表 2.7.4.7-80. すべての有害事象（MedDRA SOC 及び PT 別，重症度別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	Adalimumab (N=55) n (%)
筋骨格系および結合組織障害 (Cont.)	
関節痛	4 (7.3)
Mild	4 (7.3)
背部痛	1 (1.8)
Moderate	1 (1.8)
成長不全	1 (1.8)
Moderate	1 (1.8)
若年性特発性関節炎	1 (1.8)
Mild	1 (1.8)
脊椎痛	1 (1.8)
Mild	1 (1.8)
神経系障害	6 (10.9)
Mild	6 (10.9)
頭痛	5 (9.1)
Mild	5 (9.1)

表 2.7.4.7-80.　すべての有害事象（MedDRA SOC 及び PT 別，重症度別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	Adalimumab (N=55) n (%)
神経系障害 (Cont.)	
傾眠	1 (1.8)
Mild	1 (1.8)
精神障害	2 (3.6)
Mild	1 (1.8)
Moderate	1 (1.8)
うつ病	2 (3.6)
Mild	1 (1.8)
Moderate	1 (1.8)
腎および尿路障害	3 (5.5)
Mild	3 (5.5)
血尿	1 (1.8)
Mild	1 (1.8)
腎結石症	1 (1.8)
Mild	1 (1.8)
腎仙痛	1 (1.8)
Mild	1 (1.8)

表 2.7.4.7-80. すべての有害事象（MedDRA SOC 及び PT 別，重症度別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	Adalimumab (N=55) n (%)
生殖系および乳房障害	3 (5.5)
Mild	2 (3.6)
Moderate	1 (1.8)
月経困難症	1 (1.8)
Mild	1 (1.8)
卵巣嚢胞	2 (3.6)
Mild	1 (1.8)
Moderate	1 (1.8)
呼吸器、胸郭および縦隔障害	4 (7.3)
Mild	4 (7.3)
喘息	1 (1.8)
Mild	1 (1.8)
鼻出血	1 (1.8)
Mild	1 (1.8)
アレルギー性鼻炎	2 (3.6)
Mild	2 (3.6)

表 2.7.4.7-80. すべての有害事象（MedDRA SOC 及び PT 別，重症度別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	Adalimumab (N=55) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)	
鼻漏	1 (1.8)
Mild	1 (1.8)
皮膚および皮下組織障害	4 (7.3)
Mild	4 (7.3)
乾癬様皮膚炎	1 (1.8)
Mild	1 (1.8)
乾癬	1 (1.8)
Mild	1 (1.8)
発疹	1 (1.8)
Mild	1 (1.8)
皮膚障害	1 (1.8)
Mild	1 (1.8)
血管障害	1 (1.8)
Mild	1 (1.8)

表 2.7.4.7-80.　すべての有害事象（MedDRA SOC 及び PT 別，重症度別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	Adalimumab (N=55) n (%)
血管障害 (Cont.)	
高血圧	1 (1.8)
Mild	1 (1.8)

Note: Table depicts the most servere adverse event for each preferred term as assessed for each subject. Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown severity, then the subject will be counted in the severity category of "unknown", even if the subject has another occurrence of the same event with a severity present. The only exception is if the subject has another occurrence of the same AE with the most extreme severity - "Severe". In this case, the subject will be counted under the "Severe" category.

Cross reference: M10-870 Main-study CSR_Interim Table 14.3__1.3.2

表 2.7.4.7-81. 導入療法期中に発現した重篤な有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
Any adverse event	5 (16.7)	4 (8.5)	1 (6.3)	10 (10.8)
血液およびリンパ系障害	2 (6.7)	0	0	2 (2.2)
貧血	2 (6.7)	0	0	2 (2.2)
心臓障害	1 (3.3)	0	0	1 (1.1)
心膜炎	1 (3.3)	0	0	1 (1.1)
胃腸障害	2 (6.7)	3 (6.4)	1 (6.3)	6 (6.5)
潰瘍性大腸炎	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
膵炎	0	1 (2.1)	0	1 (1.1)
傷害、中毒および処置合併症	0	1 (2.1)	0	1 (1.1)
手首関節骨折	0	1 (2.1)	0	1 (1.1)
神経系障害	1 (3.3)	0	0	1 (1.1)
頭痛	1 (3.3)	0	0	1 (1.1)
意識消失	1 (3.3)	0	0	1 (1.1)

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.1.1.1.1

表 2.7.4.7-82. 導入療法期中に発現した重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）
（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) (PYS=4.4) Events (E/100PY)	I-HD (N=47) (PYS=7.1) Events (E/100PY)	I-HD-OL (N=16) (PYS=2.3) Events (E/100PY)	Total (N=93) (PYS=13.9) Events (E/100PY)
Any adverse event	7 (159.1)	4 (56.3)	1 (43.5)	12 (86.3)
血液およびリンパ系障害	2 (45.5)	0	0	2 (14.4)
貧血	2 (45.5)	0	0	2 (14.4)
心臓障害	1 (22.7)	0	0	1 (7.2)
心膜炎	1 (22.7)	0	0	1 (7.2)
胃腸障害	2 (45.5)	3 (42.3)	1 (43.5)	6 (43.2)
潰瘍性大腸炎	2 (45.5)	2 (28.2)	1 (43.5)	5 (36.0)
膵炎	0	1 (14.1)	0	1 (7.2)
傷害、中毒および処置合併症	0	1 (14.1)	0	1 (7.2)
手首関節骨折	0	1 (14.1)	0	1 (7.2)
神経系障害	2 (45.5)	0	0	2 (14.4)
頭痛	1 (22.7)	0	0	1 (7.2)
意識消失	1 (22.7)	0	0	1 (7.2)

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: E/100PY = Events per 100 patient-years.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.1.1.2.1

表 2.7.4.7-83. 導入療法期中に発現した治験薬と関連ありの重篤な有害事象（MedDRA SOC 及び PT 別）
（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
Any adverse event	2 (6.7)	1 (2.1)	1 (6.3)	4 (4.3)
心臓障害	1 (3.3)	0	0	1 (1.1)
心膜炎	1 (3.3)	0	0	1 (1.1)
胃腸障害	0	1 (2.1)	1 (6.3)	2 (2.2)
潰瘍性大腸炎	0	0	1 (6.3)	1 (1.1)
膵炎	0	1 (2.1)	0	1 (1.1)
神経系障害	1 (3.3)	0	0	1 (1.1)
頭痛	1 (3.3)	0	0	1 (1.1)
意識消失	1 (3.3)	0	0	1 (1.1)

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.1.2.1.1

表 2.7.4.7-84. 維持療法期中に発現した重篤な有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
Any adverse event	4 (12.9)	5 (15.6)	9 (14.3)	1 (8.3)	10 (13.3)
血液およびリンパ系障害	1 (3.2)	0	1 (1.6)	0	1 (1.3)
貧血	1 (3.2)	0	1 (1.6)	0	1 (1.3)
胃腸障害	3 (9.7)	1 (3.1)	4 (6.3)	0	4 (5.3)
潰瘍性大腸炎	3 (9.7)	0	3 (4.8)	0	3 (4.0)
消化不良	0	1 (3.1)	1 (1.6)	0	1 (1.3)
小腸炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
感染症および寄生虫症	2 (6.5)	3 (9.4)	5 (7.9)	0	5 (6.7)
胃腸炎	2 (6.5)	0	2 (3.2)	0	2 (2.7)
無菌性髄膜炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
咽頭炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
尿路感染	0	1 (3.1)	1 (1.6)	0	1 (1.3)
傷害、中毒および処置合併症	0	1 (3.1)	1 (1.6)	0	1 (1.3)
手骨折	0	1 (3.1)	1 (1.6)	0	1 (1.3)
皮膚および皮下組織障害	0	1 (3.1)	1 (1.6)	1 (8.3)	2 (2.7)
結節性紅斑	0	1 (3.1)	1 (1.6)	0	1 (1.3)
乾癬	0	0	0	1 (8.3)	1 (1.3)

表 2.7.4.7-84.　維持療法期中に発現した重篤な有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.1.1.1.2

表 2.7.4.7-85. 維持療法期中に発現した重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) (PYS=20.2) Events (E/100PY)	M-HD (N=32) (PYS=21.2) Events (E/100PY)	Total-ADA (N=63) (PYS=41.4) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=75) (PYS=47.4) Events (E/100PY)
Any adverse event	9 (44.6)	6 (28.3)	15 (36.2)	1 (16.4)	16 (33.8)
血液およびリンパ系障害	2 (9.9)	0	2 (4.8)	0	2 (4.2)
貧血	2 (9.9)	0	2 (4.8)	0	2 (4.2)
胃腸障害	5 (24.8)	1 (4.7)	6 (14.5)	0	6 (12.7)
潰瘍性大腸炎	4 (19.8)	0	4 (9.7)	0	4 (8.4)
消化不良	0	1 (4.7)	1 (2.4)	0	1 (2.1)
小腸炎	1 (5.0)	0	1 (2.4)	0	1 (2.1)
感染症および寄生虫症	2 (9.9)	3 (14.2)	5 (12.1)	0	5 (10.5)
胃腸炎	2 (9.9)	0	2 (4.8)	0	2 (4.2)
無菌性髄膜炎	0	1 (4.7)	1 (2.4)	0	1 (2.1)
咽頭炎	0	1 (4.7)	1 (2.4)	0	1 (2.1)
尿路感染	0	1 (4.7)	1 (2.4)	0	1 (2.1)
傷害、中毒および処置合併症	0	1 (4.7)	1 (2.4)	0	1 (2.1)
手骨折	0	1 (4.7)	1 (2.4)	0	1 (2.1)
皮膚および皮下組織障害	0	1 (4.7)	1 (2.4)	1 (16.4)	2 (4.2)
結節性紅斑	0	1 (4.7)	1 (2.4)	0	1 (2.1)
乾癬	0	0	0	1 (16.4)	1 (2.1)

表 2.7.4.7-85.　維持療法期中に発現した重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: E/100PY = Events per 100 patient-years.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.1.1.2.2

表 2.7.4.7-86. 維持療法期中に発現した治験薬と関連ありの重篤な有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
Any adverse event	0	1 (3.1)	1 (1.6)	1 (8.3)	2 (2.7)
感染症および寄生虫症	0	1 (3.1)	1 (1.6)	0	1 (1.3)
無菌性髄膜炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
皮膚および皮下組織障害	0	0	0	1 (8.3)	1 (1.3)
乾癬	0	0	0	1 (8.3)	1 (1.3)

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.1.2.1.2

表 2.7.4.7-87.　重篤な有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
Any adverse event	8 (14.5)
血液およびリンパ系障害	2 (3.6)
貧血	2 (3.6)
失血性貧血	1 (1.8)
胃腸障害	3 (5.5)
潰瘍性大腸炎	2 (3.6)
大腸ポリープ	1 (1.8)
直腸出血	1 (1.8)
肝胆道系障害	1 (1.8)
胆嚢炎	1 (1.8)
感染症および寄生虫症	1 (1.8)
気管支炎	1 (1.8)
傷害、中毒および処置合併症	1 (1.8)
上肢骨折	1 (1.8)
筋骨格系および結合組織障害	1 (1.8)
成長不全	1 (1.8)
生殖系および乳房障害	1 (1.8)
卵巣嚢胞	1 (1.8)

表 2.7.4.7-87.　重篤な有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
呼吸器、胸郭および縦隔障害	1 (1.8)
喘息	1 (1.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M10-870 Main-study CSR_Interim Table 14.3__2.1.1.1

表 2.7.4.7-88.　重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) (PYS=79.8) Events (E/100PY)
Any adverse event	14 (17.5)
血液およびリンパ系障害	3 (3.8)
貧血	2 (2.5)
失血性貧血	1 (1.3)
胃腸障害	4 (5.0)
潰瘍性大腸炎	2 (2.5)
大腸ポリープ	1 (1.3)
直腸出血	1 (1.3)
肝胆道系障害	1 (1.3)
胆嚢炎	1 (1.3)
感染症および寄生虫症	1 (1.3)
気管支炎	1 (1.3)
傷害、中毒および処置合併症	1 (1.3)
上肢骨折	1 (1.3)
筋骨格系および結合組織障害	1 (1.3)
成長不全	1 (1.3)
生殖系および乳房障害	2 (2.5)
卵巣嚢胞	2 (2.5)

表 2.7.4.7-88. 重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) (PYS=79.8) Events (E/100PY)
呼吸器、胸郭および縦隔障害	1 (1.3)
喘息	1 (1.3)

PYS = sum((last dose date of ADA in study M10-870 - first dose date of ADA in study M10-870 + min([redacted]20[redacted] - last dose date of ADA in study M10-870 + 1, 14)) days)/365.25 for ongoing patients; otherwise =sum(last dose date of ADA in study M10-870 - first dose date of ADA in study M10-870 + 14 days)/365.25.
E/100PY = Events per 100 patient-years.

