTS DISCONTINUED STUDY MEDICATION DUE TO ADVERSE EVENTS	17 (14.4)	1 (1.7)	18 (10.2)
SUBJECTS WHO DIED	0 (0.0)	0 (0.0)	0 (0.0)

<資料番号5.3.5.3-02：JT-8.1>

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
血液およびリンパ系障害			
貧血	3 (2.5)	1 (1.7)	4 (2.3)
鉄欠乏性貧血	4 (3.4)	3 (5.1)	7 (4.0)
リンパ節症	0 (0.0)	1 (1.7)	1 (0.6)
脾臓障害	1 (0.8)	0 (0.0)	1 (0.6)
心臓障害			
狭心症	2 (1.7)	0 (0.0)	2 (1.1)
不整脈	2 (1.7)	2 (3.4)	4 (2.3)
房室ブロック	1 (0.8)	0 (0.0)	1 (0.6)
徐脈	2 (1.7)	0 (0.0)	2 (1.1)
右脚ブロック	1 (0.8)	0 (0.0)	1 (0.6)
心臓瘤	0 (0.0)	1 (1.7)	1 (0.6)
左室不全	1 (0.8)	0 (0.0)	1 (0.6)
僧帽弁閉鎖不全症	1 (0.8)	0 (0.0)	1 (0.6)
動悸	10 (8.5)	0 (0.0)	10 (5.6)
洞性徐脈	1 (0.8)	0 (0.0)	1 (0.6)
上室性頻脈	1 (0.8)	0 (0.0)	1 (0.6)
頻脈	3 (2.5)	0 (0.0)	3 (1.7)
心室性期外収縮	3 (2.5)	0 (0.0)	3 (1.7)
先天性、家族性および遺伝性障害			
多発性内分泌腺腫症	0 (0.0)	1 (1.7)	1 (0.6)
耳および迷路障害			
耳閉	0 (0.0)	1 (1.7)	1 (0.6)
耳不快感	0 (0.0)	1 (1.7)	1 (0.6)
内リンパ水腫	0 (0.0)	1 (1.7)	1 (0.6)
耳鳴	2 (1.7)	0 (0.0)	2 (1.1)
回転性めまい	3 (2.5)	1 (1.7)	4 (2.3)
頭位性回転性めまい	2 (1.7)	0 (0.0)	2 (1.1)
内分泌障害			
続発性副甲状腺機能亢進症	0 (0.0)	1 (1.7)	1 (0.6)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
眼障害			
霰粒腫	1 (0.8)	0 (0.0)	1 (0.6)
結膜出血	1 (0.8)	2 (3.4)	3 (1.7)
結膜充血	0 (0.0)	1 (1.7)	1 (0.6)
結膜炎	3 (2.5)	1 (1.7)	4 (2.3)
アレルギー性結膜炎	3 (2.5)	1 (1.7)	4 (2.3)
眼乾燥	6 (5.1)	1 (1.7)	7 (4.0)
眼痛	1 (0.8)	1 (1.7)	2 (1.1)
眼瞼浮腫	2 (1.7)	0 (0.0)	2 (1.1)
眼瞼下垂	2 (1.7)	0 (0.0)	2 (1.1)
眼瞼皮膚乾燥	1 (0.8)	0 (0.0)	1 (0.6)
眼瞼そう痒症	0 (0.0)	1 (1.7)	1 (0.6)
緑内障	2 (1.7)	0 (0.0)	2 (1.1)
羞明	1 (0.8)	0 (0.0)	1 (0.6)
強膜出血	0 (0.0)	1 (1.7)	1 (0.6)
強膜炎	1 (0.8)	1 (1.7)	2 (1.1)
胃腸障害			
腹部不快感	7 (5.9)	2 (3.4)	9 (5.1)
腹部膨満	7 (5.9)	4 (6.8)	11 (6.2)
腹痛	10 (8.5)	6 (10.2)	16 (9.0)
下腹部痛	2 (1.7)	0 (0.0)	2 (1.1)
上腹部痛	16 (13.6)	7 (11.9)	23 (13.0)
アフタ性口内炎	1 (0.8)	0 (0.0)	1 (0.6)
口唇炎	2 (1.7)	0 (0.0)	2 (1.1)
大腸炎	0 (0.0)	3 (5.1)	3 (1.7)
結腸ポリープ	2 (1.7)	0 (0.0)	2 (1.1)
便秘	19 (16.1)	4 (6.8)	23 (13.0)
齲歯	3 (2.5)	3 (5.1)	6 (3.4)
下痢	15 (12.7)	10 (16.9)	25 (14.1)
腸憩室	3 (2.5)	0 (0.0)	3 (1.7)
口内乾燥	1 (0.8)	0 (0.0)	1 (0.6)
十二指腸潰瘍	1 (0.8)	0 (0.0)	1 (0.6)
十二指腸炎	2 (1.7)	0 (0.0)	2 (1.1)
消化不良	7 (5.9)	1 (1.7)	8 (4.5)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
小腸炎	4 (3.4)	1 (1.7)	5 (2.8)
腸炎	0 (0.0)	2 (3.4)	2 (1.1)
心窩部不快感	3 (2.5)	0 (0.0)	3 (1.7)
胃ポリープ	1 (0.8)	1 (1.7)	2 (1.1)
胃炎	4 (3.4)	1 (1.7)	5 (2.8)
胃腸音異常	1 (0.8)	0 (0.0)	1 (0.6)
胃食道逆流性疾患	11 (9.3)	4 (6.8)	15 (8.5)
歯肉痛	0 (0.0)	1 (1.7)	1 (0.6)
歯肉炎	3 (2.5)	3 (5.1)	6 (3.4)
舌炎	0 (0.0)	1 (1.7)	1 (0.6)
血便排泄	0 (0.0)	1 (1.7)	1 (0.6)
痔出血	1 (0.8)	0 (0.0)	1 (0.6)
痔核	6 (5.1)	1 (1.7)	7 (4.0)
裂孔ヘルニア	2 (1.7)	0 (0.0)	2 (1.1)
イレウス	1 (0.8)	0 (0.0)	1 (0.6)
過敏性腸症候群	0 (0.0)	1 (1.7)	1 (0.6)
口唇乾燥	3 (2.5)	0 (0.0)	3 (1.7)
悪心	16 (13.6)	5 (8.5)	21 (11.9)
急性膵炎	0 (0.0)	1 (1.7)	1 (0.6)
再発性膵炎	0 (0.0)	1 (1.7)	1 (0.6)
歯周病	1 (0.8)	0 (0.0)	1 (0.6)
歯周炎	2 (1.7)	1 (1.7)	3 (1.7)
結腸直腸ポリープ	1 (0.8)	0 (0.0)	1 (0.6)
歯根嚢胞	1 (0.8)	0 (0.0)	1 (0.6)
唾液管の炎症	0 (0.0)	1 (1.7)	1 (0.6)
口内炎	4 (3.4)	1 (1.7)	5 (2.8)
歯の障害	1 (0.8)	0 (0.0)	1 (0.6)
歯痛	1 (0.8)	5 (8.5)	6 (3.4)
臍ヘルニア	1 (0.8)	0 (0.0)	1 (0.6)
嘔吐	12 (10.2)	3 (5.1)	15 (8.5)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態			
無力症	0 (0.0)	2 (3.4)	2 (1.1)
胸部不快感	0 (0.0)	3 (5.1)	3 (1.7)
胸痛	6 (5.1)	3 (5.1)	9 (5.1)
嚢胞	1 (0.8)	0 (0.0)	1 (0.6)
疲労	13 (11.0)	2 (3.4)	15 (8.5)
異常感	0 (0.0)	1 (1.7)	1 (0.6)
熱感	1 (0.8)	0 (0.0)	1 (0.6)
高熱	0 (0.0)	1 (1.7)	1 (0.6)
炎症	1 (0.8)	0 (0.0)	1 (0.6)
局所腫脹	1 (0.8)	0 (0.0)	1 (0.6)
倦怠感	12 (10.2)	1 (1.7)	13 (7.3)
浮腫	6 (5.1)	2 (3.4)	8 (4.5)
末梢性浮腫	7 (5.9)	6 (10.2)	13 (7.3)
疼痛	2 (1.7)	0 (0.0)	2 (1.1)
発熱	13 (11.0)	9 (15.3)	22 (12.4)
口渇	106 (89.8)	18 (30.5)	124 (70.1)
肝胆道系障害			
細胆管炎	0 (0.0)	1 (1.7)	1 (0.6)
胆石症	0 (0.0)	1 (1.7)	1 (0.6)
胆嚢ポリープ	4 (3.4)	2 (3.4)	6 (3.4)
肝嚢胞	1 (0.8)	1 (1.7)	2 (1.1)
肝機能異常	12 (10.2)	2 (3.4)	14 (7.9)
脂肪肝	2 (1.7)	0 (0.0)	2 (1.1)
肝障害	4 (3.4)	0 (0.0)	4 (2.3)
免疫系障害			
節足動物咬傷アレルギー	1 (0.8)	0 (0.0)	1 (0.6)
節足動物刺傷アレルギー	1 (0.8)	0 (0.0)	1 (0.6)
アナフィラキシー様反応	1 (0.8)	0 (0.0)	1 (0.6)
家塵アレルギー	1 (0.8)	0 (0.0)	1 (0.6)
季節性アレルギー	8 (6.8)	0 (0.0)	8 (4.5)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
急性副鼻腔炎	0 (0.0)	1 (1.7)	1 (0.6)
急性扁桃炎	1 (0.8)	0 (0.0)	1 (0.6)
アデノイド咽頭炎	1 (0.8)	0 (0.0)	1 (0.6)
虫垂炎	0 (0.0)	1 (1.7)	1 (0.6)
β溶血性レンサ球菌感染	0 (0.0)	1 (1.7)	1 (0.6)
気管支炎	4 (3.4)	3 (5.1)	7 (4.0)
蜂巣炎	1 (0.8)	0 (0.0)	1 (0.6)
感染性結膜炎	1 (0.8)	0 (0.0)	1 (0.6)
膀胱炎	4 (3.4)	5 (8.5)	9 (5.1)
憩室炎	1 (0.8)	0 (0.0)	1 (0.6)
感染性腸炎	0 (0.0)	1 (1.7)	1 (0.6)
感染性小腸結腸炎	1 (0.8)	0 (0.0)	1 (0.6)
胃腸炎	3 (2.5)	6 (10.2)	9 (5.1)
ウイルス性胃腸炎	2 (1.7)	0 (0.0)	2 (1.1)
肝嚢胞感染	0 (0.0)	1 (1.7)	1 (0.6)
B型肝炎	1 (0.8)	0 (0.0)	1 (0.6)
単純ヘルペス	2 (1.7)	0 (0.0)	2 (1.1)
ヘルペスウイルス感染	2 (1.7)	0 (0.0)	2 (1.1)
帯状疱疹	2 (1.7)	3 (5.1)	5 (2.8)
麦粒腫	3 (2.5)	2 (3.4)	5 (2.8)
感染	1 (0.8)	1 (1.7)	2 (1.1)
インフルエンザ	7 (5.9)	6 (10.2)	13 (7.3)
喉頭炎	1 (0.8)	0 (0.0)	1 (0.6)
鼓膜炎	0 (0.0)	1 (1.7)	1 (0.6)
鼻咽頭炎	68 (57.6)	45 (76.3)	113 (63.8)
口腔ヘルペス	0 (0.0)	2 (3.4)	2 (1.1)
外耳炎	0 (0.0)	2 (3.4)	2 (1.1)
中耳炎	0 (0.0)	1 (1.7)	1 (0.6)
耳下腺炎	1 (0.8)	1 (1.7)	2 (1.1)
歯冠周囲炎	0 (0.0)	1 (1.7)	1 (0.6)
扁桃周囲炎	1 (0.8)	0 (0.0)	1 (0.6)
咽頭炎	3 (2.5)	6 (10.2)	9 (5.1)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
腎嚢胞感染	2 (1.7)	3 (5.1)	5 (2.8)
気道感染	1 (0.8)	1 (1.7)	2 (1.1)
鼻炎	3 (2.5)	1 (1.7)	4 (2.3)
副鼻腔炎	2 (1.7)	0 (0.0)	2 (1.1)
軟部組織感染	1 (0.8)	0 (0.0)	1 (0.6)
皮下組織膿瘍	1 (0.8)	0 (0.0)	1 (0.6)
扁桃炎	2 (1.7)	2 (3.4)	4 (2.3)
トリコモナス症	1 (0.8)	0 (0.0)	1 (0.6)
上気道感染	6 (5.1)	4 (6.8)	10 (5.6)
尿路感染	0 (0.0)	2 (3.4)	2 (1.1)
外陰部膣カンジダ症	1 (0.8)	0 (0.0)	1 (0.6)
傷害、中毒および処置合併症			
節足動物刺傷	1 (0.8)	1 (1.7)	2 (1.1)
剥離骨折	1 (0.8)	0 (0.0)	1 (0.6)
凍瘡	1 (0.8)	0 (0.0)	1 (0.6)
鎖骨骨折	1 (0.8)	0 (0.0)	1 (0.6)
挫傷	4 (3.4)	3 (5.1)	7 (4.0)
擦過傷	1 (0.8)	0 (0.0)	1 (0.6)
眼外傷	1 (0.8)	0 (0.0)	1 (0.6)
足骨折	1 (0.8)	0 (0.0)	1 (0.6)
骨折	0 (0.0)	1 (1.7)	1 (0.6)
外傷性血尿	0 (0.0)	1 (1.7)	1 (0.6)
熱射病	2 (1.7)	0 (0.0)	2 (1.1)
靱帯捻挫	2 (1.7)	2 (3.4)	4 (2.3)
半月板障害	0 (0.0)	2 (3.4)	2 (1.1)
肉離れ	0 (0.0)	1 (1.7)	1 (0.6)
外傷後疼痛	0 (0.0)	1 (1.7)	1 (0.6)
処置による疼痛	1 (0.8)	0 (0.0)	1 (0.6)
処置による嘔吐	1 (0.8)	0 (0.0)	1 (0.6)
脊椎圧迫骨折	1 (0.8)	0 (0.0)	1 (0.6)
刺創	1 (0.8)	0 (0.0)	1 (0.6)
サンバーン	0 (0.0)	1 (1.7)	1 (0.6)
熱傷	1 (0.8)	1 (1.7)	2 (1.1)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症			
脛骨骨折	1 (0.8)	0 (0.0)	1 (0.6)
創傷	0 (0.0)	1 (1.7)	1 (0.6)
臨床検査			
活性化部分トロンボプラスチン時間延長	0 (0.0)	1 (1.7)	1 (0.6)
アラニン・アミノトランスフェラーゼ増加	3 (2.5)	0 (0.0)	3 (1.7)
アスパラギン酸アミノトランスフェラーゼ増加	3 (2.5)	0 (0.0)	3 (1.7)
細菌検査陽性	0 (0.0)	1 (1.7)	1 (0.6)
血中クレアチンホスホキナーゼ増加	3 (2.5)	1 (1.7)	4 (2.3)
血中クレアチニン増加	7 (5.9)	4 (6.8)	11 (6.2)
血中カリウム減少	1 (0.8)	0 (0.0)	1 (0.6)
血圧上昇	3 (2.5)	2 (3.4)	5 (2.8)
血中尿酸増加	5 (4.2)	0 (0.0)	5 (2.8)
体温上昇	1 (0.8)	0 (0.0)	1 (0.6)
シスタチンC増加	0 (0.0)	1 (1.7)	1 (0.6)
心電図Q T間隔	1 (0.8)	0 (0.0)	1 (0.6)
γ-グルタミルトランスフェラーゼ増加	1 (0.8)	2 (3.4)	3 (1.7)
尿中ブドウ糖	1 (0.8)	0 (0.0)	1 (0.6)
炎症マーカー上昇	0 (0.0)	1 (1.7)	1 (0.6)
腎触知	1 (0.8)	0 (0.0)	1 (0.6)
便潜血	1 (0.8)	0 (0.0)	1 (0.6)
尿蛋白	0 (0.0)	1 (1.7)	1 (0.6)
トランスアミナーゼ上昇	3 (2.5)	0 (0.0)	3 (1.7)
尿検査異常	0 (0.0)	1 (1.7)	1 (0.6)
尿浸透圧上昇	1 (0.8)	0 (0.0)	1 (0.6)
体重減少	8 (6.8)	0 (0.0)	8 (4.5)
体重増加	3 (2.5)	0 (0.0)	3 (1.7)
白血球数増加	1 (0.8)	0 (0.0)	1 (0.6)
代謝および栄養障害			
食欲減退	12 (10.2)	1 (1.7)	13 (7.3)
脱水	2 (1.7)	1 (1.7)	3 (1.7)
糖尿病	2 (1.7)	0 (0.0)	2 (1.1)
コントロール不良の糖尿病	1 (0.8)	0 (0.0)	1 (0.6)
脂質異常症	1 (0.8)	0 (0.0)	1 (0.6)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
代謝および栄養障害			
痛風	2 (1.7)	2 (3.4)	4 (2.3)
高カルシウム血症	1 (0.8)	0 (0.0)	1 (0.6)
高コレステロール血症	3 (2.5)	0 (0.0)	3 (1.7)
高血糖	0 (0.0)	1 (1.7)	1 (0.6)
高脂血症	3 (2.5)	1 (1.7)	4 (2.3)
高トリグリセリド血症	2 (1.7)	1 (1.7)	3 (1.7)
高尿酸血症	14 (11.9)	3 (5.1)	17 (9.6)
低アルブミン血症	0 (0.0)	1 (1.7)	1 (0.6)
鉄欠乏	1 (0.8)	0 (0.0)	1 (0.6)
筋骨格系および結合組織障害			
関節痛	6 (5.1)	5 (8.5)	11 (6.2)
背部痛	28 (23.7)	18 (30.5)	46 (26.0)
骨痛	0 (0.0)	1 (1.7)	1 (0.6)
側腹部痛	0 (0.0)	3 (5.1)	3 (1.7)
足変形	0 (0.0)	1 (1.7)	1 (0.6)
椎間板突出	3 (2.5)	2 (3.4)	5 (2.8)
筋痙縮	2 (1.7)	4 (6.8)	6 (3.4)
筋骨格痛	7 (5.9)	2 (3.4)	9 (5.1)
筋骨格硬直	5 (4.2)	1 (1.7)	6 (3.4)
筋肉痛	11 (9.3)	5 (8.5)	16 (9.0)
頸部痛	4 (3.4)	2 (3.4)	6 (3.4)
変形性関節症	0 (0.0)	2 (3.4)	2 (1.1)
四肢痛	6 (5.1)	2 (3.4)	8 (4.5)
顎痛	0 (0.0)	1 (1.7)	1 (0.6)
関節周囲炎	1 (0.8)	2 (3.4)	3 (1.7)
変形性脊椎症	0 (0.0)	2 (3.4)	2 (1.1)
滑液嚢腫	1 (0.8)	0 (0.0)	1 (0.6)
腱鞘炎	2 (1.7)	0 (0.0)	2 (1.1)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)			
脂漏性角化症	1 (0.8)	0 (0.0)	1 (0.6)
皮膚乳頭腫	2 (1.7)	0 (0.0)	2 (1.1)
汗腺腫瘍	1 (0.8)	0 (0.0)	1 (0.6)
子宮平滑筋腫	3 (2.5)	0 (0.0)	3 (1.7)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
味覚消失	1 (0.8)	0 (0.0)	1 (0.6)
くも膜嚢胞	1 (0.8)	2 (3.4)	3 (1.7)
平衡障害	0 (0.0)	2 (3.4)	2 (1.1)
頸動脈瘤	1 (0.8)	1 (1.7)	2 (1.1)
脳出血	1 (0.8)	0 (0.0)	1 (0.6)
脳梗塞	1 (0.8)	0 (0.0)	1 (0.6)
脳虚血	1 (0.8)	0 (0.0)	1 (0.6)
群発頭痛	1 (0.8)	0 (0.0)	1 (0.6)
注意力障害	1 (0.8)	0 (0.0)	1 (0.6)
浮動性めまい	17 (14.4)	8 (13.6)	25 (14.1)
体位性めまい	2 (1.7)	0 (0.0)	2 (1.1)
異常感覚	1 (0.8)	0 (0.0)	1 (0.6)
味覚異常	4 (3.4)	0 (0.0)	4 (2.3)
頭痛	37 (31.4)	15 (25.4)	52 (29.4)
感覚鈍麻	3 (2.5)	5 (8.5)	8 (4.5)
頭蓋内動脈瘤	5 (4.2)	0 (0.0)	5 (2.8)
意識消失	1 (0.8)	0 (0.0)	1 (0.6)
片頭痛	1 (0.8)	0 (0.0)	1 (0.6)
神経痛	1 (0.8)	0 (0.0)	1 (0.6)
末梢性ニューロパチー	0 (0.0)	1 (1.7)	1 (0.6)
嗅覚錯誤	0 (0.0)	1 (1.7)	1 (0.6)
気脳体	1 (0.8)	0 (0.0)	1 (0.6)
坐骨神経痛	1 (0.8)	0 (0.0)	1 (0.6)
傾眠	3 (2.5)	1 (1.7)	4 (2.3)
くも膜下出血	0 (0.0)	1 (1.7)	1 (0.6)
失神	0 (0.0)	1 (1.7)	1 (0.6)
緊張性頭痛	0 (0.0)	1 (1.7)	1 (0.6)
精神障害			
異常行動	0 (0.0)	1 (1.7)	1 (0.6)
不安	1 (0.8)	0 (0.0)	1 (0.6)
不安障害	2 (1.7)	0 (0.0)	2 (1.1)
閉所恐怖症	1 (0.8)	0 (0.0)	1 (0.6)
うつ病	4 (3.4)	3 (5.1)	7 (4.0)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
精神障害			
不眠症	10 (8.5)	2 (3.4)	12 (6.8)
中期不眠症	1 (0.8)	0 (0.0)	1 (0.6)
睡眠障害	1 (0.8)	1 (1.7)	2 (1.1)
自殺企図	1 (0.8)	0 (0.0)	1 (0.6)
腎および尿路障害			
膀胱刺激症状	1 (0.8)	0 (0.0)	1 (0.6)
膀胱痛	1 (0.8)	0 (0.0)	1 (0.6)
尿路結石	1 (0.8)	1 (1.7)	2 (1.1)
排尿困難	3 (2.5)	0 (0.0)	3 (1.7)
血尿	7 (5.9)	7 (11.9)	14 (7.9)
腎結石症	0 (0.0)	1 (1.7)	1 (0.6)
夜間頻尿	2 (1.7)	2 (3.4)	4 (2.3)
頻尿	63 (53.4)	4 (6.8)	67 (37.9)
多尿	40 (33.9)	5 (8.5)	45 (25.4)
蛋白尿	1 (0.8)	1 (1.7)	2 (1.1)
腎嚢胞出血	0 (0.0)	2 (3.4)	2 (1.1)
腎不全	0 (0.0)	1 (1.7)	1 (0.6)
腎機能障害	2 (1.7)	1 (1.7)	3 (1.7)
腎臓痛	12 (10.2)	11 (18.6)	23 (13.0)
終末尿滴下	1 (0.8)	0 (0.0)	1 (0.6)
生殖系および乳房障害			
無月経	0 (0.0)	1 (1.7)	1 (0.6)
乳房嚢胞	1 (0.8)	0 (0.0)	1 (0.6)
乳房腫瘍	0 (0.0)	1 (1.7)	1 (0.6)
月経困難症	1 (0.8)	0 (0.0)	1 (0.6)
射精障害	1 (0.8)	0 (0.0)	1 (0.6)
子宮内膜症	0 (0.0)	1 (1.7)	1 (0.6)
精巣上体炎	1 (0.8)	0 (0.0)	1 (0.6)
乳汁漏出症	1 (0.8)	0 (0.0)	1 (0.6)
性器出血	2 (1.7)	2 (3.4)	4 (2.3)
血精液症	1 (0.8)	0 (0.0)	1 (0.6)
閉経期症状	0 (0.0)	1 (1.7)	1 (0.6)
月経障害	1 (0.8)	0 (0.0)	1 (0.6)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
生殖系および乳房障害			
不規則月経	0 (0.0)	1 (1.7)	1 (0.6)
不正子宮出血	0 (0.0)	1 (1.7)	1 (0.6)
性機能不全	0 (0.0)	1 (1.7)	1 (0.6)
子宮ポリープ	0 (0.0)	2 (3.4)	2 (1.1)
子宮腔脱	1 (0.8)	0 (0.0)	1 (0.6)
呼吸器、胸郭および縦隔障害			
喘息	4 (3.4)	0 (0.0)	4 (2.3)
慢性気管支炎	1 (0.8)	0 (0.0)	1 (0.6)
咳嗽	3 (2.5)	7 (11.9)	10 (5.6)
呼吸困難	2 (1.7)	0 (0.0)	2 (1.1)
喉頭浮腫	1 (0.8)	0 (0.0)	1 (0.6)
鼻乾燥	1 (0.8)	1 (1.7)	2 (1.1)
鼻閉塞	1 (0.8)	1 (1.7)	2 (1.1)
口腔咽頭痛	11 (9.3)	7 (11.9)	18 (10.2)
咽頭紅斑	1 (0.8)	0 (0.0)	1 (0.6)
咽頭の炎症	1 (0.8)	0 (0.0)	1 (0.6)
湿性咳嗽	1 (0.8)	0 (0.0)	1 (0.6)
鼻痛	1 (0.8)	0 (0.0)	1 (0.6)
アレルギー性鼻炎	2 (1.7)	0 (0.0)	2 (1.1)
鼻漏	6 (5.1)	2 (3.4)	8 (4.5)
上気道の炎症	3 (2.5)	1 (1.7)	4 (2.3)
皮膚および皮下組織障害			
ざ瘡	3 (2.5)	1 (1.7)	4 (2.3)
血性水疱	1 (0.8)	0 (0.0)	1 (0.6)
冷汗	1 (0.8)	0 (0.0)	1 (0.6)
アレルギー性皮膚炎	0 (0.0)	1 (1.7)	1 (0.6)
アトピー性皮膚炎	1 (0.8)	1 (1.7)	2 (1.1)
接触性皮膚炎	2 (1.7)	3 (5.1)	5 (2.8)
薬疹	0 (0.0)	1 (1.7)	1 (0.6)
皮膚乾燥	6 (5.1)	1 (1.7)	7 (4.0)
湿疹	7 (5.9)	2 (3.4)	9 (5.1)
紅斑	2 (1.7)	0 (0.0)	2 (1.1)
多形紅斑	1 (0.8)	0 (0.0)	1 (0.6)

表2.7.4.7-16

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JT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term（日本の被験者）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
皮膚および皮下組織障害			
紅色汗疹	1 (0.8)	0 (0.0)	1 (0.6)
過角化	1 (0.8)	2 (3.4)	3 (1.7)
乏汗症	1 (0.8)	0 (0.0)	1 (0.6)
網状皮斑	1 (0.8)	0 (0.0)	1 (0.6)
爪の障害	2 (1.7)	0 (0.0)	2 (1.1)
点状出血	1 (0.8)	0 (0.0)	1 (0.6)
ばら色秕糠疹	0 (0.0)	1 (1.7)	1 (0.6)
そう痒症	8 (6.8)	1 (1.7)	9 (5.1)
乾癬	1 (0.8)	0 (0.0)	1 (0.6)
発疹	11 (9.3)	4 (6.8)	15 (8.5)
酒さ	1 (0.8)	0 (0.0)	1 (0.6)
脂漏性皮膚炎	0 (0.0)	1 (1.7)	1 (0.6)
皮膚変色	1 (0.8)	0 (0.0)	1 (0.6)
蕁麻疹	6 (5.1)	2 (3.4)	8 (4.5)
慢性蕁麻疹	1 (0.8)	0 (0.0)	1 (0.6)
血管障害			
大動脈拡張	1 (0.8)	0 (0.0)	1 (0.6)
動脈硬化症	1 (0.8)	0 (0.0)	1 (0.6)
潮紅	1 (0.8)	0 (0.0)	1 (0.6)
血腫	1 (0.8)	0 (0.0)	1 (0.6)
ほてり	0 (0.0)	1 (1.7)	1 (0.6)
高血圧	27 (22.9)	15 (25.4)	42 (23.7)
低血圧	2 (1.7)	2 (3.4)	4 (2.3)
不安定血圧	1 (0.8)	0 (0.0)	1 (0.6)
起立性低血圧	1 (0.8)	2 (3.4)	3 (1.7)
TOTAL	117 (99.2)	59 (100.0)	176 (99.4)

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<資料番号5.3.5.3-02 : JT-8.2.2>

表2.7.4.7-17

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NT-8.1 Adverse Events (All Causalities) - Within Treatment Period (海外の被験者)

	Tolvaptan	Placebo	Total
Number of:	N %	N %	N %
SUBJECTS TREATED	843	424	1267
SUBJECT YEARS OF DRUG EXPOSURE	2042	1138.4	3180.4
SUBJECTS WITH ADVERSE EVENTS	824 (97.7)	410 (96.7)	1234 (97.4)
ADVERSE EVENTS	9369	4229	13598
SUBJECTS WITH TREATMENT-EMERGENT ADVERSE EVENTS	824 (97.7)	410 (96.7)	1234 (97.4)
TREATMENT-EMERGENT ADVERSE EVENTS	7385	3271	10656
SUBJECTS WITH SERIOUS TREATMENT-EMERGENT ADVERSE EVENTS	154 (18.3)	85 (20.0)	239 (18.9)
SUBJECTS WITH SEVERE TREATMENT-EMERGENT ADVERSE EVENTS	190 (22.5)	82 (19.3)	272 (21.5)
SUBJECTS DISCONTINUED STUDY MEDICATION DUE TO ADVERSE EVENTS	127 (15.1)	20 (4.7)	147 (11.6)
SUBJECTS WHO DIED	0 (0.0)	0 (0.0)	0 (0.0)

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表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
血液およびリンパ系障害			
貧血	24 (2.8)	23 (5.4)	47 (3.7)
凝血異常	1 (0.1)	1 (0.2)	2 (0.2)
好酸球増加症	2 (0.2)	2 (0.5)	4 (0.3)
低色素性貧血	1 (0.1)	0 (0.0)	1 (0.1)
鉄欠乏性貧血	2 (0.2)	1 (0.2)	3 (0.2)
白血球増加症	3 (0.4)	2 (0.5)	5 (0.4)
白血球減少症	1 (0.1)	4 (0.9)	5 (0.4)
リンパ節症	5 (0.6)	1 (0.2)	6 (0.5)
腎性貧血	0 (0.0)	1 (0.2)	1 (0.1)
好中球増加症	3 (0.4)	1 (0.2)	4 (0.3)
正色素性正球性貧血	1 (0.1)	0 (0.0)	1 (0.1)
汎血球減少症	2 (0.2)	0 (0.0)	2 (0.2)
赤血球増加症	1 (0.1)	0 (0.0)	1 (0.1)
血小板減少症	1 (0.1)	1 (0.2)	2 (0.2)
血小板増加症	1 (0.1)	0 (0.0)	1 (0.1)
心臓障害			
急性心筋梗塞	0 (0.0)	2 (0.5)	2 (0.2)
狭心症	8 (0.9)	3 (0.7)	11 (0.9)
大動脈弁閉鎖不全症	0 (0.0)	1 (0.2)	1 (0.1)
不整脈	5 (0.6)	0 (0.0)	5 (0.4)
心房細動	5 (0.6)	3 (0.7)	8 (0.6)
第一度房室ブロック	1 (0.1)	0 (0.0)	1 (0.1)
徐脈	10 (1.2)	6 (1.4)	16 (1.3)
心臓瘤	0 (0.0)	1 (0.2)	1 (0.1)
心不全	0 (0.0)	1 (0.2)	1 (0.1)
心臓弁膜疾患	1 (0.1)	0 (0.0)	1 (0.1)
心拡大	1 (0.1)	0 (0.0)	1 (0.1)
心筋症	1 (0.1)	0 (0.0)	1 (0.1)
伝導障害	1 (0.1)	0 (0.0)	1 (0.1)
冠動脈疾患	1 (0.1)	0 (0.0)	1 (0.1)
チアノーゼ	1 (0.1)	0 (0.0)	1 (0.1)
期外収縮	1 (0.1)	1 (0.2)	2 (0.2)
左房肥大	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
心臓障害			
左室機能不全	1 (0.1)	0 (0.0)	1 (0.1)
左室肥大	5 (0.6)	1 (0.2)	6 (0.5)
僧帽弁疾患	1 (0.1)	0 (0.0)	1 (0.1)
僧帽弁閉鎖不全症	0 (0.0)	2 (0.5)	2 (0.2)
僧帽弁逸脱	2 (0.2)	1 (0.2)	3 (0.2)
心筋梗塞	1 (0.1)	0 (0.0)	1 (0.1)
心筋虚血	1 (0.1)	0 (0.0)	1 (0.1)
動悸	24 (2.8)	6 (1.4)	30 (2.4)
心嚢液貯留	2 (0.2)	0 (0.0)	2 (0.2)
心膜炎	2 (0.2)	0 (0.0)	2 (0.2)
洞不全症候群	1 (0.1)	0 (0.0)	1 (0.1)
洞性不整脈	1 (0.1)	0 (0.0)	1 (0.1)
洞性徐脈	1 (0.1)	1 (0.2)	2 (0.2)
上室性期外収縮	1 (0.1)	0 (0.0)	1 (0.1)
上室性頻脈	3 (0.4)	0 (0.0)	3 (0.2)
頻脈	10 (1.2)	5 (1.2)	15 (1.2)
三尖弁閉鎖不全症	0 (0.0)	1 (0.2)	1 (0.1)
心室性期外収縮	6 (0.7)	0 (0.0)	6 (0.5)
ウォルフ・パーキンソン・ホワイ ト症候群	0 (0.0)	1 (0.2)	1 (0.1)
先天性、家族性および遺伝性障害			
心房中隔欠損症	0 (0.0)	2 (0.5)	2 (0.2)
第Ⅴ因子ライデン変異	0 (0.0)	1 (0.2)	1 (0.1)
多嚢胞性肝疾患	3 (0.4)	2 (0.5)	5 (0.4)
脊椎奇形	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺管嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
耳および迷路障害			
耳垢栓塞	2 (0.2)	0 (0.0)	2 (0.2)
難聴	1 (0.1)	2 (0.5)	3 (0.2)
耳閉	3 (0.4)	0 (0.0)	3 (0.2)
耳不快感	2 (0.2)	0 (0.0)	2 (0.2)
耳痛	7 (0.8)	3 (0.7)	10 (0.8)
耳そう痒症	0 (0.0)	1 (0.2)	1 (0.1)
耳管障害	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
耳および迷路障害			
聴覚障害	1 (0.1)	0 (0.0)	1 (0.1)
聴力低下	1 (0.1)	0 (0.0)	1 (0.1)
内耳障害	0 (0.0)	1 (0.2)	1 (0.1)
メニエール病	0 (0.0)	1 (0.2)	1 (0.1)
中耳滲出液	0 (0.0)	1 (0.2)	1 (0.1)
乗物酔い	3 (0.4)	1 (0.2)	4 (0.3)
耳鳴	9 (1.1)	2 (0.5)	11 (0.9)
回転性めまい	21 (2.5)	17 (4.0)	38 (3.0)
頭位性回転性めまい	0 (0.0)	1 (0.2)	1 (0.1)
内分泌障害			
アンドロゲン欠乏症	1 (0.1)	0 (0.0)	1 (0.1)
自己免疫性甲状腺炎	1 (0.1)	1 (0.2)	2 (0.2)
バセドウ病	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺腫	1 (0.1)	1 (0.2)	2 (0.2)
副甲状腺機能亢進症	1 (0.1)	0 (0.0)	1 (0.1)
続発性副甲状腺機能低下症	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺機能低下症	6 (0.7)	2 (0.5)	8 (0.6)
エストロゲン欠乏症	1 (0.1)	0 (0.0)	1 (0.1)
甲状腺炎	1 (0.1)	1 (0.2)	2 (0.2)
眼障害			
調節障害	1 (0.1)	0 (0.0)	1 (0.1)
眼瞼炎	3 (0.4)	1 (0.2)	4 (0.3)
白内障	1 (0.1)	0 (0.0)	1 (0.1)
結膜出血	6 (0.7)	0 (0.0)	6 (0.5)
結膜炎	11 (1.3)	6 (1.4)	17 (1.3)
アレルギー性結膜炎	0 (0.0)	1 (0.2)	1 (0.1)
角膜障害	0 (0.0)	1 (0.2)	1 (0.1)
眼の隈	0 (0.0)	1 (0.2)	1 (0.1)
眼乾燥	9 (1.1)	6 (1.4)	15 (1.2)
外眼筋不全麻痺	0 (0.0)	1 (0.2)	1 (0.1)
眼の障害	1 (0.1)	1 (0.2)	2 (0.2)
眼出血	1 (0.1)	1 (0.2)	2 (0.2)
眼の炎症	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
眼障害			
眼痛	4 (0.5)	0 (0.0)	4 (0.3)
眼部腫脹	1 (0.1)	2 (0.5)	3 (0.2)
眼瞼浮腫	2 (0.2)	1 (0.2)	3 (0.2)
緑内障	3 (0.4)	1 (0.2)	4 (0.3)
遠視	1 (0.1)	0 (0.0)	1 (0.1)
虹彩炎	1 (0.1)	1 (0.2)	2 (0.2)
流涙増加	0 (0.0)	1 (0.2)	1 (0.1)
眼充血	2 (0.2)	1 (0.2)	3 (0.2)
開放隅角緑内障	0 (0.0)	1 (0.2)	1 (0.1)
眼窩周囲浮腫	0 (0.0)	1 (0.2)	1 (0.1)
光視症	1 (0.1)	0 (0.0)	1 (0.1)
老視	1 (0.1)	0 (0.0)	1 (0.1)
翼状片	1 (0.1)	0 (0.0)	1 (0.1)
網膜剥離	2 (0.2)	1 (0.2)	3 (0.2)
暗点	1 (0.1)	0 (0.0)	1 (0.1)
ブドウ膜炎	0 (0.0)	1 (0.2)	1 (0.1)
霧視	3 (0.4)	2 (0.5)	5 (0.4)
視力低下	2 (0.2)	0 (0.0)	2 (0.2)
視力障害	2 (0.2)	3 (0.7)	5 (0.4)
硝子体剥離	3 (0.4)	0 (0.0)	3 (0.2)
硝子体浮遊物	2 (0.2)	0 (0.0)	2 (0.2)
眼球乾燥	0 (0.0)	1 (0.2)	1 (0.1)
胃腸障害			
腹部癒着	0 (0.0)	1 (0.2)	1 (0.1)
腹部不快感	22 (2.6)	8 (1.9)	30 (2.4)
腹部膨満	40 (4.7)	12 (2.8)	52 (4.1)
腹部ヘルニア	5 (0.6)	6 (1.4)	11 (0.9)
閉塞を伴う腹部ヘルニア	0 (0.0)	1 (0.2)	1 (0.1)
腹部腫瘤	1 (0.1)	1 (0.2)	2 (0.2)
腹痛	52 (6.2)	26 (6.1)	78 (6.2)
下腹部痛	5 (0.6)	4 (0.9)	9 (0.7)
上腹部痛	47 (5.6)	35 (8.3)	82 (6.5)
腹部硬直	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
腹部圧痛	8 (0.9)	2 (0.5)	10 (0.8)
裂肛	4 (0.5)	1 (0.2)	5 (0.4)
痔瘻	1 (0.1)	0 (0.0)	1 (0.1)
肛門そう痒症	1 (0.1)	0 (0.0)	1 (0.1)
アフタ性口内炎	6 (0.7)	1 (0.2)	7 (0.6)
腹水	0 (0.0)	1 (0.2)	1 (0.1)
便通不規則	1 (0.1)	0 (0.0)	1 (0.1)
呼気臭	2 (0.2)	0 (0.0)	2 (0.2)
口唇のひび割れ	1 (0.1)	0 (0.0)	1 (0.1)
口唇炎	3 (0.4)	0 (0.0)	3 (0.2)
大腸炎	1 (0.1)	1 (0.2)	2 (0.2)
結腸ポリープ	2 (0.2)	2 (0.5)	4 (0.3)
便秘	62 (7.4)	8 (1.9)	70 (5.5)
クローン病	1 (0.1)	0 (0.0)	1 (0.1)
齲歯	5 (0.6)	2 (0.5)	7 (0.6)
歯不快感	4 (0.5)	1 (0.2)	5 (0.4)
下痢	113 (13.4)	43 (10.1)	156 (12.3)
憩室	1 (0.1)	0 (0.0)	1 (0.1)
腸憩室	1 (0.1)	2 (0.5)	3 (0.2)
口内乾燥	153 (18.1)	60 (14.2)	213 (16.8)
十二指腸潰瘍	0 (0.0)	1 (0.2)	1 (0.1)
十二指腸炎	1 (0.1)	0 (0.0)	1 (0.1)
消化不良	69 (8.2)	15 (3.5)	84 (6.6)
嚥下障害	6 (0.7)	1 (0.2)	7 (0.6)
小腸炎	4 (0.5)	1 (0.2)	5 (0.4)
心窩部不快感	1 (0.1)	2 (0.5)	3 (0.2)
びらん性十二指腸炎	1 (0.1)	0 (0.0)	1 (0.1)
おくび	1 (0.1)	0 (0.0)	1 (0.1)
糞塊	0 (0.0)	1 (0.2)	1 (0.1)
大腿ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
鼓腸	8 (0.9)	1 (0.2)	9 (0.7)
食中毒	4 (0.5)	2 (0.5)	6 (0.5)
機能的胃腸障害	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
胃障害	2 (0.2)	1 (0.2)	3 (0.2)
胃ポリープ	1 (0.1)	1 (0.2)	2 (0.2)
胃潰瘍	0 (0.0)	1 (0.2)	1 (0.1)
胃炎	10 (1.2)	5 (1.2)	15 (1.2)
びらん性胃炎	1 (0.1)	0 (0.0)	1 (0.1)
胃腸障害	5 (0.6)	2 (0.5)	7 (0.6)
消化管運動過剰	1 (0.1)	0 (0.0)	1 (0.1)
胃腸の炎症	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動障害	1 (0.1)	0 (0.0)	1 (0.1)
消化器痛	1 (0.1)	1 (0.2)	2 (0.2)
胃腸音異常	0 (0.0)	1 (0.2)	1 (0.1)
胃食道逆流性疾患	32 (3.8)	12 (2.8)	44 (3.5)
歯肉障害	0 (0.0)	1 (0.2)	1 (0.1)
歯肉痛	0 (0.0)	1 (0.2)	1 (0.1)
歯肉退縮	1 (0.1)	2 (0.5)	3 (0.2)
歯肉炎	1 (0.1)	1 (0.2)	2 (0.2)
舌痛	3 (0.4)	0 (0.0)	3 (0.2)
血便排泄	3 (0.4)	3 (0.7)	6 (0.5)
痔核	8 (0.9)	8 (1.9)	16 (1.3)
裂孔ヘルニア	6 (0.7)	4 (0.9)	10 (0.8)
胃酸過多	1 (0.1)	2 (0.5)	3 (0.2)
口の感覚鈍麻	1 (0.1)	1 (0.2)	2 (0.2)
回腸炎	1 (0.1)	0 (0.0)	1 (0.1)
臍径ヘルニア	7 (0.8)	6 (1.4)	13 (1.0)
内ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
腸出血	0 (0.0)	1 (0.2)	1 (0.1)
過敏性腸症候群	1 (0.1)	4 (0.9)	5 (0.4)
口唇乾燥	3 (0.4)	2 (0.5)	5 (0.4)
口唇腫脹	1 (0.1)	0 (0.0)	1 (0.1)
弛緩歯	1 (0.1)	0 (0.0)	1 (0.1)
下部消化管出血	1 (0.1)	0 (0.0)	1 (0.1)
吸収不良	1 (0.1)	1 (0.2)	2 (0.2)
メレナ	0 (0.0)	2 (0.5)	2 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
口腔嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
口腔内出血	0 (0.0)	1 (0.2)	1 (0.1)
口腔内潰瘍形成	0 (0.0)	1 (0.2)	1 (0.1)
悪心	82 (9.7)	52 (12.3)	134 (10.6)
嚥下痛	0 (0.0)	1 (0.2)	1 (0.1)
食道炎	5 (0.6)	2 (0.5)	7 (0.6)
口腔障害	1 (0.1)	0 (0.0)	1 (0.1)
口腔扁平苔癬	1 (0.1)	0 (0.0)	1 (0.1)
口腔内痛	1 (0.1)	0 (0.0)	1 (0.1)
腭嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
口の錯感覚	1 (0.1)	0 (0.0)	1 (0.1)
腹膜出血	0 (0.0)	1 (0.2)	1 (0.1)
肛門周囲痛	1 (0.1)	0 (0.0)	1 (0.1)
直腸出血	5 (0.6)	0 (0.0)	5 (0.4)
直腸脱	0 (0.0)	1 (0.2)	1 (0.1)
吐き戻し	1 (0.1)	0 (0.0)	1 (0.1)
レッチング	1 (0.1)	1 (0.2)	2 (0.2)
S状結腸炎	0 (0.0)	1 (0.2)	1 (0.1)
口内炎	2 (0.2)	0 (0.0)	2 (0.2)
舌苔	2 (0.2)	0 (0.0)	2 (0.2)
舌変色	3 (0.4)	0 (0.0)	3 (0.2)
舌障害	1 (0.1)	1 (0.2)	2 (0.2)
舌乾燥	1 (0.1)	2 (0.5)	3 (0.2)
舌粘膜剥脱	1 (0.1)	0 (0.0)	1 (0.1)
変色歯	0 (0.0)	1 (0.2)	1 (0.1)
歯の障害	2 (0.2)	3 (0.7)	5 (0.4)
歯痛	9 (1.1)	7 (1.7)	16 (1.3)
臍ヘルニア	20 (2.4)	7 (1.7)	27 (2.1)
閉塞性臍ヘルニア	0 (0.0)	1 (0.2)	1 (0.1)
嘔吐	67 (7.9)	37 (8.7)	104 (8.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態			
無力症	57 (6.8)	25 (5.9)	82 (6.5)
腋窩痛	1 (0.1)	1 (0.2)	2 (0.2)
胸部不快感	13 (1.5)	1 (0.2)	14 (1.1)
胸痛	36 (4.3)	9 (2.1)	45 (3.6)
悪寒	12 (1.4)	2 (0.5)	14 (1.1)
嚢胞	5 (0.6)	5 (1.2)	10 (0.8)
医療機器位置異常	0 (0.0)	1 (0.2)	1 (0.1)
異形成	0 (0.0)	1 (0.2)	1 (0.1)
早期満腹	1 (0.1)	2 (0.5)	3 (0.2)
運動耐性低下	3 (0.4)	0 (0.0)	3 (0.2)
顔面浮腫	2 (0.2)	0 (0.0)	2 (0.2)
脂肪組織増加	1 (0.1)	0 (0.0)	1 (0.1)
疲労	118 (14.0)	45 (10.6)	163 (12.9)
異常感	1 (0.1)	0 (0.0)	1 (0.1)
冷感	9 (1.1)	0 (0.0)	9 (0.7)
酩酊感	1 (0.1)	0 (0.0)	1 (0.1)
熱感	2 (0.2)	2 (0.5)	4 (0.3)
びくびく感	1 (0.1)	0 (0.0)	1 (0.1)
ヘルニア	2 (0.2)	1 (0.2)	3 (0.2)
治癒不良	1 (0.1)	0 (0.0)	1 (0.1)
インフルエンザ様疾患	7 (0.8)	5 (1.2)	12 (0.9)
易刺激性	5 (0.6)	1 (0.2)	6 (0.5)
局所腫脹	0 (0.0)	1 (0.2)	1 (0.1)
倦怠感	12 (1.4)	9 (2.1)	21 (1.7)
粘膜乾燥	8 (0.9)	2 (0.5)	10 (0.8)
小結節	2 (0.2)	0 (0.0)	2 (0.2)
非心臓性胸痛	0 (0.0)	2 (0.5)	2 (0.2)
浮腫	10 (1.2)	7 (1.7)	17 (1.3)
末梢性浮腫	74 (8.8)	40 (9.4)	114 (9.0)
疼痛	14 (1.7)	4 (0.9)	18 (1.4)
発熱	32 (3.8)	33 (7.8)	65 (5.1)
不活発	1 (0.1)	1 (0.2)	2 (0.2)
恥骨上痛	1 (0.1)	1 (0.2)	2 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態			
腫脹	1 (0.1)	0 (0.0)	1 (0.1)
温度変化不耐症	7 (0.8)	1 (0.2)	8 (0.6)
口渇	425 (50.4)	81 (19.1)	506 (39.9)
ワクチン接種部位反応	0 (0.0)	1 (0.2)	1 (0.1)
血管穿刺部位血腫	1 (0.1)	0 (0.0)	1 (0.1)
肝胆道系障害			
胆道ジスキネジー	1 (0.1)	0 (0.0)	1 (0.1)
胆管炎	2 (0.2)	0 (0.0)	2 (0.2)
胆嚢炎	1 (0.1)	0 (0.0)	1 (0.1)
胆石症	3 (0.4)	0 (0.0)	3 (0.2)
胆嚢痛	1 (0.1)	0 (0.0)	1 (0.1)
肝嚢胞	12 (1.4)	9 (2.1)	21 (1.7)
肝嚢胞破裂	1 (0.1)	0 (0.0)	1 (0.1)
肝臓痛	7 (0.8)	3 (0.7)	10 (0.8)
脂肪肝	1 (0.1)	0 (0.0)	1 (0.1)
肝炎	1 (0.1)	0 (0.0)	1 (0.1)
肝腫大	9 (1.1)	3 (0.7)	12 (0.9)
高ビリルビン血症	1 (0.1)	1 (0.2)	2 (0.2)
肝障害	1 (0.1)	1 (0.2)	2 (0.2)
肝圧痛	3 (0.4)	0 (0.0)	3 (0.2)
門脈圧亢進症	0 (0.0)	1 (0.2)	1 (0.1)
免疫系障害			
アレルギー性浮腫	1 (0.1)	0 (0.0)	1 (0.1)
節足動物咬傷アレルギー	3 (0.4)	0 (0.0)	3 (0.2)
節足動物刺傷アレルギー	1 (0.1)	0 (0.0)	1 (0.1)
アナフィラキシーショック	1 (0.1)	0 (0.0)	1 (0.1)
造影剤アレルギー	0 (0.0)	1 (0.2)	1 (0.1)
薬物過敏症	3 (0.4)	2 (0.5)	5 (0.4)
食物アレルギー	3 (0.4)	0 (0.0)	3 (0.2)
過敏症	7 (0.8)	2 (0.5)	9 (0.7)
複合アレルギー	2 (0.2)	0 (0.0)	2 (0.2)
季節性アレルギー	18 (2.1)	10 (2.4)	28 (2.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
膿瘍	1 (0.1)	2 (0.5)	3 (0.2)
四肢膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
急性副鼻腔炎	3 (0.4)	1 (0.2)	4 (0.3)
急性扁桃炎	5 (0.6)	4 (0.9)	9 (0.7)
真菌性肛門感染	1 (0.1)	0 (0.0)	1 (0.1)
肛門感染	1 (0.1)	0 (0.0)	1 (0.1)
虫垂炎	2 (0.2)	3 (0.7)	5 (0.4)
細菌性関節炎	1 (0.1)	1 (0.2)	2 (0.2)
感染性関節炎	1 (0.1)	0 (0.0)	1 (0.1)
回虫症	0 (0.0)	1 (0.2)	1 (0.1)
細菌尿	3 (0.4)	1 (0.2)	4 (0.3)
バルトリン腺膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
乳房感染	0 (0.0)	2 (0.5)	2 (0.2)
気管支炎	54 (6.4)	30 (7.1)	84 (6.6)
ウイルス性気管支炎	2 (0.2)	1 (0.2)	3 (0.2)
気管支肺炎	0 (0.0)	1 (0.2)	1 (0.1)
カンジダ症	2 (0.2)	3 (0.7)	5 (0.4)
蜂巣炎	5 (0.6)	1 (0.2)	6 (0.5)
眼窩蜂巣炎	0 (0.0)	1 (0.2)	1 (0.1)
子宮頸管炎	1 (0.1)	0 (0.0)	1 (0.1)
慢性副鼻腔炎	0 (0.0)	1 (0.2)	1 (0.1)
クロストリジウム性大腸炎	1 (0.1)	0 (0.0)	1 (0.1)
膀胱炎	7 (0.8)	7 (1.7)	14 (1.1)
サイトメガロウイルス感染	1 (0.1)	0 (0.0)	1 (0.1)
憩室炎	3 (0.4)	1 (0.2)	4 (0.3)
耳感染	22 (2.6)	7 (1.7)	29 (2.3)
耳垂感染	1 (0.1)	0 (0.0)	1 (0.1)
感染性腸炎	1 (0.1)	0 (0.0)	1 (0.1)
伝染性紅斑	0 (0.0)	1 (0.2)	1 (0.1)
遊走性紅斑	1 (0.1)	0 (0.0)	1 (0.1)
眼感染	1 (0.1)	3 (0.7)	4 (0.3)
眼瞼感染	0 (0.0)	1 (0.2)	1 (0.1)
熱性感染症	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
毛包炎	1 (0.1)	0 (0.0)	1 (0.1)
真菌感染	5 (0.6)	4 (0.9)	9 (0.7)
皮膚真菌感染	2 (0.2)	1 (0.2)	3 (0.2)
せつ	1 (0.1)	0 (0.0)	1 (0.1)
胃感染	1 (0.1)	0 (0.0)	1 (0.1)
胃腸炎	51 (6.0)	15 (3.5)	66 (5.2)
ノロウイルス性胃腸炎	2 (0.2)	0 (0.0)	2 (0.2)
ウイルス性胃腸炎	18 (2.1)	6 (1.4)	24 (1.9)
細菌性消化管感染	1 (0.1)	0 (0.0)	1 (0.1)
真菌性消化管感染	1 (0.1)	0 (0.0)	1 (0.1)
消化管感染	4 (0.5)	2 (0.5)	6 (0.5)
ウイルス性消化管感染	3 (0.4)	2 (0.5)	5 (0.4)
陰部ヘルペス	1 (0.1)	0 (0.0)	1 (0.1)
泌尿生殖器感染	1 (0.1)	0 (0.0)	1 (0.1)
ジアルジア症	1 (0.1)	1 (0.2)	2 (0.2)
歯肉膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
H1N1インフルエンザ	0 (0.0)	4 (0.9)	4 (0.3)
ヘリコバクター性胃炎	0 (0.0)	1 (0.2)	1 (0.1)
ヘリコバクター感染	2 (0.2)	1 (0.2)	3 (0.2)
肝嚢胞感染	0 (0.0)	1 (0.2)	1 (0.1)
B型肝炎	1 (0.1)	0 (0.0)	1 (0.1)
C型肝炎	1 (0.1)	0 (0.0)	1 (0.1)
単純ヘルペス	2 (0.2)	2 (0.5)	4 (0.3)
ヘルペスウイルス感染	1 (0.1)	1 (0.2)	2 (0.2)
带状疱疹	5 (0.6)	4 (0.9)	9 (0.7)
麦粒腫	4 (0.5)	3 (0.7)	7 (0.6)
切開部位膿瘍	0 (0.0)	1 (0.2)	1 (0.1)
感染性嚢腫	1 (0.1)	0 (0.0)	1 (0.1)
感染	0 (0.0)	1 (0.2)	1 (0.1)
伝染性単核症	1 (0.1)	1 (0.2)	2 (0.2)
インフルエンザ	68 (8.1)	32 (7.5)	100 (7.9)
腎感染	5 (0.6)	2 (0.5)	7 (0.6)
迷路炎	2 (0.2)	1 (0.2)	3 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
喉頭炎	3 (0.4)	4 (0.9)	7 (0.6)
肝膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
限局性感染	4 (0.5)	1 (0.2)	5 (0.4)
下気道感染	7 (0.8)	3 (0.7)	10 (0.8)
ライム病	2 (0.2)	0 (0.0)	2 (0.2)
リンパ節感染	0 (0.0)	1 (0.2)	1 (0.1)
リンパ管炎	2 (0.2)	0 (0.0)	2 (0.2)
マラリア	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス性髄膜炎	0 (0.0)	1 (0.2)	1 (0.1)
マイコプラズマ感染	1 (0.1)	0 (0.0)	1 (0.1)
爪感染	0 (0.0)	1 (0.2)	1 (0.1)
鼻咽頭炎	143 (17.0)	66 (15.6)	209 (16.5)
線虫症	1 (0.1)	0 (0.0)	1 (0.1)
オンコセルカ症	1 (0.1)	0 (0.0)	1 (0.1)
爪真菌症	3 (0.4)	3 (0.7)	6 (0.5)
口腔カンジダ症	6 (0.7)	0 (0.0)	6 (0.5)
口腔真菌感染	3 (0.4)	0 (0.0)	3 (0.2)
口腔ヘルペス	8 (0.9)	3 (0.7)	11 (0.9)
口腔感染	0 (0.0)	1 (0.2)	1 (0.1)
精巣炎	0 (0.0)	1 (0.2)	1 (0.1)
外耳炎	1 (0.1)	0 (0.0)	1 (0.1)
中耳炎	5 (0.6)	2 (0.5)	7 (0.6)
急性中耳炎	1 (0.1)	0 (0.0)	1 (0.1)
乳頭腫ウイルス感染	1 (0.1)	1 (0.2)	2 (0.2)
爪囲炎	1 (0.1)	0 (0.0)	1 (0.1)
耳下腺炎	1 (0.1)	1 (0.2)	2 (0.2)
骨盤内感染	0 (0.0)	1 (0.2)	1 (0.1)
会陰膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
百日咳	1 (0.1)	1 (0.2)	2 (0.2)
咽頭炎	13 (1.5)	10 (2.4)	23 (1.8)
レンサ球菌性咽頭炎	7 (0.8)	4 (0.9)	11 (0.9)
肺炎	11 (1.3)	5 (1.2)	16 (1.3)
前立腺感染	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
歯髄炎	0 (0.0)	1 (0.2)	1 (0.1)
腎盂腎炎	8 (0.9)	9 (2.1)	17 (1.3)
腎嚢胞感染	7 (0.8)	10 (2.4)	17 (1.3)
気道感染	5 (0.6)	3 (0.7)	8 (0.6)
ウイルス性気道感染	5 (0.6)	0 (0.0)	5 (0.4)
鼻炎	11 (1.3)	10 (2.4)	21 (1.7)
卵管卵巣炎	1 (0.1)	0 (0.0)	1 (0.1)
敗血症	0 (0.0)	2 (0.5)	2 (0.2)
副鼻腔炎	51 (6.0)	23 (5.4)	74 (5.8)
皮膚感染	3 (0.4)	0 (0.0)	3 (0.2)
ブドウ球菌感染	1 (0.1)	1 (0.2)	2 (0.2)
ブドウ球菌性咽頭炎	1 (0.1)	0 (0.0)	1 (0.1)
ブドウ球菌皮膚感染	0 (0.0)	1 (0.2)	1 (0.1)
糞線虫症	1 (0.1)	0 (0.0)	1 (0.1)
梅毒	1 (0.1)	0 (0.0)	1 (0.1)
足部白癬	2 (0.2)	0 (0.0)	2 (0.2)
癬風	0 (0.0)	1 (0.2)	1 (0.1)
扁桃炎	11 (1.3)	4 (0.9)	15 (1.2)
歯膿瘍	7 (0.8)	5 (1.2)	12 (0.9)
歯感染	8 (0.9)	5 (1.2)	13 (1.0)
気管炎	2 (0.2)	1 (0.2)	3 (0.2)
気管気管支炎	1 (0.1)	0 (0.0)	1 (0.1)
上気道感染	76 (9.0)	38 (9.0)	114 (9.0)
尿路感染	81 (9.6)	59 (13.9)	140 (11.0)
泌尿生殖器細菌感染	1 (0.1)	0 (0.0)	1 (0.1)
膣感染	1 (0.1)	2 (0.5)	3 (0.2)
細菌性膣炎	1 (0.1)	0 (0.0)	1 (0.1)
水痘	0 (0.0)	1 (0.2)	1 (0.1)
ウイルス感染	21 (2.5)	13 (3.1)	34 (2.7)
ウイルス性鼻炎	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス性上気道感染	4 (0.5)	1 (0.2)	5 (0.4)
外陰部膣カンジダ症	4 (0.5)	3 (0.7)	7 (0.6)
外陰膣真菌感染	4 (0.5)	4 (0.9)	8 (0.6)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
創傷感染	2 (0.2)	1 (0.2)	3 (0.2)
膿創	1 (0.1)	0 (0.0)	1 (0.1)
傷害、中毒および処置合併症			
腹部損傷	1 (0.1)	0 (0.0)	1 (0.1)
動物咬傷	2 (0.2)	0 (0.0)	2 (0.2)
足関節部骨折	2 (0.2)	1 (0.2)	3 (0.2)
節足動物咬傷	8 (0.9)	3 (0.7)	11 (0.9)
節足動物刺傷	0 (0.0)	1 (0.2)	1 (0.1)
背部損傷	2 (0.2)	0 (0.0)	2 (0.2)
咬刺傷	1 (0.1)	0 (0.0)	1 (0.1)
滑液包損傷	1 (0.1)	0 (0.0)	1 (0.1)
軟骨損傷	4 (0.5)	0 (0.0)	4 (0.3)
胸部損傷	0 (0.0)	1 (0.2)	1 (0.1)
挫傷	14 (1.7)	3 (0.7)	17 (1.3)
角膜擦過傷	2 (0.2)	0 (0.0)	2 (0.2)
上顎炎	2 (0.2)	0 (0.0)	2 (0.2)
擦過傷	4 (0.5)	0 (0.0)	4 (0.3)
眼外傷	1 (0.1)	0 (0.0)	1 (0.1)
眼の貫通性外傷	1 (0.1)	0 (0.0)	1 (0.1)
転倒	5 (0.6)	6 (1.4)	11 (0.9)
足骨折	5 (0.6)	3 (0.7)	8 (0.6)
眼内異物	1 (0.1)	0 (0.0)	1 (0.1)
手骨折	1 (0.1)	1 (0.2)	2 (0.2)
頭部損傷	1 (0.1)	1 (0.2)	2 (0.2)
熱疲労	1 (0.1)	0 (0.0)	1 (0.1)
熱射病	1 (0.1)	0 (0.0)	1 (0.1)
腸脛靱帯症候群	1 (0.1)	0 (0.0)	1 (0.1)
ステント内動脈再狭窄	0 (0.0)	1 (0.2)	1 (0.1)
切開部位痛	1 (0.1)	0 (0.0)	1 (0.1)
人工流産による出血	1 (0.1)	0 (0.0)	1 (0.1)
損傷	0 (0.0)	1 (0.2)	1 (0.1)
顎の骨折	0 (0.0)	1 (0.2)	1 (0.1)
関節脱臼	3 (0.4)	3 (0.7)	6 (0.5)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症			
関節損傷	9 (1.1)	7 (1.7)	16 (1.3)
裂傷	6 (0.7)	4 (0.9)	10 (0.8)
靱帯損傷	1 (0.1)	1 (0.2)	2 (0.2)
靱帯断裂	2 (0.2)	4 (0.9)	6 (0.5)
靱帯捻挫	12 (1.4)	9 (2.1)	21 (1.7)
四肢損傷	3 (0.4)	5 (1.2)	8 (0.6)
口唇損傷	1 (0.1)	0 (0.0)	1 (0.1)
下肢骨折	0 (0.0)	1 (0.2)	1 (0.1)
腰椎骨折	1 (0.1)	0 (0.0)	1 (0.1)
半月板障害	5 (0.6)	5 (1.2)	10 (0.8)
多発骨折	2 (0.2)	1 (0.2)	3 (0.2)
筋断裂	2 (0.2)	1 (0.2)	3 (0.2)
肉離れ	9 (1.1)	5 (1.2)	14 (1.1)
頸部損傷	1 (0.1)	0 (0.0)	1 (0.1)
眼窩周囲血腫	2 (0.2)	1 (0.2)	3 (0.2)
処置後合併症	0 (0.0)	1 (0.2)	1 (0.1)
処置後血尿	0 (0.0)	1 (0.2)	1 (0.1)
処置後出血	1 (0.1)	0 (0.0)	1 (0.1)
外傷後疼痛	2 (0.2)	2 (0.5)	4 (0.3)
処置による疼痛	8 (0.9)	6 (1.4)	14 (1.1)
恥骨骨折	0 (0.0)	1 (0.2)	1 (0.1)
橈骨骨折	1 (0.1)	0 (0.0)	1 (0.1)
肋骨骨折	4 (0.5)	1 (0.2)	5 (0.4)
骨格損傷	3 (0.4)	1 (0.2)	4 (0.3)
軟部組織損傷	1 (0.1)	0 (0.0)	1 (0.1)
脊椎骨折	1 (0.1)	0 (0.0)	1 (0.1)
ストレス骨折	2 (0.2)	0 (0.0)	2 (0.2)
サンバーン	3 (0.4)	0 (0.0)	3 (0.2)
眼の擦過傷	1 (0.1)	0 (0.0)	1 (0.1)
腱損傷	1 (0.1)	1 (0.2)	2 (0.2)
腱断裂	1 (0.1)	0 (0.0)	1 (0.1)
熱傷	3 (0.4)	1 (0.2)	4 (0.3)
脛骨骨折	0 (0.0)	3 (0.7)	3 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症			
歯牙破折	2 (0.2)	0 (0.0)	2 (0.2)
外傷性血腫	1 (0.1)	0 (0.0)	1 (0.1)
尺骨骨折	1 (0.1)	0 (0.0)	1 (0.1)
上肢骨折	0 (0.0)	1 (0.2)	1 (0.1)
創傷	2 (0.2)	1 (0.2)	3 (0.2)
手首関節骨折	1 (0.1)	2 (0.5)	3 (0.2)
臨床検査			
活性化部分トロンボプラスチン時間延長	2 (0.2)	1 (0.2)	3 (0.2)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	1 (0.2)	1 (0.1)
アラニン・アミノトランスフェラーゼ増加	36 (4.3)	17 (4.0)	53 (4.2)
アスパラギン酸アミノトランスフェラーゼ増加	33 (3.9)	16 (3.8)	49 (3.9)
細菌検査陽性	2 (0.2)	2 (0.5)	4 (0.3)
血中アルカリホスファターゼ増加	3 (0.4)	1 (0.2)	4 (0.3)
血中ビリルビン増加	2 (0.2)	2 (0.5)	4 (0.3)
血中カルシウム増加	6 (0.7)	0 (0.0)	6 (0.5)
血中コレステロール増加	14 (1.7)	7 (1.7)	21 (1.7)
血中クレアチンホスホキナーゼ増加	3 (0.4)	0 (0.0)	3 (0.2)
血中クレアチニン増加	128 (15.2)	67 (15.8)	195 (15.4)
血中ブドウ糖減少	0 (0.0)	2 (0.5)	2 (0.2)
血中ブドウ糖増加	7 (0.8)	1 (0.2)	8 (0.6)
血中乳酸脱水素酵素増加	5 (0.6)	1 (0.2)	6 (0.5)
血中エストロゲン減少	0 (0.0)	1 (0.2)	1 (0.1)
血中副甲状腺ホルモン増加	1 (0.1)	0 (0.0)	1 (0.1)
血中カリウム減少	3 (0.4)	0 (0.0)	3 (0.2)
血中カリウム増加	6 (0.7)	3 (0.7)	9 (0.7)
血圧低下	1 (0.1)	1 (0.2)	2 (0.2)
拡張期血圧上昇	1 (0.1)	1 (0.2)	2 (0.2)
血圧上昇	7 (0.8)	5 (1.2)	12 (0.9)
血中ナトリウム減少	1 (0.1)	0 (0.0)	1 (0.1)
血中ナトリウム増加	14 (1.7)	1 (0.2)	15 (1.2)
血中テストステロン減少	1 (0.1)	0 (0.0)	1 (0.1)
血中甲状腺刺激ホルモン増加	3 (0.4)	0 (0.0)	3 (0.2)
血中トリグリセリド増加	0 (0.0)	2 (0.5)	2 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
臨床検査			
血中尿素増加	10 (1.2)	12 (2.8)	22 (1.7)
血中尿酸増加	19 (2.3)	6 (1.4)	25 (2.0)
尿中血陽性	1 (0.1)	0 (0.0)	1 (0.1)
C-反応性蛋白増加	1 (0.1)	0 (0.0)	1 (0.1)
癌胎児性抗原増加	0 (0.0)	1 (0.2)	1 (0.1)
心雑音	5 (0.6)	3 (0.7)	8 (0.6)
腎クレアチニン・クリアランス増加	1 (0.1)	0 (0.0)	1 (0.1)
尿中クレアチニン増加	0 (0.0)	1 (0.2)	1 (0.1)
シスタチンC増加	6 (0.7)	6 (1.4)	12 (0.9)
心電図再分極異常	1 (0.1)	1 (0.2)	2 (0.2)
心電図異常T波	1 (0.1)	0 (0.0)	1 (0.1)
心電図T波逆転	1 (0.1)	1 (0.2)	2 (0.2)
好酸球数増加	3 (0.4)	2 (0.5)	5 (0.4)
大腸菌検査陽性	1 (0.1)	1 (0.2)	2 (0.2)
γ-グルタミルトランスフェラーゼ増加	22 (2.6)	9 (2.1)	31 (2.4)
胃内pH低下	1 (0.1)	0 (0.0)	1 (0.1)
ヘマトクリット減少	1 (0.1)	2 (0.5)	3 (0.2)
ヘマトクリット増加	1 (0.1)	0 (0.0)	1 (0.1)
ヘモグロビン減少	2 (0.2)	3 (0.7)	5 (0.4)
心拍数増加	0 (0.0)	1 (0.2)	1 (0.1)
心拍数不整	1 (0.1)	0 (0.0)	1 (0.1)
心音異常	0 (0.0)	1 (0.2)	1 (0.1)
肝酵素異常	1 (0.1)	0 (0.0)	1 (0.1)
肝酵素上昇	17 (2.0)	1 (0.2)	18 (1.4)
ヒト乳頭腫ウイルス検査陽性	1 (0.1)	0 (0.0)	1 (0.1)
INR増加	7 (0.8)	0 (0.0)	7 (0.6)
眼圧上昇	2 (0.2)	0 (0.0)	2 (0.2)
腎触知	2 (0.2)	2 (0.5)	4 (0.3)
リバーゼ増加	0 (0.0)	1 (0.2)	1 (0.1)
肝機能検査異常	6 (0.7)	3 (0.7)	9 (0.7)
季肋下肝触知	1 (0.1)	0 (0.0)	1 (0.1)
低比重リポ蛋白減少	0 (0.0)	1 (0.2)	1 (0.1)
リンパ球数増加	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
臨床検査			
リンパ球形態異常	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球容積減少	1 (0.1)	2 (0.5)	3 (0.2)
平均赤血球容積増加	4 (0.5)	1 (0.2)	5 (0.4)
好中球数減少	1 (0.1)	3 (0.7)	4 (0.3)
好中球数増加	1 (0.1)	2 (0.5)	3 (0.2)
便潜血陽性	1 (0.1)	0 (0.0)	1 (0.1)
血小板数減少	1 (0.1)	2 (0.5)	3 (0.2)
血小板数増加	1 (0.1)	0 (0.0)	1 (0.1)
尿蛋白	1 (0.1)	0 (0.0)	1 (0.1)
プロトロンビン時間異常	1 (0.1)	0 (0.0)	1 (0.1)
プロトロンビン時間延長	5 (0.6)	0 (0.0)	5 (0.4)
QOL低下	1 (0.1)	0 (0.0)	1 (0.1)
赤血球数減少	1 (0.1)	4 (0.9)	5 (0.4)
尿中赤血球陽性	0 (0.0)	1 (0.2)	1 (0.1)
子宮頸部スミア異常	0 (0.0)	1 (0.2)	1 (0.1)
トランスアミナーゼ上昇	8 (0.9)	2 (0.5)	10 (0.8)
卵巣超音波検査異常	1 (0.1)	0 (0.0)	1 (0.1)
尿検査異常	0 (0.0)	1 (0.2)	1 (0.1)
尿浸透圧低下	9 (1.1)	1 (0.2)	10 (0.8)
尿量増加	15 (1.8)	2 (0.5)	17 (1.3)
ビタミンD減少	0 (0.0)	3 (0.7)	3 (0.2)
ウエスト周囲径増加	1 (0.1)	0 (0.0)	1 (0.1)
体重減少	38 (4.5)	16 (3.8)	54 (4.3)
体重増加	43 (5.1)	19 (4.5)	62 (4.9)
白血球数減少	1 (0.1)	2 (0.5)	3 (0.2)
白血球数増加	2 (0.2)	4 (0.9)	6 (0.5)
尿中白血球	1 (0.1)	1 (0.2)	2 (0.2)
尿中白血球陽性	1 (0.1)	1 (0.2)	2 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
代謝および栄養障害			
アシドーシス	0 (0.0)	2 (0.5)	2 (0.2)
食欲減退	57 (6.8)	4 (0.9)	61 (4.8)
脱水	16 (1.9)	10 (2.4)	26 (2.1)
糖尿病	5 (0.6)	0 (0.0)	5 (0.4)
脂質異常症	3 (0.4)	0 (0.0)	3 (0.2)
体液貯留	1 (0.1)	1 (0.2)	2 (0.2)
食物渴望	2 (0.2)	0 (0.0)	2 (0.2)
食物不耐性	1 (0.1)	0 (0.0)	1 (0.1)
耐糖能障害	1 (0.1)	1 (0.2)	2 (0.2)
痛風	26 (3.1)	5 (1.2)	31 (2.4)
高アミラーゼ血症	0 (0.0)	1 (0.2)	1 (0.1)
高カルシウム血症	4 (0.5)	2 (0.5)	6 (0.5)
高コレステロール血症	23 (2.7)	12 (2.8)	35 (2.8)
高クレアチニン血症	0 (0.0)	1 (0.2)	1 (0.1)
高血糖	6 (0.7)	9 (2.1)	15 (1.2)
高カリウム血症	7 (0.8)	3 (0.7)	10 (0.8)
高脂血症	9 (1.1)	2 (0.5)	11 (0.9)
高ナトリウム血症	27 (3.2)	5 (1.2)	32 (2.5)
高リン酸塩血症	2 (0.2)	0 (0.0)	2 (0.2)
高尿酸血症	23 (2.7)	6 (1.4)	29 (2.3)
低アルブミン血症	1 (0.1)	0 (0.0)	1 (0.1)
低カルシウム血症	1 (0.1)	2 (0.5)	3 (0.2)
低血糖症	6 (0.7)	0 (0.0)	6 (0.5)
低カリウム血症	6 (0.7)	2 (0.5)	8 (0.6)
低マグネシウム血症	1 (0.1)	0 (0.0)	1 (0.1)
低ナトリウム血症	5 (0.6)	2 (0.5)	7 (0.6)
低リン酸血症	2 (0.2)	0 (0.0)	2 (0.2)
血液量減少症	2 (0.2)	0 (0.0)	2 (0.2)
食欲亢進	1 (0.1)	1 (0.2)	2 (0.2)
鉄欠乏	3 (0.4)	0 (0.0)	3 (0.2)
ラクトース不耐性	1 (0.1)	0 (0.0)	1 (0.1)
代謝性アシドーシス	1 (0.1)	0 (0.0)	1 (0.1)
肥満	0 (0.0)	2 (0.5)	2 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
代謝および栄養障害			
過体重	3 (0.4)	0 (0.0)	3 (0.2)
多飲症	100 (11.9)	17 (4.0)	117 (9.2)
2 型糖尿病	2 (0.2)	0 (0.0)	2 (0.2)
ビタミンB 1 2 欠乏	1 (0.1)	0 (0.0)	1 (0.1)
ビタミンD 欠乏	9 (1.1)	5 (1.2)	14 (1.1)
体重変動	2 (0.2)	0 (0.0)	2 (0.2)
筋骨格系および結合組織障害			
関節痛	63 (7.5)	23 (5.4)	86 (6.8)
関節炎	6 (0.7)	1 (0.2)	7 (0.6)
反応性関節炎	1 (0.1)	0 (0.0)	1 (0.1)
関節障害	1 (0.1)	0 (0.0)	1 (0.1)
背部痛	105 (12.5)	70 (16.5)	175 (13.8)
骨痛	3 (0.4)	3 (0.7)	6 (0.5)
滑液包石灰化	1 (0.1)	0 (0.0)	1 (0.1)
滑液包炎	5 (0.6)	1 (0.2)	6 (0.5)
軟骨肥厚	1 (0.1)	0 (0.0)	1 (0.1)
頸部脊柱管狭窄症	1 (0.1)	0 (0.0)	1 (0.1)
ピロリン酸カルシウム結晶性軟骨石灰化症	2 (0.2)	0 (0.0)	2 (0.2)
軟骨軟化症	0 (0.0)	1 (0.2)	1 (0.1)
軟骨疾患	0 (0.0)	1 (0.2)	1 (0.1)
尾骨痛	0 (0.0)	2 (0.5)	2 (0.2)
肋軟骨炎	2 (0.2)	0 (0.0)	2 (0.2)
歯槽異常	1 (0.1)	0 (0.0)	1 (0.1)
外骨腫	2 (0.2)	1 (0.2)	3 (0.2)
筋膜炎	1 (0.1)	0 (0.0)	1 (0.1)
線維筋痛	2 (0.2)	1 (0.2)	3 (0.2)
瘻孔	1 (0.1)	0 (0.0)	1 (0.1)
側腹部痛	11 (1.3)	7 (1.7)	18 (1.4)
足変形	2 (0.2)	1 (0.2)	3 (0.2)
痛風性関節炎	1 (0.1)	0 (0.0)	1 (0.1)
腓径部痛	2 (0.2)	1 (0.2)	3 (0.2)
椎間板変性症	3 (0.4)	0 (0.0)	3 (0.2)
椎間板障害	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
筋骨格系および結合組織障害			
椎間板突出	10 (1.2)	5 (1.2)	15 (1.2)
関節滲出液	4 (0.5)	0 (0.0)	4 (0.3)
関節可動域低下	1 (0.1)	0 (0.0)	1 (0.1)
関節硬直	0 (0.0)	1 (0.2)	1 (0.1)
関節腫脹	9 (1.1)	5 (1.2)	14 (1.1)
靱帯障害	0 (0.0)	1 (0.2)	1 (0.1)
靱帯痛	2 (0.2)	0 (0.0)	2 (0.2)
四肢非対称	1 (0.1)	0 (0.0)	1 (0.1)
四肢不快感	2 (0.2)	0 (0.0)	2 (0.2)
筋肉疲労	1 (0.1)	0 (0.0)	1 (0.1)
筋痙縮	33 (3.9)	13 (3.1)	46 (3.6)
筋緊張	2 (0.2)	2 (0.5)	4 (0.3)
筋攣縮	2 (0.2)	1 (0.2)	3 (0.2)
筋力低下	1 (0.1)	4 (0.9)	5 (0.4)
筋骨格系胸痛	9 (1.1)	3 (0.7)	12 (0.9)
筋骨格不快感	6 (0.7)	0 (0.0)	6 (0.5)
筋骨格痛	30 (3.6)	15 (3.5)	45 (3.6)
筋骨格硬直	6 (0.7)	1 (0.2)	7 (0.6)
筋肉痛	39 (4.6)	11 (2.6)	50 (3.9)
筋炎	1 (0.1)	0 (0.0)	1 (0.1)
頸部腫瘍	1 (0.1)	0 (0.0)	1 (0.1)
頸部痛	21 (2.5)	10 (2.4)	31 (2.4)
変形性関節症	7 (0.8)	4 (0.9)	11 (0.9)
骨関節障害	1 (0.1)	0 (0.0)	1 (0.1)
骨端症	1 (0.1)	0 (0.0)	1 (0.1)
骨壊死	0 (0.0)	1 (0.2)	1 (0.1)
骨減少症	3 (0.4)	2 (0.5)	5 (0.4)
骨粗鬆症	1 (0.1)	0 (0.0)	1 (0.1)
四肢痛	36 (4.3)	25 (5.9)	61 (4.8)
顎痛	3 (0.4)	1 (0.2)	4 (0.3)
膝蓋大腿関節痛症候群	0 (0.0)	1 (0.2)	1 (0.1)
関節周囲炎	3 (0.4)	2 (0.5)	5 (0.4)
足底筋膜炎	7 (0.8)	1 (0.2)	8 (0.6)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
筋骨格系および結合組織障害			
恥骨痛	1 (0.1)	2 (0.5)	3 (0.2)
関節リウマチ	3 (0.4)	0 (0.0)	3 (0.2)
肩回旋筋腱板症候群	3 (0.4)	0 (0.0)	3 (0.2)
仙腸骨炎	3 (0.4)	0 (0.0)	3 (0.2)
側弯症	1 (0.1)	1 (0.2)	2 (0.2)
重感	1 (0.1)	4 (0.9)	5 (0.4)
脊椎障害	1 (0.1)	0 (0.0)	1 (0.1)
変形性脊椎症	1 (0.1)	2 (0.5)	3 (0.2)
脊椎炎	0 (0.0)	1 (0.2)	1 (0.1)
脊椎すべり症	0 (0.0)	1 (0.2)	1 (0.1)
滑液嚢腫	2 (0.2)	1 (0.2)	3 (0.2)
滑膜炎	0 (0.0)	1 (0.2)	1 (0.1)
腱障害	2 (0.2)	1 (0.2)	3 (0.2)
腱痛	3 (0.4)	1 (0.2)	4 (0.3)
腱炎	16 (1.9)	10 (2.4)	26 (2.1)
腱鞘炎	0 (0.0)	1 (0.2)	1 (0.1)
斜頸	5 (0.6)	0 (0.0)	5 (0.4)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)			
アクロコルドン	1 (0.1)	0 (0.0)	1 (0.1)
基底細胞癌	8 (0.9)	1 (0.2)	9 (0.7)
乳房の良性新生物	2 (0.2)	2 (0.5)	4 (0.3)
甲状腺の良性新生物	1 (0.1)	0 (0.0)	1 (0.1)
乳癌	3 (0.4)	1 (0.2)	4 (0.3)
子宮頸部癌第0期	1 (0.1)	0 (0.0)	1 (0.1)
真珠腫	0 (0.0)	1 (0.2)	1 (0.1)
慢性骨髄性白血病	1 (0.1)	0 (0.0)	1 (0.1)
異形成母斑	0 (0.0)	1 (0.2)	1 (0.1)
血管腫	1 (0.1)	0 (0.0)	1 (0.1)
肝臓血管腫	0 (0.0)	1 (0.2)	1 (0.1)
カボジ肉腫	1 (0.1)	0 (0.0)	1 (0.1)
脂肪腫	4 (0.5)	2 (0.5)	6 (0.5)
悪性黒色腫	2 (0.2)	0 (0.0)	2 (0.2)
表皮内悪性黒色腫	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）			
メラノサイト性母斑	3 (0.4)	2 (0.5)	5 (0.4)
下垂体の良性腫瘍	1 (0.1)	0 (0.0)	1 (0.1)
脂漏性角化症	1 (0.1)	2 (0.5)	3 (0.2)
皮膚乳頭腫	3 (0.4)	3 (0.7)	6 (0.5)
扁平上皮癌	0 (0.0)	1 (0.2)	1 (0.1)
甲状腺新生物	0 (0.0)	1 (0.2)	1 (0.1)
子宮平滑筋腫	7 (0.8)	5 (1.2)	12 (0.9)
神経系障害			
味覚消失	0 (0.0)	1 (0.2)	1 (0.1)
健忘	2 (0.2)	1 (0.2)	3 (0.2)
失声症	1 (0.1)	1 (0.2)	2 (0.2)
くも膜嚢胞	1 (0.1)	1 (0.2)	2 (0.2)
平衡障害	1 (0.1)	0 (0.0)	1 (0.1)
灼熱感	1 (0.1)	1 (0.2)	2 (0.2)
手根管症候群	2 (0.2)	0 (0.0)	2 (0.2)
痙攣	0 (0.0)	1 (0.2)	1 (0.1)
協調運動異常	1 (0.1)	0 (0.0)	1 (0.1)
脳神経障害	0 (0.0)	1 (0.2)	1 (0.1)
意識レベルの低下	1 (0.1)	0 (0.0)	1 (0.1)
注意力障害	7 (0.8)	1 (0.2)	8 (0.6)
浮動性めまい	92 (10.9)	34 (8.0)	126 (9.9)
労作性めまい	1 (0.1)	0 (0.0)	1 (0.1)
体位性めまい	4 (0.5)	0 (0.0)	4 (0.3)
異常感覚	1 (0.1)	0 (0.0)	1 (0.1)
味覚異常	17 (2.0)	7 (1.7)	24 (1.9)
脳症	1 (0.1)	0 (0.0)	1 (0.1)
頭部不快感	1 (0.1)	0 (0.0)	1 (0.1)
頭痛	204 (24.2)	106 (25.0)	310 (24.5)
味覚過敏	1 (0.1)	0 (0.0)	1 (0.1)
感覚鈍麻	12 (1.4)	7 (1.7)	19 (1.5)
反射減弱	0 (0.0)	1 (0.2)	1 (0.1)
筋緊張低下	2 (0.2)	0 (0.0)	2 (0.2)
頭蓋内動脈瘤	2 (0.2)	3 (0.7)	5 (0.4)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
虚血性脳卒中	0 (0.0)	1 (0.2)	1 (0.1)
嗜眠	5 (0.6)	3 (0.7)	8 (0.6)
意識消失	3 (0.4)	0 (0.0)	3 (0.2)
記憶障害	2 (0.2)	2 (0.5)	4 (0.3)
精神的機能障害	1 (0.1)	1 (0.2)	2 (0.2)
片頭痛	21 (2.5)	10 (2.4)	31 (2.4)
前兆を伴う片頭痛	1 (0.1)	0 (0.0)	1 (0.1)
単麻痺	1 (0.1)	0 (0.0)	1 (0.1)
不随意性筋収縮	3 (0.4)	0 (0.0)	3 (0.2)
ナルコレプシー	3 (0.4)	0 (0.0)	3 (0.2)
神経圧迫	1 (0.1)	0 (0.0)	1 (0.1)
神経根圧迫	1 (0.1)	0 (0.0)	1 (0.1)
神経痛	2 (0.2)	1 (0.2)	3 (0.2)
末梢性ニューロパチー	1 (0.1)	1 (0.2)	2 (0.2)
起立不耐性	1 (0.1)	0 (0.0)	1 (0.1)
錯感覚	19 (2.3)	13 (3.1)	32 (2.5)
パーキンソン病	1 (0.1)	0 (0.0)	1 (0.1)
パーキンソニズム	1 (0.1)	0 (0.0)	1 (0.1)
嗅覚錯誤	1 (0.1)	0 (0.0)	1 (0.1)
多発ニューロパチー	0 (0.0)	1 (0.2)	1 (0.1)
失神寸前の状態	3 (0.4)	0 (0.0)	3 (0.2)
根症候群	0 (0.0)	1 (0.2)	1 (0.1)
下肢静止不能症候群	2 (0.2)	3 (0.7)	5 (0.4)
坐骨神経痛	8 (0.9)	6 (1.4)	14 (1.1)
感覚障害	2 (0.2)	0 (0.0)	2 (0.2)
副鼻腔炎に伴う頭痛	1 (0.1)	1 (0.2)	2 (0.2)
傾眠	0 (0.0)	2 (0.5)	2 (0.2)
くも膜下出血	1 (0.1)	1 (0.2)	2 (0.2)
失神	16 (1.9)	2 (0.5)	18 (1.4)
緊張性頭痛	3 (0.4)	2 (0.5)	5 (0.4)
一過性脳虚血発作	0 (0.0)	2 (0.5)	2 (0.2)
振戦	2 (0.2)	1 (0.2)	3 (0.2)
トンネル状視野	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
神経系障害			
椎骨動脈解離	1 (0.1)	0 (0.0)	1 (0.1)
第7脳神経麻痺	1 (0.1)	2 (0.5)	3 (0.2)
精神障害			
異常な夢	2 (0.2)	2 (0.5)	4 (0.3)
激越	2 (0.2)	0 (0.0)	2 (0.2)
怒り	0 (0.0)	1 (0.2)	1 (0.1)
不安	29 (3.4)	8 (1.9)	37 (2.9)
注意欠陥多動性障害	1 (0.1)	0 (0.0)	1 (0.1)
自閉症スペクトラム障害	1 (0.1)	0 (0.0)	1 (0.1)
精神緩慢	1 (0.1)	0 (0.0)	1 (0.1)
燃え尽き症候群	1 (0.1)	0 (0.0)	1 (0.1)
抑うつ気分	2 (0.2)	2 (0.5)	4 (0.3)
うつ病	38 (4.5)	18 (4.2)	56 (4.4)
睡眠異常	1 (0.1)	0 (0.0)	1 (0.1)
初期不眠症	1 (0.1)	0 (0.0)	1 (0.1)
不眠症	45 (5.3)	19 (4.5)	64 (5.1)
リビドー減退	5 (0.6)	1 (0.2)	6 (0.5)
性欲障害	1 (0.1)	1 (0.2)	2 (0.2)
リビドー消失	1 (0.1)	0 (0.0)	1 (0.1)
大うつ病	2 (0.2)	0 (0.0)	2 (0.2)
精神障害	0 (0.0)	1 (0.2)	1 (0.1)
気分変化	1 (0.1)	0 (0.0)	1 (0.1)
気分動揺	1 (0.1)	1 (0.2)	2 (0.2)
神経過敏	5 (0.6)	1 (0.2)	6 (0.5)
ニコチン依存	1 (0.1)	2 (0.5)	3 (0.2)
悪夢	1 (0.1)	0 (0.0)	1 (0.1)
パニック発作	5 (0.6)	2 (0.5)	7 (0.6)
パニック反応	2 (0.2)	0 (0.0)	2 (0.2)
外傷後ストレス障害	0 (0.0)	1 (0.2)	1 (0.1)
心身症	0 (0.0)	1 (0.2)	1 (0.1)
落ち着きのなさ	1 (0.1)	0 (0.0)	1 (0.1)
統合失調感情障害	0 (0.0)	1 (0.2)	1 (0.1)
統合失調症	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
精神障害			
睡眠障害	5 (0.6)	2 (0.5)	7 (0.6)
夢遊症	1 (0.1)	0 (0.0)	1 (0.1)
ストレス	9 (1.1)	10 (2.4)	19 (1.5)
自殺企図	0 (0.0)	1 (0.2)	1 (0.1)
腎および尿路障害			
アルブミン尿	1 (0.1)	0 (0.0)	1 (0.1)
高窒素血症	0 (0.0)	1 (0.2)	1 (0.1)
膀胱不快感	0 (0.0)	1 (0.2)	1 (0.1)
膀胱痛	1 (0.1)	0 (0.0)	1 (0.1)
膀胱脱	2 (0.2)	1 (0.2)	3 (0.2)
膀胱痙縮	1 (0.1)	0 (0.0)	1 (0.1)
尿路結石	0 (0.0)	2 (0.5)	2 (0.2)
着色尿	1 (0.1)	1 (0.2)	2 (0.2)
非感染性膀胱炎	1 (0.1)	0 (0.0)	1 (0.1)
排尿困難	14 (1.7)	9 (2.1)	23 (1.8)
遺尿	2 (0.2)	0 (0.0)	2 (0.2)
糖尿	0 (0.0)	1 (0.2)	1 (0.1)
血尿	68 (8.1)	61 (14.4)	129 (10.2)
水腎症	1 (0.1)	0 (0.0)	1 (0.1)
緊張性膀胱	1 (0.1)	0 (0.0)	1 (0.1)
失禁	2 (0.2)	0 (0.0)	2 (0.2)
腎腫大	3 (0.4)	3 (0.7)	6 (0.5)
白血球尿	2 (0.2)	4 (0.9)	6 (0.5)
尿意切迫	8 (0.9)	2 (0.5)	10 (0.8)
腎炎	0 (0.0)	1 (0.2)	1 (0.1)
腎結石症	15 (1.8)	13 (3.1)	28 (2.2)
夜間頻尿	278 (33.0)	61 (14.4)	339 (26.8)
乏尿	2 (0.2)	0 (0.0)	2 (0.2)
頻尿	160 (19.0)	22 (5.2)	182 (14.4)
多尿	328 (38.9)	78 (18.4)	406 (32.0)
蛋白尿	3 (0.4)	7 (1.7)	10 (0.8)
腎仙痛	3 (0.4)	5 (1.2)	8 (0.6)
腎嚢胞	1 (0.1)	1 (0.2)	2 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
腎および尿路障害			
腎嚢胞出血	6 (0.7)	7 (1.7)	13 (1.0)
腎嚢胞破裂	7 (0.8)	5 (1.2)	12 (0.9)
腎障害	0 (0.0)	1 (0.2)	1 (0.1)
急性腎不全	2 (0.2)	2 (0.5)	4 (0.3)
慢性腎不全	2 (0.2)	0 (0.0)	2 (0.2)
腎機能障害	11 (1.3)	7 (1.7)	18 (1.4)
腎臓痛	248 (29.4)	160 (37.7)	408 (32.2)
有痛性排尿困難	1 (0.1)	0 (0.0)	1 (0.1)
腹圧性尿失禁	0 (0.0)	1 (0.2)	1 (0.1)
尿道狭窄	1 (0.1)	0 (0.0)	1 (0.1)
切迫性尿失禁	1 (0.1)	1 (0.2)	2 (0.2)
排尿躊躇	1 (0.1)	0 (0.0)	1 (0.1)
尿失禁	9 (1.1)	2 (0.5)	11 (0.9)
尿閉	1 (0.1)	2 (0.5)	3 (0.2)
尿路障害	0 (0.0)	2 (0.5)	2 (0.2)
尿流量減少	2 (0.2)	0 (0.0)	2 (0.2)
尿臭異常	0 (0.0)	1 (0.2)	1 (0.1)
生殖系および乳房障害			
子宮付属器痛	1 (0.1)	0 (0.0)	1 (0.1)
無月経	4 (0.5)	4 (0.9)	8 (0.6)
精子無力症	0 (0.0)	1 (0.2)	1 (0.1)
萎縮性外陰陰炎	1 (0.1)	0 (0.0)	1 (0.1)
無精子症	0 (0.0)	1 (0.2)	1 (0.1)
バルトリン腺炎	0 (0.0)	1 (0.2)	1 (0.1)
良性前立腺肥大症	0 (0.0)	1 (0.2)	1 (0.1)
乳房嚢胞	1 (0.1)	1 (0.2)	2 (0.2)
乳房不快感	0 (0.0)	1 (0.2)	1 (0.1)
乳房腫瘍	2 (0.2)	0 (0.0)	2 (0.2)
乳房痛	1 (0.1)	0 (0.0)	1 (0.1)
子宮頸部上皮異形成	2 (0.2)	1 (0.2)	3 (0.2)
子宮頸管ポリープ	2 (0.2)	0 (0.0)	2 (0.2)
性交出血	1 (0.1)	0 (0.0)	1 (0.1)
膀胱瘤	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
生殖系および乳房障害			
月経困難症	2 (0.2)	4 (0.9)	6 (0.5)
性交困難	1 (0.1)	1 (0.2)	2 (0.2)
子宮内膜症	0 (0.0)	1 (0.2)	1 (0.1)
精巣上体嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
精巣上体炎	1 (0.1)	1 (0.2)	2 (0.2)
勃起不全	10 (1.2)	2 (0.5)	12 (0.9)
線維嚢胞性乳腺疾患	0 (0.0)	1 (0.2)	1 (0.1)
乳汁漏出症	1 (0.1)	0 (0.0)	1 (0.1)
性器出血	1 (0.1)	0 (0.0)	1 (0.1)
血精液症	3 (0.4)	0 (0.0)	3 (0.2)
出血性卵巣嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
過少月経	1 (0.1)	0 (0.0)	1 (0.1)
子宮瘤	0 (0.0)	1 (0.2)	1 (0.1)
不妊症	0 (0.0)	2 (0.5)	2 (0.2)
機能性子宮出血	1 (0.1)	0 (0.0)	1 (0.1)
月経過多	14 (1.7)	9 (2.1)	23 (1.8)
月経障害	2 (0.2)	0 (0.0)	2 (0.2)
月経遅延	0 (0.0)	2 (0.5)	2 (0.2)
不規則月経	8 (0.9)	3 (0.7)	11 (0.9)
不正子宮出血	2 (0.2)	3 (0.7)	5 (0.4)
卵巣嚢胞	6 (0.7)	6 (1.4)	12 (0.9)
卵巣障害	0 (0.0)	1 (0.2)	1 (0.1)
卵巣捻転	2 (0.2)	0 (0.0)	2 (0.2)
排卵痛	1 (0.1)	0 (0.0)	1 (0.1)
骨盤不快感	1 (0.1)	0 (0.0)	1 (0.1)
骨盤痛	2 (0.2)	0 (0.0)	2 (0.2)
骨盤脱	1 (0.1)	0 (0.0)	1 (0.1)
会陰痛	1 (0.1)	0 (0.0)	1 (0.1)
ペイロニー病	2 (0.2)	0 (0.0)	2 (0.2)
閉経後出血	1 (0.1)	0 (0.0)	1 (0.1)
月経前症候群	1 (0.1)	0 (0.0)	1 (0.1)
前立腺炎	4 (0.5)	3 (0.7)	7 (0.6)
前立腺腫大	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
生殖系および乳房障害			
精嚢嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
性機能不全	2 (0.2)	0 (0.0)	2 (0.2)
精嚢嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
精嚢腫瘍	1 (0.1)	1 (0.2)	2 (0.2)
精嚢痛	2 (0.2)	3 (0.7)	5 (0.4)
子宮ポリープ	0 (0.0)	2 (0.5)	2 (0.2)
子宮脱	3 (0.4)	1 (0.2)	4 (0.3)
膣嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
膣分泌物	1 (0.1)	2 (0.5)	3 (0.2)
膣出血	6 (0.7)	1 (0.2)	7 (0.6)
精索静脈瘤	1 (0.1)	1 (0.2)	2 (0.2)
外陰膣乾燥	3 (0.4)	3 (0.7)	6 (0.5)
呼吸器、胸郭および縦隔障害			
喘息	7 (0.8)	4 (0.9)	11 (0.9)
運動誘発喘息	0 (0.0)	1 (0.2)	1 (0.1)
気管支痙攣	1 (0.1)	1 (0.2)	2 (0.2)
咳嗽	74 (8.8)	31 (7.3)	105 (8.3)
咽喉乾燥	6 (0.7)	2 (0.5)	8 (0.6)
発声障害	3 (0.4)	0 (0.0)	3 (0.2)
呼吸困難	20 (2.4)	6 (1.4)	26 (2.1)
安静時呼吸困難	1 (0.1)	0 (0.0)	1 (0.1)
労作性呼吸困難	4 (0.5)	1 (0.2)	5 (0.4)
鼻出血	7 (0.8)	5 (1.2)	12 (0.9)
過換気	1 (0.1)	0 (0.0)	1 (0.1)
喉頭嚢腫	1 (0.1)	0 (0.0)	1 (0.1)
喉頭浮腫	1 (0.1)	1 (0.2)	2 (0.2)
肺障害	2 (0.2)	0 (0.0)	2 (0.2)
鼻閉	7 (0.8)	5 (1.2)	12 (0.9)
鼻乾燥	1 (0.1)	1 (0.2)	2 (0.2)
鼻の炎症	0 (0.0)	1 (0.2)	1 (0.1)
鼻閉塞	1 (0.1)	0 (0.0)	1 (0.1)
鼻中隔弯曲	2 (0.2)	0 (0.0)	2 (0.2)
夜間呼吸困難	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害			
口腔咽頭痛	35 (4.2)	11 (2.6)	46 (3.6)
咽頭紅斑	0 (0.0)	1 (0.2)	1 (0.1)
咽頭浮腫	0 (0.0)	1 (0.2)	1 (0.1)
胸水	1 (0.1)	0 (0.0)	1 (0.1)
胸膜痛	1 (0.1)	0 (0.0)	1 (0.1)
肺臓炎	1 (0.1)	0 (0.0)	1 (0.1)
湿性咳嗽	1 (0.1)	0 (0.0)	1 (0.1)
肺塞栓症	1 (0.1)	0 (0.0)	1 (0.1)
肺線維症	1 (0.1)	0 (0.0)	1 (0.1)
呼吸不全	1 (0.1)	0 (0.0)	1 (0.1)
気道うっ血	2 (0.2)	0 (0.0)	2 (0.2)
鼻痛	1 (0.1)	0 (0.0)	1 (0.1)
アレルギー性鼻炎	7 (0.8)	4 (0.9)	11 (0.9)
鼻漏	4 (0.5)	1 (0.2)	5 (0.4)
低音性連続性ラ音	1 (0.1)	0 (0.0)	1 (0.1)
副鼻腔うっ血	6 (0.7)	2 (0.5)	8 (0.6)
睡眠時無呼吸症候群	5 (0.6)	0 (0.0)	5 (0.4)
くしゃみ	1 (0.1)	1 (0.2)	2 (0.2)
いびき	2 (0.2)	1 (0.2)	3 (0.2)
咽喉絞扼感	0 (0.0)	1 (0.2)	1 (0.1)
扁桃肥大	1 (0.1)	0 (0.0)	1 (0.1)
扁桃の炎症	0 (0.0)	1 (0.2)	1 (0.1)
扁桃結石	1 (0.1)	0 (0.0)	1 (0.1)
上気道咳症候群	1 (0.1)	0 (0.0)	1 (0.1)
喘鳴	2 (0.2)	5 (1.2)	7 (0.6)
皮膚および皮下組織障害			
ざ瘡	11 (1.3)	7 (1.7)	18 (1.4)
日光性角化症	1 (0.1)	0 (0.0)	1 (0.1)
脱毛症	15 (1.8)	7 (1.7)	22 (1.7)
円形脱毛症	0 (0.0)	1 (0.2)	1 (0.1)
アンドロゲン性脱毛症	1 (0.1)	0 (0.0)	1 (0.1)
血管浮腫	2 (0.2)	0 (0.0)	2 (0.2)
水疱	2 (0.2)	0 (0.0)	2 (0.2)