Cross reference: M10-870 Main-study CSR_Interim Table 14.3__2.1.1.2

表 2.7.4.7-89. 治験薬と関連ありの重篤な有害事象（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
Any adverse event	2 (3.6)
肝胆道系障害	1 (1.8)
胆嚢炎	1 (1.8)
生殖系および乳房障害	1 (1.8)
卵巣嚢胞	1 (1.8)

AEs with unknown relationship were counted as 'reasonable possibility of being related'.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M10-870 Main-study CSR_Interim Table 14.3__2.1.2.1

表 2.7.4.7-90.　導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（主試験安全性解析対象集団，M11-290 試験）

	I-SD (N=30) (PYS=4.4) Events (E/100PY)	I-HD (N=47) (PYS=7.1) Events (E/100PY)	I-HD-OL (N=16) (PYS=2.3) Events (E/100PY)	Total (N=93) (PYS=13.9) Events (E/100PY)
Any treatment-emergent				
Adverse event (AE)	43 (977.3)	57 (802.8)	31 (1347.8)	131 (942.4)
Serious AE	7 (159.1)	4 (56.3)	1 (43.5)	12 (86.3)
Severe AE	5 (113.6)	1 (14.1)	0	6 (43.2)
AEs leading to discontinuation of study drug	3 (68.2)	1 (14.1)	0	4 (28.8)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	7 (159.1)	15 (211.3)	2 (87.0)	24 (172.7)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (68.2)	1 (14.1)	1 (43.5)	5 (36.0)
AEs leading to Death	0	0	0	0
Infections	7 (159.1)	10 (140.8)	7 (304.3)	24 (172.7)
Serious infections	0	0	0	0
Legionella infections	0	0	0	0
Diverticulitis	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0

表 2.7.4.7-90. 導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（主試験安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=30) (PYS=4.4) Events (E/100PY)	I-HD (N=47) (PYS=7.1) Events (E/100PY)	I-HD-OL (N=16) (PYS=2.3) Events (E/100PY)	Total (N=93) (PYS=13.9) Events (E/100PY)
Oral candidiasis	0	0	0	0
Tuberculosis	0	0	0	0
Active tuberculosis	0	0	0	0
Latent tuberculosis	0	0	0	0
Parasitic infections	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0
Malignancies	0	0	0	0
Lymphoma	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0
Melanoma	0	0	0	0
Leukemia	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0

表 2.7.4.7-90. 導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（主試験安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=30) (PYS=4.4) Events (E/100PY)	I-HD (N=47) (PYS=7.1) Events (E/100PY)	I-HD-OL (N=16) (PYS=2.3) Events (E/100PY)	Total (N=93) (PYS=13.9) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	1 (14.1)	0	1 (7.2)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0
Vasculitis	0	0	0	0
Cutaneous vasculitis	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0
Sarcoidosis	0	0	0	0
Autoimmune Hepatitis	0	0	0	0
Myocardial infarction (MI)	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0
Pulmonary embolism	0	0	0	0
Interstitial lung disease	0	0	0	0
Intestinal perforation	0	0	0	0
Pancreatitis	0	1 (14.1)	0	1 (7.2)

表 2.7.4.7-90. 導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（主試験安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=30) (PYS=4.4) Events (E/100PY)	I-HD (N=47) (PYS=7.1) Events (E/100PY)	I-HD-OL (N=16) (PYS=2.3) Events (E/100PY)	Total (N=93) (PYS=13.9) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0
Erythema multiforme	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0
Demyelinating disorder	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0
Hematologic disorders including pancytopenia	3 (68.2)	3 (42.3)	1 (43.5)	7 (50.4)
Liver failure and other liver events	0	0	0	0
Humira administration related medication error	0	0	0	0
Injection site reaction	0	4 (56.3)	0	4 (28.8)
All deaths	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0
Occurring >70 days after last dose	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__1.1.2.1

表 2.7.4.7-91. 維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）

	M-SD (N=31) (PYS=20.2) Events (E/100PY)	M-HD (N=32) (PYS=21.2) Events (E/100PY)	Total-ADA (N=63) (PYS=41.4) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=75) (PYS=47.4) Events (E/100PY)
Any treatment-emergent					
Adverse event (AE)	73 (361.4)	69 (325.5)	142 (343.0)	26 (426.2)	168 (354.4)
Serious AE	9 (44.6)	6 (28.3)	15 (36.2)	1 (16.4)	16 (33.8)
Severe AE	5 (24.8)	1 (4.7)	6 (14.5)	0	6 (12.7)
AEs leading to discontinuation of study drug	3 (14.9)	0	3 (7.2)	0	3 (6.3)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	14 (69.3)	18 (84.9)	32 (77.3)	6 (98.4)	38 (80.2)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (4.7)	1 (2.4)	1 (16.4)	2 (4.2)
AEs leading to Death	0	0	0	0	0
Infections	17 (84.2)	19 (89.6)	36 (87.0)	9 (147.5)	45 (94.9)
Serious infections	2 (9.9)	3 (14.2)	5 (12.1)	0	5 (10.5)
Legionella infections	0	0	0	0	0
Diverticulitis	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0

表 2.7.4.7-91. 維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=31) (PYS=20.2) Events (E/100PY)	M-HD (N=32) (PYS=21.2) Events (E/100PY)	Total-ADA (N=63) (PYS=41.4) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=75) (PYS=47.4) Events (E/100PY)
Oral candidiasis	0	0	0	0	0
Tuberculosis	0	1 (4.7)	1 (2.4)	0	1 (2.1)
Active tuberculosis	0	0	0	0	0
Latent tuberculosis	0	1 (4.7)	1 (2.4)	0	1 (2.1)
Parasitic infections	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0
Malignancies	0	0	0	0	0
Lymphoma	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0
Melanoma	0	0	0	0	0
Leukemia	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0

表 2.7.4.7-91. 維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=31) (PYS=20.2) Events (E/100PY)	M-HD (N=32) (PYS=21.2) Events (E/100PY)	Total-ADA (N=63) (PYS=41.4) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=75) (PYS=47.4) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (9.9)	2 (9.4)	4 (9.7)	0	4 (8.4)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0
Vasculitis	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0
Sarcoidosis	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0
Intestinal perforation	0	0	0	0	0
Pancreatitis	0	0	0	0	0

表 2.7.4.7-91. 維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=31) (PYS=20.2) Events (E/100PY)	M-HD (N=32) (PYS=21.2) Events (E/100PY)	Total-ADA (N=63) (PYS=41.4) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=75) (PYS=47.4) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0
Erythema multiforme	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (16.4)	1 (2.1)
Demyelinating disorder	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0
Hematologic disorders including pancytopenia	5 (24.8)	1 (4.7)	6 (14.5)	2 (32.8)	8 (16.9)
Liver failure and other liver events	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0
Injection site reaction	6 (29.7)	3 (14.2)	9 (21.7)	0	9 (19.0)
All deaths	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0

表 2.7.4.7-91.　維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__1.1.2.2

表 2.7.4.7-92.　有害事象の 100 人年あたりの発現頻度の概要（主試験 FAS 集団，M10-870 試験）

	Adalimumab (N=55) (PYS=79.8) Events (E/100PY)
Any treatment-emergent	
Adverse event (AE)	139 (174.2)
Serious AE	14 (17.5)
Severe AE	3 (3.8)
AEs leading to discontinuation of study drug	2 (2.5)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	16 (20.1)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (3.8)
AEs leading to death	0
Infections	40 (50.1)
Serious infections	1 (1.3)
Legionella infections	0
Diverticulitis	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0
Oral candidiasis	0

表 2.7.4.7-92. 有害事象の 100 人年あたりの発現頻度の概要（主試験 FAS 集団，M10-870 試験）（続き）

	Adalimumab (N=55) (PYS=79.8) Events (E/100PY)
Tuberculosis	4 (5.0)
Active tuberculosis	0
Latent tuberculosis	4 (5.0)
Parasitic infections	0
Reactivation of Hepatitis B	0
Progressive multifocal leukoencephalopathy (PML)	0
Malignancies	0
Lymphoma	0
Hepatosplenic T-cell lymphoma (HSTCL)	0
Non-melanoma skin cancer (NMSC)	0
Melanoma	0
Leukemia	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0
Allergic reactions including angioedema/anaphylaxis	2 (2.5)
Lupus-like reactions and systemic lupus erythematosus	0

表 2.7.4.7-92. 有害事象の 100 人年あたりの発現頻度の概要（主試験 FAS 集団，M10-870 試験）（続き）

	Adalimumab (N=55) (PYS=79.8) Events (E/100PY)
Vasculitis	0
Cutaneous vasculitis	0
Non-cutaneous vasculitis	0
Sarcoidosis	0
Autoimmune Hepatitis	0
Myocardial infarction (MI)	0
Cerebrovascular accident (CVA)	0
Congestive heart failure (CHF)	0
Pulmonary embolism	0
Interstitial lung disease	0
Intestinal perforation	0
Pancreatitis	0
Stevens-Johnson syndrome	0
Erythema multiforme	0
Worsening or new onset of psoriasis	2 (2.5)

表 2.7.4.7-92.　有害事象の 100 人年あたりの発現頻度の概要（主試験 FAS 集団，M10-870 試験）（続き）

	Adalimumab (N=55) (PYS=79.8) Events (E/100PY)
Demyelinating disorder	0
Amyotrophic lateral sclerosis	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0
Hematologic disorders including pancytopenia	4 (5.0)
Liver failure and other liver events	0
Humira administration related medication error	0
Injection site reaction	0
All deaths	0
Occurring <=70 days after last dose	0
Occurring >70 days after last dose	0

Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug and up to 70 days after the last dose of the study drug.
PYS = sum((last dose date of ADA in study M10-870 - first dose date of ADA in study M10-870 + min([redacted]20[redacted] - last dose date of ADA in study M10-870 + 1, 14)) days)/365.25 for ongoing patients; otherwise = sum(last dose date of ADA in study M10-870 - first dose date of ADA in study M10-870 + 14 days)/365.25.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: M10-870 Main-study CSR_Interim Table 14.3__1.1.2

表 2.7.4.7-93.　導入療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=30) n (%)	I-HD (N=47) n (%)	I-HD-OL (N=16) n (%)	Total (N=93) n (%)
Any adverse event	6 (20.0)	8 (17.0)	6 (37.5)	20 (21.5)
感染症および寄生虫症	6 (20.0)	8 (17.0)	6 (37.5)	20 (21.5)
気管支炎	0	0	1 (6.3)	1 (1.1)
せつ	0	1 (2.1)	0	1 (1.1)
サルモネラ菌性胃腸炎	1 (3.3)	0	0	1 (1.1)
上咽頭炎	2 (6.7)	2 (4.3)	1 (6.3)	5 (5.4)
口腔ヘルペス	1 (3.3)	2 (4.3)	0	3 (3.2)
咽頭炎	2 (6.7)	1 (2.1)	1 (6.3)	4 (4.3)
レンサ球菌感染	0	0	1 (6.3)	1 (1.1)
上気道感染	0	1 (2.1)	0	1 (1.1)
尿路感染	1 (3.3)	0	0	1 (1.1)
水痘	0	1 (2.1)	0	1 (1.1)
ウイルス感染	0	0	1 (6.3)	1 (1.1)
ウイルス性上気道感染	0	1 (2.1)	0	1 (1.1)
外陰膣真菌感染	0	0	1 (6.3)	1 (1.1)

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.4.1.1

表 2.7.4.7-94.　維持療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=31) n (%)	M-HD (N=32) n (%)	Total-ADA (N=63) n (%)	M-PL (N=12) n (%)	Total (N=75) n (%)
Any adverse event	10 (32.3)	13 (40.6)	23 (36.5)	5 (41.7)	28 (37.3)
感染症および寄生虫症	10 (32.3)	13 (40.6)	23 (36.5)	5 (41.7)	28 (37.3)
気管支炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
胃腸炎	2 (6.5)	0	2 (3.2)	1 (8.3)	3 (4.0)
感染性嚢腫	0	1 (3.1)	1 (1.6)	0	1 (1.3)
インフルエンザ	0	1 (3.1)	1 (1.6)	0	1 (1.3)
喉頭炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
無菌性髄膜炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
上咽頭炎	3 (9.7)	4 (12.5)	7 (11.1)	1 (8.3)	8 (10.7)
口腔ヘルペス	0	1 (3.1)	1 (1.6)	0	1 (1.3)
中耳炎	0	1 (3.1)	1 (1.6)	0	1 (1.3)
咽頭炎	2 (6.5)	2 (6.3)	4 (6.3)	1 (8.3)	5 (6.7)
気道感染	1 (3.2)	0	1 (1.6)	0	1 (1.3)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.3)
鼻炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
癜風	1 (3.2)	0	1 (1.6)	0	1 (1.3)
歯膿瘍	0	0	0	1 (8.3)	1 (1.3)
気管炎	1 (3.2)	0	1 (1.6)	0	1 (1.3)
上気道感染	2 (6.5)	3 (9.4)	5 (7.9)	2 (16.7)	7 (9.3)
尿路感染	1 (3.2)	2 (6.3)	3 (4.8)	0	3 (4.0)
水痘	0	1 (3.1)	1 (1.6)	0	1 (1.3)

表 2.7.4.7-94.　維持療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた主試験安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 Main-study CSR_Interim Table 14.3__2.4.1.2

表 2.7.4.7-95.　すべての感染症（MedDRA SOC 及び PT 別）（主試験 FAS 集団，M10-870 試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab (N=55) n (%)
Any adverse event	20 (36.4)
感染症および寄生虫症	20 (36.4)
肛門膿瘍	1 (1.8)
気管支炎	3 (5.5)
ウイルス性胃腸炎	2 (3.6)
帯状疱疹	1 (1.8)
上咽頭炎	3 (5.5)
口腔ヘルペス	1 (1.8)
中耳炎	1 (1.8)
咽頭炎	2 (3.6)
副鼻腔炎	1 (1.8)
歯膿瘍	1 (1.8)
上気道感染	6 (10.9)
尿路感染	2 (3.6)
ウイルス感染	2 (3.6)
ウイルス性上気道感染	2 (3.6)
外陰膣炎	1 (1.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M10-870 Main-study CSR_Interim Table 14.3__2.4.1

表 2.7.4.7-96.　性別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Gender	
	Male (N=42) n (%)	Female (N=51) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	36 (85.7)	44 (86.3)
Serious AE	12 (28.6)	14 (27.5)
Severe AE	6 (14.3)	6 (11.8)
AEs leading to discontinuation of study drug	5 (11.9)	2 (3.9)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	20 (47.6)	17 (33.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	4 (9.5)	4 (7.8)
AEs leading to death	0	0
Infections	27 (64.3)	23 (45.1)
Serious infections	3 (7.1)	3 (5.9)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	1 (2.4)	0
Oral candidiasis	0	0
Tuberculosis	2 (4.8)	3 (5.9)
Active tuberculosis	0	0

表 2.7.4.7-96.　性別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Gender	
	Male (N=42) n (%)	Female (N=51) n (%)
Latent tuberculosis	2 (4.8)	3 (5.9)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	3 (7.1)	3 (5.9)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-96.　性別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Gender	
	Male (N=42) n (%)	Female (N=51) n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (2.4)	0
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	2 (4.8)	0
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	5 (11.9)	10 (19.6)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-96.　性別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Gender	
	Male (N=42) n (%)	Female (N=51) n (%)
Injection site reaction	3 (7.1)	5 (9.8)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.1

表 2.7.4.7-97.　　年齢区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Age Categories	
	< 13 Years (N=25) n (%)	>= 13 Years (N=68) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	22 (88.0)	58 (85.3)
Serious AE	5 (20.0)	21 (30.9)
Severe AE	1 (4.0)	11 (16.2)
AEs leading to discontinuation of study drug	1 (4.0)	6 (8.8)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	9 (36.0)	28 (41.2)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (8.0)	6 (8.8)
AEs leading to death	0	0
Infections	15 (60.0)	35 (51.5)
Serious infections	1 (4.0)	5 (7.4)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (1.5)
Oral candidiasis	0	0
Tuberculosis	1 (4.0)	4 (5.9)
Active tuberculosis	0	0

表 2.7.4.7-97. 年齢区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Age Categories	
	< 13 Years (N=25) n (%)	>= 13 Years (N=68) n (%)
Latent tuberculosis	1 (4.0)	4 (5.9)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	2 (8.0)	4 (5.9)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-97. 年齢区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Age Categories	
	< 13 Years (N=25) n (%)	>= 13 Years (N=68) n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (1.5)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (4.0)	1 (1.5)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	4 (16.0)	11 (16.2)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-97. 年齢区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
Injection site reaction	1 (4.0)	7 (10.3)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.2

表 2.7.4.7-98. 人種別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Race	
	White (N=88) n (%)	Non-White (N=5) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	75 (85.2)	5 (100)
Serious AE	24 (27.3)	2 (40.0)
Severe AE	11 (12.5)	1 (20.0)
AEs leading to discontinuation of study drug	7 (8.0)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	33 (37.5)	4 (80.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	7 (8.0)	1 (20.0)
AEs leading to death	0	0
Infections	47 (53.4)	3 (60.0)
Serious infections	6 (6.8)	0
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	1 (1.1)	0
Oral candidiasis	0	0
Tuberculosis	5 (5.7)	0
Active tuberculosis	0	0

表 2.7.4.7-98. 人種別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Race	
	White (N=88) n (%)	Non-White (N=5) n (%)
Latent tuberculosis	5 (5.7)	0
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	6 (6.8)	0
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-98.　人種別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Race	
	White (N=88) n (%)	Non-White (N=5) n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (1.1)	0
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	2 (2.3)	0
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	15 (17.0)	0
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-98. 人種別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Race	
	White (N=88) n (%)	Non-White (N=5) n (%)
Injection site reaction	7 (8.0)	1 (20.0)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.3

表 2.7.4.7-99.　　体重区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) n (%)	>= 40 kg (N=78) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	13 (86.7)	67 (85.9)
Serious AE	4 (26.7)	22 (28.2)
Severe AE	1 (6.7)	11 (14.1)
AEs leading to discontinuation of study drug	1 (6.7)	6 (7.7)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	7 (46.7)	30 (38.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (6.7)	7 (9.0)
AEs leading to death	0	0
Infections	7 (46.7)	43 (55.1)
Serious infections	2 (13.3)	4 (5.1)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (1.3)
Oral candidiasis	0	0
Tuberculosis	1 (6.7)	4 (5.1)
Active tuberculosis	0	0

表 2.7.4.7-99. 体重区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) n (%)	>= 40 kg (N=78) n (%)
Latent tuberculosis	1 (6.7)	4 (5.1)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	2 (13.3)	4 (5.1)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-99. 体重区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) n (%)	>= 40 kg (N=78) n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (1.3)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (6.7)	1 (1.3)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	2 (13.3)	13 (16.7)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-99. 体重区分別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) n (%)	>= 40 kg (N=78) n (%)
Injection site reaction	2 (13.3)	6 (7.7)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.4

表 2.7.4.7-100.　性別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Gender	
	Male (N=42) (PYS=68.6) Events (E/100PY)	Female (N=51) (PYS=76.4) Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	235 (342.6)	230 (301.0)
Serious AE	22 (32.1)	22 (28.8)
Severe AE	10 (14.6)	8 (10.5)
AEs leading to discontinuation of study drug	7 (10.2)	2 (2.6)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	47 (68.5)	32 (41.9)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	4 (5.8)	6 (7.9)
AEs leading to death	0	0
Infections	57 (83.1)	60 (78.5)
Serious infections	3 (4.4)	3 (3.9)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	1 (1.5)	0

表 2.7.4.7-100.　性別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Gender	
	Male (N=42) (PYS=68.6) Events (E/100PY)	Female (N=51) (PYS=76.4) Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	2 (2.9)	3 (3.9)
Active tuberculosis	0	0
Latent tuberculosis	2 (2.9)	3 (3.9)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-100.　性別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Gender	
	Male (N=42) (PYS=68.6) Events (E/100PY)	Female (N=51) (PYS=76.4) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	4 (5.8)	3 (3.9)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (1.5)	0

表 2.7.4.7-100.　性別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Gender	
	Male (N=42) (PYS=68.6) Events (E/100PY)	Female (N=51) (PYS=76.4) Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	2 (2.9)	0
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	7 (10.2)	11 (14.4)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	7 (10.2)	6 (7.9)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.2.2.1

表 2.7.4.7-101.　年齢区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Age Categories	
	< 13 Years (N=25) (PYS=46.5) Events (E/100PY)	>= 13 Years (N=68) (PYS=98.5) Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	156 (335.5)	309 (313.7)
Serious AE	12 (25.8)	32 (32.5)
Severe AE	2 (4.3)	16 (16.2)
AEs leading to discontinuation of study drug	1 (2.2)	8 (8.1)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	17 (36.6)	62 (62.9)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (4.3)	8 (8.1)
AEs leading to death	0	0
Infections	55 (118.3)	62 (62.9)
Serious infections	1 (2.2)	5 (5.1)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (1.0)

表 2.7.4.7-101. 年齢区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Age Categories	
	< 13 Years (N=25) (PYS=46.5) Events (E/100PY)	>= 13 Years (N=68) (PYS=98.5) Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	1 (2.2)	4 (4.1)
Active tuberculosis	0	0
Latent tuberculosis	1 (2.2)	4 (4.1)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-101. 年齢区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Age Categories	
	< 13 Years (N=25) (PYS=46.5) Events (E/100PY)	>= 13 Years (N=68) (PYS=98.5) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	3 (6.5)	4 (4.1)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (1.0)

表 2.7.4.7-101. 年齢区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Age Categories	
	< 13 Years (N=25) (PYS=46.5) Events (E/100PY)	>= 13 Years (N=68) (PYS=98.5) Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (2.2)	1 (1.0)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	4 (8.6)	14 (14.2)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	1 (2.2)	12 (12.2)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.2.2.2

表 2.7.4.7-102.　人種別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Race	
	White (N=88) (PYS=140.2) Events (E/100PY)	Non-White (N=5) (PYS=4.8) Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	425 (303.1)	40 (833.3)
Serious AE	42 (30.0)	2 (41.7)
Severe AE	17 (12.1)	1 (20.8)
AEs leading to discontinuation of study drug	9 (6.4)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	63 (44.9)	16 (333.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	9 (6.4)	1 (20.8)
AEs leading to death	0	0
Infections	112 (79.9)	5 (104.2)
Serious infections	6 (4.3)	0
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	1 (0.7)	0

表 2.7.4.7-102. 人種別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Race	
	White (N=88) (PYS=140.2) Events (E/100PY)	Non-White (N=5) (PYS=4.8) Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	5 (3.6)	0
Active tuberculosis	0	0
Latent tuberculosis	5 (3.6)	0
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-102. 人種別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Race	
	White (N=88) (PYS=140.2) Events (E/100PY)	Non-White (N=5) (PYS=4.8) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	7 (5.0)	0
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (0.7)	0

表 2.7.4.7-102. 人種別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Race	
	White (N=88) (PYS=140.2) Events (E/100PY)	Non-White (N=5) (PYS=4.8) Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	2 (1.4)	0
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	18 (12.8)	0
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	10 (7.1)	3 (62.5)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.2.2.3

表 2.7.4.7-103.　体重区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) (PYS=30.8) Events (E/100PY)	>= 40 kg (N=78) (PYS=114.2) Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	84 (272.7)	381 (333.6)
Serious AE	12 (39.0)	32 (28.0)
Severe AE	2 (6.5)	16 (14.0)
AEs leading to discontinuation of study drug	1 (3.2)	8 (7.0)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	14 (45.5)	65 (56.9)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (3.2)	9 (7.9)
AEs leading to death	0	0
Infections	20 (64.9)	97 (84.9)
Serious infections	2 (6.5)	4 (3.5)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (0.9)

表 2.7.4.7-103. 体重区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) (PYS=30.8) Events (E/100PY)	>= 40 kg (N=78) (PYS=114.2) Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	1 (3.2)	4 (3.5)
Active tuberculosis	0	0
Latent tuberculosis	1 (3.2)	4 (3.5)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-103. 体重区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) (PYS=30.8) Events (E/100PY)	>= 40 kg (N=78) (PYS=114.2) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (6.5)	5 (4.4)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (0.9)

表 2.7.4.7-103. 体重区分別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Weight	
	< 40 kg (N=15) (PYS=30.8) Events (E/100PY)	>= 40 kg (N=78) (PYS=114.2) Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (3.2)	1 (0.9)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	2 (6.5)	16 (14.0)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	3 (9.7)	10 (8.8)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.2.2.4

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
Any adverse event	36 (85.7)	44 (86.3)
血液およびリンパ系障害	7 (16.7)	12 (23.5)
貧血	5 (11.9)	10 (19.6)
失血性貧血	0	1 (2.0)
鉄欠乏性貧血	2 (4.8)	0
リンパ節炎	0	1 (2.0)
リンパ節症	0	1 (2.0)
血小板増加症	0	1 (2.0)
心臓障害	1 (2.4)	0
心膜炎	1 (2.4)	0
耳および迷路障害	0	1 (2.0)
耳痛	0	1 (2.0)
内分泌障害	0	1 (2.0)
甲状腺腫	0	1 (2.0)
眼障害	1 (2.4)	1 (2.0)
角膜炎	0	1 (2.0)
非感染性結膜炎	1 (2.4)	0

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
胃腸障害	25 (59.5)	22 (43.1)
腹部不快感	1 (2.4)	0
腹痛	3 (7.1)	3 (5.9)
上腹部痛	3 (7.1)	3 (5.9)
アフタ性潰瘍	1 (2.4)	0
口唇症	0	1 (2.0)
潰瘍性大腸炎	16 (38.1)	13 (25.5)
便秘	0	3 (5.9)
下痢	1 (2.4)	2 (3.9)
血性下痢	1 (2.4)	0
消化不良	1 (2.4)	1 (2.0)
小腸炎	2 (4.8)	1 (2.0)
腸炎	0	1 (2.0)
鼓腸	1 (2.4)	0
排便回数増加	1 (2.4)	0
胃炎	1 (2.4)	2 (3.9)
胃食道逆流性疾患	1 (2.4)	1 (2.0)

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
胃腸障害 (Cont.)		
血便排泄	4 (9.5)	0
大腸ポリープ	2 (4.8)	0
悪心	3 (7.1)	2 (3.9)
膵炎	1 (2.4)	0
直腸出血	0	1 (2.0)
嘔吐	3 (7.1)	1 (2.0)
一般・全身障害および投与部位の状態	6 (14.3)	12 (23.5)
腋窩痛	0	1 (2.0)
胸痛	0	1 (2.0)
疲労	2 (4.8)	1 (2.0)
炎症	1 (2.4)	0
インフルエンザ様疾患	1 (2.4)	0
注射部位紅斑	0	1 (2.0)
注射部位炎症	0	1 (2.0)
注射部位浮腫	1 (2.4)	0
注射部位疼痛	1 (2.4)	1 (2.0)
注射部位そう痒感	0	1 (2.0)

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	1 (2.4)	0
注射部位蕁麻疹	0	2 (3.9)
倦怠感	0	1 (2.0)
末梢性浮腫	0	1 (2.0)
末梢腫脹	1 (2.4)	0
発熱	1 (2.4)	4 (7.8)
肝胆道系障害	2 (4.8)	0
胆嚢炎	1 (2.4)	0
高ビリルビン血症	1 (2.4)	0
免疫系障害	1 (2.4)	1 (2.0)
薬物過敏症	0	1 (2.0)
季節性アレルギー	1 (2.4)	0
感染症および寄生虫症	27 (64.3)	23 (45.1)
肛門膿瘍	1 (2.4)	0
気管支炎	4 (9.5)	1 (2.0)
クロストリジウム・ディフィシレ感染	1 (2.4)	0
サイトメガロウイルス性腸炎	1 (2.4)	0

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
感染症および寄生虫症 (Cont.)		
せつ	0	1 (2.0)
胃腸炎	2 (4.8)	1 (2.0)
サルモネラ菌性胃腸炎	1 (2.4)	0
ウイルス性胃腸炎	1 (2.4)	1 (2.0)
帯状疱疹	0	1 (2.0)
膿痂疹	1 (2.4)	0
感染性嚢腫	0	1 (2.0)
インフルエンザ	1 (2.4)	0
喉頭炎	0	1 (2.0)
無菌性髄膜炎	0	1 (2.0)
上咽頭炎	4 (9.5)	7 (13.7)
口腔ヘルペス	1 (2.4)	2 (3.9)
中耳炎	0	1 (2.0)
咽頭炎	5 (11.9)	6 (11.8)
気道感染	2 (4.8)	0
ウイルス性気道感染	1 (2.4)	0
鼻炎	1 (2.4)	0

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	0	1 (2.0)
レンサ球菌感染	1 (2.4)	0
癜風	1 (2.4)	0
扁桃炎	0	1 (2.0)
歯膿瘍	1 (2.4)	1 (2.0)
気管炎	1 (2.4)	0
上気道感染	10 (23.8)	4 (7.8)
尿路感染	3 (7.1)	4 (7.8)
水痘	1 (2.4)	1 (2.0)
ウイルス感染	2 (4.8)	1 (2.0)
ウイルス性上気道感染	2 (4.8)	1 (2.0)
外陰腟真菌感染	0	1 (2.0)
外陰腟炎	0	1 (2.0)
傷害、中毒および処置合併症	7 (16.7)	4 (7.8)
足関節部骨折	1 (2.4)	0
節足動物咬傷	1 (2.4)	0
転倒	1 (2.4)	0

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	1 (2.4)	1 (2.0)
注入に伴う反応	1 (2.4)	0
靱帯捻挫	0	1 (2.0)
四肢損傷	0	1 (2.0)
処置による疼痛	0	1 (2.0)
上肢骨折	1 (2.4)	0
手首関節骨折	2 (4.8)	0
臨床検査	10 (23.8)	8 (15.7)
血中アルカリホスファターゼ増加	1 (2.4)	0
血中ビリルビン増加	1 (2.4)	1 (2.0)
血中カルシウム減少	1 (2.4)	0
血圧上昇	1 (2.4)	0
血中ナトリウム減少	1 (2.4)	0
体温上昇	0	1 (2.0)
骨密度減少	0	1 (2.0)
Ｃ－反応性蛋白増加	4 (9.5)	1 (2.0)
好酸球数増加	1 (2.4)	0

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	1 (2.4)	0
ヘモグロビン減少	1 (2.4)	0
肝酵素上昇	1 (2.4)	0
リンパ節触知	0	1 (2.0)
結核菌群検査陽性	2 (4.8)	3 (5.9)
好中球数減少	1 (2.4)	0
体重減少	1 (2.4)	1 (2.0)
白血球数減少	1 (2.4)	0
筋骨格系および結合組織障害	6 (14.3)	6 (11.8)
関節痛	2 (4.8)	3 (5.9)
背部痛	1 (2.4)	2 (3.9)
成長不全	1 (2.4)	0
若年性特発性関節炎	0	1 (2.0)
靭帯障害	1 (2.4)	0
四肢痛	1 (2.4)	0
脊椎痛	1 (2.4)	0

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
神経系障害	11 (26.2)	15 (29.4)
頭痛	10 (23.8)	13 (25.5)
感覚鈍麻	0	1 (2.0)
意識消失	0	1 (2.0)
片頭痛	1 (2.4)	0
錯感覚	1 (2.4)	1 (2.0)
傾眠	0	1 (2.0)
振戦	0	2 (3.9)
精神障害	2 (4.8)	2 (3.9)
うつ病	2 (4.8)	2 (3.9)
腎および尿路障害	2 (4.8)	2 (3.9)
糖尿	0	1 (2.0)
血尿	1 (2.4)	0
腎結石症	0	1 (2.0)
腎仙痛	1 (2.4)	0
生殖系および乳房障害	0	5 (9.8)
乳房痛	0	1 (2.0)
月経困難症	0	2 (3.9)