表2.7.4.7-18

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NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
皮膚および皮下組織障害			
皮膚嚢腫	0 (0.0)	1 (0.2)	1 (0.1)
皮膚炎	4 (0.5)	1 (0.2)	5 (0.4)
アレルギー性皮膚炎	5 (0.6)	3 (0.7)	8 (0.6)
接触性皮膚炎	7 (0.8)	1 (0.2)	8 (0.6)
皮膚症	1 (0.1)	0 (0.0)	1 (0.1)
皮膚乾燥	41 (4.9)	7 (1.7)	48 (3.8)
斑状出血	1 (0.1)	1 (0.2)	2 (0.2)
湿疹	12 (1.4)	1 (0.2)	13 (1.0)
湿潤性湿疹	0 (0.0)	1 (0.2)	1 (0.1)
紅斑	7 (0.8)	2 (0.5)	9 (0.7)
多形紅斑	0 (0.0)	1 (0.2)	1 (0.1)
過剰皮膚	1 (0.1)	0 (0.0)	1 (0.1)
毛髪成長異常	0 (0.0)	1 (0.2)	1 (0.1)
紅色汗疹	1 (0.1)	0 (0.0)	1 (0.1)
汗腺炎	1 (0.1)	0 (0.0)	1 (0.1)
多汗症	5 (0.6)	4 (0.9)	9 (0.7)
乏汗症	1 (0.1)	0 (0.0)	1 (0.1)
内出血発生の増加傾向	2 (0.2)	0 (0.0)	2 (0.2)
嵌入爪	1 (0.1)	0 (0.0)	1 (0.1)
間擦疹	1 (0.1)	0 (0.0)	1 (0.1)
斑	0 (0.0)	1 (0.2)	1 (0.1)
機械性蕁麻疹	2 (0.2)	0 (0.0)	2 (0.2)
爪の障害	3 (0.4)	0 (0.0)	3 (0.2)
爪成長異常	0 (0.0)	1 (0.2)	1 (0.1)
神経皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
寝汗	5 (0.6)	2 (0.5)	7 (0.6)
爪破損	1 (0.1)	0 (0.0)	1 (0.1)
皮膚疼痛	1 (0.1)	0 (0.0)	1 (0.1)
丘疹	1 (0.1)	1 (0.2)	2 (0.2)
光線過敏性反応	1 (0.1)	0 (0.0)	1 (0.1)
色素沈着障害	3 (0.4)	1 (0.2)	4 (0.3)
皰糠疹	0 (0.0)	1 (0.2)	1 (0.1)
ばら色皰糠疹	1 (0.1)	1 (0.2)	2 (0.2)

表2.7.4.7-18

156-251

NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
皮膚および皮下組織障害			
そう痒症	25 (3.0)	12 (2.8)	37 (2.9)
全身性そう痒症	1 (0.1)	0 (0.0)	1 (0.1)
発疹	29 (3.4)	5 (1.2)	34 (2.7)
紅斑性皮疹	3 (0.4)	2 (0.5)	5 (0.4)
斑状丘疹状皮疹	0 (0.0)	1 (0.2)	1 (0.1)
そう痒性皮疹	3 (0.4)	0 (0.0)	3 (0.2)
酒さ	4 (0.5)	0 (0.0)	4 (0.3)
脂腺障害	1 (0.1)	0 (0.0)	1 (0.1)
脂漏性皮膚炎	2 (0.2)	0 (0.0)	2 (0.2)
皮膚色素脱失	1 (0.1)	0 (0.0)	1 (0.1)
皮膚変色	3 (0.4)	0 (0.0)	3 (0.2)
皮膚色素過剰	1 (0.1)	0 (0.0)	1 (0.1)
皮膚刺激	2 (0.2)	2 (0.5)	4 (0.3)
皮膚病変	4 (0.5)	2 (0.5)	6 (0.5)
皮膚反応	0 (0.0)	1 (0.2)	1 (0.1)
皮膚潰瘍	1 (0.1)	1 (0.2)	2 (0.2)
うつ滞性皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
顔面腫脹	1 (0.1)	1 (0.2)	2 (0.2)
蕁麻疹	8 (0.9)	2 (0.5)	10 (0.8)
慢性蕁麻疹	1 (0.1)	0 (0.0)	1 (0.1)
尋常性白斑	1 (0.1)	0 (0.0)	1 (0.1)
乾皮症	1 (0.1)	0 (0.0)	1 (0.1)
社会環境			
閉経	2 (0.2)	1 (0.2)	3 (0.2)
外科および内科処置			
収れん薬療法	1 (0.1)	0 (0.0)	1 (0.1)
ジフテリア免疫	1 (0.1)	0 (0.0)	1 (0.1)
子宮頸管拡張および子宮内搔爬	0 (0.0)	1 (0.2)	1 (0.1)
ビタミン補給	1 (0.1)	0 (0.0)	1 (0.1)
血管障害			
血管障害	1 (0.1)	0 (0.0)	1 (0.1)
大動脈拡張	0 (0.0)	2 (0.5)	2 (0.2)
動脈硬化症	2 (0.2)	0 (0.0)	2 (0.2)

表2.7.4.7-18

156-251

NT-8.2.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
血管障害			
コントロール不良の血圧	2 (0.2)	1 (0.2)	3 (0.2)
循環虚脱	0 (0.0)	1 (0.2)	1 (0.1)
深部静脈血栓症	1 (0.1)	1 (0.2)	2 (0.2)
血腫	5 (0.6)	4 (0.9)	9 (0.7)
出血	1 (0.1)	0 (0.0)	1 (0.1)
ほてり	8 (0.9)	2 (0.5)	10 (0.8)
高血圧	283 (33.6)	159 (37.5)	442 (34.9)
高血圧クリーゼ	2 (0.2)	0 (0.0)	2 (0.2)
低血圧	28 (3.3)	13 (3.1)	41 (3.2)
腸骨動脈狭窄	0 (0.0)	1 (0.2)	1 (0.1)
微小血管症	1 (0.1)	0 (0.0)	1 (0.1)
起立性低血圧	4 (0.5)	3 (0.7)	7 (0.6)
末梢冷感	11 (1.3)	3 (0.7)	14 (1.1)
静脈炎	1 (0.1)	0 (0.0)	1 (0.1)
レイノー現象	3 (0.4)	1 (0.2)	4 (0.3)
血栓性静脈炎	1 (0.1)	1 (0.2)	2 (0.2)
表在性血栓性静脈炎	3 (0.4)	0 (0.0)	3 (0.2)
血栓性静脈瘤	1 (0.1)	0 (0.0)	1 (0.1)
血栓症	2 (0.2)	0 (0.0)	2 (0.2)
静脈瘤	7 (0.8)	1 (0.2)	8 (0.6)
血管圧迫	0 (0.0)	1 (0.2)	1 (0.1)
静脈不全	1 (0.1)	0 (0.0)	1 (0.1)
TOTAL	824 (97.7)	410 (96.7)	1234 (97.4)

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<資料番号5.3.5.3-02 : NT-8.2.2>

表2.7.4.7-19

156-■■-251

CT-8.2.1 Incidence of All Treatment-emergent Adverse Events by System Organ Class (全体)

	Tolvaptan (N=961)	Placebo (N=483)	Total (N=1444)
System organ class	n (%)	n (%)	n (%)
血液およびリンパ系障害	51 (5.3)	36 (7.5)	87 (6.0)
心臓障害	99 (10.3)	33 (6.8)	132 (9.1)
先天性、家族性および遺伝性障害	4 (0.4)	6 (1.2)	10 (0.7)
耳および迷路障害	53 (5.5)	28 (5.8)	81 (5.6)
内分泌障害	14 (1.5)	6 (1.2)	20 (1.4)
眼障害	73 (7.6)	41 (8.5)	114 (7.9)
胃腸障害	557 (58.0)	246 (50.9)	803 (55.6)
一般・全身障害および投与部位の状態	658 (68.5)	218 (45.1)	876 (60.7)
肝胆道系障害	62 (6.5)	21 (4.3)	83 (5.7)
免疫系障害	50 (5.2)	15 (3.1)	65 (4.5)
感染症および寄生虫症	551 (57.3)	302 (62.5)	853 (59.1)
傷害、中毒および処置合併症	145 (15.1)	83 (17.2)	228 (15.8)
臨床検査	353 (36.7)	166 (34.4)	519 (35.9)
代謝および栄養障害	322 (33.5)	93 (19.3)	415 (28.7)
筋骨格系および結合組織障害	364 (37.9)	186 (38.5)	550 (38.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	45 (4.7)	19 (3.9)	64 (4.4)
神経系障害	387 (40.3)	185 (38.3)	572 (39.6)
精神障害	156 (16.2)	65 (13.5)	221 (15.3)
腎および尿路障害	757 (78.8)	296 (61.3)	1053 (72.9)
生殖系および乳房障害	93 (9.7)	64 (13.3)	157 (10.9)
呼吸器、胸郭および縦隔障害	196 (20.4)	90 (18.6)	286 (19.8)
皮膚および皮下組織障害	218 (22.7)	81 (16.8)	299 (20.7)
社会環境	2 (0.2)	1 (0.2)	3 (0.2)
外科および内科処置	3 (0.3)	1 (0.2)	4 (0.3)
血管障害	362 (37.7)	194 (40.2)	556 (38.5)
TOTAL	941 (97.9)	469 (97.1)	1410 (97.6)

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<資料番号5.3.5.1-01 : CT-8.2.1>

表2.7.4.7-20

156-251

CT-8.3.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class (全体)

	Tolvaptan (N=961)	Placebo (N=483)	Total (N=1444)
System organ class	n (%)	n (%)	n (%)
血液およびリンパ系障害	6 (0.6)	7 (1.4)	13 (0.9)
心臓障害	33 (3.4)	7 (1.4)	40 (2.8)
耳および迷路障害	22 (2.3)	6 (1.2)	28 (1.9)
内分泌障害	1 (0.1)	0 (0.0)	1 (0.1)
眼障害	22 (2.3)	10 (2.1)	32 (2.2)
胃腸障害	322 (33.5)	103 (21.3)	425 (29.4)
一般・全身障害および投与部位の状態	587 (61.1)	123 (25.5)	710 (49.2)
肝胆道系障害	18 (1.9)	1 (0.2)	19 (1.3)
免疫系障害	2 (0.2)	0 (0.0)	2 (0.1)
感染症および寄生虫症	39 (4.1)	22 (4.6)	61 (4.2)
傷害、中毒および処置合併症	4 (0.4)	2 (0.4)	6 (0.4)
臨床検査	227 (23.6)	86 (17.8)	313 (21.7)
代謝および栄養障害	240 (25.0)	50 (10.4)	290 (20.1)
筋骨格系および結合組織障害	66 (6.9)	30 (6.2)	96 (6.6)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.2)	0 (0.0)	2 (0.1)
神経系障害	221 (23.0)	66 (13.7)	287 (19.9)
精神障害	64 (6.7)	7 (1.4)	71 (4.9)
腎および尿路障害	687 (71.5)	151 (31.3)	838 (58.0)
生殖系および乳房障害	15 (1.6)	9 (1.9)	24 (1.7)
呼吸器、胸郭および縦隔障害	43 (4.5)	14 (2.9)	57 (3.9)
皮膚および皮下組織障害	82 (8.5)	25 (5.2)	107 (7.4)
外科および内科処置	1 (0.1)	0 (0.0)	1 (0.1)
血管障害	76 (7.9)	29 (6.0)	105 (7.3)
TOTAL	851 (88.6)	302 (62.5)	1153 (79.8)

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<資料番号5.3.5.1-01 : CT-8.3.1>

表2.7.4.7-21

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JT-8.2.1 Incidence of All Treatment-emergent Adverse Events by System Organ Class（日本の被験者）

	Tolvaptan (N=118)	Placebo (N=59)	Total (N=177)
System organ class	n (%)	n (%)	n (%)
血液およびリンパ系障害	8 (6.8)	5 (8.5)	13 (7.3)
心臓障害	22 (18.6)	2 (3.4)	24 (13.6)
先天性、家族性および遺伝性障害	0 (0.0)	1 (1.7)	1 (0.6)
耳および迷路障害	7 (5.9)	3 (5.1)	10 (5.6)
内分泌障害	0 (0.0)	1 (1.7)	1 (0.6)
眼障害	16 (13.6)	9 (15.3)	25 (14.1)
胃腸障害	82 (69.5)	36 (61.0)	118 (66.7)
一般・全身障害および投与部位の状態	112 (94.9)	32 (54.2)	144 (81.4)
肝胆道系障害	21 (17.8)	6 (10.2)	27 (15.3)
免疫系障害	12 (10.2)	0 (0.0)	12 (6.8)
感染症および寄生虫症	82 (69.5)	51 (86.4)	133 (75.1)
傷害、中毒および処置合併症	18 (15.3)	12 (20.3)	30 (16.9)
臨床検査	30 (25.4)	14 (23.7)	44 (24.9)
代謝および栄養障害	34 (28.8)	11 (18.6)	45 (25.4)
筋骨格系および結合組織障害	49 (41.5)	35 (59.3)	84 (47.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	6 (5.1)	0 (0.0)	6 (3.4)
神経系障害	58 (49.2)	25 (42.4)	83 (46.9)
精神障害	20 (16.9)	6 (10.2)	26 (14.7)
腎および尿路障害	98 (83.1)	25 (42.4)	123 (69.5)
生殖系および乳房障害	9 (7.6)	8 (13.6)	17 (9.6)
呼吸器、胸郭および縦隔障害	29 (24.6)	16 (27.1)	45 (25.4)
皮膚および皮下組織障害	40 (33.9)	17 (28.8)	57 (32.2)
血管障害	31 (26.3)	18 (30.5)	49 (27.7)
TOTAL	117 (99.2)	59 (100.0)	176 (99.4)

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<資料番号5.3.5.3-02：JT-8.2.1>

表2.7.4.7-22

156-XXXX-251

JT-8.3.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class （日本の被験者）

	Tolvaptan (N=118)	Placebo (N=59)	Total (N=177)
System organ class	n (%)	n (%)	n (%)
血液およびリンパ系障害	1 (0.8)	1 (1.7)	2 (1.1)
心臓障害	13 (11.0)	2 (3.4)	15 (8.5)
耳および迷路障害	5 (4.2)	0 (0.0)	5 (2.8)
眼障害	7 (5.9)	2 (3.4)	9 (5.1)
胃腸障害	39 (33.1)	12 (20.3)	51 (28.8)
一般・全身障害および投与部位の状態	109 (92.4)	19 (32.2)	128 (72.3)
肝胆道系障害	13 (11.0)	1 (1.7)	14 (7.9)
免疫系障害	1 (0.8)	0 (0.0)	1 (0.6)
感染症および寄生虫症	8 (6.8)	4 (6.8)	12 (6.8)
傷害、中毒および処置合併症	1 (0.8)	2 (3.4)	3 (1.7)
臨床検査	19 (16.1)	5 (8.5)	24 (13.6)
代謝および栄養障害	29 (24.6)	5 (8.5)	34 (19.2)
筋骨格系および結合組織障害	11 (9.3)	8 (13.6)	19 (10.7)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.8)	0 (0.0)	1 (0.6)
神経系障害	29 (24.6)	9 (15.3)	38 (21.5)
精神障害	7 (5.9)	1 (1.7)	8 (4.5)
腎および尿路障害	95 (80.5)	13 (22.0)	108 (61.0)
生殖系および乳房障害	4 (3.4)	4 (6.8)	8 (4.5)
呼吸器、胸郭および縦隔障害	8 (6.8)	2 (3.4)	10 (5.6)
皮膚および皮下組織障害	18 (15.3)	2 (3.4)	20 (11.3)
血管障害	14 (11.9)	6 (10.2)	20 (11.3)
TOTAL	117 (99.2)	42 (71.2)	159 (89.8)

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<資料番号5.3.5.3-02 : JT-8.3.1>

表2.7.4.7-23

156-■■■-251

NT-8.2.1 Incidence of All Treatment-emergent Adverse Events by System Organ Class (海外の被験者)

	Tolvaptan (N=843)	Placebo (N=424)	Total (N=1267)
System organ class	n (%)	n (%)	n (%)
血液およびリンパ系障害	43 (5.1)	31 (7.3)	74 (5.8)
心臓障害	77 (9.1)	31 (7.3)	108 (8.5)
先天性、家族性および遺伝性障害	4 (0.5)	5 (1.2)	9 (0.7)
耳および迷路障害	46 (5.5)	25 (5.9)	71 (5.6)
内分泌障害	14 (1.7)	5 (1.2)	19 (1.5)
眼障害	57 (6.8)	32 (7.5)	89 (7.0)
胃腸障害	475 (56.3)	210 (49.5)	685 (54.1)
一般・全身障害および投与部位の状態	546 (64.8)	186 (43.9)	732 (57.8)
肝胆道系障害	41 (4.9)	15 (3.5)	56 (4.4)
免疫系障害	38 (4.5)	15 (3.5)	53 (4.2)
感染症および寄生虫症	469 (55.6)	251 (59.2)	720 (56.8)
傷害、中毒および処置合併症	127 (15.1)	71 (16.7)	198 (15.6)
臨床検査	323 (38.3)	152 (35.8)	475 (37.5)
代謝および栄養障害	288 (34.2)	82 (19.3)	370 (29.2)
筋骨格系および結合組織障害	315 (37.4)	151 (35.6)	466 (36.8)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	39 (4.6)	19 (4.5)	58 (4.6)
神経系障害	329 (39.0)	160 (37.7)	489 (38.6)
精神障害	136 (16.1)	59 (13.9)	195 (15.4)
腎および尿路障害	659 (78.2)	271 (63.9)	930 (73.4)
生殖系および乳房障害	84 (10.0)	56 (13.2)	140 (11.0)
呼吸器、胸郭および縦隔障害	167 (19.8)	74 (17.5)	241 (19.0)
皮膚および皮下組織障害	178 (21.1)	64 (15.1)	242 (19.1)
社会環境	2 (0.2)	1 (0.2)	3 (0.2)
外科および内科処置	3 (0.4)	1 (0.2)	4 (0.3)
血管障害	331 (39.3)	176 (41.5)	507 (40.0)
TOTAL	824 (97.7)	410 (96.7)	1234 (97.4)

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<資料番号5.3.5.3-02 : NT-8.2.1>

表2.7.4.7-24

156-XXXX-251

NT-8.3.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class（海外の被験者）

	Tolvaptan (N=843)	Placebo (N=424)	Total (N=1267)
System organ class	n (%)	n (%)	n (%)
血液およびリンパ系障害	5 (0.6)	6 (1.4)	11 (0.9)
心臓障害	20 (2.4)	5 (1.2)	25 (2.0)
耳および迷路障害	17 (2.0)	6 (1.4)	23 (1.8)
内分泌障害	1 (0.1)	0 (0.0)	1 (0.1)
眼障害	15 (1.8)	8 (1.9)	23 (1.8)
胃腸障害	283 (33.6)	91 (21.5)	374 (29.5)
一般・全身障害および投与部位の状態	478 (56.7)	104 (24.5)	582 (45.9)
肝胆道系障害	5 (0.6)	0 (0.0)	5 (0.4)
免疫系障害	1 (0.1)	0 (0.0)	1 (0.1)
感染症および寄生虫症	31 (3.7)	18 (4.2)	49 (3.9)
傷害、中毒および処置合併症	3 (0.4)	0 (0.0)	3 (0.2)
臨床検査	208 (24.7)	81 (19.1)	289 (22.8)
代謝および栄養障害	211 (25.0)	45 (10.6)	256 (20.2)
筋骨格系および結合組織障害	55 (6.5)	22 (5.2)	77 (6.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.1)	0 (0.0)	1 (0.1)
神経系障害	192 (22.8)	57 (13.4)	249 (19.7)
精神障害	57 (6.8)	6 (1.4)	63 (5.0)
腎および尿路障害	592 (70.2)	138 (32.5)	730 (57.6)
生殖系および乳房障害	11 (1.3)	5 (1.2)	16 (1.3)
呼吸器、胸郭および縦隔障害	35 (4.2)	12 (2.8)	47 (3.7)
皮膚および皮下組織障害	64 (7.6)	23 (5.4)	87 (6.9)
外科および内科処置	1 (0.1)	0 (0.0)	1 (0.1)
血管障害	62 (7.4)	23 (5.4)	85 (6.7)
TOTAL	734 (87.1)	260 (61.3)	994 (78.5)

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表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血液およびリンパ系障害								
貧血	18 (1.9)	8 (0.8)	1 (0.1)	27 (2.8)	17 (3.5)	7 (1.4)	0 (0.0)	24 (5.0)
凝血異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好酸球増加症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
低色素性貧血	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
白血球増加症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
白血球減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
リンパ節症	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好中球増加症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
正色素性正球性貧血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球増加症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血小板増加症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害								
急性心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.4)
狭心症	6 (0.6)	3 (0.3)	1 (0.1)	10 (1.0)	1 (0.2)	2 (0.4)	0 (0.0)	3 (0.6)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不整脈	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
心房細動	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
房室ブロック	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	11 (1.1)	1 (0.1)	0 (0.0)	12 (1.2)	5 (1.0)	0 (0.0)	1 (0.2)	6 (1.2)
右脚ブロック	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
心臓弁膜疾患	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拡大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
心臓障害								
伝導障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
チアノーゼ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
左室機能不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
僧帽弁疾患	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
僧帽弁逸脱	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心筋梗塞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	31 (3.2)	3 (0.3)	0 (0.0)	34 (3.5)	3 (0.6)	3 (0.6)	0 (0.0)	6 (1.2)
心嚢液貯留	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心膜炎	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞不全症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
上室性期外収縮	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	13 (1.4)	0 (0.0)	0 (0.0)	13 (1.4)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
三尖弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心室性期外収縮	5 (0.5)	4 (0.4)	0 (0.0)	9 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
先天性、家族性および遺伝性障害								
心房中隔欠損症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
第Ⅴ因子ライデン変異	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
多嚢胞性肝疾患	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
脊椎奇形	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
耳および迷路障害								
耳垢栓塞	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
耳閉	0 (0.0)	3 (0.3)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳不快感	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳痛	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳管障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴覚障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内耳障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乗物酔い	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	9 (0.9)	2 (0.2)	0 (0.0)	11 (1.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
回転性めまい	20 (2.1)	2 (0.2)	2 (0.2)	24 (2.5)	14 (2.9)	4 (0.8)	0 (0.0)	18 (3.7)
頭位性回転性めまい	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
内分泌障害								
アンドロゲン欠乏症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
バセドウ病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
副甲状腺機能亢進症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
続発性副甲状腺機能低下症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
エストロゲン欠乏症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
眼障害								
調節障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
白内障	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
結膜炎	11 (1.1)	2 (0.2)	1 (0.1)	14 (1.5)	6 (1.2)	1 (0.2)	0 (0.0)	7 (1.4)
アレルギー性結膜炎	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼の隈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼乾燥	14 (1.5)	1 (0.1)	0 (0.0)	15 (1.6)	3 (0.6)	3 (0.6)	1 (0.2)	7 (1.4)
外眼筋不全麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
眼の障害	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
眼出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼痛	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼部腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
眼瞼浮腫	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
眼瞼下垂	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
緑内障	4 (0.4)	0 (0.0)	1 (0.1)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
遠視	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虹彩炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
流涙増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼充血	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
羞明	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光視症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
老視	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
翼状片	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
眼障害								
網膜剥離	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
強膜炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
暗点	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
霧視	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
視力低下	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
硝子体剥離	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害								
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腹部不快感	21 (2.2)	7 (0.7)	1 (0.1)	29 (3.0)	7 (1.4)	2 (0.4)	1 (0.2)	10 (2.1)
腹部膨満	35 (3.6)	12 (1.2)	0 (0.0)	47 (4.9)	13 (2.7)	2 (0.4)	1 (0.2)	16 (3.3)
腹部ヘルニア	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	5 (1.0)	1 (0.2)	0 (0.0)	6 (1.2)
閉塞を伴う腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腹部腫瘤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腹痛	35 (3.6)	19 (2.0)	8 (0.8)	62 (6.5)	20 (4.1)	8 (1.7)	4 (0.8)	32 (6.6)
下腹部痛	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	1 (0.2)	3 (0.6)	0 (0.0)	4 (0.8)
上腹部痛	44 (4.6)	16 (1.7)	3 (0.3)	63 (6.6)	33 (6.8)	8 (1.7)	1 (0.2)	42 (8.7)
腹部硬直	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部圧痛	6 (0.6)	2 (0.2)	0 (0.0)	8 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
裂肛	1 (0.1)	3 (0.3)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
痔瘻	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
便通不規則	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
口唇炎	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
結腸ポリープ	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
便秘	69 (7.2)	11 (1.1)	1 (0.1)	81 (8.4)	8 (1.7)	3 (0.6)	1 (0.2)	12 (2.5)
クローン病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	3 (0.3)	5 (0.5)	0 (0.0)	8 (0.8)	3 (0.6)	2 (0.4)	0 (0.0)	5 (1.0)
歯不快感	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
下痢	97 (10.1)	26 (2.7)	5 (0.5)	128 (13.3)	42 (8.7)	11 (2.3)	0 (0.0)	53 (11.0)
憩室	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸憩室	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
口内乾燥	116 (12.1)	30 (3.1)	8 (0.8)	154 (16.0)	47 (9.7)	11 (2.3)	2 (0.4)	60 (12.4)
十二指腸潰瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
十二指腸炎	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	62 (6.5)	12 (1.2)	2 (0.2)	76 (7.9)	12 (2.5)	4 (0.8)	0 (0.0)	16 (3.3)
嚥下障害	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
小腸炎	8 (0.8)	0 (0.0)	0 (0.0)	8 (0.8)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
心窩部不快感	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
びらん性十二指腸炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
大腿ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	6 (0.6)	2 (0.2)	0 (0.0)	8 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
食中毒	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
機能的胃腸障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃ポリープ	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
胃潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
胃炎	11 (1.1)	3 (0.3)	0 (0.0)	14 (1.5)	3 (0.6)	3 (0.6)	0 (0.0)	6 (1.2)
びらん性胃炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
消化管運動過剰	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
胃腸の炎症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸音異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃食道逆流性疾患	30 (3.1)	12 (1.2)	1 (0.1)	43 (4.5)	12 (2.5)	4 (0.8)	0 (0.0)	16 (3.3)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
歯肉退縮	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
歯肉炎	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
舌痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
痔出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	13 (1.4)	1 (0.1)	0 (0.0)	14 (1.5)	8 (1.7)	1 (0.2)	0 (0.0)	9 (1.9)
裂孔ヘルニア	6 (0.6)	2 (0.2)	0 (0.0)	8 (0.8)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
胃酸過多	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
口の感覚鈍麻	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
回腸炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単径ヘルニア	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	3 (0.6)	3 (0.6)	0 (0.0)	6 (1.2)
内ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
過敏性腸症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	3 (0.6)	0 (0.0)	5 (1.0)
口唇乾燥	6 (0.6)	0 (0.0)	0 (0.0)	6 (0.6)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
口唇腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下部消化管出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吸収不良	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
メレナ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
悪心	76 (7.9)	22 (2.3)	0 (0.0)	98 (10.2)	39 (8.1)	18 (3.7)	0 (0.0)	57 (11.8)
嚥下痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
食道炎	2 (0.2)	3 (0.3)	0 (0.0)	5 (0.5)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
口腔障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
口の錯感覚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
結腸直腸ポリープ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門周囲痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
吐き戻し	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
S状結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
口内炎	6 (0.6)	0 (0.0)	0 (0.0)	6 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
舌苔	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
舌乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
舌粘膜剥脱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯の障害	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
歯痛	4 (0.4)	6 (0.6)	0 (0.0)	10 (1.0)	10 (2.1)	2 (0.4)	0 (0.0)	12 (2.5)
臍ヘルニア	16 (1.7)	4 (0.4)	1 (0.1)	21 (2.2)	5 (1.0)	2 (0.4)	0 (0.0)	7 (1.4)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
閉塞性臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
嘔吐	55 (5.7)	22 (2.3)	2 (0.2)	79 (8.2)	26 (5.4)	13 (2.7)	1 (0.2)	40 (8.3)
一般・全身障害および投与部位の状態								
無力症	30 (3.1)	21 (2.2)	6 (0.6)	57 (5.9)	14 (2.9)	9 (1.9)	4 (0.8)	27 (5.6)
腋窩痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胸部不快感	12 (1.2)	1 (0.1)	0 (0.0)	13 (1.4)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
胸痛	21 (2.2)	18 (1.9)	3 (0.3)	42 (4.4)	7 (1.4)	5 (1.0)	0 (0.0)	12 (2.5)
悪寒	9 (0.9)	3 (0.3)	0 (0.0)	12 (1.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
嚢胞	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
医療機器位置異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
早期満腹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
運動耐性低下	2 (0.2)	0 (0.0)	1 (0.1)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪組織増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	94 (9.8)	30 (3.1)	7 (0.7)	131 (13.6)	33 (6.8)	12 (2.5)	2 (0.4)	47 (9.7)
異常感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
冷感	6 (0.6)	2 (0.2)	1 (0.1)	9 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
びくびく感	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルニア	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
治癒不良	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	3 (0.3)	4 (0.4)	0 (0.0)	7 (0.7)	3 (0.6)	2 (0.4)	0 (0.0)	5 (1.0)
易刺激性	4 (0.4)	0 (0.0)	1 (0.1)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
局所腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
倦怠感	22 (2.3)	2 (0.2)	0 (0.0)	24 (2.5)	5 (1.0)	4 (0.8)	1 (0.2)	10 (2.1)
粘膜乾燥	6 (0.6)	1 (0.1)	1 (0.1)	8 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
小結節	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
一般・全身障害および投与部位の状態								
浮腫	13 (1.4)	3 (0.3)	0 (0.0)	16 (1.7)	7 (1.4)	1 (0.2)	1 (0.2)	9 (1.9)
末梢性浮腫	70 (7.3)	11 (1.1)	0 (0.0)	81 (8.4)	37 (7.7)	9 (1.9)	0 (0.0)	46 (9.5)
疼痛	10 (1.0)	6 (0.6)	0 (0.0)	16 (1.7)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
発熱	31 (3.2)	14 (1.5)	0 (0.0)	45 (4.7)	24 (5.0)	17 (3.5)	1 (0.2)	42 (8.7)
不活発	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
恥骨上痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口渇	344 (35.8)	157 (16.3)	30 (3.1)	531 (55.3)	83 (17.2)	12 (2.5)	4 (0.8)	99 (20.5)
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管穿刺部位血腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害								
胆道ジスキネジー	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胆管炎	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胆嚢痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
肝嚢胞	8 (0.8)	5 (0.5)	0 (0.0)	13 (1.4)	2 (0.4)	7 (1.4)	1 (0.2)	10 (2.1)
肝嚢胞破裂	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	6 (0.6)	5 (0.5)	1 (0.1)	12 (1.2)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
肝臓痛	4 (0.4)	2 (0.2)	1 (0.1)	7 (0.7)	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.6)
脂肪肝	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	6 (0.6)	3 (0.3)	0 (0.0)	9 (0.9)	1 (0.2)	0 (0.0)	2 (0.4)	3 (0.6)
高ビリルビン血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝障害	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝圧痛	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
免疫系障害								
アレルギー性浮腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷アレルギー	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシーショック	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
造影剤アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
薬物過敏症	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.3)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
食物アレルギー	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	3 (0.3)	4 (0.4)	0 (0.0)	7 (0.7)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
複合アレルギー	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	24 (2.5)	2 (0.2)	0 (0.0)	26 (2.7)	5 (1.0)	5 (1.0)	0 (0.0)	10 (2.1)
感染症および寄生虫症								
膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.4)
四肢膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
急性扁桃炎	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
アデノイド咽頭炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性肛門感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	4 (0.8)	4 (0.8)
細菌性関節炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
感染性関節炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
細菌尿	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
バルトリン腺膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
乳房感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
気管支炎	36 (3.7)	21 (2.2)	1 (0.1)	58 (6.0)	21 (4.3)	12 (2.5)	0 (0.0)	33 (6.8)
ウイルス性気管支炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
カンジダ症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
蜂巣炎	5 (0.5)	0 (0.0)	1 (0.1)	6 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
眼窩蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
子宮頸管炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
クロストリジウム性大腸炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	10 (1.0)	1 (0.1)	0 (0.0)	11 (1.1)	12 (2.5)	0 (0.0)	0 (0.0)	12 (2.5)
サイトメガロウイルス感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	1 (0.1)	3 (0.3)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳感染	6 (0.6)	16 (1.7)	0 (0.0)	22 (2.3)	4 (0.8)	3 (0.6)	0 (0.0)	7 (1.4)
耳垂感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
感染性小腸結腸炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
遊走性紅斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	2 (0.4)	0 (0.0)	3 (0.6)
眼瞼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
熱性感染症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
毛包炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
皮膚真菌感染	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
せつ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	31 (3.2)	20 (2.1)	3 (0.3)	54 (5.6)	12 (2.5)	8 (1.7)	1 (0.2)	21 (4.3)
ノロウイルス性胃腸炎	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	12 (1.2)	5 (0.5)	3 (0.3)	20 (2.1)	4 (0.8)	2 (0.4)	0 (0.0)	6 (1.2)
細菌性消化管感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性消化管感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
ウイルス性消化管感染	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
陰部ヘルペス	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
泌尿生殖器感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジアルジア症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
歯肉膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H 1 N 1 インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.6)	0 (0.0)	4 (0.8)
ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
ヘリコバクター感染	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)
B型肝炎	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C型肝炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
ヘルペスウイルス感染	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
带状疱疹	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	5 (1.0)	2 (0.4)	0 (0.0)	7 (1.4)
麦粒腫	7 (0.7)	0 (0.0)	0 (0.0)	7 (0.7)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
感染性嚢腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
伝染性単核症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
インフルエンザ	53 (5.5)	22 (2.3)	0 (0.0)	75 (7.8)	22 (4.6)	15 (3.1)	1 (0.2)	38 (7.9)
腎感染	2 (0.2)	1 (0.1)	2 (0.2)	5 (0.5)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
迷路炎	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
喉頭炎	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
肝膿瘍	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
下気道感染	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	0 (0.0)	3 (0.6)	0 (0.0)	3 (0.6)
ライム病	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
リンパ管炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マラリア	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
マイコプラズマ感染	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
爪感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
鼻咽頭炎	174 (18.1)	37 (3.9)	0 (0.0)	211 (22.0)	92 (19.0)	19 (3.9)	0 (0.0)	111 (23.0)
線虫症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
口腔カンジダ症	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔真菌感染	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	8 (0.8)	0 (0.0)	0 (0.0)	8 (0.8)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
外耳炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
中耳炎	2 (0.2)	3 (0.3)	0 (0.0)	5 (0.5)	1 (0.2)	2 (0.4)	0 (0.0)	3 (0.6)
急性中耳炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳頭腫ウイルス感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
爪囲炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
会陰膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
百日咳	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
咽頭炎	13 (1.4)	3 (0.3)	0 (0.0)	16 (1.7)	14 (2.9)	2 (0.4)	0 (0.0)	16 (3.3)
レンサ球菌性咽頭炎	3 (0.3)	4 (0.4)	0 (0.0)	7 (0.7)	0 (0.0)	4 (0.8)	0 (0.0)	4 (0.8)
肺炎	4 (0.4)	5 (0.5)	2 (0.2)	11 (1.1)	2 (0.4)	3 (0.6)	0 (0.0)	5 (1.0)
前立腺感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腎盂腎炎	1 (0.1)	7 (0.7)	0 (0.0)	8 (0.8)	1 (0.2)	6 (1.2)	2 (0.4)	9 (1.9)
腎嚢胞感染	3 (0.3)	6 (0.6)	0 (0.0)	9 (0.9)	6 (1.2)	5 (1.0)	2 (0.4)	13 (2.7)
気道感染	2 (0.2)	4 (0.4)	0 (0.0)	6 (0.6)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
ウイルス性気道感染	3 (0.3)	1 (0.1)	1 (0.1)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	14 (1.5)	0 (0.0)	0 (0.0)	14 (1.5)	11 (2.3)	0 (0.0)	0 (0.0)	11 (2.3)
卵管卵巣炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
副鼻腔炎	36 (3.7)	16 (1.7)	1 (0.1)	53 (5.5)	13 (2.7)	10 (2.1)	0 (0.0)	23 (4.8)
皮膚感染	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ブドウ球菌性咽頭炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
糞線虫症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癬風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
扁桃炎	5 (0.5)	8 (0.8)	0 (0.0)	13 (1.4)	5 (1.0)	1 (0.2)	0 (0.0)	6 (1.2)
歯膿瘍	3 (0.3)	4 (0.4)	0 (0.0)	7 (0.7)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
歯感染	7 (0.7)	1 (0.1)	0 (0.0)	8 (0.8)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
気管炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
気管気管支炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	50 (5.2)	31 (3.2)	1 (0.1)	82 (8.5)	30 (6.2)	12 (2.5)	0 (0.0)	42 (8.7)
尿路感染	52 (5.4)	28 (2.9)	1 (0.1)	81 (8.4)	31 (6.4)	27 (5.6)	3 (0.6)	61 (12.6)
泌尿生殖器細菌感染	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
細菌性腔炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
ウイルス感染	14 (1.5)	6 (0.6)	1 (0.1)	21 (2.2)	11 (2.3)	2 (0.4)	0 (0.0)	13 (2.7)
ウイルス性鼻炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
外陰部腔カンジダ症	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
外陰腔真菌感染	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
創傷感染	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膿創	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
傷害、中毒および処置合併症								
腹部損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足関節部骨折	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
節足動物咬傷	8 (0.8)	0 (0.0)	0 (0.0)	8 (0.8)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
節足動物刺傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
剥離骨折	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部損傷	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咬刺傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨損傷	0 (0.0)	2 (0.2)	2 (0.2)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
凍瘡	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	13 (1.4)	5 (0.5)	0 (0.0)	18 (1.9)	4 (0.8)	2 (0.4)	0 (0.0)	6 (1.2)
角膜擦過傷	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
擦過傷	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の貫通性外傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	3 (0.3)	1 (0.1)	1 (0.1)	5 (0.5)	6 (1.2)	0 (0.0)	0 (0.0)	6 (1.2)
足骨折	1 (0.1)	5 (0.5)	0 (0.0)	6 (0.6)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
眼内異物	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
手骨折	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
頭部損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
熱疲労	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸脛靱帯症候群	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
切開部位痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
傷害、中毒および処置合併症								
損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
関節脱臼	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	2 (0.4)	0 (0.0)	3 (0.6)
関節損傷	4 (0.4)	5 (0.5)	0 (0.0)	9 (0.9)	3 (0.6)	3 (0.6)	1 (0.2)	7 (1.4)
裂傷	3 (0.3)	2 (0.2)	1 (0.1)	6 (0.6)	1 (0.2)	2 (0.4)	1 (0.2)	4 (0.8)
靱帯損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
靱帯断裂	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
靱帯捻挫	9 (0.9)	5 (0.5)	0 (0.0)	14 (1.5)	9 (1.9)	2 (0.4)	0 (0.0)	11 (2.3)
四肢損傷	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	5 (1.0)	0 (0.0)	5 (1.0)
口唇損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腰椎骨折	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	2 (0.2)	2 (0.2)	1 (0.1)	5 (0.5)	0 (0.0)	7 (1.4)	0 (0.0)	7 (1.4)
多発骨折	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
筋断裂	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肉離れ	7 (0.7)	2 (0.2)	0 (0.0)	9 (0.9)	5 (1.0)	1 (0.2)	0 (0.0)	6 (1.2)
頸部損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲血腫	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
処置後合併症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
処置後血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
処置後出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
処置による疼痛	3 (0.3)	6 (0.6)	0 (0.0)	9 (0.9)	2 (0.4)	4 (0.8)	0 (0.0)	6 (1.2)
処置による嘔吐	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
橈骨骨折	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	1 (0.1)	1 (0.1)	2 (0.2)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
骨格損傷	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
軟部組織損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎骨折	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
傷害、中毒および処置合併症								
ストレス骨折	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼の擦過傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腱断裂	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
脛骨骨折	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
歯牙破折	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
創傷	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
手首関節骨折	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
臨床検査								
活性化部分トロンボプラスチン時間延長	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
アラニン・アミノトランスフェラーゼ増加	26 (2.7)	10 (1.0)	3 (0.3)	39 (4.1)	16 (3.3)	1 (0.2)	0 (0.0)	17 (3.5)
アスパラギン酸アミノトランスフェラーゼ増加	26 (2.7)	8 (0.8)	2 (0.2)	36 (3.7)	15 (3.1)	1 (0.2)	0 (0.0)	16 (3.3)
細菌検査陽性	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
血中アルカリホスファターゼ増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中ビリルビン増加	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
血中カルシウム増加	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	13 (1.4)	1 (0.1)	0 (0.0)	14 (1.5)	7 (1.4)	0 (0.0)	0 (0.0)	7 (1.4)
血中クレアチンホスホキナーゼ増加	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中クレアチニン増加	105 (10.9)	30 (3.1)	0 (0.0)	135 (14.0)	55 (11.4)	16 (3.3)	0 (0.0)	71 (14.7)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
血中ブドウ糖増加	7 (0.7)	0 (0.0)	0 (0.0)	7 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血中乳酸脱水素酵素増加	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中副甲状腺ホルモン増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
血圧低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
拡張期血圧上昇	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血圧上昇	8 (0.8)	2 (0.2)	0 (0.0)	10 (1.0)	5 (1.0)	2 (0.4)	0 (0.0)	7 (1.4)
血中ナトリウム減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム増加	13 (1.4)	1 (0.1)	0 (0.0)	14 (1.5)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血中テストステロン減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
血中尿素増加	8 (0.8)	2 (0.2)	0 (0.0)	10 (1.0)	9 (1.9)	3 (0.6)	0 (0.0)	12 (2.5)
血中尿酸増加	21 (2.2)	3 (0.3)	0 (0.0)	24 (2.5)	5 (1.0)	1 (0.2)	0 (0.0)	6 (1.2)
尿中血陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C-反応性蛋白増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心雑音	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
腎クレアチニン・クリアランス増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
シスタチンC増加	6 (0.6)	0 (0.0)	0 (0.0)	6 (0.6)	6 (1.2)	1 (0.2)	0 (0.0)	7 (1.4)
心電図QT間隔	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図再分極異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心電図異常T波	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好酸球数増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
大腸菌検査陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
γ-グルタミルトランスフェラーゼ増加	16 (1.7)	7 (0.7)	0 (0.0)	23 (2.4)	10 (2.1)	0 (0.0)	1 (0.2)	11 (2.3)
胃内pH低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
ヘマトクリット増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心拍数不整	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝酵素異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	9 (0.9)	7 (0.7)	1 (0.1)	17 (1.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ヒト乳頭腫ウイルス検査陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
I N R 増加	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼圧上昇	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
リパーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝機能検査異常	2 (0.2)	4 (0.4)	0 (0.0)	6 (0.6)	2 (0.4)	0 (0.0)	1 (0.2)	3 (0.6)
季肋下肝触知	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低比重リポ蛋白減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
リンパ球形態異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球容積減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
平均赤血球容積増加	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好中球数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
好中球数増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
便潜血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
血小板数増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
プロトロンビン時間異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Q O L 低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
トランスアミナーゼ上昇	5 (0.5)	4 (0.4)	2 (0.2)	11 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
卵巣超音波検査異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
尿浸透圧低下	7 (0.7)	2 (0.2)	0 (0.0)	9 (0.9)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿浸透圧上昇	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量増加	12 (1.2)	2 (0.2)	1 (0.1)	15 (1.6)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
ビタミンD減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
ウエスト周囲径増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	37 (3.9)	9 (0.9)	0 (0.0)	46 (4.8)	9 (1.9)	7 (1.4)	0 (0.0)	16 (3.3)
体重増加	35 (3.6)	11 (1.1)	0 (0.0)	46 (4.8)	14 (2.9)	5 (1.0)	0 (0.0)	19 (3.9)
白血球数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
白血球数増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
尿中白血球	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿中白血球陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
代謝および栄養障害								
アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
食欲減退	52 (5.4)	16 (1.7)	1 (0.1)	69 (7.2)	2 (0.4)	3 (0.6)	0 (0.0)	5 (1.0)
脱水	8 (0.8)	7 (0.7)	3 (0.3)	18 (1.9)	3 (0.6)	6 (1.2)	2 (0.4)	11 (2.3)
糖尿病	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体液貯留	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
食物渴望	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
痛風	14 (1.5)	14 (1.5)	0 (0.0)	28 (2.9)	4 (0.8)	3 (0.6)	0 (0.0)	7 (1.4)
高アマラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
高カルシウム血症	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
高コレステロール血症	22 (2.3)	4 (0.4)	0 (0.0)	26 (2.7)	10 (2.1)	2 (0.4)	0 (0.0)	12 (2.5)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
高血糖	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	10 (2.1)	0 (0.0)	0 (0.0)	10 (2.1)
高カリウム血症	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
高脂血症	11 (1.1)	1 (0.1)	0 (0.0)	12 (1.2)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
高ナトリウム血症	22 (2.3)	5 (0.5)	0 (0.0)	27 (2.8)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
代謝および栄養障害								
高リン酸塩血症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高尿酸血症	31 (3.2)	6 (0.6)	0 (0.0)	37 (3.9)	8 (1.7)	1 (0.2)	0 (0.0)	9 (1.9)
低アルブミン血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
低カルシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
低血糖症	6 (0.6)	0 (0.0)	0 (0.0)	6 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	3 (0.3)	3 (0.3)	0 (0.0)	6 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
低マグネシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
低リン酸血症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鉄欠乏	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ラクトース不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝性アシドーシス	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
過体重	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	50 (5.2)	44 (4.6)	6 (0.6)	100 (10.4)	12 (2.5)	5 (1.0)	0 (0.0)	17 (3.5)
2型糖尿病	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンB 1 2 欠乏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD欠乏	8 (0.8)	1 (0.1)	0 (0.0)	9 (0.9)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
体重変動	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害								
関節痛	48 (5.0)	21 (2.2)	0 (0.0)	69 (7.2)	20 (4.1)	7 (1.4)	1 (0.2)	28 (5.8)
関節炎	4 (0.4)	2 (0.2)	0 (0.0)	6 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
反応性関節炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	89 (9.3)	37 (3.9)	7 (0.7)	133 (13.8)	57 (11.8)	26 (5.4)	5 (1.0)	88 (18.2)
骨痛	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
滑液包石灰化	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
軟骨肥厚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
筋骨格系および結合組織障害								
頸部脊柱管狭窄症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
尾骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
肋軟骨炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外骨腫	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋膜炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
瘻孔	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	7 (0.7)	4 (0.4)	0 (0.0)	11 (1.1)	8 (1.7)	2 (0.4)	0 (0.0)	10 (2.1)
足変形	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
痛風性関節炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腓距部痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
椎間板変性症	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板障害	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	4 (0.4)	9 (0.9)	0 (0.0)	13 (1.4)	4 (0.8)	2 (0.4)	1 (0.2)	7 (1.4)
関節滲出液	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節可動域低下	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
関節腫脹	9 (0.9)	0 (0.0)	0 (0.0)	9 (0.9)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
靱帯障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
靱帯痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢非対称	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	27 (2.8)	8 (0.8)	0 (0.0)	35 (3.6)	13 (2.7)	4 (0.8)	0 (0.0)	17 (3.5)
筋緊張	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
筋攣縮	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
筋力低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
筋骨格系胸痛	6 (0.6)	3 (0.3)	0 (0.0)	9 (0.9)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
筋骨格系および結合組織障害								
筋骨格不快感	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格痛	26 (2.7)	10 (1.0)	1 (0.1)	37 (3.9)	12 (2.5)	4 (0.8)	1 (0.2)	17 (3.5)
筋骨格硬直	9 (0.9)	1 (0.1)	1 (0.1)	11 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
筋肉痛	38 (4.0)	12 (1.2)	0 (0.0)	50 (5.2)	12 (2.5)	3 (0.6)	1 (0.2)	16 (3.3)
筋炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部痛	14 (1.5)	10 (1.0)	1 (0.1)	25 (2.6)	8 (1.7)	4 (0.8)	0 (0.0)	12 (2.5)
変形性関節症	4 (0.4)	1 (0.1)	2 (0.2)	7 (0.7)	3 (0.6)	2 (0.4)	1 (0.2)	6 (1.2)
骨関節障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
骨減少症	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
骨粗鬆症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	32 (3.3)	10 (1.0)	0 (0.0)	42 (4.4)	17 (3.5)	10 (2.1)	0 (0.0)	27 (5.6)
顎痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
関節周囲炎	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
足底筋膜炎	4 (0.4)	3 (0.3)	0 (0.0)	7 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
恥骨痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
関節リウマチ	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
仙腸骨炎	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側弯症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
重感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
脊椎障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
脊椎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
滑液嚢腫	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腱障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腱痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
筋骨格系および結合組織障害								
腱炎	11 (1.1)	5 (0.5)	0 (0.0)	16 (1.7)	6 (1.2)	4 (0.8)	0 (0.0)	10 (2.1)
腱鞘炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
斜頸	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）								
アクロコルドン	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
基底細胞癌	5 (0.5)	3 (0.3)	0 (0.0)	8 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房の良性新生物	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
甲状腺の良性新生物	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳癌	0 (0.0)	1 (0.1)	2 (0.2)	3 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
子宮頸部癌第0期	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真珠腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
慢性骨髄性白血病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
カボジ肉腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
悪性黒色腫	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表皮内悪性黒色腫	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メラノサイト性母斑	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
下垂体の良性腫瘍	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性角化症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
皮膚乳頭腫	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
扁平上皮癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
汗腺腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
子宮平滑筋腫	7 (0.7)	3 (0.3)	0 (0.0)	10 (1.0)	3 (0.6)	1 (0.2)	1 (0.2)	5 (1.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
味覚消失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
健忘	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
失声症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
くも膜嚢胞	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
平衡障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
灼熱感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
頸動脈瘤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
手根管症候群	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
協調運動異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳神経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
意識レベルの低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	4 (0.4)	3 (0.3)	1 (0.1)	8 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
浮動性めまい	86 (8.9)	22 (2.3)	1 (0.1)	109 (11.3)	30 (6.2)	11 (2.3)	1 (0.2)	42 (8.7)
労作性めまい	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	17 (1.8)	4 (0.4)	0 (0.0)	21 (2.2)	6 (1.2)	1 (0.2)	0 (0.0)	7 (1.4)
脳症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	178 (18.5)	46 (4.8)	17 (1.8)	241 (25.1)	94 (19.5)	22 (4.6)	5 (1.0)	121 (25.1)
味覚過敏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	12 (1.2)	3 (0.3)	0 (0.0)	15 (1.6)	9 (1.9)	3 (0.6)	0 (0.0)	12 (2.5)
反射減弱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋緊張低下	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	6 (0.6)	0 (0.0)	1 (0.1)	7 (0.7)	0 (0.0)	2 (0.4)	1 (0.2)	3 (0.6)
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
嗜眠	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
意識消失	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
精神的機能障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
片頭痛	17 (1.8)	4 (0.4)	1 (0.1)	22 (2.3)	7 (1.4)	3 (0.6)	0 (0.0)	10 (2.1)
前兆を伴う片頭痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
末梢性ニューロパチー	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
起立不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	13 (1.4)	5 (0.5)	1 (0.1)	19 (2.0)	11 (2.3)	2 (0.4)	0 (0.0)	13 (2.7)
パーキンソン病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パーキンソニズム	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
気脳体	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
失神寸前の状態	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
根症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
下肢静止不能症候群	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
坐骨神経痛	4 (0.4)	4 (0.4)	1 (0.1)	9 (0.9)	3 (0.6)	2 (0.4)	1 (0.2)	6 (1.2)
感覚障害	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
傾眠	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
くも膜下出血	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.4)
失神	6 (0.6)	10 (1.0)	0 (0.0)	16 (1.7)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
緊張性頭痛	0 (0.0)	3 (0.3)	0 (0.0)	3 (0.3)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
一過性脳虚血発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.4)
振戦	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
トンネル状視野	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎骨動脈解離	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第7脳神経麻痺	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
精神障害								
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
異常な夢	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
激越	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不安	17 (1.8)	10 (1.0)	3 (0.3)	30 (3.1)	5 (1.0)	3 (0.6)	0 (0.0)	8 (1.7)
不安障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意欠陥多動性障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自閉症スペクトラム障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神緩慢	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
燃え尽き症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
うつ病	23 (2.4)	16 (1.7)	3 (0.3)	42 (4.4)	12 (2.5)	9 (1.9)	0 (0.0)	21 (4.3)
睡眠異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	29 (3.0)	20 (2.1)	6 (0.6)	55 (5.7)	12 (2.5)	9 (1.9)	0 (0.0)	21 (4.3)
リビドー減退	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
性欲障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
リビド消失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大うつ病	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
中期不眠症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分変化	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分動揺	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
神経過敏	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ニコチン依存	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
悪夢	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	2 (0.2)	3 (0.3)	0 (0.0)	5 (0.5)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
精神障害								
パニック反応	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
心身症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
落ち着きのなさ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
統合失調症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
夢遊症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス	8 (0.8)	1 (0.1)	0 (0.0)	9 (0.9)	9 (1.9)	1 (0.2)	0 (0.0)	10 (2.1)
自殺企図	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腎および尿路障害								
アルブミン尿	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱刺激症状	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱脱	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
膀胱痙縮	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	2 (0.4)	0 (0.0)	3 (0.6)
着色尿	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
非感染性膀胱炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	14 (1.5)	3 (0.3)	0 (0.0)	17 (1.8)	7 (1.4)	2 (0.4)	0 (0.0)	9 (1.9)
遺尿	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血尿	54 (5.6)	16 (1.7)	5 (0.5)	75 (7.8)	50 (10.4)	16 (3.3)	2 (0.4)	68 (14.1)
水腎症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎腫大	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
白血球尿	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
尿意切迫	6 (0.6)	2 (0.2)	0 (0.0)	8 (0.8)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
腎および尿路障害								
腎結石症	5 (0.5)	8 (0.8)	2 (0.2)	15 (1.6)	6 (1.2)	5 (1.0)	3 (0.6)	14 (2.9)
夜間頻尿	178 (18.5)	92 (9.6)	10 (1.0)	280 (29.1)	54 (11.2)	9 (1.9)	0 (0.0)	63 (13.0)
乏尿	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	133 (13.8)	68 (7.1)	22 (2.3)	223 (23.2)	18 (3.7)	6 (1.2)	2 (0.4)	26 (5.4)
多尿	184 (19.1)	142 (14.8)	42 (4.4)	368 (38.3)	65 (13.5)	16 (3.3)	2 (0.4)	83 (17.2)
蛋白尿	2 (0.2)	1 (0.1)	1 (0.1)	4 (0.4)	8 (1.7)	0 (0.0)	0 (0.0)	8 (1.7)
腎仙痛	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.3)	0 (0.0)	5 (1.0)	0 (0.0)	5 (1.0)
腎嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腎嚢胞出血	1 (0.1)	4 (0.4)	1 (0.1)	6 (0.6)	4 (0.8)	3 (0.6)	2 (0.4)	9 (1.9)
腎嚢胞破裂	3 (0.3)	4 (0.4)	0 (0.0)	7 (0.7)	1 (0.2)	3 (0.6)	1 (0.2)	5 (1.0)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
急性腎不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.4)
慢性腎不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	8 (0.8)	5 (0.5)	0 (0.0)	13 (1.4)	5 (1.0)	3 (0.6)	0 (0.0)	8 (1.7)
腎臓痛	134 (13.9)	98 (10.2)	28 (2.9)	260 (27.1)	81 (16.8)	66 (13.7)	24 (5.0)	171 (35.4)
有痛性排尿困難	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
終末尿滴下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿道狭窄	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
排尿躊躇	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	5 (0.5)	4 (0.4)	0 (0.0)	9 (0.9)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
尿閉	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)
尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
尿流量減少	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
生殖系および乳房障害								
子宮付属器痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	1 (0.1)	3 (0.3)	0 (0.0)	4 (0.4)	2 (0.4)	3 (0.6)	0 (0.0)	5 (1.0)
精子無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
萎縮性外陰陰炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
生殖系および乳房障害								
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房嚢胞	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房腫瘤	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部上皮異形成	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
子宮頸管ポリープ	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性交出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱瘤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
性交困難	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
射精障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
精巣上体嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精巣上体炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
勃起不全	5 (0.5)	3 (0.3)	2 (0.2)	10 (1.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳汁漏出症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
血精液症	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過少月経	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
機能性子宮出血	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
月経過多	8 (0.8)	6 (0.6)	0 (0.0)	14 (1.5)	7 (1.4)	2 (0.4)	0 (0.0)	9 (1.9)
月経障害	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
不規則月経	7 (0.7)	1 (0.1)	0 (0.0)	8 (0.8)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
生殖系および乳房障害								
不正子宮出血	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
卵巣嚢胞	4 (0.4)	1 (0.1)	1 (0.1)	6 (0.6)	6 (1.2)	0 (0.0)	0 (0.0)	6 (1.2)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
卵巣捻転	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤脱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ペイロニー病	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経後出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.4)	1 (0.2)	2 (0.4)	0 (0.0)	3 (0.6)
前立腺腫大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性功能不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精嚢嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
精嚢痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
子宮脱	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
子宮腔脱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔分泌物	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
腔出血	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精索静脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
外陰腔乾燥	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
呼吸器、胸郭および縦隔障害								
喘息	6 (0.6)	5 (0.5)	0 (0.0)	11 (1.1)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
慢性気管支炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支痙攣	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
呼吸器、胸郭および縦隔障害								
咳嗽	61 (6.3)	16 (1.7)	0 (0.0)	77 (8.0)	30 (6.2)	8 (1.7)	0 (0.0)	38 (7.9)
咽喉乾燥	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
発声障害	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	13 (1.4)	7 (0.7)	2 (0.2)	22 (2.3)	1 (0.2)	5 (1.0)	0 (0.0)	6 (1.2)
安静時呼吸困難	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	1 (0.1)	3 (0.3)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻出血	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
過換気	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭嚢腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肺障害	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
鼻乾燥	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
鼻閉塞	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻中隔弯曲	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
口腔咽頭痛	43 (4.5)	3 (0.3)	0 (0.0)	46 (4.8)	16 (3.3)	2 (0.4)	0 (0.0)	18 (3.7)
咽頭紅斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
咽頭の炎症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
胸水	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺塞栓症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺線維症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気道うつ血	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	7 (0.7)	2 (0.2)	0 (0.0)	9 (0.9)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
鼻漏	9 (0.9)	1 (0.1)	0 (0.0)	10 (1.0)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
呼吸器、胸郭および縦隔障害								
低音性連続性ラ音	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔うっ血	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
睡眠時無呼吸症候群	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
いびき	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
咽喉絞扼感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
扁桃肥大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
扁桃結石	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
上気道咳症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
皮膚および皮下組織障害								
ざ瘡	10 (1.0)	4 (0.4)	0 (0.0)	14 (1.5)	6 (1.2)	2 (0.4)	0 (0.0)	8 (1.7)
日光性角化症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	12 (1.2)	3 (0.3)	0 (0.0)	15 (1.6)	2 (0.4)	5 (1.0)	0 (0.0)	7 (1.4)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
アンドロゲン性脱毛症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚炎	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
アレルギー性皮膚炎	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
アトピー性皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
接触性皮膚炎	8 (0.8)	1 (0.1)	0 (0.0)	9 (0.9)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
皮膚症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚乾燥	45 (4.7)	1 (0.1)	1 (0.1)	47 (4.9)	8 (1.7)	0 (0.0)	0 (0.0)	8 (1.7)
斑状出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
湿疹	17 (1.8)	2 (0.2)	0 (0.0)	19 (2.0)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
紅斑	9 (0.9)	0 (0.0)	0 (0.0)	9 (0.9)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
多形紅斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
過剰皮膚	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
紅色汗疹	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	3 (0.3)	2 (0.2)	0 (0.0)	5 (0.5)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
過角化	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
乏汗症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内出血発生の増加傾向	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嵌入爪	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
機械性蕁麻疹	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
神経皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	3 (0.3)	1 (0.1)	1 (0.1)	5 (0.5)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.4)
爪破損	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚疼痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
点状出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光線過敏性反応	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
枇糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ばら色枇糠疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
そう痒症	29 (3.0)	4 (0.4)	0 (0.0)	33 (3.4)	10 (2.1)	3 (0.6)	0 (0.0)	13 (2.7)
全身性そう痒症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	35 (3.6)	5 (0.5)	0 (0.0)	40 (4.2)	7 (1.4)	2 (0.4)	0 (0.0)	9 (1.9)