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
生殖系および乳房障害（Cont.）		
卵巣嚢胞	0	2 (3.9)
呼吸器、胸郭および縦隔障害	11 (26.2)	9 (17.6)
喘息	2 (4.8)	0
咳嗽	3 (7.1)	1 (2.0)
鼻出血	2 (4.8)	1 (2.0)
鼻閉	2 (4.8)	0
鼻浮腫	0	1 (2.0)
口腔咽頭痛	4 (9.5)	3 (5.9)
アレルギー性鼻炎	1 (2.4)	2 (3.9)
鼻漏	1 (2.4)	3 (5.9)
喘鳴	1 (2.4)	0
皮膚および皮下組織障害	8 (19.0)	7 (13.7)
脱毛症	0	1 (2.0)
皮膚炎	1 (2.4)	1 (2.0)
乾癬様皮膚炎	1 (2.4)	0
紅斑	0	1 (2.0)
結節性紅斑	1 (2.4)	2 (3.9)

表 2.7.4.7-104.　性別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Gender Male (N=42) n (%)	Any Adalimumab Gender Female (N=51) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	1 (2.4)	0
乾癬	1 (2.4)	0
発疹	3 (7.1)	2 (3.9)
痂皮	0	1 (2.0)
脂漏	1 (2.4)	0
皮膚障害	1 (2.4)	0
皮膚病変	0	1 (2.0)
血管障害	1 (2.4)	0
高血圧	1 (2.4)	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.1

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
Any adverse event	22 (88.0)	58 (85.3)
血液およびリンパ系障害	5 (20.0)	14 (20.6)
貧血	4 (16.0)	11 (16.2)
失血性貧血	0	1 (1.5)
鉄欠乏性貧血	0	2 (2.9)
リンパ節炎	0	1 (1.5)
リンパ節症	1 (4.0)	0
血小板増加症	1 (4.0)	0
心臓障害	0	1 (1.5)
心膜炎	0	1 (1.5)
耳および迷路障害	1 (4.0)	0
耳痛	1 (4.0)	0
内分泌障害	0	1 (1.5)
甲状腺腫	0	1 (1.5)
眼障害	1 (4.0)	1 (1.5)
角膜炎	0	1 (1.5)
非感染性結膜炎	1 (4.0)	0

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
胃腸障害	11 (44.0)	36 (52.9)
腹部不快感	0	1 (1.5)
腹痛	1 (4.0)	5 (7.4)
上腹部痛	2 (8.0)	4 (5.9)
アフタ性潰瘍	0	1 (1.5)
口唇症	1 (4.0)	0
潰瘍性大腸炎	7 (28.0)	22 (32.4)
便秘	1 (4.0)	2 (2.9)
下痢	2 (8.0)	1 (1.5)
血性下痢	0	1 (1.5)
消化不良	0	2 (2.9)
小腸炎	1 (4.0)	2 (2.9)
腸炎	1 (4.0)	0
鼓腸	0	1 (1.5)
排便回数増加	0	1 (1.5)
胃炎	1 (4.0)	2 (2.9)
胃食道逆流性疾患	0	2 (2.9)

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
胃腸障害 (Cont.)		
血便排泄	2 (8.0)	2 (2.9)
大腸ポリープ	1 (4.0)	1 (1.5)
悪心	2 (8.0)	3 (4.4)
膵炎	0	1 (1.5)
直腸出血	0	1 (1.5)
嘔吐	3 (12.0)	1 (1.5)
一般・全身障害および投与部位の状態	4 (16.0)	14 (20.6)
腋窩痛	0	1 (1.5)
胸痛	0	1 (1.5)
疲労	1 (4.0)	2 (2.9)
炎症	0	1 (1.5)
インフルエンザ様疾患	0	1 (1.5)
注射部位紅斑	0	1 (1.5)
注射部位炎症	0	1 (1.5)
注射部位浮腫	0	1 (1.5)
注射部位疼痛	0	2 (2.9)
注射部位そう痒感	0	1 (1.5)

表 2.7.4.7-105. 年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	1 (4.0)	0
注射部位蕁麻疹	0	2 (2.9)
倦怠感	0	1 (1.5)
末梢性浮腫	0	1 (1.5)
末梢腫脹	0	1 (1.5)
発熱	2 (8.0)	3 (4.4)
肝胆道系障害	0	2 (2.9)
胆嚢炎	0	1 (1.5)
高ビリルビン血症	0	1 (1.5)
免疫系障害	1 (4.0)	1 (1.5)
薬物過敏症	0	1 (1.5)
季節性アレルギー	1 (4.0)	0
感染症および寄生虫症	15 (60.0)	35 (51.5)
肛門膿瘍	0	1 (1.5)
気管支炎	3 (12.0)	2 (2.9)
クロストリジウム・ディフィシレ感染	0	1 (1.5)
サイトメガロウイルス性腸炎	0	1 (1.5)

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
感染症および寄生虫症 (Cont.)		
せつ	0	1 (1.5)
胃腸炎	1 (4.0)	2 (2.9)
サルモネラ菌性胃腸炎	0	1 (1.5)
ウイルス性胃腸炎	2 (8.0)	0
帯状疱疹	0	1 (1.5)
膿痂疹	1 (4.0)	0
感染性嚢腫	1 (4.0)	0
インフルエンザ	0	1 (1.5)
喉頭炎	1 (4.0)	0
無菌性髄膜炎	0	1 (1.5)
上咽頭炎	8 (32.0)	3 (4.4)
口腔ヘルペス	1 (4.0)	2 (2.9)
中耳炎	1 (4.0)	0
咽頭炎	3 (12.0)	8 (11.8)
気道感染	1 (4.0)	1 (1.5)
ウイルス性気道感染	0	1 (1.5)
鼻炎	0	1 (1.5)

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	1 (4.0)	0
レンサ球菌感染	0	1 (1.5)
癜風	1 (4.0)	0
扁桃炎	0	1 (1.5)
歯膿瘍	1 (4.0)	1 (1.5)
気管炎	1 (4.0)	0
上気道感染	4 (16.0)	10 (14.7)
尿路感染	3 (12.0)	4 (5.9)
水痘	0	2 (2.9)
ウイルス感染	1 (4.0)	2 (2.9)
ウイルス性上気道感染	1 (4.0)	2 (2.9)
外陰腟真菌感染	1 (4.0)	0
外陰腟炎	0	1 (1.5)
傷害、中毒および処置合併症	4 (16.0)	7 (10.3)
足関節部骨折	0	1 (1.5)
節足動物咬傷	0	1 (1.5)
転倒	0	1 (1.5)

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	2 (8.0)	0
注入に伴う反応	0	1 (1.5)
靱帯捻挫	1 (4.0)	0
四肢損傷	0	1 (1.5)
処置による疼痛	0	1 (1.5)
上肢骨折	1 (4.0)	0
手首関節骨折	1 (4.0)	1 (1.5)
臨床検査	4 (16.0)	14 (20.6)
血中アルカリホスファターゼ増加	0	1 (1.5)
血中ビリルビン増加	0	2 (2.9)
血中カルシウム減少	1 (4.0)	0
血圧上昇	0	1 (1.5)
血中ナトリウム減少	0	1 (1.5)
体温上昇	1 (4.0)	0
骨密度減少	1 (4.0)	0
Ｃ－反応性蛋白増加	1 (4.0)	4 (5.9)
好酸球数増加	0	1 (1.5)

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	0	1 (1.5)
ヘモグロビン減少	0	1 (1.5)
肝酵素上昇	0	1 (1.5)
リンパ節触知	0	1 (1.5)
結核菌群検査陽性	1 (4.0)	4 (5.9)
好中球数減少	1 (4.0)	0
体重減少	0	2 (2.9)
白血球数減少	1 (4.0)	0
筋骨格系および結合組織障害	2 (8.0)	10 (14.7)
関節痛	0	5 (7.4)
背部痛	1 (4.0)	2 (2.9)
成長不全	1 (4.0)	0
若年性特発性関節炎	0	1 (1.5)
靭帯障害	0	1 (1.5)
四肢痛	0	1 (1.5)
脊椎痛	0	1 (1.5)

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
神経系障害	8 (32.0)	18 (26.5)
頭痛	8 (32.0)	15 (22.1)
感覚鈍麻	0	1 (1.5)
意識消失	0	1 (1.5)
片頭痛	0	1 (1.5)
錯感覚	0	2 (2.9)
傾眠	0	1 (1.5)
振戦	1 (4.0)	1 (1.5)
精神障害	1 (4.0)	3 (4.4)
うつ病	1 (4.0)	3 (4.4)
腎および尿路障害	1 (4.0)	3 (4.4)
糖尿	1 (4.0)	0
血尿	0	1 (1.5)
腎結石症	0	1 (1.5)
腎仙痛	0	1 (1.5)
生殖系および乳房障害	3 (12.0)	2 (2.9)
乳房痛	0	1 (1.5)
月経困難症	2 (8.0)	0

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
生殖系および乳房障害 (Cont.)		
卵巣嚢胞	1 (4.0)	1 (1.5)
呼吸器、胸郭および縦隔障害	7 (28.0)	13 (19.1)
喘息	2 (8.0)	0
咳嗽	1 (4.0)	3 (4.4)
鼻出血	1 (4.0)	2 (2.9)
鼻閉	0	2 (2.9)
鼻浮腫	0	1 (1.5)
口腔咽頭痛	1 (4.0)	6 (8.8)
アレルギー性鼻炎	1 (4.0)	2 (2.9)
鼻漏	2 (8.0)	2 (2.9)
喘鳴	0	1 (1.5)
皮膚および皮下組織障害	4 (16.0)	11 (16.2)
脱毛症	0	1 (1.5)
皮膚炎	1 (4.0)	1 (1.5)
乾癬様皮膚炎	1 (4.0)	0
紅斑	1 (4.0)	0
結節性紅斑	1 (4.0)	2 (2.9)

表 2.7.4.7-105.　年齢区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Age Categories < 13 Years (N=25) n (%)	Any Adalimumab Age Categories >= 13 Years (N=68) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	0	1 (1.5)
乾癬	0	1 (1.5)
発疹	1 (4.0)	4 (5.9)
痂皮	0	1 (1.5)
脂漏	1 (4.0)	0
皮膚障害	0	1 (1.5)
皮膚病変	0	1 (1.5)
血管障害	0	1 (1.5)
高血圧	0	1 (1.5)

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.2

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
Any adverse event	75 (85.2)	5 (100)
血液およびリンパ系障害	18 (20.5)	1 (20.0)
貧血	15 (17.0)	0
失血性貧血	1 (1.1)	0
鉄欠乏性貧血	1 (1.1)	1 (20.0)
リンパ節炎	1 (1.1)	0
リンパ節症	1 (1.1)	0
血小板増加症	1 (1.1)	0
心臓障害	1 (1.1)	0
心膜炎	1 (1.1)	0
耳および迷路障害	1 (1.1)	0
耳痛	1 (1.1)	0
内分泌障害	1 (1.1)	0
甲状腺腫	1 (1.1)	0
眼障害	2 (2.3)	0
角膜炎	1 (1.1)	0
非感染性結膜炎	1 (1.1)	0

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
胃腸障害	43 (48.9)	4 (80.0)
腹部不快感	1 (1.1)	0
腹痛	6 (6.8)	0
上腹部痛	5 (5.7)	1 (20.0)
アフタ性潰瘍	0	1 (20.0)
口唇症	1 (1.1)	0
潰瘍性大腸炎	26 (29.5)	3 (60.0)
便秘	2 (2.3)	1 (20.0)
下痢	3 (3.4)	0
血性下痢	1 (1.1)	0
消化不良	2 (2.3)	0
小腸炎	3 (3.4)	0
腸炎	1 (1.1)	0
鼓腸	1 (1.1)	0
排便回数増加	0	1 (20.0)
胃炎	3 (3.4)	0
胃食道逆流性疾患	2 (2.3)	0

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
胃腸障害 (Cont.)		
血便排泄	3 (3.4)	1 (20.0)
大腸ポリープ	2 (2.3)	0
悪心	4 (4.5)	1 (20.0)
膵炎	1 (1.1)	0
直腸出血	1 (1.1)	0
嘔吐	2 (2.3)	2 (40.0)
一般・全身障害および投与部位の状態	17 (19.3)	1 (20.0)
腋窩痛	1 (1.1)	0
胸痛	1 (1.1)	0
疲労	2 (2.3)	1 (20.0)
炎症	1 (1.1)	0
インフルエンザ様疾患	1 (1.1)	0
注射部位紅斑	1 (1.1)	0
注射部位炎症	1 (1.1)	0
注射部位浮腫	1 (1.1)	0
注射部位疼痛	1 (1.1)	1 (20.0)
注射部位そう痒感	1 (1.1)	0

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	1 (1.1)	0
注射部位蕁麻疹	2 (2.3)	0
倦怠感	1 (1.1)	0
末梢性浮腫	1 (1.1)	0
末梢腫脹	1 (1.1)	0
発熱	4 (4.5)	1 (20.0)
肝胆道系障害	2 (2.3)	0
胆嚢炎	1 (1.1)	0
高ビリルビン血症	1 (1.1)	0
免疫系障害	2 (2.3)	0
薬物過敏症	1 (1.1)	0
季節性アレルギー	1 (1.1)	0
感染症および寄生虫症	47 (53.4)	3 (60.0)
肛門膿瘍	1 (1.1)	0
気管支炎	5 (5.7)	0
クロストリジウム・ディフィシレ感染	1 (1.1)	0
サイトメガロウイルス性腸炎	1 (1.1)	0

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
感染症および寄生虫症 (Cont.)		
せつ	1 (1.1)	0
胃腸炎	3 (3.4)	0
サルモネラ菌性胃腸炎	1 (1.1)	0
ウイルス性胃腸炎	2 (2.3)	0
帯状疱疹	1 (1.1)	0
膿痂疹	1 (1.1)	0
感染性嚢腫	1 (1.1)	0
インフルエンザ	1 (1.1)	0
喉頭炎	1 (1.1)	0
無菌性髄膜炎	1 (1.1)	0
上咽頭炎	11 (12.5)	0
口腔ヘルペス	3 (3.4)	0
中耳炎	1 (1.1)	0
咽頭炎	11 (12.5)	0
気道感染	2 (2.3)	0
ウイルス性気道感染	0	1 (20.0)
鼻炎	1 (1.1)	0