表2.7.4.7-25

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CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
紅斑性皮疹	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	2 (0.4)	0 (0.0)	2 (0.4)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
そう痒性皮疹	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂腺障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚色素脱失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素過剰	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
皮膚病変	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚潰瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
うつ滞性皮膚炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
蕁麻疹	8 (0.8)	4 (0.4)	2 (0.2)	14 (1.5)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.8)
慢性蕁麻疹	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尋常性白斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
社会環境								
閉経	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
外科および内科処置								
収れん薬療法	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジフテリア免疫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管拡張および子宮内搔爬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ビタミン補給	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害								
血管障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈拡張	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
動脈硬化症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の血圧	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

表2.7.4.7-25

156-251

CT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血管障害								
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
深部静脈血栓症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
潮紅	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	4 (0.4)	1 (0.1)	1 (0.1)	6 (0.6)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	6 (0.6)	1 (0.1)	1 (0.1)	8 (0.8)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
高血圧	233 (24.2)	74 (7.7)	3 (0.3)	310 (32.3)	122 (25.3)	48 (9.9)	4 (0.8)	174 (36.0)
高血圧クリーゼ	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	19 (2.0)	9 (0.9)	2 (0.2)	30 (3.1)	9 (1.9)	5 (1.0)	1 (0.2)	15 (3.1)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
不安定血圧	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
微小血管症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	4 (0.4)	0 (0.0)	1 (0.1)	5 (0.5)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
末梢冷感	11 (1.1)	0 (0.0)	0 (0.0)	11 (1.1)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
静脈炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レイノー現象	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血栓性静脈炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
表在性血栓性静脈炎	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
静脈瘤	4 (0.4)	3 (0.3)	0 (0.0)	7 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
静脈不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表2.7.4.7-26

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血液およびリンパ系障害								
貧血	2 (1.7)	1 (0.8)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
鉄欠乏性貧血	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
脾臓障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害								
狭心症	0 (0.0)	1 (0.8)	1 (0.8)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
房室ブロック	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
左室不全	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	10 (8.5)	0 (0.0)	0 (0.0)	10 (8.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害								
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
耳および迷路障害								
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
耳鳴	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
頭位性回転性めまい	0 (0.0)	2 (1.7)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害								
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)

表2.7.4.7-26

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
眼障害								
霰粒腫	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
結膜炎	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
アレルギー性結膜炎	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
眼乾燥	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
眼痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
眼瞼浮腫	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
緑内障	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
強膜炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
胃腸障害								
腹部不快感	7 (5.9)	0 (0.0)	0 (0.0)	7 (5.9)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
腹部膨満	6 (5.1)	1 (0.8)	0 (0.0)	7 (5.9)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
腹痛	9 (7.6)	0 (0.0)	1 (0.8)	10 (8.5)	6 (10.2)	0 (0.0)	0 (0.0)	6 (10.2)
下腹部痛	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	15 (12.7)	1 (0.8)	0 (0.0)	16 (13.6)	6 (10.2)	1 (1.7)	0 (0.0)	7 (11.9)
アフタ性口内炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
結腸ポリープ	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	19 (16.1)	0 (0.0)	0 (0.0)	19 (16.1)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
齲齒	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
下痢	15 (12.7)	0 (0.0)	0 (0.0)	15 (12.7)	10 (16.9)	0 (0.0)	0 (0.0)	10 (16.9)
腸憩室	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内乾燥	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-26

156-251

JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
消化不良	7 (5.9)	0 (0.0)	0 (0.0)	7 (5.9)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
小腸炎	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
心窩部不快感	2 (1.7)	1 (0.8)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
胃炎	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
胃腸音異常	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	8 (6.8)	3 (2.5)	0 (0.0)	11 (9.3)	3 (5.1)	1 (1.7)	0 (0.0)	4 (6.8)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
歯肉炎	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
痔出血	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
裂孔ヘルニア	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
口唇乾燥	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	15 (12.7)	1 (0.8)	0 (0.0)	16 (13.6)	4 (6.8)	1 (1.7)	0 (0.0)	5 (8.5)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)
歯周病	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
結腸直腸ポリープ	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
口内炎	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
歯の障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	5 (8.5)	0 (0.0)	0 (0.0)	5 (8.5)
臍ヘルニア	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	12 (10.2)	0 (0.0)	0 (0.0)	12 (10.2)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)

表2.7.4.7-26

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
一般・全身障害および投与部位の状態								
無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
胸痛	5 (4.2)	1 (0.8)	0 (0.0)	6 (5.1)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
嚢胞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	10 (8.5)	2 (1.7)	1 (0.8)	13 (11.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
熱感	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
炎症	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	11 (9.3)	1 (0.8)	0 (0.0)	12 (10.2)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
浮腫	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
末梢性浮腫	7 (5.9)	0 (0.0)	0 (0.0)	7 (5.9)	4 (6.8)	2 (3.4)	0 (0.0)	6 (10.2)
疼痛	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	13 (11.0)	0 (0.0)	0 (0.0)	13 (11.0)	7 (11.9)	2 (3.4)	0 (0.0)	9 (15.3)
口渇	89 (75.4)	17 (14.4)	0 (0.0)	106 (89.8)	18 (30.5)	0 (0.0)	0 (0.0)	18 (30.5)
肝胆道系障害								
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
胆嚢ポリープ	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
肝嚢胞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
肝機能異常	6 (5.1)	5 (4.2)	1 (0.8)	12 (10.2)	0 (0.0)	2 (3.4)	0 (0.0)	2 (3.4)
脂肪肝	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害								
節足動物咬傷アレルギー	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	8 (6.8)	0 (0.0)	0 (0.0)	8 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
急性扁桃炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
気管支炎	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
蜂巣炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	5 (8.5)	0 (0.0)	0 (0.0)	5 (8.5)
憩室炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
感染性小腸結腸炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	5 (8.5)	1 (1.7)	0 (0.0)	6 (10.2)
ウイルス性胃腸炎	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
B型肝炎	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
带状疱疹	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
麦粒腫	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
感染	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
インフルエンザ	5 (4.2)	2 (1.7)	0 (0.0)	7 (5.9)	3 (5.1)	3 (5.1)	0 (0.0)	6 (10.2)
喉頭炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
鼻咽頭炎	65 (55.1)	3 (2.5)	0 (0.0)	68 (57.6)	44 (74.6)	1 (1.7)	0 (0.0)	45 (76.3)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
耳下腺炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
扁桃周囲炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	6 (10.2)	0 (0.0)	0 (0.0)	6 (10.2)
腎嚢胞感染	0 (0.0)	2 (1.7)	0 (0.0)	2 (1.7)	0 (0.0)	2 (3.4)	1 (1.7)	3 (5.1)

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System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
気道感染	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
鼻炎	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
副鼻腔炎	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
トリコモナス症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
尿路感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
外陰部腔カンジダ症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症								
節足動物刺傷	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
剥離骨折	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
擦過傷	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足骨折	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
熱射病	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	2 (3.4)
肉離れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
外傷後疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
処置による疼痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による嘔吐	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
熱傷	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
傷害、中毒および処置合併症								
脛骨骨折	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
臨床検査								
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
アラニン・アミノトランスフェラーゼ増加	1 (0.8)	1 (0.8)	1 (0.8)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.8)	1 (0.8)	1 (0.8)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
血中クレアチンホスホキナーゼ増加	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
血中クレアチニン増加	6 (5.1)	1 (0.8)	0 (0.0)	7 (5.9)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
血中カリウム減少	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
血中尿酸増加	5 (4.2)	0 (0.0)	0 (0.0)	5 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
心電図Q T間隔	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
尿中ブドウ糖	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
腎触知	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
トランスアミナーゼ上昇	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
尿浸透圧上昇	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	8 (6.8)	0 (0.0)	0 (0.0)	8 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
代謝および栄養障害								
食欲減退	9 (7.6)	3 (2.5)	0 (0.0)	12 (10.2)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
脱水	0 (0.0)	1 (0.8)	1 (0.8)	2 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)
糖尿病	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
高カルシウム血症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	2 (1.7)	1 (0.8)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
高脂血症	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
高トリグリセリド血症	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
高尿酸血症	13 (11.0)	1 (0.8)	0 (0.0)	14 (11.9)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
鉄欠乏	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害								
関節痛	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	4 (6.8)	1 (1.7)	0 (0.0)	5 (8.5)
背部痛	23 (19.5)	4 (3.4)	1 (0.8)	28 (23.7)	18 (30.5)	0 (0.0)	0 (0.0)	18 (30.5)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
側腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
椎間板突出	1 (0.8)	2 (1.7)	0 (0.0)	3 (2.5)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
筋痙縮	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
筋骨格痛	7 (5.9)	0 (0.0)	0 (0.0)	7 (5.9)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
筋骨格硬直	5 (4.2)	0 (0.0)	0 (0.0)	5 (4.2)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
筋肉痛	10 (8.5)	1 (0.8)	0 (0.0)	11 (9.3)	5 (8.5)	0 (0.0)	0 (0.0)	5 (8.5)
頸部痛	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
変形性関節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
四肢痛	5 (4.2)	1 (0.8)	0 (0.0)	6 (5.1)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
関節周囲炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
筋骨格系および結合組織障害								
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
滑液嚢腫	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱鞘炎	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）								
脂漏性角化症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害								
味覚消失	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
頸動脈瘤	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
脳出血	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	16 (13.6)	1 (0.8)	0 (0.0)	17 (14.4)	8 (13.6)	0 (0.0)	0 (0.0)	8 (13.6)
体位性めまい	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	3 (2.5)	1 (0.8)	0 (0.0)	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	36 (30.5)	0 (0.0)	1 (0.8)	37 (31.4)	15 (25.4)	0 (0.0)	0 (0.0)	15 (25.4)
感覚鈍麻	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	5 (8.5)	0 (0.0)	0 (0.0)	5 (8.5)
頭蓋内動脈瘤	5 (4.2)	0 (0.0)	0 (0.0)	5 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
気脳体	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)
失神	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
精神障害								
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
不安	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安障害	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	3 (2.5)	1 (0.8)	0 (0.0)	4 (3.4)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
不眠症	6 (5.1)	4 (3.4)	0 (0.0)	10 (8.5)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
中期不眠症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
自殺企図	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害								
膀胱刺激症状	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
排尿困難	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	7 (5.9)	0 (0.0)	0 (0.0)	7 (5.9)	7 (11.9)	0 (0.0)	0 (0.0)	7 (11.9)
腎結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
夜間頻尿	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
頻尿	48 (40.7)	12 (10.2)	3 (2.5)	63 (53.4)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
多尿	32 (27.1)	7 (5.9)	1 (0.8)	40 (33.9)	3 (5.1)	1 (1.7)	1 (1.7)	5 (8.5)
蛋白尿	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
腎機能障害	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
腎臓痛	9 (7.6)	3 (2.5)	0 (0.0)	12 (10.2)	10 (16.9)	1 (1.7)	0 (0.0)	11 (18.6)
終末尿滴下	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
生殖系および乳房障害								
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
乳房嚢胞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
月経困難症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
精巣上体炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳汁漏出症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
血精液症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
月経障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
子宮腔脱	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害								
喘息	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	7 (11.9)	0 (0.0)	0 (0.0)	7 (11.9)
呼吸困難	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
鼻閉塞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
口腔咽頭痛	11 (9.3)	0 (0.0)	0 (0.0)	11 (9.3)	7 (11.9)	0 (0.0)	0 (0.0)	7 (11.9)
咽頭紅斑	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
上気道の炎症	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)

表2.7.4.7-26

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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
ざ瘡	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
血性水疱	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
アトピー性皮膚炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
接触性皮膚炎	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
皮膚乾燥	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
湿疹	7 (5.9)	0 (0.0)	0 (0.0)	7 (5.9)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
紅斑	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多形紅斑	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
乏汗症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色粒糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
そう痒症	8 (6.8)	0 (0.0)	0 (0.0)	8 (6.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
乾癬	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	11 (9.3)	0 (0.0)	0 (0.0)	11 (9.3)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
酒さ	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
皮膚変色	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	5 (4.2)	1 (0.8)	0 (0.0)	6 (5.1)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
慢性蕁麻疹	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害								
大動脈拡張	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
高血圧	25 (21.2)	2 (1.7)	0 (0.0)	27 (22.9)	13 (22.0)	2 (3.4)	0 (0.0)	15 (25.4)

表2.7.4.7-26
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JT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血管障害								
低血圧	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
不安定血圧	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)

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表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血液およびリンパ系障害								
貧血	16 (1.9)	7 (0.8)	1 (0.1)	24 (2.8)	16 (3.8)	7 (1.7)	0 (0.0)	23 (5.4)
凝血異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好酸球増加症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
低色素性貧血	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
白血球増加症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
白血球減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
リンパ節症	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好中球増加症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
正色素性正球性貧血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球増加症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血小板増加症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害								
急性心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	2 (0.5)
狭心症	6 (0.7)	2 (0.2)	0 (0.0)	8 (0.9)	1 (0.2)	2 (0.5)	0 (0.0)	3 (0.7)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不整脈	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心房細動	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
第一度房室ブロック	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	9 (1.1)	1 (0.1)	0 (0.0)	10 (1.2)	5 (1.2)	0 (0.0)	1 (0.2)	6 (1.4)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
心臓弁膜疾患	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拡大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝導障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
チアノーゼ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
心臓障害								
左室機能不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
僧帽弁疾患	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
僧帽弁逸脱	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心筋梗塞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	21 (2.5)	3 (0.4)	0 (0.0)	24 (2.8)	3 (0.7)	3 (0.7)	0 (0.0)	6 (1.4)
心嚢液貯留	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心膜炎	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞不全症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
上室性期外収縮	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	10 (1.2)	0 (0.0)	0 (0.0)	10 (1.2)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
三尖弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心室性期外収縮	2 (0.2)	4 (0.5)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
先天性、家族性および遺伝性障害								
心房中隔欠損症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
第Ⅴ因子ライデン変異	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
多嚢胞性肝疾患	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
脊椎奇形	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳および迷路障害								
耳垢栓塞	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
耳閉	0 (0.0)	3 (0.4)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	6 (0.7)	1 (0.1)	0 (0.0)	7 (0.8)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳管障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
耳および迷路障害								
聴覚障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内耳障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乗物酔い	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	7 (0.8)	2 (0.2)	0 (0.0)	9 (1.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
回転性めまい	17 (2.0)	2 (0.2)	2 (0.2)	21 (2.5)	13 (3.1)	4 (0.9)	0 (0.0)	17 (4.0)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
内分泌障害								
アンドロゲン欠乏症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
バセドウ病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
副甲状腺機能亢進症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能低下症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
エストロゲン欠乏症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼障害								
調節障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
白内障	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	8 (0.9)	2 (0.2)	1 (0.1)	11 (1.3)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼の隈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼乾燥	8 (0.9)	1 (0.1)	0 (0.0)	9 (1.1)	2 (0.5)	3 (0.7)	1 (0.2)	6 (1.4)
外眼筋不全麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
眼の障害	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
眼出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-27

156-251

NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
眼障害								
眼痛	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼部腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
眼瞼浮腫	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
緑内障	2 (0.2)	0 (0.0)	1 (0.1)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
遠視	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虹彩炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
流涙増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼充血	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
光視症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
老視	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
翼状片	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
暗点	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
霧視	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
視力低下	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
硝子体剥離	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害								
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腹部不快感	14 (1.7)	7 (0.8)	1 (0.1)	22 (2.6)	5 (1.2)	2 (0.5)	1 (0.2)	8 (1.9)
腹部膨満	29 (3.4)	11 (1.3)	0 (0.0)	40 (4.7)	9 (2.1)	2 (0.5)	1 (0.2)	12 (2.8)
腹部ヘルニア	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
閉塞を伴う腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腹部腫瘤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腹痛	26 (3.1)	19 (2.3)	7 (0.8)	52 (6.2)	14 (3.3)	8 (1.9)	4 (0.9)	26 (6.1)
下腹部痛	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	1 (0.2)	3 (0.7)	0 (0.0)	4 (0.9)
上腹部痛	29 (3.4)	15 (1.8)	3 (0.4)	47 (5.6)	27 (6.4)	7 (1.7)	1 (0.2)	35 (8.3)
腹部硬直	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-27

156-251

NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
腹部圧痛	6 (0.7)	2 (0.2)	0 (0.0)	8 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
裂肛	1 (0.1)	3 (0.4)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
痔瘻	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
便通不規則	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
結腸ポリープ	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
便秘	50 (5.9)	11 (1.3)	1 (0.1)	62 (7.4)	4 (0.9)	3 (0.7)	1 (0.2)	8 (1.9)
クローン病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
齲菌	0 (0.0)	5 (0.6)	0 (0.0)	5 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
歯不快感	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
下痢	82 (9.7)	26 (3.1)	5 (0.6)	113 (13.4)	32 (7.5)	11 (2.6)	0 (0.0)	43 (10.1)
憩室	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸憩室	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
口内乾燥	115 (13.6)	30 (3.6)	8 (0.9)	153 (18.1)	47 (11.1)	11 (2.6)	2 (0.5)	60 (14.2)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
十二指腸炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	55 (6.5)	12 (1.4)	2 (0.2)	69 (8.2)	11 (2.6)	4 (0.9)	0 (0.0)	15 (3.5)
嚥下障害	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
小腸炎	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
心窩部不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
びらん性十二指腸炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
大腿ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	6 (0.7)	2 (0.2)	0 (0.0)	8 (0.9)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
食中毒	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
機能的胃腸障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
胃障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃ポリープ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
胃潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
胃炎	7 (0.8)	3 (0.4)	0 (0.0)	10 (1.2)	2 (0.5)	3 (0.7)	0 (0.0)	5 (1.2)
びらん性胃炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
消化管運動過剰	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸の炎症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃食道逆流性疾患	22 (2.6)	9 (1.1)	1 (0.1)	32 (3.8)	9 (2.1)	3 (0.7)	0 (0.0)	12 (2.8)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
歯肉退縮	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
歯肉炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
舌痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
痔核	7 (0.8)	1 (0.1)	0 (0.0)	8 (0.9)	7 (1.7)	1 (0.2)	0 (0.0)	8 (1.9)
裂孔ヘルニア	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
胃酸過多	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
口の感覚鈍麻	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
回腸炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単径ヘルニア	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	3 (0.7)	3 (0.7)	0 (0.0)	6 (1.4)
内ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
過敏性腸症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
口唇乾燥	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
口唇腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下部消化管出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吸収不良	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
メレナ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
悪心	61 (7.2)	21 (2.5)	0 (0.0)	82 (9.7)	35 (8.3)	17 (4.0)	0 (0.0)	52 (12.3)
嚥下痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
食道炎	2 (0.2)	3 (0.4)	0 (0.0)	5 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
口腔障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腭嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
肛門周囲痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
吐き戻し	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
S状結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
口内炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌苔	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
舌乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
舌粘膜剥脱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯の障害	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
歯痛	3 (0.4)	6 (0.7)	0 (0.0)	9 (1.1)	5 (1.2)	2 (0.5)	0 (0.0)	7 (1.7)
臍ヘルニア	15 (1.8)	4 (0.5)	1 (0.1)	20 (2.4)	5 (1.2)	2 (0.5)	0 (0.0)	7 (1.7)
閉塞性臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
嘔吐	43 (5.1)	22 (2.6)	2 (0.2)	67 (7.9)	24 (5.7)	12 (2.8)	1 (0.2)	37 (8.7)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
一般・全身障害および投与部位の状態								
無力症	30 (3.6)	21 (2.5)	6 (0.7)	57 (6.8)	13 (3.1)	8 (1.9)	4 (0.9)	25 (5.9)
腋窩痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胸部不快感	12 (1.4)	1 (0.1)	0 (0.0)	13 (1.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胸痛	16 (1.9)	17 (2.0)	3 (0.4)	36 (4.3)	4 (0.9)	5 (1.2)	0 (0.0)	9 (2.1)
悪寒	9 (1.1)	3 (0.4)	0 (0.0)	12 (1.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
嚢胞	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	4 (0.9)	1 (0.2)	0 (0.0)	5 (1.2)
医療機器位置異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
早期満腹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
運動耐性低下	2 (0.2)	0 (0.0)	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪組織増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	84 (10.0)	28 (3.3)	6 (0.7)	118 (14.0)	31 (7.3)	12 (2.8)	2 (0.5)	45 (10.6)
異常感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	6 (0.7)	2 (0.2)	1 (0.1)	9 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
びくびく感	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルニア	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
治癒不良	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	3 (0.4)	4 (0.5)	0 (0.0)	7 (0.8)	3 (0.7)	2 (0.5)	0 (0.0)	5 (1.2)
易刺激性	4 (0.5)	0 (0.0)	1 (0.1)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
倦怠感	11 (1.3)	1 (0.1)	0 (0.0)	12 (1.4)	4 (0.9)	4 (0.9)	1 (0.2)	9 (2.1)
粘膜乾燥	6 (0.7)	1 (0.1)	1 (0.1)	8 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
小結節	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
浮腫	7 (0.8)	3 (0.4)	0 (0.0)	10 (1.2)	5 (1.2)	1 (0.2)	1 (0.2)	7 (1.7)
末梢性浮腫	63 (7.5)	11 (1.3)	0 (0.0)	74 (8.8)	33 (7.8)	7 (1.7)	0 (0.0)	40 (9.4)
疼痛	8 (0.9)	6 (0.7)	0 (0.0)	14 (1.7)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
発熱	18 (2.1)	14 (1.7)	0 (0.0)	32 (3.8)	17 (4.0)	15 (3.5)	1 (0.2)	33 (7.8)
不活発	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
恥骨上痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
一般・全身障害および投与部位の状態								
腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口渇	255 (30.2)	140 (16.6)	30 (3.6)	425 (50.4)	65 (15.3)	12 (2.8)	4 (0.9)	81 (19.1)
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管穿刺部位血腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害								
胆道ジスキネジー	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	7 (0.8)	5 (0.6)	0 (0.0)	12 (1.4)	1 (0.2)	7 (1.7)	1 (0.2)	9 (2.1)
肝嚢胞破裂	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓痛	4 (0.5)	2 (0.2)	1 (0.1)	7 (0.8)	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.7)
脂肪肝	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	6 (0.7)	3 (0.4)	0 (0.0)	9 (1.1)	1 (0.2)	0 (0.0)	2 (0.5)	3 (0.7)
高ビリルビン血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝圧痛	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
免疫系障害								
アレルギー性浮腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷アレルギー	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシーショック	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
造影剤アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
薬物過敏症	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.4)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
食物アレルギー	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	3 (0.4)	4 (0.5)	0 (0.0)	7 (0.8)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
複合アレルギー	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	16 (1.9)	2 (0.2)	0 (0.0)	18 (2.1)	5 (1.2)	5 (1.2)	0 (0.0)	10 (2.4)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.5)
四肢膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
急性扁桃炎	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
真菌性肛門感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	3 (0.7)	3 (0.7)
細菌性関節炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
感染性関節炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
細菌尿	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
バルトリン腺膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
気管支炎	32 (3.8)	21 (2.5)	1 (0.1)	54 (6.4)	19 (4.5)	11 (2.6)	0 (0.0)	30 (7.1)
ウイルス性気管支炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
カンジダ症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
蜂巣炎	4 (0.5)	0 (0.0)	1 (0.1)	5 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
眼窩蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
子宮頸管炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
クロストリジウム性大腸炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	6 (0.7)	1 (0.1)	0 (0.0)	7 (0.8)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
サイトメガロウイルス感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	3 (0.4)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳感染	6 (0.7)	16 (1.9)	0 (0.0)	22 (2.6)	4 (0.9)	3 (0.7)	0 (0.0)	7 (1.7)
耳垂感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
遊走性紅斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	2 (0.5)	0 (0.0)	3 (0.7)
眼瞼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
熱性感染症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
毛包炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
皮膚真菌感染	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
せつ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	28 (3.3)	20 (2.4)	3 (0.4)	51 (6.0)	7 (1.7)	7 (1.7)	1 (0.2)	15 (3.5)
ノロウイルス性胃腸炎	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	10 (1.2)	5 (0.6)	3 (0.4)	18 (2.1)	4 (0.9)	2 (0.5)	0 (0.0)	6 (1.4)
細菌性消化管感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性消化管感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
ウイルス性消化管感染	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
陰部ヘルペス	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
泌尿生殖器感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジアルジア症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
歯肉膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H 1 N 1 インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.7)	0 (0.0)	4 (0.9)
ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
ヘリコバクター感染	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
B型肝炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C型肝炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
ヘルペスウイルス感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
帯状疱疹	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
麦粒腫	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
感染性嚢腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
伝染性単核症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
インフルエンザ	48 (5.7)	20 (2.4)	0 (0.0)	68 (8.1)	19 (4.5)	12 (2.8)	1 (0.2)	32 (7.5)
腎感染	2 (0.2)	1 (0.1)	2 (0.2)	5 (0.6)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
迷路炎	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
喉頭炎	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
肝膿瘍	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
下気道感染	6 (0.7)	1 (0.1)	0 (0.0)	7 (0.8)	0 (0.0)	3 (0.7)	0 (0.0)	3 (0.7)
ライム病	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
リンパ管炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マラリア	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
マイコプラズマ感染	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻咽頭炎	109 (12.9)	34 (4.0)	0 (0.0)	143 (17.0)	48 (11.3)	18 (4.2)	0 (0.0)	66 (15.6)
線虫症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
口腔カンジダ症	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔真菌感染	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	8 (0.9)	0 (0.0)	0 (0.0)	8 (0.9)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
外耳炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	2 (0.2)	3 (0.4)	0 (0.0)	5 (0.6)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
急性中耳炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳頭腫ウイルス感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
爪囲炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
会陰膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
百日咳	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
咽頭炎	10 (1.2)	3 (0.4)	0 (0.0)	13 (1.5)	8 (1.9)	2 (0.5)	0 (0.0)	10 (2.4)
レンサ球菌性咽頭炎	3 (0.4)	4 (0.5)	0 (0.0)	7 (0.8)	0 (0.0)	4 (0.9)	0 (0.0)	4 (0.9)
肺炎	4 (0.5)	5 (0.6)	2 (0.2)	11 (1.3)	2 (0.5)	3 (0.7)	0 (0.0)	5 (1.2)
前立腺感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腎盂腎炎	1 (0.1)	7 (0.8)	0 (0.0)	8 (0.9)	1 (0.2)	6 (1.4)	2 (0.5)	9 (2.1)
腎嚢胞感染	3 (0.4)	4 (0.5)	0 (0.0)	7 (0.8)	6 (1.4)	3 (0.7)	1 (0.2)	10 (2.4)
気道感染	1 (0.1)	4 (0.5)	0 (0.0)	5 (0.6)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
ウイルス性気道感染	3 (0.4)	1 (0.1)	1 (0.1)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	11 (1.3)	0 (0.0)	0 (0.0)	11 (1.3)	10 (2.4)	0 (0.0)	0 (0.0)	10 (2.4)
卵管卵巣炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
副鼻腔炎	35 (4.2)	15 (1.8)	1 (0.1)	51 (6.0)	13 (3.1)	10 (2.4)	0 (0.0)	23 (5.4)
皮膚感染	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ブドウ球菌性咽頭炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
糞線虫症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癩風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
扁桃炎	4 (0.5)	7 (0.8)	0 (0.0)	11 (1.3)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
歯膿瘍	3 (0.4)	4 (0.5)	0 (0.0)	7 (0.8)	4 (0.9)	1 (0.2)	0 (0.0)	5 (1.2)
歯感染	7 (0.8)	1 (0.1)	0 (0.0)	8 (0.9)	4 (0.9)	1 (0.2)	0 (0.0)	5 (1.2)
気管炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
気管気管支炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	44 (5.2)	31 (3.7)	1 (0.1)	76 (9.0)	26 (6.1)	12 (2.8)	0 (0.0)	38 (9.0)
尿路感染	52 (6.2)	28 (3.3)	1 (0.1)	81 (9.6)	29 (6.8)	27 (6.4)	3 (0.7)	59 (13.9)
泌尿生殖器細菌感染	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膣感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
細菌性膣炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
ウイルス感染	14 (1.7)	6 (0.7)	1 (0.1)	21 (2.5)	11 (2.6)	2 (0.5)	0 (0.0)	13 (3.1)
ウイルス性鼻炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
外陰部膣カンジダ症	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
外陰膣真菌感染	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	4 (0.9)	0 (0.0)	0 (0.0)	4 (0.9)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
創傷感染	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膿創	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症								
腹部損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足関節部骨折	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
節足動物咬傷	8 (0.9)	0 (0.0)	0 (0.0)	8 (0.9)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
背部損傷	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咬刺傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨損傷	0 (0.0)	2 (0.2)	2 (0.2)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
挫傷	9 (1.1)	5 (0.6)	0 (0.0)	14 (1.7)	1 (0.2)	2 (0.5)	0 (0.0)	3 (0.7)
角膜擦過傷	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
擦過傷	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の貫通性外傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	3 (0.4)	1 (0.1)	1 (0.1)	5 (0.6)	6 (1.4)	0 (0.0)	0 (0.0)	6 (1.4)
足骨折	0 (0.0)	5 (0.6)	0 (0.0)	5 (0.6)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
眼内異物	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
頭部損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
熱疲労	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸脛靱帯症候群	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
切開部位痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
関節脱臼	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	2 (0.5)	0 (0.0)	3 (0.7)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
傷害、中毒および処置合併症								
関節損傷	4 (0.5)	5 (0.6)	0 (0.0)	9 (1.1)	3 (0.7)	3 (0.7)	1 (0.2)	7 (1.7)
裂傷	3 (0.4)	2 (0.2)	1 (0.1)	6 (0.7)	1 (0.2)	2 (0.5)	1 (0.2)	4 (0.9)
靱帯損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
靱帯断裂	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
靱帯捻挫	7 (0.8)	5 (0.6)	0 (0.0)	12 (1.4)	7 (1.7)	2 (0.5)	0 (0.0)	9 (2.1)
四肢損傷	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	5 (1.2)	0 (0.0)	5 (1.2)
口唇損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腰椎骨折	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	2 (0.2)	2 (0.2)	1 (0.1)	5 (0.6)	0 (0.0)	5 (1.2)	0 (0.0)	5 (1.2)
多発骨折	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
筋断裂	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肉離れ	7 (0.8)	2 (0.2)	0 (0.0)	9 (1.1)	4 (0.9)	1 (0.2)	0 (0.0)	5 (1.2)
頸部損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲血腫	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
処置後合併症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
処置後血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
処置後出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
処置による疼痛	2 (0.2)	6 (0.7)	0 (0.0)	8 (0.9)	2 (0.5)	4 (0.9)	0 (0.0)	6 (1.4)
恥骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
橈骨骨折	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	1 (0.1)	1 (0.1)	2 (0.2)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
骨格損傷	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
軟部組織損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎骨折	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス骨折	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の擦過傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱損傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腱断裂	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
脛骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
傷害、中毒および処置合併症								
歯牙破折	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
創傷	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
手首関節骨折	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
臨床検査								
活性化部分トロンボプラスチン時間延長	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
アラニン・アミノトランスフェラーゼ増加	25 (3.0)	9 (1.1)	2 (0.2)	36 (4.3)	16 (3.8)	1 (0.2)	0 (0.0)	17 (4.0)
アスパラギン酸アミノトランスフェラーゼ増加	25 (3.0)	7 (0.8)	1 (0.1)	33 (3.9)	15 (3.5)	1 (0.2)	0 (0.0)	16 (3.8)
細菌検査陽性	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
血中アルカリホスファターゼ増加	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中ビリルビン増加	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
血中カルシウム増加	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	13 (1.5)	1 (0.1)	0 (0.0)	14 (1.7)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
血中クレアチンホスホキナーゼ増加	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	99 (11.7)	29 (3.4)	0 (0.0)	128 (15.2)	51 (12.0)	16 (3.8)	0 (0.0)	67 (15.8)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
血中ブドウ糖増加	7 (0.8)	0 (0.0)	0 (0.0)	7 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血中乳酸脱水素酵素増加	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中副甲状腺ホルモン増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
血圧低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
拡張期血圧上昇	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血圧上昇	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	3 (0.7)	2 (0.5)	0 (0.0)	5 (1.2)
血中ナトリウム減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム増加	13 (1.5)	1 (0.1)	0 (0.0)	14 (1.7)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血中テストステロン減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
血中尿素増加	8 (0.9)	2 (0.2)	0 (0.0)	10 (1.2)	9 (2.1)	3 (0.7)	0 (0.0)	12 (2.8)
血中尿酸増加	16 (1.9)	3 (0.4)	0 (0.0)	19 (2.3)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
尿中血陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C-反応性蛋白増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心雑音	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
腎クレアチニン・クリアランス増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
シスタチンC増加	6 (0.7)	0 (0.0)	0 (0.0)	6 (0.7)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
心電図再分極異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心電図異常T波	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好酸球数増加	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
大腸菌検査陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
γ-グルタミルトランスフェラーゼ増加	16 (1.9)	6 (0.7)	0 (0.0)	22 (2.6)	8 (1.9)	0 (0.0)	1 (0.2)	9 (2.1)
胃内pH低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
ヘマトクリット増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心拍数不整	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝酵素異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	9 (1.1)	7 (0.8)	1 (0.1)	17 (2.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ヒト乳頭腫ウイルス検査陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
INR増加	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼圧上昇	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
リパーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝機能検査異常	2 (0.2)	4 (0.5)	0 (0.0)	6 (0.7)	2 (0.5)	0 (0.0)	1 (0.2)	3 (0.7)
季肋下肝触知	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低比重リポ蛋白減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
リンパ球形態異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球容積減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
平均赤血球容積増加	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好中球数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
好中球数増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
便潜血陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
血小板数増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
QOL低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
トランスアミナーゼ上昇	2 (0.2)	4 (0.5)	2 (0.2)	8 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
卵巣超音波検査異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿浸透圧低下	7 (0.8)	2 (0.2)	0 (0.0)	9 (1.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿量増加	12 (1.4)	2 (0.2)	1 (0.1)	15 (1.8)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
ビタミンD減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
ウエスト周囲径増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	29 (3.4)	9 (1.1)	0 (0.0)	38 (4.5)	9 (2.1)	7 (1.7)	0 (0.0)	16 (3.8)
体重増加	32 (3.8)	11 (1.3)	0 (0.0)	43 (5.1)	14 (3.3)	5 (1.2)	0 (0.0)	19 (4.5)
白血球数減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
白血球数増加	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	4 (0.9)	0 (0.0)	0 (0.0)	4 (0.9)
尿中白血球	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿中白血球陽性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
代謝および栄養障害								
アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
食欲減退	43 (5.1)	13 (1.5)	1 (0.1)	57 (6.8)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
脱水	8 (0.9)	6 (0.7)	2 (0.2)	16 (1.9)	3 (0.7)	6 (1.4)	1 (0.2)	10 (2.4)
糖尿病	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体液貯留	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
食物渴望	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
痛風	12 (1.4)	14 (1.7)	0 (0.0)	26 (3.1)	3 (0.7)	2 (0.5)	0 (0.0)	5 (1.2)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
高カルシウム血症	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
高コレステロール血症	20 (2.4)	3 (0.4)	0 (0.0)	23 (2.7)	10 (2.4)	2 (0.5)	0 (0.0)	12 (2.8)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
高血糖	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	9 (2.1)	0 (0.0)	0 (0.0)	9 (2.1)
高カリウム血症	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
高脂血症	8 (0.9)	1 (0.1)	0 (0.0)	9 (1.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
高ナトリウム血症	22 (2.6)	5 (0.6)	0 (0.0)	27 (3.2)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
高リン酸塩血症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	18 (2.1)	5 (0.6)	0 (0.0)	23 (2.7)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
低アルブミン血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
低血糖症	6 (0.7)	0 (0.0)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	3 (0.4)	3 (0.4)	0 (0.0)	6 (0.7)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
低マグネシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
低リン酸血症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鉄欠乏	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ラクトース不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝性アシドーシス	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
代謝および栄養障害								
過体重	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	50 (5.9)	44 (5.2)	6 (0.7)	100 (11.9)	12 (2.8)	5 (1.2)	0 (0.0)	17 (4.0)
2 型糖尿病	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン B 1 2 欠乏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン D 欠乏	8 (0.9)	1 (0.1)	0 (0.0)	9 (1.1)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
体重変動	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害								
関節痛	42 (5.0)	21 (2.5)	0 (0.0)	63 (7.5)	16 (3.8)	6 (1.4)	1 (0.2)	23 (5.4)
関節炎	4 (0.5)	2 (0.2)	0 (0.0)	6 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
反応性関節炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	66 (7.8)	33 (3.9)	6 (0.7)	105 (12.5)	39 (9.2)	26 (6.1)	5 (1.2)	70 (16.5)
骨痛	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
滑液包石灰化	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
軟骨肥厚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部脊柱管狭窄症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
尾骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
肋軟骨炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外骨腫	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋膜炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
瘻孔	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	7 (0.8)	4 (0.5)	0 (0.0)	11 (1.3)	5 (1.2)	2 (0.5)	0 (0.0)	7 (1.7)
足変形	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
痛風性関節炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単径部痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
椎間板変性症	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板障害	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
筋骨格系および結合組織障害								
椎間板突出	3 (0.4)	7 (0.8)	0 (0.0)	10 (1.2)	3 (0.7)	1 (0.2)	1 (0.2)	5 (1.2)
関節滲出液	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節可動域低下	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
関節腫脹	9 (1.1)	0 (0.0)	0 (0.0)	9 (1.1)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
靱帯障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
靱帯痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢非対称	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	25 (3.0)	8 (0.9)	0 (0.0)	33 (3.9)	9 (2.1)	4 (0.9)	0 (0.0)	13 (3.1)
筋緊張	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
筋攣縮	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
筋力低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
筋骨格系胸痛	6 (0.7)	3 (0.4)	0 (0.0)	9 (1.1)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
筋骨格不快感	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格痛	19 (2.3)	10 (1.2)	1 (0.1)	30 (3.6)	10 (2.4)	4 (0.9)	1 (0.2)	15 (3.5)
筋骨格硬直	4 (0.5)	1 (0.1)	1 (0.1)	6 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋肉痛	28 (3.3)	11 (1.3)	0 (0.0)	39 (4.6)	7 (1.7)	3 (0.7)	1 (0.2)	11 (2.6)
筋炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部痛	10 (1.2)	10 (1.2)	1 (0.1)	21 (2.5)	7 (1.7)	3 (0.7)	0 (0.0)	10 (2.4)
変形性関節症	4 (0.5)	1 (0.1)	2 (0.2)	7 (0.8)	2 (0.5)	1 (0.2)	1 (0.2)	4 (0.9)
骨関節障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
骨減少症	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
骨粗鬆症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	27 (3.2)	9 (1.1)	0 (0.0)	36 (4.3)	15 (3.5)	10 (2.4)	0 (0.0)	25 (5.9)
顎痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
関節周囲炎	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
足底筋膜炎	4 (0.5)	3 (0.4)	0 (0.0)	7 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
筋骨格系および結合組織障害								
恥骨痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
関節リウマチ	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
仙腸骨炎	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側弯症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
重感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
脊椎障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
脊椎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
滑液嚢腫	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腱障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腱痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腱炎	11 (1.3)	5 (0.6)	0 (0.0)	16 (1.9)	6 (1.4)	4 (0.9)	0 (0.0)	10 (2.4)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
斜頸	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）								
アクロコルドン	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
基底細胞癌	5 (0.6)	3 (0.4)	0 (0.0)	8 (0.9)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房の良性新生物	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
甲状腺の良性新生物	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳癌	0 (0.0)	1 (0.1)	2 (0.2)	3 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
子宮頸部癌第0期	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真珠腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
慢性骨髄性白血病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
カポジ肉腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
悪性黒色腫	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表皮内悪性黒色腫	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）								
メラノサイト性母斑	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
下垂体の良性腫瘍	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性角化症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
皮膚乳頭腫	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
扁平上皮癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
甲状腺新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
子宮平滑筋腫	4 (0.5)	3 (0.4)	0 (0.0)	7 (0.8)	3 (0.7)	1 (0.2)	1 (0.2)	5 (1.2)
神経系障害								
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
健忘	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
失声症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
くも膜嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平衡障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
手根管症候群	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
協調運動異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳神経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
意識レベルの低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	3 (0.4)	3 (0.4)	1 (0.1)	7 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
浮動性めまい	70 (8.3)	21 (2.5)	1 (0.1)	92 (10.9)	22 (5.2)	11 (2.6)	1 (0.2)	34 (8.0)
労作性めまい	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	14 (1.7)	3 (0.4)	0 (0.0)	17 (2.0)	6 (1.4)	1 (0.2)	0 (0.0)	7 (1.7)
脳症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	142 (16.8)	46 (5.5)	16 (1.9)	204 (24.2)	79 (18.6)	22 (5.2)	5 (1.2)	106 (25.0)
味覚過敏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	9 (1.1)	3 (0.4)	0 (0.0)	12 (1.4)	4 (0.9)	3 (0.7)	0 (0.0)	7 (1.7)
反射減弱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋緊張低下	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	2 (0.5)	1 (0.2)	3 (0.7)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
嗜眠	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
意識消失	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
精神的機能障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
片頭痛	16 (1.9)	4 (0.5)	1 (0.1)	21 (2.5)	7 (1.7)	3 (0.7)	0 (0.0)	10 (2.4)
前兆を伴う片頭痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
末梢性ニューロパチー	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
起立不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	13 (1.5)	5 (0.6)	1 (0.1)	19 (2.3)	11 (2.6)	2 (0.5)	0 (0.0)	13 (3.1)
パーキンソン病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パーキンソニズム	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
失神寸前の状態	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
根症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
下肢静止不能症候群	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
坐骨神経痛	3 (0.4)	4 (0.5)	1 (0.1)	8 (0.9)	3 (0.7)	2 (0.5)	1 (0.2)	6 (1.4)
感覚障害	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
くも膜下出血	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
失神	6 (0.7)	10 (1.2)	0 (0.0)	16 (1.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
緊張性頭痛	0 (0.0)	3 (0.4)	0 (0.0)	3 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
一過性脳虚血発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	2 (0.5)
振戦	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
トンネル状視野	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
椎骨動脈解離	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第7脳神経麻痺	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
精神障害								
異常な夢	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
激越	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不安	16 (1.9)	10 (1.2)	3 (0.4)	29 (3.4)	5 (1.2)	3 (0.7)	0 (0.0)	8 (1.9)
注意欠陥多動性障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自閉症スペクトラム障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神緩慢	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
燃え尽き症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
うつ病	20 (2.4)	15 (1.8)	3 (0.4)	38 (4.5)	10 (2.4)	8 (1.9)	0 (0.0)	18 (4.2)
睡眠異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	23 (2.7)	16 (1.9)	6 (0.7)	45 (5.3)	11 (2.6)	8 (1.9)	0 (0.0)	19 (4.5)
リビドー減退	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
性欲障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
リビドー消失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大うつ病	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
気分変化	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分動揺	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
神経過敏	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ニコチン依存	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
悪夢	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	2 (0.2)	3 (0.4)	0 (0.0)	5 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
パニック反応	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
心身症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
落ち着きのなさ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
統合失調症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
精神障害								
睡眠障害	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
夢遊症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス	8 (0.9)	1 (0.1)	0 (0.0)	9 (1.1)	9 (2.1)	1 (0.2)	0 (0.0)	10 (2.4)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腎および尿路障害								
アルブミン尿	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱脱	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
膀胱痙縮	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
着色尿	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
非感染性膀胱炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	11 (1.3)	3 (0.4)	0 (0.0)	14 (1.7)	7 (1.7)	2 (0.5)	0 (0.0)	9 (2.1)
遺尿	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血尿	47 (5.6)	16 (1.9)	5 (0.6)	68 (8.1)	43 (10.1)	16 (3.8)	2 (0.5)	61 (14.4)
水腎症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎腫大	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
白血球尿	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	4 (0.9)	0 (0.0)	0 (0.0)	4 (0.9)
尿意切迫	6 (0.7)	2 (0.2)	0 (0.0)	8 (0.9)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
腎結石症	5 (0.6)	8 (0.9)	2 (0.2)	15 (1.8)	5 (1.2)	5 (1.2)	3 (0.7)	13 (3.1)
夜間頻尿	177 (21.0)	91 (10.8)	10 (1.2)	278 (33.0)	53 (12.5)	8 (1.9)	0 (0.0)	61 (14.4)
乏尿	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	85 (10.1)	56 (6.6)	19 (2.3)	160 (19.0)	14 (3.3)	6 (1.4)	2 (0.5)	22 (5.2)
多尿	152 (18.0)	135 (16.0)	41 (4.9)	328 (38.9)	62 (14.6)	15 (3.5)	1 (0.2)	78 (18.4)
蛋白尿	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.4)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
腎仙痛	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.4)	0 (0.0)	5 (1.2)	0 (0.0)	5 (1.2)
腎嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
腎および尿路障害								
腎嚢胞出血	1 (0.1)	4 (0.5)	1 (0.1)	6 (0.7)	2 (0.5)	3 (0.7)	2 (0.5)	7 (1.7)
腎嚢胞破裂	3 (0.4)	4 (0.5)	0 (0.0)	7 (0.8)	1 (0.2)	3 (0.7)	1 (0.2)	5 (1.2)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
急性腎不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.5)
慢性腎不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	7 (0.8)	4 (0.5)	0 (0.0)	11 (1.3)	4 (0.9)	3 (0.7)	0 (0.0)	7 (1.7)
腎臓痛	125 (14.8)	95 (11.3)	28 (3.3)	248 (29.4)	71 (16.7)	65 (15.3)	24 (5.7)	160 (37.7)
有痛性排尿困難	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿道狭窄	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
排尿躊躇	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	5 (0.6)	4 (0.5)	0 (0.0)	9 (1.1)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
尿閉	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
尿流量減少	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
生殖系および乳房障害								
子宮付属器痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	1 (0.1)	3 (0.4)	0 (0.0)	4 (0.5)	1 (0.2)	3 (0.7)	0 (0.0)	4 (0.9)
精子無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
萎縮性外陰陰炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳房腫瘍	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部上皮異形成	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
子宮頸管ポリープ	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性交出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱瘤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
生殖系および乳房障害								
月経困難症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.5)	2 (0.5)	0 (0.0)	4 (0.9)
性交困難	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
精巣上体嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精巣上体炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
勃起不全	5 (0.6)	3 (0.4)	2 (0.2)	10 (1.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳汁漏出症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血精液症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過少月経	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
機能性子宮出血	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多	8 (0.9)	6 (0.7)	0 (0.0)	14 (1.7)	7 (1.7)	2 (0.5)	0 (0.0)	9 (2.1)
月経障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
不規則月経	7 (0.8)	1 (0.1)	0 (0.0)	8 (0.9)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
不正子宮出血	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.2)	2 (0.5)	0 (0.0)	3 (0.7)
卵巣嚢胞	4 (0.5)	1 (0.1)	1 (0.1)	6 (0.7)	6 (1.4)	0 (0.0)	0 (0.0)	6 (1.4)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
卵巣捻転	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤脱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ペイロニー病	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経後出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.5)	1 (0.2)	2 (0.5)	0 (0.0)	3 (0.7)
前立腺腫大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
生殖系および乳房障害								
精嚢嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
精嚢痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
子宮脱	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
嚢嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚢分泌物	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
嚢出血	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精索静脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
外陰陰乾燥	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
呼吸器、胸郭および縦隔障害								
喘息	2 (0.2)	5 (0.6)	0 (0.0)	7 (0.8)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
気管支痙攣	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
咳嗽	58 (6.9)	16 (1.9)	0 (0.0)	74 (8.8)	23 (5.4)	8 (1.9)	0 (0.0)	31 (7.3)
咽喉乾燥	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
発声障害	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	12 (1.4)	6 (0.7)	2 (0.2)	20 (2.4)	1 (0.2)	5 (1.2)	0 (0.0)	6 (1.4)
安静時呼吸困難	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	1 (0.1)	3 (0.4)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻出血	6 (0.7)	1 (0.1)	0 (0.0)	7 (0.8)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
過換気	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭嚢腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肺障害	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
鼻乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
鼻閉塞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻中隔彎曲	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
呼吸器、胸郭および縦隔障害								
口腔咽頭痛	32 (3.8)	3 (0.4)	0 (0.0)	35 (4.2)	9 (2.1)	2 (0.5)	0 (0.0)	11 (2.6)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
胸水	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺塞栓症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺線維症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気道うっ血	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	4 (0.9)	0 (0.0)	0 (0.0)	4 (0.9)
鼻漏	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
低音性連続性ラ音	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔うっ血	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
睡眠時無呼吸症候群	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
いびき	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
咽喉絞扼感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
扁桃肥大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
扁桃結石	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
皮膚および皮下組織障害								
ざ瘡	7 (0.8)	4 (0.5)	0 (0.0)	11 (1.3)	5 (1.2)	2 (0.5)	0 (0.0)	7 (1.7)
日光性角化症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	12 (1.4)	3 (0.4)	0 (0.0)	15 (1.8)	2 (0.5)	5 (1.2)	0 (0.0)	7 (1.7)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
アンドロゲン性脱毛症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
皮膚嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚炎	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
アレルギー性皮膚炎	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
接触性皮膚炎	6 (0.7)	1 (0.1)	0 (0.0)	7 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	39 (4.6)	1 (0.1)	1 (0.1)	41 (4.9)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
斑状出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
湿疹	10 (1.2)	2 (0.2)	0 (0.0)	12 (1.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
紅斑	7 (0.8)	0 (0.0)	0 (0.0)	7 (0.8)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
過剰皮膚	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
紅色汗疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	3 (0.4)	2 (0.2)	0 (0.0)	5 (0.6)	4 (0.9)	0 (0.0)	0 (0.0)	4 (0.9)
乏汗症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内出血発生の増加傾向	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嵌入爪	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
機械性蕁麻疹	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
神経皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	3 (0.4)	1 (0.1)	1 (0.1)	5 (0.6)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.5)
爪破損	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚疼痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
光線過敏性反応	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
秕糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ばら色秕糠疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
そう痒症	21 (2.5)	4 (0.5)	0 (0.0)	25 (3.0)	9 (2.1)	3 (0.7)	0 (0.0)	12 (2.8)
全身性そう痒症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	24 (2.8)	5 (0.6)	0 (0.0)	29 (3.4)	3 (0.7)	2 (0.5)	0 (0.0)	5 (1.2)
紅斑性皮疹	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
そう痒性皮疹	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂腺障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素過剰	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
皮膚病変	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.5)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚潰瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
うっ滞性皮膚炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
蕁麻疹	3 (0.4)	3 (0.4)	2 (0.2)	8 (0.9)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
慢性蕁麻疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尋常性白斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
社会環境								
閉経	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
外科および内科処置								
収れん薬療法	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジフテリア免疫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管拡張および子宮内搔爬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ビタミン補給	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-27