表 2.7.4.7-106.　人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	1 (1.1)	0
レンサ球菌感染	1 (1.1)	0
癜風	1 (1.1)	0
扁桃炎	1 (1.1)	0
歯膿瘍	2 (2.3)	0
気管炎	1 (1.1)	0
上気道感染	13 (14.8)	1 (20.0)
尿路感染	7 (8.0)	0
水痘	2 (2.3)	0
ウイルス感染	2 (2.3)	1 (20.0)
ウイルス性上気道感染	3 (3.4)	0
外陰腟真菌感染	0	1 (20.0)
外陰腟炎	1 (1.1)	0
傷害、中毒および処置合併症	9 (10.2)	2 (40.0)
足関節部骨折	0	1 (20.0)
節足動物咬傷	1 (1.1)	0
転倒	0	1 (20.0)

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	2 (2.3)	0
注入に伴う反応	1 (1.1)	0
靱帯捻挫	1 (1.1)	0
四肢損傷	1 (1.1)	0
処置による疼痛	1 (1.1)	0
上肢骨折	1 (1.1)	0
手首関節骨折	2 (2.3)	0
臨床検査	16 (18.2)	2 (40.0)
血中アルカリホスファターゼ増加	1 (1.1)	0
血中ビリルビン増加	2 (2.3)	0
血中カルシウム減少	1 (1.1)	0
血圧上昇	1 (1.1)	0
血中ナトリウム減少	0	1 (20.0)
体温上昇	1 (1.1)	0
骨密度減少	1 (1.1)	0
Ｃ－反応性蛋白増加	3 (3.4)	2 (40.0)
好酸球数増加	0	1 (20.0)

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	1 (1.1)	0
ヘモグロビン減少	1 (1.1)	0
肝酵素上昇	1 (1.1)	0
リンパ節触知	1 (1.1)	0
結核菌群検査陽性	5 (5.7)	0
好中球数減少	1 (1.1)	0
体重減少	1 (1.1)	1 (20.0)
白血球数減少	1 (1.1)	0
筋骨格系および結合組織障害	11 (12.5)	1 (20.0)
関節痛	5 (5.7)	0
背部痛	3 (3.4)	0
成長不全	1 (1.1)	0
若年性特発性関節炎	1 (1.1)	0
靭帯障害	1 (1.1)	0
四肢痛	0	1 (20.0)
脊椎痛	1 (1.1)	0

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
神経系障害	23 (26.1)	3 (60.0)
頭痛	21 (23.9)	2 (40.0)
感覚鈍麻	1 (1.1)	0
意識消失	1 (1.1)	0
片頭痛	0	1 (20.0)
錯感覚	1 (1.1)	1 (20.0)
傾眠	1 (1.1)	0
振戦	2 (2.3)	0
精神障害	4 (4.5)	0
うつ病	4 (4.5)	0
腎および尿路障害	4 (4.5)	0
糖尿	1 (1.1)	0
血尿	1 (1.1)	0
腎結石症	1 (1.1)	0
腎仙痛	1 (1.1)	0
生殖系および乳房障害	5 (5.7)	0
乳房痛	1 (1.1)	0
月経困難症	2 (2.3)	0

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
生殖系および乳房障害 (Cont.)		
卵巣嚢胞	2 (2.3)	0
呼吸器、胸郭および縦隔障害	18 (20.5)	2 (40.0)
喘息	2 (2.3)	0
咳嗽	4 (4.5)	0
鼻出血	3 (3.4)	0
鼻閉	2 (2.3)	0
鼻浮腫	1 (1.1)	0
口腔咽頭痛	6 (6.8)	1 (20.0)
アレルギー性鼻炎	3 (3.4)	0
鼻漏	4 (4.5)	0
喘鳴	0	1 (20.0)
皮膚および皮下組織障害	15 (17.0)	0
脱毛症	1 (1.1)	0
皮膚炎	2 (2.3)	0
乾癬様皮膚炎	1 (1.1)	0
紅斑	1 (1.1)	0
結節性紅斑	3 (3.4)	0

表 2.7.4.7-106. 人種別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Race White (N=88) n (%)	Any Adalimumab Race Non-White (N=5) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	1 (1.1)	0
乾癬	1 (1.1)	0
発疹	5 (5.7)	0
痂皮	1 (1.1)	0
脂漏	1 (1.1)	0
皮膚障害	1 (1.1)	0
皮膚病変	1 (1.1)	0
血管障害	1 (1.1)	0
高血圧	1 (1.1)	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.3

表 2.7.4.7-107.　体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
Any adverse event	13 (86.7)	67 (85.9)
血液およびリンパ系障害	3 (20.0)	16 (20.5)
貧血	2 (13.3)	13 (16.7)
失血性貧血	0	1 (1.3)
鉄欠乏性貧血	0	2 (2.6)
リンパ節炎	0	1 (1.3)
リンパ節症	1 (6.7)	0
血小板増加症	1 (6.7)	0
心臓障害	0	1 (1.3)
心膜炎	0	1 (1.3)
耳および迷路障害	1 (6.7)	0
耳痛	1 (6.7)	0
内分泌障害	0	1 (1.3)
甲状腺腫	0	1 (1.3)
眼障害	0	2 (2.6)
角膜炎	0	1 (1.3)
非感染性結膜炎	0	1 (1.3)

表 2.7.4.7-107.　体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
胃腸障害	7 (46.7)	40 (51.3)
腹部不快感	0	1 (1.3)
腹痛	0	6 (7.7)
上腹部痛	1 (6.7)	5 (6.4)
アフタ性潰瘍	0	1 (1.3)
口唇症	1 (6.7)	0
潰瘍性大腸炎	4 (26.7)	25 (32.1)
便秘	0	3 (3.8)
下痢	1 (6.7)	2 (2.6)
血性下痢	0	1 (1.3)
消化不良	0	2 (2.6)
小腸炎	1 (6.7)	2 (2.6)
腸炎	1 (6.7)	0
鼓腸	0	1 (1.3)
排便回数増加	0	1 (1.3)
胃炎	1 (6.7)	2 (2.6)
胃食道逆流性疾患	0	2 (2.6)

表 2.7.4.7-107.　体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
胃腸障害 (Cont.)		
血便排泄	2 (13.3)	2 (2.6)
大腸ポリープ	1 (6.7)	1 (1.3)
悪心	1 (6.7)	4 (5.1)
膵炎	0	1 (1.3)
直腸出血	0	1 (1.3)
嘔吐	2 (13.3)	2 (2.6)
一般・全身障害および投与部位の状態	3 (20.0)	15 (19.2)
腋窩痛	0	1 (1.3)
胸痛	0	1 (1.3)
疲労	0	3 (3.8)
炎症	0	1 (1.3)
インフルエンザ様疾患	0	1 (1.3)
注射部位紅斑	1 (6.7)	0
注射部位炎症	0	1 (1.3)
注射部位浮腫	0	1 (1.3)
注射部位疼痛	0	2 (2.6)
注射部位そう痒感	0	1 (1.3)

表 2.7.4.7-107.　体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	1 (6.7)	0
注射部位蕁麻疹	1 (6.7)	1 (1.3)
倦怠感	0	1 (1.3)
末梢性浮腫	0	1 (1.3)
末梢腫脹	0	1 (1.3)
発熱	1 (6.7)	4 (5.1)
肝胆道系障害	0	2 (2.6)
胆嚢炎	0	1 (1.3)
高ビリルビン血症	0	1 (1.3)
免疫系障害	1 (6.7)	1 (1.3)
薬物過敏症	0	1 (1.3)
季節性アレルギー	1 (6.7)	0
感染症および寄生虫症	7 (46.7)	43 (55.1)
肛門膿瘍	0	1 (1.3)
気管支炎	3 (20.0)	2 (2.6)
クロストリジウム・ディフィシレ感染	0	1 (1.3)
サイトメガロウイルス性腸炎	0	1 (1.3)

表 2.7.4.7-107.　体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
感染症および寄生虫症 (Cont.)		
せつ	0	1 (1.3)
胃腸炎	0	3 (3.8)
サルモネラ菌性胃腸炎	0	1 (1.3)
ウイルス性胃腸炎	1 (6.7)	1 (1.3)
帯状疱疹	0	1 (1.3)
膿痂疹	0	1 (1.3)
感染性嚢腫	0	1 (1.3)
インフルエンザ	0	1 (1.3)
喉頭炎	1 (6.7)	0
無菌性髄膜炎	0	1 (1.3)
上咽頭炎	4 (26.7)	7 (9.0)
口腔ヘルペス	0	3 (3.8)
中耳炎	0	1 (1.3)
咽頭炎	1 (6.7)	10 (12.8)
気道感染	1 (6.7)	1 (1.3)
ウイルス性気道感染	0	1 (1.3)
鼻炎	0	1 (1.3)

表 2.7.4.7-107. 体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	0	1 (1.3)
レンサ球菌感染	0	1 (1.3)
癜風	0	1 (1.3)
扁桃炎	0	1 (1.3)
歯膿瘍	0	2 (2.6)
気管炎	0	1 (1.3)
上気道感染	2 (13.3)	12 (15.4)
尿路感染	1 (6.7)	6 (7.7)
水痘	0	2 (2.6)
ウイルス感染	1 (6.7)	2 (2.6)
ウイルス性上気道感染	0	3 (3.8)
外陰腟真菌感染	0	1 (1.3)
外陰腟炎	0	1 (1.3)
傷害、中毒および処置合併症	3 (20.0)	8 (10.3)
足関節部骨折	0	1 (1.3)
節足動物咬傷	0	1 (1.3)
転倒	0	1 (1.3)

表 2.7.4.7-107. 体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	1 (6.7)	1 (1.3)
注入に伴う反応	0	1 (1.3)
靱帯捻挫	1 (6.7)	0
四肢損傷	0	1 (1.3)
処置による疼痛	0	1 (1.3)
上肢骨折	1 (6.7)	0
手首関節骨折	1 (6.7)	1 (1.3)
臨床検査	3 (20.0)	15 (19.2)
血中アルカリホスファターゼ増加	0	1 (1.3)
血中ビリルビン増加	0	2 (2.6)
血中カルシウム減少	1 (6.7)	0
血圧上昇	0	1 (1.3)
血中ナトリウム減少	0	1 (1.3)
体温上昇	1 (6.7)	0
骨密度減少	0	1 (1.3)
Ｃ－反応性蛋白増加	1 (6.7)	4 (5.1)
好酸球数増加	0	1 (1.3)

表 2.7.4.7-107.　体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	0	1 (1.3)
ヘモグロビン減少	0	1 (1.3)
肝酵素上昇	0	1 (1.3)
リンパ節触知	0	1 (1.3)
結核菌群検査陽性	1 (6.7)	4 (5.1)
好中球数減少	1 (6.7)	0
体重減少	0	2 (2.6)
白血球数減少	1 (6.7)	0
筋骨格系および結合組織障害	1 (6.7)	11 (14.1)
関節痛	0	5 (6.4)
背部痛	0	3 (3.8)
成長不全	1 (6.7)	0
若年性特発性関節炎	0	1 (1.3)
靭帯障害	0	1 (1.3)
四肢痛	0	1 (1.3)
脊椎痛	0	1 (1.3)

表 2.7.4.7-107. 体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
神経系障害	5 (33.3)	21 (26.9)
頭痛	5 (33.3)	18 (23.1)
感覚鈍麻	0	1 (1.3)
意識消失	0	1 (1.3)
片頭痛	0	1 (1.3)
錯感覚	0	2 (2.6)
傾眠	0	1 (1.3)
振戦	0	2 (2.6)
精神障害	1 (6.7)	3 (3.8)
うつ病	1 (6.7)	3 (3.8)
腎および尿路障害	1 (6.7)	3 (3.8)
糖尿	1 (6.7)	0
血尿	0	1 (1.3)
腎結石症	0	1 (1.3)
腎仙痛	0	1 (1.3)
生殖系および乳房障害	0	5 (6.4)
乳房痛	0	1 (1.3)
月経困難症	0	2 (2.6)

表 2.7.4.7-107. 体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
生殖系および乳房障害 (Cont.)		
卵巣嚢胞	0	2 (2.6)
呼吸器、胸郭および縦隔障害	4 (26.7)	16 (20.5)
喘息	1 (6.7)	1 (1.3)
咳嗽	2 (13.3)	2 (2.6)
鼻出血	0	3 (3.8)
鼻閉	0	2 (2.6)
鼻浮腫	0	1 (1.3)
口腔咽頭痛	0	7 (9.0)
アレルギー性鼻炎	0	3 (3.8)
鼻漏	2 (13.3)	2 (2.6)
喘鳴	0	1 (1.3)
皮膚および皮下組織障害	2 (13.3)	13 (16.7)
脱毛症	0	1 (1.3)
皮膚炎	0	2 (2.6)
乾癬様皮膚炎	1 (6.7)	0
紅斑	0	1 (1.3)
結節性紅斑	1 (6.7)	2 (2.6)

表 2.7.4.7-107. 体重区分別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Weight < 40 kg (N=15) n (%)	Any Adalimumab Weight >= 40 kg (N=78) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	0	1 (1.3)
乾癬	0	1 (1.3)
発疹	0	5 (6.4)
痂皮	0	1 (1.3)
脂漏	0	1 (1.3)
皮膚障害	0	1 (1.3)
皮膚病変	0	1 (1.3)
血管障害	0	1 (1.3)
高血圧	0	1 (1.3)

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.4

表 2.7.4.7-108.　性別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	Male				Female			
	I-SD (N=17) n (%)	I-HD (N=28) n (%)	I-HD-OL (N=5) n (%)	Total (N=50) n (%)	I-SD (N=15) n (%)	I-HD (N=23) n (%)	I-HD-OL (N=13) n (%)	Total (N=51) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	10 (58.8)	15 (53.6)	5 (100)	30 (60.0)	9 (60.0)	12 (52.2)	9 (69.2)	30 (58.8)
Serious AE	2 (11.8)	2 (7.1)	0	4 (8.0)	3 (20.0)	2 (8.7)	1 (7.7)	6 (11.8)
Severe AE	3 (17.6)	0	0	3 (6.0)	1 (6.7)	1 (4.3)	0	2 (3.9)
AEs leading to discontinuation of study drug	3 (17.6)	0	0	3 (6.0)	0	1 (4.3)	0	1 (2.0)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	4 (23.5)	6 (21.4)	1 (20.0)	11 (22.0)	1 (6.7)	2 (8.7)	1 (7.7)	4 (7.8)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (5.9)	1 (3.6)	0	2 (4.0)	1 (6.7)	0	1 (7.7)	2 (3.9)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (23.5)	8 (28.6)	2 (40.0)	14 (28.0)	2 (13.3)	3 (13.0)	4 (30.8)	9 (17.6)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-108.　性別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	I-SD (N=17) n (%)	I-HD (N=28) n (%)	I-HD-OL (N=5) n (%)	Total (N=50) n (%)	I-SD (N=15) n (%)	I-HD (N=23) n (%)	I-HD-OL (N=13) n (%)	Total (N=51) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (4.3)	0	1 (2.0)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-108. 性別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	I-SD (N=17) n (%)	I-HD (N=28) n (%)	I-HD-OL (N=5) n (%)	Total (N=50) n (%)	I-SD (N=15) n (%)	I-HD (N=23) n (%)	I-HD-OL (N=13) n (%)	Total (N=51) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (3.6)	0	1 (2.0)	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	2 (11.8)	0	0	2 (4.0)	1 (6.7)	3 (13.0)	1 (7.7)	5 (9.8)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-108.　性別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	I-SD (N=17) n (%)	I-HD (N=28) n (%)	I-HD-OL (N=5) n (%)	Total (N=50) n (%)	I-SD (N=15) n (%)	I-HD (N=23) n (%)	I-HD-OL (N=13) n (%)	Total (N=51) n (%)
Injection site reaction	1 (5.9)	2 (7.1)	0	3 (6.0)	0	1 (4.3)	0	1 (2.0)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.1_J