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NT-8.2.3 Incidence of All Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血管障害								
血管障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
動脈硬化症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の血圧	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
深部静脈血栓症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
血腫	3 (0.4)	1 (0.1)	1 (0.1)	5 (0.6)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	6 (0.7)	1 (0.1)	1 (0.1)	8 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
高血圧	208 (24.7)	72 (8.5)	3 (0.4)	283 (33.6)	109 (25.7)	46 (10.8)	4 (0.9)	159 (37.5)
高血圧クリーゼ	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	17 (2.0)	9 (1.1)	2 (0.2)	28 (3.3)	7 (1.7)	5 (1.2)	1 (0.2)	13 (3.1)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
微小血管症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	3 (0.4)	0 (0.0)	1 (0.1)	4 (0.5)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
末梢冷感	11 (1.3)	0 (0.0)	0 (0.0)	11 (1.3)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
静脈炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レイノー現象	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血栓性静脈炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
表在性血栓性静脈炎	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
静脈瘤	4 (0.5)	3 (0.4)	0 (0.0)	7 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
静脈不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
血液およびリンパ系障害			
貧血	1 (0.1)	2 (0.4)	3 (0.2)
好酸球増加症	1 (0.1)	1 (0.2)	2 (0.1)
鉄欠乏性貧血	1 (0.1)	0 (0.0)	1 (0.1)
白血球増加症	1 (0.1)	0 (0.0)	1 (0.1)
白血球減少症	1 (0.1)	1 (0.2)	2 (0.1)
リンパ節症	0 (0.0)	2 (0.4)	2 (0.1)
腎性貧血	0 (0.0)	1 (0.2)	1 (0.1)
血小板減少症	1 (0.1)	0 (0.0)	1 (0.1)
心臓障害			
狭心症	1 (0.1)	0 (0.0)	1 (0.1)
不整脈	2 (0.2)	2 (0.4)	4 (0.3)
心房細動	0 (0.0)	1 (0.2)	1 (0.1)
房室ブロック	1 (0.1)	0 (0.0)	1 (0.1)
右脚ブロック	1 (0.1)	0 (0.0)	1 (0.1)
心臓瘤	0 (0.0)	1 (0.2)	1 (0.1)
左室機能不全	1 (0.1)	0 (0.0)	1 (0.1)
左室不全	1 (0.1)	0 (0.0)	1 (0.1)
左室肥大	1 (0.1)	0 (0.0)	1 (0.1)
僧帽弁疾患	1 (0.1)	0 (0.0)	1 (0.1)
動悸	22 (2.3)	2 (0.4)	24 (1.7)
上室性頻脈	1 (0.1)	0 (0.0)	1 (0.1)
頻脈	5 (0.5)	2 (0.4)	7 (0.5)
心室性期外収縮	3 (0.3)	0 (0.0)	3 (0.2)
耳および迷路障害			
難聴	1 (0.1)	0 (0.0)	1 (0.1)
耳痛	1 (0.1)	1 (0.2)	2 (0.1)
耳鳴	2 (0.2)	0 (0.0)	2 (0.1)
回転性めまい	17 (1.8)	6 (1.2)	23 (1.6)
頭位性回転性めまい	1 (0.1)	0 (0.0)	1 (0.1)
内分泌障害			
続発性副甲状腺機能低下症	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
眼障害			
眼瞼炎	1 (0.1)	0 (0.0)	1 (0.1)
霰粒腫	1 (0.1)	0 (0.0)	1 (0.1)
結膜出血	1 (0.1)	0 (0.0)	1 (0.1)
結膜充血	0 (0.0)	1 (0.2)	1 (0.1)
眼乾燥	10 (1.0)	6 (1.2)	16 (1.1)
眼瞼浮腫	1 (0.1)	0 (0.0)	1 (0.1)
緑内障	3 (0.3)	0 (0.0)	3 (0.2)
眼充血	1 (0.1)	0 (0.0)	1 (0.1)
眼窩周囲浮腫	0 (0.0)	1 (0.2)	1 (0.1)
羞明	1 (0.1)	0 (0.0)	1 (0.1)
光視症	1 (0.1)	0 (0.0)	1 (0.1)
網膜剥離	1 (0.1)	0 (0.0)	1 (0.1)
霧視	2 (0.2)	0 (0.0)	2 (0.1)
視力障害	0 (0.0)	1 (0.2)	1 (0.1)
硝子体浮遊物	1 (0.1)	0 (0.0)	1 (0.1)
眼球乾燥	0 (0.0)	1 (0.2)	1 (0.1)
胃腸障害			
腹部不快感	8 (0.8)	2 (0.4)	10 (0.7)
腹部膨満	25 (2.6)	4 (0.8)	29 (2.0)
腹痛	13 (1.4)	7 (1.4)	20 (1.4)
上腹部痛	23 (2.4)	10 (2.1)	33 (2.3)
アフタ性口内炎	1 (0.1)	0 (0.0)	1 (0.1)
呼気臭	2 (0.2)	0 (0.0)	2 (0.1)
口唇のひび割れ	1 (0.1)	0 (0.0)	1 (0.1)
口唇炎	1 (0.1)	0 (0.0)	1 (0.1)
結腸ポリープ	2 (0.2)	0 (0.0)	2 (0.1)
便秘	52 (5.4)	3 (0.6)	55 (3.8)
齲歯	1 (0.1)	0 (0.0)	1 (0.1)
下痢	29 (3.0)	9 (1.9)	38 (2.6)
口内乾燥	152 (15.8)	56 (11.6)	208 (14.4)
十二指腸炎	1 (0.1)	0 (0.0)	1 (0.1)
消化不良	31 (3.2)	6 (1.2)	37 (2.6)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
嚥下障害	3 (0.3)	0 (0.0)	3 (0.2)
心窩部不快感	2 (0.2)	0 (0.0)	2 (0.1)
糞塊	0 (0.0)	1 (0.2)	1 (0.1)
鼓腸	4 (0.4)	0 (0.0)	4 (0.3)
胃障害	1 (0.1)	0 (0.0)	1 (0.1)
胃炎	3 (0.3)	1 (0.2)	4 (0.3)
胃腸障害	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動過剰	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動障害	1 (0.1)	0 (0.0)	1 (0.1)
胃食道逆流性疾患	12 (1.2)	5 (1.0)	17 (1.2)
歯肉炎	1 (0.1)	0 (0.0)	1 (0.1)
舌痛	3 (0.3)	0 (0.0)	3 (0.2)
血便排泄	1 (0.1)	0 (0.0)	1 (0.1)
痔出血	1 (0.1)	0 (0.0)	1 (0.1)
痔核	2 (0.2)	1 (0.2)	3 (0.2)
裂孔ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
胃酸過多	1 (0.1)	0 (0.0)	1 (0.1)
口 of 感覚鈍麻	1 (0.1)	1 (0.2)	2 (0.1)
過敏性腸症候群	0 (0.0)	1 (0.2)	1 (0.1)
口唇乾燥	6 (0.6)	2 (0.4)	8 (0.6)
弛緩歯	1 (0.1)	0 (0.0)	1 (0.1)
悪心	39 (4.1)	22 (4.6)	61 (4.2)
食道炎	2 (0.2)	0 (0.0)	2 (0.1)
口腔扁平苔癬	1 (0.1)	0 (0.0)	1 (0.1)
口腔内痛	1 (0.1)	0 (0.0)	1 (0.1)
口の錯感覚	1 (0.1)	0 (0.0)	1 (0.1)
レッチング	1 (0.1)	0 (0.0)	1 (0.1)
口内炎	0 (0.0)	1 (0.2)	1 (0.1)
舌苔	2 (0.2)	0 (0.0)	2 (0.1)
舌変色	2 (0.2)	0 (0.0)	2 (0.1)
舌乾燥	1 (0.1)	1 (0.2)	2 (0.1)
歯痛	1 (0.1)	1 (0.2)	2 (0.1)
臍ヘルニア	3 (0.3)	0 (0.0)	3 (0.2)
嘔吐	15 (1.6)	3 (0.6)	18 (1.2)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
一般・全身障害および投与部位の状態			
無力症	41 (4.3)	8 (1.7)	49 (3.4)
腋窩痛	1 (0.1)	0 (0.0)	1 (0.1)
胸部不快感	6 (0.6)	2 (0.4)	8 (0.6)
胸痛	11 (1.1)	1 (0.2)	12 (0.8)
悪寒	1 (0.1)	0 (0.0)	1 (0.1)
嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
運動耐性低下	1 (0.1)	0 (0.0)	1 (0.1)
疲労	94 (9.8)	23 (4.8)	117 (8.1)
異常感	1 (0.1)	1 (0.2)	2 (0.1)
冷感	7 (0.7)	0 (0.0)	7 (0.5)
酩酊感	1 (0.1)	0 (0.0)	1 (0.1)
熱感	2 (0.2)	0 (0.0)	2 (0.1)
びくびく感	1 (0.1)	0 (0.0)	1 (0.1)
易刺激性	3 (0.3)	0 (0.0)	3 (0.2)
倦怠感	9 (0.9)	4 (0.8)	13 (0.9)
粘膜乾燥	8 (0.8)	2 (0.4)	10 (0.7)
浮腫	7 (0.7)	2 (0.4)	9 (0.6)
末梢性浮腫	21 (2.2)	11 (2.3)	32 (2.2)
疼痛	2 (0.2)	0 (0.0)	2 (0.1)
発熱	3 (0.3)	1 (0.2)	4 (0.3)
不活発	0 (0.0)	1 (0.2)	1 (0.1)
腫脹	1 (0.1)	0 (0.0)	1 (0.1)
温度変化不耐症	1 (0.1)	0 (0.0)	1 (0.1)
口渇	525 (54.6)	93 (19.3)	618 (42.8)
肝胆道系障害			
胆管炎	1 (0.1)	0 (0.0)	1 (0.1)
胆嚢痛	1 (0.1)	0 (0.0)	1 (0.1)
肝嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
肝機能異常	11 (1.1)	1 (0.2)	12 (0.8)
肝炎	1 (0.1)	0 (0.0)	1 (0.1)
肝障害	4 (0.4)	0 (0.0)	4 (0.3)
免疫系障害			
過敏症	1 (0.1)	0 (0.0)	1 (0.1)
季節性アレルギー	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
感染症および寄生虫症			
急性扁桃炎	1 (0.1)	0 (0.0)	1 (0.1)
気管支炎	2 (0.2)	1 (0.2)	3 (0.2)
カンジダ症	0 (0.0)	1 (0.2)	1 (0.1)
蜂巣炎	0 (0.0)	1 (0.2)	1 (0.1)
膀胱炎	1 (0.1)	0 (0.0)	1 (0.1)
憩室炎	2 (0.2)	0 (0.0)	2 (0.1)
耳感染	0 (0.0)	1 (0.2)	1 (0.1)
耳垂感染	1 (0.1)	0 (0.0)	1 (0.1)
胃腸炎	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス性胃腸炎	2 (0.2)	0 (0.0)	2 (0.1)
歯肉膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
単純ヘルペス	0 (0.0)	1 (0.2)	1 (0.1)
帯状疱疹	0 (0.0)	3 (0.6)	3 (0.2)
麦粒腫	1 (0.1)	0 (0.0)	1 (0.1)
インフルエンザ	1 (0.1)	0 (0.0)	1 (0.1)
腎感染	1 (0.1)	0 (0.0)	1 (0.1)
喉頭炎	0 (0.0)	1 (0.2)	1 (0.1)
鼻咽頭炎	9 (0.9)	3 (0.6)	12 (0.8)
口腔カンジダ症	3 (0.3)	0 (0.0)	3 (0.2)
口腔真菌感染	2 (0.2)	0 (0.0)	2 (0.1)
口腔ヘルペス	1 (0.1)	0 (0.0)	1 (0.1)
中耳炎	1 (0.1)	0 (0.0)	1 (0.1)
咽頭炎	0 (0.0)	1 (0.2)	1 (0.1)
レンサ球菌性咽頭炎	0 (0.0)	1 (0.2)	1 (0.1)
肺炎	1 (0.1)	0 (0.0)	1 (0.1)
腎盂腎炎	0 (0.0)	1 (0.2)	1 (0.1)
腎嚢胞感染	0 (0.0)	2 (0.4)	2 (0.1)
副鼻腔炎	2 (0.2)	1 (0.2)	3 (0.2)
ブドウ球菌感染	1 (0.1)	0 (0.0)	1 (0.1)
扁桃炎	1 (0.1)	0 (0.0)	1 (0.1)
上気道感染	4 (0.4)	1 (0.2)	5 (0.3)
尿路感染	4 (0.4)	4 (0.8)	8 (0.6)
ウイルス感染	1 (0.1)	0 (0.0)	1 (0.1)
外陰部腔カンジダ症	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
傷害、中毒および処置合併症			
挫傷	1 (0.1)	1 (0.2)	2 (0.1)
熱疲労	1 (0.1)	0 (0.0)	1 (0.1)
熱射病	1 (0.1)	0 (0.0)	1 (0.1)
半月板障害	0 (0.0)	1 (0.2)	1 (0.1)
外傷後疼痛	1 (0.1)	0 (0.0)	1 (0.1)
臨床検査			
アラニン・アミノトランスフェラーゼ増加	35 (3.6)	12 (2.5)	47 (3.3)
アスパラギン酸アミノトランスフェラーゼ増加	30 (3.1)	10 (2.1)	40 (2.8)
細菌検査陽性	0 (0.0)	1 (0.2)	1 (0.1)
血中アルカリホスファターゼ増加	3 (0.3)	0 (0.0)	3 (0.2)
血中ビリルビン増加	2 (0.2)	0 (0.0)	2 (0.1)
血中カルシウム増加	3 (0.3)	0 (0.0)	3 (0.2)
血中コレステロール増加	3 (0.3)	1 (0.2)	4 (0.3)
血中クレアチニン増加	95 (9.9)	48 (9.9)	143 (9.9)
血中ブドウ糖増加	1 (0.1)	0 (0.0)	1 (0.1)
血中乳酸脱水素酵素増加	3 (0.3)	0 (0.0)	3 (0.2)
血中カリウム減少	1 (0.1)	0 (0.0)	1 (0.1)
血中カリウム増加	2 (0.2)	0 (0.0)	2 (0.1)
血圧低下	1 (0.1)	1 (0.2)	2 (0.1)
拡張期血圧上昇	0 (0.0)	1 (0.2)	1 (0.1)
血圧上昇	4 (0.4)	2 (0.4)	6 (0.4)
血中ナトリウム増加	11 (1.1)	1 (0.2)	12 (0.8)
血中尿素増加	5 (0.5)	8 (1.7)	13 (0.9)
血中尿酸増加	16 (1.7)	4 (0.8)	20 (1.4)
心雑音	0 (0.0)	1 (0.2)	1 (0.1)
シスタチンC増加	3 (0.3)	4 (0.8)	7 (0.5)
心電図異常T波	1 (0.1)	0 (0.0)	1 (0.1)
好酸球数増加	1 (0.1)	0 (0.0)	1 (0.1)
γ-グルタミルトランスフェラーゼ増加	16 (1.7)	3 (0.6)	19 (1.3)
ヘマトクリット減少	1 (0.1)	2 (0.4)	3 (0.2)
ヘマトクリット増加	1 (0.1)	0 (0.0)	1 (0.1)
ヘモグロビン減少	2 (0.2)	1 (0.2)	3 (0.2)
心拍数増加	0 (0.0)	1 (0.2)	1 (0.1)
肝酵素異常	1 (0.1)	0 (0.0)	1 (0.1)
肝酵素上昇	10 (1.0)	0 (0.0)	10 (0.7)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
臨床検査			
I N R 増加	1 (0.1)	0 (0.0)	1 (0.1)
リパーゼ増加	0 (0.0)	1 (0.2)	1 (0.1)
肝機能検査異常	5 (0.5)	0 (0.0)	5 (0.3)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球容積減少	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球容積増加	4 (0.4)	1 (0.2)	5 (0.3)
好中球数増加	0 (0.0)	1 (0.2)	1 (0.1)
血小板数減少	0 (0.0)	1 (0.2)	1 (0.1)
Q O L 低下	1 (0.1)	0 (0.0)	1 (0.1)
赤血球数減少	0 (0.0)	2 (0.4)	2 (0.1)
トランスアミナーゼ上昇	9 (0.9)	0 (0.0)	9 (0.6)
尿浸透圧低下	8 (0.8)	1 (0.2)	9 (0.6)
尿浸透圧上昇	1 (0.1)	0 (0.0)	1 (0.1)
尿量増加	15 (1.6)	2 (0.4)	17 (1.2)
ウェスト周囲径増加	1 (0.1)	0 (0.0)	1 (0.1)
体重減少	28 (2.9)	3 (0.6)	31 (2.1)
体重増加	16 (1.7)	5 (1.0)	21 (1.5)
白血球数増加	1 (0.1)	1 (0.2)	2 (0.1)
代謝および栄養障害			
食欲減退	55 (5.7)	1 (0.2)	56 (3.9)
脱水	15 (1.6)	7 (1.4)	22 (1.5)
糖尿病	2 (0.2)	0 (0.0)	2 (0.1)
脂質異常症	1 (0.1)	0 (0.0)	1 (0.1)
食物渴望	2 (0.2)	0 (0.0)	2 (0.1)
食物不耐性	1 (0.1)	0 (0.0)	1 (0.1)
耐糖能障害	1 (0.1)	1 (0.2)	2 (0.1)
痛風	15 (1.6)	4 (0.8)	19 (1.3)
高アミラーゼ血症	0 (0.0)	1 (0.2)	1 (0.1)
高カルシウム血症	3 (0.3)	2 (0.4)	5 (0.3)
高コレステロール血症	4 (0.4)	1 (0.2)	5 (0.3)
高クレアチニン血症	0 (0.0)	1 (0.2)	1 (0.1)
高血糖	3 (0.3)	3 (0.6)	6 (0.4)
高カリウム血症	3 (0.3)	1 (0.2)	4 (0.3)
高脂血症	2 (0.2)	2 (0.4)	4 (0.3)
高ナトリウム血症	26 (2.7)	5 (1.0)	31 (2.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
代謝および栄養障害			
高トリグリセリド血症	1 (0.1)	0 (0.0)	1 (0.1)
高尿酸血症	23 (2.4)	5 (1.0)	28 (1.9)
低カルシウム血症	1 (0.1)	0 (0.0)	1 (0.1)
低血糖症	5 (0.5)	0 (0.0)	5 (0.3)
低カリウム血症	4 (0.4)	1 (0.2)	5 (0.3)
低ナトリウム血症	2 (0.2)	1 (0.2)	3 (0.2)
低リン酸血症	2 (0.2)	0 (0.0)	2 (0.1)
血液量減少症	2 (0.2)	0 (0.0)	2 (0.1)
過体重	1 (0.1)	0 (0.0)	1 (0.1)
多飲症	100 (10.4)	17 (3.5)	117 (8.1)
ビタミンB 1 2 欠乏	1 (0.1)	0 (0.0)	1 (0.1)
体重変動	2 (0.2)	0 (0.0)	2 (0.1)
筋骨格系および結合組織障害			
関節痛	11 (1.1)	3 (0.6)	14 (1.0)
背部痛	12 (1.2)	10 (2.1)	22 (1.5)
骨痛	0 (0.0)	1 (0.2)	1 (0.1)
線維筋痛	0 (0.0)	1 (0.2)	1 (0.1)
側腹部痛	2 (0.2)	1 (0.2)	3 (0.2)
椎間板変性症	1 (0.1)	0 (0.0)	1 (0.1)
椎間板突出	0 (0.0)	1 (0.2)	1 (0.1)
関節腫脹	2 (0.2)	0 (0.0)	2 (0.1)
筋肉疲労	1 (0.1)	0 (0.0)	1 (0.1)
筋痙縮	19 (2.0)	7 (1.4)	26 (1.8)
筋骨格痛	3 (0.3)	0 (0.0)	3 (0.2)
筋骨格硬直	3 (0.3)	0 (0.0)	3 (0.2)
筋肉痛	11 (1.1)	2 (0.4)	13 (0.9)
頸部痛	1 (0.1)	0 (0.0)	1 (0.1)
四肢痛	8 (0.8)	5 (1.0)	13 (0.9)
重感	1 (0.1)	0 (0.0)	1 (0.1)
変形性脊椎症	0 (0.0)	2 (0.4)	2 (0.1)
腱炎	1 (0.1)	1 (0.2)	2 (0.1)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)			
皮膚乳頭腫	1 (0.1)	0 (0.0)	1 (0.1)
汗腺腫瘍	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
神経系障害			
味覚消失	1 (0.1)	1 (0.2)	2 (0.1)
平衡障害	1 (0.1)	1 (0.2)	2 (0.1)
脳梗塞	1 (0.1)	0 (0.0)	1 (0.1)
群発頭痛	1 (0.1)	0 (0.0)	1 (0.1)
協調運動異常	1 (0.1)	0 (0.0)	1 (0.1)
注意力障害	7 (0.7)	1 (0.2)	8 (0.6)
浮動性めまい	72 (7.5)	22 (4.6)	94 (6.5)
労作性めまい	1 (0.1)	0 (0.0)	1 (0.1)
体位性めまい	2 (0.2)	0 (0.0)	2 (0.1)
異常感覚	1 (0.1)	0 (0.0)	1 (0.1)
味覚異常	14 (1.5)	3 (0.6)	17 (1.2)
頭部不快感	1 (0.1)	0 (0.0)	1 (0.1)
頭痛	129 (13.4)	44 (9.1)	173 (12.0)
味覚過敏	1 (0.1)	0 (0.0)	1 (0.1)
感覚鈍麻	4 (0.4)	2 (0.4)	6 (0.4)
虚血性脳卒中	0 (0.0)	1 (0.2)	1 (0.1)
嗜眠	2 (0.2)	3 (0.6)	5 (0.3)
意識消失	4 (0.4)	0 (0.0)	4 (0.3)
記憶障害	0 (0.0)	1 (0.2)	1 (0.1)
精神的機能障害	0 (0.0)	1 (0.2)	1 (0.1)
片頭痛	2 (0.2)	1 (0.2)	3 (0.2)
前兆を伴う片頭痛	1 (0.1)	0 (0.0)	1 (0.1)
不随意性筋収縮	2 (0.2)	0 (0.0)	2 (0.1)
ナルコレプシー	3 (0.3)	0 (0.0)	3 (0.2)
錯感覚	5 (0.5)	0 (0.0)	5 (0.3)
嗅覚錯誤	1 (0.1)	0 (0.0)	1 (0.1)
失神寸前の状態	2 (0.2)	0 (0.0)	2 (0.1)
下肢静止不能症候群	1 (0.1)	1 (0.2)	2 (0.1)
坐骨神経痛	1 (0.1)	0 (0.0)	1 (0.1)
傾眠	2 (0.2)	1 (0.2)	3 (0.2)
失神	8 (0.8)	0 (0.0)	8 (0.6)
緊張性頭痛	2 (0.2)	0 (0.0)	2 (0.1)
振戦	1 (0.1)	1 (0.2)	2 (0.1)
第7脳神経麻痺	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
精神障害			
異常な夢	1 (0.1)	2 (0.4)	3 (0.2)
激越	1 (0.1)	0 (0.0)	1 (0.1)
不安	4 (0.4)	0 (0.0)	4 (0.3)
抑うつ気分	1 (0.1)	0 (0.0)	1 (0.1)
うつ病	7 (0.7)	0 (0.0)	7 (0.5)
初期不眠症	1 (0.1)	0 (0.0)	1 (0.1)
不眠症	40 (4.2)	6 (1.2)	46 (3.2)
リビドー減退	3 (0.3)	0 (0.0)	3 (0.2)
リビドー消失	1 (0.1)	0 (0.0)	1 (0.1)
大うつ病	1 (0.1)	0 (0.0)	1 (0.1)
中期不眠症	1 (0.1)	0 (0.0)	1 (0.1)
神経過敏	2 (0.2)	0 (0.0)	2 (0.1)
パニック発作	2 (0.2)	0 (0.0)	2 (0.1)
パニック反応	1 (0.1)	0 (0.0)	1 (0.1)
睡眠障害	4 (0.4)	1 (0.2)	5 (0.3)
夢遊症	1 (0.1)	0 (0.0)	1 (0.1)
腎および尿路障害			
高窒素血症	0 (0.0)	1 (0.2)	1 (0.1)
膀胱不快感	0 (0.0)	1 (0.2)	1 (0.1)
膀胱刺激症状	1 (0.1)	0 (0.0)	1 (0.1)
膀胱痛	2 (0.2)	0 (0.0)	2 (0.1)
尿路結石	1 (0.1)	0 (0.0)	1 (0.1)
着色尿	0 (0.0)	1 (0.2)	1 (0.1)
排尿困難	5 (0.5)	1 (0.2)	6 (0.4)
遺尿	2 (0.2)	0 (0.0)	2 (0.1)
血尿	10 (1.0)	7 (1.4)	17 (1.2)
緊張性膀胱	1 (0.1)	0 (0.0)	1 (0.1)
失禁	1 (0.1)	0 (0.0)	1 (0.1)
尿意切迫	6 (0.6)	2 (0.4)	8 (0.6)
腎結石症	2 (0.2)	1 (0.2)	3 (0.2)
夜間頻尿	280 (29.1)	61 (12.6)	341 (23.6)
乏尿	2 (0.2)	0 (0.0)	2 (0.1)
頻尿	223 (23.2)	25 (5.2)	248 (17.2)
多尿	366 (38.1)	80 (16.6)	446 (30.9)
腎仙痛	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
腎および尿路障害			
腎嚢胞出血	0 (0.0)	1 (0.2)	1 (0.1)
腎嚢胞破裂	0 (0.0)	2 (0.4)	2 (0.1)
急性腎不全	2 (0.2)	1 (0.2)	3 (0.2)
腎機能障害	7 (0.7)	3 (0.6)	10 (0.7)
腎臓痛	46 (4.8)	26 (5.4)	72 (5.0)
終末尿滴下	1 (0.1)	0 (0.0)	1 (0.1)
切迫性尿失禁	0 (0.0)	1 (0.2)	1 (0.1)
尿失禁	3 (0.3)	0 (0.0)	3 (0.2)
尿閉	1 (0.1)	0 (0.0)	1 (0.1)
生殖系および乳房障害			
無月経	1 (0.1)	0 (0.0)	1 (0.1)
乳房嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
乳房腫瘍	0 (0.0)	1 (0.2)	1 (0.1)
月経困難症	0 (0.0)	1 (0.2)	1 (0.1)
射精障害	1 (0.1)	0 (0.0)	1 (0.1)
勃起不全	4 (0.4)	1 (0.2)	5 (0.3)
乳汁漏出症	1 (0.1)	0 (0.0)	1 (0.1)
性器出血	0 (0.0)	1 (0.2)	1 (0.1)
閉経期症状	0 (0.0)	1 (0.2)	1 (0.1)
月経過多	2 (0.2)	1 (0.2)	3 (0.2)
月経障害	1 (0.1)	0 (0.0)	1 (0.1)
月経遅延	0 (0.0)	1 (0.2)	1 (0.1)
不規則月経	2 (0.2)	0 (0.0)	2 (0.1)
性機能不全	1 (0.1)	1 (0.2)	2 (0.1)
精巣痛	0 (0.0)	1 (0.2)	1 (0.1)
外陰腔乾燥	1 (0.1)	1 (0.2)	2 (0.1)
呼吸器、胸郭および縦隔障害			
喘息	4 (0.4)	0 (0.0)	4 (0.3)
運動誘発喘息	0 (0.0)	1 (0.2)	1 (0.1)
慢性気管支炎	1 (0.1)	0 (0.0)	1 (0.1)
咳嗽	15 (1.6)	5 (1.0)	20 (1.4)
咽喉乾燥	5 (0.5)	1 (0.2)	6 (0.4)
発声障害	2 (0.2)	0 (0.0)	2 (0.1)
呼吸困難	7 (0.7)	0 (0.0)	7 (0.5)
安静時呼吸困難	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961) n (%)	Placebo (N=483) n (%)	Total (N=1444) n (%)
呼吸器、胸郭および縦隔障害			
労作性呼吸困難	3 (0.3)	0 (0.0)	3 (0.2)
鼻出血	3 (0.3)	1 (0.2)	4 (0.3)
喉頭浮腫	0 (0.0)	1 (0.2)	1 (0.1)
鼻乾燥	2 (0.2)	2 (0.4)	4 (0.3)
口腔咽頭痛	3 (0.3)	0 (0.0)	3 (0.2)
咽頭浮腫	0 (0.0)	1 (0.2)	1 (0.1)
肺塞栓症	1 (0.1)	0 (0.0)	1 (0.1)
肺線維症	1 (0.1)	0 (0.0)	1 (0.1)
アレルギー性鼻炎	1 (0.1)	0 (0.0)	1 (0.1)
鼻漏	1 (0.1)	0 (0.0)	1 (0.1)
くしゃみ	1 (0.1)	1 (0.2)	2 (0.1)
いびき	1 (0.1)	0 (0.0)	1 (0.1)
上気道の炎症	1 (0.1)	0 (0.0)	1 (0.1)
喘鳴	0 (0.0)	1 (0.2)	1 (0.1)
皮膚および皮下組織障害			
ざ瘡	4 (0.4)	0 (0.0)	4 (0.3)
脱毛症	5 (0.5)	4 (0.8)	9 (0.6)
円形脱毛症	0 (0.0)	1 (0.2)	1 (0.1)
血性水疱	1 (0.1)	0 (0.0)	1 (0.1)
冷汗	1 (0.1)	0 (0.0)	1 (0.1)
皮膚炎	1 (0.1)	1 (0.2)	2 (0.1)
接触性皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
皮膚乾燥	30 (3.1)	6 (1.2)	36 (2.5)
斑状出血	1 (0.1)	0 (0.0)	1 (0.1)
湿疹	3 (0.3)	0 (0.0)	3 (0.2)
紅斑	0 (0.0)	1 (0.2)	1 (0.1)
毛髪成長異常	0 (0.0)	1 (0.2)	1 (0.1)
多汗症	2 (0.2)	1 (0.2)	3 (0.2)
乏汗症	2 (0.2)	0 (0.0)	2 (0.1)
機械性蕁麻疹	1 (0.1)	0 (0.0)	1 (0.1)
爪の障害	3 (0.3)	0 (0.0)	3 (0.2)
寝汗	2 (0.2)	1 (0.2)	3 (0.2)
爪破損	1 (0.1)	0 (0.0)	1 (0.1)
光線過敏性反応	1 (0.1)	0 (0.0)	1 (0.1)
色素沈着障害	2 (0.2)	1 (0.2)	3 (0.2)

表2.7.4.7-28

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CT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
皮膚および皮下組織障害			
そう痒症	19 (2.0)	6 (1.2)	25 (1.7)
乾癬	1 (0.1)	0 (0.0)	1 (0.1)
発疹	10 (1.0)	2 (0.4)	12 (0.8)
そう痒性皮疹	1 (0.1)	0 (0.0)	1 (0.1)
皮膚色素脱失	1 (0.1)	0 (0.0)	1 (0.1)
皮膚変色	1 (0.1)	0 (0.0)	1 (0.1)
皮膚病変	1 (0.1)	0 (0.0)	1 (0.1)
皮膚反応	0 (0.0)	1 (0.2)	1 (0.1)
顔面腫脹	0 (0.0)	1 (0.2)	1 (0.1)
蕁麻疹	4 (0.4)	0 (0.0)	4 (0.3)
慢性蕁麻疹	2 (0.2)	0 (0.0)	2 (0.1)
乾皮症	1 (0.1)	0 (0.0)	1 (0.1)
外科および内科処置			
収れん薬療法	1 (0.1)	0 (0.0)	1 (0.1)
血管障害			
コントロール不良の血圧	1 (0.1)	0 (0.0)	1 (0.1)
深部静脈血栓症	0 (0.0)	1 (0.2)	1 (0.1)
潮紅	1 (0.1)	0 (0.0)	1 (0.1)
ほてり	4 (0.4)	0 (0.0)	4 (0.3)
高血圧	46 (4.8)	19 (3.9)	65 (4.5)
高血圧クリーゼ	1 (0.1)	0 (0.0)	1 (0.1)
低血圧	16 (1.7)	9 (1.9)	25 (1.7)
不安定血圧	1 (0.1)	0 (0.0)	1 (0.1)
起立性低血圧	2 (0.2)	2 (0.4)	4 (0.3)
末梢冷感	5 (0.5)	2 (0.4)	7 (0.5)
レイノー現象	1 (0.1)	1 (0.2)	2 (0.1)
TOTAL	851 (88.6)	302 (62.5)	1153 (79.8)

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表2.7.4.7-29

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JT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
血液およびリンパ系障害			
鉄欠乏性貧血	1 (0.8)	0 (0.0)	1 (0.6)
リンパ節症	0 (0.0)	1 (1.7)	1 (0.6)
心臓障害			
狭心症	1 (0.8)	0 (0.0)	1 (0.6)
不整脈	2 (1.7)	2 (3.4)	4 (2.3)
房室ブロック	1 (0.8)	0 (0.0)	1 (0.6)
右脚ブロック	1 (0.8)	0 (0.0)	1 (0.6)
心臓瘤	0 (0.0)	1 (1.7)	1 (0.6)
左室不全	1 (0.8)	0 (0.0)	1 (0.6)
動悸	7 (5.9)	0 (0.0)	7 (4.0)
頻脈	2 (1.7)	0 (0.0)	2 (1.1)
心室性期外収縮	3 (2.5)	0 (0.0)	3 (1.7)
耳および迷路障害			
耳鳴	1 (0.8)	0 (0.0)	1 (0.6)
回転性めまい	3 (2.5)	0 (0.0)	3 (1.7)
頭位性回転性めまい	1 (0.8)	0 (0.0)	1 (0.6)
眼障害			
霰粒腫	1 (0.8)	0 (0.0)	1 (0.6)
結膜充血	0 (0.0)	1 (1.7)	1 (0.6)
眼乾燥	3 (2.5)	1 (1.7)	4 (2.3)
眼瞼浮腫	1 (0.8)	0 (0.0)	1 (0.6)
緑内障	2 (1.7)	0 (0.0)	2 (1.1)
羞明	1 (0.8)	0 (0.0)	1 (0.6)
胃腸障害			
腹部不快感	2 (1.7)	1 (1.7)	3 (1.7)
腹部膨満	6 (5.1)	2 (3.4)	8 (4.5)
腹痛	2 (1.7)	2 (3.4)	4 (2.3)
上腹部痛	8 (6.8)	3 (5.1)	11 (6.2)
口唇炎	1 (0.8)	0 (0.0)	1 (0.6)
結腸ポリープ	2 (1.7)	0 (0.0)	2 (1.1)

表2.7.4.7-29

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JT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
便秘	11 (9.3)	0 (0.0)	11 (6.2)
下痢	2 (1.7)	1 (1.7)	3 (1.7)
口内乾燥	1 (0.8)	0 (0.0)	1 (0.6)
十二指腸炎	1 (0.8)	0 (0.0)	1 (0.6)
消化不良	4 (3.4)	0 (0.0)	4 (2.3)
心窩部不快感	1 (0.8)	0 (0.0)	1 (0.6)
胃炎	2 (1.7)	0 (0.0)	2 (1.1)
胃食道逆流性疾患	4 (3.4)	3 (5.1)	7 (4.0)
歯肉炎	1 (0.8)	0 (0.0)	1 (0.6)
痔出血	1 (0.8)	0 (0.0)	1 (0.6)
痔核	1 (0.8)	0 (0.0)	1 (0.6)
裂孔ヘルニア	1 (0.8)	0 (0.0)	1 (0.6)
口唇乾燥	3 (2.5)	0 (0.0)	3 (1.7)
悪心	5 (4.2)	1 (1.7)	6 (3.4)
口内炎	0 (0.0)	1 (1.7)	1 (0.6)
臍ヘルニア	1 (0.8)	0 (0.0)	1 (0.6)
嘔吐	2 (1.7)	0 (0.0)	2 (1.1)
一般・全身障害および投与部位の状態			
胸部不快感	0 (0.0)	2 (3.4)	2 (1.1)
胸痛	4 (3.4)	0 (0.0)	4 (2.3)
疲労	11 (9.3)	0 (0.0)	11 (6.2)
異常感	0 (0.0)	1 (1.7)	1 (0.6)
熱感	1 (0.8)	0 (0.0)	1 (0.6)
倦怠感	8 (6.8)	0 (0.0)	8 (4.5)
浮腫	3 (2.5)	0 (0.0)	3 (1.7)
末梢性浮腫	4 (3.4)	3 (5.1)	7 (4.0)
疼痛	1 (0.8)	0 (0.0)	1 (0.6)
発熱	2 (1.7)	0 (0.0)	2 (1.1)
口渇	106 (89.8)	17 (28.8)	123 (69.5)

表2.7.4.7-29

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JT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
肝胆道系障害			
肝機能異常	11 (9.3)	1 (1.7)	12 (6.8)
肝障害	3 (2.5)	0 (0.0)	3 (1.7)
免疫系障害			
季節性アレルギー	1 (0.8)	0 (0.0)	1 (0.6)
感染症および寄生虫症			
急性扁桃炎	1 (0.8)	0 (0.0)	1 (0.6)
気管支炎	1 (0.8)	0 (0.0)	1 (0.6)
膀胱炎	1 (0.8)	0 (0.0)	1 (0.6)
憩室炎	1 (0.8)	0 (0.0)	1 (0.6)
带状疱疹	0 (0.0)	1 (1.7)	1 (0.6)
麦粒腫	1 (0.8)	0 (0.0)	1 (0.6)
鼻咽頭炎	4 (3.4)	2 (3.4)	6 (3.4)
腎嚢胞感染	0 (0.0)	1 (1.7)	1 (0.6)
上気道感染	2 (1.7)	0 (0.0)	2 (1.1)
傷害、中毒および処置合併症			
挫傷	0 (0.0)	1 (1.7)	1 (0.6)
熱射病	1 (0.8)	0 (0.0)	1 (0.6)
半月板障害	0 (0.0)	1 (1.7)	1 (0.6)
臨床検査			
アラニン・アミノトランスフェラーゼ増加	2 (1.7)	0 (0.0)	2 (1.1)
アスパラギン酸アミノトランスフェラーゼ増加	2 (1.7)	0 (0.0)	2 (1.1)
細菌検査陽性	0 (0.0)	1 (1.7)	1 (0.6)
血中クレアチニン増加	5 (4.2)	3 (5.1)	8 (4.5)
血中カリウム減少	1 (0.8)	0 (0.0)	1 (0.6)
血圧上昇	1 (0.8)	1 (1.7)	2 (1.1)
血中尿酸増加	4 (3.4)	0 (0.0)	4 (2.3)
シスタチンC増加	0 (0.0)	1 (1.7)	1 (0.6)
γ-グルタミルトランスフェラーゼ増加	1 (0.8)	0 (0.0)	1 (0.6)
トランスアミナーゼ上昇	2 (1.7)	0 (0.0)	2 (1.1)
尿浸透圧上昇	1 (0.8)	0 (0.0)	1 (0.6)

表2.7.4.7-29

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JT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
臨床検査			
体重減少	8 (6.8)	0 (0.0)	8 (4.5)
体重増加	1 (0.8)	0 (0.0)	1 (0.6)
白血球数増加	1 (0.8)	0 (0.0)	1 (0.6)
代謝および栄養障害			
食欲減退	11 (9.3)	0 (0.0)	11 (6.2)
脱水	2 (1.7)	0 (0.0)	2 (1.1)
糖尿病	1 (0.8)	0 (0.0)	1 (0.6)
痛風	2 (1.7)	0 (0.0)	2 (1.1)
高カルシウム血症	1 (0.8)	0 (0.0)	1 (0.6)
高コレステロール血症	2 (1.7)	0 (0.0)	2 (1.1)
高血糖	0 (0.0)	1 (1.7)	1 (0.6)
高脂血症	2 (1.7)	1 (1.7)	3 (1.7)
高トリグリセリド血症	1 (0.8)	0 (0.0)	1 (0.6)
高尿酸血症	13 (11.0)	3 (5.1)	16 (9.0)
筋骨格系および結合組織障害			
関節痛	1 (0.8)	1 (1.7)	2 (1.1)
背部痛	6 (5.1)	2 (3.4)	8 (4.5)
側腹部痛	0 (0.0)	1 (1.7)	1 (0.6)
椎間板突出	0 (0.0)	1 (1.7)	1 (0.6)
筋痙縮	1 (0.8)	1 (1.7)	2 (1.1)
筋骨格痛	2 (1.7)	0 (0.0)	2 (1.1)
筋骨格硬直	2 (1.7)	0 (0.0)	2 (1.1)
筋肉痛	1 (0.8)	2 (3.4)	3 (1.7)
四肢痛	2 (1.7)	0 (0.0)	2 (1.1)
変形性脊椎症	0 (0.0)	2 (3.4)	2 (1.1)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)			
汗腺腫瘍	1 (0.8)	0 (0.0)	1 (0.6)
神経系障害			
味覚消失	1 (0.8)	0 (0.0)	1 (0.6)
平衡障害	0 (0.0)	1 (1.7)	1 (0.6)

表2.7.4.7-29

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JT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
脳梗塞	1 (0.8)	0 (0.0)	1 (0.6)
群発頭痛	1 (0.8)	0 (0.0)	1 (0.6)
注意力障害	1 (0.8)	0 (0.0)	1 (0.6)
浮動性めまい	7 (5.9)	5 (8.5)	12 (6.8)
異常感覚	1 (0.8)	0 (0.0)	1 (0.6)
味覚異常	2 (1.7)	0 (0.0)	2 (1.1)
頭痛	20 (16.9)	5 (8.5)	25 (14.1)
感覚鈍麻	0 (0.0)	1 (1.7)	1 (0.6)
意識消失	1 (0.8)	0 (0.0)	1 (0.6)
坐骨神経痛	1 (0.8)	0 (0.0)	1 (0.6)
傾眠	2 (1.7)	1 (1.7)	3 (1.7)
精神障害			
不眠症	6 (5.1)	0 (0.0)	6 (3.4)
中期不眠症	1 (0.8)	0 (0.0)	1 (0.6)
睡眠障害	0 (0.0)	1 (1.7)	1 (0.6)
腎および尿路障害			
膀胱刺激症状	1 (0.8)	0 (0.0)	1 (0.6)
膀胱痛	1 (0.8)	0 (0.0)	1 (0.6)
尿路結石	1 (0.8)	0 (0.0)	1 (0.6)
排尿困難	2 (1.7)	0 (0.0)	2 (1.1)
血尿	1 (0.8)	2 (3.4)	3 (1.7)
夜間頻尿	2 (1.7)	2 (3.4)	4 (2.3)
頻尿	63 (53.4)	4 (6.8)	67 (37.9)
多尿	40 (33.9)	5 (8.5)	45 (25.4)
腎機能障害	2 (1.7)	0 (0.0)	2 (1.1)
腎臓痛	6 (5.1)	4 (6.8)	10 (5.6)
終末尿滴下	1 (0.8)	0 (0.0)	1 (0.6)
生殖系および乳房障害			
乳房嚢胞	1 (0.8)	0 (0.0)	1 (0.6)
乳房腫瘍	0 (0.0)	1 (1.7)	1 (0.6)

表2.7.4.7-29

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JT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
生殖系および乳房障害			
射精障害	1 (0.8)	0 (0.0)	1 (0.6)
乳汁漏出症	1 (0.8)	0 (0.0)	1 (0.6)
性器出血	0 (0.0)	1 (1.7)	1 (0.6)
閉経期症状	0 (0.0)	1 (1.7)	1 (0.6)
月経障害	1 (0.8)	0 (0.0)	1 (0.6)
性機能不全	0 (0.0)	1 (1.7)	1 (0.6)
呼吸器、胸郭および縦隔障害			
喘息	3 (2.5)	0 (0.0)	3 (1.7)
慢性気管支炎	1 (0.8)	0 (0.0)	1 (0.6)
咳嗽	1 (0.8)	1 (1.7)	2 (1.1)
呼吸困難	1 (0.8)	0 (0.0)	1 (0.6)
鼻乾燥	1 (0.8)	1 (1.7)	2 (1.1)
アレルギー性鼻炎	1 (0.8)	0 (0.0)	1 (0.6)
上気道の炎症	1 (0.8)	0 (0.0)	1 (0.6)
皮膚および皮下組織障害			
ざ瘡	1 (0.8)	0 (0.0)	1 (0.6)
血性水疱	1 (0.8)	0 (0.0)	1 (0.6)
冷汗	1 (0.8)	0 (0.0)	1 (0.6)
接触性皮膚炎	1 (0.8)	0 (0.0)	1 (0.6)
皮膚乾燥	5 (4.2)	1 (1.7)	6 (3.4)
湿疹	1 (0.8)	0 (0.0)	1 (0.6)
乏汗症	1 (0.8)	0 (0.0)	1 (0.6)
爪の障害	1 (0.8)	0 (0.0)	1 (0.6)
そう痒症	3 (2.5)	0 (0.0)	3 (1.7)
乾癬	1 (0.8)	0 (0.0)	1 (0.6)
発疹	2 (1.7)	1 (1.7)	3 (1.7)
蕁麻疹	2 (1.7)	0 (0.0)	2 (1.1)
慢性蕁麻疹	1 (0.8)	0 (0.0)	1 (0.6)

表2.7.4.7-29

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JT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term（日本の被験者）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
血管障害			
潮紅	1 (0.8)	0 (0.0)	1 (0.6)
高血圧	11 (9.3)	4 (6.8)	15 (8.5)
低血圧	1 (0.8)	1 (1.7)	2 (1.1)
不安定血圧	1 (0.8)	0 (0.0)	1 (0.6)
起立性低血圧	0 (0.0)	1 (1.7)	1 (0.6)
TOTAL	117 (99.2)	42 (71.2)	159 (89.8)

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表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
血液およびリンパ系障害			
貧血	1 (0.1)	2 (0.5)	3 (0.2)
好酸球増加症	1 (0.1)	1 (0.2)	2 (0.2)
白血球増加症	1 (0.1)	0 (0.0)	1 (0.1)
白血球減少症	1 (0.1)	1 (0.2)	2 (0.2)
リンパ節症	0 (0.0)	1 (0.2)	1 (0.1)
腎性貧血	0 (0.0)	1 (0.2)	1 (0.1)
血小板減少症	1 (0.1)	0 (0.0)	1 (0.1)
心臓障害			
心房細動	0 (0.0)	1 (0.2)	1 (0.1)
左室機能不全	1 (0.1)	0 (0.0)	1 (0.1)
左室肥大	1 (0.1)	0 (0.0)	1 (0.1)
僧帽弁疾患	1 (0.1)	0 (0.0)	1 (0.1)
動悸	15 (1.8)	2 (0.5)	17 (1.3)
上室性頻脈	1 (0.1)	0 (0.0)	1 (0.1)
頻脈	3 (0.4)	2 (0.5)	5 (0.4)
耳および迷路障害			
難聴	1 (0.1)	0 (0.0)	1 (0.1)
耳痛	1 (0.1)	1 (0.2)	2 (0.2)
耳鳴	1 (0.1)	0 (0.0)	1 (0.1)
回転性めまい	14 (1.7)	6 (1.4)	20 (1.6)
内分泌障害			
続発性副甲状腺機能低下症	1 (0.1)	0 (0.0)	1 (0.1)
眼障害			
眼瞼炎	1 (0.1)	0 (0.0)	1 (0.1)
結膜出血	1 (0.1)	0 (0.0)	1 (0.1)
眼乾燥	7 (0.8)	5 (1.2)	12 (0.9)
緑内障	1 (0.1)	0 (0.0)	1 (0.1)
眼充血	1 (0.1)	0 (0.0)	1 (0.1)
眼窩周囲浮腫	0 (0.0)	1 (0.2)	1 (0.1)
光視症	1 (0.1)	0 (0.0)	1 (0.1)
網膜剥離	1 (0.1)	0 (0.0)	1 (0.1)
霧視	2 (0.2)	0 (0.0)	2 (0.2)
視力障害	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
眼障害			
硝子体浮遊物	1 (0.1)	0 (0.0)	1 (0.1)
眼球乾燥	0 (0.0)	1 (0.2)	1 (0.1)
胃腸障害			
腹部不快感	6 (0.7)	1 (0.2)	7 (0.6)
腹部膨満	19 (2.3)	2 (0.5)	21 (1.7)
腹痛	11 (1.3)	5 (1.2)	16 (1.3)
上腹部痛	15 (1.8)	7 (1.7)	22 (1.7)
アフタ性口内炎	1 (0.1)	0 (0.0)	1 (0.1)
呼気臭	2 (0.2)	0 (0.0)	2 (0.2)
口唇のひび割れ	1 (0.1)	0 (0.0)	1 (0.1)
便秘	41 (4.9)	3 (0.7)	44 (3.5)
齲歯	1 (0.1)	0 (0.0)	1 (0.1)
下痢	27 (3.2)	8 (1.9)	35 (2.8)
口内乾燥	151 (17.9)	56 (13.2)	207 (16.3)
消化不良	27 (3.2)	6 (1.4)	33 (2.6)
嚥下障害	3 (0.4)	0 (0.0)	3 (0.2)
心窩部不快感	1 (0.1)	0 (0.0)	1 (0.1)
糞塊	0 (0.0)	1 (0.2)	1 (0.1)
鼓腸	4 (0.5)	0 (0.0)	4 (0.3)
胃障害	1 (0.1)	0 (0.0)	1 (0.1)
胃炎	1 (0.1)	1 (0.2)	2 (0.2)
胃腸障害	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動過剰	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動障害	1 (0.1)	0 (0.0)	1 (0.1)
胃食道逆流性疾患	8 (0.9)	2 (0.5)	10 (0.8)
舌痛	3 (0.4)	0 (0.0)	3 (0.2)
血便排泄	1 (0.1)	0 (0.0)	1 (0.1)
痔核	1 (0.1)	1 (0.2)	2 (0.2)
胃酸過多	1 (0.1)	0 (0.0)	1 (0.1)
口の感覚鈍麻	1 (0.1)	1 (0.2)	2 (0.2)
過敏性腸症候群	0 (0.0)	1 (0.2)	1 (0.1)
口唇乾燥	3 (0.4)	2 (0.5)	5 (0.4)
弛緩歯	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
悪心	34 (4.0)	21 (5.0)	55 (4.3)
食道炎	2 (0.2)	0 (0.0)	2 (0.2)
口腔扁平苔癬	1 (0.1)	0 (0.0)	1 (0.1)
口腔内痛	1 (0.1)	0 (0.0)	1 (0.1)
口の錯感覚	1 (0.1)	0 (0.0)	1 (0.1)
レッチング	1 (0.1)	0 (0.0)	1 (0.1)
舌苔	2 (0.2)	0 (0.0)	2 (0.2)
舌変色	2 (0.2)	0 (0.0)	2 (0.2)
舌乾燥	1 (0.1)	1 (0.2)	2 (0.2)
歯痛	1 (0.1)	1 (0.2)	2 (0.2)
臍ヘルニア	2 (0.2)	0 (0.0)	2 (0.2)
嘔吐	13 (1.5)	3 (0.7)	16 (1.3)
一般・全身障害および投与部位の状態			
無力症	41 (4.9)	8 (1.9)	49 (3.9)
腋窩痛	1 (0.1)	0 (0.0)	1 (0.1)
胸部不快感	6 (0.7)	0 (0.0)	6 (0.5)
胸痛	7 (0.8)	1 (0.2)	8 (0.6)
悪寒	1 (0.1)	0 (0.0)	1 (0.1)
嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
運動耐性低下	1 (0.1)	0 (0.0)	1 (0.1)
疲労	83 (9.8)	23 (5.4)	106 (8.4)
異常感	1 (0.1)	0 (0.0)	1 (0.1)
冷感	7 (0.8)	0 (0.0)	7 (0.6)
酩酊感	1 (0.1)	0 (0.0)	1 (0.1)
熱感	1 (0.1)	0 (0.0)	1 (0.1)
びくびく感	1 (0.1)	0 (0.0)	1 (0.1)
易刺激性	3 (0.4)	0 (0.0)	3 (0.2)
倦怠感	1 (0.1)	4 (0.9)	5 (0.4)
粘膜乾燥	8 (0.9)	2 (0.5)	10 (0.8)
浮腫	4 (0.5)	2 (0.5)	6 (0.5)
末梢性浮腫	17 (2.0)	8 (1.9)	25 (2.0)
疼痛	1 (0.1)	0 (0.0)	1 (0.1)
発熱	1 (0.1)	1 (0.2)	2 (0.2)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態			
不活発	0 (0.0)	1 (0.2)	1 (0.1)
腫脹	1 (0.1)	0 (0.0)	1 (0.1)
温度変化不耐症	1 (0.1)	0 (0.0)	1 (0.1)
口渇	419 (49.7)	76 (17.9)	495 (39.1)
肝胆道系障害			
胆管炎	1 (0.1)	0 (0.0)	1 (0.1)
胆嚢痛	1 (0.1)	0 (0.0)	1 (0.1)
肝嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
肝炎	1 (0.1)	0 (0.0)	1 (0.1)
肝障害	1 (0.1)	0 (0.0)	1 (0.1)
免疫系障害			
過敏症	1 (0.1)	0 (0.0)	1 (0.1)
感染症および寄生虫症			
気管支炎	1 (0.1)	1 (0.2)	2 (0.2)
カンジダ症	0 (0.0)	1 (0.2)	1 (0.1)
蜂巣炎	0 (0.0)	1 (0.2)	1 (0.1)
憩室炎	1 (0.1)	0 (0.0)	1 (0.1)
耳感染	0 (0.0)	1 (0.2)	1 (0.1)
耳垂感染	1 (0.1)	0 (0.0)	1 (0.1)
胃腸炎	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス性胃腸炎	2 (0.2)	0 (0.0)	2 (0.2)
歯肉膿瘍	1 (0.1)	0 (0.0)	1 (0.1)
単純ヘルペス	0 (0.0)	1 (0.2)	1 (0.1)
帯状疱疹	0 (0.0)	2 (0.5)	2 (0.2)
インフルエンザ	1 (0.1)	0 (0.0)	1 (0.1)
腎感染	1 (0.1)	0 (0.0)	1 (0.1)
喉頭炎	0 (0.0)	1 (0.2)	1 (0.1)
鼻咽頭炎	5 (0.6)	1 (0.2)	6 (0.5)
口腔カンジダ症	3 (0.4)	0 (0.0)	3 (0.2)
口腔真菌感染	2 (0.2)	0 (0.0)	2 (0.2)
口腔ヘルペス	1 (0.1)	0 (0.0)	1 (0.1)
中耳炎	1 (0.1)	0 (0.0)	1 (0.1)
咽頭炎	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
レンサ球菌性咽頭炎	0 (0.0)	1 (0.2)	1 (0.1)
肺炎	1 (0.1)	0 (0.0)	1 (0.1)
腎盂腎炎	0 (0.0)	1 (0.2)	1 (0.1)
腎嚢胞感染	0 (0.0)	1 (0.2)	1 (0.1)
副鼻腔炎	2 (0.2)	1 (0.2)	3 (0.2)
ブドウ球菌感染	1 (0.1)	0 (0.0)	1 (0.1)
扁桃炎	1 (0.1)	0 (0.0)	1 (0.1)
上気道感染	2 (0.2)	1 (0.2)	3 (0.2)
尿路感染	4 (0.5)	4 (0.9)	8 (0.6)
ウイルス感染	1 (0.1)	0 (0.0)	1 (0.1)
外陰部腭カンジダ症	1 (0.1)	0 (0.0)	1 (0.1)
傷害、中毒および処置合併症			
挫傷	1 (0.1)	0 (0.0)	1 (0.1)
熱疲労	1 (0.1)	0 (0.0)	1 (0.1)
外傷後疼痛	1 (0.1)	0 (0.0)	1 (0.1)
臨床検査			
アラニン・アミノトランスフェラーゼ増加	33 (3.9)	12 (2.8)	45 (3.6)
アスパラギン酸アミノトランスフェラーゼ増加	28 (3.3)	10 (2.4)	38 (3.0)
血中アルカリホスファターゼ増加	3 (0.4)	0 (0.0)	3 (0.2)
血中ビリルビン増加	2 (0.2)	0 (0.0)	2 (0.2)
血中カルシウム増加	3 (0.4)	0 (0.0)	3 (0.2)
血中コレステロール増加	3 (0.4)	1 (0.2)	4 (0.3)
血中クレアチニン増加	90 (10.7)	45 (10.6)	135 (10.7)
血中ブドウ糖増加	1 (0.1)	0 (0.0)	1 (0.1)
血中乳酸脱水素酵素増加	3 (0.4)	0 (0.0)	3 (0.2)
血中カリウム増加	2 (0.2)	0 (0.0)	2 (0.2)
血圧低下	1 (0.1)	1 (0.2)	2 (0.2)
拡張期血圧上昇	0 (0.0)	1 (0.2)	1 (0.1)
血圧上昇	3 (0.4)	1 (0.2)	4 (0.3)
血中ナトリウム増加	11 (1.3)	1 (0.2)	12 (0.9)
血中尿素増加	5 (0.6)	8 (1.9)	13 (1.0)
血中尿酸増加	12 (1.4)	4 (0.9)	16 (1.3)
心雑音	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
臨床検査			
シスタチンC増加	3 (0.4)	3 (0.7)	6 (0.5)
心電図異常T波	1 (0.1)	0 (0.0)	1 (0.1)
好酸球数増加	1 (0.1)	0 (0.0)	1 (0.1)
γ-グルタミルトランスフェラーゼ増加	15 (1.8)	3 (0.7)	18 (1.4)
ヘマトクリット減少	1 (0.1)	2 (0.5)	3 (0.2)
ヘマトクリット増加	1 (0.1)	0 (0.0)	1 (0.1)
ヘモグロビン減少	2 (0.2)	1 (0.2)	3 (0.2)
心拍数増加	0 (0.0)	1 (0.2)	1 (0.1)
肝酵素異常	1 (0.1)	0 (0.0)	1 (0.1)
肝酵素上昇	10 (1.2)	0 (0.0)	10 (0.8)
I N R 増加	1 (0.1)	0 (0.0)	1 (0.1)
リパーゼ増加	0 (0.0)	1 (0.2)	1 (0.1)
肝機能検査異常	5 (0.6)	0 (0.0)	5 (0.4)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球容積減少	0 (0.0)	1 (0.2)	1 (0.1)
平均赤血球容積増加	4 (0.5)	1 (0.2)	5 (0.4)
好中球数増加	0 (0.0)	1 (0.2)	1 (0.1)
血小板数減少	0 (0.0)	1 (0.2)	1 (0.1)
Q O L 低下	1 (0.1)	0 (0.0)	1 (0.1)
赤血球数減少	0 (0.0)	2 (0.5)	2 (0.2)
トランスアミナーゼ上昇	7 (0.8)	0 (0.0)	7 (0.6)
尿浸透圧低下	8 (0.9)	1 (0.2)	9 (0.7)
尿量増加	15 (1.8)	2 (0.5)	17 (1.3)
ウエスト周囲径増加	1 (0.1)	0 (0.0)	1 (0.1)
体重減少	20 (2.4)	3 (0.7)	23 (1.8)
体重増加	15 (1.8)	5 (1.2)	20 (1.6)
白血球数増加	0 (0.0)	1 (0.2)	1 (0.1)
代謝および栄養障害			
食欲減退	44 (5.2)	1 (0.2)	45 (3.6)
脱水	13 (1.5)	7 (1.7)	20 (1.6)
糖尿病	1 (0.1)	0 (0.0)	1 (0.1)
脂質異常症	1 (0.1)	0 (0.0)	1 (0.1)
食物渴望	2 (0.2)	0 (0.0)	2 (0.2)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
代謝および栄養障害			
食物不耐性	1 (0.1)	0 (0.0)	1 (0.1)
耐糖能障害	1 (0.1)	1 (0.2)	2 (0.2)
痛風	13 (1.5)	4 (0.9)	17 (1.3)
高アマラーゼ血症	0 (0.0)	1 (0.2)	1 (0.1)
高カルシウム血症	2 (0.2)	2 (0.5)	4 (0.3)
高コレステロール血症	2 (0.2)	1 (0.2)	3 (0.2)
高クレアチニン血症	0 (0.0)	1 (0.2)	1 (0.1)
高血糖	3 (0.4)	2 (0.5)	5 (0.4)
高カリウム血症	3 (0.4)	1 (0.2)	4 (0.3)
高脂血症	0 (0.0)	1 (0.2)	1 (0.1)
高ナトリウム血症	26 (3.1)	5 (1.2)	31 (2.4)
高尿酸血症	10 (1.2)	2 (0.5)	12 (0.9)
低カルシウム血症	1 (0.1)	0 (0.0)	1 (0.1)
低血糖症	5 (0.6)	0 (0.0)	5 (0.4)
低カリウム血症	4 (0.5)	1 (0.2)	5 (0.4)
低ナトリウム血症	2 (0.2)	1 (0.2)	3 (0.2)
低リン酸血症	2 (0.2)	0 (0.0)	2 (0.2)
血液量減少症	2 (0.2)	0 (0.0)	2 (0.2)
過体重	1 (0.1)	0 (0.0)	1 (0.1)
多飲症	100 (11.9)	17 (4.0)	117 (9.2)
ビタミンB 1 2 欠乏	1 (0.1)	0 (0.0)	1 (0.1)
体重変動	2 (0.2)	0 (0.0)	2 (0.2)
筋骨格系および結合組織障害			
関節痛	10 (1.2)	2 (0.5)	12 (0.9)
背部痛	6 (0.7)	8 (1.9)	14 (1.1)
骨痛	0 (0.0)	1 (0.2)	1 (0.1)
線維筋痛	0 (0.0)	1 (0.2)	1 (0.1)
側腹部痛	2 (0.2)	0 (0.0)	2 (0.2)
椎間板変性症	1 (0.1)	0 (0.0)	1 (0.1)
関節腫脹	2 (0.2)	0 (0.0)	2 (0.2)
筋肉疲労	1 (0.1)	0 (0.0)	1 (0.1)
筋痙縮	18 (2.1)	6 (1.4)	24 (1.9)
筋骨格痛	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
筋骨格系および結合組織障害			
筋骨格硬直	1 (0.1)	0 (0.0)	1 (0.1)
筋肉痛	10 (1.2)	0 (0.0)	10 (0.8)
頸部痛	1 (0.1)	0 (0.0)	1 (0.1)
四肢痛	6 (0.7)	5 (1.2)	11 (0.9)
重感	1 (0.1)	0 (0.0)	1 (0.1)
腱炎	1 (0.1)	1 (0.2)	2 (0.2)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)			
皮膚乳頭腫	1 (0.1)	0 (0.0)	1 (0.1)
神経系障害			
味覚消失	0 (0.0)	1 (0.2)	1 (0.1)
平衡障害	1 (0.1)	0 (0.0)	1 (0.1)
協調運動異常	1 (0.1)	0 (0.0)	1 (0.1)
注意力障害	6 (0.7)	1 (0.2)	7 (0.6)
浮動性めまい	65 (7.7)	17 (4.0)	82 (6.5)
労作性めまい	1 (0.1)	0 (0.0)	1 (0.1)
体位性めまい	2 (0.2)	0 (0.0)	2 (0.2)
味覚異常	12 (1.4)	3 (0.7)	15 (1.2)
頭部不快感	1 (0.1)	0 (0.0)	1 (0.1)
頭痛	109 (12.9)	39 (9.2)	148 (11.7)
味覚過敏	1 (0.1)	0 (0.0)	1 (0.1)
感覚鈍麻	4 (0.5)	1 (0.2)	5 (0.4)
虚血性脳卒中	0 (0.0)	1 (0.2)	1 (0.1)
嗜眠	2 (0.2)	3 (0.7)	5 (0.4)
意識消失	3 (0.4)	0 (0.0)	3 (0.2)
記憶障害	0 (0.0)	1 (0.2)	1 (0.1)
精神的機能障害	0 (0.0)	1 (0.2)	1 (0.1)
片頭痛	2 (0.2)	1 (0.2)	3 (0.2)
前兆を伴う片頭痛	1 (0.1)	0 (0.0)	1 (0.1)
不随意性筋収縮	2 (0.2)	0 (0.0)	2 (0.2)
ナルコレプシー	3 (0.4)	0 (0.0)	3 (0.2)
錯感覚	5 (0.6)	0 (0.0)	5 (0.4)
嗅覚錯誤	1 (0.1)	0 (0.0)	1 (0.1)
失神寸前の状態	2 (0.2)	0 (0.0)	2 (0.2)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
下肢静止不能症候群	1 (0.1)	1 (0.2)	2 (0.2)
失神	8 (0.9)	0 (0.0)	8 (0.6)
緊張性頭痛	2 (0.2)	0 (0.0)	2 (0.2)
振戦	1 (0.1)	1 (0.2)	2 (0.2)
第7脳神経麻痺	1 (0.1)	0 (0.0)	1 (0.1)
精神障害			
異常な夢	1 (0.1)	2 (0.5)	3 (0.2)
激越	1 (0.1)	0 (0.0)	1 (0.1)
不安	4 (0.5)	0 (0.0)	4 (0.3)
抑うつ気分	1 (0.1)	0 (0.0)	1 (0.1)
うつ病	7 (0.8)	0 (0.0)	7 (0.6)
初期不眠症	1 (0.1)	0 (0.0)	1 (0.1)
不眠症	34 (4.0)	6 (1.4)	40 (3.2)
リビドー減退	3 (0.4)	0 (0.0)	3 (0.2)
リビドー消失	1 (0.1)	0 (0.0)	1 (0.1)
大うつ病	1 (0.1)	0 (0.0)	1 (0.1)
神経過敏	2 (0.2)	0 (0.0)	2 (0.2)
パニック発作	2 (0.2)	0 (0.0)	2 (0.2)
パニック反応	1 (0.1)	0 (0.0)	1 (0.1)
睡眠障害	4 (0.5)	0 (0.0)	4 (0.3)
夢遊症	1 (0.1)	0 (0.0)	1 (0.1)
腎および尿路障害			
高窒素血症	0 (0.0)	1 (0.2)	1 (0.1)
膀胱不快感	0 (0.0)	1 (0.2)	1 (0.1)
膀胱痛	1 (0.1)	0 (0.0)	1 (0.1)
着色尿	0 (0.0)	1 (0.2)	1 (0.1)
排尿困難	3 (0.4)	1 (0.2)	4 (0.3)
遺尿	2 (0.2)	0 (0.0)	2 (0.2)
血尿	9 (1.1)	5 (1.2)	14 (1.1)
緊張性膀胱	1 (0.1)	0 (0.0)	1 (0.1)
失禁	1 (0.1)	0 (0.0)	1 (0.1)
尿意切迫	6 (0.7)	2 (0.5)	8 (0.6)
腎結石症	2 (0.2)	1 (0.2)	3 (0.2)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
腎および尿路障害			
夜間頻尿	278 (33.0)	59 (13.9)	337 (26.6)
乏尿	2 (0.2)	0 (0.0)	2 (0.2)
頻尿	160 (19.0)	21 (5.0)	181 (14.3)
多尿	326 (38.7)	75 (17.7)	401 (31.6)
腎仙痛	1 (0.1)	0 (0.0)	1 (0.1)
腎嚢胞出血	0 (0.0)	1 (0.2)	1 (0.1)
腎嚢胞破裂	0 (0.0)	2 (0.5)	2 (0.2)
急性腎不全	2 (0.2)	1 (0.2)	3 (0.2)
腎機能障害	5 (0.6)	3 (0.7)	8 (0.6)
腎臓痛	40 (4.7)	22 (5.2)	62 (4.9)
切迫性尿失禁	0 (0.0)	1 (0.2)	1 (0.1)
尿失禁	3 (0.4)	0 (0.0)	3 (0.2)
尿閉	1 (0.1)	0 (0.0)	1 (0.1)
生殖系および乳房障害			
無月経	1 (0.1)	0 (0.0)	1 (0.1)
月経困難症	0 (0.0)	1 (0.2)	1 (0.1)
勃起不全	4 (0.5)	1 (0.2)	5 (0.4)
月経過多	2 (0.2)	1 (0.2)	3 (0.2)
月経遅延	0 (0.0)	1 (0.2)	1 (0.1)
不規則月経	2 (0.2)	0 (0.0)	2 (0.2)
性機能不全	1 (0.1)	0 (0.0)	1 (0.1)
精巣痛	0 (0.0)	1 (0.2)	1 (0.1)
外陰腔乾燥	1 (0.1)	1 (0.2)	2 (0.2)
呼吸器、胸郭および縦隔障害			
喘息	1 (0.1)	0 (0.0)	1 (0.1)
運動誘発喘息	0 (0.0)	1 (0.2)	1 (0.1)
咳嗽	14 (1.7)	4 (0.9)	18 (1.4)
咽喉乾燥	5 (0.6)	1 (0.2)	6 (0.5)
発声障害	2 (0.2)	0 (0.0)	2 (0.2)
呼吸困難	6 (0.7)	0 (0.0)	6 (0.5)
安静時呼吸困難	1 (0.1)	0 (0.0)	1 (0.1)
労作性呼吸困難	3 (0.4)	0 (0.0)	3 (0.2)
鼻出血	3 (0.4)	1 (0.2)	4 (0.3)

表2.7.4.7-30

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NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害			
喉頭浮腫	0 (0.0)	1 (0.2)	1 (0.1)
鼻乾燥	1 (0.1)	1 (0.2)	2 (0.2)
口腔咽頭痛	3 (0.4)	0 (0.0)	3 (0.2)
咽頭浮腫	0 (0.0)	1 (0.2)	1 (0.1)
肺塞栓症	1 (0.1)	0 (0.0)	1 (0.1)
肺線維症	1 (0.1)	0 (0.0)	1 (0.1)
鼻漏	1 (0.1)	0 (0.0)	1 (0.1)
くしゃみ	1 (0.1)	1 (0.2)	2 (0.2)
いびき	1 (0.1)	0 (0.0)	1 (0.1)
喘鳴	0 (0.0)	1 (0.2)	1 (0.1)
皮膚および皮下組織障害			
ざ瘡	3 (0.4)	0 (0.0)	3 (0.2)
脱毛症	5 (0.6)	4 (0.9)	9 (0.7)
円形脱毛症	0 (0.0)	1 (0.2)	1 (0.1)
皮膚炎	1 (0.1)	1 (0.2)	2 (0.2)
皮膚乾燥	25 (3.0)	5 (1.2)	30 (2.4)
斑状出血	1 (0.1)	0 (0.0)	1 (0.1)
湿疹	2 (0.2)	0 (0.0)	2 (0.2)
紅斑	0 (0.0)	1 (0.2)	1 (0.1)
毛髪成長異常	0 (0.0)	1 (0.2)	1 (0.1)
多汗症	2 (0.2)	1 (0.2)	3 (0.2)
乏汗症	1 (0.1)	0 (0.0)	1 (0.1)
機械性蕁麻疹	1 (0.1)	0 (0.0)	1 (0.1)
爪の障害	2 (0.2)	0 (0.0)	2 (0.2)
寝汗	2 (0.2)	1 (0.2)	3 (0.2)
爪破損	1 (0.1)	0 (0.0)	1 (0.1)
光線過敏性反応	1 (0.1)	0 (0.0)	1 (0.1)
色素沈着障害	2 (0.2)	1 (0.2)	3 (0.2)
そう痒症	16 (1.9)	6 (1.4)	22 (1.7)
発疹	8 (0.9)	1 (0.2)	9 (0.7)
そう痒性皮疹	1 (0.1)	0 (0.0)	1 (0.1)
皮膚色素脱失	1 (0.1)	0 (0.0)	1 (0.1)
皮膚変色	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-30

156-XXXX-251

NT-8.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
皮膚および皮下組織障害			
皮膚病変	1 (0.1)	0 (0.0)	1 (0.1)
皮膚反応	0 (0.0)	1 (0.2)	1 (0.1)
顔面腫脹	0 (0.0)	1 (0.2)	1 (0.1)
蕁麻疹	2 (0.2)	0 (0.0)	2 (0.2)
慢性蕁麻疹	1 (0.1)	0 (0.0)	1 (0.1)
乾皮症	1 (0.1)	0 (0.0)	1 (0.1)
外科および内科処置			
収れん薬療法	1 (0.1)	0 (0.0)	1 (0.1)
血管障害			
コントロール不良の血圧	1 (0.1)	0 (0.0)	1 (0.1)
深部静脈血栓症	0 (0.0)	1 (0.2)	1 (0.1)
ほてり	4 (0.5)	0 (0.0)	4 (0.3)
高血圧	35 (4.2)	15 (3.5)	50 (3.9)
高血圧クリーゼ	1 (0.1)	0 (0.0)	1 (0.1)
低血圧	15 (1.8)	8 (1.9)	23 (1.8)
起立性低血圧	2 (0.2)	1 (0.2)	3 (0.2)
末梢冷感	5 (0.6)	2 (0.5)	7 (0.6)
レイノー現象	1 (0.1)	1 (0.2)	2 (0.2)
TOTAL	734 (87.1)	260 (61.3)	994 (78.5)

MedDRA/J version14.1

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表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血液およびリンパ系障害								
貧血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
好酸球増加症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鉄欠乏性貧血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球増加症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血小板減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害								
狭心症	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
房室ブロック	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
左室機能不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁疾患	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	20 (2.1)	2 (0.2)	0 (0.0)	22 (2.3)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
上室性頻脈	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
心室性期外収縮	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害								
難聴	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	15 (1.6)	1 (0.1)	1 (0.1)	17 (1.8)	6 (1.2)	0 (0.0)	0 (0.0)	6 (1.2)
頭位性回転性めまい	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害								
続発性副甲状腺機能低下症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
眼障害								
眼瞼炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼乾燥	10 (1.0)	0 (0.0)	0 (0.0)	10 (1.0)	2 (0.4)	3 (0.6)	1 (0.2)	6 (1.2)
眼瞼浮腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	2 (0.2)	0 (0.0)	1 (0.1)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
羞明	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光視症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霧視	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
硝子体浮遊物	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害								
腹部不快感	6 (0.6)	1 (0.1)	1 (0.1)	8 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
腹部膨満	19 (2.0)	6 (0.6)	0 (0.0)	25 (2.6)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
腹痛	5 (0.5)	6 (0.6)	2 (0.2)	13 (1.4)	4 (0.8)	2 (0.4)	1 (0.2)	7 (1.4)
上腹部痛	14 (1.5)	8 (0.8)	1 (0.1)	23 (2.4)	8 (1.7)	2 (0.4)	0 (0.0)	10 (2.1)
アフタ性口内炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	44 (4.6)	7 (0.7)	1 (0.1)	52 (5.4)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
齲歯	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下痢	20 (2.1)	7 (0.7)	2 (0.2)	29 (3.0)	7 (1.4)	2 (0.4)	0 (0.0)	9 (1.9)
口内乾燥	114 (11.9)	30 (3.1)	8 (0.8)	152 (15.8)	43 (8.9)	11 (2.3)	2 (0.4)	56 (11.6)
十二指腸炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
消化不良	24 (2.5)	5 (0.5)	2 (0.2)	31 (3.2)	5 (1.0)	1 (0.2)	0 (0.0)	6 (1.2)
嚥下障害	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼓腸	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動過剰	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	8 (0.8)	4 (0.4)	0 (0.0)	12 (1.2)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
歯肉炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
裂孔ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃酸過多	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の感覚鈍麻	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口唇乾燥	6 (0.6)	0 (0.0)	0 (0.0)	6 (0.6)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
弛緩歯	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	30 (3.1)	9 (0.9)	0 (0.0)	39 (4.1)	19 (3.9)	3 (0.6)	0 (0.0)	22 (4.6)
食道炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
舌苔	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
臍ヘルニア	2 (0.2)	0 (0.0)	1 (0.1)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	12 (1.2)	3 (0.3)	0 (0.0)	15 (1.6)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
一般・全身障害および投与部位の状態								
無力症	17 (1.8)	18 (1.9)	6 (0.6)	41 (4.3)	3 (0.6)	4 (0.8)	1 (0.2)	8 (1.7)
腋窩痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
胸痛	6 (0.6)	5 (0.5)	0 (0.0)	11 (1.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
悪寒	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	66 (6.9)	21 (2.2)	7 (0.7)	94 (9.8)	13 (2.7)	8 (1.7)	2 (0.4)	23 (4.8)
異常感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
冷感	4 (0.4)	2 (0.2)	1 (0.1)	7 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びくびく感	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
易刺激性	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	9 (0.9)	0 (0.0)	0 (0.0)	9 (0.9)	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.8)
粘膜乾燥	6 (0.6)	1 (0.1)	1 (0.1)	8 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
浮腫	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.4)
末梢性浮腫	18 (1.9)	3 (0.3)	0 (0.0)	21 (2.2)	8 (1.7)	3 (0.6)	0 (0.0)	11 (2.3)
疼痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不活発	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	338 (35.2)	157 (16.3)	30 (3.1)	525 (54.6)	78 (16.1)	11 (2.3)	4 (0.8)	93 (19.3)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
肝胆道系障害								
胆管炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	5 (0.5)	5 (0.5)	1 (0.1)	11 (1.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害								
過敏症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症								
急性扁桃炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
膀胱炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳垂感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
麦粒腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻咽頭炎	7 (0.7)	2 (0.2)	0 (0.0)	9 (0.9)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
口腔カンジダ症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔真菌感染	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
レンサ球菌性咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肺炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎盂腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腎嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)
副鼻腔炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ブドウ球菌感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿路感染	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
ウイルス感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部腔カンジダ症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症								
挫傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
熱疲労	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
外傷後疼痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査								
アラニン・アミノトランスフェラーゼ増加	22 (2.3)	10 (1.0)	3 (0.3)	35 (3.6)	11 (2.3)	1 (0.2)	0 (0.0)	12 (2.5)
アスパラギン酸アミノトランスフェラーゼ増加	20 (2.1)	8 (0.8)	2 (0.2)	30 (3.1)	9 (1.9)	1 (0.2)	0 (0.0)	10 (2.1)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中アルカリホスファターゼ増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ビリルビン増加	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カルシウム増加	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
血中コレステロール増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中クレアチニン増加	66 (6.9)	29 (3.0)	0 (0.0)	95 (9.9)	39 (8.1)	9 (1.9)	0 (0.0)	48 (9.9)
血中ブドウ糖増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
拡張期血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血圧上昇	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
血中ナトリウム増加	10 (1.0)	1 (0.1)	0 (0.0)	11 (1.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血中尿素増加	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	7 (1.4)	1 (0.2)	0 (0.0)	8 (1.7)
血中尿酸増加	14 (1.5)	2 (0.2)	0 (0.0)	16 (1.7)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
心雑音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
シスタチンC増加	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	4 (0.8)	0 (0.0)	0 (0.0)	4 (0.8)
心電図異常T波	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	11 (1.1)	5 (0.5)	0 (0.0)	16 (1.7)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
ヘマトクリット減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
ヘマトクリット増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肝酵素異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	3 (0.3)	6 (0.6)	1 (0.1)	10 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
I N R 増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リパーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝機能検査異常	1 (0.1)	4 (0.4)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球容積減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球容積増加	4 (0.4)	0 (0.0)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好中球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血小板数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
Q O L 低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
トランスアミナーゼ上昇	4 (0.4)	3 (0.3)	2 (0.2)	9 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧低下	6 (0.6)	2 (0.2)	0 (0.0)	8 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿浸透圧上昇	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量増加	12 (1.2)	2 (0.2)	1 (0.1)	15 (1.6)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
ウエスト周囲径増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	24 (2.5)	4 (0.4)	0 (0.0)	28 (2.9)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
体重増加	13 (1.4)	3 (0.3)	0 (0.0)	16 (1.7)	3 (0.6)	2 (0.4)	0 (0.0)	5 (1.0)
白血球数増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
代謝および栄養障害								
食欲減退	40 (4.2)	14 (1.5)	1 (0.1)	55 (5.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
脱水	7 (0.7)	5 (0.5)	3 (0.3)	15 (1.6)	1 (0.2)	5 (1.0)	1 (0.2)	7 (1.4)
糖尿病	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物渴望	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
痛風	7 (0.7)	8 (0.8)	0 (0.0)	15 (1.6)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
高カルシウム血症	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
高コレステロール血症	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
高血糖	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
高カリウム血症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高脂血症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
高ナトリウム血症	21 (2.2)	5 (0.5)	0 (0.0)	26 (2.7)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
高トリグリセリド血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	20 (2.1)	3 (0.3)	0 (0.0)	23 (2.4)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
代謝および栄養障害								
低カルシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血糖症	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	1 (0.1)	3 (0.3)	0 (0.0)	4 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
低ナトリウム血症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
低リン酸血症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過体重	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	50 (5.2)	44 (4.6)	6 (0.6)	100 (10.4)	12 (2.5)	5 (1.0)	0 (0.0)	17 (3.5)
ビタミンB 1 2 欠乏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重変動	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害								
関節痛	8 (0.8)	3 (0.3)	0 (0.0)	11 (1.1)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
背部痛	7 (0.7)	3 (0.3)	2 (0.2)	12 (1.2)	7 (1.4)	2 (0.4)	1 (0.2)	10 (2.1)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
線維筋痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
側腹部痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
椎間板変性症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
関節腫脹	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙攣	13 (1.4)	6 (0.6)	0 (0.0)	19 (2.0)	5 (1.0)	2 (0.4)	0 (0.0)	7 (1.4)
筋骨格痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	5 (0.5)	6 (0.6)	0 (0.0)	11 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
頸部痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	3 (0.3)	5 (0.5)	0 (0.0)	8 (0.8)	2 (0.4)	3 (0.6)	0 (0.0)	5 (1.0)
重感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
腱炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）								
皮膚乳頭腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
味覚消失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平衡障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
脳梗塞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	3 (0.3)	3 (0.3)	1 (0.1)	7 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
浮動性めまい	57 (5.9)	14 (1.5)	1 (0.1)	72 (7.5)	16 (3.3)	6 (1.2)	0 (0.0)	22 (4.6)
労作性めまい	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	10 (1.0)	4 (0.4)	0 (0.0)	14 (1.5)	2 (0.4)	1 (0.2)	0 (0.0)	3 (0.6)
頭部不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	97 (10.1)	26 (2.7)	6 (0.6)	129 (13.4)	37 (7.7)	6 (1.2)	1 (0.2)	44 (9.1)
味覚過敏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
嗜眠	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
意識消失	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
片頭痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
前兆を伴う片頭痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	3 (0.3)	1 (0.1)	1 (0.1)	5 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神寸前の状態	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
坐骨神経痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
失神	2 (0.2)	6 (0.6)	0 (0.0)	8 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
第7脳神経麻痺	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害								
異常な夢	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
激越	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	5 (0.5)	2 (0.2)	0 (0.0)	7 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	21 (2.2)	13 (1.4)	6 (0.6)	40 (4.2)	5 (1.0)	1 (0.2)	0 (0.0)	6 (1.2)
リビドー減退	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リビドー消失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大うつ病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経過敏	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック反応	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
夢遊症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害								
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱刺激症状	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
排尿困難	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
遺尿	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
腎および尿路障害								
血尿	6 (0.6)	3 (0.3)	1 (0.1)	10 (1.0)	4 (0.8)	2 (0.4)	1 (0.2)	7 (1.4)
緊張性膀胱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿意切迫	5 (0.5)	1 (0.1)	0 (0.0)	6 (0.6)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)
腎結石症	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
夜間頻尿	178 (18.5)	92 (9.6)	10 (1.0)	280 (29.1)	52 (10.8)	9 (1.9)	0 (0.0)	61 (12.6)
乏尿	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	134 (13.9)	67 (7.0)	22 (2.3)	223 (23.2)	18 (3.7)	5 (1.0)	2 (0.4)	25 (5.2)
多尿	182 (18.9)	142 (14.8)	42 (4.4)	366 (38.1)	62 (12.8)	16 (3.3)	2 (0.4)	80 (16.6)
腎仙痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腎嚢胞破裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)
急性腎不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腎機能障害	6 (0.6)	1 (0.1)	0 (0.0)	7 (0.7)	1 (0.2)	2 (0.4)	0 (0.0)	3 (0.6)
腎臓痛	24 (2.5)	16 (1.7)	6 (0.6)	46 (4.8)	6 (1.2)	11 (2.3)	9 (1.9)	26 (5.4)
終末尿滴下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
尿失禁	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿閉	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害								
無月経	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
射精障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
勃起不全	0 (0.0)	2 (0.2)	2 (0.2)	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乳汁漏出症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
月経過多	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
月経障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
生殖系および乳房障害								
不規則月経	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
精巣痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
外陰腔乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
呼吸器、胸郭および縦隔障害								
喘息	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
慢性気管支炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	13 (1.4)	2 (0.2)	0 (0.0)	15 (1.6)	4 (0.8)	1 (0.2)	0 (0.0)	5 (1.0)
咽喉乾燥	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
発声障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	3 (0.3)	4 (0.4)	0 (0.0)	7 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
安静時呼吸困難	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	0 (0.0)	3 (0.3)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
鼻乾燥	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
口腔咽頭痛	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
肺塞栓症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺線維症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
いびき	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-31