表 2.7.4.7-109. 年齢区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	< 13 Years				>= 13 Years			
	I-SD (N=4) n (%)	I-HD (N=17) n (%)	I-HD-OL (N=5) n (%)	Total (N=26) n (%)	I-SD (N=28) n (%)	I-HD (N=34) n (%)	I-HD-OL (N=13) n (%)	Total (N=75) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	3 (75.0)	7 (41.2)	4 (80.0)	14 (53.8)	16 (57.1)	20 (58.8)	10 (76.9)	46 (61.3)
Serious AE	0	1 (5.9)	1 (20.0)	2 (7.7)	5 (17.9)	3 (8.8)	0	8 (10.7)
Severe AE	0	0	0	0	4 (14.3)	1 (2.9)	0	5 (6.7)
AEs leading to discontinuation of study drug	0	0	0	0	3 (10.7)	1 (2.9)	0	4 (5.3)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (5.9)	1 (20.0)	2 (7.7)	5 (17.9)	7 (20.6)	1 (7.7)	13 (17.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	1 (20.0)	1 (3.8)	2 (7.1)	1 (2.9)	0	3 (4.0)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	2 (50.0)	3 (17.6)	1 (20.0)	6 (23.1)	4 (14.3)	8 (23.5)	5 (38.5)	17 (22.7)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-109. 年齢区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 13 Years				>= 13 Years			
	I-SD (N=4) n (%)	I-HD (N=17) n (%)	I-HD-OL (N=5) n (%)	Total (N=26) n (%)	I-SD (N=28) n (%)	I-HD (N=34) n (%)	I-HD-OL (N=13) n (%)	Total (N=75) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (2.9)	0	1 (1.3)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-109. 年齢区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 13 Years				>= 13 Years			
	I-SD (N=4) n (%)	I-HD (N=17) n (%)	I-HD-OL (N=5) n (%)	Total (N=26) n (%)	I-SD (N=28) n (%)	I-HD (N=34) n (%)	I-HD-OL (N=13) n (%)	Total (N=75) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (2.9)	0	1 (1.3)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	1 (5.9)	1 (20.0)	2 (7.7)	3 (10.7)	2 (5.9)	0	5 (6.7)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-109.　年齢区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 13 Years				>= 13 Years			
	I-SD (N=4) n (%)	I-HD (N=17) n (%)	I-HD-OL (N=5) n (%)	Total (N=26) n (%)	I-SD (N=28) n (%)	I-HD (N=34) n (%)	I-HD-OL (N=13) n (%)	Total (N=75) n (%)
Injection site reaction	0	0	0	0	1 (3.6)	3 (8.8)	0	4 (5.3)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.2_J

表 2.7.4.7-110.　人種別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	White				Non-White			
	I-SD (N=28) n (%)	I-HD (N=45) n (%)	I-HD-OL (N=15) n (%)	Total (N=88) n (%)	I-SD (N=4) n (%)	I-HD (N=6) n (%)	I-HD-OL (N=3) n (%)	Total (N=13) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	16 (57.1)	21 (46.7)	11 (73.3)	48 (54.5)	3 (75.0)	6 (100)	3 (100)	12 (92.3)
Serious AE	5 (17.9)	4 (8.9)	0	9 (10.2)	0	0	1 (33.3)	1 (7.7)
Severe AE	4 (14.3)	1 (2.2)	0	5 (5.7)	0	0	0	0
AEs leading to discontinuation of study drug	2 (7.1)	1 (2.2)	0	3 (3.4)	1 (25.0)	0	0	1 (7.7)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (10.7)	5 (11.1)	0	8 (9.1)	2 (50.0)	3 (50.0)	2 (66.7)	7 (53.8)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (7.1)	1 (2.2)	0	3 (3.4)	0	0	1 (33.3)	1 (7.7)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	6 (21.4)	7 (15.6)	5 (33.3)	18 (20.5)	0	4 (66.7)	1 (33.3)	5 (38.5)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-110.　人種別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	I-SD (N=28) n (%)	I-HD (N=45) n (%)	I-HD-OL (N=15) n (%)	Total (N=88) n (%)	I-SD (N=4) n (%)	I-HD (N=6) n (%)	I-HD-OL (N=3) n (%)	Total (N=13) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	1 (2.2)	0	1 (1.1)	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-110. 人種別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	I-SD (N=28) n (%)	I-HD (N=45) n (%)	I-HD-OL (N=15) n (%)	Total (N=88) n (%)	I-SD (N=4) n (%)	I-HD (N=6) n (%)	I-HD-OL (N=3) n (%)	Total (N=13) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (2.2)	0	1 (1.1)	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (10.7)	3 (6.7)	1 (6.7)	7 (8.0)	0	0	0	0
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-110. 人種別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	I-SD (N=28) n (%)	I-HD (N=45) n (%)	I-HD-OL (N=15) n (%)	Total (N=88) n (%)	I-SD (N=4) n (%)	I-HD (N=6) n (%)	I-HD-OL (N=3) n (%)	Total (N=13) n (%)
Injection site reaction	0	1 (2.2)	0	1 (1.1)	1 (25.0)	2 (33.3)	0	3 (23.1)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.3_J

表 2.7.4.7-111.　体重区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	< 40 kg				>= 40 kg			
	I-SD (N=3) n (%)	I-HD (N=10) n (%)	I-HD-OL (N=3) n (%)	Total (N=16) n (%)	I-SD (N=29) n (%)	I-HD (N=41) n (%)	I-HD-OL (N=15) n (%)	Total (N=85) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	3 (100)	3 (30.0)	3 (100)	9 (56.3)	16 (55.2)	24 (58.5)	11 (73.3)	51 (60.0)
Serious AE	0	1 (10.0)	0	1 (6.3)	5 (17.2)	3 (7.3)	1 (6.7)	9 (10.6)
Severe AE	0	0	0	0	4 (13.8)	1 (2.4)	0	5 (5.9)
AEs leading to discontinuation of study drug	0	0	0	0	3 (10.3)	1 (2.4)	0	4 (4.7)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (10.0)	0	1 (6.3)	5 (17.2)	7 (17.1)	2 (13.3)	14 (16.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	2 (6.9)	1 (2.4)	1 (6.7)	4 (4.7)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	1 (33.3)	1 (10.0)	0	2 (12.5)	5 (17.2)	10 (24.4)	6 (40.0)	21 (24.7)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-111. 体重区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	I-SD (N=3) n (%)	I-HD (N=10) n (%)	I-HD-OL (N=3) n (%)	Total (N=16) n (%)	I-SD (N=29) n (%)	I-HD (N=41) n (%)	I-HD-OL (N=15) n (%)	Total (N=85) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (2.4)	0	1 (1.2)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-111. 体重区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	I-SD (N=3) n (%)	I-HD (N=10) n (%)	I-HD-OL (N=3) n (%)	Total (N=16) n (%)	I-SD (N=29) n (%)	I-HD (N=41) n (%)	I-HD-OL (N=15) n (%)	Total (N=85) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (2.4)	0	1 (1.2)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	0	1 (33.3)	1 (6.3)	3 (10.3)	3 (7.3)	0	6 (7.1)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-111.　体重区分別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	I-SD (N=3) n (%)	I-HD (N=10) n (%)	I-HD-OL (N=3) n (%)	Total (N=16) n (%)	I-SD (N=29) n (%)	I-HD (N=41) n (%)	I-HD-OL (N=15) n (%)	Total (N=85) n (%)
Injection site reaction	0	0	0	0	1 (3.4)	3 (7.3)	0	4 (4.7)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.4_J

表 2.7.4.7-112.　性別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	Male				Female			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=9) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=3) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	11 (73.3)	11 (64.7)	22 (68.8)	7 (77.8)	10 (55.6)	15 (78.9)	25 (67.6)	3 (100)
Serious AE	4 (26.7)	1 (5.9)	5 (15.6)	0	1 (5.6)	4 (21.1)	5 (13.5)	1 (33.3)
Severe AE	2 (13.3)	0	2 (6.3)	0	1 (5.6)	1 (5.3)	2 (5.4)	0
AEs leading to discontinuation of study drug	2 (13.3)	0	2 (6.3)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	4 (26.7)	4 (23.5)	8 (25.0)	3 (33.3)	4 (22.2)	7 (36.8)	11 (29.7)	2 (66.7)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	0	1 (5.3)	1 (2.7)	1 (33.3)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	8 (53.3)	6 (35.3)	14 (43.8)	4 (44.4)	3 (16.7)	10 (52.6)	13 (35.1)	1 (33.3)
Serious infections	3 (20.0)	0	3 (9.4)	0	0	3 (15.8)	3 (8.1)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (5.3)	1 (2.7)	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-112.　性別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=9) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=3) n (%)
Latent tuberculosis	0	0	0	0	0	1 (5.3)	1 (2.7)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	1 (6.7)	0	1 (3.1)	0	0	2 (10.5)	2 (5.4)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-112.　性別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=9) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=3) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (33.3)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	1 (6.7)	0	1 (3.1)	1 (11.1)	2 (11.1)	1 (5.3)	3 (8.1)	1 (33.3)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-112.　性別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=9) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=3) n (%)
Injection site reaction	2 (13.3)	0	2 (6.3)	0	2 (11.1)	2 (10.5)	4 (10.8)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.1_J

表 2.7.4.7-113.　年齢区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	< 13 Years				>= 13 Years			
	M-SD (N=12) n (%)	M-HD (N=9) n (%)	Total-ADA (N=21) n (%)	M-PL (N=2) n (%)	M-SD (N=21) n (%)	M-HD (N=27) n (%)	Total-ADA (N=48) n (%)	M-PL (N=10) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	8 (66.7)	7 (77.8)	15 (71.4)	2 (100)	13 (61.9)	19 (70.4)	32 (66.7)	8 (80.0)
Serious AE	1 (8.3)	1 (11.1)	2 (9.5)	0	4 (19.0)	4 (14.8)	8 (16.7)	1 (10.0)
Severe AE	1 (8.3)	0	1 (4.8)	0	2 (9.5)	1 (3.7)	3 (6.3)	0
AEs leading to discontinuation of study drug	0	0	0	0	2 (9.5)	0	2 (4.2)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (16.7)	2 (22.2)	4 (19.0)	1 (50.0)	6 (28.6)	9 (33.3)	15 (31.3)	4 (40.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	0	1 (3.7)	1 (2.1)	1 (10.0)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	5 (41.7)	6 (66.7)	11 (52.4)	2 (100)	6 (28.6)	10 (37.0)	16 (33.3)	3 (30.0)
Serious infections	0	0	0	0	3 (14.3)	3 (11.1)	6 (12.5)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (3.7)	1 (2.1)	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-113. 年齢区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 13 Years				>= 13 Years			
	M-SD (N=12) n (%)	M-HD (N=9) n (%)	Total-ADA (N=21) n (%)	M-PL (N=2) n (%)	M-SD (N=21) n (%)	M-HD (N=27) n (%)	Total-ADA (N=48) n (%)	M-PL (N=10) n (%)
Latent tuberculosis	0	0	0	0	0	1 (3.7)	1 (2.1)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	1 (8.3)	0	1 (4.8)	0	0	2 (7.4)	2 (4.2)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-113. 年齢区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 13 Years				>= 13 Years			
	M-SD (N=12) n (%)	M-HD (N=9) n (%)	Total-ADA (N=21) n (%)	M-PL (N=2) n (%)	M-SD (N=21) n (%)	M-HD (N=27) n (%)	Total-ADA (N=48) n (%)	M-PL (N=10) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (10.0)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	1 (11.1)	1 (4.8)	0	3 (14.3)	0	3 (6.3)	2 (20.0)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-113. 年齢区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 13 Years				>= 13 Years			
	M-SD (N=12) n (%)	M-HD (N=9) n (%)	Total-ADA (N=21) n (%)	M-PL (N=2) n (%)	M-SD (N=21) n (%)	M-HD (N=27) n (%)	Total-ADA (N=48) n (%)	M-PL (N=10) n (%)
Injection site reaction	1 (8.3)	0	1 (4.8)	0	3 (14.3)	2 (7.4)	5 (10.4)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.2_J

表 2.7.4.7-114.　人種別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	White				Non-White			
	M-SD (N=29) n (%)	M-HD (N=31) n (%)	Total-ADA (N=60) n (%)	M-PL (N=11) n (%)	M-SD (N=4) n (%)	M-HD (N=5) n (%)	Total-ADA (N=9) n (%)	M-PL (N=1) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	18 (62.1)	21 (67.7)	39 (65.0)	9 (81.8)	3 (75.0)	5 (100)	8 (88.9)	1 (100)
Serious AE	3 (10.3)	5 (16.1)	8 (13.3)	1 (9.1)	2 (50.0)	0	2 (22.2)	0
Severe AE	2 (6.9)	1 (3.2)	3 (5.0)	0	1 (25.0)	0	1 (11.1)	0
AEs leading to discontinuation of study drug	2 (6.9)	0	2 (3.3)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	7 (24.1)	9 (29.0)	16 (26.7)	4 (36.4)	1 (25.0)	2 (40.0)	3 (33.3)	1 (100)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (3.2)	1 (1.7)	1 (9.1)	0	0	0	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	10 (34.5)	13 (41.9)	23 (38.3)	4 (36.4)	1 (25.0)	3 (60.0)	4 (44.4)	1 (100)
Serious infections	2 (6.9)	3 (9.7)	5 (8.3)	0	1 (25.0)	0	1 (11.1)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (3.2)	1 (1.7)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-114. 人種別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	M-SD (N=29) n (%)	M-HD (N=31) n (%)	Total-ADA (N=60) n (%)	M-PL (N=11) n (%)	M-SD (N=4) n (%)	M-HD (N=5) n (%)	Total-ADA (N=9) n (%)	M-PL (N=1) n (%)
Latent tuberculosis	0	1 (3.2)	1 (1.7)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	1 (3.4)	2 (6.5)	3 (5.0)	0	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-114. 人種別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	M-SD (N=29) n (%)	M-HD (N=31) n (%)	Total-ADA (N=60) n (%)	M-PL (N=11) n (%)	M-SD (N=4) n (%)	M-HD (N=5) n (%)	Total-ADA (N=9) n (%)	M-PL (N=1) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (9.1)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (10.3)	1 (3.2)	4 (6.7)	1 (9.1)	0	0	0	1 (100)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-114.　人種別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	M-SD (N=29) n (%)	M-HD (N=31) n (%)	Total-ADA (N=60) n (%)	M-PL (N=11) n (%)	M-SD (N=4) n (%)	M-HD (N=5) n (%)	Total-ADA (N=9) n (%)	M-PL (N=1) n (%)
Injection site reaction	4 (13.8)	2 (6.5)	6 (10.0)	0	0	0	0	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.3_J