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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
ざ瘡	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	4 (0.4)	1 (0.1)	0 (0.0)	5 (0.5)	1 (0.2)	3 (0.6)	0 (0.0)	4 (0.8)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血性水疱	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
接触性皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	28 (2.9)	1 (0.1)	1 (0.1)	30 (3.1)	6 (1.2)	0 (0.0)	0 (0.0)	6 (1.2)
斑状出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
多汗症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乏汗症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機械性蕁麻疹	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
爪破損	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光線過敏性反応	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
そう痒症	17 (1.8)	2 (0.2)	0 (0.0)	19 (2.0)	5 (1.0)	1 (0.2)	0 (0.0)	6 (1.2)
乾癬	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	8 (0.8)	2 (0.2)	0 (0.0)	10 (1.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
そう痒性皮疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚病変	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
顔面腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
蕁麻疹	3 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性蕁麻疹	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-31
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CT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity（全体）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=961)				Placebo (N=483)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
外科および内科処置								
収れん薬療法	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害								
コントロール不良の血圧	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
潮紅	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	2 (0.2)	1 (0.1)	1 (0.1)	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	32 (3.3)	14 (1.5)	0 (0.0)	46 (4.8)	12 (2.5)	7 (1.4)	0 (0.0)	19 (3.9)
高血圧クリーゼ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	10 (1.0)	6 (0.6)	0 (0.0)	16 (1.7)	5 (1.0)	4 (0.8)	0 (0.0)	9 (1.9)
不安定血圧	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
末梢冷感	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.5)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
レイノー現象	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

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表2.7.4.7-32

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JT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血液およびリンパ系障害								
鉄欠乏性貧血	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
心臓障害								
狭心症	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
房室ブロック	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
左室不全	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	7 (5.9)	0 (0.0)	0 (0.0)	7 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害								
耳鳴	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭位性回転性めまい	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害								
霰粒腫	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
眼乾燥	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
眼瞼浮腫	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害								
腹部不快感	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
腹部膨満	6 (5.1)	0 (0.0)	0 (0.0)	6 (5.1)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
腹痛	1 (0.8)	0 (0.0)	1 (0.8)	2 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
上腹部痛	8 (6.8)	0 (0.0)	0 (0.0)	8 (6.8)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
口唇炎	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	11 (9.3)	0 (0.0)	0 (0.0)	11 (9.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下痢	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
口内乾燥	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-32

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JT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild	Mod	Sev	Total	Mild	Mod	Sev	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害								
十二指腸炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	2 (1.7)	2 (1.7)	0 (0.0)	4 (3.4)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
歯肉炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
裂孔ヘルニア	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	4 (3.4)	1 (0.8)	0 (0.0)	5 (4.2)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
臍ヘルニア	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態								
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
胸痛	3 (2.5)	1 (0.8)	0 (0.0)	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	8 (6.8)	2 (1.7)	1 (0.8)	11 (9.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
熱感	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	8 (6.8)	0 (0.0)	0 (0.0)	8 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性浮腫	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	2 (3.4)	1 (1.7)	0 (0.0)	3 (5.1)
疼痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	89 (75.4)	17 (14.4)	0 (0.0)	106 (89.8)	17 (28.8)	0 (0.0)	0 (0.0)	17 (28.8)
肝胆道系障害								
肝機能異常	5 (4.2)	5 (4.2)	1 (0.8)	11 (9.3)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
肝障害	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害								
季節性アレルギー	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-32

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JT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild	Mod	Sev	Total	Mild	Mod	Sev	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症								
急性扁桃炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
带状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
麦粒腫	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	3 (2.5)	1 (0.8)	0 (0.0)	4 (3.4)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
腎嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
上気道感染	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症								
挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
熱射病	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)
臨床検査								
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	1 (0.8)	1 (0.8)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	1 (0.8)	1 (0.8)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
血中クレアチニン増加	4 (3.4)	1 (0.8)	0 (0.0)	5 (4.2)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
血中カリウム減少	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
血中尿酸増加	4 (3.4)	0 (0.0)	0 (0.0)	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
γ-グルタミルトランスフェラーゼ増加	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧上昇	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	8 (6.8)	0 (0.0)	0 (0.0)	8 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害								
食欲減退	8 (6.8)	3 (2.5)	0 (0.0)	11 (9.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	0 (0.0)	1 (0.8)	1 (0.8)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-32

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JT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
代謝および栄養障害								
高カルシウム血症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
高脂血症	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
高トリグリセリド血症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	12 (10.2)	1 (0.8)	0 (0.0)	13 (11.0)	3 (5.1)	0 (0.0)	0 (0.0)	3 (5.1)
筋骨格系および結合組織障害								
関節痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
背部痛	4 (3.4)	1 (0.8)	1 (0.8)	6 (5.1)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
側腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
筋痙縮	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
筋骨格痛	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
四肢痛	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）								
汗腺腫瘍	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害								
味覚消失	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
脳梗塞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	6 (5.1)	1 (0.8)	0 (0.0)	7 (5.9)	5 (8.5)	0 (0.0)	0 (0.0)	5 (8.5)
異常感覚	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	19 (16.1)	0 (0.0)	1 (0.8)	20 (16.9)	5 (8.5)	0 (0.0)	0 (0.0)	5 (8.5)
感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
意識消失	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)

表2.7.4.7-32

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JT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
精神障害								
不眠症	3 (2.5)	3 (2.5)	0 (0.0)	6 (5.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
腎および尿路障害								
膀胱刺激症状	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	0 (0.0)	0 (0.0)	2 (3.4)
夜間頻尿	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)
頻尿	48 (40.7)	12 (10.2)	3 (2.5)	63 (53.4)	4 (6.8)	0 (0.0)	0 (0.0)	4 (6.8)
多尿	32 (27.1)	7 (5.9)	1 (0.8)	40 (33.9)	3 (5.1)	1 (1.7)	1 (1.7)	5 (8.5)
腎機能障害	1 (0.8)	1 (0.8)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎臓痛	4 (3.4)	2 (1.7)	0 (0.0)	6 (5.1)	3 (5.1)	1 (1.7)	0 (0.0)	4 (6.8)
終末尿滴下	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害								
乳房嚢胞	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
射精障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳汁漏出症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
月経障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
呼吸器、胸郭および縦隔障害								
喘息	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
呼吸困難	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
アレルギー性鼻炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-32

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JT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=118)				Placebo (N=59)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
ざ瘡	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	5 (4.2)	0 (0.0)	0 (0.0)	5 (4.2)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
湿疹	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏汗症	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	3 (2.5)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
蕁麻疹	2 (1.7)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性蕁麻疹	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害								
潮紅	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	9 (7.6)	2 (1.7)	0 (0.0)	11 (9.3)	3 (5.1)	1 (1.7)	0 (0.0)	4 (6.8)
低血圧	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)
不安定血圧	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)

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表2.7.4.7-33

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
血液およびリンパ系障害								
貧血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
好酸球増加症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
白血球増加症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血小板減少症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害								
心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
左室機能不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁疾患	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	13 (1.5)	2 (0.2)	0 (0.0)	15 (1.8)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
上室性頻脈	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
耳および迷路障害								
難聴	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	12 (1.4)	1 (0.1)	1 (0.1)	14 (1.7)	6 (1.4)	0 (0.0)	0 (0.0)	6 (1.4)
内分泌障害								
続発性副甲状腺機能低下症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害								
眼瞼炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	7 (0.8)	0 (0.0)	0 (0.0)	7 (0.8)	1 (0.2)	3 (0.7)	1 (0.2)	5 (1.2)
緑内障	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
光視症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霧視	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

表2.7.4.7-33

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
眼障害								
硝子体浮遊物	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害								
腹部不快感	4 (0.5)	1 (0.1)	1 (0.1)	6 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腹部膨満	13 (1.5)	6 (0.7)	0 (0.0)	19 (2.3)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
腹痛	4 (0.5)	6 (0.7)	1 (0.1)	11 (1.3)	2 (0.5)	2 (0.5)	1 (0.2)	5 (1.2)
上腹部痛	6 (0.7)	8 (0.9)	1 (0.1)	15 (1.8)	6 (1.4)	1 (0.2)	0 (0.0)	7 (1.7)
アフタ性口内炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	33 (3.9)	7 (0.8)	1 (0.1)	41 (4.9)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
齲歯	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下痢	18 (2.1)	7 (0.8)	2 (0.2)	27 (3.2)	6 (1.4)	2 (0.5)	0 (0.0)	8 (1.9)
口内乾燥	113 (13.4)	30 (3.6)	8 (0.9)	151 (17.9)	43 (10.1)	11 (2.6)	2 (0.5)	56 (13.2)
消化不良	20 (2.4)	5 (0.6)	2 (0.2)	27 (3.2)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
嚥下障害	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼓腸	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動過剰	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	6 (0.7)	2 (0.2)	0 (0.0)	8 (0.9)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
舌痛	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃酸過多	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の感覚鈍麻	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口唇乾燥	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
弛緩歯	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-33

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
胃腸障害								
悪心	26 (3.1)	8 (0.9)	0 (0.0)	34 (4.0)	18 (4.2)	3 (0.7)	0 (0.0)	21 (5.0)
食道炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌苔	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
臍ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	10 (1.2)	3 (0.4)	0 (0.0)	13 (1.5)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
一般・全身障害および投与部位の状態								
無力症	17 (2.0)	18 (2.1)	6 (0.7)	41 (4.9)	3 (0.7)	4 (0.9)	1 (0.2)	8 (1.9)
腋窩痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	3 (0.4)	4 (0.5)	0 (0.0)	7 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
悪寒	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	58 (6.9)	19 (2.3)	6 (0.7)	83 (9.8)	13 (3.1)	8 (1.9)	2 (0.5)	23 (5.4)
異常感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	4 (0.5)	2 (0.2)	1 (0.1)	7 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びくびく感	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
易刺激性	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	1 (0.2)	1 (0.2)	4 (0.9)
粘膜乾燥	6 (0.7)	1 (0.1)	1 (0.1)	8 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
浮腫	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	1 (0.2)	2 (0.5)
末梢性浮腫	14 (1.7)	3 (0.4)	0 (0.0)	17 (2.0)	6 (1.4)	2 (0.5)	0 (0.0)	8 (1.9)
疼痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
一般・全身障害および投与部位の状態								
不活発	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
腫脹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	249 (29.5)	140 (16.6)	30 (3.6)	419 (49.7)	61 (14.4)	11 (2.6)	4 (0.9)	76 (17.9)
肝胆道系障害								
胆管炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害								
過敏症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症								
気管支炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
憩室炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳垂感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
インフルエンザ	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻咽頭炎	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔カンジダ症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔真菌感染	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
感染症および寄生虫症								
レンサ球菌性咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肺炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎盂腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腎嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
副鼻腔炎	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ブドウ球菌感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿路感染	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	4 (0.9)	0 (0.0)	0 (0.0)	4 (0.9)
ウイルス感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部膺カンジダ症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症								
挫傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱疲労	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査								
アラニン・アミノトランスフェラーゼ増加	22 (2.6)	9 (1.1)	2 (0.2)	33 (3.9)	11 (2.6)	1 (0.2)	0 (0.0)	12 (2.8)
アスパラギン酸アミノトランスフェラーゼ増加	20 (2.4)	7 (0.8)	1 (0.1)	28 (3.3)	9 (2.1)	1 (0.2)	0 (0.0)	10 (2.4)
血中アルカリホスファターゼ増加	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ビリルビン増加	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カルシウム増加	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中クレアチニン増加	62 (7.4)	28 (3.3)	0 (0.0)	90 (10.7)	36 (8.5)	9 (2.1)	0 (0.0)	45 (10.6)
血中ブドウ糖増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
拡張期血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血圧上昇	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血中ナトリウム増加	10 (1.2)	1 (0.1)	0 (0.0)	11 (1.3)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血中尿素増加	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	7 (1.7)	1 (0.2)	0 (0.0)	8 (1.9)
血中尿酸増加	10 (1.2)	2 (0.2)	0 (0.0)	12 (1.4)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
心雑音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
臨床検査								
シスタチンC増加	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
心電図異常T波	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	11 (1.3)	4 (0.5)	0 (0.0)	15 (1.8)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
ヘマトクリット減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
ヘマトクリット増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肝酵素異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	3 (0.4)	6 (0.7)	1 (0.1)	10 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
I N R 増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リパーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
肝機能検査異常	1 (0.1)	4 (0.5)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球容積減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平均赤血球容積増加	4 (0.5)	0 (0.0)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
好中球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血小板数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
Q O L 低下	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
トランスアミナーゼ上昇	2 (0.2)	3 (0.4)	2 (0.2)	7 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧低下	6 (0.7)	2 (0.2)	0 (0.0)	8 (0.9)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
尿量増加	12 (1.4)	2 (0.2)	1 (0.1)	15 (1.8)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
ウエスト周囲径増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	16 (1.9)	4 (0.5)	0 (0.0)	20 (2.4)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
体重増加	12 (1.4)	3 (0.4)	0 (0.0)	15 (1.8)	3 (0.7)	2 (0.5)	0 (0.0)	5 (1.2)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
代謝および栄養障害								
食欲減退	32 (3.8)	11 (1.3)	1 (0.1)	44 (5.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
脱水	7 (0.8)	4 (0.5)	2 (0.2)	13 (1.5)	1 (0.2)	5 (1.2)	1 (0.2)	7 (1.7)
糖尿病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物渴望	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-33

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
代謝および栄養障害								
食物不耐性	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
痛風	5 (0.6)	8 (0.9)	0 (0.0)	13 (1.5)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
高カルシウム血症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
高コレステロール血症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
高血糖	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
高カリウム血症	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高ナトリウム血症	21 (2.5)	5 (0.6)	0 (0.0)	26 (3.1)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
高尿酸血症	8 (0.9)	2 (0.2)	0 (0.0)	10 (1.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
低カルシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血糖症	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	1 (0.1)	3 (0.4)	0 (0.0)	4 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
低ナトリウム血症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
低リン酸血症	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過体重	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	50 (5.9)	44 (5.2)	6 (0.7)	100 (11.9)	12 (2.8)	5 (1.2)	0 (0.0)	17 (4.0)
ビタミンB 1 2 欠乏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重変動	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害								
関節痛	7 (0.8)	3 (0.4)	0 (0.0)	10 (1.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
背部痛	3 (0.4)	2 (0.2)	1 (0.1)	6 (0.7)	5 (1.2)	2 (0.5)	1 (0.2)	8 (1.9)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
線維筋痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
側腹部痛	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板変性症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	12 (1.4)	6 (0.7)	0 (0.0)	18 (2.1)	4 (0.9)	2 (0.5)	0 (0.0)	6 (1.4)
筋骨格痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
筋骨格系および結合組織障害								
筋骨格硬直	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	4 (0.5)	6 (0.7)	0 (0.0)	10 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	2 (0.2)	4 (0.5)	0 (0.0)	6 (0.7)	2 (0.5)	3 (0.7)	0 (0.0)	5 (1.2)
重感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)								
皮膚乳頭腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害								
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
平衡障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	2 (0.2)	3 (0.4)	1 (0.1)	6 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
浮動性めまい	51 (6.0)	13 (1.5)	1 (0.1)	65 (7.7)	11 (2.6)	6 (1.4)	0 (0.0)	17 (4.0)
労作性めまい	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	9 (1.1)	3 (0.4)	0 (0.0)	12 (1.4)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
頭部不快感	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	78 (9.3)	26 (3.1)	5 (0.6)	109 (12.9)	32 (7.5)	6 (1.4)	1 (0.2)	39 (9.2)
味覚過敏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
嗜眠	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
意識消失	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
片頭痛	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
前兆を伴う片頭痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	3 (0.4)	1 (0.1)	1 (0.1)	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神寸前の状態	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
神経系障害								
下肢静止不能症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
失神	2 (0.2)	6 (0.7)	0 (0.0)	8 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
第7脳神経麻痺	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害								
異常な夢	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
激越	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	5 (0.6)	2 (0.2)	0 (0.0)	7 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	18 (2.1)	10 (1.2)	6 (0.7)	34 (4.0)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
リビドー減退	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リビドー消失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大うつ病	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経過敏	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック反応	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夢遊症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害								
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
排尿困難	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
遺尿	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	5 (0.6)	3 (0.4)	1 (0.1)	9 (1.1)	2 (0.5)	2 (0.5)	1 (0.2)	5 (1.2)
緊張性膀胱	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿意切迫	5 (0.6)	1 (0.1)	0 (0.0)	6 (0.7)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
腎結石症	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)

表2.7.4.7-33

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
腎および尿路障害								
夜間頻尿	177 (21.0)	91 (10.8)	10 (1.2)	278 (33.0)	51 (12.0)	8 (1.9)	0 (0.0)	59 (13.9)
乏尿	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	86 (10.2)	55 (6.5)	19 (2.3)	160 (19.0)	14 (3.3)	5 (1.2)	2 (0.5)	21 (5.0)
多尿	150 (17.8)	135 (16.0)	41 (4.9)	326 (38.7)	59 (13.9)	15 (3.5)	1 (0.2)	75 (17.7)
腎仙痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腎嚢胞破裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
急性腎不全	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
腎機能障害	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	1 (0.2)	2 (0.5)	0 (0.0)	3 (0.7)
腎臓痛	20 (2.4)	14 (1.7)	6 (0.7)	40 (4.7)	3 (0.7)	10 (2.4)	9 (2.1)	22 (5.2)
切迫性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
尿失禁	1 (0.1)	2 (0.2)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿閉	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害								
無月経	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
勃起不全	0 (0.0)	2 (0.2)	2 (0.2)	4 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
月経過多	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不規則月経	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
外陰腔乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
呼吸器、胸郭および縦隔障害								
喘息	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
咳嗽	12 (1.4)	2 (0.2)	0 (0.0)	14 (1.7)	3 (0.7)	1 (0.2)	0 (0.0)	4 (0.9)
咽喉乾燥	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
発声障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	3 (0.4)	3 (0.4)	0 (0.0)	6 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
安静時呼吸困難	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	0 (0.0)	3 (0.4)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

2.7.4 臨床的安全性

表2.7.4.7-33

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
呼吸器、胸郭および縦隔障害								
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
鼻乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔咽頭痛	3 (0.4)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
肺塞栓症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺線維症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
いびき	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚および皮下組織障害								
ざ瘡	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	4 (0.5)	1 (0.1)	0 (0.0)	5 (0.6)	1 (0.2)	3 (0.7)	0 (0.0)	4 (0.9)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚乾燥	23 (2.7)	1 (0.1)	1 (0.1)	25 (3.0)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
斑状出血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
多汗症	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乏汗症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機械性蕁麻疹	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
爪破損	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光線過敏性反応	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
そう痒症	14 (1.7)	2 (0.2)	0 (0.0)	16 (1.9)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.4)
発疹	6 (0.7)	2 (0.2)	0 (0.0)	8 (0.9)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
そう痒性皮疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-33

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NT-8.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843)				Placebo (N=424)			
	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)	Mild n (%)	Mod n (%)	Sev n (%)	Total n (%)
皮膚および皮下組織障害								
皮膚病変	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
顔面腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
蕁麻疹	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性蕁麻疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外科および内科処置								
収れん薬療法	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害								
コントロール不良の血圧	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
ほてり	2 (0.2)	1 (0.1)	1 (0.1)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	23 (2.7)	12 (1.4)	0 (0.0)	35 (4.2)	9 (2.1)	6 (1.4)	0 (0.0)	15 (3.5)
高血圧クリーゼ	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	9 (1.1)	6 (0.7)	0 (0.0)	15 (1.8)	4 (0.9)	4 (0.9)	0 (0.0)	8 (1.9)
起立性低血圧	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
末梢冷感	5 (0.6)	0 (0.0)	0 (0.0)	5 (0.6)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
レイノー現象	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

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表2.7.4.7-34
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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period（全体）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
血液およびリンパ系障害			
貧血	2 (0.2)	3 (0.6)	5 (0.3)
好酸球増加症	2 (0.2)	0 (0.0)	2 (0.1)
白血球減少症	1 (0.1)	1 (0.2)	2 (0.1)
リンパ節症	1 (0.1)	0 (0.0)	1 (0.1)
心臓障害			
狭心症	1 (0.1)	0 (0.0)	1 (0.1)
不整脈	2 (0.2)	0 (0.0)	2 (0.1)
徐脈	4 (0.4)	2 (0.4)	6 (0.4)
右脚ブロック	1 (0.1)	0 (0.0)	1 (0.1)
伝導障害	1 (0.1)	0 (0.0)	1 (0.1)
左室肥大	1 (0.1)	0 (0.0)	1 (0.1)
動悸	13 (1.4)	2 (0.4)	15 (1.0)
洞不全症候群	1 (0.1)	0 (0.0)	1 (0.1)
洞性徐脈	0 (0.0)	1 (0.2)	1 (0.1)
頻脈	7 (0.7)	1 (0.2)	8 (0.6)
先天性、家族性および遺伝性障害			
多嚢胞性肝疾患	1 (0.1)	0 (0.0)	1 (0.1)
耳および迷路障害			
難聴	1 (0.1)	0 (0.0)	1 (0.1)
耳痛	2 (0.2)	1 (0.2)	3 (0.2)
耳そう痒症	0 (0.0)	1 (0.2)	1 (0.1)
耳鳴	0 (0.0)	1 (0.2)	1 (0.1)
回転性めまい	8 (0.8)	2 (0.4)	10 (0.7)
眼障害			
結膜炎	0 (0.0)	1 (0.2)	1 (0.1)
眼乾燥	6 (0.6)	5 (1.0)	11 (0.8)
眼部腫脹	0 (0.0)	1 (0.2)	1 (0.1)
眼充血	0 (0.0)	1 (0.2)	1 (0.1)
開放隅角緑内障	0 (0.0)	1 (0.2)	1 (0.1)
光視症	1 (0.1)	0 (0.0)	1 (0.1)
霧視	2 (0.2)	0 (0.0)	2 (0.1)
視力障害	0 (0.0)	1 (0.2)	1 (0.1)
硝子体浮遊物	1 (0.1)	0 (0.0)	1 (0.1)
眼球乾燥	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
腹部不快感	5 (0.5)	1 (0.2)	6 (0.4)
腹部膨満	7 (0.7)	3 (0.6)	10 (0.7)
腹部ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
腹部腫瘍	1 (0.1)	0 (0.0)	1 (0.1)
腹痛	10 (1.0)	10 (2.1)	20 (1.4)
下腹部痛	2 (0.2)	0 (0.0)	2 (0.1)
上腹部痛	15 (1.6)	8 (1.7)	23 (1.6)
腹部圧痛	1 (0.1)	0 (0.0)	1 (0.1)
肛門そう痒症	1 (0.1)	0 (0.0)	1 (0.1)
アフタ性口内炎	2 (0.2)	0 (0.0)	2 (0.1)
便通不規則	1 (0.1)	0 (0.0)	1 (0.1)
呼気臭	2 (0.2)	0 (0.0)	2 (0.1)
口唇のひび割れ	1 (0.1)	0 (0.0)	1 (0.1)
便秘	45 (4.7)	4 (0.8)	49 (3.4)
下痢	36 (3.7)	9 (1.9)	45 (3.1)
口内乾燥	142 (14.8)	51 (10.6)	193 (13.4)
消化不良	21 (2.2)	3 (0.6)	24 (1.7)
嚥下障害	4 (0.4)	0 (0.0)	4 (0.3)
心窩部不快感	2 (0.2)	0 (0.0)	2 (0.1)
鼓腸	3 (0.3)	0 (0.0)	3 (0.2)
胃障害	1 (0.1)	0 (0.0)	1 (0.1)
胃炎	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動障害	1 (0.1)	0 (0.0)	1 (0.1)
胃食道逆流性疾患	3 (0.3)	0 (0.0)	3 (0.2)
舌痛	2 (0.2)	0 (0.0)	2 (0.1)
痔出血	1 (0.1)	0 (0.0)	1 (0.1)
胃酸過多	1 (0.1)	0 (0.0)	1 (0.1)
口の感覚鈍麻	1 (0.1)	1 (0.2)	2 (0.1)
鼠径ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
過敏性腸症候群	1 (0.1)	1 (0.2)	2 (0.1)
口唇乾燥	4 (0.4)	1 (0.2)	5 (0.3)
口腔内出血	0 (0.0)	1 (0.2)	1 (0.1)
悪心	33 (3.4)	19 (3.9)	52 (3.6)
口腔扁平苔癬	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
口腔内痛	1 (0.1)	0 (0.0)	1 (0.1)
口の錯感覚	1 (0.1)	0 (0.0)	1 (0.1)
口内炎	0 (0.0)	1 (0.2)	1 (0.1)
舌苔	2 (0.2)	0 (0.0)	2 (0.1)
舌変色	2 (0.2)	0 (0.0)	2 (0.1)
舌障害	1 (0.1)	1 (0.2)	2 (0.1)
舌乾燥	1 (0.1)	2 (0.4)	3 (0.2)
舌粘膜剥脱	1 (0.1)	0 (0.0)	1 (0.1)
変色歯	0 (0.0)	1 (0.2)	1 (0.1)
歯の障害	0 (0.0)	1 (0.2)	1 (0.1)
歯痛	2 (0.2)	0 (0.0)	2 (0.1)
臍ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
嘔吐	16 (1.7)	5 (1.0)	21 (1.5)
一般・全身障害および投与部位の状態			
無力症	29 (3.0)	5 (1.0)	34 (2.4)
腋窩痛	1 (0.1)	0 (0.0)	1 (0.1)
胸部不快感	5 (0.5)	0 (0.0)	5 (0.3)
胸痛	7 (0.7)	0 (0.0)	7 (0.5)
悪寒	4 (0.4)	1 (0.2)	5 (0.3)
異形成	0 (0.0)	1 (0.2)	1 (0.1)
運動耐性低下	1 (0.1)	0 (0.0)	1 (0.1)
顔面浮腫	1 (0.1)	0 (0.0)	1 (0.1)
疲労	56 (5.8)	18 (3.7)	74 (5.1)
冷感	5 (0.5)	0 (0.0)	5 (0.3)
酩酊感	1 (0.1)	0 (0.0)	1 (0.1)
熱感	1 (0.1)	1 (0.2)	2 (0.1)
びくびく感	1 (0.1)	0 (0.0)	1 (0.1)
高熱	0 (0.0)	1 (0.2)	1 (0.1)
炎症	1 (0.1)	0 (0.0)	1 (0.1)
インフルエンザ様疾患	1 (0.1)	0 (0.0)	1 (0.1)
易刺激性	3 (0.3)	0 (0.0)	3 (0.2)
倦怠感	3 (0.3)	2 (0.4)	5 (0.3)
粘膜乾燥	5 (0.5)	2 (0.4)	7 (0.5)
浮腫	1 (0.1)	4 (0.8)	5 (0.3)
末梢性浮腫	12 (1.2)	10 (2.1)	22 (1.5)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態			
疼痛	1 (0.1)	0 (0.0)	1 (0.1)
発熱	6 (0.6)	3 (0.6)	9 (0.6)
不活発	0 (0.0)	1 (0.2)	1 (0.1)
腫脹	1 (0.1)	0 (0.0)	1 (0.1)
温度変化不耐症	4 (0.4)	1 (0.2)	5 (0.3)
口渇	494 (51.4)	86 (17.8)	580 (40.2)
肝胆道系障害			
肝嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
肝臓痛	0 (0.0)	1 (0.2)	1 (0.1)
高ビリルビン血症	1 (0.1)	0 (0.0)	1 (0.1)
肝障害	2 (0.2)	0 (0.0)	2 (0.1)
免疫系障害			
過敏症	2 (0.2)	0 (0.0)	2 (0.1)
季節性アレルギー	4 (0.4)	0 (0.0)	4 (0.3)
感染症および寄生虫症			
急性扁桃炎	0 (0.0)	1 (0.2)	1 (0.1)
細菌尿	1 (0.1)	0 (0.0)	1 (0.1)
気管支炎	5 (0.5)	3 (0.6)	8 (0.6)
カンジダ症	1 (0.1)	2 (0.4)	3 (0.2)
膀胱炎	1 (0.1)	1 (0.2)	2 (0.1)
真菌感染	0 (0.0)	2 (0.4)	2 (0.1)
胃腸炎	2 (0.2)	4 (0.8)	6 (0.4)
帯状疱疹	0 (0.0)	1 (0.2)	1 (0.1)
インフルエンザ	8 (0.8)	2 (0.4)	10 (0.7)
喉頭炎	1 (0.1)	0 (0.0)	1 (0.1)
鼻咽頭炎	21 (2.2)	16 (3.3)	37 (2.6)
口腔カンジダ症	2 (0.2)	0 (0.0)	2 (0.1)
口腔ヘルペス	3 (0.3)	0 (0.0)	3 (0.2)
中耳炎	1 (0.1)	0 (0.0)	1 (0.1)
咽頭炎	1 (0.1)	4 (0.8)	5 (0.3)
腎盂腎炎	1 (0.1)	1 (0.2)	2 (0.1)
気道感染	1 (0.1)	1 (0.2)	2 (0.1)
鼻炎	3 (0.3)	2 (0.4)	5 (0.3)
副鼻腔炎	4 (0.4)	1 (0.2)	5 (0.3)
扁桃炎	2 (0.2)	0 (0.0)	2 (0.1)
上気道感染	8 (0.8)	4 (0.8)	12 (0.8)
尿路感染	10 (1.0)	4 (0.8)	14 (1.0)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
感染症および寄生虫症			
膣感染	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス感染	2 (0.2)	0 (0.0)	2 (0.1)
ウイルス性上気道感染	0 (0.0)	1 (0.2)	1 (0.1)
外陰部膣カンジダ症	0 (0.0)	2 (0.4)	2 (0.1)
外陰膣真菌感染	1 (0.1)	0 (0.0)	1 (0.1)
傷害、中毒および処置合併症			
挫傷	1 (0.1)	0 (0.0)	1 (0.1)
熱射病	1 (0.1)	0 (0.0)	1 (0.1)
関節脱臼	1 (0.1)	0 (0.0)	1 (0.1)
四肢損傷	0 (0.0)	1 (0.2)	1 (0.1)
肉離れ	0 (0.0)	1 (0.2)	1 (0.1)
処置による疼痛	0 (0.0)	1 (0.2)	1 (0.1)
軟部組織損傷	1 (0.1)	0 (0.0)	1 (0.1)
サンバーン	1 (0.1)	0 (0.0)	1 (0.1)
熱傷	1 (0.1)	0 (0.0)	1 (0.1)
歯牙破折	1 (0.1)	0 (0.0)	1 (0.1)
臨床検査			
アラニン・アミノトランスフェラーゼ増加	10 (1.0)	1 (0.2)	11 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	8 (0.8)	2 (0.4)	10 (0.7)
細菌検査陽性	0 (0.0)	1 (0.2)	1 (0.1)
血中ビリルビン増加	0 (0.0)	2 (0.4)	2 (0.1)
血中コレステロール増加	2 (0.2)	1 (0.2)	3 (0.2)
血中クレアチンホスホキナーゼ増加	1 (0.1)	0 (0.0)	1 (0.1)
血中クレアチニン増加	11 (1.1)	1 (0.2)	12 (0.8)
血中ブドウ糖減少	0 (0.0)	1 (0.2)	1 (0.1)
血中ブドウ糖増加	3 (0.3)	0 (0.0)	3 (0.2)
血中乳酸脱水素酵素増加	2 (0.2)	1 (0.2)	3 (0.2)
血中カリウム減少	2 (0.2)	0 (0.0)	2 (0.1)
血中カリウム増加	2 (0.2)	1 (0.2)	3 (0.2)
血圧低下	1 (0.1)	1 (0.2)	2 (0.1)
拡張期血圧上昇	0 (0.0)	1 (0.2)	1 (0.1)
血圧上昇	2 (0.2)	1 (0.2)	3 (0.2)
血中ナトリウム増加	3 (0.3)	1 (0.2)	4 (0.3)
血中尿素増加	1 (0.1)	0 (0.0)	1 (0.1)
血中尿酸増加	7 (0.7)	0 (0.0)	7 (0.5)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
臨床検査			
シスタチンC増加	1 (0.1)	0 (0.0)	1 (0.1)
心電図再分極異常	1 (0.1)	0 (0.0)	1 (0.1)
心電図T波逆転	0 (0.0)	1 (0.2)	1 (0.1)
好酸球数増加	2 (0.2)	0 (0.0)	2 (0.1)
γ-グルタミルトランスフェラーゼ増加	6 (0.6)	1 (0.2)	7 (0.5)
胃内pH低下	1 (0.1)	0 (0.0)	1 (0.1)
心音異常	0 (0.0)	1 (0.2)	1 (0.1)
肝酵素異常	1 (0.1)	0 (0.0)	1 (0.1)
肝酵素上昇	3 (0.3)	1 (0.2)	4 (0.3)
INR増加	2 (0.2)	0 (0.0)	2 (0.1)
腎触知	1 (0.1)	0 (0.0)	1 (0.1)
リパーゼ増加	0 (0.0)	1 (0.2)	1 (0.1)
肝機能検査異常	1 (0.1)	2 (0.4)	3 (0.2)
リンパ球数増加	0 (0.0)	1 (0.2)	1 (0.1)
好中球数減少	0 (0.0)	1 (0.2)	1 (0.1)
血小板数減少	1 (0.1)	0 (0.0)	1 (0.1)
血小板数増加	1 (0.1)	0 (0.0)	1 (0.1)
プロトロンビン時間異常	1 (0.1)	0 (0.0)	1 (0.1)
プロトロンビン時間延長	2 (0.2)	0 (0.0)	2 (0.1)
トランスアミナーゼ上昇	1 (0.1)	1 (0.2)	2 (0.1)
尿浸透圧低下	2 (0.2)	0 (0.0)	2 (0.1)
尿量増加	14 (1.5)	2 (0.4)	16 (1.1)
体重減少	24 (2.5)	1 (0.2)	25 (1.7)
体重増加	3 (0.3)	5 (1.0)	8 (0.6)
尿中白血球陽性	1 (0.1)	0 (0.0)	1 (0.1)
代謝および栄養障害			
食欲減退	47 (4.9)	0 (0.0)	47 (3.3)
脱水	8 (0.8)	1 (0.2)	9 (0.6)
食物渴望	2 (0.2)	0 (0.0)	2 (0.1)
痛風	2 (0.2)	1 (0.2)	3 (0.2)
高アミラーゼ血症	0 (0.0)	1 (0.2)	1 (0.1)
高カルシウム血症	2 (0.2)	1 (0.2)	3 (0.2)
高コレステロール血症	2 (0.2)	3 (0.6)	5 (0.3)
高血糖	1 (0.1)	2 (0.4)	3 (0.2)
高カリウム血症	4 (0.4)	1 (0.2)	5 (0.3)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
代謝および栄養障害			
高脂血症	1 (0.1)	0 (0.0)	1 (0.1)
高ナトリウム血症	9 (0.9)	0 (0.0)	9 (0.6)
高尿酸血症	4 (0.4)	0 (0.0)	4 (0.3)
低アルブミン血症	0 (0.0)	1 (0.2)	1 (0.1)
低血糖症	4 (0.4)	0 (0.0)	4 (0.3)
低カリウム血症	1 (0.1)	1 (0.2)	2 (0.1)
低ナトリウム血症	1 (0.1)	1 (0.2)	2 (0.1)
血液量減少症	1 (0.1)	0 (0.0)	1 (0.1)
食欲亢進	1 (0.1)	0 (0.0)	1 (0.1)
多飲症	90 (9.4)	14 (2.9)	104 (7.2)
体重変動	2 (0.2)	0 (0.0)	2 (0.1)
筋骨格系および結合組織障害			
関節痛	4 (0.4)	3 (0.6)	7 (0.5)
背部痛	16 (1.7)	8 (1.7)	24 (1.7)
尾骨痛	0 (0.0)	1 (0.2)	1 (0.1)
側腹部痛	3 (0.3)	0 (0.0)	3 (0.2)
筋痙縮	7 (0.7)	7 (1.4)	14 (1.0)
筋緊張	0 (0.0)	1 (0.2)	1 (0.1)
筋攣縮	1 (0.1)	0 (0.0)	1 (0.1)
筋骨格不快感	1 (0.1)	0 (0.0)	1 (0.1)
筋骨格痛	0 (0.0)	2 (0.4)	2 (0.1)
筋骨格硬直	3 (0.3)	0 (0.0)	3 (0.2)
筋肉痛	10 (1.0)	1 (0.2)	11 (0.8)
頸部痛	4 (0.4)	1 (0.2)	5 (0.3)
四肢痛	3 (0.3)	4 (0.8)	7 (0.5)
関節リウマチ	1 (0.1)	0 (0.0)	1 (0.1)
肩回旋筋腱板症候群	1 (0.1)	0 (0.0)	1 (0.1)
重感	0 (0.0)	1 (0.2)	1 (0.1)
腱炎	2 (0.2)	0 (0.0)	2 (0.1)
腱鞘炎	0 (0.0)	1 (0.2)	1 (0.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）			
メラノサイト性母斑	0 (0.0)	1 (0.2)	1 (0.1)
皮膚乳頭腫	1 (0.1)	0 (0.0)	1 (0.1)
汗腺腫瘍	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
味覚消失	1 (0.1)	0 (0.0)	1 (0.1)
平衡障害	0 (0.0)	1 (0.2)	1 (0.1)
群発頭痛	1 (0.1)	0 (0.0)	1 (0.1)
注意力障害	4 (0.4)	0 (0.0)	4 (0.3)
浮動性めまい	45 (4.7)	17 (3.5)	62 (4.3)
体位性めまい	1 (0.1)	0 (0.0)	1 (0.1)
異常感覚	1 (0.1)	0 (0.0)	1 (0.1)
味覚異常	15 (1.6)	6 (1.2)	21 (1.5)
頭痛	110 (11.4)	54 (11.2)	164 (11.4)
味覚過敏	1 (0.1)	0 (0.0)	1 (0.1)
感覚鈍麻	3 (0.3)	1 (0.2)	4 (0.3)
頭蓋内動脈瘤	1 (0.1)	0 (0.0)	1 (0.1)
嗜眠	1 (0.1)	2 (0.4)	3 (0.2)
精神的機能障害	0 (0.0)	1 (0.2)	1 (0.1)
片頭痛	4 (0.4)	1 (0.2)	5 (0.3)
不随意性筋収縮	1 (0.1)	0 (0.0)	1 (0.1)
ナルコレプシー	2 (0.2)	0 (0.0)	2 (0.1)
錯感覚	5 (0.5)	2 (0.4)	7 (0.5)
嗅覚錯誤	1 (0.1)	0 (0.0)	1 (0.1)
坐骨神経痛	1 (0.1)	0 (0.0)	1 (0.1)
感覚障害	1 (0.1)	0 (0.0)	1 (0.1)
副鼻腔炎に伴う頭痛	1 (0.1)	0 (0.0)	1 (0.1)
傾眠	2 (0.2)	2 (0.4)	4 (0.3)
失神	2 (0.2)	0 (0.0)	2 (0.1)
緊張性頭痛	1 (0.1)	0 (0.0)	1 (0.1)
振戦	1 (0.1)	0 (0.0)	1 (0.1)
精神障害			
異常な夢	2 (0.2)	2 (0.4)	4 (0.3)
激越	1 (0.1)	0 (0.0)	1 (0.1)
不安	5 (0.5)	2 (0.4)	7 (0.5)
抑うつ気分	1 (0.1)	0 (0.0)	1 (0.1)
うつ病	3 (0.3)	2 (0.4)	5 (0.3)
不眠症	25 (2.6)	4 (0.8)	29 (2.0)
リビドー減退	2 (0.2)	0 (0.0)	2 (0.1)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
精神障害			
性欲障害	0 (0.0)	1 (0.2)	1 (0.1)
リビド消失	1 (0.1)	0 (0.0)	1 (0.1)
気分変化	1 (0.1)	0 (0.0)	1 (0.1)
気分動揺	0 (0.0)	1 (0.2)	1 (0.1)
神経過敏	3 (0.3)	0 (0.0)	3 (0.2)
パニック発作	1 (0.1)	0 (0.0)	1 (0.1)
腎および尿路障害			
アルブミン尿	1 (0.1)	0 (0.0)	1 (0.1)
膀胱不快感	0 (0.0)	1 (0.2)	1 (0.1)
膀胱痛	1 (0.1)	0 (0.0)	1 (0.1)
尿路結石	1 (0.1)	1 (0.2)	2 (0.1)
着色尿	0 (0.0)	1 (0.2)	1 (0.1)
排尿困難	2 (0.2)	0 (0.0)	2 (0.1)
血尿	8 (0.8)	5 (1.0)	13 (0.9)
腎腫大	1 (0.1)	0 (0.0)	1 (0.1)
白血球尿	1 (0.1)	0 (0.0)	1 (0.1)
尿意切迫	3 (0.3)	2 (0.4)	5 (0.3)
腎結石症	2 (0.2)	1 (0.2)	3 (0.2)
夜間頻尿	247 (25.7)	48 (9.9)	295 (20.4)
乏尿	2 (0.2)	0 (0.0)	2 (0.1)
頻尿	212 (22.1)	22 (4.6)	234 (16.2)
多尿	325 (33.8)	63 (13.0)	388 (26.9)
蛋白尿	1 (0.1)	1 (0.2)	2 (0.1)
腎仙痛	0 (0.0)	2 (0.4)	2 (0.1)
腎嚢胞出血	0 (0.0)	1 (0.2)	1 (0.1)
腎嚢胞破裂	0 (0.0)	1 (0.2)	1 (0.1)
腎障害	0 (0.0)	1 (0.2)	1 (0.1)
腎機能障害	1 (0.1)	0 (0.0)	1 (0.1)
腎臓痛	52 (5.4)	24 (5.0)	76 (5.3)
切迫性尿失禁	1 (0.1)	0 (0.0)	1 (0.1)
排尿躊躇	1 (0.1)	0 (0.0)	1 (0.1)
尿失禁	1 (0.1)	0 (0.0)	1 (0.1)
尿流量減少	1 (0.1)	0 (0.0)	1 (0.1)
尿臭異常	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-34

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CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (全体)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
生殖系および乳房障害			
月経困難症	0 (0.0)	2 (0.4)	2 (0.1)
勃起不全	3 (0.3)	1 (0.2)	4 (0.3)
過少月経	1 (0.1)	0 (0.0)	1 (0.1)
月経過多	2 (0.2)	2 (0.4)	4 (0.3)
月経障害	1 (0.1)	0 (0.0)	1 (0.1)
不規則月経	2 (0.2)	0 (0.0)	2 (0.1)
不正子宮出血	0 (0.0)	1 (0.2)	1 (0.1)
卵巣嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
精巣痛	1 (0.1)	0 (0.0)	1 (0.1)
膣分泌物	0 (0.0)	2 (0.4)	2 (0.1)
膣出血	1 (0.1)	0 (0.0)	1 (0.1)
外陰膣乾燥	1 (0.1)	3 (0.6)	4 (0.3)
呼吸器、胸郭および縦隔障害			
喘息	2 (0.2)	0 (0.0)	2 (0.1)
咳嗽	13 (1.4)	4 (0.8)	17 (1.2)
咽喉乾燥	2 (0.2)	1 (0.2)	3 (0.2)
呼吸困難	2 (0.2)	1 (0.2)	3 (0.2)
労作性呼吸困難	1 (0.1)	0 (0.0)	1 (0.1)
鼻閉	1 (0.1)	0 (0.0)	1 (0.1)
鼻乾燥	0 (0.0)	2 (0.4)	2 (0.1)
鼻の炎症	0 (0.0)	1 (0.2)	1 (0.1)
鼻閉塞	1 (0.1)	0 (0.0)	1 (0.1)
口腔咽頭痛	8 (0.8)	2 (0.4)	10 (0.7)
アレルギー性鼻炎	0 (0.0)	1 (0.2)	1 (0.1)
鼻漏	3 (0.3)	0 (0.0)	3 (0.2)
睡眠時無呼吸症候群	1 (0.1)	0 (0.0)	1 (0.1)
くしゃみ	0 (0.0)	1 (0.2)	1 (0.1)
皮膚および皮下組織障害			
ざ瘡	3 (0.3)	1 (0.2)	4 (0.3)
脱毛症	1 (0.1)	0 (0.0)	1 (0.1)
冷汗	1 (0.1)	0 (0.0)	1 (0.1)
皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
アレルギー性皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
接触性皮膚炎	1 (0.1)	1 (0.2)	2 (0.1)
皮膚乾燥	26 (2.7)	4 (0.8)	30 (2.1)
湿疹	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-34
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 CT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period（全体）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=961)	(N=483)	(N=1444)
(MedDRA preferred term)	n (%)	n (%)	n (%)
皮膚および皮下組織障害			
紅斑	1 (0.1)	0 (0.0)	1 (0.1)
毛髪成長異常	0 (0.0)	1 (0.2)	1 (0.1)
乏汗症	1 (0.1)	0 (0.0)	1 (0.1)
内出血発生の増加傾向	1 (0.1)	0 (0.0)	1 (0.1)
機械性蕁麻疹	2 (0.2)	0 (0.0)	2 (0.1)
寝汗	1 (0.1)	0 (0.0)	1 (0.1)
そう痒症	11 (1.1)	2 (0.4)	13 (0.9)
発疹	9 (0.9)	1 (0.2)	10 (0.7)
脂漏性皮膚炎	2 (0.2)	0 (0.0)	2 (0.1)
皮膚病変	1 (0.1)	2 (0.4)	3 (0.2)
皮膚反応	0 (0.0)	1 (0.2)	1 (0.1)
蕁麻疹	0 (0.0)	1 (0.2)	1 (0.1)
慢性蕁麻疹	1 (0.1)	0 (0.0)	1 (0.1)
血管障害			
血腫	1 (0.1)	0 (0.0)	1 (0.1)
出血	1 (0.1)	0 (0.0)	1 (0.1)
ほてり	2 (0.2)	0 (0.0)	2 (0.1)
高血圧	66 (6.9)	35 (7.2)	101 (7.0)
低血圧	11 (1.1)	4 (0.8)	15 (1.0)
起立性低血圧	1 (0.1)	0 (0.0)	1 (0.1)
末梢冷感	4 (0.4)	0 (0.0)	4 (0.3)
TOTAL	820 (85.3)	301 (62.3)	1121 (77.6)

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<資料番号5.3.5.1-01：CT-8.9.2>

表2.7.4.7-35

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JT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period（日本の被験者）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
心臓障害			
徐脈	1 (0.8)	0 (0.0)	1 (0.6)
右脚ブロック	1 (0.8)	0 (0.0)	1 (0.6)
動悸	3 (2.5)	0 (0.0)	3 (1.7)
頻脈	2 (1.7)	0 (0.0)	2 (1.1)
眼障害			
眼乾燥	1 (0.8)	1 (1.7)	2 (1.1)
胃腸障害			
腹部膨満	3 (2.5)	0 (0.0)	3 (1.7)
腹痛	1 (0.8)	2 (3.4)	3 (1.7)
下腹部痛	1 (0.8)	0 (0.0)	1 (0.6)
上腹部痛	3 (2.5)	1 (1.7)	4 (2.3)
便秘	9 (7.6)	1 (1.7)	10 (5.6)
下痢	4 (3.4)	1 (1.7)	5 (2.8)
消化不良	1 (0.8)	0 (0.0)	1 (0.6)
心窩部不快感	1 (0.8)	0 (0.0)	1 (0.6)
痔出血	1 (0.8)	0 (0.0)	1 (0.6)
口唇乾燥	2 (1.7)	0 (0.0)	2 (1.1)
悪心	3 (2.5)	2 (3.4)	5 (2.8)
口内炎	0 (0.0)	1 (1.7)	1 (0.6)
嘔吐	2 (1.7)	1 (1.7)	3 (1.7)
一般・全身障害および投与部位の状態			
胸痛	3 (2.5)	0 (0.0)	3 (1.7)
疲労	6 (5.1)	0 (0.0)	6 (3.4)
高熱	0 (0.0)	1 (1.7)	1 (0.6)
炎症	1 (0.8)	0 (0.0)	1 (0.6)
倦怠感	3 (2.5)	1 (1.7)	4 (2.3)
浮腫	0 (0.0)	1 (1.7)	1 (0.6)
末梢性浮腫	0 (0.0)	1 (1.7)	1 (0.6)
発熱	2 (1.7)	1 (1.7)	3 (1.7)
口渇	98 (83.1)	18 (30.5)	116 (65.5)

表2.7.4.7-35

156-251

JT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (日本の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
肝胆道系障害			
肝障害	2 (1.7)	0 (0.0)	2 (1.1)
感染症および寄生虫症			
気管支炎	1 (0.8)	0 (0.0)	1 (0.6)
膀胱炎	1 (0.8)	0 (0.0)	1 (0.6)
胃腸炎	0 (0.0)	1 (1.7)	1 (0.6)
喉頭炎	1 (0.8)	0 (0.0)	1 (0.6)
鼻咽頭炎	6 (5.1)	3 (5.1)	9 (5.1)
咽頭炎	0 (0.0)	1 (1.7)	1 (0.6)
気道感染	1 (0.8)	0 (0.0)	1 (0.6)
傷害、中毒および処置合併症			
熱射病	1 (0.8)	0 (0.0)	1 (0.6)
臨床検査			
アラニン・アミノトランスフェラーゼ増加	1 (0.8)	0 (0.0)	1 (0.6)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.8)	0 (0.0)	1 (0.6)
細菌検査陽性	0 (0.0)	1 (1.7)	1 (0.6)
血中クレアチニン増加	1 (0.8)	0 (0.0)	1 (0.6)
血中カリウム減少	1 (0.8)	0 (0.0)	1 (0.6)
血中尿酸増加	3 (2.5)	0 (0.0)	3 (1.7)
γ-グルタミルトランスフェラーゼ増加	1 (0.8)	0 (0.0)	1 (0.6)
トランスアミナーゼ上昇	1 (0.8)	0 (0.0)	1 (0.6)
体重減少	6 (5.1)	0 (0.0)	6 (3.4)
代謝および栄養障害			
食欲減退	5 (4.2)	0 (0.0)	5 (2.8)
痛風	0 (0.0)	1 (1.7)	1 (0.6)
低アルブミン血症	0 (0.0)	1 (1.7)	1 (0.6)
筋骨格系および結合組織障害			
背部痛	3 (2.5)	0 (0.0)	3 (1.7)

表2.7.4.7-35

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JT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period（日本の被験者）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
筋骨格系および結合組織障害			
筋痙縮	1 (0.8)	1 (1.7)	2 (1.1)
筋骨格硬直	1 (0.8)	0 (0.0)	1 (0.6)
筋肉痛	1 (0.8)	0 (0.0)	1 (0.6)
四肢痛	0 (0.0)	1 (1.7)	1 (0.6)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）			
汗腺腫瘍	1 (0.8)	0 (0.0)	1 (0.6)
神経系障害			
味覚消失	1 (0.8)	0 (0.0)	1 (0.6)
平衡障害	0 (0.0)	1 (1.7)	1 (0.6)
群発頭痛	1 (0.8)	0 (0.0)	1 (0.6)
浮動性めまい	6 (5.1)	2 (3.4)	8 (4.5)
味覚異常	1 (0.8)	0 (0.0)	1 (0.6)
頭痛	11 (9.3)	7 (11.9)	18 (10.2)
傾眠	2 (1.7)	1 (1.7)	3 (1.7)
精神障害			
うつ病	0 (0.0)	1 (1.7)	1 (0.6)
不眠症	4 (3.4)	1 (1.7)	5 (2.8)
腎および尿路障害			
尿路結石	1 (0.8)	0 (0.0)	1 (0.6)
血尿	0 (0.0)	1 (1.7)	1 (0.6)
夜間頻尿	2 (1.7)	1 (1.7)	3 (1.7)
頻尿	60 (50.8)	4 (6.8)	64 (36.2)
多尿	37 (31.4)	3 (5.1)	40 (22.6)
腎機能障害	1 (0.8)	0 (0.0)	1 (0.6)
腎臓痛	3 (2.5)	1 (1.7)	4 (2.3)
呼吸器、胸郭および縦隔障害			
咳嗽	2 (1.7)	0 (0.0)	2 (1.1)
鼻乾燥	0 (0.0)	1 (1.7)	1 (0.6)
口腔咽頭痛	0 (0.0)	1 (1.7)	1 (0.6)
鼻漏	2 (1.7)	0 (0.0)	2 (1.1)

表2.7.4.7-35

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JT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period（日本の被験者）

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=118)	(N=59)	(N=177)
(MedDRA preferred term)	n (%)	n (%)	n (%)
皮膚および皮下組織障害			
冷汗	1 (0.8)	0 (0.0)	1 (0.6)
皮膚乾燥	2 (1.7)	1 (1.7)	3 (1.7)
乏汗症	1 (0.8)	0 (0.0)	1 (0.6)
そう痒症	2 (1.7)	0 (0.0)	2 (1.1)
発疹	4 (3.4)	0 (0.0)	4 (2.3)
血管障害			
高血圧	1 (0.8)	1 (1.7)	2 (1.1)
低血圧	1 (0.8)	0 (0.0)	1 (0.6)
TOTAL	113 (95.8)	31 (52.5)	144 (81.4)

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表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
血液およびリンパ系障害			
貧血	2 (0.2)	3 (0.7)	5 (0.4)
好酸球増加症	2 (0.2)	0 (0.0)	2 (0.2)
白血球減少症	1 (0.1)	1 (0.2)	2 (0.2)
リンパ節症	1 (0.1)	0 (0.0)	1 (0.1)
心臓障害			
狭心症	1 (0.1)	0 (0.0)	1 (0.1)
不整脈	2 (0.2)	0 (0.0)	2 (0.2)
徐脈	3 (0.4)	2 (0.5)	5 (0.4)
伝導障害	1 (0.1)	0 (0.0)	1 (0.1)
左室肥大	1 (0.1)	0 (0.0)	1 (0.1)
動悸	10 (1.2)	2 (0.5)	12 (0.9)
洞不全症候群	1 (0.1)	0 (0.0)	1 (0.1)
洞性徐脈	0 (0.0)	1 (0.2)	1 (0.1)
頻脈	5 (0.6)	1 (0.2)	6 (0.5)
先天性、家族性および遺伝性障害			
多嚢胞性肝疾患	1 (0.1)	0 (0.0)	1 (0.1)
耳および迷路障害			
難聴	1 (0.1)	0 (0.0)	1 (0.1)
耳痛	2 (0.2)	1 (0.2)	3 (0.2)
耳そう痒症	0 (0.0)	1 (0.2)	1 (0.1)
耳鳴	0 (0.0)	1 (0.2)	1 (0.1)
回転性めまい	8 (0.9)	2 (0.5)	10 (0.8)
眼障害			
結膜炎	0 (0.0)	1 (0.2)	1 (0.1)
眼乾燥	5 (0.6)	4 (0.9)	9 (0.7)
眼部腫脹	0 (0.0)	1 (0.2)	1 (0.1)
眼充血	0 (0.0)	1 (0.2)	1 (0.1)
開放隅角緑内障	0 (0.0)	1 (0.2)	1 (0.1)
光視症	1 (0.1)	0 (0.0)	1 (0.1)
霧視	2 (0.2)	0 (0.0)	2 (0.2)
視力障害	0 (0.0)	1 (0.2)	1 (0.1)
硝子体浮遊物	1 (0.1)	0 (0.0)	1 (0.1)
眼球乾燥	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
胃腸障害			
腹部不快感	5 (0.6)	1 (0.2)	6 (0.5)
腹部膨満	4 (0.5)	3 (0.7)	7 (0.6)
腹部ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
腹部腫瘍	1 (0.1)	0 (0.0)	1 (0.1)
腹痛	9 (1.1)	8 (1.9)	17 (1.3)
下腹部痛	1 (0.1)	0 (0.0)	1 (0.1)
上腹部痛	12 (1.4)	7 (1.7)	19 (1.5)
腹部圧痛	1 (0.1)	0 (0.0)	1 (0.1)
肛門そう痒症	1 (0.1)	0 (0.0)	1 (0.1)
アフタ性口内炎	2 (0.2)	0 (0.0)	2 (0.2)
便通不規則	1 (0.1)	0 (0.0)	1 (0.1)
呼気臭	2 (0.2)	0 (0.0)	2 (0.2)
口唇のひび割れ	1 (0.1)	0 (0.0)	1 (0.1)
便秘	36 (4.3)	3 (0.7)	39 (3.1)
下痢	32 (3.8)	8 (1.9)	40 (3.2)
口内乾燥	142 (16.8)	51 (12.0)	193 (15.2)
消化不良	20 (2.4)	3 (0.7)	23 (1.8)
嚥下障害	4 (0.5)	0 (0.0)	4 (0.3)
心窩部不快感	1 (0.1)	0 (0.0)	1 (0.1)
鼓腸	3 (0.4)	0 (0.0)	3 (0.2)
胃障害	1 (0.1)	0 (0.0)	1 (0.1)
胃炎	1 (0.1)	0 (0.0)	1 (0.1)
消化管運動障害	1 (0.1)	0 (0.0)	1 (0.1)
胃食道逆流性疾患	3 (0.4)	0 (0.0)	3 (0.2)
舌痛	2 (0.2)	0 (0.0)	2 (0.2)
胃酸過多	1 (0.1)	0 (0.0)	1 (0.1)
口の感覚鈍麻	1 (0.1)	1 (0.2)	2 (0.2)
単径ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
過敏性腸症候群	1 (0.1)	1 (0.2)	2 (0.2)
口唇乾燥	2 (0.2)	1 (0.2)	3 (0.2)
口腔内出血	0 (0.0)	1 (0.2)	1 (0.1)
悪心	30 (3.6)	17 (4.0)	47 (3.7)
口腔扁平苔癬	1 (0.1)	0 (0.0)	1 (0.1)
口腔内痛	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-36

156-251

NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
胃腸障害			
口の錯感覚	1 (0.1)	0 (0.0)	1 (0.1)
舌苔	2 (0.2)	0 (0.0)	2 (0.2)
舌変色	2 (0.2)	0 (0.0)	2 (0.2)
舌障害	1 (0.1)	1 (0.2)	2 (0.2)
舌乾燥	1 (0.1)	2 (0.5)	3 (0.2)
舌粘膜剥脱	1 (0.1)	0 (0.0)	1 (0.1)
変色歯	0 (0.0)	1 (0.2)	1 (0.1)
歯の障害	0 (0.0)	1 (0.2)	1 (0.1)
歯痛	2 (0.2)	0 (0.0)	2 (0.2)
臍ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)
嘔吐	14 (1.7)	4 (0.9)	18 (1.4)
一般・全身障害および投与部位の状態			
無力症	29 (3.4)	5 (1.2)	34 (2.7)
腋窩痛	1 (0.1)	0 (0.0)	1 (0.1)
胸部不快感	5 (0.6)	0 (0.0)	5 (0.4)
胸痛	4 (0.5)	0 (0.0)	4 (0.3)
悪寒	4 (0.5)	1 (0.2)	5 (0.4)
異形成	0 (0.0)	1 (0.2)	1 (0.1)
運動耐性低下	1 (0.1)	0 (0.0)	1 (0.1)
顔面浮腫	1 (0.1)	0 (0.0)	1 (0.1)
疲労	50 (5.9)	18 (4.2)	68 (5.4)
冷感	5 (0.6)	0 (0.0)	5 (0.4)
酩酊感	1 (0.1)	0 (0.0)	1 (0.1)
熱感	1 (0.1)	1 (0.2)	2 (0.2)
びくびく感	1 (0.1)	0 (0.0)	1 (0.1)
インフルエンザ様疾患	1 (0.1)	0 (0.0)	1 (0.1)
易刺激性	3 (0.4)	0 (0.0)	3 (0.2)
倦怠感	0 (0.0)	1 (0.2)	1 (0.1)
粘膜乾燥	5 (0.6)	2 (0.5)	7 (0.6)
浮腫	1 (0.1)	3 (0.7)	4 (0.3)
末梢性浮腫	12 (1.4)	9 (2.1)	21 (1.7)
疼痛	1 (0.1)	0 (0.0)	1 (0.1)
発熱	4 (0.5)	2 (0.5)	6 (0.5)
不活発	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
一般・全身障害および投与部位の状態			
腫脹	1 (0.1)	0 (0.0)	1 (0.1)
温度変化不耐症	4 (0.5)	1 (0.2)	5 (0.4)
口渇	396 (47.0)	68 (16.0)	464 (36.6)
肝胆道系障害			
肝嚢胞	1 (0.1)	0 (0.0)	1 (0.1)
肝臓痛	0 (0.0)	1 (0.2)	1 (0.1)
高ビリルビン血症	1 (0.1)	0 (0.0)	1 (0.1)
免疫系障害			
過敏症	2 (0.2)	0 (0.0)	2 (0.2)
季節性アレルギー	4 (0.5)	0 (0.0)	4 (0.3)
感染症および寄生虫症			
急性扁桃炎	0 (0.0)	1 (0.2)	1 (0.1)
細菌尿	1 (0.1)	0 (0.0)	1 (0.1)
気管支炎	4 (0.5)	3 (0.7)	7 (0.6)
カンジダ症	1 (0.1)	2 (0.5)	3 (0.2)
膀胱炎	0 (0.0)	1 (0.2)	1 (0.1)
真菌感染	0 (0.0)	2 (0.5)	2 (0.2)
胃腸炎	2 (0.2)	3 (0.7)	5 (0.4)
帯状疱疹	0 (0.0)	1 (0.2)	1 (0.1)
インフルエンザ	8 (0.9)	2 (0.5)	10 (0.8)
鼻咽頭炎	15 (1.8)	13 (3.1)	28 (2.2)
口腔カンジダ症	2 (0.2)	0 (0.0)	2 (0.2)
口腔ヘルペス	3 (0.4)	0 (0.0)	3 (0.2)
中耳炎	1 (0.1)	0 (0.0)	1 (0.1)
咽頭炎	1 (0.1)	3 (0.7)	4 (0.3)
腎盂腎炎	1 (0.1)	1 (0.2)	2 (0.2)
気道感染	0 (0.0)	1 (0.2)	1 (0.1)
鼻炎	3 (0.4)	2 (0.5)	5 (0.4)
副鼻腔炎	4 (0.5)	1 (0.2)	5 (0.4)
扁桃炎	2 (0.2)	0 (0.0)	2 (0.2)
上気道感染	8 (0.9)	4 (0.9)	12 (0.9)
尿路感染	10 (1.2)	4 (0.9)	14 (1.1)
膣感染	1 (0.1)	0 (0.0)	1 (0.1)
ウイルス感染	2 (0.2)	0 (0.0)	2 (0.2)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
感染症および寄生虫症			
ウイルス性上気道感染	0 (0.0)	1 (0.2)	1 (0.1)
外陰部腔カンジダ症	0 (0.0)	2 (0.5)	2 (0.2)
外陰腔真菌感染	1 (0.1)	0 (0.0)	1 (0.1)
傷害、中毒および処置合併症			
挫傷	1 (0.1)	0 (0.0)	1 (0.1)
関節脱臼	1 (0.1)	0 (0.0)	1 (0.1)
四肢損傷	0 (0.0)	1 (0.2)	1 (0.1)
肉離れ	0 (0.0)	1 (0.2)	1 (0.1)
処置による疼痛	0 (0.0)	1 (0.2)	1 (0.1)
軟部組織損傷	1 (0.1)	0 (0.0)	1 (0.1)
サンバーン	1 (0.1)	0 (0.0)	1 (0.1)
熱傷	1 (0.1)	0 (0.0)	1 (0.1)
歯牙破折	1 (0.1)	0 (0.0)	1 (0.1)
臨床検査			
アラニン・アミノトランスフェラーゼ増加	9 (1.1)	1 (0.2)	10 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	7 (0.8)	2 (0.5)	9 (0.7)
血中ビリルビン増加	0 (0.0)	2 (0.5)	2 (0.2)
血中コレステロール増加	2 (0.2)	1 (0.2)	3 (0.2)
血中クレアチンホスホキナーゼ増加	1 (0.1)	0 (0.0)	1 (0.1)
血中クレアチニン増加	10 (1.2)	1 (0.2)	11 (0.9)
血中ブドウ糖減少	0 (0.0)	1 (0.2)	1 (0.1)
血中ブドウ糖増加	3 (0.4)	0 (0.0)	3 (0.2)
血中乳酸脱水素酵素増加	2 (0.2)	1 (0.2)	3 (0.2)
血中カリウム減少	1 (0.1)	0 (0.0)	1 (0.1)
血中カリウム増加	2 (0.2)	1 (0.2)	3 (0.2)
血圧低下	1 (0.1)	1 (0.2)	2 (0.2)
拡張期血圧上昇	0 (0.0)	1 (0.2)	1 (0.1)
血圧上昇	2 (0.2)	1 (0.2)	3 (0.2)
血中ナトリウム増加	3 (0.4)	1 (0.2)	4 (0.3)
血中尿素増加	1 (0.1)	0 (0.0)	1 (0.1)
血中尿酸増加	4 (0.5)	0 (0.0)	4 (0.3)
シスタチンC増加	1 (0.1)	0 (0.0)	1 (0.1)
心電図再分極異常	1 (0.1)	0 (0.0)	1 (0.1)
心電図T波逆転	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
臨床検査			
好酸球数増加	2 (0.2)	0 (0.0)	2 (0.2)
γ-グルタミルトランスフェラーゼ増加	5 (0.6)	1 (0.2)	6 (0.5)
胃内pH低下	1 (0.1)	0 (0.0)	1 (0.1)
心音異常	0 (0.0)	1 (0.2)	1 (0.1)
肝酵素異常	1 (0.1)	0 (0.0)	1 (0.1)
肝酵素上昇	3 (0.4)	1 (0.2)	4 (0.3)
INR増加	2 (0.2)	0 (0.0)	2 (0.2)
腎触知	1 (0.1)	0 (0.0)	1 (0.1)
リパーゼ増加	0 (0.0)	1 (0.2)	1 (0.1)
肝機能検査異常	1 (0.1)	2 (0.5)	3 (0.2)
リンパ球数増加	0 (0.0)	1 (0.2)	1 (0.1)
好中球数減少	0 (0.0)	1 (0.2)	1 (0.1)
血小板数減少	1 (0.1)	0 (0.0)	1 (0.1)
血小板数増加	1 (0.1)	0 (0.0)	1 (0.1)
プロトロンビン時間異常	1 (0.1)	0 (0.0)	1 (0.1)
プロトロンビン時間延長	2 (0.2)	0 (0.0)	2 (0.2)
トランスアミナーゼ上昇	0 (0.0)	1 (0.2)	1 (0.1)
尿浸透圧低下	2 (0.2)	0 (0.0)	2 (0.2)
尿量増加	14 (1.7)	2 (0.5)	16 (1.3)
体重減少	18 (2.1)	1 (0.2)	19 (1.5)
体重増加	3 (0.4)	5 (1.2)	8 (0.6)
尿中白血球陽性	1 (0.1)	0 (0.0)	1 (0.1)
代謝および栄養障害			
食欲減退	42 (5.0)	0 (0.0)	42 (3.3)
脱水	8 (0.9)	1 (0.2)	9 (0.7)
食物渴望	2 (0.2)	0 (0.0)	2 (0.2)
痛風	2 (0.2)	0 (0.0)	2 (0.2)
高アミラーゼ血症	0 (0.0)	1 (0.2)	1 (0.1)
高カルシウム血症	2 (0.2)	1 (0.2)	3 (0.2)
高コレステロール血症	2 (0.2)	3 (0.7)	5 (0.4)
高血糖	1 (0.1)	2 (0.5)	3 (0.2)
高カリウム血症	4 (0.5)	1 (0.2)	5 (0.4)
高脂血症	1 (0.1)	0 (0.0)	1 (0.1)
高ナトリウム血症	9 (1.1)	0 (0.0)	9 (0.7)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
代謝および栄養障害			
高尿酸血症	4 (0.5)	0 (0.0)	4 (0.3)
低血糖症	4 (0.5)	0 (0.0)	4 (0.3)
低カリウム血症	1 (0.1)	1 (0.2)	2 (0.2)
低ナトリウム血症	1 (0.1)	1 (0.2)	2 (0.2)
血液量減少症	1 (0.1)	0 (0.0)	1 (0.1)
食欲亢進	1 (0.1)	0 (0.0)	1 (0.1)
多飲症	90 (10.7)	14 (3.3)	104 (8.2)
体重変動	2 (0.2)	0 (0.0)	2 (0.2)
筋骨格系および結合組織障害			
関節痛	4 (0.5)	3 (0.7)	7 (0.6)
背部痛	13 (1.5)	8 (1.9)	21 (1.7)
尾骨痛	0 (0.0)	1 (0.2)	1 (0.1)
側腹部痛	3 (0.4)	0 (0.0)	3 (0.2)
筋痙縮	6 (0.7)	6 (1.4)	12 (0.9)
筋緊張	0 (0.0)	1 (0.2)	1 (0.1)
筋攣縮	1 (0.1)	0 (0.0)	1 (0.1)
筋骨格不快感	1 (0.1)	0 (0.0)	1 (0.1)
筋骨格痛	0 (0.0)	2 (0.5)	2 (0.2)
筋骨格硬直	2 (0.2)	0 (0.0)	2 (0.2)
筋肉痛	9 (1.1)	1 (0.2)	10 (0.8)
頸部痛	4 (0.5)	1 (0.2)	5 (0.4)
四肢痛	3 (0.4)	3 (0.7)	6 (0.5)
関節リウマチ	1 (0.1)	0 (0.0)	1 (0.1)
肩回旋筋腱板症候群	1 (0.1)	0 (0.0)	1 (0.1)
重感	0 (0.0)	1 (0.2)	1 (0.1)
腱炎	2 (0.2)	0 (0.0)	2 (0.2)
腱鞘炎	0 (0.0)	1 (0.2)	1 (0.1)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)			
メラノサイト性母斑	0 (0.0)	1 (0.2)	1 (0.1)
皮膚乳頭腫	1 (0.1)	0 (0.0)	1 (0.1)
神経系障害			
注意力障害	4 (0.5)	0 (0.0)	4 (0.3)
浮動性めまい	39 (4.6)	15 (3.5)	54 (4.3)
体位性めまい	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class	Tolvaptan	Placebo	Total
Adverse event	(N=843)	(N=424)	(N=1267)
(MedDRA preferred term)	n (%)	n (%)	n (%)
神経系障害			
異常感覚	1 (0.1)	0 (0.0)	1 (0.1)
味覚異常	14 (1.7)	6 (1.4)	20 (1.6)
頭痛	99 (11.7)	47 (11.1)	146 (11.5)
味覚過敏	1 (0.1)	0 (0.0)	1 (0.1)
感覚鈍麻	3 (0.4)	1 (0.2)	4 (0.3)
頭蓋内動脈瘤	1 (0.1)	0 (0.0)	1 (0.1)
嗜眠	1 (0.1)	2 (0.5)	3 (0.2)
精神的機能障害	0 (0.0)	1 (0.2)	1 (0.1)
片頭痛	4 (0.5)	1 (0.2)	5 (0.4)
不随意性筋収縮	1 (0.1)	0 (0.0)	1 (0.1)
ナルコレプシー	2 (0.2)	0 (0.0)	2 (0.2)
錯感覚	5 (0.6)	2 (0.5)	7 (0.6)
嗅覚錯誤	1 (0.1)	0 (0.0)	1 (0.1)
坐骨神経痛	1 (0.1)	0 (0.0)	1 (0.1)
感覚障害	1 (0.1)	0 (0.0)	1 (0.1)
副鼻腔炎に伴う頭痛	1 (0.1)	0 (0.0)	1 (0.1)
傾眠	0 (0.0)	1 (0.2)	1 (0.1)
失神	2 (0.2)	0 (0.0)	2 (0.2)
緊張性頭痛	1 (0.1)	0 (0.0)	1 (0.1)
振戦	1 (0.1)	0 (0.0)	1 (0.1)
精神障害			
異常な夢	2 (0.2)	2 (0.5)	4 (0.3)
激越	1 (0.1)	0 (0.0)	1 (0.1)
不安	5 (0.6)	2 (0.5)	7 (0.6)
抑うつ気分	1 (0.1)	0 (0.0)	1 (0.1)
うつ病	3 (0.4)	1 (0.2)	4 (0.3)
不眠症	21 (2.5)	3 (0.7)	24 (1.9)
リビドー減退	2 (0.2)	0 (0.0)	2 (0.2)
性欲障害	0 (0.0)	1 (0.2)	1 (0.1)
リビドー消失	1 (0.1)	0 (0.0)	1 (0.1)
気分変化	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
精神障害			
気分動揺	0 (0.0)	1 (0.2)	1 (0.1)
神経過敏	3 (0.4)	0 (0.0)	3 (0.2)
パニック発作	1 (0.1)	0 (0.0)	1 (0.1)
腎および尿路障害			
アルブミン尿	1 (0.1)	0 (0.0)	1 (0.1)
膀胱不快感	0 (0.0)	1 (0.2)	1 (0.1)
膀胱痛	1 (0.1)	0 (0.0)	1 (0.1)
尿路結石	0 (0.0)	1 (0.2)	1 (0.1)
着色尿	0 (0.0)	1 (0.2)	1 (0.1)
排尿困難	2 (0.2)	0 (0.0)	2 (0.2)
血尿	8 (0.9)	4 (0.9)	12 (0.9)
腎腫大	1 (0.1)	0 (0.0)	1 (0.1)
白血球尿	1 (0.1)	0 (0.0)	1 (0.1)
尿意切迫	3 (0.4)	2 (0.5)	5 (0.4)
腎結石症	2 (0.2)	1 (0.2)	3 (0.2)
夜間頻尿	245 (29.1)	47 (11.1)	292 (23.0)
乏尿	2 (0.2)	0 (0.0)	2 (0.2)
頻尿	152 (18.0)	18 (4.2)	170 (13.4)
多尿	288 (34.2)	60 (14.2)	348 (27.5)
蛋白尿	1 (0.1)	1 (0.2)	2 (0.2)
腎仙痛	0 (0.0)	2 (0.5)	2 (0.2)
腎嚢胞出血	0 (0.0)	1 (0.2)	1 (0.1)
腎嚢胞破裂	0 (0.0)	1 (0.2)	1 (0.1)
腎障害	0 (0.0)	1 (0.2)	1 (0.1)
腎臓痛	49 (5.8)	23 (5.4)	72 (5.7)
切迫性尿失禁	1 (0.1)	0 (0.0)	1 (0.1)
排尿躊躇	1 (0.1)	0 (0.0)	1 (0.1)
尿失禁	1 (0.1)	0 (0.0)	1 (0.1)
尿流量減少	1 (0.1)	0 (0.0)	1 (0.1)
尿臭異常	0 (0.0)	1 (0.2)	1 (0.1)
生殖系および乳房障害			
月経困難症	0 (0.0)	2 (0.5)	2 (0.2)
勃起不全	3 (0.4)	1 (0.2)	4 (0.3)
過少月経	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
生殖系および乳房障害			
月経過多	2 (0.2)	2 (0.5)	4 (0.3)
月経障害	1 (0.1)	0 (0.0)	1 (0.1)
不規則月経	2 (0.2)	0 (0.0)	2 (0.2)
不正子宮出血	0 (0.0)	1 (0.2)	1 (0.1)
卵巣嚢胞	0 (0.0)	1 (0.2)	1 (0.1)
精巣痛	1 (0.1)	0 (0.0)	1 (0.1)
膺分泌物	0 (0.0)	2 (0.5)	2 (0.2)
膺出血	1 (0.1)	0 (0.0)	1 (0.1)
外陰膺乾燥	1 (0.1)	3 (0.7)	4 (0.3)
呼吸器、胸郭および縦隔障害			
喘息	2 (0.2)	0 (0.0)	2 (0.2)
咳嗽	11 (1.3)	4 (0.9)	15 (1.2)
咽喉乾燥	2 (0.2)	1 (0.2)	3 (0.2)
呼吸困難	2 (0.2)	1 (0.2)	3 (0.2)
労作性呼吸困難	1 (0.1)	0 (0.0)	1 (0.1)
鼻閉	1 (0.1)	0 (0.0)	1 (0.1)
鼻乾燥	0 (0.0)	1 (0.2)	1 (0.1)
鼻の炎症	0 (0.0)	1 (0.2)	1 (0.1)
鼻閉塞	1 (0.1)	0 (0.0)	1 (0.1)
口腔咽頭痛	8 (0.9)	1 (0.2)	9 (0.7)
アレルギー性鼻炎	0 (0.0)	1 (0.2)	1 (0.1)
鼻漏	1 (0.1)	0 (0.0)	1 (0.1)
睡眠時無呼吸症候群	1 (0.1)	0 (0.0)	1 (0.1)
くしゃみ	0 (0.0)	1 (0.2)	1 (0.1)
皮膚および皮下組織障害			
ざ瘡	3 (0.4)	1 (0.2)	4 (0.3)
脱毛症	1 (0.1)	0 (0.0)	1 (0.1)
皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
アレルギー性皮膚炎	1 (0.1)	0 (0.0)	1 (0.1)
接触性皮膚炎	1 (0.1)	1 (0.2)	2 (0.2)
皮膚乾燥	24 (2.8)	3 (0.7)	27 (2.1)
湿疹	1 (0.1)	0 (0.0)	1 (0.1)
紅斑	1 (0.1)	0 (0.0)	1 (0.1)
毛髪成長異常	0 (0.0)	1 (0.2)	1 (0.1)

表2.7.4.7-36

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NT-8.9.2 Incidence of All Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term - Titration Period (海外の被験者)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan (N=843) n (%)	Placebo (N=424) n (%)	Total (N=1267) n (%)
皮膚および皮下組織障害			
内出血発生の増加傾向	1 (0.1)	0 (0.0)	1 (0.1)
機械性蕁麻疹	2 (0.2)	0 (0.0)	2 (0.2)
寝汗	1 (0.1)	0 (0.0)	1 (0.1)
そう痒症	9 (1.1)	2 (0.5)	11 (0.9)
発疹	5 (0.6)	1 (0.2)	6 (0.5)
脂漏性皮膚炎	2 (0.2)	0 (0.0)	2 (0.2)
皮膚病変	1 (0.1)	2 (0.5)	3 (0.2)
皮膚反応	0 (0.0)	1 (0.2)	1 (0.1)
蕁麻疹	0 (0.0)	1 (0.2)	1 (0.1)
慢性蕁麻疹	1 (0.1)	0 (0.0)	1 (0.1)
血管障害			
血腫	1 (0.1)	0 (0.0)	1 (0.1)
出血	1 (0.1)	0 (0.0)	1 (0.1)
ほてり	2 (0.2)	0 (0.0)	2 (0.2)
高血圧	65 (7.7)	34 (8.0)	99 (7.8)
低血圧	10 (1.2)	4 (0.9)	14 (1.1)
起立性低血圧	1 (0.1)	0 (0.0)	1 (0.1)
末梢冷感	4 (0.5)	0 (0.0)	4 (0.3)
TOTAL	707 (83.9)	270 (63.7)	977 (77.1)

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表2.7.4.7-37

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CT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (全体)

System organ class	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961)	(N=878)	(N=844)	(N=825)	(N=809)	(N=796)	(N=781)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血液およびリンパ系障害	8 (0.8)	5 (0.6)	1 (0.1)	3 (0.4)	3 (0.4)	6 (0.8)	9 (1.2)
心臓障害	38 (4.0)	8 (0.9)	13 (1.5)	4 (0.5)	6 (0.7)	4 (0.5)	7 (0.9)
先天性、家族性および遺伝性障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	16 (1.7)	4 (0.5)	3 (0.4)	5 (0.6)	4 (0.5)	3 (0.4)	8 (1.0)
内分泌障害	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.3)
眼障害	17 (1.8)	6 (0.7)	4 (0.5)	6 (0.7)	4 (0.5)	6 (0.8)	8 (1.0)
胃腸障害	343 (35.7)	82 (9.3)	58 (6.9)	41 (5.0)	52 (6.4)	54 (6.8)	46 (5.9)
一般・全身障害および投与部位の状態	578 (60.1)	50 (5.7)	43 (5.1)	26 (3.2)	30 (3.7)	34 (4.3)	26 (3.3)
肝胆道系障害	9 (0.9)	9 (1.0)	11 (1.3)	7 (0.8)	2 (0.2)	5 (0.6)	2 (0.3)
免疫系障害	10 (1.0)	9 (1.0)	4 (0.5)	3 (0.4)	1 (0.1)	5 (0.6)	8 (1.0)
感染症および寄生虫症	158 (16.4)	103 (11.7)	89 (10.5)	78 (9.5)	72 (8.9)	52 (6.5)	56 (7.2)
傷害、中毒および処置合併症	18 (1.9)	12 (1.4)	14 (1.7)	17 (2.1)	6 (0.7)	15 (1.9)	16 (2.0)
臨床検査	116 (12.1)	53 (6.0)	50 (5.9)	37 (4.5)	25 (3.1)	44 (5.5)	32 (4.1)
代謝および栄養障害	195 (20.3)	31 (3.5)	26 (3.1)	16 (1.9)	14 (1.7)	13 (1.6)	16 (2.0)
筋骨格系および結合組織障害	88 (9.2)	59 (6.7)	52 (6.2)	46 (5.6)	38 (4.7)	41 (5.2)	26 (3.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (0.3)	4 (0.5)	2 (0.2)	5 (0.6)	7 (0.9)	1 (0.1)	3 (0.4)
神経系障害	227 (23.6)	33 (3.8)	41 (4.9)	30 (3.6)	10 (1.2)	30 (3.8)	22 (2.8)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	57 (5.9)	16 (1.8)	15 (1.8)	13 (1.6)	7 (0.9)	12 (1.5)	8 (1.0)
腎および尿路障害	667 (69.4)	65 (7.4)	60 (7.1)	40 (4.8)	28 (3.5)	35 (4.4)	26 (3.3)
生殖系および乳房障害	29 (3.0)	17 (1.9)	11 (1.3)	7 (0.8)	7 (0.9)	8 (1.0)	10 (1.3)
呼吸器、胸郭および縦隔障害	50 (5.2)	23 (2.6)	22 (2.6)	27 (3.3)	20 (2.5)	17 (2.1)	10 (1.3)
皮膚および皮下組織障害	88 (9.2)	33 (3.8)	20 (2.4)	17 (2.1)	17 (2.1)	10 (1.3)	14 (1.8)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
外科および内科処置	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
血管障害	121 (12.6)	37 (4.2)	29 (3.4)	30 (3.6)	19 (2.3)	37 (4.6)	20 (2.6)
TOTAL	864 (89.9)	26 (3.0)	17 (2.0)	11 (1.3)	2 (0.2)	5 (0.6)	4 (0.5)

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表2.7.4.7-37

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CT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (全体)

System organ class	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769)	(N=762)	(N=755)	(N=749)	(N=739)	(N=961)	(N=483)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血液およびリンパ系障害	4 (0.5)	2 (0.3)	4 (0.5)	6 (0.8)	3 (0.4)	5 (0.5)	8 (1.7)
心臓障害	6 (0.8)	8 (1.0)	3 (0.4)	5 (0.7)	10 (1.4)	2 (0.2)	8 (1.7)
先天性、家族性および遺伝性障害	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)
耳および迷路障害	4 (0.5)	5 (0.7)	2 (0.3)	3 (0.4)	0 (0.0)	1 (0.1)	8 (1.7)
内分泌障害	2 (0.3)	3 (0.4)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	1 (0.2)
眼障害	4 (0.5)	7 (0.9)	5 (0.7)	8 (1.1)	7 (0.9)	4 (0.4)	12 (2.5)
胃腸障害	41 (5.3)	40 (5.2)	41 (5.4)	37 (4.9)	33 (4.5)	22 (2.3)	118 (24.4)
一般・全身障害および投与部位の状態	14 (1.8)	17 (2.2)	16 (2.1)	14 (1.9)	30 (4.1)	17 (1.8)	139 (28.8)
肝胆道系障害	5 (0.7)	3 (0.4)	2 (0.3)	2 (0.3)	6 (0.8)	1 (0.1)	2 (0.4)
免疫系障害	3 (0.4)	5 (0.7)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.6)
感染症および寄生虫症	76 (9.9)	55 (7.2)	56 (7.4)	44 (5.9)	60 (8.1)	41 (4.3)	95 (19.7)
傷害、中毒および処置合併症	13 (1.7)	20 (2.6)	10 (1.3)	10 (1.3)	18 (2.4)	7 (0.7)	12 (2.5)
臨床検査	24 (3.1)	19 (2.5)	29 (3.8)	17 (2.3)	31 (4.2)	21 (2.2)	37 (7.7)
代謝および栄養障害	10 (1.3)	9 (1.2)	16 (2.1)	15 (2.0)	18 (2.4)	5 (0.5)	35 (7.2)
筋骨格系および結合組織障害	50 (6.5)	33 (4.3)	36 (4.8)	31 (4.1)	35 (4.7)	13 (1.4)	45 (9.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (0.4)	6 (0.8)	4 (0.5)	3 (0.4)	5 (0.7)	1 (0.1)	5 (1.0)
神経系障害	25 (3.3)	20 (2.6)	17 (2.3)	11 (1.5)	27 (3.7)	8 (0.8)	89 (18.4)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
精神障害	8 (1.0)	7 (0.9)	6 (0.8)	9 (1.2)	14 (1.9)	1 (0.1)	17 (3.5)
腎および尿路障害	24 (3.1)	21 (2.8)	15 (2.0)	20 (2.7)	25 (3.4)	10 (1.0)	155 (32.1)
生殖系および乳房障害	6 (0.8)	6 (0.8)	1 (0.1)	6 (0.8)	6 (0.8)	2 (0.2)	16 (3.3)
呼吸器、胸郭および縦隔障害	11 (1.4)	12 (1.6)	13 (1.7)	16 (2.1)	14 (1.9)	8 (0.8)	22 (4.6)
皮膚および皮下組織障害	21 (2.7)	11 (1.4)	10 (1.3)	10 (1.3)	13 (1.8)	11 (1.1)	23 (4.8)
社会環境	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外科および内科処置	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	25 (3.3)	15 (2.0)	20 (2.6)	24 (3.2)	22 (3.0)	18 (1.9)	54 (11.2)
TOTAL	5 (0.7)	1 (0.1)	3 (0.4)	1 (0.1)	2 (0.3)	1 (0.1)	359 (74.3)

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表2.7.4.7-37

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CT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (全体)

System organ class	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473)	(N=465)	(N=460)	(N=455)	(N=448)	(N=441)	(N=435)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血液およびリンパ系障害	4 (0.8)	5 (1.1)	2 (0.4)	1 (0.2)	3 (0.7)	4 (0.9)	1 (0.2)
心臓障害	1 (0.2)	4 (0.9)	2 (0.4)	1 (0.2)	7 (1.6)	2 (0.5)	3 (0.7)
先天性、家族性および遺伝性障害	0 (0.0)	1 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	2 (0.4)	3 (0.6)	2 (0.4)	2 (0.4)	2 (0.4)	2 (0.5)	3 (0.7)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
眼障害	4 (0.8)	3 (0.6)	3 (0.7)	7 (1.5)	3 (0.7)	1 (0.2)	4 (0.9)
胃腸障害	34 (7.2)	33 (7.1)	26 (5.7)	33 (7.3)	24 (5.4)	36 (8.2)	19 (4.4)
一般・全身障害および投与部位の状態	14 (3.0)	28 (6.0)	13 (2.8)	11 (2.4)	15 (3.3)	22 (5.0)	10 (2.3)
肝胆道系障害	1 (0.2)	3 (0.6)	2 (0.4)	1 (0.2)	3 (0.7)	2 (0.5)	3 (0.7)
免疫系障害	1 (0.2)	1 (0.2)	0 (0.0)	3 (0.7)	1 (0.2)	0 (0.0)	1 (0.2)
感染症および寄生虫症	55 (11.6)	47 (10.1)	39 (8.5)	32 (7.0)	45 (10.0)	37 (8.4)	39 (9.0)
傷害、中毒および処置合併症	3 (0.6)	9 (1.9)	11 (2.4)	4 (0.9)	11 (2.5)	12 (2.7)	7 (1.6)
臨床検査	22 (4.7)	17 (3.7)	16 (3.5)	11 (2.4)	25 (5.6)	22 (5.0)	18 (4.1)
代謝および栄養障害	13 (2.7)	6 (1.3)	9 (2.0)	5 (1.1)	2 (0.4)	7 (1.6)	6 (1.4)
筋骨格系および結合組織障害	17 (3.6)	26 (5.6)	31 (6.7)	15 (3.3)	20 (4.5)	24 (5.4)	22 (5.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	3 (0.6)	1 (0.2)	1 (0.2)	2 (0.4)	1 (0.2)	2 (0.5)
神経系障害	16 (3.4)	21 (4.5)	12 (2.6)	11 (2.4)	11 (2.5)	16 (3.6)	10 (2.3)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	7 (1.5)	5 (1.1)	7 (1.5)	5 (1.1)	5 (1.1)	5 (1.1)	6 (1.4)
腎および尿路障害	35 (7.4)	38 (8.2)	33 (7.2)	16 (3.5)	22 (4.9)	23 (5.2)	15 (3.4)
生殖系および乳房障害	11 (2.3)	5 (1.1)	7 (1.5)	4 (0.9)	6 (1.3)	4 (0.9)	3 (0.7)
呼吸器、胸郭および縦隔障害	11 (2.3)	11 (2.4)	12 (2.6)	8 (1.8)	13 (2.9)	5 (1.1)	6 (1.4)
皮膚および皮下組織障害	7 (1.5)	8 (1.7)	8 (1.7)	6 (1.3)	8 (1.8)	5 (1.1)	8 (1.8)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
外科および内科処置	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	25 (5.3)	24 (5.2)	23 (5.0)	8 (1.8)	12 (2.7)	18 (4.1)	11 (2.5)
TOTAL	37 (7.8)	21 (4.5)	13 (2.8)	8 (1.8)	8 (1.8)	8 (1.8)	4 (0.9)

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表2.7.4.7-37

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CT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (全体)

System organ class	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
血液およびリンパ系障害	1 (0.2)	2 (0.5)	2 (0.5)	5 (1.2)	2 (0.4)	16 (1.1)	9 (0.7)
心臓障害	5 (1.2)	0 (0.0)	1 (0.2)	2 (0.5)	2 (0.4)	46 (3.2)	9 (0.7)
先天性、家族性および遺伝性障害	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.1)	0 (0.0)
耳および迷路障害	3 (0.7)	1 (0.2)	1 (0.2)	2 (0.5)	0 (0.0)	24 (1.7)	6 (0.4)
内分泌障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.2)	0 (0.0)
眼障害	1 (0.2)	1 (0.2)	3 (0.7)	4 (1.0)	1 (0.2)	29 (2.0)	10 (0.7)
胃腸障害	22 (5.2)	12 (2.8)	17 (4.1)	23 (5.5)	8 (1.7)	461 (31.9)	116 (8.6)
一般・全身障害および投与部位の状態	12 (2.8)	16 (3.8)	5 (1.2)	15 (3.6)	2 (0.4)	717 (49.7)	64 (4.7)
肝胆道系障害	2 (0.5)	1 (0.2)	0 (0.0)	2 (0.5)	1 (0.2)	11 (0.8)	10 (0.7)
免疫系障害	1 (0.2)	3 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	13 (0.9)	10 (0.7)
感染症および寄生虫症	29 (6.8)	40 (9.4)	31 (7.4)	35 (8.4)	14 (2.9)	253 (17.5)	158 (11.7)
傷害、中毒および処置合併症	6 (1.4)	8 (1.9)	8 (1.9)	6 (1.4)	5 (1.0)	30 (2.1)	15 (1.1)
臨床検査	10 (2.3)	21 (5.0)	13 (3.1)	23 (5.5)	9 (1.9)	153 (10.6)	75 (5.6)
代謝および栄養障害	3 (0.7)	3 (0.7)	9 (2.1)	5 (1.2)	5 (1.0)	230 (15.9)	44 (3.3)
筋骨格系および結合組織障害	21 (4.9)	19 (4.5)	16 (3.8)	22 (5.3)	6 (1.2)	133 (9.2)	76 (5.6)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.5)	3 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	8 (0.6)	4 (0.3)
神経系障害	7 (1.6)	10 (2.4)	13 (3.1)	11 (2.6)	7 (1.4)	316 (21.9)	49 (3.6)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	3 (0.7)	4 (0.9)	3 (0.7)	7 (1.7)	2 (0.4)	74 (5.1)	23 (1.7)
腎および尿路障害	21 (4.9)	13 (3.1)	15 (3.6)	23 (5.5)	9 (1.9)	822 (56.9)	100 (7.4)
生殖系および乳房障害	1 (0.2)	3 (0.7)	6 (1.4)	4 (1.0)	2 (0.4)	45 (3.1)	28 (2.1)
呼吸器、胸郭および縦隔障害	2 (0.5)	4 (0.9)	3 (0.7)	6 (1.4)	2 (0.4)	72 (5.0)	34 (2.5)
皮膚および皮下組織障害	3 (0.7)	7 (1.7)	7 (1.7)	2 (0.5)	2 (0.4)	111 (7.7)	40 (3.0)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外科および内科処置	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血管障害	7 (1.6)	12 (2.8)	8 (1.9)	10 (2.4)	5 (1.0)	175 (12.1)	62 (4.6)
TOTAL	1 (0.2)	6 (1.4)	2 (0.5)	2 (0.5)	3 (0.6)	1223 (84.7)	63 (4.7)

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表2.7.4.7-37

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CT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (全体)

System organ class	Total						
	6-9 Months (N=1309)	9-12 Months (N=1285)	12-15 Months (N=1264)	15-18 Months (N=1244)	18-21 Months (N=1222)	21-24 Months (N=1204)	24-27 Months (N=1189)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血液およびリンパ系障害	6 (0.5)	5 (0.4)	4 (0.3)	9 (0.7)	13 (1.1)	5 (0.4)	3 (0.3)
心臓障害	17 (1.3)	6 (0.5)	7 (0.6)	11 (0.9)	9 (0.7)	9 (0.7)	13 (1.1)
先天性、家族性および遺伝性障害	1 (0.1)	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
耳および迷路障害	6 (0.5)	7 (0.5)	6 (0.5)	5 (0.4)	10 (0.8)	7 (0.6)	8 (0.7)
内分泌障害	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	3 (0.2)	4 (0.3)	4 (0.3)
眼障害	7 (0.5)	9 (0.7)	11 (0.9)	9 (0.7)	9 (0.7)	8 (0.7)	8 (0.7)
胃腸障害	91 (7.0)	67 (5.2)	85 (6.7)	78 (6.3)	82 (6.7)	60 (5.0)	62 (5.2)
一般・全身障害および投与部位の状態	71 (5.4)	39 (3.0)	41 (3.2)	49 (3.9)	48 (3.9)	24 (2.0)	29 (2.4)
肝胆道系障害	14 (1.1)	9 (0.7)	3 (0.2)	8 (0.6)	4 (0.3)	8 (0.7)	5 (0.4)
免疫系障害	5 (0.4)	3 (0.2)	4 (0.3)	6 (0.5)	8 (0.7)	4 (0.3)	6 (0.5)
感染症および寄生虫症	136 (10.4)	117 (9.1)	104 (8.2)	97 (7.8)	93 (7.6)	115 (9.6)	84 (7.1)
傷害、中毒および処置合併症	23 (1.8)	28 (2.2)	10 (0.8)	26 (2.1)	28 (2.3)	20 (1.7)	26 (2.2)
臨床検査	67 (5.1)	53 (4.1)	36 (2.8)	69 (5.5)	54 (4.4)	42 (3.5)	29 (2.4)
代謝および栄養障害	32 (2.4)	25 (1.9)	19 (1.5)	15 (1.2)	23 (1.9)	16 (1.3)	12 (1.0)
筋骨格系および結合組織障害	78 (6.0)	77 (6.0)	53 (4.2)	61 (4.9)	50 (4.1)	72 (6.0)	54 (4.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	5 (0.4)	6 (0.5)	8 (0.6)	3 (0.2)	4 (0.3)	5 (0.4)	8 (0.7)
神経系障害	62 (4.7)	42 (3.3)	21 (1.7)	41 (3.3)	38 (3.1)	35 (2.9)	27 (2.3)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	20 (1.5)	20 (1.6)	12 (0.9)	17 (1.4)	13 (1.1)	14 (1.2)	10 (0.8)
腎および尿路障害	98 (7.5)	73 (5.7)	44 (3.5)	57 (4.6)	49 (4.0)	39 (3.2)	42 (3.5)
生殖系および乳房障害	16 (1.2)	14 (1.1)	11 (0.9)	14 (1.1)	14 (1.1)	9 (0.7)	7 (0.6)
呼吸器、胸郭および縦隔障害	33 (2.5)	39 (3.0)	28 (2.2)	30 (2.4)	15 (1.2)	17 (1.4)	14 (1.2)
皮膚および皮下組織障害	28 (2.1)	25 (1.9)	23 (1.8)	18 (1.4)	19 (1.6)	29 (2.4)	14 (1.2)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
外科および内科処置	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	53 (4.0)	53 (4.1)	27 (2.1)	49 (3.9)	38 (3.1)	36 (3.0)	22 (1.9)
TOTAL	38 (2.9)	24 (1.9)	10 (0.8)	13 (1.0)	12 (1.0)	9 (0.7)	2 (0.2)

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表2.7.4.7-37

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CT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (全体)

System organ class	Total			
	27-30 Months (N=1179) n (%)	30-33 Months (N=1168) n (%)	33-36 Months (N=1156) n (%)	Post withdraw (N=1444) n (%)
血液およびリンパ系障害	6 (0.5)	8 (0.7)	8 (0.7)	7 (0.5)
心臓障害	3 (0.3)	6 (0.5)	12 (1.0)	4 (0.3)
先天性、家族性および遺伝性障害	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)
耳および迷路障害	3 (0.3)	4 (0.3)	2 (0.2)	1 (0.1)
内分泌障害	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.1)
眼障害	6 (0.5)	11 (0.9)	11 (1.0)	5 (0.3)
胃腸障害	53 (4.5)	54 (4.6)	56 (4.8)	30 (2.1)
一般・全身障害および投与部位の状態	32 (2.7)	19 (1.6)	45 (3.9)	19 (1.3)
肝胆道系障害	3 (0.3)	2 (0.2)	8 (0.7)	2 (0.1)
免疫系障害	4 (0.3)	2 (0.2)	1 (0.1)	1 (0.1)
感染症および寄生虫症	96 (8.1)	75 (6.4)	95 (8.2)	55 (3.8)
傷害、中毒および処置合併症	18 (1.5)	18 (1.5)	24 (2.1)	12 (0.8)
臨床検査	50 (4.2)	30 (2.6)	54 (4.7)	30 (2.1)
代謝および栄養障害	19 (1.6)	24 (2.1)	23 (2.0)	10 (0.7)
筋骨格系および結合組織障害	55 (4.7)	47 (4.0)	57 (4.9)	19 (1.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	7 (0.6)	3 (0.3)	6 (0.5)	1 (0.1)
神経系障害	27 (2.3)	24 (2.1)	38 (3.3)	15 (1.0)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
精神障害	10 (0.8)	12 (1.0)	21 (1.8)	3 (0.2)
腎および尿路障害	28 (2.4)	35 (3.0)	48 (4.2)	19 (1.3)
生殖系および乳房障害	4 (0.3)	12 (1.0)	10 (0.9)	4 (0.3)
呼吸器、胸郭および縦隔障害	17 (1.4)	19 (1.6)	20 (1.7)	10 (0.7)
皮膚および皮下組織障害	17 (1.4)	17 (1.5)	15 (1.3)	13 (0.9)
社会環境	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
外科および内科処置	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	32 (2.7)	32 (2.7)	32 (2.8)	23 (1.6)
TOTAL	9 (0.8)	3 (0.3)	4 (0.3)	4 (0.3)

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<資料番号5.3.5.1-01 : CT-8.7.1>

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
血液およびリンパ系障害							
貧血	3 (0.3)	2 (0.2)	0 (0.0)	2 (0.2)	2 (0.2)	5 (0.6)	3 (0.4)
凝血異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
好酸球増加症	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低色素性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
白血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
白血球減少症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球増加症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
正色素性正球性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
赤血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
急性心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
狭心症	3 (0.3)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心房細動	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	5 (0.5)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	3 (0.4)
右脚ブロック	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓弁膜疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心拡大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
心臓障害							
心筋症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝導障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
チアノーゼ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
僧帽弁疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁逸脱	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心筋虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
動悸	16 (1.7)	3 (0.3)	6 (0.7)	0 (0.0)	3 (0.4)	1 (0.1)	0 (0.0)
心嚢液貯留	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
洞不全症候群	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	8 (0.8)	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
三尖弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.4)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
先天性、家族性および遺伝性障害							
心房中隔欠損症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第V因子ライデン変異	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多嚢胞性肝疾患	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎奇形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害							
耳垢栓塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
難聴	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳閉	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
耳痛	3 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴覚障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内耳障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乗物酔い	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.3)	1 (0.1)
回転性めまい	9 (0.9)	3 (0.3)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	3 (0.4)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
内分泌障害							
アンドロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
バセドウ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
副甲状腺機能亢進症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能低下症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
エストロゲン欠乏症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害							
調節障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	3 (0.3)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	4 (0.5)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の隈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	7 (0.7)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.3)
外眼筋不全麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
眼障害							
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
遠視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
虹彩炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涙増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光視症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
老視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
翼状片	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
暗点	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霧視	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
視力低下	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
硝子体変性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体剥離	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
胃腸障害							
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	7 (0.7)	4 (0.5)	2 (0.2)	5 (0.6)	3 (0.4)	3 (0.4)	2 (0.3)
腹部膨満	13 (1.4)	4 (0.5)	2 (0.2)	2 (0.2)	1 (0.1)	7 (0.9)	2 (0.3)
腹部ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
閉塞を伴う腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	19 (2.0)	5 (0.6)	4 (0.5)	7 (0.8)	3 (0.4)	5 (0.6)	6 (0.8)
下腹部痛	3 (0.3)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
上腹部痛	22 (2.3)	12 (1.4)	2 (0.2)	3 (0.4)	3 (0.4)	5 (0.6)	4 (0.5)
腹部硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腹部圧痛	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)
裂肛	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
痔瘻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	3 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便通不規則	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.3)	0 (0.0)
便秘	47 (4.9)	7 (0.8)	5 (0.6)	6 (0.7)	2 (0.2)	3 (0.4)	3 (0.4)
クローン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
胃腸障害							
歯不快感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
下痢	49 (5.1)	12 (1.4)	8 (0.9)	2 (0.2)	9 (1.1)	10 (1.3)	7 (0.9)
憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腸憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
口内乾燥	148 (15.4)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
十二指腸炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
消化不良	32 (3.3)	16 (1.8)	4 (0.5)	1 (0.1)	6 (0.7)	1 (0.1)	1 (0.1)
嚥下障害	5 (0.5)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
びらん性十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
おくび	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腿ヘルニア	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	4 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
食中毒	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
機能性胃腸障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胃障害	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胃潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	3 (0.3)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.3)	1 (0.1)
びらん性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
胃腸の炎症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
胃腸障害							
胃食道逆流性疾患	10 (1.0)	6 (0.7)	5 (0.6)	0 (0.0)	4 (0.5)	5 (0.6)	1 (0.1)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉退縮	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌痛	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	3 (0.3)	1 (0.1)	3 (0.4)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
裂孔ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
胃酸過多	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の感覚鈍麻	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
単径ヘルニア	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
内ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	4 (0.4)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
下部消化管出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
吸収不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
メレナ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	42 (4.4)	13 (1.5)	7 (0.8)	5 (0.6)	8 (1.0)	4 (0.5)	5 (0.6)
嚥下痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
胃腸障害							
食道炎	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
口腔障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
肛門周囲痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
歯根嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吐き戻し	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
S状結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
舌苔	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌乾燥	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌粘膜剥脱	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯の障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	3 (0.3)	2 (0.2)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
臍ヘルニア	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.2)	2 (0.2)	2 (0.3)	2 (0.3)
閉塞性臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	23 (2.4)	8 (0.9)	8 (0.9)	7 (0.8)	5 (0.6)	7 (0.9)	2 (0.3)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
一般・全身障害および投与部位の状態							
無力症	37 (3.9)	3 (0.3)	5 (0.6)	1 (0.1)	4 (0.5)	1 (0.1)	0 (0.0)
腋窩痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	8 (0.8)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	2 (0.3)
胸痛	15 (1.6)	8 (0.9)	3 (0.4)	1 (0.1)	4 (0.5)	0 (0.0)	2 (0.3)
悪寒	8 (0.8)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
医療機器位置異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
顔面浮腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脂肪組織増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	65 (6.8)	14 (1.6)	12 (1.4)	6 (0.7)	7 (0.9)	6 (0.8)	8 (1.0)
異常感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	7 (0.7)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びくびく感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
治癒不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
炎症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	2 (0.2)	0 (0.0)	1 (0.1)	3 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)
易刺激性	4 (0.4)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	11 (1.1)	4 (0.5)	1 (0.1)	2 (0.2)	2 (0.2)	1 (0.1)	1 (0.1)
粘膜乾燥	5 (0.5)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
小結節	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	3 (0.3)	2 (0.2)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)
末梢性浮腫	15 (1.6)	5 (0.6)	7 (0.8)	5 (0.6)	5 (0.6)	9 (1.1)	7 (0.9)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
一般・全身障害および投与部位の状態							
疼痛	3 (0.3)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)
発熱	11 (1.1)	4 (0.5)	5 (0.6)	1 (0.1)	1 (0.1)	5 (0.6)	4 (0.5)
不活発	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨上痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫脹	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	5 (0.5)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
口渇	511 (53.2)	7 (0.8)	5 (0.6)	0 (0.0)	3 (0.4)	2 (0.3)	0 (0.0)
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肝胆道系障害							
胆道ジスキネジー	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
胆石症	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
肝嚢胞	2 (0.2)	0 (0.0)	3 (0.4)	2 (0.2)	0 (0.0)	2 (0.3)	0 (0.0)
肝嚢胞破裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	4 (0.4)	4 (0.5)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
肝臓痛	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.2)	0 (0.0)	2 (0.3)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
肝炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
高ビリルビン血症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝圧痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
免疫系障害							
アレルギー性浮腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	2 (0.3)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシーショック	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
造影剤アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
食物アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
家塵アレルギー	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)
複合アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	6 (0.6)	6 (0.7)	4 (0.5)	1 (0.1)	0 (0.0)	2 (0.3)	2 (0.3)
感染症および寄生虫症							
膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢膿瘍	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	1 (0.1)	3 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
真菌性肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性関節炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性関節炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌尿	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
バルトリン腺膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	14 (1.5)	4 (0.5)	3 (0.4)	7 (0.8)	4 (0.5)	2 (0.3)	0 (0.0)
ウイルス性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カンジダ症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
感染症および寄生虫症							
蜂巣炎	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
眼窩蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
クロストリジウム性大腸炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
角膜感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	2 (0.3)	0 (0.0)
サイトメガロウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
耳感染	1 (0.1)	3 (0.3)	2 (0.2)	0 (0.0)	4 (0.5)	1 (0.1)	2 (0.3)
耳垂感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
伝染性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
遊走性紅斑	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱性感染症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
皮膚真菌感染	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	9 (0.9)	5 (0.6)	5 (0.6)	2 (0.2)	4 (0.5)	4 (0.5)	3 (0.4)
ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
ウイルス性胃腸炎	1 (0.1)	5 (0.6)	1 (0.1)	1 (0.1)	1 (0.1)	5 (0.6)	1 (0.1)
細菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
真菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ウイルス性消化管感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
陰部ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
感染症および寄生虫症							
泌尿生殖器感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジアルジア症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H 1 N 1 インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター感染	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
C型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	4 (0.5)	0 (0.0)	0 (0.0)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性単核症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	16 (1.7)	8 (0.9)	4 (0.5)	11 (1.3)	4 (0.5)	5 (0.6)	6 (0.8)
腎感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
迷路炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
喉頭炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
肝膿瘍	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下気道感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
ライム病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
リンパ節感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ管炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
マラリア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マイコプラズマ感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
感染症および寄生虫症							
鼻咽喉炎	44 (4.6)	28 (3.2)	29 (3.4)	23 (2.8)	14 (1.7)	11 (1.4)	12 (1.5)
線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
爪真菌症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口腔カンジダ症	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
口腔真菌感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	4 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性中耳炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳頭腫ウイルス感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪囲炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
扁桃周囲炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
百日咳	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	3 (0.3)	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.4)	1 (0.1)
レンサ球菌性咽頭炎	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
肺炎	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎盂腎炎	3 (0.3)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腎嚢胞感染	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)
気道感染	2 (0.2)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性気道感染	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
鼻炎	4 (0.4)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	2 (0.3)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
感染症および寄生虫症							
卵管卵巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	12 (1.2)	8 (0.9)	3 (0.4)	5 (0.6)	7 (0.9)	0 (0.0)	4 (0.5)
皮膚感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
軟部組織感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌性咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癬風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	2 (0.2)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
歯膿瘍	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
歯感染	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
気管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
気管気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	14 (1.5)	9 (1.0)	11 (1.3)	3 (0.4)	6 (0.7)	1 (0.1)	7 (0.9)
尿路感染	20 (2.1)	8 (0.9)	8 (0.9)	5 (0.6)	7 (0.9)	5 (0.6)	5 (0.6)
泌尿生殖器細菌感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膣感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性膣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	3 (0.3)	3 (0.3)	4 (0.5)	3 (0.4)	0 (0.0)	0 (0.0)	1 (0.1)
ウイルス性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)
外陰部膣カンジダ症	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
外陰膣真菌感染	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
創傷感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
膿創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
傷害、中毒および処置合併症							
腹部損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足関節部骨折	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
節足動物咬傷	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
背部損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咬刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
軟骨損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
挫傷	1 (0.1)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	4 (0.5)
角膜擦過傷	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の貫通性外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼内異物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腕骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸脛靱帯症候群	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
傷害、中毒および処置合併症							
切開部位痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
企図的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
関節損傷	2 (0.2)	0 (0.0)	1 (0.1)	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)
裂傷	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
靱帯損傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
靱帯捻挫	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.3)
四肢損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
口唇損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腰椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋断裂	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
頸部損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後合併症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.3)	1 (0.1)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
橈骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
骨格損傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
軟部組織損傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
傷害、中毒および処置合併症							
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ストレス骨折	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
眼の擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腱損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
熱傷	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
歯牙破折	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手首関節骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	11 (1.1)	6 (0.7)	9 (1.1)	4 (0.5)	1 (0.1)	6 (0.8)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	9 (0.9)	4 (0.5)	7 (0.8)	4 (0.5)	1 (0.1)	4 (0.5)	2 (0.3)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルブミン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血中カルシウム増加	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中コレステロール増加	3 (0.3)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)	2 (0.3)	0 (0.0)
血中クレアチンホスホキナーゼ増加	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
血中クレアチニン増加	14 (1.5)	17 (1.9)	14 (1.7)	12 (1.5)	11 (1.4)	20 (2.5)	18 (2.3)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ブドウ糖増加	3 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
臨床検査							
血中乳酸脱水素酵素増加	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中副甲状腺ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中カリウム減少	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	3 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血圧低下	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
拡張期血圧上昇	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
血中ナトリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム増加	3 (0.3)	2 (0.2)	3 (0.4)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)
血中テストステロン減少	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿素増加	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)
血中尿酸増加	9 (0.9)	0 (0.0)	0 (0.0)	5 (0.6)	3 (0.4)	0 (0.0)	0 (0.0)
尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
C-反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心雑音	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
腎クレアチニン・クリアランス増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図再分極異常	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図異常T波	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
大腸菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	6 (0.6)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.1)	1 (0.1)	3 (0.4)
胃内pH低下	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
臨床検査							
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット減少	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数不整	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素異常	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	5 (0.5)	2 (0.2)	3 (0.4)	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)
A型肝炎ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヒト乳頭腫ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
I N R 増加	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腎触知	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
リパーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査異常	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
季肋下肝触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低比重リポ蛋白減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球形態異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血陽性	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数減少	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数増加	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間異常	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
臨床検査							
プロトロンビン時間延長	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Q O L 低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	3 (0.3)	1 (0.1)	3 (0.4)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
卵巣超音波検査異常	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧低下	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)
尿浸透圧上昇	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量増加	14 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウエスト周囲径増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	24 (2.5)	7 (0.8)	5 (0.6)	0 (0.0)	0 (0.0)	3 (0.4)	2 (0.3)
体重増加	6 (0.6)	6 (0.7)	8 (0.9)	2 (0.2)	2 (0.2)	6 (0.8)	1 (0.1)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿中白血球	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害							
アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	55 (5.7)	6 (0.7)	2 (0.2)	1 (0.1)	0 (0.0)	2 (0.3)	1 (0.1)
脱水	10 (1.0)	0 (0.0)	3 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
糖尿病	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)
体液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物渴望	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	3 (0.3)	4 (0.5)	4 (0.5)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.1)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
代謝および栄養障害							
高カルシウム血症	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	3 (0.3)	2 (0.2)	3 (0.4)	2 (0.2)	3 (0.4)	3 (0.4)	0 (0.0)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
高カリウム血症	3 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
高脂血症	2 (0.2)	2 (0.2)	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)
高ナトリウム血症	11 (1.1)	4 (0.5)	2 (0.2)	2 (0.2)	2 (0.2)	0 (0.0)	2 (0.3)
高リン酸塩血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	10 (1.0)	2 (0.2)	0 (0.0)	6 (0.7)	5 (0.6)	1 (0.1)	4 (0.5)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
低血糖症	4 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
低カリウム血症	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
低マグネシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低リン酸血症	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ラクトース不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
代謝性アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過体重	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
多飲症	96 (10.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
2 型糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンB 1 2 欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD 欠乏	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
体重変動	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
筋骨格系および結合組織障害							
関節痛	10 (1.0)	11 (1.3)	7 (0.8)	9 (1.1)	2 (0.2)	8 (1.0)	1 (0.1)
関節炎	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
反応性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	24 (2.5)	13 (1.5)	18 (2.1)	13 (1.6)	6 (0.7)	8 (1.0)	6 (0.8)
骨痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包石灰化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
軟骨肥厚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
頸部脊柱管狭窄症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尾骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋軟骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外骨腫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
瘻孔	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	5 (0.5)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
痛風性関節炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単径部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
椎間板変性症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
椎間板障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	3 (0.3)	1 (0.1)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	1 (0.1)
関節滲出液	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
関節可動域低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
筋骨格系および結合組織障害							
靱帯障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
四肢非対称	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
筋肉疲労	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	11 (1.1)	5 (0.6)	4 (0.5)	7 (0.8)	2 (0.2)	1 (0.1)	2 (0.3)
筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋攣縮	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
筋骨格不快感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
筋骨格痛	0 (0.0)	6 (0.7)	1 (0.1)	2 (0.2)	3 (0.4)	4 (0.5)	1 (0.1)
筋骨格硬直	4 (0.4)	1 (0.1)	4 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	16 (1.7)	5 (0.6)	5 (0.6)	3 (0.4)	3 (0.4)	3 (0.4)	3 (0.4)
筋炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部痛	5 (0.5)	3 (0.3)	1 (0.1)	0 (0.0)	3 (0.4)	0 (0.0)	1 (0.1)
変形性関節症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)
骨関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨減少症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨粗鬆症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	4 (0.4)	4 (0.5)	2 (0.2)	4 (0.5)	2 (0.2)	5 (0.6)	2 (0.3)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
恥骨痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節リウマチ	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
仙腸骨炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
筋骨格系および結合組織障害							
側弯症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
重感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脊椎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脊椎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腱炎	5 (0.5)	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.4)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
斜頸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.3)	0 (0.0)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)							
アクリコルドン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
基底細胞癌	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)
乳房の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳癌	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部癌第0期	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真珠腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性骨髄性白血病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
肝臓血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カポジ肉腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
表皮内悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メラノサイト性母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
下垂体の良性腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
脂漏性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁平上皮癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	5 (0.6)	0 (0.0)	0 (0.0)
神経系障害							
味覚消失	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
健忘	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
失声症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頰動脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手根管症候群	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳神経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識レベルの低下	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	5 (0.5)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
浮動性めまい	58 (6.0)	8 (0.9)	8 (0.9)	5 (0.6)	1 (0.1)	5 (0.6)	4 (0.5)
労作性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
体位性めまい	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
異常感覚	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	21 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
神経系障害							
脳症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
頭部不快感	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	138 (14.4)	11 (1.3)	19 (2.3)	12 (1.5)	5 (0.6)	9 (1.1)	9 (1.2)
味覚過敏	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	4 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.1)
反射減弱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
頭蓋内動脈瘤	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗜眠	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
意識消失	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
片頭痛	7 (0.7)	1 (0.1)	2 (0.2)	3 (0.4)	0 (0.0)	2 (0.3)	1 (0.1)
前兆を伴う片頭痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
錯感覚	7 (0.7)	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)	2 (0.3)	0 (0.0)
パーキンソン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
パーキンソニズム	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神寸前の状態	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
根症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)
坐骨神経痛	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
神経系障害							
感覚障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神	4 (0.4)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
緊張性頭痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
一過性脳虚血発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トンネル状視野	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎骨動脈解離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第7脳神経麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
妊娠、産褥および周産期の状態							
自然流産	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常な夢	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
激越	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	6 (0.6)	3 (0.3)	2 (0.2)	4 (0.5)	2 (0.2)	2 (0.3)	1 (0.1)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自閉症スペクトラム障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神緩慢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
燃え尽き症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	5 (0.5)	5 (0.6)	5 (0.6)	4 (0.5)	2 (0.2)	3 (0.4)	3 (0.4)
睡眠異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
不眠症	29 (3.0)	7 (0.8)	4 (0.5)	2 (0.2)	1 (0.1)	4 (0.5)	0 (0.0)
リビドー減退	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
性欲障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リビドー消失	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
精神障害							
大うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分変化	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
神経過敏	3 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ニコチン依存	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪夢	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
パニック反応	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心身症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
落ち着きのなさ	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
夢遊症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス	3 (0.3)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
自殺企図	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
アルブミン尿	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿路結石	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
非感染性膀胱炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	2 (0.2)	4 (0.5)	4 (0.5)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
遺尿	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
腎および尿路障害							
血尿	19 (2.0)	7 (0.8)	7 (0.8)	9 (1.1)	6 (0.7)	3 (0.4)	4 (0.5)
水腎症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎腫大	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球尿	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿意切迫	3 (0.3)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎結石症	4 (0.4)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.1)	2 (0.3)	1 (0.1)
夜間頻尿	259 (27.0)	6 (0.7)	5 (0.6)	3 (0.4)	2 (0.2)	3 (0.4)	0 (0.0)
閉塞性尿路疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏尿	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	215 (22.4)	5 (0.6)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	340 (35.4)	9 (1.0)	6 (0.7)	3 (0.4)	3 (0.4)	2 (0.3)	2 (0.3)
蛋白尿	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
腎仙痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
腎嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞破裂	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性腎不全	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎機能障害	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	5 (0.6)	1 (0.1)
腎臓痛	75 (7.8)	31 (3.5)	30 (3.6)	17 (2.1)	15 (1.9)	16 (2.0)	17 (2.2)
有痛性排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
終末尿滴下	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿道狭窄	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿躊躇	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	4 (0.4)	3 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
尿閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
腎および尿路障害							
尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿流量減少	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害							
子宮付属器痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
精子無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
萎縮性外陰陰炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
子宮頸部上皮異形成	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管ポリープ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
性交出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱瘤	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
性交困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
勃起不全	4 (0.4)	2 (0.2)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳汁漏出症	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
血精液症	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過少月経	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
生殖系および乳房障害							
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機能性子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多	6 (0.6)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)
月経障害	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	4 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
不正子宮出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
卵巣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
卵巣捻転	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤不快感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
骨盤脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ペイロニー病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)
閉経後出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.3)	0 (0.0)
前立腺腫大	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮脱	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
膣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膣分泌物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
膣出血	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
生殖系および乳房障害							
精索静脈瘤	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰腔乾燥	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害							
喘息	3 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	25 (2.6)	7 (0.8)	4 (0.5)	6 (0.7)	8 (1.0)	2 (0.3)	1 (0.1)
咽喉乾燥	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発声障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	5 (0.5)	2 (0.2)	3 (0.4)	2 (0.2)	3 (0.4)	3 (0.4)	0 (0.0)
安静時呼吸困難	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	1 (0.1)	1 (0.1)	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)
過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
肺障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉塞	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻中隔彎曲	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
夜間呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	13 (1.4)	5 (0.6)	7 (0.8)	5 (0.6)	1 (0.1)	4 (0.5)	4 (0.5)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸水	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
呼吸器、胸郭および縦隔障害							
肺塞栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺線維症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
呼吸不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気道うっ血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.3)
鼻漏	4 (0.4)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
低音性連続性ラ音	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔うっ血	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)
睡眠時無呼吸症候群	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
くしゃみ	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
いびき	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽喉絞扼感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃結石	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害							
ざ瘡	7 (0.7)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
日光性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	4 (0.4)	4 (0.5)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンドロゲン性脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
皮膚および皮下組織障害							
皮膚炎	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	3 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
皮膚症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	34 (3.5)	2 (0.2)	4 (0.5)	0 (0.0)	3 (0.4)	0 (0.0)	2 (0.3)
斑状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	4 (0.4)	2 (0.2)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
多形紅斑	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過剰皮膚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
汗腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏汗症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
内出血発生の増加傾向	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嵌入爪	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機械性蕁麻疹	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪破損	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
皮膚および皮下組織障害							
光線過敏性反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
色素沈着障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
糝糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色糝糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
そう痒症	16 (1.7)	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	4 (0.5)
全身性そう痒症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	12 (1.2)	7 (0.8)	4 (0.5)	3 (0.4)	1 (0.1)	2 (0.3)	2 (0.3)
紅斑性皮疹	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒性皮疹	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脂腺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
皮膚色素過剰	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚病変	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚潰瘍	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ滞性皮膚炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	2 (0.2)	4 (0.5)	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)	2 (0.3)
慢性蕁麻疹	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尋常性白斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
社会環境							
閉経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
外科および内科処置							
収れん薬療法	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジフテリア免疫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
子宮頸管拡張および子宮内搔爬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン補給	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血管障害							
動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の血圧	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	3 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
高血圧	92 (9.6)	28 (3.2)	25 (3.0)	22 (2.7)	16 (2.0)	30 (3.8)	18 (2.3)
高血圧クリーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
低血圧	15 (1.6)	4 (0.5)	0 (0.0)	1 (0.1)	2 (0.2)	2 (0.3)	0 (0.0)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
微小血管症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	3 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢冷感	5 (0.5)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レイノー現象	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
表在性血栓性静脈炎	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈瘤	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（全体）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=961) n (%)	(N=878) n (%)	(N=844) n (%)	(N=825) n (%)	(N=809) n (%)	(N=796) n (%)	(N=781) n (%)
血管障害							
静脈瘤	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
静脈不全	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	864 (89.9)	26 (3.0)	17 (2.0)	11 (1.3)	2 (0.2)	5 (0.6)	4 (0.5)

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表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
血液およびリンパ系障害							
貧血	2 (0.3)	0 (0.0)	4 (0.5)	1 (0.1)	3 (0.4)	3 (0.3)	4 (0.8)
凝血異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
好酸球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
低色素性貧血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
白血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
好中球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
正色素性正球性貧血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血小板増加症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
急性心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
狭心症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心房細動	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
房室ブロック	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.6)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓弁膜疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拡大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心筋症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝導障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
心臓障害							
チアノーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
左室肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
僧帽弁疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁逸脱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	3 (0.4)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.4)
心嚢液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
洞不全症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.2)
上室性期外収縮	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
三尖弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
先天性、家族性および遺伝性障害							
心房中隔欠損症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第Ⅴ因子ライデン変異	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多嚢胞性肝疾患	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎奇形	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
耳および迷路障害							
耳垢栓塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳閉	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳管障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内耳障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乗物酔い	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	0 (0.0)	1 (0.1)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
回転性めまい	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.1)	5 (1.0)
頭位性回転性めまい	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害							
アンドロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バセドウ病	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
続発性副甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
エストロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害							
調節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
眼障害							
結膜出血	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.3)	1 (0.1)	0 (0.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	2 (0.4)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の隈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	5 (1.0)
外眼筋不全麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼出血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼痛	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)
眼瞼浮腫	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
遠視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虹彩炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涙増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光視症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
老視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
翼状片	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
暗点	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
眼障害							
霧視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
硝子体変性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
硝子体剥離	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害							
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
腹部膨満	4 (0.5)	0 (0.0)	1 (0.1)	4 (0.5)	7 (0.9)	3 (0.3)	6 (1.2)
腹部ヘルニア	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
閉塞を伴う腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	1 (0.1)	5 (0.7)	1 (0.1)	4 (0.5)	2 (0.3)	1 (0.1)	14 (2.9)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	5 (0.7)	2 (0.3)	2 (0.3)	2 (0.3)	1 (0.1)	1 (0.1)	11 (2.3)
腹部硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部圧痛	0 (0.0)	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)
裂肛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔瘻	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
便通不規則	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	0 (0.0)	2 (0.3)	2 (0.3)	2 (0.3)	2 (0.3)	0 (0.0)	5 (1.0)
クローン病	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	2 (0.3)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	3 (0.6)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
胃腸障害							
歯不快感	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
下痢	8 (1.0)	8 (1.0)	7 (0.9)	5 (0.7)	3 (0.4)	5 (0.5)	14 (2.9)
憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸憩室	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
口内乾燥	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	51 (10.6)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
十二指腸炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	4 (0.5)	5 (0.7)	3 (0.4)	1 (0.1)	2 (0.3)	2 (0.2)	4 (0.8)
嚥下障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びらん性十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腿ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
食中毒	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機能性胃腸障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	0 (0.0)	2 (0.3)	2 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)
びらん性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	4 (0.5)	2 (0.3)	2 (0.3)	3 (0.4)	1 (0.1)	0 (0.0)	1 (0.2)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
胃腸障害							
歯肉退縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)
裂孔ヘルニア	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.3)	0 (0.0)	1 (0.2)
胃酸過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
回腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵径ヘルニア	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
内ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
口唇乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口唇腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吸収不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メレナ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	1 (0.1)	5 (0.7)	3 (0.4)	2 (0.3)	3 (0.4)	4 (0.4)	26 (5.4)
嚥下痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
口腔障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口腔扁平苔癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
胃腸障害							
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門周囲痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
吐き戻し	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
S状結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
舌苔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
舌乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
舌粘膜剥脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯の障害	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)
臍ヘルニア	2 (0.3)	1 (0.1)	1 (0.1)	3 (0.4)	3 (0.4)	0 (0.0)	0 (0.0)
閉塞性臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	2 (0.3)	4 (0.5)	5 (0.7)	4 (0.5)	4 (0.5)	3 (0.3)	8 (1.7)
一般・全身障害および投与部位の状態							
無力症	3 (0.4)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	8 (1.7)
腋窩痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
胸痛	2 (0.3)	1 (0.1)	1 (0.1)	0 (0.0)	5 (0.7)	1 (0.1)	1 (0.2)
悪寒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
一般・全身障害および投与部位の状態							
医療機器位置異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
早期満腹	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪組織増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	4 (0.5)	1 (0.1)	0 (0.0)	2 (0.3)	6 (0.8)	1 (0.1)	20 (4.1)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
冷感	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
びくびく感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ヘルニア	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
治癒不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
易刺激性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.2)
粘膜乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.4)
小結節	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	4 (0.5)	3 (0.3)	4 (0.8)
末梢性浮腫	2 (0.3)	5 (0.7)	4 (0.5)	4 (0.5)	13 (1.8)	7 (0.7)	18 (3.7)
疼痛	1 (0.1)	2 (0.3)	2 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.2)
発熱	2 (0.3)	5 (0.7)	2 (0.3)	3 (0.4)	2 (0.3)	0 (0.0)	6 (1.2)
不活発	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
恥骨上痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
温度変化不耐症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口渇	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	88 (18.2)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
一般・全身障害および投与部位の状態							
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害							
胆道ジスキネジー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
胆管炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
肝嚢胞	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
肝嚢胞破裂	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
脂肪肝	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	3 (0.4)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
高ビリルビン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
肝圧痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害							
アレルギー性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
アナフィラキシーショック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
造影剤アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
食物アレルギー	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
免疫系障害							
複合アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	2 (0.3)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
感染症および寄生虫症							
膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
真菌性肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
細菌性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	5 (0.7)	3 (0.4)	6 (0.8)	5 (0.7)	5 (0.7)	1 (0.1)	5 (1.0)
ウイルス性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カンジダ症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
蜂巣炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
クロストリジウム性大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
膀胱炎	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
サイトメガロウイルス感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
感染症および寄生虫症							
耳感染	3 (0.4)	4 (0.5)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳垂感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
游走性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
眼瞼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱性感染症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
皮膚真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	4 (0.5)	3 (0.4)	4 (0.5)	4 (0.5)	7 (0.9)	2 (0.2)	5 (1.0)
ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)
細菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
ウイルス性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
陰部ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
泌尿生殖器感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジアルジア症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H 1 N 1 インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C型肝炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
感染症および寄生虫症							
帯状疱疹	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	2 (0.4)
麦粒腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
伝染性単核症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	2 (0.3)	6 (0.8)	5 (0.7)	2 (0.3)	6 (0.8)	3 (0.3)	3 (0.6)
腎感染	2 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
迷路炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下気道感染	1 (0.1)	1 (0.1)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ライム病	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マラリア	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マイコプラズマ感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	12 (1.6)	13 (1.7)	7 (0.9)	5 (0.7)	13 (1.8)	10 (1.0)	36 (7.5)
線虫症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔カンジダ症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
口腔真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
口腔ヘルペス	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.2)
急性中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
感染症および寄生虫症							
乳頭腫ウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
爪囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
百日咳	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	4 (0.4)	5 (1.0)
レンサ球菌性咽頭炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
肺炎	1 (0.1)	2 (0.3)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ウイルス性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
前立腺感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎盂腎炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎嚢胞感染	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)	1 (0.1)	1 (0.1)	2 (0.4)
気道感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
ウイルス性気道感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.4)
卵管卵巣炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	2 (0.3)	2 (0.3)	5 (0.7)	0 (0.0)	5 (0.7)	3 (0.3)	8 (1.7)
皮膚感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌性咽頭炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
癬風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
感染症および寄生虫症							
扁桃炎	2 (0.3)	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
歯感染	3 (0.4)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
気管気管支炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	10 (1.3)	3 (0.4)	5 (0.7)	5 (0.7)	8 (1.1)	5 (0.5)	8 (1.7)
尿路感染	9 (1.2)	3 (0.4)	3 (0.4)	4 (0.5)	4 (0.5)	7 (0.7)	11 (2.3)
泌尿生殖器細菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	5 (0.7)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
外陰部腔カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
外陰腔真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
創傷感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
膿創	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症							
腹部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足関節部骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)
節足動物刺傷	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
咬刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
滑液包損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨損傷	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
傷害、中毒および処置合併症							
挫傷	5 (0.7)	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.4)
角膜擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
擦過傷	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼外傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
眼の貫通性外傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
足骨折	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼内異物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
上腕骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腸脛靱帯症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切開部位痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
企図的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
関節損傷	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
裂傷	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
靱帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯断裂	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	4 (0.5)	1 (0.1)	1 (0.2)
四肢損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
口唇損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腰椎骨折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
傷害、中毒および処置合併症							
半月板障害	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
多発骨折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
筋断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	0 (0.0)	2 (0.3)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.4)
頸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲血腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
処置後合併症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)
処置による疼痛	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
処置による嘔吐	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
橈骨骨折	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨格損傷	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス骨折	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)
手首関節骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.2)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	2 (0.3)	1 (0.1)	2 (0.4)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中アルブミン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.4)
血中カルシウム増加	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	0 (0.0)	1 (0.1)	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.6)
血中クレアチンホスホキナーゼ増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血中クレアチニン増加	8 (1.0)	5 (0.7)	8 (1.1)	5 (0.7)	3 (0.4)	5 (0.5)	2 (0.4)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)
血中ブドウ糖増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.2)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中副甲状腺ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
血圧低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
拡張期血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
血圧上昇	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.4)
血中ナトリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
血中テストステロン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿素増加	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.3)	1 (0.1)	2 (0.2)	0 (0.0)
血中尿酸増加	4 (0.5)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)
尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C－反応性蛋白増加	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
臨床検査							
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心雑音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)
腎クレアチニン・クリアランス増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図再分極異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
心電図異常T波	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心電図T波逆転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
好酸球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	2 (0.3)	0 (0.0)	3 (0.4)	0 (0.0)	3 (0.4)	1 (0.1)	1 (0.2)
胃内pH低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ヘマトクリット減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ヘマトクリット増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
心拍数不整	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肝酵素異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.3)	1 (0.1)	1 (0.2)
A型肝炎ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヒト乳頭腫ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
I N R増加	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リバーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肝機能検査異常	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
季肋下肝触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
低比重リポ蛋白減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
臨床検査							
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
リンパ球形態異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
平均赤血球容積増加	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
好中球数減少	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
好中球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
QOL低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
卵巣超音波検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧低下	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿量増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
ビタミンD減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウエスト周囲径増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	2 (0.3)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)
体重増加	1 (0.1)	5 (0.7)	3 (0.4)	0 (0.0)	6 (0.8)	0 (0.0)	8 (1.7)
白血球数減少	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿中白血球	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿中白血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
代謝および栄養障害							
アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	3 (0.6)
糖尿病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
食物渴望	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	0 (0.0)	0 (0.0)	4 (0.5)	3 (0.4)	5 (0.7)	0 (0.0)	2 (0.4)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
高カルシウム血症	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
高コレステロール血症	3 (0.4)	1 (0.1)	1 (0.1)	3 (0.4)	2 (0.3)	0 (0.0)	3 (0.6)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	2 (0.2)	2 (0.4)
高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.2)
高脂血症	0 (0.0)	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高ナトリウム血症	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)
高リン酸塩血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
高トリグリセリド血症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	2 (0.3)	1 (0.1)	2 (0.3)	2 (0.3)	2 (0.3)	3 (0.3)	1 (0.2)
低アルブミン血症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
低カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血糖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
低マグネシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)
低リン酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ラクトース不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
代謝および栄養障害							
代謝性アシドーシス	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
過体重	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	15 (3.1)
2 型糖尿病	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
ビタミンB 1 2 欠乏	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD 欠乏	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.3)	1 (0.1)	0 (0.0)	1 (0.2)
体重変動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	5 (0.7)	1 (0.1)	6 (0.8)	4 (0.5)	5 (0.7)	1 (0.1)	2 (0.4)
関節炎	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
反応性関節炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	17 (2.2)	5 (0.7)	10 (1.3)	5 (0.7)	8 (1.1)	6 (0.6)	13 (2.7)
骨痛	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包石灰化	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨肥厚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部脊柱管狭窄症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尾骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肋軟骨炎	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外骨腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
線維筋痛	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
瘻孔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.2)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
痛風性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腓脛部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
筋骨格系および結合組織障害							
椎間板変性症	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
関節滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
関節可動域低下	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
関節腫脹	1 (0.1)	2 (0.3)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
靱帯障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢非対称	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	7 (1.4)
筋緊張	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
筋攣縮	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	3 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)
筋骨格不快感	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格痛	5 (0.7)	3 (0.4)	2 (0.3)	6 (0.8)	4 (0.5)	0 (0.0)	4 (0.8)
筋骨格硬直	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	2 (0.3)	2 (0.3)	2 (0.3)	1 (0.1)	5 (0.7)	2 (0.2)	1 (0.2)
筋炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
頸部腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
頸部痛	2 (0.3)	3 (0.4)	2 (0.3)	3 (0.4)	2 (0.3)	0 (0.0)	2 (0.4)
変形性関節症	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
骨端症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨減少症	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
骨粗鬆症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	5 (0.7)	5 (0.7)	5 (0.7)	3 (0.4)	1 (0.1)	0 (0.0)	6 (1.2)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
筋骨格系および結合組織障害							
関節周囲炎	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節リウマチ	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
仙腸骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側弯症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
重感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
脊椎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
腱痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腱炎	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.4)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
斜頸	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
アクロコルドン	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
基底細胞癌	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
乳房の良性新生物	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
甲状腺の良性新生物	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
子宮頸部癌第0期	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真珠腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性骨髄性白血病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カボジ肉腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
悪性黒色腫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表皮内悪性黒色腫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メラノサイト性母斑	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)
下垂体の良性腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性角化症	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)
扁平上皮癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.4)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
灼熱感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手根管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳神経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識レベルの低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	6 (0.8)	4 (0.5)	2 (0.3)	4 (0.5)	4 (0.5)	0 (0.0)	19 (3.9)
労作性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.2)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
神経系障害							
脳症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	8 (1.0)	6 (0.8)	9 (1.2)	3 (0.4)	12 (1.6)	4 (0.4)	63 (13.0)
味覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.4)	0 (0.0)	2 (0.4)
反射減弱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗜眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.6)
意識消失	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
片頭痛	2 (0.3)	2 (0.3)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.4)
前兆を伴う片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	1 (0.1)	0 (0.0)	2 (0.3)	1 (0.1)	2 (0.3)	1 (0.1)	2 (0.4)
パーキンソン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パーキンソニズム	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神寸前の状態	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
根症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
坐骨神経痛	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.4)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
神経系障害							
感覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神	3 (0.4)	3 (0.4)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
一過性脳虚血発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
トンネル状視野	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎骨動脈解離	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第7 脳神経麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
妊娠、産褥および周産期の状態							
自然流産	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
不安	2 (0.3)	2 (0.3)	0 (0.0)	2 (0.3)	4 (0.5)	0 (0.0)	2 (0.4)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
自閉症スペクトラム障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
精神緩慢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
燃え尽き症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
抑うつ気分	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	3 (0.4)	3 (0.4)	2 (0.3)	3 (0.4)	4 (0.5)	0 (0.0)	2 (0.4)
睡眠異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	1 (0.1)	2 (0.3)	1 (0.1)	2 (0.3)	2 (0.3)	0 (0.0)	6 (1.2)
リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
性欲障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
リビド消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
精神障害							
大うつ病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分変化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
神経過敏	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ニコチン依存	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)
パニック反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心身症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
夢遊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
アルブミン尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱脱	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.2)
膀胱痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
着色尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.2)
非感染性膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.4)	1 (0.1)	1 (0.1)	1 (0.2)
遺尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
腎および尿路障害							
血尿	4 (0.5)	5 (0.7)	3 (0.4)	3 (0.4)	5 (0.7)	0 (0.0)	9 (1.9)
水腎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腎腫大	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿意切迫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎結石症	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.4)
夜間頻尿	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	50 (10.4)
閉塞性尿路疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	22 (4.6)
多尿	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	68 (14.1)
蛋白尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎仙痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
腎嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.4)
腎嚢胞破裂	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
急性腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性腎不全	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)
腎臓痛	17 (2.2)	14 (1.8)	6 (0.8)	11 (1.5)	11 (1.5)	6 (0.6)	41 (8.5)
有痛性排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿道狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿躊躇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿閉	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
腎および尿路障害							
尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿流量減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
生殖系および乳房障害							
子宮付属器痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.6)
精子無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
萎縮性外陰腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
乳房嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部上皮異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性交出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
性交困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
勃起不全	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
過少月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
生殖系および乳房障害							
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機能性子宮出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.6)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
不規則月経	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
卵巣嚢胞	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.2)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
卵巣捻転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤脱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ペイロニー病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺腫大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮脱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔分泌物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
腔出血	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
生殖系および乳房障害							
精索静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰腔乾燥	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.6)
呼吸器、胸郭および縦隔障害							
喘息	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
気管支痙攣	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	6 (0.8)	1 (0.1)	5 (0.7)	6 (0.8)	6 (0.8)	1 (0.1)	8 (1.7)
咽喉乾燥	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
発声障害	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.4)
安静時呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
過換気	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
喉頭囊腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
鼻中隔弯曲	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	1 (0.1)	2 (0.3)	3 (0.4)	1 (0.1)	0 (0.0)	4 (0.4)	5 (1.0)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
呼吸器、胸郭および縦隔障害							
肺塞栓症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺線維症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
気道うっ血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)
鼻漏	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
低音性連続性ラ音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔うっ血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠時無呼吸症候群	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
いびき	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽喉絞扼感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害							
ざ瘡	2 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
日光性角化症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンドロゲン性脱毛症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚囊腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
皮膚および皮下組織障害							
皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アトピー性皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	1 (0.2)
皮膚症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	5 (1.0)
斑状出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	3 (0.4)	2 (0.3)	0 (0.0)	0 (0.0)	2 (0.3)	2 (0.2)	0 (0.0)
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.2)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過剰皮膚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
過角化	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内出血発生の増加傾向	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嵌入爪	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機械性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
爪破損	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚疼痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
皮膚および皮下組織障害							
光線過敏性反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
柑糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色柑糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	2 (0.3)	3 (0.4)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	4 (0.8)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	1 (0.1)	2 (0.3)	2 (0.3)	3 (0.4)	1 (0.1)	1 (0.1)	3 (0.6)
紅斑性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
斑状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
そう痒性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脂腺障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
皮膚色素過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚病変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.4)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ滞性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尋常性白斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
社会環境							
閉経	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
外科および内科処置							
収れん薬療法	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジフテリア免疫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管拡張および子宮内搔爬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン補給	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)
コントロール不良の血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血腫	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)
高血圧	21 (2.7)	10 (1.3)	16 (2.1)	18 (2.4)	14 (1.9)	15 (1.6)	45 (9.3)
高血圧クリーゼ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	0 (0.0)	1 (0.1)	3 (0.4)	0 (0.0)	2 (0.3)	0 (0.0)	6 (1.2)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
微小血管症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
レイノー現象	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表在性血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=769) n (%)	(N=762) n (%)	(N=755) n (%)	(N=749) n (%)	(N=739) n (%)	(N=961) n (%)	(N=483) n (%)
血管障害							
静脈瘤	3 (0.4)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
静脈不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	5 (0.7)	1 (0.1)	3 (0.4)	1 (0.1)	2 (0.3)	1 (0.1)	359 (74.3)