表 2.7.4.7-115.　体重区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	< 40 kg				>= 40 kg			
	M-SD (N=7) n (%)	M-HD (N=8) n (%)	Total-ADA (N=15) n (%)	M-PL (N=0) n (%)	M-SD (N=26) n (%)	M-HD (N=28) n (%)	Total-ADA (N=54) n (%)	M-PL (N=12) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	5 (71.4)	6 (75.0)	11 (73.3)	0	16 (61.5)	20 (71.4)	36 (66.7)	10 (83.3)
Serious AE	1 (14.3)	1 (12.5)	2 (13.3)	0	4 (15.4)	4 (14.3)	8 (14.8)	1 (8.3)
Severe AE	1 (14.3)	0	1 (6.7)	0	2 (7.7)	1 (3.6)	3 (5.6)	0
AEs leading to discontinuation of study drug	0	0	0	0	2 (7.7)	0	2 (3.7)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (28.6)	2 (25.0)	4 (26.7)	0	6 (23.1)	9 (32.1)	15 (27.8)	5 (41.7)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	0	1 (3.6)	1 (1.9)	1 (8.3)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	3 (42.9)	4 (50.0)	7 (46.7)	0	8 (30.8)	12 (42.9)	20 (37.0)	5 (41.7)
Serious infections	0	1 (12.5)	1 (6.7)	0	3 (11.5)	2 (7.1)	5 (9.3)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (3.6)	1 (1.9)	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-115. 体重区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	M-SD (N=7) n (%)	M-HD (N=8) n (%)	Total-ADA (N=15) n (%)	M-PL (N=0) n (%)	M-SD (N=26) n (%)	M-HD (N=28) n (%)	Total-ADA (N=54) n (%)	M-PL (N=12) n (%)
Latent tuberculosis	0	0	0	0	0	1 (3.6)	1 (1.9)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	1 (12.5)	1 (6.7)	0	1 (3.8)	1 (3.6)	2 (3.7)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-115.　体重区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	M-SD (N=7) n (%)	M-HD (N=8) n (%)	Total-ADA (N=15) n (%)	M-PL (N=0) n (%)	M-SD (N=26) n (%)	M-HD (N=28) n (%)	Total-ADA (N=54) n (%)	M-PL (N=12) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (8.3)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	0	0	0	3 (11.5)	1 (3.6)	4 (7.4)	2 (16.7)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-115.　体重区分別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	M-SD (N=7) n (%)	M-HD (N=8) n (%)	Total-ADA (N=15) n (%)	M-PL (N=0) n (%)	M-SD (N=26) n (%)	M-HD (N=28) n (%)	Total-ADA (N=54) n (%)	M-PL (N=12) n (%)
Injection site reaction	1 (14.3)	1 (12.5)	2 (13.3)	0	3 (11.5)	1 (3.6)	4 (7.4)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.4_J

表 2.7.4.7-116. 性別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	Male				Female			
	I-SD (N=17) (PYS=2.3) Events (E/100PY)	I-HD (N=28) (PYS=4.3) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.8) Events (E/100PY)	Total (N=50) (PYS=7.4) Events (E/100PY)	I-SD (N=15) (PYS=2.3) Events (E/100PY)	I-HD (N=23) (PYS=3.5) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=51) (PYS=7.7) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	29 (1260.9)	35 (814.0)	10 (1250.0)	74 (1000.0)	17 (739.1)	27 (771.4)	25 (1315.8)	69 (896.1)
Serious AE	3 (130.4)	2 (46.5)	0	5 (67.6)	4 (173.9)	2 (57.1)	1 (52.6)	7 (90.9)
Severe AE	4 (173.9)	0	0	4 (54.1)	1 (43.5)	1 (28.6)	0	2 (26.0)
AEs leading to discontinuation of study drug	4 (173.9)	0	0	4 (54.1)	0	1 (28.6)	0	1 (13.0)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	6 (260.9)	14 (325.6)	3 (375.0)	23 (310.8)	2 (87.0)	2 (57.1)	2 (105.3)	6 (77.9)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (43.5)	1 (23.3)	0	2 (27.0)	2 (87.0)	0	1 (52.6)	3 (39.0)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (173.9)	10 (232.6)	2 (250.0)	16 (216.2)	3 (130.4)	3 (85.7)	5 (263.2)	11 (142.9)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-116. 性別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	I-SD (N=17) (PYS=2.3) Events (E/100PY)	I-HD (N=28) (PYS=4.3) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.8) Events (E/100PY)	Total (N=50) (PYS=7.4) Events (E/100PY)	I-SD (N=15) (PYS=2.3) Events (E/100PY)	I-HD (N=23) (PYS=3.5) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=51) (PYS=7.7) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-116. 性別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	I-SD (N=17) (PYS=2.3) Events (E/100PY)	I-HD (N=28) (PYS=4.3) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.8) Events (E/100PY)	Total (N=50) (PYS=7.4) Events (E/100PY)	I-SD (N=15) (PYS=2.3) Events (E/100PY)	I-HD (N=23) (PYS=3.5) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=51) (PYS=7.7) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (28.6)	0	1 (13.0)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (23.3)	0	1 (13.5)	0	0	0	0

表 2.7.4.7-116. 性別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	I-SD (N=17) (PYS=2.3) Events (E/100PY)	I-HD (N=28) (PYS=4.3) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.8) Events (E/100PY)	Total (N=50) (PYS=7.4) Events (E/100PY)	I-SD (N=15) (PYS=2.3) Events (E/100PY)	I-HD (N=23) (PYS=3.5) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=51) (PYS=7.7) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	2 (87.0)	0	0	2 (27.0)	1 (43.5)	3 (85.7)	1 (52.6)	5 (64.9)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	1 (43.5)	4 (93.0)	0	5 (67.6)	0	1 (28.6)	0	1 (13.0)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-116.　性別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.1_J

表 2.7.4.7-117. 年齢区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	<13 Years				>=13 Years			
	I-SD (N=4) (PYS=0.6) Events (E/100PY)	I-HD (N=17) (PYS=2.6) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.7) Events (E/100PY)	Total (N=26) (PYS=3.9) Events (E/100PY)	I-SD (N=28) (PYS=4.0) Events (E/100PY)	I-HD (N=34) (PYS=5.1) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=75) (PYS=11.1) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	5 (833.3)	14 (538.5)	12 (1714.3)	31 (794.9)	41 (1025.0)	48 (941.2)	23 (1210.5)	112 (1009.0)
Serious AE	0	1 (38.5)	1 (142.9)	2 (51.3)	7 (175.0)	3 (58.8)	0	10 (90.1)
Severe AE	0	0	0	0	5 (125.0)	1 (19.6)	0	6 (54.1)
AEs leading to discontinuation of study drug	0	0	0	0	4 (100.0)	1 (19.6)	0	5 (45.0)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	3 (115.4)	2 (285.7)	5 (128.2)	8 (200.0)	13 (254.9)	3 (157.9)	24 (216.2)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	1 (142.9)	1 (25.6)	3 (75.0)	1 (19.6)	0	4 (36.0)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	3 (500.0)	4 (153.8)	1 (142.9)	8 (205.1)	4 (100.0)	9 (176.5)	6 (315.8)	19 (171.2)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-117. 年齢区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<13 Years				>=13 Years			
	I-SD (N=4) (PYS=0.6) Events (E/100PY)	I-HD (N=17) (PYS=2.6) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.7) Events (E/100PY)	Total (N=26) (PYS=3.9) Events (E/100PY)	I-SD (N=28) (PYS=4.0) Events (E/100PY)	I-HD (N=34) (PYS=5.1) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=75) (PYS=11.1) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-117. 年齢区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<13 Years				>=13 Years			
	I-SD (N=4) (PYS=0.6) Events (E/100PY)	I-HD (N=17) (PYS=2.6) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.7) Events (E/100PY)	Total (N=26) (PYS=3.9) Events (E/100PY)	I-SD (N=28) (PYS=4.0) Events (E/100PY)	I-HD (N=34) (PYS=5.1) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=75) (PYS=11.1) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (19.6)	0	1 (9.0)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (19.6)	0	1 (9.0)

表 2.7.4.7-117. 年齢区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 13 Years				>= 13 Years			
	I-SD (N=4) (PYS=0.6) Events (E/100PY)	I-HD (N=17) (PYS=2.6) Events (E/100PY)	I-HD-OL (N=5) (PYS=0.7) Events (E/100PY)	Total (N=26) (PYS=3.9) Events (E/100PY)	I-SD (N=28) (PYS=4.0) Events (E/100PY)	I-HD (N=34) (PYS=5.1) Events (E/100PY)	I-HD-OL (N=13) (PYS=1.9) Events (E/100PY)	Total (N=75) (PYS=11.1) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	1 (38.5)	1 (142.9)	2 (51.3)	3 (75.0)	2 (39.2)	0	5 (45.0)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	0	0	0	0	1 (25.0)	5 (98.0)	0	6 (54.1)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-117. 年齢区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.2_J

表 2.7.4.7-118. 人種別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	White				Non-White			
	I-SD (N=28) (PYS=4.1) Events (E/100PY)	I-HD (N=45) (PYS=6.8) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=88) (PYS=13.2) Events (E/100PY)	I-SD (N=4) (PYS=0.5) Events (E/100PY)	I-HD (N=6) (PYS=0.9) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=13) (PYS=1.8) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	38 (926.8)	48 (705.9)	26 (1181.8)	112 (848.5)	8 (1600.0)	14 (1555.6)	9 (2250.0)	31 (1722.2)
Serious AE	7 (170.7)	4 (58.8)	0	11 (83.3)	0	0	1 (250.0)	1 (55.6)
Severe AE	5 (122.0)	1 (14.7)	0	6 (45.5)	0	0	0	0
AEs leading to discontinuation of study drug	3 (73.2)	1 (14.7)	0	4 (30.3)	1 (200.0)	0	0	1 (55.6)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	4 (97.6)	8 (117.6)	0	12 (90.9)	4 (800.0)	8 (888.9)	5 (1250.0)	17 (944.4)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (73.2)	1 (14.7)	0	4 (30.3)	0	0	1 (250.0)	1 (55.6)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	7 (170.7)	8 (117.6)	6 (272.7)	21 (159.1)	0	5 (555.6)	1 (250.0)	6 (333.3)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-118. 人種別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	I-SD (N=28) (PYS=4.1) Events (E/100PY)	I-HD (N=45) (PYS=6.8) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=88) (PYS=13.2) Events (E/100PY)	I-SD (N=4) (PYS=0.5) Events (E/100PY)	I-HD (N=6) (PYS=0.9) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=13) (PYS=1.8) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-118. 人種別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	I-SD (N=28) (PYS=4.1) Events (E/100PY)	I-HD (N=45) (PYS=6.8) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=88) (PYS=13.2) Events (E/100PY)	I-SD (N=4) (PYS=0.5) Events (E/100PY)	I-HD (N=6) (PYS=0.9) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=13) (PYS=1.8) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	1 (14.7)	0	1 (7.6)	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (14.7)	0	1 (7.6)	0	0	0	0

表 2.7.4.7-118. 人種別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	I-SD (N=28) (PYS=4.1) Events (E/100PY)	I-HD (N=45) (PYS=6.8) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=88) (PYS=13.2) Events (E/100PY)	I-SD (N=4) (PYS=0.5) Events (E/100PY)	I-HD (N=6) (PYS=0.9) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=13) (PYS=1.8) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (73.2)	3 (44.1)	1 (45.5)	7 (53.0)	0	0	0	0
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	0	1 (14.7)	0	1 (7.6)	1 (200.0)	4 (444.4)	0	5 (277.8)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-118.　人種別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.3_J

表 2.7.4.7-119. 体重区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	< 40 kg				>= 40 kg			
	I-SD (N=3) (PYS=0.5) Events (E/100PY)	I-HD (N=10) (PYS=1.5) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=29) (PYS=4.2) Events (E/100PY)	I-HD (N=41) (PYS=6.2) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	3 (600.0)	5 (333.3)	8 (2000.0)	16 (666.7)	43 (1023.8)	57 (919.4)	27 (1227.3)	127 (1007.9)
Serious AE	0	1 (66.7)	0	1 (41.7)	7 (166.7)	3 (48.4)	1 (45.5)	11 (87.3)
Severe AE	0	0	0	0	5 (119.0)	1 (16.1)	0	6 (47.6)
AEs leading to discontinuation of study drug	0	0	0	0	4 (95.2)	1 (16.1)	0	5 (39.7)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	3 (200.0)	0	3 (125.0)	8 (190.5)	13 (209.7)	5 (227.3)	26 (206.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	3 (71.4)	1 (16.1)	1 (45.5)	5 (39.7)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	1 (200.0)	1 (66.7)	0	2 (83.3)	6 (142.9)	12 (193.5)	7 (318.2)	25 (198.4)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-119. 体重区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	I-SD (N=3) (PYS=0.5) Events (E/100PY)	I-HD (N=10) (PYS=1.5) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=29) (PYS=4.2) Events (E/100PY)	I-HD (N=41) (PYS=6.2) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-119. 体重区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	I-SD (N=3) (PYS=0.5) Events (E/100PY)	I-HD (N=10) (PYS=1.5) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=29) (PYS=4.2) Events (E/100PY)	I-HD (N=41) (PYS=6.2) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (16.1)	0	1 (7.9)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (16.1)	0	1 (7.9)

表 2.7.4.7-119. 体重区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	I-SD (N=3) (PYS=0.5) Events (E/100PY)	I-HD (N=10) (PYS=1.5) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.4) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=29) (PYS=4.2) Events (E/100PY)	I-HD (N=41) (PYS=6.2) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	0	1 (250.0)	1 (41.7)	3 (71.4)	3 (48.4)	0	6 (47.6)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	0	0	0	0	1 (23.8)	5 (80.6)	0	6 (47.6)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-119. 体重区分別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

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I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study
      drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period
      and prior to the first dose date of the study drug in the maintenance period if applicable.
      E/100PY = Events per 100 patient-years.
      AEs with unknown relationship were counted as 'reasonable possibility of being related'.
      AEs with unknown severity were counted as 'severe'.
# As assessed by investigator.
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Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.4_J