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表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
血液およびリンパ系障害							
貧血	3 (0.6)	5 (1.1)	1 (0.2)	1 (0.2)	2 (0.4)	2 (0.5)	1 (0.2)
凝血異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
低色素性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
白血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球減少症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
正色素性正球性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
急性心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
狭心症	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
心房細動	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心臓弁膜疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拡大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝導障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
心臓障害							
チアノーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
左室機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
僧帽弁疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁逸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)
心嚢液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞不全症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)
三尖弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害							
心房中隔欠損症	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第Ⅴ因子ライデン変異	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多嚢胞性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎奇形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
耳および迷路障害							
耳垢栓塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内耳障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
回転性めまい	2 (0.4)	3 (0.6)	0 (0.0)	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害							
アンドロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
バセドウ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
エストロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
眼障害							
調節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
眼障害							
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.5)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
眼の隈	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外眼筋不全麻痺	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
眼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
遠視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虹彩炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涙増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光視症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
老視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
翼状片	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
強膜炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
暗点	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
眼障害							
霧視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体変性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体剥離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害							
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
腹部不快感	1 (0.2)	1 (0.2)	0 (0.0)	3 (0.7)	1 (0.2)	0 (0.0)	1 (0.2)
腹部膨満	4 (0.8)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)
腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.5)
閉塞を伴う腹部ヘルニア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腹痛	3 (0.6)	0 (0.0)	2 (0.4)	2 (0.4)	1 (0.2)	5 (1.1)	0 (0.0)
下腹部痛	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	4 (0.8)	3 (0.6)	4 (0.9)	4 (0.9)	2 (0.4)	5 (1.1)	2 (0.5)
腹部硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部圧痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
裂肛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
痔瘻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便通不規則	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)
クローン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
胃腸障害							
歯不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下痢	2 (0.4)	6 (1.3)	6 (1.3)	6 (1.3)	2 (0.4)	7 (1.6)	0 (0.0)
憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
口内乾燥	0 (0.0)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	3 (0.6)	1 (0.2)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)
嚥下障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
びらん性十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
大腿ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
食中毒	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
機能性胃腸障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
びらん性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	0 (0.0)	1 (0.2)	2 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
胃腸障害							
歯肉退縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
歯肉炎	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
舌痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	1 (0.2)	1 (0.2)	0 (0.0)	3 (0.7)	0 (0.0)	2 (0.5)	0 (0.0)
裂孔ヘルニア	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胃酸過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵径ヘルニア	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
内ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吸収不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
メレナ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	5 (1.1)	5 (1.1)	3 (0.7)	2 (0.4)	6 (1.3)	2 (0.5)	1 (0.2)
嚥下痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
口腔障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
胃腸障害							
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門周囲痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
吐き戻し	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
S状結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌苔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌粘膜剥脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.4)	2 (0.5)	1 (0.2)
臍ヘルニア	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)
閉塞性臍ヘルニア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	5 (1.1)	3 (0.6)	3 (0.7)	3 (0.7)	6 (1.3)	3 (0.7)	2 (0.5)
一般・全身障害および投与部位の状態							
無力症	0 (0.0)	5 (1.1)	1 (0.2)	1 (0.2)	2 (0.4)	2 (0.5)	1 (0.2)
腋窩痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胸痛	2 (0.4)	1 (0.2)	0 (0.0)	1 (0.2)	3 (0.7)	1 (0.2)	0 (0.0)
悪寒	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚢胞	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
一般・全身障害および投与部位の状態							
医療機器位置異常	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪組織増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	2 (0.4)	8 (1.7)	0 (0.0)	0 (0.0)	2 (0.4)	4 (0.9)	3 (0.7)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
びくびく感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
治癒不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	3 (0.7)	0 (0.0)
易刺激性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
倦怠感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
粘膜乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小結節	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
浮腫	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
末梢性浮腫	3 (0.6)	4 (0.9)	2 (0.4)	1 (0.2)	3 (0.7)	1 (0.2)	1 (0.2)
疼痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	2 (0.4)	2 (0.4)	6 (1.3)	6 (1.3)	1 (0.2)	6 (1.4)	4 (0.9)
不活発	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨上痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	1 (0.2)	3 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	3 (0.7)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
一般・全身障害および投与部位の状態							
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害							
胆道ジスキネジー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	1 (0.2)	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
肝嚢胞破裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肝臓痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
高ビリルビン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肝障害	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝圧痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
免疫系障害							
アレルギー性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシーショック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
造影剤アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
食物アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
免疫系障害							
複合アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症							
膿瘍	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
四肢膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
細菌性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
細菌尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	4 (0.8)	3 (0.6)	4 (0.9)	1 (0.2)	4 (0.9)	1 (0.2)	2 (0.5)
ウイルス性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
カンジダ症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩蜂巣炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
クロストリジウム性大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	3 (0.6)	2 (0.4)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
サイトメガロウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
感染症および寄生虫症							
耳感染	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.5)	0 (0.0)
耳垂感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性紅斑	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
游走性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
熱性感染症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	2 (0.4)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	2 (0.5)	2 (0.5)
ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
細菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰部ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
泌尿生殖器感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジアルジア症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H 1 N 1 インフルエンザ	0 (0.0)	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター性胃炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
感染症および寄生虫症							
帯状疱疹	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.5)
麦粒腫	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
感染性嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
伝染性単核症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
インフルエンザ	5 (1.1)	2 (0.4)	4 (0.9)	5 (1.1)	6 (1.3)	3 (0.7)	1 (0.2)
腎感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
迷路炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肝膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
下気道感染	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
ライム病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マラリア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
マイコプラズマ感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
爪感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	11 (2.3)	11 (2.4)	6 (1.3)	3 (0.7)	8 (1.8)	5 (1.1)	8 (1.8)
線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口腔カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
精巣炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
急性中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
感染症および寄生虫症							
乳頭腫ウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
歯冠周囲炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
百日咳	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
咽頭炎	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.5)	1 (0.2)
レンサ球菌性咽頭炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺炎	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎盂腎炎	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
腎嚢胞感染	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.4)	2 (0.4)	0 (0.0)	4 (0.9)
気道感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
卵管卵巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
副鼻腔炎	0 (0.0)	2 (0.4)	4 (0.9)	0 (0.0)	2 (0.4)	1 (0.2)	3 (0.7)
皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌性咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癬風	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
感染症および寄生虫症							
扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)
歯膿瘍	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
歯感染	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
気管炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
気管気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	2 (0.4)	7 (1.5)	2 (0.4)	1 (0.2)	2 (0.4)	4 (0.9)	2 (0.5)
尿路感染	9 (1.9)	5 (1.1)	5 (1.1)	0 (0.0)	3 (0.7)	7 (1.6)	2 (0.5)
泌尿生殖器細菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
細菌性腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)
ウイルス性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部腔カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰腔真菌感染	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
創傷感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膿創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症							
腹部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足関節部骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咬刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
傷害、中毒および処置合併症							
挫傷	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
角膜擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の貫通性外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
足骨折	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼内異物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腕骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸脛靱帯症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切開部位痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
企図的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
関節脱臼	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節損傷	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
裂傷	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
靱帯損傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯断裂	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.5)	1 (0.2)
四肢損傷	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口唇損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腰椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
傷害、中毒および処置合併症							
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	1 (0.2)	1 (0.2)
多発骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋断裂	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)
頸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
処置後合併症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
橈骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨格損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手首関節骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
臨床検査							
活性化部分トロンボプラスチン時間延長	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
アラニン・アミノトランスフェラーゼ増加	5 (1.1)	1 (0.2)	4 (0.9)	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.4)	0 (0.0)	3 (0.7)	1 (0.2)	0 (0.0)	2 (0.5)	1 (0.2)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルブミン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カルシウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
血中クレアチンホスホキナーゼ増加	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	8 (1.7)	11 (2.4)	4 (0.9)	6 (1.3)	9 (2.0)	9 (2.0)	6 (1.4)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
血中副甲状腺ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血圧低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
拡張期血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
血中ナトリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中テストステロン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血中尿素増加	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
血中尿酸増加	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
臨床検査							
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
心雑音	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎クレアチニン・クリアランス増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
心電図QT間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図再分極異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図異常T波	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	1 (0.2)	1 (0.2)	2 (0.4)	1 (0.2)	4 (0.9)	0 (0.0)	1 (0.2)
胃内pH低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ヘマトクリット増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数不整	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
A型肝炎ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヒト乳頭腫ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
I N R増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リバーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季肋下肝触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低比重リポ蛋白減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
臨床検査							
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球形態異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
平均赤血球容積増加	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数減少	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
プロトロンビン時間異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
QOL低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
卵巣超音波検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
尿浸透圧低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
ウエスト周囲径増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	3 (0.6)	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.9)	1 (0.2)
体重増加	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
尿中白血球	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
代謝および栄養障害							
アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
食欲減退	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	2 (0.5)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物渴望	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	1 (0.2)	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)
高クレアチニン血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
高カリウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高脂血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高ナトリウム血症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
高リン酸塩血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血糖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低マグネシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低リン酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ラクトース不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
代謝および栄養障害							
代謝性アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過体重	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 型糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンB 1 2 欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD 欠乏	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
体重変動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	3 (0.6)	2 (0.4)	3 (0.7)	1 (0.2)	2 (0.4)	2 (0.5)	2 (0.5)
関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
反応性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	8 (1.7)	6 (1.3)	12 (2.6)	3 (0.7)	8 (1.8)	7 (1.6)	8 (1.8)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.5)	0 (0.0)
滑液包石灰化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨肥厚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部脊柱管狭窄症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
尾骨痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋軟骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外骨腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
瘻孔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	0 (0.0)	2 (0.4)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腓脛部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
筋骨格系および結合組織障害							
椎間板変性症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	2 (0.4)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)
関節滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節可動域低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
靱帯障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢非対称	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋力低下	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格痛	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
筋肉痛	2 (0.4)	0 (0.0)	2 (0.4)	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)
筋炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部痛	0 (0.0)	4 (0.9)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
変形性関節症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	3 (0.7)
骨関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
骨粗鬆症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	2 (0.4)	4 (0.9)	4 (0.9)	2 (0.4)	2 (0.4)	5 (1.1)	0 (0.0)
顎痛	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
筋骨格系および結合組織障害							
関節周囲炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
足底筋膜炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
関節リウマチ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
仙腸骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側弯症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
重感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
脊椎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
脊椎炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
腱障害	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
腱炎	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斜頸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
アクロコルドン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
基底細胞癌	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
乳房の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
子宮頸部癌第0期	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真珠腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性骨髄性白血病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カボジ肉腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表皮内悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メラノサイト性母斑	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下垂体の良性腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
扁平上皮癌	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺新生物	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
平衡障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手根管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳神経障害	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識レベルの低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
浮動性めまい	4 (0.8)	6 (1.3)	1 (0.2)	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.9)
労作性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
神経系障害							
脳症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	9 (1.9)	12 (2.6)	5 (1.1)	7 (1.5)	5 (1.1)	4 (0.9)	3 (0.7)
味覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)
反射減弱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗜眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
前兆を伴う片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
起立不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	3 (0.7)	0 (0.0)	1 (0.2)
パーキンソン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パーキンソニズム	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
失神寸前の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
根症候群	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
坐骨神経痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
神経系障害							
感覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)
失神	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)
一過性脳虚血発作	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トンネル状視野	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎骨動脈解離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第7 脳神経麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
妊娠、産褥および周産期の状態							
自然流産	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自閉症スペクトラム障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神緩慢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
燃え尽き症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	1 (0.2)	2 (0.4)	2 (0.4)	2 (0.4)	2 (0.4)	1 (0.2)	4 (0.9)
睡眠異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	1 (0.2)	2 (0.4)	1 (0.2)	2 (0.4)	1 (0.2)	2 (0.5)	1 (0.2)
リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性欲障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リビド消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
精神障害							
大うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分変化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経過敏	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
ニコチン依存	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
パニック反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
心身症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
統合失調症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
夢遊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス	1 (0.2)	1 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
自殺企図	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
アルブミン尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高窒素血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非感染性膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)
遺尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
腎および尿路障害							
血尿	5 (1.1)	11 (2.4)	5 (1.1)	5 (1.1)	6 (1.3)	6 (1.4)	2 (0.5)
水腎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎腫大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
白血球尿	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
尿意切迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎結石症	3 (0.6)	2 (0.4)	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
夜間頻尿	1 (0.2)	2 (0.4)	5 (1.1)	0 (0.0)	3 (0.7)	1 (0.2)	0 (0.0)
閉塞性尿路疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	2 (0.4)	4 (0.9)	4 (0.9)	1 (0.2)	0 (0.0)	2 (0.5)	0 (0.0)
蛋白尿	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
腎仙痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
腎嚢胞出血	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎嚢胞破裂	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
慢性腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	2 (0.4)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)
腎臓痛	16 (3.4)	21 (4.5)	17 (3.7)	11 (2.4)	12 (2.7)	11 (2.5)	9 (2.1)
有痛性排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿道狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿躊躇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
腎および尿路障害							
尿路障害	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿流量減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害							
子宮付属器痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
精子無力症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
萎縮性外陰腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房不快感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部上皮異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
子宮頸管ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性交出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性交困難	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
精巣上体嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過少月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮瘤	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
生殖系および乳房障害							
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
機能性子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多	0 (0.0)	1 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
卵巣嚢胞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.7)	0 (0.0)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
卵巣捻転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ペイロニー病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺腫大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
子宮脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔分泌物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
生殖系および乳房障害							
精索静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰腔乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害							
喘息	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
運動誘発喘息	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	5 (1.1)	4 (0.9)	3 (0.7)	4 (0.9)	4 (0.9)	2 (0.5)	2 (0.5)
咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
発声障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
安静時呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.5)
過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
鼻中隔弯曲	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間呼吸困難	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	2 (0.4)	2 (0.4)	2 (0.4)	2 (0.4)	2 (0.4)	0 (0.0)	1 (0.2)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
呼吸器、胸郭および縦隔障害							
肺塞栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺線維症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気道うっ血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
鼻漏	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低音性連続性ラ音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔うっ血	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠時無呼吸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
いびき	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽喉絞扼感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
扁桃結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
皮膚および皮下組織障害							
ざ瘡	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)
日光性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)
円形脱毛症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンドロゲン性脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚囊腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
皮膚および皮下組織障害							
皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
斑状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
湿疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多形紅斑	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過剰皮膚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内出血発生の増加傾向	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嵌入爪	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
機械性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
神経皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
爪破損	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
皮膚および皮下組織障害							
光線過敏性反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糝糠疹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色糝糠疹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
そう痒症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	2 (0.4)	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑性皮疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂腺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
皮膚病変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚潰瘍	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ滞性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尋常性白斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
社会環境							
閉経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473) n (%)	(N=465) n (%)	(N=460) n (%)	(N=455) n (%)	(N=448) n (%)	(N=441) n (%)	(N=435) n (%)
外科および内科処置							
収れん薬療法	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジフテリア免疫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管拡張および子宮内搔爬	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン補給	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈拡張	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
深部静脈血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	22 (4.7)	20 (4.3)	19 (4.1)	5 (1.1)	10 (2.2)	15 (3.4)	9 (2.1)
高血圧クリーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	2 (0.4)	3 (0.6)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
微小血管症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レイノー現象	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表在性血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=473)	(N=465)	(N=460)	(N=455)	(N=448)	(N=441)	(N=435)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血管障害							
静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血管閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
静脈不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	37 (7.8)	21 (4.5)	13 (2.8)	8 (1.8)	8 (1.8)	8 (1.8)	4 (0.9)

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表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
血液およびリンパ系障害							
貧血	0 (0.0)	2 (0.5)	1 (0.2)	2 (0.5)	2 (0.4)	7 (0.5)	5 (0.4)
凝血異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
好酸球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
低色素性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	3 (0.2)
白血球増加症	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
リンパ節症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
好中球増加症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
正色素性正球性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血小板増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
急性心筋梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
狭心症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	2 (0.1)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (0.6)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓弁膜疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拡大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
伝導障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
冠動脈疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
心臓障害							
チアノーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
僧帽弁疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁逸脱	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	18 (1.2)	4 (0.3)
心嚢液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞不全症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
洞性不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	9 (0.6)	1 (0.1)
三尖弁閉鎖不全症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
先天性、家族性および遺伝性障害							
心房中隔欠損症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第Ⅴ因子ライデン変異	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多嚢胞性肝疾患	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
脊椎奇形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
耳および迷路障害							
耳垢栓塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
耳閉	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
耳痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
内耳障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乗物酔い	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
回転性めまい	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	14 (1.0)	5 (0.4)
頭位性回転性めまい	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害							
アンドロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バセドウ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	0 (0.0)
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
続発性副甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
エストロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害							
調節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼瞼炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
眼障害							
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	1 (0.1)	0 (0.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.3)	1 (0.1)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の隈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	12 (0.8)	2 (0.1)
外眼筋不全麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼の障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
眼出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼部腫脹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
遠視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虹彩炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
流涙増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
光視症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
老視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
翼状片	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
暗点	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
眼障害							
霧視	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
視力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
硝子体変性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体剥離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胃腸障害							
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (0.6)	5 (0.4)
腹部膨満	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	19 (1.3)	8 (0.6)
腹部ヘルニア	2 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
閉塞を伴う腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腹部腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腹痛	1 (0.2)	1 (0.2)	2 (0.5)	1 (0.2)	1 (0.2)	33 (2.3)	8 (0.6)
下腹部痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
上腹部痛	2 (0.5)	2 (0.5)	2 (0.5)	1 (0.2)	2 (0.4)	33 (2.3)	16 (1.2)
腹部硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部圧痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
裂肛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
痔瘻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
アフタ性口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
腹水	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便通不規則	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
呼気臭	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
口唇のひび割れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
便秘	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	52 (3.6)	7 (0.5)
クローン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
胃腸障害							
歯不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
下痢	2 (0.5)	1 (0.2)	2 (0.5)	5 (1.2)	1 (0.2)	63 (4.4)	14 (1.0)
憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸憩室	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	199 (13.8)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
消化不良	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	36 (2.5)	19 (1.4)
嚥下障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.3)	1 (0.1)
小腸炎	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
びらん性十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腿ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
食中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
機能性胃腸障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
胃潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	2 (0.1)
びらん性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.1)
消化管運動過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
消化器痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
胃食道逆流性疾患	3 (0.7)	3 (0.7)	2 (0.5)	1 (0.2)	0 (0.0)	11 (0.8)	6 (0.4)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
歯肉痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
胃腸障害							
歯肉退縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
血便排泄	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
痔核	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	3 (0.2)	2 (0.1)
裂孔ヘルニア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
胃酸過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
回腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵径ヘルニア	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.1)	0 (0.0)
内ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	1 (0.1)
口唇乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.3)	1 (0.1)
口唇腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吸収不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メレナ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	1 (0.2)	1 (0.2)	1 (0.2)	4 (1.0)	2 (0.4)	68 (4.7)	18 (1.3)
嚥下痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
口腔障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
口腔扁平苔癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口腔内痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
膵嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
胃腸障害							
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門周囲痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
直腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吐き戻し	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
S状結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.1)	1 (0.1)
舌苔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
舌変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
舌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
舌乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
舌粘膜剥脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
歯の障害	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.1)	0 (0.0)
歯痛	1 (0.2)	1 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	4 (0.3)	2 (0.1)
臍ヘルニア	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
閉塞性臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
嘔吐	2 (0.5)	0 (0.0)	1 (0.2)	4 (1.0)	0 (0.0)	31 (2.1)	13 (1.0)
一般・全身障害および投与部位の状態							
無力症	3 (0.7)	0 (0.0)	1 (0.2)	3 (0.7)	0 (0.0)	45 (3.1)	3 (0.2)
腋窩痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	9 (0.6)	1 (0.1)
胸痛	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	16 (1.1)	10 (0.7)
悪寒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (0.6)	1 (0.1)
嚢胞	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
一般・全身障害および投与部位の状態							
医療機器位置異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
早期満腹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脂肪組織増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
疲労	2 (0.5)	1 (0.2)	1 (0.2)	4 (1.0)	0 (0.0)	85 (5.9)	16 (1.2)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.5)	1 (0.1)
酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
びくびく感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
全身性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
治癒不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
インフルエンザ様疾患	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
易刺激性	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	17 (1.2)	4 (0.3)
粘膜乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.5)	0 (0.0)
小結節	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	7 (0.5)	2 (0.1)
末梢性浮腫	3 (0.7)	5 (1.2)	1 (0.2)	4 (1.0)	0 (0.0)	33 (2.3)	8 (0.6)
疼痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	4 (0.3)
発熱	2 (0.5)	4 (0.9)	1 (0.2)	2 (0.5)	1 (0.2)	17 (1.2)	6 (0.4)
不活発	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
恥骨上痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
温度変化不耐症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (0.4)	1 (0.1)
口渇	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	599 (41.5)	8 (0.6)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
一般・全身障害および投与部位の状態							
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害							
胆道ジスキネジー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)
胆嚢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
胆嚢ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
肝嚢胞破裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	4 (0.3)
肝臓痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
高ビリルビン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肝障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
肝圧痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害							
アレルギー性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシーショック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
造影剤アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
食物アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
過敏症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
免疫系障害							
複合アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	3 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	8 (0.6)	7 (0.5)
感染症および寄生虫症							
膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
四肢膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
急性扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	3 (0.2)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性関節炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
感染性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
バルトリン腺膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
乳房感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	3 (0.7)	2 (0.5)	2 (0.5)	2 (0.5)	3 (0.6)	19 (1.3)	8 (0.6)
ウイルス性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.2)	0 (0.0)
蜂巣炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼窩蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
クロストリジウム性大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)	1 (0.2)	2 (0.1)	4 (0.3)
サイトメガロウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
感染症および寄生虫症							
耳感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	6 (0.4)
耳垂感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
游走性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼瞼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱性感染症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.1)
皮膚真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.2)	3 (0.7)	1 (0.2)	2 (0.5)	0 (0.0)	14 (1.0)	7 (0.5)
ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	6 (0.4)
細菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性消化管感染	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰部ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
泌尿生殖器感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ジアルジア症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
H 1 N 1 インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
肝嚢胞感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
ヘルペスウイルス感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
感染症および寄生虫症							
帯状疱疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	2 (0.1)
麦粒腫	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性単核症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	1 (0.2)	2 (0.5)	4 (1.0)	2 (0.5)	0 (0.0)	19 (1.3)	13 (1.0)
腎感染	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)	1 (0.1)	0 (0.0)
迷路炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
喉頭炎	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
肝膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
下気道感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ライム病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
マラリア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マイコプラズマ感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	6 (1.4)	5 (1.2)	5 (1.2)	7 (1.7)	0 (0.0)	80 (5.5)	39 (2.9)
線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
口腔カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
口腔真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
急性中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
感染症および寄生虫症							
乳頭腫ウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
爪囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
百日咳	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	3 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	8 (0.6)	4 (0.3)
レンサ球菌性咽頭炎	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.1)
肺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	3 (0.2)	2 (0.1)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎盂腎炎	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.3)	1 (0.1)
腎嚢胞感染	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
気道感染	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	3 (0.2)
ウイルス性気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	1 (0.2)	1 (0.2)	1 (0.2)	2 (0.5)	0 (0.0)	6 (0.4)	1 (0.1)
卵管卵巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
副鼻腔炎	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	20 (1.4)	8 (0.6)
皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ブドウ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌性咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癬風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
感染症および寄生虫症							
扁桃炎	2 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.1)
歯膿瘍	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	2 (0.1)
歯感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	3 (0.7)	5 (1.2)	2 (0.5)	4 (1.0)	0 (0.0)	22 (1.5)	11 (0.8)
尿路感染	2 (0.5)	7 (1.7)	5 (1.2)	5 (1.2)	4 (0.8)	31 (2.1)	17 (1.3)
泌尿生殖器細菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
細菌性腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	2 (0.5)	2 (0.5)	2 (0.5)	0 (0.0)	1 (0.2)	3 (0.2)	5 (0.4)
ウイルス性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
外陰部腔カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	4 (0.3)	1 (0.1)
外陰腔真菌感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.2)
創傷感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
膿創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症							
腹部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
足関節部骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
節足動物咬傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
咬刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
傷害、中毒および処置合併症							
挫傷	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	4 (0.3)
角膜擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
上顎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の貫通性外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
足骨折	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼内異物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
上腕骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸脛靱帯症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
切開部位痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
企図的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.1)	0 (0.0)
関節損傷	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	3 (0.2)	1 (0.1)
裂傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
靱帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
靱帯断裂	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	2 (0.5)	1 (0.2)	1 (0.2)	1 (0.2)	2 (0.1)	1 (0.1)
四肢損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口唇損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腰椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
傷害、中毒および処置合併症							
半月板障害	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
多発骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
頸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼窩周囲血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後合併症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後血尿	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
橈骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨格損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
軟部組織損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼の擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱損傷	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腱断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
脛骨骨折	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
手首関節骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	12 (0.8)	11 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.5)	2 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	11 (0.8)	6 (0.4)
細菌検査陽性	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルブミン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
血中カルシウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	6 (0.4)	1 (0.1)
血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
血中クレアチニン増加	1 (0.2)	6 (1.4)	4 (1.0)	5 (1.2)	0 (0.0)	16 (1.1)	25 (1.9)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
血中乳酸脱水素酵素増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.2)	0 (0.0)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中副甲状腺ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	1 (0.1)
血圧低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
拡張期血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血圧上昇	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	6 (0.4)	0 (0.0)
血中ナトリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	2 (0.1)
血中テストステロン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
血中トリグリセリド増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿素増加	0 (0.0)	7 (1.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	9 (0.6)	0 (0.0)
尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
臨床検査							
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心雑音	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎クレアチニン・クリアランス増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
尿中クレアチニン増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	1 (0.1)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図再分極異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
心電図異常T波	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
好酸球数増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.1)	0 (0.0)
大腸菌検査陽性	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.5)	2 (0.1)
胃内pH低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット減少	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ヘマトクリット増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心拍数不整	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肝酵素異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肝酵素上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	6 (0.4)	2 (0.1)
A型肝炎ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ヒト乳頭腫ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
I N R 増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
眼圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)
リバーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肝機能検査異常	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	3 (0.2)	2 (0.1)
季肋下肝触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低比重リポ蛋白減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
臨床検査							
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
リンパ球形態異常	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積減少	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	1 (0.1)	0 (0.0)
好中球数増加	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血小板数減少	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
プロトロンビン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
QOL低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	1 (0.1)
卵巣超音波検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
尿検査異常	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.1)	0 (0.0)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	16 (1.1)	0 (0.0)
ビタミンD減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウエスト周囲径増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
体重減少	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	25 (1.7)	10 (0.7)
体重増加	0 (0.0)	1 (0.2)	2 (0.5)	2 (0.5)	0 (0.0)	14 (1.0)	6 (0.4)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)
尿中白血球	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
尿中白血球陽性	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
代謝および栄養障害							
アシドーシス	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	55 (3.8)	7 (0.5)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	13 (0.9)	2 (0.1)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体液貯留	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物渴望	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
食物不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
痛風	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.3)	5 (0.4)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
高カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
高コレステロール血症	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.4)	6 (0.4)	3 (0.2)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
高血糖	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.5)	1 (0.2)	3 (0.2)	3 (0.2)
高カリウム血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	4 (0.3)	2 (0.1)
高脂血症	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.1)	3 (0.2)
高ナトリウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	12 (0.8)	6 (0.4)
高リン酸塩血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	11 (0.8)	2 (0.1)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
低カルシウム血症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低血糖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
低カリウム血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	3 (0.2)	2 (0.1)
低マグネシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
低ナトリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.1)
低リン酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
血液量減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
鉄欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ラクトース不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
代謝および栄養障害							
代謝性アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
過体重	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	111 (7.7)	3 (0.2)
2 型糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンB 1 2 欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD 欠乏	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
体重変動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	3 (0.7)	5 (1.2)	1 (0.2)	2 (0.5)	1 (0.2)	12 (0.8)	14 (1.0)
関節炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
反応性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	6 (1.4)	6 (1.4)	6 (1.4)	5 (1.2)	3 (0.6)	37 (2.6)	21 (1.6)
骨痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
滑液包石灰化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
軟骨肥厚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部脊柱管狭窄症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尾骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肋軟骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
外骨腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
瘻孔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
側腹部痛	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	6 (0.4)	1 (0.1)
足変形	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
痛風性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腓径部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
筋骨格系および結合組織障害							
椎間板変性症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	3 (0.2)	3 (0.2)
関節滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
関節可動域低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
関節腫脹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
靱帯障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢非対称	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
筋肉疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
筋痙縮	0 (0.0)	3 (0.7)	0 (0.0)	1 (0.2)	0 (0.0)	18 (1.2)	7 (0.5)
筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
筋力低下	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.1)	0 (0.0)
筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
筋骨格痛	2 (0.5)	0 (0.0)	0 (0.0)	5 (1.2)	0 (0.0)	4 (0.3)	7 (0.5)
筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	1 (0.1)
筋肉痛	2 (0.5)	0 (0.0)	1 (0.2)	4 (1.0)	1 (0.2)	17 (1.2)	7 (0.5)
筋炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部痛	1 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	7 (0.5)	3 (0.2)
変形性関節症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
骨関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
骨減少症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
骨粗鬆症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	10 (0.7)	6 (0.4)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
筋骨格系および結合組織障害							
関節周囲炎	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
恥骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節リウマチ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
肩回旋筋腱板症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
仙腸骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側弯症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
重感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脊椎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
滑液嚢腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱炎	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	7 (0.5)	2 (0.1)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
斜頸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
アクロコルドン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
基底細胞癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
乳房の良性新生物	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
甲状腺の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部癌第0期	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
真珠腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性骨髄性白血病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓血管腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カボジ肉腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表皮内悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メラノサイト性母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
下垂体の良性腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性角化症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
扁平上皮癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
甲状腺新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	3 (0.2)	1 (0.1)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
健忘	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
灼熱感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
手根管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳神経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識レベルの低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.3)	1 (0.1)
浮動性めまい	2 (0.5)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	77 (5.3)	12 (0.9)
労作性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
味覚異常	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	27 (1.9)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
神経系障害							
脳症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
頭痛	0 (0.0)	4 (0.9)	4 (1.0)	5 (1.2)	2 (0.4)	201 (13.9)	20 (1.5)
味覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
感覚鈍麻	1 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	6 (0.4)	2 (0.1)
反射減弱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	2 (0.1)
虚血性脳卒中	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗜眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	4 (0.3)	1 (0.1)
意識消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
片頭痛	2 (0.5)	2 (0.5)	0 (0.0)	1 (0.2)	1 (0.2)	9 (0.6)	1 (0.1)
前兆を伴う片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
ナルコレプシー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
神経圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
起立不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	2 (0.5)	1 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	9 (0.6)	1 (0.1)
パーキンソン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パーキンソニズム	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神寸前の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
根症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.2)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
神経系障害							
感覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
副鼻腔炎に伴う頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	0 (0.0)
傾眠	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
失神	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	4 (0.3)	1 (0.1)
緊張性頭痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
一過性脳虚血発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
トンネル状視野	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
椎骨動脈解離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第7脳神経麻痺	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
妊娠、産褥および周産期の状態							
自然流産	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
不安	0 (0.0)	1 (0.2)	0 (0.0)	2 (0.5)	0 (0.0)	8 (0.6)	5 (0.4)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自閉症スペクトラム障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神緩慢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
燃え尽き症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
うつ病	1 (0.2)	1 (0.2)	1 (0.2)	2 (0.5)	0 (0.0)	7 (0.5)	6 (0.4)
睡眠異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	1 (0.2)	0 (0.0)	2 (0.5)	2 (0.5)	2 (0.4)	35 (2.4)	8 (0.6)
リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
性欲障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
リビドー消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
精神障害							
大うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
気分変化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
神経過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
ニコチン依存	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
パニック発作	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
パニック反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心身症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)
夢遊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ストレス	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	4 (0.3)	1 (0.1)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腎および尿路障害							
アルブミン尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
膀胱脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
膀胱痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
着色尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
非感染性膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	3 (0.2)	6 (0.4)
遺尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
腎および尿路障害							
血尿	6 (1.4)	4 (0.9)	3 (0.7)	6 (1.4)	1 (0.2)	28 (1.9)	12 (0.9)
水腎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
緊張性膀胱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎腫大	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
白血球尿	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
尿意切迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.3)	2 (0.1)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎結石症	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)	6 (0.4)	5 (0.4)
夜間頻尿	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	309 (21.4)	7 (0.5)
閉塞性尿路疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
乏尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
頻尿	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	237 (16.4)	7 (0.5)
多尿	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	408 (28.3)	11 (0.8)
蛋白尿	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.1)	1 (0.1)
腎仙痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	2 (0.1)
腎嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.1)	5 (0.4)
腎嚢胞破裂	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.1)	3 (0.2)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
急性腎不全	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	1 (0.1)
慢性腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	3 (0.2)
腎臓痛	12 (2.8)	4 (0.9)	9 (2.1)	8 (1.9)	2 (0.4)	116 (8.0)	47 (3.5)
有痛性排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿道狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
排尿躊躇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	4 (0.3)	3 (0.2)
尿閉	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
腎および尿路障害							
尿路障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿流量減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
生殖系および乳房障害							
子宮付属器痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	3 (0.2)
精子無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
萎縮性外陰腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
乳房不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
乳房痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部上皮異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
子宮頸管ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)
性交出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
膀胱瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	3 (0.2)
性交困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.3)	2 (0.1)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過少月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
子宮瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
生殖系および乳房障害							
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機能性子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	9 (0.6)	1 (0.1)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
不規則月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	2 (0.1)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
卵巣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	1 (0.1)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
卵巣捻転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
骨盤不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
骨盤痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ペイロニー病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
前立腺腫大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘍	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢痛	0 (0.0)	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
子宮脱	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔分泌物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
腔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
生殖系および乳房障害							
精索静脈瘤	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰腔乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	1 (0.1)
呼吸器、胸郭および縦隔障害							
喘息	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支痙攣	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	1 (0.2)	0 (0.0)	2 (0.5)	3 (0.7)	0 (0.0)	33 (2.3)	12 (0.9)
咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
発声障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	7 (0.5)	3 (0.2)
安静時呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
労作性呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.2)
鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭囊腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	1 (0.1)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
鼻中隔弯曲	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	18 (1.2)	7 (0.5)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
呼吸器、胸郭および縦隔障害							
肺塞栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肺線維症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気道うっ血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (0.4)	2 (0.1)
低音性連続性ラ音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
副鼻腔うっ血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
睡眠時無呼吸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
くしゃみ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
いびき	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
咽喉絞扼感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
上気道咳症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
皮膚および皮下組織障害							
ざ瘡	0 (0.0)	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	8 (0.6)	3 (0.2)
日光性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	5 (0.3)	4 (0.3)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンドロゲン性脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
皮膚囊腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
皮膚および皮下組織障害							
皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
アレルギー性皮膚炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
皮膚症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	39 (2.7)	2 (0.1)
斑状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	2 (0.1)
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	1 (0.1)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
過剰皮膚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
内出血発生の増加傾向	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
嵌入爪	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機械性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
爪破損	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
皮膚疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
皮膚および皮下組織障害							
光線過敏性反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
柑糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色柑糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)	0 (0.0)	20 (1.4)	2 (0.1)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	15 (1.0)	9 (0.7)
紅斑性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
そう痒性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
酒さ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脂腺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
皮膚色素脱失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
皮膚病変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
皮膚潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
うつ滞性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
蕁麻疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	4 (0.3)	4 (0.3)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
尋常性白斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
社会環境							
閉経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427) n (%)	(N=424) n (%)	(N=419) n (%)	(N=417) n (%)	(N=483) n (%)	(N=1444) n (%)	(N=1351) n (%)
外科および内科処置							
収れん薬療法	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ジフテリア免疫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管拡張および子宮内搔爬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン補給	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ほてり	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
高血圧	4 (0.9)	9 (2.1)	7 (1.7)	9 (2.2)	3 (0.6)	137 (9.5)	50 (3.7)
高血圧クリーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	21 (1.5)	6 (0.4)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
微小血管症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.3)	1 (0.1)
末梢冷感	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	5 (0.3)	0 (0.0)
静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レイノー現象	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表在性血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血栓性静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=427)	(N=424)	(N=419)	(N=417)	(N=483)	(N=1444)	(N=1351)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血管障害							
静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
静脈不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
TOTAL	1 (0.2)	6 (1.4)	2 (0.5)	2 (0.5)	3 (0.6)	1223 (84.7)	63 (4.7)

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表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
血液およびリンパ系障害							
貧血	5 (0.4)	3 (0.2)	3 (0.2)	7 (0.6)	5 (0.4)	3 (0.2)	0 (0.0)
凝血異常	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
低色素性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
鉄欠乏性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)
白血球増加症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
白血球減少症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球増加症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
正色素性正球性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
赤血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
急性心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
狭心症	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)
心房細動	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
第一度房室ブロック	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.2)	3 (0.2)	1 (0.1)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
心臓弁膜疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
心拡大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝導障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
心臓障害							
チアノーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
左室機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
僧帽弁疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
僧帽弁逸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	6 (0.5)	0 (0.0)	3 (0.2)	4 (0.3)	0 (0.0)	3 (0.2)	1 (0.1)
心嚢液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
洞不全症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
上室性頻脈	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
頻脈	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)
三尖弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	1 (0.1)	1 (0.1)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害							
心房中隔欠損症	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第Ⅴ因子ライデン変異	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発性内分泌腺腫症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多嚢胞性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脊椎奇形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺舌管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
耳および迷路障害							
耳垢栓塞	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
難聴	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.3)
耳不快感	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
耳管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
聴覚障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内耳障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
乗物酔い	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
耳鳴	0 (0.0)	1 (0.1)	1 (0.1)	3 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)
回転性めまい	4 (0.3)	2 (0.2)	3 (0.2)	2 (0.2)	4 (0.3)	2 (0.2)	3 (0.3)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
内分泌障害							
アンドロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
バセドウ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
甲状腺腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	2 (0.2)
エストロゲン欠乏症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
眼障害							
調節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
眼障害							
結膜出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
結膜充血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)	4 (0.3)	2 (0.2)	2 (0.2)
アレルギー性結膜炎	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
角膜障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の隈	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)
外眼筋不全麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)
眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
遠視	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
虹彩炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涙増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
光視症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
老視	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
翼状片	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
暗点	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
眼障害							
霧視	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
視力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体変性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体剥離	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
硝子体浮遊物	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害							
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	3 (0.2)	5 (0.4)	6 (0.5)	4 (0.3)	2 (0.2)	1 (0.1)	3 (0.3)
腹部膨満	2 (0.2)	2 (0.2)	2 (0.2)	9 (0.7)	3 (0.2)	4 (0.3)	1 (0.1)
腹部ヘルニア	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.2)	4 (0.3)
閉塞を伴う腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腹痛	4 (0.3)	9 (0.7)	5 (0.4)	6 (0.5)	11 (0.9)	1 (0.1)	6 (0.5)
下腹部痛	2 (0.2)	2 (0.2)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
上腹部痛	5 (0.4)	7 (0.5)	7 (0.6)	7 (0.6)	9 (0.7)	7 (0.6)	4 (0.3)
腹部硬直	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腹部圧痛	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
裂肛	2 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
痔瘻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
便通不規則	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	6 (0.5)	7 (0.5)	3 (0.2)	3 (0.2)	4 (0.3)	1 (0.1)	2 (0.2)
クローン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
齲歯	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	3 (0.2)	1 (0.1)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
胃腸障害							
歯不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)
下痢	14 (1.1)	8 (0.6)	15 (1.2)	12 (1.0)	14 (1.1)	8 (0.7)	10 (0.8)
憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腸憩室	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
口内乾燥	4 (0.3)	2 (0.2)	1 (0.1)	0 (0.0)	4 (0.3)	1 (0.1)	1 (0.1)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
消化不良	5 (0.4)	2 (0.2)	8 (0.6)	1 (0.1)	1 (0.1)	5 (0.4)	6 (0.5)
嚥下障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
小腸炎	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)
腸炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
びらん性十二指腸炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腿ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
食中毒	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
機能性胃腸障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	3 (0.2)	0 (0.0)	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)	3 (0.3)
びらん性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
消化管運動過剰	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸の炎症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	6 (0.5)	2 (0.2)	7 (0.6)	5 (0.4)	1 (0.1)	4 (0.3)	5 (0.4)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
胃腸障害							
歯肉退縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
歯肉炎	3 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
舌痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	4 (0.3)	0 (0.0)	5 (0.4)	1 (0.1)	3 (0.2)	1 (0.1)	1 (0.1)
裂孔ヘルニア	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)
胃酸過多	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単径ヘルニア	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)
内ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇腫脹	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吸収不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
メレナ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	12 (0.9)	8 (0.6)	10 (0.8)	10 (0.8)	7 (0.6)	2 (0.2)	6 (0.5)
嚥下痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道炎	2 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
口腔障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
胃腸障害							
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門周囲痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吐き戻し	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
S状結腸炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
舌苔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌粘膜剥脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
歯痛	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.2)	2 (0.2)	1 (0.1)	1 (0.1)
膺ヘルニア	2 (0.2)	3 (0.2)	3 (0.2)	2 (0.2)	3 (0.2)	3 (0.2)	1 (0.1)
閉塞性膺ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	11 (0.8)	10 (0.8)	8 (0.6)	13 (1.0)	5 (0.4)	4 (0.3)	6 (0.5)
一般・全身障害および投与部位の状態							
無力症	10 (0.8)	2 (0.2)	5 (0.4)	3 (0.2)	2 (0.2)	4 (0.3)	3 (0.3)
腋窩痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)
胸痛	4 (0.3)	1 (0.1)	5 (0.4)	3 (0.2)	3 (0.2)	2 (0.2)	2 (0.2)
悪寒	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
嚢胞	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
一般・全身障害および投与部位の状態							
医療機器位置異常	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脂肪組織増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	20 (1.5)	6 (0.5)	7 (0.6)	8 (0.6)	12 (1.0)	7 (0.6)	3 (0.3)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
びくびく感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
治癒不良	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	1 (0.1)	3 (0.2)	2 (0.2)	0 (0.0)	3 (0.2)	0 (0.0)	1 (0.1)
易刺激性	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
倦怠感	1 (0.1)	3 (0.2)	2 (0.2)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)
粘膜乾燥	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小結節	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
浮腫	4 (0.3)	3 (0.2)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性浮腫	11 (0.8)	7 (0.5)	6 (0.5)	12 (1.0)	8 (0.7)	3 (0.2)	8 (0.7)
疼痛	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.2)	0 (0.0)	1 (0.1)	3 (0.3)
発熱	7 (0.5)	7 (0.5)	7 (0.6)	6 (0.5)	10 (0.8)	6 (0.5)	7 (0.6)
不活発	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨上痛	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	8 (0.6)	1 (0.1)	4 (0.3)	2 (0.2)	3 (0.2)	0 (0.0)	3 (0.3)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
一般・全身障害および投与部位の状態							
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害							
胆道ジスキネジー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
肝嚢胞	4 (0.3)	4 (0.3)	0 (0.0)	3 (0.2)	1 (0.1)	3 (0.2)	3 (0.3)
肝嚢胞破裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
肝臓痛	4 (0.3)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
脂肪肝	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
肝炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	3 (0.2)	0 (0.0)
高ビリルビン血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝圧痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害							
アレルギー性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシーショック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
造影剤アレルギー	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
食物アレルギー	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	2 (0.2)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
免疫系障害							
複合アレルギー	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	5 (0.4)	1 (0.1)	2 (0.2)	2 (0.2)	2 (0.2)	2 (0.2)	3 (0.3)
感染症および寄生虫症							
膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
四肢膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
細菌性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌尿	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	6 (0.5)	11 (0.9)	5 (0.4)	6 (0.5)	1 (0.1)	7 (0.6)	6 (0.5)
ウイルス性気管支炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
カンジダ症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
蜂巣炎	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
眼窩蜂巣炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
クロストリジウム性大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
角膜感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	4 (0.3)	2 (0.2)	1 (0.1)	3 (0.2)	0 (0.0)	1 (0.1)	2 (0.2)
サイトメガロウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
憩室炎	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
感染症および寄生虫症							
耳感染	2 (0.2)	0 (0.0)	4 (0.3)	2 (0.2)	4 (0.3)	3 (0.2)	4 (0.3)
耳垂感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
伝染性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
遊走性紅斑	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼瞼感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱性感染症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)
皮膚真菌感染	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	5 (0.4)	2 (0.2)	7 (0.6)	4 (0.3)	5 (0.4)	6 (0.5)	4 (0.3)
ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	3 (0.2)	2 (0.2)	1 (0.1)	6 (0.5)	2 (0.2)	1 (0.1)	1 (0.1)
細菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性消化管感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
ウイルス性消化管感染	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
陰部ヘルペス	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
泌尿生殖器感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジアルジア症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H 1 N 1 インフルエンザ	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター感染	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
B型肝炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
C型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
単純ヘルペス	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
感染症および寄生虫症							
帯状疱疹	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.2)
麦粒腫	0 (0.0)	4 (0.3)	4 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
感染性嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
伝染性単核症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
インフルエンザ	6 (0.5)	15 (1.2)	9 (0.7)	11 (0.9)	9 (0.7)	3 (0.2)	7 (0.6)
腎感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
迷路炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
喉頭炎	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
肝膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
下気道感染	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
ライム病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
リンパ節感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ管炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マラリア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マイコプラズマ感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
爪感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	40 (3.1)	29 (2.3)	17 (1.3)	19 (1.5)	17 (1.4)	20 (1.7)	19 (1.6)
線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.2)	0 (0.0)
口腔カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
口腔真菌感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	3 (0.2)	1 (0.1)	1 (0.1)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
精巣炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
急性中耳炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
感染症および寄生虫症							
乳頭腫ウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪囲炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
百日咳	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
咽頭炎	3 (0.2)	1 (0.1)	2 (0.2)	3 (0.2)	3 (0.2)	1 (0.1)	0 (0.0)
レンサ球菌性咽頭炎	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
肺炎	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.2)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎盂腎炎	2 (0.2)	2 (0.2)	0 (0.0)	1 (0.1)	2 (0.2)	3 (0.2)	0 (0.0)
腎嚢胞感染	1 (0.1)	2 (0.2)	3 (0.2)	3 (0.2)	0 (0.0)	4 (0.3)	1 (0.1)
気道感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性気道感染	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
鼻炎	3 (0.2)	1 (0.1)	2 (0.2)	3 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)
卵管卵巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
敗血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
副鼻腔炎	5 (0.4)	9 (0.7)	7 (0.6)	2 (0.2)	5 (0.4)	5 (0.4)	3 (0.3)
皮膚感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ブドウ球菌性咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ブドウ球菌皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
糞線虫症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癬風	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（全体）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
感染症および寄生虫症							
扁桃炎	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	3 (0.2)	5 (0.4)
歯膿瘍	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)
歯感染	1 (0.1)	4 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	4 (0.3)	0 (0.0)
気管炎	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
気管気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
トリコモナス症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	18 (1.4)	5 (0.4)	7 (0.6)	3 (0.2)	11 (0.9)	12 (1.0)	6 (0.5)
尿路感染	13 (1.0)	10 (0.8)	7 (0.6)	8 (0.6)	12 (1.0)	11 (0.9)	5 (0.4)
泌尿生殖器細菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	5 (0.4)	4 (0.3)	0 (0.0)	1 (0.1)	2 (0.2)	6 (0.5)	3 (0.3)
ウイルス性鼻炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
外陰部腔カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
外陰腔真菌感染	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
創傷感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膿創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
傷害、中毒および処置合併症							
腹部損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
足関節部骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
節足動物咬傷	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	3 (0.2)	1 (0.1)	1 (0.1)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咬刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
軟骨損傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
傷害、中毒および処置合併症							
挫傷	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	5 (0.4)	5 (0.4)	2 (0.2)
角膜擦過傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
擦過傷	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼の貫通性外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
転倒	2 (0.2)	2 (0.2)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)
足骨折	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.3)
眼内異物	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
熱疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腕骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸脛靱帯症候群	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切開部位痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
企図的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
関節脱臼	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
関節損傷	1 (0.1)	3 (0.2)	1 (0.1)	3 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
裂傷	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.3)
靱帯損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯断裂	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
靱帯捻挫	2 (0.2)	0 (0.0)	0 (0.0)	5 (0.4)	4 (0.3)	1 (0.1)	0 (0.0)
四肢損傷	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口唇損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腰椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
傷害、中毒および処置合併症							
半月板障害	1 (0.1)	0 (0.0)	0 (0.0)	3 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)
多発骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
筋断裂	0 (0.0)	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.2)
頸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
処置後合併症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	2 (0.2)	3 (0.2)	1 (0.1)	3 (0.2)	1 (0.1)	2 (0.2)	2 (0.2)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
恥骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
橈骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肋骨骨折	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)
骨格損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
軟部組織損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脊椎骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
サンバーン	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腱損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手首関節骨折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	10 (0.8)	8 (0.6)	2 (0.2)	8 (0.6)	1 (0.1)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	7 (0.5)	7 (0.5)	2 (0.2)	4 (0.3)	4 (0.3)	1 (0.1)	2 (0.2)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルブミン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カルシウム増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
血中コレステロール増加	2 (0.2)	1 (0.1)	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)	1 (0.1)
血中クレアチンホスホキナーゼ増加	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
血中クレアチニン増加	25 (1.9)	16 (1.2)	17 (1.3)	29 (2.3)	27 (2.2)	14 (1.2)	6 (0.5)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ブドウ糖増加	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中副甲状腺ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
血圧低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
拡張期血圧上昇	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	0 (0.0)	1 (0.1)	1 (0.1)	3 (0.2)	0 (0.0)	3 (0.2)	1 (0.1)
血中ナトリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム増加	3 (0.2)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
血中テストステロン減少	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
血中尿素増加	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	3 (0.2)	1 (0.1)	0 (0.0)
血中尿酸増加	0 (0.0)	6 (0.5)	3 (0.2)	0 (0.0)	0 (0.0)	7 (0.6)	1 (0.1)
尿中血陽性	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
臨床検査							
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心雑音	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
腎クレアチニン・クリアランス増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
シスタチンC増加	0 (0.0)	4 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	4 (0.3)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図再分極異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図異常T波	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
大腸菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	1 (0.1)	5 (0.4)	2 (0.2)	5 (0.4)	3 (0.2)	3 (0.2)	0 (0.0)
胃内pH低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット減少	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ヘマトクリット増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数不整	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	3 (0.2)	3 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
A型肝炎ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヒト乳頭腫ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
I N R増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腎触知	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
リバーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査異常	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
季肋下肝触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低比重リポ蛋白減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
臨床検査							
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球形態異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
平均赤血球容積増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)
好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
好中球数増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数減少	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
プロトロンビン時間異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
QOL低下	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	3 (0.2)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
卵巣超音波検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尿浸透圧低下	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
尿浸透圧上昇	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ビタミンD減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
ウエスト周囲径増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	7 (0.5)	1 (0.1)	1 (0.1)	4 (0.3)	6 (0.5)	3 (0.2)	2 (0.2)
体重増加	9 (0.7)	2 (0.2)	4 (0.3)	7 (0.6)	2 (0.2)	2 (0.2)	5 (0.4)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
代謝および栄養障害							
アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
食欲減退	3 (0.2)	2 (0.2)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)
脱水	4 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	4 (0.3)	3 (0.2)	1 (0.1)
糖尿病	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)
体液貯留	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物渴望	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	4 (0.3)	2 (0.2)	0 (0.0)	3 (0.2)	3 (0.2)	0 (0.0)	1 (0.1)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
高コレステロール血症	4 (0.3)	4 (0.3)	3 (0.2)	4 (0.3)	1 (0.1)	4 (0.3)	2 (0.2)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
高脂血症	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
高ナトリウム血症	2 (0.2)	2 (0.2)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
高リン酸塩血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	0 (0.0)	8 (0.6)	6 (0.5)	2 (0.2)	5 (0.4)	3 (0.2)	1 (0.1)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
低血糖症	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
低マグネシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低リン酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ラクトース不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
代謝および栄養障害							
代謝性アシドーシス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過体重	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
多飲症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
2型糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ビタミンB 1 2 欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ビタミンD 欠乏	3 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
体重変動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	9 (0.7)	12 (0.9)	3 (0.2)	10 (0.8)	3 (0.2)	7 (0.6)	4 (0.3)
関節炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
反応性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
関節障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	24 (1.8)	25 (1.9)	9 (0.7)	16 (1.3)	13 (1.1)	25 (2.1)	11 (0.9)
骨痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	3 (0.3)
滑液包石灰化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
滑液包炎	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
軟骨肥厚	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部脊柱管狭窄症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
尾骨痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋軟骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外骨腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)
瘻孔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	3 (0.2)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
痛風性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腓脛部痛	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
筋骨格系および結合組織障害							
椎間板変性症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
椎間板障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	2 (0.2)	0 (0.0)	4 (0.3)	0 (0.0)	2 (0.2)	2 (0.2)	1 (0.1)
関節滲出液	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
関節可動域低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	1 (0.1)	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)
靱帯障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
靱帯痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢非対称	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	6 (0.5)	7 (0.5)	2 (0.2)	1 (0.1)	3 (0.2)	2 (0.2)	0 (0.0)
筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
筋力低下	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
筋骨格系胸痛	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	3 (0.2)	1 (0.1)
筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)
筋骨格痛	3 (0.2)	3 (0.2)	3 (0.2)	5 (0.4)	2 (0.2)	5 (0.4)	5 (0.4)
筋骨格硬直	4 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
筋肉痛	5 (0.4)	5 (0.4)	4 (0.3)	5 (0.4)	3 (0.2)	3 (0.2)	4 (0.3)
筋炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部痛	5 (0.4)	0 (0.0)	3 (0.2)	2 (0.2)	1 (0.1)	2 (0.2)	4 (0.3)
変形性関節症	0 (0.0)	2 (0.2)	3 (0.2)	1 (0.1)	0 (0.0)	3 (0.2)	0 (0.0)
骨関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
骨粗鬆症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	6 (0.5)	8 (0.6)	4 (0.3)	7 (0.6)	7 (0.6)	5 (0.4)	6 (0.5)
顎痛	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
筋骨格系および結合組織障害							
関節周囲炎	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.3)
足底筋膜炎	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)
恥骨痛	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
関節リウマチ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
仙腸骨炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
側弯症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
重感	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
脊椎炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腱障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
腱炎	0 (0.0)	1 (0.1)	4 (0.3)	1 (0.1)	3 (0.2)	2 (0.2)	1 (0.1)
腱鞘炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
斜頸	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
アクロコルドン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
基底細胞癌	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
乳房の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)
甲状腺の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
乳癌	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
子宮頸部癌第0期	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真珠腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性骨髄性白血病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成母斑	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
肝臓血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カボジ肉腫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
悪性黒色腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
表皮内悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
メラノサイト性母斑	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
下垂体の良性腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
皮膚乳頭腫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)
扁平上皮癌	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺新生物	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	1 (0.1)	0 (0.0)	5 (0.4)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
健忘	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
平衡障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
頸動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手根管症候群	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脳神経障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識レベルの低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
浮動性めまい	14 (1.1)	6 (0.5)	3 (0.2)	6 (0.5)	5 (0.4)	10 (0.8)	6 (0.5)
労作性めまい	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
神経系障害							
脳症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	31 (2.4)	17 (1.3)	12 (0.9)	14 (1.1)	13 (1.1)	11 (0.9)	6 (0.5)
味覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	0 (0.0)	1 (0.1)	1 (0.1)	4 (0.3)	2 (0.2)	1 (0.1)	2 (0.2)
反射減弱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張低下	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
虚血性脳卒中	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗜眠	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
意識消失	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
記憶障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	2 (0.2)	4 (0.3)	0 (0.0)	2 (0.2)	3 (0.2)	2 (0.2)	4 (0.3)
前兆を伴う片頭痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
神経痛	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
末梢性ニューロパチー	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
起立不耐性	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	2 (0.2)	2 (0.2)	0 (0.0)	5 (0.4)	0 (0.0)	2 (0.2)	2 (0.2)
パーキンソン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
パーキンソニズム	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
失神寸前の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
根症候群	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)	0 (0.0)
坐骨神経痛	2 (0.2)	2 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)	3 (0.2)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
神経系障害							
感覚障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
くも膜下出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
失神	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)	3 (0.2)	4 (0.3)
緊張性頭痛	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
一過性脳虚血発作	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トンネル状視野	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎骨動脈解離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
第7 脳神経麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
妊娠、産褥および周産期の状態							
自然流産	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	2 (0.2)	4 (0.3)	2 (0.2)	2 (0.2)	1 (0.1)	3 (0.2)	2 (0.2)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自閉症スペクトラム障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神緩慢	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
燃え尽き症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
うつ病	7 (0.5)	6 (0.5)	4 (0.3)	5 (0.4)	4 (0.3)	7 (0.6)	4 (0.3)
睡眠異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	6 (0.5)	3 (0.2)	3 (0.2)	5 (0.4)	2 (0.2)	2 (0.2)	3 (0.3)
リビドー減退	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性欲障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リビド消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
精神障害							
大うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分変化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分動揺	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経過敏	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ニコチン依存	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
パニック反応	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心身症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
統合失調症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)
夢遊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス	3 (0.2)	4 (0.3)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
自殺企図	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
アルブミン尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱刺激症状	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
膀胱痙攣	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非感染性膀胱炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	5 (0.4)	3 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
遺尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
腎および尿路障害							
血尿	18 (1.4)	14 (1.1)	11 (0.9)	9 (0.7)	10 (0.8)	6 (0.5)	11 (0.9)
水腎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎腫大	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
白血球尿	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿意切迫	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎結石症	2 (0.2)	4 (0.3)	1 (0.1)	4 (0.3)	1 (0.1)	0 (0.0)	1 (0.1)
夜間頻尿	7 (0.5)	8 (0.6)	2 (0.2)	6 (0.5)	1 (0.1)	0 (0.0)	1 (0.1)
閉塞性尿路疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
多尿	10 (0.8)	7 (0.5)	4 (0.3)	2 (0.2)	4 (0.3)	0 (0.0)	2 (0.2)
蛋白尿	1 (0.1)	2 (0.2)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	1 (0.1)
腎仙痛	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎嚢胞	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
腎嚢胞破裂	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
慢性腎不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	2 (0.2)	0 (0.0)	1 (0.1)	5 (0.4)	2 (0.2)	2 (0.2)	0 (0.0)
腎臓痛	51 (3.9)	34 (2.6)	26 (2.1)	28 (2.3)	28 (2.3)	26 (2.2)	26 (2.2)
有痛性排尿困難	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿道狭窄	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿躊躇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
腎および尿路障害							
尿路障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿流量減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害							
子宮付属器痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
精子無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
萎縮性外陰腔炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
乳房不快感	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
子宮頸部上皮異形成	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管ポリープ	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性交出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
性交困難	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
勃起不全	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳汁漏出症	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
血精液症	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過少月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
生殖系および乳房障害							
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
機能性子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多	1 (0.1)	5 (0.4)	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
不正子宮出血	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
卵巣嚢胞	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	3 (0.2)	1 (0.1)	1 (0.1)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
卵巣捻転	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ペイロニー病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
閉経後出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺腫大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
精嚢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
子宮ポリープ	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
子宮脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腔分泌物	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
生殖系および乳房障害							
精索静脈瘤	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
外陰腔乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
呼吸器、胸郭および縦隔障害							
喘息	1 (0.1)	1 (0.1)	0 (0.0)	4 (0.3)	0 (0.0)	0 (0.0)	2 (0.2)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
咳嗽	8 (0.6)	9 (0.7)	12 (0.9)	6 (0.5)	3 (0.2)	8 (0.7)	2 (0.2)
咽喉乾燥	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
発声障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
呼吸困難	3 (0.2)	2 (0.2)	3 (0.2)	5 (0.4)	0 (0.0)	0 (0.0)	2 (0.2)
安静時呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	2 (0.2)	3 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)
過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肺障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
鼻閉	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
鼻中隔彎曲	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
夜間呼吸困難	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	9 (0.7)	7 (0.5)	3 (0.2)	6 (0.5)	4 (0.3)	2 (0.2)	2 (0.2)
咽頭紅斑	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸水	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
肺臓炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
呼吸器、胸郭および縦隔障害							
肺塞栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
肺線維症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気道うっ血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	2 (0.2)	1 (0.1)	2 (0.2)	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)
鼻漏	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
低音性連続性ラ音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔うっ血	0 (0.0)	5 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠時無呼吸症候群	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
いびき	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
咽喉絞扼感	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃肥大	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
扁桃結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
上気道咳症候群	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害							
ざ瘡	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)	0 (0.0)	3 (0.2)	1 (0.1)
日光性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	3 (0.2)	0 (0.0)	3 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)
円形脱毛症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンドロゲン性脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
皮膚および皮下組織障害							
皮膚炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
アトピー性皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
接触性皮膚炎	3 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	2 (0.2)
皮膚症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	4 (0.3)	0 (0.0)	3 (0.2)	2 (0.2)	2 (0.2)	1 (0.1)	0 (0.0)
斑状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
湿疹	2 (0.2)	2 (0.2)	1 (0.1)	2 (0.2)	1 (0.1)	4 (0.3)	2 (0.2)
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
紅斑	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過剰皮膚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
汗腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
多汗症	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
過角化	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内出血発生の増加傾向	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嵌入爪	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
機械性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
神経皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
爪破損	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
丘疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309) n (%)	(N=1285) n (%)	(N=1264) n (%)	(N=1244) n (%)	(N=1222) n (%)	(N=1204) n (%)	(N=1189) n (%)
皮膚および皮下組織障害							
光線過敏性反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
色素沈着障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
柑糠疹	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色柑糠疹	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	2 (0.2)	2 (0.2)	1 (0.1)	2 (0.2)	5 (0.4)	4 (0.3)	3 (0.3)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
発疹	6 (0.5)	3 (0.2)	3 (0.2)	2 (0.2)	2 (0.2)	1 (0.1)	2 (0.2)
紅斑性皮疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒性皮疹	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
脂腺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素過剰	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
皮膚病変	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚潰瘍	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ滞性皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尋常性白斑	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
社会環境							
閉経	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309)	(N=1285)	(N=1264)	(N=1244)	(N=1222)	(N=1204)	(N=1189)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
外科および内科処置							
収れん薬療法	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジフテリア免疫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管拡張および子宮内搔爬	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン補給	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
大動脈拡張	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の血圧	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
深部静脈血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)
出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
高血圧	45 (3.4)	41 (3.2)	21 (1.7)	40 (3.2)	33 (2.7)	30 (2.5)	14 (1.2)
高血圧クリーゼ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
低血圧	3 (0.2)	1 (0.1)	3 (0.2)	3 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
不安定血圧	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
微小血管症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢冷感	1 (0.1)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レイノー現象	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
血栓性静脈炎	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表在性血栓性静脈炎	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1309)	(N=1285)	(N=1264)	(N=1244)	(N=1222)	(N=1204)	(N=1189)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血管障害							
静脈瘤	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)	1 (0.1)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血管閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
静脈不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	38 (2.9)	24 (1.9)	10 (0.8)	13 (1.0)	12 (1.0)	9 (0.7)	2 (0.2)

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表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
血液およびリンパ系障害				
貧血	6 (0.5)	2 (0.2)	5 (0.4)	5 (0.3)
凝血異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低色素性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
白血球増加症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
腎性貧血	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
好中球増加症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
正色素性正球形貧血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
汎血球減少症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
赤血球増加症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板減少症	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
血小板増加症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心臓障害				
急性心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
狭心症	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
大動脈弁閉鎖不全症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
不整脈	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
心房細動	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓弁膜疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拡大	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心筋症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝導障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
心臓障害				
チアノーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左房肥大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室機能不全	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
左室肥大	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
僧帽弁疾患	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
僧帽弁逸脱	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
心筋梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
心嚢液貯留	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心膜炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
洞不全症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
三尖弁閉鎖不全症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
ウォルフ・パーキンソン・ホワイト症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害				
心房中隔欠損症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第Ⅴ因子ライデン変異	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多嚢胞性肝疾患	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
脊椎奇形	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
甲状腺管嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
耳および迷路障害				
耳垢栓塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内耳障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メニエール病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳滲出液	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乗物酔い	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
耳鳴	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
回転性めまい	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
頭位性回転性めまい	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害				
アンドロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バセドウ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
続発性副甲状腺機能低下症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
エストロゲン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害				
調節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)
白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179)	(N=1168)	(N=1156)	(N=1444)
	n (%)	n (%)	n (%)	n (%)
眼障害				
結膜出血	1 (0.1)	1 (0.1)	4 (0.3)	1 (0.1)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.1)
アレルギー性結膜炎	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の隈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
外眼筋不全麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
眼出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼痛	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
眼部腫脹	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
眼瞼浮腫	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
眼瞼下垂	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
遠視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虹彩炎	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
流涙増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
開放隅角緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
光視症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
老視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
翼状片	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜剥離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
暗点	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
眼障害				
霧視	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
視力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体変性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
硝子体剥離	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼球乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害				
腹部癒着	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	1 (0.1)	5 (0.4)	7 (0.6)	4 (0.3)
腹部ヘルニア	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.1)
閉塞を伴う腹部ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	2 (0.2)	6 (0.5)	3 (0.3)	2 (0.1)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	4 (0.3)	4 (0.3)	2 (0.2)	3 (0.2)
腹部硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部圧痛	3 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)
裂肛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔瘻	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
便通不規則	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼気臭	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	2 (0.2)	3 (0.3)	3 (0.3)	0 (0.0)
クローン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
胃腸障害				
歯不快感	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
下痢	8 (0.7)	7 (0.6)	8 (0.7)	6 (0.4)
憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸憩室	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)
口内乾燥	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	4 (0.3)	2 (0.2)	3 (0.3)	2 (0.1)
嚥下障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びらん性十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腿ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
食中毒	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
機能性胃腸障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
びらん性胃炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
胃腸障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	5 (0.4)	5 (0.4)	2 (0.2)	0 (0.0)
歯肉障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
胃腸障害				
歯肉退縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	2 (0.2)	1 (0.1)	0 (0.0)	3 (0.2)
裂孔ヘルニア	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)
胃酸過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単径ヘルニア	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)
内ヘルニア	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腸出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吸収不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メレナ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内潰瘍形成	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
悪心	4 (0.3)	3 (0.3)	7 (0.6)	6 (0.4)
嚥下痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
口腔障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
口腔扁平苔癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腭嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性腭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
胃腸障害				
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門周囲痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
吐き戻し	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
S状結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
舌苔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌粘膜剥脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯の障害	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
歯痛	1 (0.1)	3 (0.3)	2 (0.2)	0 (0.0)
臍ヘルニア	1 (0.1)	5 (0.4)	3 (0.3)	0 (0.0)
閉塞性臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	5 (0.4)	5 (0.4)	8 (0.7)	3 (0.2)
一般・全身障害および投与部位の状態				
無力症	1 (0.1)	2 (0.2)	4 (0.3)	1 (0.1)
腋窩痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
胸痛	3 (0.3)	0 (0.0)	5 (0.4)	1 (0.1)
悪寒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚢胞	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179)	(N=1168)	(N=1156)	(N=1444)
	n (%)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態				
医療機器位置異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
運動耐性低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪組織増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	1 (0.1)	3 (0.3)	10 (0.9)	1 (0.1)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びくびく感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ヘルニア	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
治癒不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
易刺激性	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
粘膜乾燥	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
小結節	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	1 (0.1)	1 (0.1)	4 (0.3)	4 (0.3)
末梢性浮腫	9 (0.8)	5 (0.4)	17 (1.5)	7 (0.5)
疼痛	2 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)
発熱	6 (0.5)	4 (0.3)	4 (0.3)	1 (0.1)
不活発	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨上痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
温度変化不耐症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
一般・全身障害および投与部位の状態				
ワクチン接種部位反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害				
胆道ジスキネジー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
胆嚢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肝嚢胞	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
肝嚢胞破裂	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腫大	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)
高ビリルビン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肝圧痛	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害				
アレルギー性浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
アナフィラキシーショック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
造影剤アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
食物アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179)	(N=1168)	(N=1156)	(N=1444)
	n (%)	n (%)	n (%)	n (%)
免疫系障害				
複合アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	3 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)
感染症および寄生虫症				
膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
急性扁桃炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
真菌性肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
細菌性関節炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
感染性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺膿瘍	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	8 (0.7)	7 (0.6)	7 (0.6)	4 (0.3)
ウイルス性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
蜂巣炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
眼窩蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
慢性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
クロストリジウム性大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
膀胱炎	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)
サイトメガロウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)

表2.7.4.7-38

156-251

CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months (N=1179)	30-33 Months (N=1168)	33-36 Months (N=1156)	Post withdraw (N=1444)
	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症				
耳感染	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
耳垂感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
伝染性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
遊走性紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱性感染症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚真菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	7 (0.6)	5 (0.4)	9 (0.8)	2 (0.1)
ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)
細菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌性消化管感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化管感染	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
ウイルス性消化管感染	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
陰部ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
泌尿生殖器感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジアルジア症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H 1 N 1 インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
感染症および寄生虫症				
帯状疱疹	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
麦粒腫	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
切開部位膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
伝染性単核症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	7 (0.6)	6 (0.5)	8 (0.7)	3 (0.2)
腎感染	1 (0.1)	0 (0.0)	2 (0.2)	2 (0.1)
迷路炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭炎	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
肝膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下気道感染	3 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)
ライム病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マラリア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性髄膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
マイコプラズマ感染	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪感染	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	12 (1.0)	10 (0.9)	20 (1.7)	10 (0.7)
線虫症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
オンコセルカ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
口腔カンジダ症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
口腔真菌感染	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
急性中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
感染症および寄生虫症				
乳頭腫ウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤内感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
百日咳	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	5 (0.4)	1 (0.1)	1 (0.1)	4 (0.3)
レンサ球菌性咽頭炎	1 (0.1)	3 (0.3)	1 (0.1)	1 (0.1)
肺炎	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ウイルス性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
前立腺感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎盂腎炎	0 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)
腎嚢胞感染	1 (0.1)	3 (0.3)	1 (0.1)	1 (0.1)
気道感染	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	2 (0.2)	2 (0.2)	3 (0.3)	0 (0.0)
卵管卵巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	5 (0.4)	1 (0.1)	6 (0.5)	3 (0.2)
皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌性咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ブドウ球菌皮膚感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞線虫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
梅毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
癬風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
感染症および寄生虫症				
扁桃炎	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
歯膿瘍	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)
歯感染	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
気管炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
気管気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	10 (0.8)	7 (0.6)	12 (1.0)	5 (0.3)
尿路感染	10 (0.8)	9 (0.8)	9 (0.8)	11 (0.8)
泌尿生殖器細菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性腔炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	2 (0.2)	3 (0.3)	0 (0.0)	1 (0.1)
ウイルス性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部腔カンジダ症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
外陰腔真菌感染	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
創傷感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膿創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症				
腹部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足関節部骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷	1 (0.1)	1 (0.1)	2 (0.2)	0 (0.0)
節足動物刺傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
咬刺傷	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
滑液包損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨損傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
傷害、中毒および処置合併症				
挫傷	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
角膜擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
眼外傷	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
眼の貫通性外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)
足骨折	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
眼内異物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
手骨折	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱疲労	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
上腕骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
腸脛靱帯症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ステント内動脈再狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切開部位痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人工流産による出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
企図的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
顎の骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.2)
関節損傷	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
裂傷	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
靱帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	3 (0.3)	2 (0.2)	5 (0.4)	2 (0.1)
四肢損傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
口唇損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腰椎骨折	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
傷害、中毒および処置合併症				
半月板障害	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)
多発骨折	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
筋断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
頸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲血腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
処置後合併症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
処置後血尿	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
処置後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨骨折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
橈骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨格損傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎骨折	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱損傷	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脛骨骨折	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯牙破折	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尺骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上肢骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)
手首関節骨折	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
臨床検査				
活性化部分トロンボプラスチン時間延長	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
活性化部分トロンボプラスチン時間短縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	2 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)
アスパラギン酸アミノトランスフェラーゼ増加	4 (0.3)	2 (0.2)	2 (0.2)	1 (0.1)
細菌検査陽性	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血中アルブミン減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中カルシウム増加	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
血中コレステロール増加	3 (0.3)	0 (0.0)	2 (0.2)	0 (0.0)
血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血中クレアチニン増加	14 (1.2)	9 (0.8)	8 (0.7)	5 (0.3)
血中ブドウ糖減少	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
血中ブドウ糖増加	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)
血中エストロゲン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中副甲状腺ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血中カリウム増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血圧低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
拡張期血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	1 (0.1)	0 (0.0)	1 (0.1)	3 (0.2)
血中ナトリウム減少	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血中ナトリウム増加	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血中テストステロン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿素増加	8 (0.7)	3 (0.3)	1 (0.1)	2 (0.1)
血中尿酸増加	0 (0.0)	0 (0.0)	4 (0.3)	1 (0.1)
尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
C－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
臨床検査				
癌胎児性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心雑音	1 (0.1)	0 (0.0)	2 (0.2)	1 (0.1)
腎クレアチニン・クリアランス増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	3 (0.3)	1 (0.1)
心電図QT間隔	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
心電図再分極異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図異常T波	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
心電図T波逆転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好酸球数増加	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
大腸菌検査陽性	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	3 (0.3)	0 (0.0)	3 (0.3)	1 (0.1)
胃内pH低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ヘマトクリット減少	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.1)
ヘマトクリット増加	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.1)
心拍数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数不整	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	1 (0.1)	0 (0.0)	2 (0.2)	3 (0.2)
A型肝炎ウイルス検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
ヒト乳頭腫ウイルス検査陽性	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
I N R増加	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
眼圧上昇	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
リバーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査異常	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
季肋下肝触知	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
低比重リポ蛋白減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
臨床検査				
リンパ球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球形態異常	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
平均赤血球ヘモグロビン濃度減少	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
平均赤血球容積減少	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
平均赤血球容積増加	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
好中球数減少	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
好中球数増加	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数減少	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
QOL低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
尿中赤血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部スミア異常	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
トランスアミナーゼ上昇	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
卵巣超音波検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿浸透圧低下	0 (0.0)	0 (0.0)	1 (0.1)	3 (0.2)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウエスト周囲径増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	0 (0.0)	2 (0.2)	1 (0.1)	1 (0.1)
体重増加	4 (0.3)	2 (0.2)	8 (0.7)	0 (0.0)
白血球数減少	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
白血球数増加	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
尿中白血球	0 (0.0)	0 (0.0)	2 (0.2)	1 (0.1)
尿中白血球陽性	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38

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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
代謝および栄養障害				
アシドーシス	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
食欲減退	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脱水	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
糖尿病	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体液貯留	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
食物渴望	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食物不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	4 (0.3)	3 (0.3)	5 (0.4)	0 (0.0)
高アミラーゼ血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	1 (0.1)	3 (0.3)	3 (0.3)	2 (0.1)
高クレアチニン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	1 (0.1)	3 (0.3)	2 (0.2)	3 (0.2)
高カリウム血症	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)
高脂血症	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)
高ナトリウム血症	2 (0.2)	1 (0.1)	1 (0.1)	0 (0.0)
高リン酸塩血症	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
高トリグリセリド血症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	3 (0.3)	3 (0.3)	2 (0.2)	3 (0.2)
低アルブミン血症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
低血糖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
低マグネシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
低リン酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ラクトース不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
代謝および栄養障害				
代謝性アシドーシス	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肥満	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過体重	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
多飲症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
2 型糖尿病	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
ビタミンB 1 2 欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD 欠乏	2 (0.2)	3 (0.3)	1 (0.1)	0 (0.0)
体重変動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害				
関節痛	11 (0.9)	5 (0.4)	7 (0.6)	2 (0.1)
関節炎	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
反応性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	16 (1.4)	11 (0.9)	13 (1.1)	9 (0.6)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包石灰化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨肥厚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸部脊柱管狭窄症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ピロリン酸カルシウム結晶性軟骨石灰化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨軟化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟骨疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尾骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋軟骨炎	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
歯槽異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外骨腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
筋膜炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
線維筋痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
瘻孔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	1 (0.1)	2 (0.2)	2 (0.2)	3 (0.2)
足変形	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
痛風性関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腓径部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
筋骨格系および結合組織障害				
椎間板変性症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)
関節滲出液	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
関節可動域低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
靱帯障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯痛	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
四肢非対称	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	4 (0.3)	0 (0.0)	2 (0.2)	1 (0.1)
筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋力低下	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
筋骨格系胸痛	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
筋骨格不快感	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
筋骨格痛	2 (0.2)	6 (0.5)	9 (0.8)	0 (0.0)
筋骨格硬直	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	2 (0.2)	2 (0.2)	9 (0.8)	3 (0.2)
筋炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
頸部腫瘤	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
頸部痛	4 (0.3)	4 (0.3)	2 (0.2)	0 (0.0)
変形性関節症	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
骨関節障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
骨端症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨減少症	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)
骨粗鬆症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	5 (0.4)	4 (0.3)	1 (0.1)	0 (0.0)
顎痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
膝蓋大腿関節痛症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
筋骨格系および結合組織障害				
関節周囲炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
恥骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節リウマチ	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
仙腸骨炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側弯症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
重感	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脊椎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
脊椎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
滑膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱障害	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
腱痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
腱炎	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斜頸	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）				
アクロコルドン	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
基底細胞癌	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
乳房の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺の良性新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳癌	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
子宮頸部癌第0期	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真珠腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性骨髄性白血病	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓血管腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
カボジ肉腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）				
悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表皮内悪性黒色腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メラノサイト性母斑	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
下垂体の良性腫瘍	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脂漏性角化症	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
皮膚乳頭腫	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
扁平上皮癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺新生物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
神経系障害				
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
健忘	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
手根管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
協調運動異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳神経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識レベルの低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	2 (0.2)	5 (0.4)	5 (0.4)	0 (0.0)
労作性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
神経系障害				
脳症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	13 (1.1)	7 (0.6)	17 (1.5)	6 (0.4)
味覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	3 (0.3)	2 (0.2)	3 (0.3)	0 (0.0)
反射減弱	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
筋緊張低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
虚血性脳卒中	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
嗜眠	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
意識消失	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	2 (0.2)	1 (0.1)	2 (0.2)	2 (0.1)
前兆を伴う片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不随意性筋収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ナルコレプシー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経根圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
起立不耐性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	3 (0.3)	4 (0.3)	2 (0.2)	1 (0.1)
パーキンソン病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パーキンソニズム	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神寸前の状態	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
根症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
神経系障害				
感覚障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
緊張性頭痛	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
一過性脳虚血発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トンネル状視野	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎骨動脈解離	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第7 脳神経麻痺	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
妊娠、産褥および周産期の状態				
自然流産	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
精神障害				
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
激越	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
怒り	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	1 (0.1)	2 (0.2)	6 (0.5)	0 (0.0)
不安障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
自閉症スペクトラム障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
精神緩慢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
燃え尽き症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	3 (0.3)	4 (0.3)	6 (0.5)	0 (0.0)
睡眠異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	1 (0.1)	4 (0.3)	4 (0.3)	2 (0.1)
リビドー減退	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
性欲障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リビドー消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
精神障害				
大うつ病	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分変化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経過敏	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
ニコチン依存	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
パニック発作	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)
パニック反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後ストレス障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心身症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調感情障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
統合失調症	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
夢遊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストレス	2 (0.2)	1 (0.1)	0 (0.0)	1 (0.1)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害				
アルブミン尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高窒素血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱脱	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
膀胱痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
非感染性膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	1 (0.1)	3 (0.3)	2 (0.2)	1 (0.1)
遺尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
腎および尿路障害				
血尿	7 (0.6)	6 (0.5)	11 (1.0)	1 (0.1)
水腎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失禁	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
腎腫大	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
白血球尿	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
尿意切迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎結石症	2 (0.2)	2 (0.2)	1 (0.1)	3 (0.2)
夜間頻尿	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)
閉塞性尿路疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
乏尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	0 (0.0)	1 (0.1)	2 (0.2)	1 (0.1)
蛋白尿	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
腎仙痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	1 (0.1)	0 (0.0)	3 (0.3)	1 (0.1)
腎嚢胞破裂	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
腎障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性腎不全	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
慢性腎不全	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	1 (0.1)	2 (0.2)	2 (0.2)	0 (0.0)
腎臓痛	10 (0.8)	20 (1.7)	19 (1.6)	8 (0.6)
有痛性排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹圧性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿道狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
切迫性尿失禁	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿躊躇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
尿閉	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
腎および尿路障害				
尿路障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
尿流量減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿臭異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害				
子宮付属器痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精子無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
萎縮性外陰腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無精子症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
バルトリン腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性前立腺肥大症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
乳房不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
乳房痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸部上皮異形成	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
性交出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性交困難	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
精巣上体嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血精液症	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)
出血性卵巣嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
過少月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179)	(N=1168)	(N=1156)	(N=1444)
	n (%)	n (%)	n (%)	n (%)
生殖系および乳房障害				
不妊症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機能性子宮出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経遅延	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
不規則月経	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
不正子宮出血	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
卵巣嚢胞	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
卵巣障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
卵巣捻転	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排卵痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
骨盤脱	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
会陰痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ペイロニー病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経後出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
前立腺腫大	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢腫瘍	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
精嚢痛	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮脱	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔分泌物	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腔出血	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
生殖系および乳房障害				
精索静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰腔乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害				
喘息	0 (0.0)	1 (0.1)	3 (0.3)	0 (0.0)
運動誘発喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
気管支痙攣	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
咳嗽	5 (0.4)	8 (0.7)	9 (0.8)	1 (0.1)
咽喉乾燥	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
発声障害	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
呼吸困難	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)
安静時呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
過換気	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
喉頭嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
肺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉塞	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
鼻中隔彎曲	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	4 (0.3)	2 (0.2)	0 (0.0)	4 (0.3)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
呼吸器、胸郭および縦隔障害				
肺塞栓症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
肺線維症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
気道うっ血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)
鼻漏	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
低音性連続性ラ音	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔うっ血	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
睡眠時無呼吸症候群	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
くしゃみ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
いびき	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽喉絞扼感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃肥大	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
扁桃の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害				
ざ瘡	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)
日光性角化症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
脱毛症	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)
円形脱毛症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンドロゲン性脱毛症	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
皮膚および皮下組織障害				
皮膚炎	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
皮膚症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	1 (0.1)	1 (0.1)	3 (0.2)
斑状出血	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.1)
湿潤性湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過剰皮膚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛髪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	2 (0.2)	0 (0.0)	2 (0.2)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内出血発生の増加傾向	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嵌入爪	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
間擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
機械性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
爪成長異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経皮膚炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
寝汗	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
爪破損	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
皮膚および皮下組織障害				
光線過敏性反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
色素沈着障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
柑糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色柑糠疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	1 (0.1)	2 (0.2)	2 (0.2)	1 (0.1)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	2 (0.2)	3 (0.3)	1 (0.1)	1 (0.1)
紅斑性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
斑状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
斑状丘疹状皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
脂腺障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚色素脱失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
皮膚色素過剰	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚刺激	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚病変	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
皮膚反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ滞性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尋常性白斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
社会環境				
閉経	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-38
156-251
CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=1179) n (%)	(N=1168) n (%)	(N=1156) n (%)	(N=1444) n (%)
外科および内科処置				
収れん薬療法	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジフテリア免疫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頸管拡張および子宮内搔爬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミン補給	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害				
動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈拡張	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)
コントロール不良の血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血腫	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)
出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
高血圧	25 (2.1)	25 (2.1)	23 (2.0)	18 (1.2)
高血圧クリーゼ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血圧	4 (0.3)	0 (0.0)	2 (0.2)	0 (0.0)
腸骨動脈狭窄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
微小血管症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
末梢冷感	0 (0.0)	2 (0.2)	1 (0.1)	0 (0.0)
静脈炎	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
レイノー現象	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
表在性血栓性静脈炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓症	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)

表2.7.4.7-38
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CT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (全体)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months (N=1179)	30-33 Months (N=1168)	33-36 Months (N=1156)	Post withdraw (N=1444)
	n (%)	n (%)	n (%)	n (%)
血管障害				
静脈瘤	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
血管圧迫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管閉塞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
血管炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
静脈不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	9 (0.8)	3 (0.3)	4 (0.3)	4 (0.3)

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<資料番号5.3.5.1-01 : CT-8.7.2>

表2.7.4.7-39

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JT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (日本の被験者)

System organ class	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
血液およびリンパ系障害	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	1 (1.0)
心臓障害	10 (8.5)	1 (0.9)	5 (4.6)	0 (0.0)	3 (2.9)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	2 (1.7)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	1 (1.0)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	3 (2.5)	2 (1.8)	2 (1.9)	2 (1.9)	1 (1.0)	0 (0.0)	3 (3.1)
胃腸障害	41 (34.7)	20 (17.9)	9 (8.3)	9 (8.7)	9 (8.8)	14 (14.1)	9 (9.3)
一般・全身障害および投与部位の状態	108 (91.5)	8 (7.1)	4 (3.7)	4 (3.8)	4 (3.9)	4 (4.0)	4 (4.1)
肝胆道系障害	6 (5.1)	5 (4.5)	2 (1.9)	1 (1.0)	1 (1.0)	2 (2.0)	0 (0.0)
免疫系障害	2 (1.7)	2 (1.8)	3 (2.8)	1 (1.0)	0 (0.0)	1 (1.0)	1 (1.0)
感染症および寄生虫症	27 (22.9)	18 (16.1)	12 (11.1)	11 (10.6)	9 (8.8)	11 (11.1)	5 (5.2)
傷害、中毒および処置合併症	3 (2.5)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	3 (3.1)
臨床検査	13 (11.0)	3 (2.7)	2 (1.9)	2 (1.9)	3 (2.9)	4 (4.0)	2 (2.1)
代謝および栄養障害	12 (10.2)	4 (3.6)	4 (3.7)	3 (2.9)	2 (2.0)	2 (2.0)	3 (3.1)
筋骨格系および結合組織障害	12 (10.2)	10 (8.9)	8 (7.4)	4 (3.8)	3 (2.9)	5 (5.1)	3 (3.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.0)	0 (0.0)	0 (0.0)
神経系障害	37 (31.4)	4 (3.6)	5 (4.6)	4 (3.8)	2 (2.0)	4 (4.0)	2 (2.1)
精神障害	5 (4.2)	3 (2.7)	1 (0.9)	1 (1.0)	1 (1.0)	3 (3.0)	1 (1.0)
腎および尿路障害	92 (78.0)	4 (3.6)	3 (2.8)	2 (1.9)	1 (1.0)	2 (2.0)	1 (1.0)
生殖系および乳房障害	3 (2.5)	1 (0.9)	0 (0.0)	1 (1.0)	1 (1.0)	2 (2.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	6 (5.1)	4 (3.6)	6 (5.6)	6 (5.8)	2 (2.0)	1 (1.0)	1 (1.0)
皮膚および皮下組織障害	16 (13.6)	5 (4.5)	2 (1.9)	5 (4.8)	5 (4.9)	3 (3.0)	4 (4.1)
血管障害	7 (5.9)	4 (3.6)	0 (0.0)	3 (2.9)	2 (2.0)	6 (6.1)	1 (1.0)
TOTAL	115 (97.5)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表2.7.4.7-39

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JT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (日本の被験者)

System organ class	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
血液およびリンパ系障害	1 (1.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	2 (1.7)	2 (3.4)
心臓障害	1 (1.0)	3 (3.2)	1 (1.1)	2 (2.1)	1 (1.1)	1 (0.8)	0 (0.0)
先天性、家族性および遺伝性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
眼障害	0 (0.0)	3 (3.2)	2 (2.1)	2 (2.1)	1 (1.1)	0 (0.0)	1 (1.7)
胃腸障害	10 (10.4)	8 (8.4)	6 (6.3)	6 (6.4)	1 (1.1)	3 (2.5)	15 (25.4)
一般・全身障害および投与部位の状態	0 (0.0)	3 (3.2)	2 (2.1)	0 (0.0)	4 (4.3)	3 (2.5)	25 (42.4)
肝胆道系障害	1 (1.0)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.2)	0 (0.0)	1 (1.7)
免疫系障害	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	4 (4.2)	10 (10.5)	6 (6.3)	0 (0.0)	8 (8.6)	11 (9.3)	17 (28.8)
傷害、中毒および処置合併症	3 (3.1)	3 (3.2)	1 (1.1)	0 (0.0)	3 (3.2)	0 (0.0)	2 (3.4)
臨床検査	1 (1.0)	3 (3.2)	3 (3.2)	1 (1.1)	1 (1.1)	4 (3.4)	2 (3.4)
代謝および栄養障害	2 (2.1)	2 (2.1)	3 (3.2)	2 (2.1)	2 (2.2)	1 (0.8)	3 (5.1)
筋骨格系および結合組織障害	5 (5.2)	5 (5.3)	8 (8.4)	3 (3.2)	6 (6.5)	3 (2.5)	6 (10.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	2 (2.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
神経系障害	5 (5.2)	3 (3.2)	3 (3.2)	2 (2.1)	7 (7.5)	2 (1.7)	10 (16.9)
精神障害	0 (0.0)	1 (1.1)	1 (1.1)	1 (1.1)	2 (2.2)	0 (0.0)	3 (5.1)
腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	2 (2.2)	1 (0.8)	16 (27.1)
生殖系および乳房障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	0 (0.0)	2 (2.1)	3 (3.2)	4 (4.3)	3 (3.2)	1 (0.8)	4 (6.8)
皮膚および皮下組織障害	6 (6.3)	4 (4.2)	0 (0.0)	1 (1.1)	3 (3.2)	1 (0.8)	4 (6.8)
血管障害	3 (3.1)	1 (1.1)	3 (3.2)	3 (3.2)	2 (2.2)	1 (0.8)	7 (11.9)
TOTAL	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	49 (83.1)

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表2.7.4.7-39

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JT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (日本の被験者)

System organ class	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
血液およびリンパ系障害	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
心臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)
先天性、家族性および遺伝性障害	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (1.8)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	2 (3.4)	1 (1.7)	0 (0.0)	2 (3.4)	0 (0.0)	1 (1.8)	1 (1.8)
胃腸障害	7 (12.1)	5 (8.6)	4 (6.9)	7 (12.1)	1 (1.8)	9 (16.1)	2 (3.6)
一般・全身障害および投与部位の状態	3 (5.2)	4 (6.9)	3 (5.2)	1 (1.7)	2 (3.5)	0 (0.0)	2 (3.6)
肝胆道系障害	0 (0.0)	1 (1.7)	1 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.8)
免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	13 (22.4)	11 (19.0)	7 (12.1)	5 (8.6)	6 (10.5)	8 (14.3)	8 (14.3)
傷害、中毒および処置合併症	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	1 (1.8)	1 (1.8)	2 (3.6)
臨床検査	3 (5.2)	1 (1.7)	0 (0.0)	0 (0.0)	2 (3.5)	1 (1.8)	1 (1.8)
代謝および栄養障害	2 (3.4)	0 (0.0)	1 (1.7)	2 (3.4)	1 (1.8)	0 (0.0)	1 (1.8)
筋骨格系および結合組織障害	4 (6.9)	5 (8.6)	3 (5.2)	4 (6.9)	2 (3.5)	3 (5.4)	8 (14.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	3 (5.2)	3 (5.2)	1 (1.7)	4 (6.9)	1 (1.8)	5 (8.9)	1 (1.8)
精神障害	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
腎および尿路障害	2 (3.4)	4 (6.9)	2 (3.4)	2 (3.4)	1 (1.8)	2 (3.6)	0 (0.0)
生殖系および乳房障害	2 (3.4)	1 (1.7)	2 (3.4)	1 (1.7)	1 (1.8)	1 (1.8)	0 (0.0)
呼吸器、胸郭および縦隔障害	3 (5.2)	2 (3.4)	2 (3.4)	0 (0.0)	3 (5.3)	2 (3.6)	1 (1.8)
皮膚および皮下組織障害	2 (3.4)	5 (8.6)	2 (3.4)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)
血管障害	2 (3.4)	2 (3.4)	3 (5.2)	2 (3.4)	1 (1.8)	1 (1.8)	0 (0.0)
TOTAL	3 (5.2)	2 (3.4)	2 (3.4)	0 (0.0)	1 (1.8)	0 (0.0)	2 (3.6)

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JT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (日本の被験者)

System organ class	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
血液およびリンパ系障害	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (1.7)	3 (1.7)	2 (1.2)
心臓障害	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (5.6)	1 (0.6)
先天性、家族性および遺伝性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	1 (0.6)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
眼障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)	0 (0.0)	4 (2.3)	4 (2.4)
胃腸障害	5 (9.1)	4 (7.3)	4 (7.3)	5 (9.1)	2 (3.4)	56 (31.6)	27 (15.9)
一般・全身障害および投与部位の状態	1 (1.8)	2 (3.6)	1 (1.8)	0 (0.0)	1 (1.7)	133 (75.1)	11 (6.5)
肝胆道系障害	0 (0.0)	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)	7 (4.0)	5 (2.9)
免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	2 (1.2)
感染症および寄生虫症	9 (16.4)	3 (5.5)	4 (7.3)	5 (9.1)	0 (0.0)	44 (24.9)	31 (18.2)
傷害、中毒および処置合併症	0 (0.0)	1 (1.8)	4 (7.3)	1 (1.8)	1 (1.7)	5 (2.8)	1 (0.6)
臨床検査	1 (1.8)	1 (1.8)	0 (0.0)	3 (5.5)	1 (1.7)	15 (8.5)	6 (3.5)
代謝および栄養障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	15 (8.5)	6 (3.5)
筋骨格系および結合組織障害	6 (10.9)	3 (5.5)	2 (3.6)	4 (7.3)	1 (1.7)	18 (10.2)	14 (8.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
神経系障害	0 (0.0)	1 (1.8)	3 (5.5)	1 (1.8)	0 (0.0)	47 (26.6)	7 (4.1)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)	0 (0.0)	8 (4.5)	3 (1.8)
腎および尿路障害	0 (0.0)	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.7)	108 (61.0)	6 (3.5)
生殖系および乳房障害	0 (0.0)	1 (1.8)	2 (3.6)	0 (0.0)	0 (0.0)	3 (1.7)	3 (1.8)
呼吸器、胸郭および縦隔障害	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	10 (5.6)	7 (4.1)
皮膚および皮下組織障害	2 (3.6)	2 (3.6)	2 (3.6)	0 (0.0)	0 (0.0)	20 (11.3)	7 (4.1)
血管障害	0 (0.0)	0 (0.0)	2 (3.6)	0 (0.0)	0 (0.0)	14 (7.9)	6 (3.5)
TOTAL	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	164 (92.7)	4 (2.4)

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表2.7.4.7-39

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JT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period（日本の被験者）

System organ class	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
血液およびリンパ系障害	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	2 (1.3)	1 (0.7)	1 (0.7)
心臓障害	5 (3.0)	0 (0.0)	3 (1.9)	0 (0.0)	1 (0.7)	2 (1.3)	4 (2.7)
先天性、家族性および遺伝性障害	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.3)	1 (0.7)	2 (1.3)	1 (0.7)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	3 (1.8)	2 (1.2)	3 (1.9)	0 (0.0)	4 (2.6)	1 (0.7)	3 (2.0)
胃腸障害	14 (8.4)	13 (8.0)	16 (10.0)	15 (9.6)	18 (11.8)	12 (7.9)	13 (8.7)
一般・全身障害および投与部位の状態	8 (4.8)	7 (4.3)	5 (3.1)	6 (3.8)	4 (2.6)	2 (1.3)	4 (2.7)
肝胆道系障害	3 (1.8)	2 (1.2)	2 (1.3)	2 (1.3)	0 (0.0)	2 (1.3)	2 (1.3)
免疫系障害	3 (1.8)	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
感染症および寄生虫症	23 (13.9)	18 (11.1)	14 (8.8)	17 (10.9)	13 (8.5)	12 (7.9)	19 (12.7)
傷害、中毒および処置合併症	0 (0.0)	2 (1.2)	1 (0.6)	2 (1.3)	4 (2.6)	5 (3.3)	3 (2.0)
臨床検査	3 (1.8)	2 (1.2)	3 (1.9)	6 (3.8)	3 (2.0)	2 (1.3)	4 (2.7)
代謝および栄養障害	4 (2.4)	4 (2.5)	4 (2.5)	3 (1.9)	3 (2.0)	3 (2.0)	2 (1.3)
筋骨格系および結合組織障害	13 (7.8)	7 (4.3)	7 (4.4)	7 (4.5)	6 (3.9)	13 (8.6)	11 (7.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	8 (4.8)	5 (3.1)	6 (3.8)	5 (3.2)	7 (4.6)	6 (3.9)	3 (2.0)
精神障害	2 (1.2)	1 (0.6)	1 (0.6)	4 (2.6)	1 (0.7)	0 (0.0)	1 (0.7)
腎および尿路障害	7 (4.2)	4 (2.5)	3 (1.9)	3 (1.9)	3 (2.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	1 (0.6)	3 (1.9)	2 (1.3)	3 (1.9)	1 (0.7)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	8 (4.8)	8 (4.9)	2 (1.3)	4 (2.6)	3 (2.0)	1 (0.7)	2 (1.3)
皮膚および皮下組織障害	7 (4.2)	7 (4.3)	5 (3.1)	3 (1.9)	5 (3.3)	7 (4.6)	6 (4.0)
血管障害	2 (1.2)	6 (3.7)	4 (2.5)	7 (4.5)	2 (1.3)	3 (2.0)	1 (0.7)
TOTAL	2 (1.2)	2 (1.2)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.3)	1 (0.7)

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表2.7.4.7-39

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JT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period（日本の被験者）

System organ class	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
血液およびリンパ系障害	0 (0.0)	2 (1.3)	0 (0.0)	3 (1.7)
心臓障害	1 (0.7)	2 (1.3)	1 (0.7)	1 (0.6)
先天性、家族性および遺伝性障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	2 (1.3)	2 (1.3)	3 (2.0)	0 (0.0)
胃腸障害	10 (6.7)	10 (6.7)	6 (4.1)	5 (2.8)
一般・全身障害および投与部位の状態	4 (2.7)	1 (0.7)	4 (2.7)	4 (2.3)
肝胆道系障害	1 (0.7)	0 (0.0)	3 (2.0)	0 (0.0)
免疫系障害	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	9 (6.0)	4 (2.7)	13 (8.8)	11 (6.2)
傷害、中毒および処置合併症	2 (1.3)	4 (2.7)	4 (2.7)	1 (0.6)
臨床検査	4 (2.7)	1 (0.7)	4 (2.7)	5 (2.8)
代謝および栄養障害	3 (2.0)	2 (1.3)	3 (2.0)	2 (1.1)
筋骨格系および結合組織障害	11 (7.3)	5 (3.4)	10 (6.8)	4 (2.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (1.3)	0 (0.0)	1 (0.7)	0 (0.0)
神経系障害	4 (2.7)	5 (3.4)	8 (5.4)	2 (1.1)
精神障害	1 (0.7)	1 (0.7)	4 (2.7)	0 (0.0)
腎および尿路障害	1 (0.7)	2 (1.3)	3 (2.0)	2 (1.1)
生殖系および乳房障害	1 (0.7)	3 (2.0)	1 (0.7)	0 (0.0)
呼吸器、胸郭および縦隔障害	3 (2.0)	5 (3.4)	3 (2.0)	1 (0.6)
皮膚および皮下組織障害	2 (1.3)	3 (2.0)	3 (2.0)	1 (0.6)
血管障害	3 (2.0)	5 (3.4)	2 (1.4)	1 (0.6)
TOTAL	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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<資料番号5.3.5.3-02 : JT-8.7.1>

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
血液およびリンパ系障害							
貧血	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	0 (0.0)
鉄欠乏性貧血	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
狭心症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
右脚ブロック	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	5 (4.2)	1 (0.9)	3 (2.8)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害							
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害							
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
回転性めまい	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
内分泌障害							
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
眼障害							
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
眼乾燥	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)
眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害							
腹部不快感	1 (0.8)	2 (1.8)	0 (0.0)	2 (1.9)	0 (0.0)	0 (0.0)	1 (1.0)
腹部膨満	4 (3.4)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	3 (2.5)	1 (0.9)	0 (0.0)	2 (1.9)	1 (1.0)	0 (0.0)	0 (0.0)
下腹部痛	1 (0.8)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	5 (4.2)	5 (4.5)	0 (0.0)	2 (1.9)	1 (1.0)	0 (0.0)	1 (1.0)
アフタ性口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
便秘	10 (8.5)	2 (1.8)	3 (2.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
下痢	4 (3.4)	1 (0.9)	0 (0.0)	0 (0.0)	2 (2.0)	3 (3.0)	1 (1.0)
腸憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
口内乾燥	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
十二指腸炎	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
胃腸障害							
消化不良	2 (1.7)	3 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
胃ポリープ	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	2 (1.7)	1 (0.9)	1 (0.9)	0 (0.0)	1 (1.0)	3 (3.0)	1 (1.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	0 (0.0)	1 (0.9)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	2 (1.7)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
裂孔ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	2 (1.7)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	3 (2.5)	4 (3.6)	1 (0.9)	2 (1.9)	0 (0.0)	1 (1.0)	1 (1.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
歯根嚢胞	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	1 (0.8)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
歯の障害	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
嘔吐	3 (2.5)	1 (0.9)	0 (0.0)	3 (2.9)	2 (2.0)	2 (2.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
一般・全身障害および投与部位の状態							
無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	4 (3.4)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
疲労	8 (6.8)	1 (0.9)	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	7 (5.9)	1 (0.9)	0 (0.0)	1 (1.0)	1 (1.0)	1 (1.0)	0 (0.0)
浮腫	1 (0.8)	1 (0.9)	0 (0.0)	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
末梢性浮腫	0 (0.0)	1 (0.9)	1 (0.9)	0 (0.0)	2 (2.0)	0 (0.0)	0 (0.0)
疼痛	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
発熱	4 (3.4)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	2 (2.0)	2 (2.1)
口渇	104 (88.1)	2 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害							
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	0 (0.0)
肝嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	4 (3.4)	4 (3.6)	2 (1.9)	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
肝障害	2 (1.7)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害							
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
家塵アレルギー	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	1 (0.8)	2 (1.8)	3 (2.8)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
感染症および寄生虫症							
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	2 (1.7)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
膀胱炎	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
胃腸炎	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
ウイルス性胃腸炎	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	2 (1.8)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.0)
喉頭炎	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	17 (14.4)	11 (9.8)	8 (7.4)	8 (7.7)	6 (5.9)	4 (4.0)	1 (1.0)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.8)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
感染症および寄生虫症							
腎嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
気道感染	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
副鼻腔炎	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
軟部組織感染	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	1 (0.8)	1 (0.9)	2 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部腭カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
傷害、中毒および処置合併症							
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
凍瘡	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
傷害、中毒および処置合併症							
熱傷	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
血中クレアチニン増加	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)
血中カリウム減少	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿酸増加	4 (3.4)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	2 (1.7)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧上昇	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	6 (5.1)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
体重増加	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
代謝および栄養障害							
食欲減退	9 (7.6)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
脱水	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高脂血症	1 (0.8)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	2 (1.7)	2 (1.8)	0 (0.0)	0 (0.0)	2 (2.0)	1 (1.0)	3 (3.1)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	0 (0.0)	1 (0.9)	2 (1.9)	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
背部痛	6 (5.1)	4 (3.6)	4 (3.7)	2 (1.9)	2 (2.0)	1 (1.0)	0 (0.0)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	2 (1.7)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格痛	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	1 (0.8)	1 (0.9)	2 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	2 (2.1)
頸部痛	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性関節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	0 (0.0)	2 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
脂漏性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.0)	0 (0.0)	0 (0.0)
神経系障害							
味覚消失	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	10 (8.5)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	19 (16.1)	1 (0.9)	5 (4.6)	1 (1.0)	1 (1.0)	2 (2.0)	1 (1.0)
感覚鈍麻	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	1 (0.8)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.0)
意識消失	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
傾眠	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
不眠症	4 (3.4)	2 (1.8)	0 (0.0)	1 (1.0)	0 (0.0)	2 (2.0)	0 (0.0)
中期不眠症	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
自殺企図	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
血尿	4 (3.4)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	61 (51.7)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	40 (33.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
腎臓痛	6 (5.1)	1 (0.9)	2 (1.9)	0 (0.0)	1 (1.0)	0 (0.0)	1 (1.0)
終末尿滴下	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害							
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
生殖系および乳房障害							
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経障害	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害							
喘息	1 (0.8)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	2 (1.7)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	1 (0.8)	2 (1.8)	2 (1.9)	3 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	2 (1.7)	2 (1.8)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	0 (0.0)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害							
ざ瘡	2 (1.7)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
皮膚および皮下組織障害							
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	5 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
湿疹	0 (0.0)	1 (0.9)	1 (0.9)	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
多形紅斑	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏汗症	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
点状出血	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色靴擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	2 (1.7)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.0)	1 (1.0)	2 (2.1)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	4 (3.4)	1 (0.9)	1 (0.9)	2 (1.9)	0 (0.0)	1 (1.0)	0 (0.0)
酒さ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
蕁麻疹	1 (0.8)	1 (0.9)	1 (0.9)	0 (0.0)	1 (1.0)	0 (0.0)	1 (1.0)
慢性蕁麻疹	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	4 (3.4)	4 (3.6)	0 (0.0)	1 (1.0)	1 (1.0)	5 (5.1)	1 (1.0)
低血圧	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=118) n (%)	(N=112) n (%)	(N=108) n (%)	(N=104) n (%)	(N=102) n (%)	(N=99) n (%)	(N=97) n (%)
血管障害							
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	115 (97.5)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
血液およびリンパ系障害							
貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
鉄欠乏性貧血	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.7)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
脾臓障害	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
狭心症	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
房室ブロック	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	1 (1.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害							
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害							
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭位性回転性めまい	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害							
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
眼障害							
霰粒腫	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.7)
眼痛	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害							
腹部不快感	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.8)	0 (0.0)
腹痛	1 (1.0)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	4 (6.8)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	1 (1.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)
アフタ性口内炎	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	0 (0.0)	1 (1.1)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.7)
齲歯	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)
下痢	2 (2.1)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	3 (5.1)
腸憩室	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
胃腸障害							
消化不良	1 (1.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	1 (1.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)
裂孔ヘルニア	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	0 (0.0)	2 (2.1)	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.8)	2 (3.4)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
歯の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
一般・全身障害および投与部位の状態							
無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.2)	0 (0.0)	1 (1.7)
末梢性浮腫	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	2 (2.2)	2 (1.7)	3 (5.1)
疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
発熱	0 (0.0)	3 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)
口渇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	18 (30.5)
肝胆道系障害							
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
肝嚢胞	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪肝	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
免疫系障害							
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
感染症および寄生虫症							
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.8)	2 (3.4)
ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	1 (1.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (1.1)	2 (1.7)	0 (0.0)
喉頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	3 (3.1)	7 (7.4)	1 (1.1)	0 (0.0)	2 (2.2)	4 (3.4)	15 (25.4)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.7)	1 (1.7)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
感染症および寄生虫症							
腎嚢胞感染	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.7)	0 (0.0)
外陰部腭カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症							
節足動物刺傷	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	2 (2.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
擦過傷	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による嘔吐	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
傷害、中毒および処置合併症							
熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
血中クレアチンホスホキナーゼ増加	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
血中クレアチニン増加	0 (0.0)	2 (2.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.8)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	1 (1.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
代謝および栄養障害							
食欲減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.2)	0 (0.0)	2 (3.4)
高カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
高脂血症	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	1 (1.0)	0 (0.0)	2 (2.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
鉄欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
背部痛	1 (1.0)	2 (2.1)	3 (3.2)	1 (1.1)	2 (2.2)	1 (0.8)	3 (5.1)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
筋骨格痛	0 (0.0)	1 (1.1)	1 (1.1)	1 (1.1)	3 (3.2)	0 (0.0)	1 (1.7)
筋骨格硬直	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	1 (1.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
頸部痛	1 (1.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
変形性関節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	1 (1.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
脂漏性角化症	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.7)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
頸動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	1 (1.0)	1 (1.1)	1 (1.1)	2 (2.1)	1 (1.1)	0 (0.0)	2 (3.4)
体位性めまい	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	3 (3.1)	1 (1.1)	1 (1.1)	0 (0.0)	2 (2.2)	1 (0.8)	8 (13.6)
感覚鈍麻	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
頭蓋内動脈瘤	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
意識消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
うつ病	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.7)
不眠症	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	2 (3.4)
腎結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)
頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.8)
多尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.8)
蛋白尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
腎機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎臓痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	6 (10.2)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害							
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
生殖系および乳房障害							
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害							
喘息	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	0 (0.0)	1 (1.1)	2 (2.1)	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.7)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)
上気道の炎症	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害							
ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アトピー性皮膚炎	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
皮膚および皮下組織障害							
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
湿疹	1 (1.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色靴擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
乾癬	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
酒さ	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	3 (3.1)	1 (1.1)	3 (3.2)	3 (3.2)	1 (1.1)	1 (0.8)	5 (8.5)
低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)

表2.7.4.7-40
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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=96) n (%)	(N=95) n (%)	(N=95) n (%)	(N=94) n (%)	(N=93) n (%)	(N=118) n (%)	(N=59) n (%)
血管障害							
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
TOTAL	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	49 (83.1)

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表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
血液およびリンパ系障害							
貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
狭心症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害							
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害							
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害							
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
眼障害							
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
強膜炎	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害							
腹部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	2 (3.4)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.8)	0 (0.0)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	2 (3.4)	0 (0.0)	2 (3.4)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.8)	0 (0.0)
齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
下痢	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)	0 (0.0)
腸憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
胃腸障害							
消化不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
裂孔ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	1 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.8)	1 (1.8)	0 (0.0)
臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
一般・全身障害および投与部位の状態							
無力症	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性浮腫	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	2 (3.4)	1 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)
口渇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害							
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害							
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
感染症および寄生虫症							
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	1 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (1.7)	1 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)
ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	1 (1.7)	1 (1.7)	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)
喉頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
鼻咽頭炎	6 (10.3)	6 (10.3)	3 (5.2)	2 (3.4)	3 (5.3)	4 (7.1)	2 (3.6)
口腔ヘルペス	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
外耳炎	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
歯冠周囲炎	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	1 (1.7)	1 (1.7)	0 (0.0)	1 (1.7)	0 (0.0)	2 (3.6)	0 (0.0)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
感染症および寄生虫症							
腎嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)
気道感染	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
外陰部腭カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症							
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (1.8)
肉離れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
傷害、中毒および処置合併症							
熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査							
活性化部分トロンボプラスチン時間延長	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼ増加	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
代謝および栄養障害							
食欲減退	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高脂血症	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)	1 (1.8)	0 (0.0)	0 (0.0)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	1 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
背部痛	2 (3.4)	1 (1.7)	2 (3.4)	1 (1.7)	0 (0.0)	2 (3.6)	3 (5.4)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
筋肉痛	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	2 (3.5)	0 (0.0)	0 (0.0)
頸部痛	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性関節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)
四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
変形性脊椎症	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
脂漏性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
平衡障害	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	1 (1.7)	2 (3.4)	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.4)	0 (0.0)	1 (1.8)	0 (0.0)
感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.8)	1 (1.8)
頭蓋内動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
失神	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	0 (0.0)	1 (1.7)	1 (1.7)	1 (1.7)	0 (0.0)	1 (1.8)	0 (0.0)
腎結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
腎臓痛	0 (0.0)	2 (3.4)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害							
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
生殖系および乳房障害							
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害							
喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	1 (1.7)	1 (1.7)	1 (1.7)	0 (0.0)	1 (1.8)	2 (3.6)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
口腔咽頭痛	2 (3.4)	1 (1.7)	0 (0.0)	0 (0.0)	2 (3.5)	0 (0.0)	0 (0.0)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害							
ざ瘡	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
皮膚および皮下組織障害							
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色靴擦疹	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	1 (1.7)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	2 (3.4)	1 (1.7)	2 (3.4)	1 (1.7)	1 (1.8)	1 (1.8)	0 (0.0)
低血圧	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40
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 JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=58) n (%)	(N=57) n (%)	(N=56) n (%)	(N=56) n (%)
血管障害							
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	3 (5.2)	2 (3.4)	2 (3.4)	0 (0.0)	1 (1.8)	0 (0.0)	2 (3.6)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
血液およびリンパ系障害							
貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.6)	1 (0.6)
鉄欠乏性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
リンパ節症	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害							
狭心症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.8)	1 (0.6)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)
心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害							
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害							
耳閉	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害							
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
眼障害							
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)
眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)
胃腸障害							
腹部不快感	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.2)
腹部膨満	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	4 (2.3)	3 (1.8)
腹痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (4.0)	1 (0.6)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
上腹部痛	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	6 (3.4)	7 (4.1)
アフタ性口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	1 (0.6)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
便秘	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	11 (6.2)	2 (1.2)
齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
下痢	2 (3.6)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	7 (4.0)	1 (0.6)
腸憩室	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
胃腸障害							
消化不良	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	3 (1.8)
小腸炎	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	0 (0.0)	2 (3.6)	0 (0.0)	1 (1.8)	0 (0.0)	2 (1.1)	1 (0.6)
歯肉痛	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
裂孔ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
悪心	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	5 (2.8)	5 (2.9)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
歯の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
歯痛	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	1 (0.6)
臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	3 (1.8)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
一般・全身障害および投与部位の状態							
無力症	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
胸痛	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	1 (0.6)
嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (5.1)	1 (0.6)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (4.5)	1 (0.6)
浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
末梢性浮腫	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	1 (0.6)
疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
発熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	6 (3.4)	3 (1.8)
口渇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	122 (68.9)	2 (1.2)
肝胆道系障害							
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	4 (2.4)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
免疫系障害							
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.2)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
感染症および寄生虫症							
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	2 (1.1)	2 (1.2)
蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.6)	2 (1.2)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	0 (0.0)	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)	2 (1.1)	0 (0.0)
ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
肝嚢胞感染	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)
麦粒腫	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)
喉頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	2 (3.6)	0 (0.0)	2 (3.6)	0 (0.0)	0 (0.0)	32 (18.1)	17 (10.0)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	2 (1.2)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
感染症および寄生虫症							
腎嚢胞感染	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
鼻炎	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)	1 (0.6)	1 (0.6)
尿路感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部腭カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症							
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	1 (0.6)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
傷害、中毒および処置合併症							
熱傷	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
脛骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	0 (0.0)	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.6)	2 (1.2)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
血圧上昇	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	1 (0.6)	0 (0.0)
血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)
心電図Q T間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (3.4)	0 (0.0)
体重増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
代謝および栄養障害							
食欲減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (5.1)	2 (1.2)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
高カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	0 (0.0)	0 (0.0)
高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.2)
高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	2 (1.2)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
鉄欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)
背部痛	3 (5.5)	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	9 (5.1)	6 (3.5)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)
足変形	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	2 (1.2)
筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	3 (1.7)	0 (0.0)
筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.6)	1 (0.6)
筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
筋肉痛	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	3 (1.7)	0 (0.0)
頸部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
変形性関節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.2)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
脂漏性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
子宮平滑筋腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
頸動脈瘤	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
浮動性めまい	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	12 (6.8)	1 (0.6)
体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	0 (0.0)
頭痛	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)	27 (15.3)	2 (1.2)
感覚鈍麻	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)
頭蓋内動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
意識消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.6)	0 (0.0)
不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	5 (2.8)	2 (1.2)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
腎および尿路障害							
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
血尿	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	6 (3.4)	1 (0.6)
腎結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	0 (0.0)
頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	65 (36.7)	1 (0.6)
多尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	44 (24.9)	0 (0.0)
蛋白尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
腎機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
腎臓痛	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)	0 (0.0)	12 (6.8)	1 (0.6)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
生殖系および乳房障害							
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
生殖系および乳房障害							
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
不規則月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害							
喘息	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	1 (0.6)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	2 (1.1)	4 (2.4)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	2 (1.2)
上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
皮膚および皮下組織障害							
ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	2 (1.2)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	2 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
皮膚および皮下組織障害							
薬疹	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (3.4)	0 (0.0)
湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
ばら色靴擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.8)	2 (1.2)
酒さ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1 (0.6)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
血管障害							
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	0 (0.0)	0 (0.0)	2 (3.6)	0 (0.0)	0 (0.0)	9 (5.1)	6 (3.5)
低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)

表2.7.4.7-40
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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=55) n (%)	(N=59) n (%)	(N=177) n (%)	(N=170) n (%)
血管障害							
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
TOTAL	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	164 (92.7)	4 (2.4)

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表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
血液およびリンパ系障害							
貧血	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)	1 (0.7)	0 (0.0)
リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
心臓障害							
狭心症	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	2 (1.3)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
僧帽弁閉鎖不全症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	3 (1.8)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性頻脈	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
先天性、家族性および遺伝性障害							
多発性内分泌腺腫症	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害							
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)
内分泌障害							
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
眼障害							
霰粒腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
結膜充血	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
アレルギー性結膜炎	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)	1 (0.7)
眼痛	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
眼瞼浮腫	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
羞明	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害							
腹部不快感	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	2 (1.3)
腹部膨満	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	0 (0.0)	2 (1.2)	2 (1.3)	0 (0.0)	1 (0.7)	1 (0.7)	2 (1.3)
下腹部痛	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	0 (0.0)	4 (2.5)	2 (1.3)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
アフタ性口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	3 (1.8)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.3)	0 (0.0)	1 (0.7)
齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	3 (2.0)	0 (0.0)
下痢	2 (1.2)	0 (0.0)	2 (1.3)	3 (1.9)	3 (2.0)	2 (1.3)	3 (2.0)
腸憩室	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
胃腸障害							
消化不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
小腸炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	1 (0.7)	0 (0.0)
腸炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	1 (0.6)	1 (0.6)	1 (0.6)	3 (1.9)	1 (0.7)	0 (0.0)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
歯肉炎	3 (1.8)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
裂孔ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	2 (1.2)	2 (1.2)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	2 (1.3)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液管の炎症	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
歯の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
臍ヘルニア	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	0 (0.0)	3 (1.9)	2 (1.3)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
一般・全身障害および投与部位の状態							
無力症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
疲労	3 (1.8)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)
浮腫	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性浮腫	2 (1.2)	0 (0.0)	3 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	2 (1.2)	2 (1.2)	0 (0.0)	2 (1.3)	2 (1.3)	2 (1.3)	3 (2.0)
口渇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害							
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢ポリープ	1 (0.6)	0 (0.0)	2 (1.3)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)
肝嚢胞	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
肝機能異常	2 (1.2)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
肝障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害							
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	3 (1.8)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
感染症および寄生虫症							
急性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (0.6)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	2 (1.3)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	1 (0.7)	0 (0.0)
ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
B型肝炎	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
帯状疱疹	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)
麦粒腫	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
感染	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	1 (0.6)	2 (1.2)	0 (0.0)	1 (0.6)	2 (1.3)	0 (0.0)	1 (0.7)
喉頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
鼻咽頭炎	14 (8.4)	11 (6.8)	8 (5.0)	7 (4.5)	5 (3.3)	5 (3.3)	9 (6.0)
口腔ヘルペス	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
外耳炎	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
感染症および寄生虫症							
腎嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.3)	1 (0.7)
気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
副鼻腔炎	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
トリコモナス症	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	2 (1.2)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
尿路感染	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
外陰部腭カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症							
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	2 (1.3)	2 (1.3)	1 (0.7)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靱帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)
肉離れ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
傷害、中毒および処置合併症							
熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脛骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査							
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼ増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)	1 (0.7)	0 (0.0)	2 (1.3)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
血中尿酸増加	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図QT間隔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
尿浸透圧上昇	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
代謝および栄養障害							
食欲減退	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
糖尿病	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
痛風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	0 (0.0)	1 (0.6)	3 (1.9)	2 (1.3)	3 (2.0)	1 (0.7)	0 (0.0)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害							
関節痛	3 (1.8)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.3)	0 (0.0)
背部痛	5 (3.0)	4 (2.5)	3 (1.9)	1 (0.6)	2 (1.3)	4 (2.6)	5 (3.3)
骨痛	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)
足変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
筋骨格硬直	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
筋肉痛	0 (0.0)	1 (0.6)	1 (0.6)	3 (1.9)	2 (1.3)	1 (0.7)	2 (1.3)
頸部痛	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
変形性関節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)
四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	1 (0.7)	1 (0.7)
顎痛	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
変形性脊椎症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
腱鞘炎	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）							
脂漏性角化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害							
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	3 (1.8)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
体位性めまい	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	6 (3.6)	1 (0.6)	3 (1.9)	2 (1.3)	2 (1.3)	3 (2.0)	1 (0.7)
感覚鈍麻	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)
頭蓋内動脈瘤	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
意識消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
失神	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
精神障害							
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
不安	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	2 (1.2)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)	1 (0.7)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害							
膀胱刺激症状	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	1 (0.6)	2 (1.2)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
腎結石症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)
腎臓痛	4 (2.4)	0 (0.0)	2 (1.3)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害							
無月経	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
生殖系および乳房障害							
乳汁漏出症	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)
血精液症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
閉経期症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害							
喘息	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	1 (0.6)	2 (1.2)	0 (0.0)	1 (0.6)	2 (1.3)	0 (0.0)	0 (0.0)
呼吸困難	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
鼻閉塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
口腔咽頭痛	3 (1.8)	3 (1.9)	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)	1 (0.7)
咽頭紅斑	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
皮膚および皮下組織障害							
ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
アトピー性皮膚炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
接触性皮膚炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.3)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
皮膚および皮下組織障害							
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
湿疹	2 (1.2)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	2 (1.3)	1 (0.7)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色靴擦疹	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.6)	2 (1.3)	1 (0.7)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
発疹	3 (1.8)	2 (1.2)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	2 (1.3)
酒さ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害							
大動脈拡張	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	1 (0.6)	3 (1.9)	2 (1.3)	6 (3.8)	2 (1.3)	3 (2.0)	1 (0.7)
低血圧	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=166) n (%)	(N=162) n (%)	(N=160) n (%)	(N=156) n (%)	(N=153) n (%)	(N=152) n (%)	(N=150) n (%)
血管障害							
不安定血圧	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	2 (1.2)	2 (1.2)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.3)	1 (0.7)

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
血液およびリンパ系障害				
貧血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
鉄欠乏性貧血	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
リンパ節症	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.6)
腎性貧血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
脾臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害				
狭心症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不整脈	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓瘤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室不全	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
僧帽弁閉鎖不全症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
洞性徐脈	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
上室性頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害				
多発性内分泌腺腫症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害				
耳閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内リンパ水腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭位性回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害				
続発性副甲状腺機能亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
眼障害				
霰粒腫	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
結膜出血	0 (0.0)	0 (0.0)	2 (1.4)	0 (0.0)
結膜充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性結膜炎	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
眼瞼皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)
羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害				
腹部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	0 (0.0)	2 (1.3)	0 (0.0)	1 (0.6)
腹痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.1)
アフタ性口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)
結腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	1 (0.7)	2 (1.3)	0 (0.0)	0 (0.0)
齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下痢	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)
腸憩室	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
胃腸障害				
消化不良	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	3 (2.0)	1 (0.7)	1 (0.7)	0 (0.0)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.1)
裂孔ヘルニア	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	1 (0.7)	0 (0.0)	2 (1.4)	2 (1.1)
急性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
再発性膵炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結腸直腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯根嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸脱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
唾液管の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯の障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
臍ヘルニア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.6)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
一般・全身障害および投与部位の状態				
無力症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
局所腫脹	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	0 (0.0)	0 (0.0)	2 (1.4)	0 (0.0)
末梢性浮腫	2 (1.3)	0 (0.0)	2 (1.4)	2 (1.1)
疼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
発熱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
口渇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害				
細胆管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
胆嚢ポリープ	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
肝嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
免疫系障害				
節足動物咬傷アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷アレルギー	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
アナフィラキシー様反応	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
家塵アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
感染症および寄生虫症				
急性副鼻腔炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
急性扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アデノイド咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
β溶血性レンサ球菌感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
蜂巣炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性小腸結腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.7)	0 (0.0)	2 (1.4)	1 (0.6)
ウイルス性胃腸炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
肝嚢胞感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
麦粒腫	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)
感染	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
インフルエンザ	2 (1.3)	1 (0.7)	1 (0.7)	2 (1.1)
喉頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻咽頭炎	1 (0.7)	2 (1.3)	2 (1.4)	4 (2.3)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳下腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯冠周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)
マイコプラズマ性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
感染症および寄生虫症				
腎嚢胞感染	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.6)
気道感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリコモナス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	1 (0.7)	1 (0.7)	1 (0.7)	0 (0.0)
尿路感染	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)
外陰部腭カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症				
節足動物刺傷	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎖骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼外傷	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
外傷性血尿	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
熱射病	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
靱帯捻挫	0 (0.0)	1 (0.7)	2 (1.4)	0 (0.0)
半月板障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉離れ	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
処置による疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
刺創	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period (日本の被験者)

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
傷害、中毒および処置合併症				
熱傷	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
脛骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査				
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アラニン・アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌検査陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁量	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
血中クレアチニン増加	1 (0.7)	1 (0.7)	1 (0.7)	1 (0.6)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	1 (0.7)	0 (0.0)	1 (0.7)	1 (0.6)
血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シスタチンC増加	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
心電図QT間隔	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
γ-グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
炎症マーカー上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎触知	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
便潜血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿蛋白	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿浸透圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
代謝および栄養障害				
食欲減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	0 (0.0)	0 (0.0)	2 (1.4)	0 (0.0)
高カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
高血糖	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)
高脂血症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	2 (1.3)	1 (0.7)	0 (0.0)	0 (0.0)
低アルブミン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害				
関節痛	1 (0.7)	1 (0.7)	0 (0.0)	1 (0.6)
背部痛	4 (2.7)	1 (0.7)	2 (1.4)	2 (1.1)
骨痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.6)
足変形	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
筋骨格痛	1 (0.7)	1 (0.7)	4 (2.7)	0 (0.0)
筋骨格硬直	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	1 (0.7)	0 (0.0)	2 (1.4)	0 (0.0)
頸部痛	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
変形性関節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
顎痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
滑液嚢腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱鞘炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）				
脂漏性角化症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乳頭腫	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)
汗腺腫瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害				
味覚消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜嚢胞	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
平衡障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頸動脈瘤	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
脳出血	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳虚血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
群発頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	1 (0.7)	3 (2.0)	1 (0.7)	0 (0.0)
体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	1 (0.7)	1 (0.7)	3 (2.0)	1 (0.6)
感覚鈍麻	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内動脈瘤	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
意識消失	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
神経痛	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
末梢性ニューロパチー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚錯誤	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気脳体	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
精神障害				
異常行動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安障害	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
閉所恐怖症	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
うつ病	1 (0.7)	1 (0.7)	1 (0.7)	0 (0.0)
不眠症	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自殺企図	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害				
膀胱刺激症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
血尿	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)
腎結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
腎嚢胞出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
腎不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎臓痛	0 (0.0)	1 (0.7)	2 (1.4)	0 (0.0)
終末尿滴下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害				
無月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘍	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
射精障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮内膜症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
精巣上体炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
生殖系および乳房障害				
乳汁漏出症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器出血	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
血精液症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
閉経期症状	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
月経障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性機能不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮腔脱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害				
喘息	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)
慢性気管支炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉塞	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
口腔咽頭痛	2 (1.3)	1 (0.7)	0 (0.0)	1 (0.6)
咽頭紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)
鼻漏	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害				
ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性水疱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触性皮膚炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)

表2.7.4.7-40

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JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months	30-33 Months	33-36 Months	Post withdraw
	(N=150) n (%)	(N=149) n (%)	(N=148) n (%)	(N=177) n (%)
皮膚および皮下組織障害				
薬疹	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
紅斑	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅色汗疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網状皮斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
点状出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ばら色靴擦疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.6)
乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
酒さ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
慢性蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害				
大動脈拡張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化症	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
潮紅	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	3 (2.0)	5 (3.4)	1 (0.7)	1 (0.6)
低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表2.7.4.7-40

156-251

JT-8.7.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and MedDRA Preferred Term by Period（日本の被験者）

System organ class Adverse event (MedDRA preferred term)	Total			
	27-30 Months (N=150)	30-33 Months (N=149)	33-36 Months (N=148)	Post withdraw (N=177)
	n (%)	n (%)	n (%)	n (%)
血管障害				
不安定血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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<資料番号5.3.5.3-02 : JT-8.7.2>

表2.7.4.7-41

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NT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (海外の被験者)

System organ class	Tolvaptan						
	0-3 Months	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months
	(N=843)	(N=766)	(N=736)	(N=721)	(N=707)	(N=697)	(N=684)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血液およびリンパ系障害	7 (0.8)	4 (0.5)	1 (0.1)	3 (0.4)	2 (0.3)	5 (0.7)	8 (1.2)
心臓障害	28 (3.3)	7 (0.9)	8 (1.1)	4 (0.6)	3 (0.4)	4 (0.6)	7 (1.0)
先天性、家族性および遺伝性障害	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	14 (1.7)	3 (0.4)	3 (0.4)	5 (0.7)	3 (0.4)	2 (0.3)	7 (1.0)
内分泌障害	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	2 (0.3)
眼障害	14 (1.7)	4 (0.5)	2 (0.3)	4 (0.6)	3 (0.4)	6 (0.9)	5 (0.7)
胃腸障害	302 (35.8)	62 (8.1)	49 (6.7)	32 (4.4)	43 (6.1)	40 (5.7)	37 (5.4)
一般・全身障害および投与部位の状態	470 (55.8)	42 (5.5)	39 (5.3)	22 (3.1)	26 (3.7)	30 (4.3)	22 (3.2)
肝胆道系障害	3 (0.4)	4 (0.5)	9 (1.2)	6 (0.8)	1 (0.1)	3 (0.4)	2 (0.3)
免疫系障害	8 (0.9)	7 (0.9)	1 (0.1)	2 (0.3)	1 (0.1)	4 (0.6)	7 (1.0)
感染症および寄生虫症	131 (15.5)	85 (11.1)	77 (10.5)	67 (9.3)	63 (8.9)	41 (5.9)	51 (7.5)
傷害、中毒および処置合併症	15 (1.8)	11 (1.4)	14 (1.9)	17 (2.4)	5 (0.7)	14 (2.0)	13 (1.9)
臨床検査	103 (12.2)	50 (6.5)	48 (6.5)	35 (4.9)	22 (3.1)	40 (5.7)	30 (4.4)
代謝および栄養障害	183 (21.7)	27 (3.5)	22 (3.0)	13 (1.8)	12 (1.7)	11 (1.6)	13 (1.9)
筋骨格系および結合組織障害	76 (9.0)	49 (6.4)	44 (6.0)	42 (5.8)	35 (5.0)	36 (5.2)	23 (3.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.1)	4 (0.5)	2 (0.3)	5 (0.7)	5 (0.7)	1 (0.1)	3 (0.4)
神経系障害	190 (22.5)	29 (3.8)	36 (4.9)	26 (3.6)	8 (1.1)	26 (3.7)	20 (2.9)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	52 (6.2)	13 (1.7)	14 (1.9)	12 (1.7)	6 (0.8)	9 (1.3)	7 (1.0)
腎および尿路障害	575 (68.2)	61 (8.0)	57 (7.7)	38 (5.3)	27 (3.8)	33 (4.7)	25 (3.7)
生殖系および乳房障害	26 (3.1)	16 (2.1)	11 (1.5)	6 (0.8)	6 (0.8)	6 (0.9)	10 (1.5)
呼吸器、胸郭および縦隔障害	44 (5.2)	19 (2.5)	16 (2.2)	21 (2.9)	18 (2.5)	16 (2.3)	9 (1.3)
皮膚および皮下組織障害	72 (8.5)	28 (3.7)	18 (2.4)	12 (1.7)	12 (1.7)	7 (1.0)	10 (1.5)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
外科および内科処置	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)
血管障害	114 (13.5)	33 (4.3)	29 (3.9)	27 (3.7)	17 (2.4)	31 (4.4)	19 (2.8)
TOTAL	749 (88.8)	25 (3.3)	17 (2.3)	11 (1.5)	2 (0.3)	5 (0.7)	4 (0.6)

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表2.7.4.7-41

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NT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (海外の被験者)

System organ class	Tolvaptan						Placebo
	21-24 Months	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months
	(N=673) n (%)	(N=667) n (%)	(N=660) n (%)	(N=655) n (%)	(N=646) n (%)	(N=843) n (%)	(N=424) n (%)
血液およびリンパ系障害	3 (0.4)	1 (0.1)	4 (0.6)	5 (0.8)	3 (0.5)	3 (0.4)	6 (1.4)
心臓障害	5 (0.7)	5 (0.7)	2 (0.3)	3 (0.5)	9 (1.4)	1 (0.1)	8 (1.9)
先天性、家族性および遺伝性障害	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)
耳および迷路障害	3 (0.4)	5 (0.7)	2 (0.3)	3 (0.5)	0 (0.0)	1 (0.1)	7 (1.7)
内分泌障害	2 (0.3)	3 (0.4)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)
眼障害	4 (0.6)	4 (0.6)	3 (0.5)	6 (0.9)	6 (0.9)	4 (0.5)	11 (2.6)
胃腸障害	31 (4.6)	32 (4.8)	35 (5.3)	31 (4.7)	32 (5.0)	19 (2.3)	103 (24.3)
一般・全身障害および投与部位の状態	14 (2.1)	14 (2.1)	14 (2.1)	14 (2.1)	26 (4.0)	14 (1.7)	114 (26.9)
肝胆道系障害	4 (0.6)	1 (0.1)	2 (0.3)	2 (0.3)	4 (0.6)	1 (0.1)	1 (0.2)
免疫系障害	3 (0.4)	4 (0.6)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.1)	3 (0.7)
感染症および寄生虫症	72 (10.7)	45 (6.7)	50 (7.6)	44 (6.7)	52 (8.0)	30 (3.6)	78 (18.4)
傷害、中毒および処置合併症	10 (1.5)	17 (2.5)	9 (1.4)	10 (1.5)	15 (2.3)	7 (0.8)	10 (2.4)
臨床検査	23 (3.4)	16 (2.4)	26 (3.9)	16 (2.4)	30 (4.6)	17 (2.0)	35 (8.3)
代謝および栄養障害	8 (1.2)	7 (1.0)	13 (2.0)	13 (2.0)	16 (2.5)	4 (0.5)	32 (7.5)
筋骨格系および結合組織障害	45 (6.7)	28 (4.2)	28 (4.2)	28 (4.3)	29 (4.5)	10 (1.2)	39 (9.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (0.4)	6 (0.9)	2 (0.3)	3 (0.5)	4 (0.6)	1 (0.1)	5 (1.2)
神経系障害	20 (3.0)	17 (2.5)	14 (2.1)	9 (1.4)	20 (3.1)	6 (0.7)	79 (18.6)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
精神障害	8 (1.2)	6 (0.9)	5 (0.8)	8 (1.2)	12 (1.9)	1 (0.1)	14 (3.3)
腎および尿路障害	24 (3.6)	21 (3.1)	15 (2.3)	19 (2.9)	23 (3.6)	9 (1.1)	139 (32.8)
生殖系および乳房障害	6 (0.9)	6 (0.9)	1 (0.2)	5 (0.8)	5 (0.8)	2 (0.2)	16 (3.8)
呼吸器、胸郭および縦隔障害	11 (1.6)	10 (1.5)	10 (1.5)	12 (1.8)	11 (1.7)	7 (0.8)	18 (4.2)
皮膚および皮下組織障害	15 (2.2)	7 (1.0)	10 (1.5)	9 (1.4)	10 (1.5)	10 (1.2)	19 (4.5)
社会環境	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外科および内科処置	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	22 (3.3)	14 (2.1)	17 (2.6)	21 (3.2)	20 (3.1)	17 (2.0)	47 (11.1)
TOTAL	5 (0.7)	0 (0.0)	3 (0.5)	1 (0.2)	2 (0.3)	1 (0.1)	310 (73.1)

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表2.7.4.7-41
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NT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (海外の被験者)

System organ class	Placebo						
	3-6 Months	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months
	(N=415) n (%)	(N=407) n (%)	(N=402) n (%)	(N=397) n (%)	(N=391) n (%)	(N=385) n (%)	(N=379) n (%)
血液およびリンパ系障害	3 (0.7)	5 (1.2)	2 (0.5)	1 (0.3)	3 (0.8)	3 (0.8)	1 (0.3)
心臓障害	1 (0.2)	4 (1.0)	2 (0.5)	1 (0.3)	7 (1.8)	1 (0.3)	2 (0.5)
先天性、家族性および遺伝性障害	0 (0.0)	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	2 (0.5)	3 (0.7)	2 (0.5)	2 (0.5)	1 (0.3)	2 (0.5)	2 (0.5)
内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)	2 (0.5)
眼障害	2 (0.5)	2 (0.5)	3 (0.7)	5 (1.3)	3 (0.8)	0 (0.0)	3 (0.8)
胃腸障害	27 (6.5)	28 (6.9)	22 (5.5)	26 (6.5)	23 (5.9)	27 (7.0)	17 (4.5)
一般・全身障害および投与部位の状態	11 (2.7)	24 (5.9)	10 (2.5)	10 (2.5)	13 (3.3)	22 (5.7)	8 (2.1)
肝胆道系障害	1 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.8)	2 (0.5)	2 (0.5)
免疫系障害	1 (0.2)	1 (0.2)	0 (0.0)	3 (0.8)	1 (0.3)	0 (0.0)	1 (0.3)
感染症および寄生虫症	42 (10.1)	36 (8.8)	32 (8.0)	27 (6.8)	39 (10.0)	29 (7.5)	31 (8.2)
傷害、中毒および処置合併症	3 (0.7)	9 (2.2)	9 (2.2)	4 (1.0)	10 (2.6)	11 (2.9)	5 (1.3)
臨床検査	19 (4.6)	16 (3.9)	16 (4.0)	11 (2.8)	23 (5.9)	21 (5.5)	17 (4.5)
代謝および栄養障害	11 (2.7)	6 (1.5)	8 (2.0)	3 (0.8)	1 (0.3)	7 (1.8)	5 (1.3)
筋骨格系および結合組織障害	13 (3.1)	21 (5.2)	28 (7.0)	11 (2.8)	18 (4.6)	21 (5.5)	14 (3.7)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	3 (0.7)	1 (0.2)	1 (0.3)	2 (0.5)	1 (0.3)	2 (0.5)
神経系障害	13 (3.1)	18 (4.4)	11 (2.7)	7 (1.8)	10 (2.6)	11 (2.9)	9 (2.4)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	7 (1.7)	4 (1.0)	7 (1.7)	5 (1.3)	4 (1.0)	5 (1.3)	6 (1.6)
腎および尿路障害	33 (8.0)	34 (8.4)	31 (7.7)	14 (3.5)	21 (5.4)	21 (5.5)	15 (4.0)
生殖系および乳房障害	9 (2.2)	4 (1.0)	5 (1.2)	3 (0.8)	5 (1.3)	3 (0.8)	3 (0.8)
呼吸器、胸郭および縦隔障害	8 (1.9)	9 (2.2)	10 (2.5)	8 (2.0)	10 (2.6)	3 (0.8)	5 (1.3)
皮膚および皮下組織障害	5 (1.2)	3 (0.7)	6 (1.5)	6 (1.5)	8 (2.0)	4 (1.0)	7 (1.8)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
外科および内科処置	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	23 (5.5)	22 (5.4)	20 (5.0)	6 (1.5)	11 (2.8)	17 (4.4)	11 (2.9)
TOTAL	34 (8.2)	19 (4.7)	11 (2.7)	8 (2.0)	7 (1.8)	8 (2.1)	2 (0.5)

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NT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (海外の被験者)

System organ class	Placebo					Total	
	24-27 Months	27-30 Months	30-33 Months	33-36 Months	Post withdraw	0-3 Months	3-6 Months
	(N=372) n (%)	(N=369) n (%)	(N=364) n (%)	(N=362) n (%)	(N=424) n (%)	(N=1267) n (%)	(N=1181) n (%)
血液およびリンパ系障害	1 (0.3)	2 (0.5)	1 (0.3)	5 (1.4)	1 (0.2)	13 (1.0)	7 (0.6)
心臓障害	4 (1.1)	0 (0.0)	1 (0.3)	2 (0.6)	2 (0.5)	36 (2.8)	8 (0.7)
先天性、家族性および遺伝性障害	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)	2 (0.2)	0 (0.0)
耳および迷路障害	2 (0.5)	1 (0.3)	1 (0.3)	2 (0.6)	0 (0.0)	21 (1.7)	5 (0.4)
内分泌障害	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.2)	0 (0.0)
眼障害	1 (0.3)	1 (0.3)	3 (0.8)	2 (0.6)	1 (0.2)	25 (2.0)	6 (0.5)
胃腸障害	17 (4.6)	8 (2.2)	13 (3.6)	18 (5.0)	6 (1.4)	405 (32.0)	89 (7.5)
一般・全身障害および投与部位の状態	11 (3.0)	14 (3.8)	4 (1.1)	15 (4.1)	1 (0.2)	584 (46.1)	53 (4.5)
肝胆道系障害	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	4 (0.3)	5 (0.4)
免疫系障害	1 (0.3)	3 (0.8)	1 (0.3)	0 (0.0)	0 (0.0)	11 (0.9)	8 (0.7)
感染症および寄生虫症	20 (5.4)	37 (10.0)	27 (7.4)	30 (8.3)	14 (3.3)	209 (16.5)	127 (10.8)
傷害、中毒および処置合併症	6 (1.6)	7 (1.9)	4 (1.1)	5 (1.4)	4 (0.9)	25 (2.0)	14 (1.2)
臨床検査	9 (2.4)	20 (5.4)	13 (3.6)	20 (5.5)	8 (1.9)	138 (10.9)	69 (5.8)
代謝および栄養障害	3 (0.8)	3 (0.8)	9 (2.5)	4 (1.1)	4 (0.9)	215 (17.0)	38 (3.2)
筋骨格系および結合組織障害	15 (4.0)	16 (4.3)	14 (3.8)	18 (5.0)	5 (1.2)	115 (9.1)	62 (5.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.5)	3 (0.8)	0 (0.0)	1 (0.3)	0 (0.0)	6 (0.5)	4 (0.3)
神経系障害	7 (1.9)	9 (2.4)	10 (2.7)	10 (2.8)	7 (1.7)	269 (21.2)	42 (3.6)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	3 (0.8)	4 (1.1)	3 (0.8)	5 (1.4)	2 (0.5)	66 (5.2)	20 (1.7)
腎および尿路障害	21 (5.6)	12 (3.3)	14 (3.8)	22 (6.1)	8 (1.9)	714 (56.4)	94 (8.0)
生殖系および乳房障害	1 (0.3)	2 (0.5)	4 (1.1)	4 (1.1)	2 (0.5)	42 (3.3)	25 (2.1)
呼吸器、胸郭および縦隔障害	2 (0.5)	4 (1.1)	2 (0.5)	6 (1.7)	2 (0.5)	62 (4.9)	27 (2.3)
皮膚および皮下組織障害	1 (0.3)	5 (1.4)	5 (1.4)	2 (0.6)	2 (0.5)	91 (7.2)	33 (2.8)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外科および内科処置	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
血管障害	7 (1.9)	12 (3.3)	6 (1.6)	10 (2.8)	5 (1.2)	161 (12.7)	56 (4.7)
TOTAL	1 (0.3)	6 (1.6)	2 (0.5)	2 (0.6)	3 (0.7)	1059 (83.6)	59 (5.0)

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表2.7.4.7-41

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NT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period (海外の被験者)

System organ class	Total						
	6-9 Months	9-12 Months	12-15 Months	15-18 Months	18-21 Months	21-24 Months	24-27 Months
	(N=1143)	(N=1123)	(N=1104)	(N=1088)	(N=1069)	(N=1052)	(N=1039)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血液およびリンパ系障害	6 (0.5)	5 (0.4)	3 (0.3)	8 (0.7)	11 (1.0)	4 (0.4)	2 (0.2)
心臓障害	12 (1.0)	6 (0.5)	4 (0.4)	11 (1.0)	8 (0.7)	7 (0.7)	9 (0.9)
先天性、家族性および遺伝性障害	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
耳および迷路障害	6 (0.5)	7 (0.6)	5 (0.5)	3 (0.3)	9 (0.8)	5 (0.5)	7 (0.7)
内分泌障害	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	3 (0.3)	4 (0.4)	4 (0.4)
眼障害	4 (0.3)	7 (0.6)	8 (0.7)	9 (0.8)	5 (0.5)	7 (0.7)	5 (0.5)
胃腸障害	77 (6.7)	54 (4.8)	69 (6.3)	63 (5.8)	64 (6.0)	48 (4.6)	49 (4.7)
一般・全身障害および投与部位の状態	63 (5.5)	32 (2.8)	36 (3.3)	43 (4.0)	44 (4.1)	22 (2.1)	25 (2.4)
肝胆道系障害	11 (1.0)	7 (0.6)	1 (0.1)	6 (0.6)	4 (0.4)	6 (0.6)	3 (0.3)
免疫系障害	2 (0.2)	2 (0.2)	4 (0.4)	5 (0.5)	7 (0.7)	4 (0.4)	5 (0.5)
感染症および寄生虫症	113 (9.9)	99 (8.8)	90 (8.2)	80 (7.4)	80 (7.5)	103 (9.8)	65 (6.3)
傷害、中毒および処置合併症	23 (2.0)	26 (2.3)	9 (0.8)	24 (2.2)	24 (2.2)	15 (1.4)	23 (2.2)
臨床検査	64 (5.6)	51 (4.5)	33 (3.0)	63 (5.8)	51 (4.8)	40 (3.8)	25 (2.4)
代謝および栄養障害	28 (2.4)	21 (1.9)	15 (1.4)	12 (1.1)	20 (1.9)	13 (1.2)	10 (1.0)
筋骨格系および結合組織障害	65 (5.7)	70 (6.2)	46 (4.2)	54 (5.0)	44 (4.1)	59 (5.6)	43 (4.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	5 (0.4)	6 (0.5)	6 (0.5)	3 (0.3)	4 (0.4)	5 (0.5)	8 (0.8)
神経系障害	54 (4.7)	37 (3.3)	15 (1.4)	36 (3.3)	31 (2.9)	29 (2.8)	24 (2.3)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	18 (1.6)	19 (1.7)	11 (1.0)	13 (1.2)	12 (1.1)	14 (1.3)	9 (0.9)
腎および尿路障害	91 (8.0)	69 (6.1)	41 (3.7)	54 (5.0)	46 (4.3)	39 (3.7)	42 (4.0)
生殖系および乳房障害	15 (1.3)	11 (1.0)	9 (0.8)	11 (1.0)	13 (1.2)	9 (0.9)	7 (0.7)
呼吸器、胸郭および縦隔障害	25 (2.2)	31 (2.8)	26 (2.4)	26 (2.4)	12 (1.1)	16 (1.5)	12 (1.2)
皮膚および皮下組織障害	21 (1.8)	18 (1.6)	18 (1.6)	15 (1.4)	14 (1.3)	22 (2.1)	8 (0.8)
社会環境	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
外科および内科処置	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	51 (4.5)	47 (4.2)	23 (2.1)	42 (3.9)	36 (3.4)	33 (3.1)	21 (2.0)
TOTAL	36 (3.1)	22 (2.0)	10 (0.9)	12 (1.1)	12 (1.1)	7 (0.7)	1 (0.1)

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表2.7.4.7-41

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NT-8.7.1 Incidence of Treatment-emergent Adverse Events by System Organ Class by Period（海外の被験者）

System organ class	Total			
	27-30 Months (N=1029)	30-33 Months (N=1019)	33-36 Months (N=1008)	Post withdraw (N=1267)
	n (%)	n (%)	n (%)	n (%)
血液およびリンパ系障害	6 (0.6)	6 (0.6)	8 (0.8)	4 (0.3)
心臓障害	2 (0.2)	4 (0.4)	11 (1.1)	3 (0.2)
先天性、家族性および遺伝性障害	1 (0.1)	2 (0.2)	1 (0.1)	0 (0.0)
耳および迷路障害	3 (0.3)	4 (0.4)	2 (0.2)	1 (0.1)
内分泌障害	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.2)
眼障害	4 (0.4)	9 (0.9)	8 (0.8)	5 (0.4)
胃腸障害	43 (4.2)	44 (4.3)	50 (5.0)	25 (2.0)
一般・全身障害および投与部位の状態	28 (2.7)	18 (1.8)	41 (4.1)	15 (1.2)
肝胆道系障害	2 (0.2)	2 (0.2)	5 (0.5)	2 (0.2)
免疫系障害	3 (0.3)	2 (0.2)	1 (0.1)	1 (0.1)
感染症および寄生虫症	87 (8.5)	71 (7.0)	82 (8.1)	44 (3.5)
傷害、中毒および処置合併症	16 (1.6)	14 (1.4)	20 (2.0)	11 (0.9)
臨床検査	46 (4.5)	29 (2.8)	50 (5.0)	25 (2.0)
代謝および栄養障害	16 (1.6)	22 (2.2)	20 (2.0)	8 (0.6)
筋骨格系および結合組織障害	44 (4.3)	42 (4.1)	47 (4.7)	15 (1.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	5 (0.5)	3 (0.3)	5 (0.5)	1 (0.1)
神経系障害	23 (2.2)	19 (1.9)	30 (3.0)	13 (1.0)
妊娠、産褥および周産期の状態	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
精神障害	9 (0.9)	11 (1.1)	17 (1.7)	3 (0.2)
腎および尿路障害	27 (2.6)	33 (3.2)	45 (4.5)	17 (1.3)
生殖系および乳房障害	3 (0.3)	9 (0.9)	9 (0.9)	4 (0.3)
呼吸器、胸郭および縦隔障害	14 (1.4)	14 (1.4)	17 (1.7)	9 (0.7)
皮膚および皮下組織障害	15 (1.5)	14 (1.4)	12 (1.2)	12 (0.9)
社会環境	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
外科および内科処置	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	29 (2.8)	27 (2.6)	30 (3.0)	22 (1.7)
TOTAL	9 (0.9)	3 (0.3)	4 (0.4)	4 (0.3)

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