表 2.7.4.7-120. 性別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	Male				Female			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=10.5) Events (E/100PY)	Total-ADA (N=32) (PYS=18.7) Events (E/100PY)	M-PL (N=9) (PYS=3.7) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=13.3) Events (E/100PY)	Total-ADA (N=37) (PYS=25.6) Events (E/100PY)	M-PL (N=3) (PYS=2.3) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	43 (524.4)	24 (228.6)	67 (358.3)	18 (486.5)	31 (252.0)	53 (398.5)	84 (328.1)	8 (347.8)
Serious AE	8 (97.6)	1 (9.5)	9 (48.1)	0	2 (16.3)	5 (37.6)	7 (27.3)	1 (43.5)
Severe AE	4 (48.8)	0	4 (21.4)	0	1 (8.1)	1 (7.5)	2 (7.8)	0
AEs leading to discontinuation of study drug	3 (36.6)	0	3 (16.0)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	10 (122.0)	6 (57.1)	16 (85.6)	4 (108.1)	4 (32.5)	14 (105.3)	18 (70.3)	2 (87.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	0	1 (7.5)	1 (3.9)	1 (43.5)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	11 (134.1)	6 (57.1)	17 (90.9)	5 (135.1)	7 (56.9)	16 (120.3)	23 (89.8)	4 (173.9)
Serious infections	3 (36.6)	0	3 (16.0)	0	0	3 (22.6)	3 (11.7)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-120. 性別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=10.5) Events (E/100PY)	Total-ADA (N=32) (PYS=18.7) Events (E/100PY)	M-PL (N=9) (PYS=3.7) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=13.3) Events (E/100PY)	Total-ADA (N=37) (PYS=25.6) Events (E/100PY)	M-PL (N=3) (PYS=2.3) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (7.5)	1 (3.9)	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	1 (7.5)	1 (3.9)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-120. 性別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=10.5) Events (E/100PY)	Total-ADA (N=32) (PYS=18.7) Events (E/100PY)	M-PL (N=9) (PYS=3.7) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=13.3) Events (E/100PY)	Total-ADA (N=37) (PYS=25.6) Events (E/100PY)	M-PL (N=3) (PYS=2.3) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (24.4)	0	2 (10.7)	0	0	2 (15.0)	2 (7.8)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-120. 性別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Male				Female			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=10.5) Events (E/100PY)	Total-ADA (N=32) (PYS=18.7) Events (E/100PY)	M-PL (N=9) (PYS=3.7) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=13.3) Events (E/100PY)	Total-ADA (N=37) (PYS=25.6) Events (E/100PY)	M-PL (N=3) (PYS=2.3) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (43.5)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (36.6)	0	3 (16.0)	1 (27.0)	2 (16.3)	1 (7.5)	3 (11.7)	1 (43.5)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	4 (48.8)	0	4 (21.4)	0	2 (16.3)	3 (22.6)	5 (19.5)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-120.　性別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.1_J

表 2.7.4.7-121. 年齢区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	<13 Years				>=13 Years			
	M-SD (N=12) (PYS=8.1) Events (E/100PY)	M-HD (N=9) (PYS=6.9) Events (E/100PY)	Total-ADA (N=21) (PYS=15.0) Events (E/100PY)	M-PL (N=2) (PYS=1.0) Events (E/100PY)	M-SD (N=21) (PYS=12.4) Events (E/100PY)	M-HD (N=27) (PYS=16.9) Events (E/100PY)	Total-ADA (N=48) (PYS=29.3) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	27 (333.3)	25 (362.3)	52 (346.7)	11 (1100.0)	47 (379.0)	52 (307.7)	99 (337.9)	15 (294.1)
Serious AE	2 (24.7)	1 (14.5)	3 (20.0)	0	8 (64.5)	5 (29.6)	13 (44.4)	1 (19.6)
Severe AE	1 (12.3)	0	1 (6.7)	0	4 (32.3)	1 (5.9)	5 (17.1)	0
AEs leading to discontinuation of study drug	0	0	0	0	3 (24.2)	0	3 (10.2)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (37.0)	3 (43.5)	6 (40.0)	1 (100.0)	11 (88.7)	17 (100.6)	28 (95.6)	5 (98.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	0	1 (5.9)	1 (3.4)	1 (19.6)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	9 (111.1)	10 (144.9)	19 (126.7)	6 (600.0)	9 (72.6)	12 (71.0)	21 (71.7)	3 (58.8)
Serious infections	0	0	0	0	3 (24.2)	3 (17.8)	6 (20.5)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-121. 年齢区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<13 Years				>=13 Years			
	M-SD (N=12) (PYS=8.1) Events (E/100PY)	M-HD (N=9) (PYS=6.9) Events (E/100PY)	Total-ADA (N=21) (PYS=15.0) Events (E/100PY)	M-PL (N=2) (PYS=1.0) Events (E/100PY)	M-SD (N=21) (PYS=12.4) Events (E/100PY)	M-HD (N=27) (PYS=16.9) Events (E/100PY)	Total-ADA (N=48) (PYS=29.3) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (5.9)	1 (3.4)	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	1 (5.9)	1 (3.4)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-121. 年齢区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<13 Years				>=13 Years			
	M-SD (N=12) (PYS=8.1) Events (E/100PY)	M-HD (N=9) (PYS=6.9) Events (E/100PY)	Total-ADA (N=21) (PYS=15.0) Events (E/100PY)	M-PL (N=2) (PYS=1.0) Events (E/100PY)	M-SD (N=21) (PYS=12.4) Events (E/100PY)	M-HD (N=27) (PYS=16.9) Events (E/100PY)	Total-ADA (N=48) (PYS=29.3) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (24.7)	0	2 (13.3)	0	0	2 (11.8)	2 (6.8)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-121. 年齢区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<13 Years				>=13 Years			
	M-SD (N=12) (PYS=8.1) Events (E/100PY)	M-HD (N=9) (PYS=6.9) Events (E/100PY)	Total-ADA (N=21) (PYS=15.0) Events (E/100PY)	M-PL (N=2) (PYS=1.0) Events (E/100PY)	M-SD (N=21) (PYS=12.4) Events (E/100PY)	M-HD (N=27) (PYS=16.9) Events (E/100PY)	Total-ADA (N=48) (PYS=29.3) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (19.6)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	1 (14.5)	1 (6.7)	0	5 (40.3)	0	5 (17.1)	2 (39.2)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	1 (12.3)	0	1 (6.7)	0	5 (40.3)	3 (17.8)	8 (27.3)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-121. 年齢区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.2_J

表 2.7.4.7-122. 人種別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	White				Non-White			
	M-SD (N=29) (PYS=19.1) Events (E/100PY)	M-HD (N=31) (PYS=21.0) Events (E/100PY)	Total-ADA (N=60) (PYS=40.1) Events (E/100PY)	M-PL (N=11) (PYS=5.2) Events (E/100PY)	M-SD (N=4) (PYS=1.3) Events (E/100PY)	M-HD (N=5) (PYS=2.8) Events (E/100PY)	Total-ADA (N=9) (PYS=4.1) Events (E/100PY)	M-PL (N=1) (PYS=0.8) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	65 (340.3)	66 (314.3)	131 (326.7)	22 (423.1)	9 (692.3)	11 (392.9)	20 (487.8)	4 (500.0)
Serious AE	8 (41.9)	6 (28.6)	14 (34.9)	1 (19.2)	2 (153.8)	0	2 (48.8)	0
Severe AE	4 (20.9)	1 (4.8)	5 (12.5)	0	1 (76.9)	0	1 (24.4)	0
AEs leading to discontinuation of study drug	3 (15.7)	0	3 (7.5)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	12 (62.8)	16 (76.2)	28 (69.8)	5 (96.2)	2 (153.8)	4 (142.9)	6 (146.3)	1 (125.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (4.8)	1 (2.5)	1 (19.2)	0	0	0	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	17 (89.0)	19 (90.5)	36 (89.8)	8 (153.8)	1 (76.9)	3 (107.1)	4 (97.6)	1 (125.0)
Serious infections	2 (10.5)	3 (14.3)	5 (12.5)	0	1 (76.9)	0	1 (24.4)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-122. 人種別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	M-SD (N=29) (PYS=19.1) Events (E/100PY)	M-HD (N=31) (PYS=21.0) Events (E/100PY)	Total-ADA (N=60) (PYS=40.1) Events (E/100PY)	M-PL (N=11) (PYS=5.2) Events (E/100PY)	M-SD (N=4) (PYS=1.3) Events (E/100PY)	M-HD (N=5) (PYS=2.8) Events (E/100PY)	Total-ADA (N=9) (PYS=4.1) Events (E/100PY)	M-PL (N=1) (PYS=0.8) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (4.8)	1 (2.5)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	1 (4.8)	1 (2.5)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-122. 人種別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	M-SD (N=29) (PYS=19.1) Events (E/100PY)	M-HD (N=31) (PYS=21.0) Events (E/100PY)	Total-ADA (N=60) (PYS=40.1) Events (E/100PY)	M-PL (N=11) (PYS=5.2) Events (E/100PY)	M-SD (N=4) (PYS=1.3) Events (E/100PY)	M-HD (N=5) (PYS=2.8) Events (E/100PY)	Total-ADA (N=9) (PYS=4.1) Events (E/100PY)	M-PL (N=1) (PYS=0.8) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (10.5)	2 (9.5)	4 (10.0)	0	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-122. 人種別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	White				Non-White			
	M-SD (N=29) (PYS=19.1) Events (E/100PY)	M-HD (N=31) (PYS=21.0) Events (E/100PY)	Total-ADA (N=60) (PYS=40.1) Events (E/100PY)	M-PL (N=11) (PYS=5.2) Events (E/100PY)	M-SD (N=4) (PYS=1.3) Events (E/100PY)	M-HD (N=5) (PYS=2.8) Events (E/100PY)	Total-ADA (N=9) (PYS=4.1) Events (E/100PY)	M-PL (N=1) (PYS=0.8) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (19.2)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	5 (26.2)	1 (4.8)	6 (15.0)	1 (19.2)	0	0	0	1 (125.0)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	6 (31.4)	3 (14.3)	9 (22.4)	0	0	0	0	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-122.　人種別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.3_J

表 2.7.4.7-123. 体重区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	< 40 kg				>= 40 kg			
	M-SD (N=7) (PYS=4.3) Events (E/100PY)	M-HD (N=8) (PYS=5.8) Events (E/100PY)	Total-ADA (N=15) (PYS=10.0) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	M-SD (N=26) (PYS=16.2) Events (E/100PY)	M-HD (N=28) (PYS=18.0) Events (E/100PY)	Total-ADA (N=54) (PYS=34.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	18 (418.6)	16 (275.9)	34 (340.0)	0	56 (345.7)	61 (338.9)	117 (342.1)	26 (426.2)
Serious AE	2 (46.5)	2 (34.5)	4 (40.0)	0	8 (49.4)	4 (22.2)	12 (35.1)	1 (16.4)
Severe AE	1 (23.3)	0	1 (10.0)	0	4 (24.7)	1 (5.6)	5 (14.6)	0
AEs leading to discontinuation of study drug	0	0	0	0	3 (18.5)	0	3 (8.8)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (69.8)	3 (51.7)	6 (60.0)	0	11 (67.9)	17 (94.4)	28 (81.9)	6 (98.4)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	0	1 (5.6)	1 (2.9)	1 (16.4)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	6 (139.5)	5 (86.2)	11 (110.0)	0	12 (74.1)	17 (94.4)	29 (84.8)	9 (147.5)
Serious infections	0	1 (17.2)	1 (10.0)	0	3 (18.5)	2 (11.1)	5 (14.6)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-123. 体重区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	M-SD (N=7) (PYS=4.3) Events (E/100PY)	M-HD (N=8) (PYS=5.8) Events (E/100PY)	Total-ADA (N=15) (PYS=10.0) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	M-SD (N=26) (PYS=16.2) Events (E/100PY)	M-HD (N=28) (PYS=18.0) Events (E/100PY)	Total-ADA (N=54) (PYS=34.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (5.6)	1 (2.9)	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	1 (5.6)	1 (2.9)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-123. 体重区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	M-SD (N=7) (PYS=4.3) Events (E/100PY)	M-HD (N=8) (PYS=5.8) Events (E/100PY)	Total-ADA (N=15) (PYS=10.0) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	M-SD (N=26) (PYS=16.2) Events (E/100PY)	M-HD (N=28) (PYS=18.0) Events (E/100PY)	Total-ADA (N=54) (PYS=34.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	1 (17.2)	1 (10.0)	0	2 (12.3)	1 (5.6)	3 (8.8)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-123. 体重区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	< 40 kg				>= 40 kg			
	M-SD (N=7) (PYS=4.3) Events (E/100PY)	M-HD (N=8) (PYS=5.8) Events (E/100PY)	Total-ADA (N=15) (PYS=10.0) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	M-SD (N=26) (PYS=16.2) Events (E/100PY)	M-HD (N=28) (PYS=18.0) Events (E/100PY)	Total-ADA (N=54) (PYS=34.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (16.4)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	0	0	0	5 (30.9)	1 (5.6)	6 (17.5)	2 (32.8)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	1 (23.3)	2 (34.5)	3 (30.0)	0	5 (30.9)	1 (5.6)	6 (17.5)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-123. 体重区分別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.4_J

表 2.7.4.7-124.　抗 TNF 製剤の投与経験の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) n (%)	No (N=78) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	12 (80.0)	68 (87.2)
Serious AE	7 (46.7)	19 (24.4)
Severe AE	2 (13.3)	10 (12.8)
AEs leading to discontinuation of study drug	1 (6.7)	6 (7.7)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	5 (33.3)	32 (41.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (20.0)	5 (6.4)
AEs leading to death	0	0
Infections	9 (60.0)	41 (52.6)
Serious infections	3 (20.0)	3 (3.8)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (1.3)
Oral candidiasis	0	0
Tuberculosis	1 (6.7)	4 (5.1)
Active tuberculosis	0	0

表 2.7.4.7-124. 抗 TNF 製剤の投与経験の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) n (%)	No (N=78) n (%)
Latent tuberculosis	1 (6.7)	4 (5.1)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	2 (13.3)	4 (5.1)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-124. 抗 TNF 製剤の投与経験の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) n (%)	No (N=78) n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (1.3)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	0	2 (2.6)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	4 (26.7)	11 (14.1)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-124.　抗 TNF 製剤の投与経験の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) n (%)	No (N=78) n (%)
Injection site reaction	1 (6.7)	7 (9.0)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.5

表 2.7.4.7-125.　ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes (N=44) n (%)	No (N=49) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	37 (84.1)	43 (87.8)
Serious AE	13 (29.5)	13 (26.5)
Severe AE	7 (15.9)	5 (10.2)
AEs leading to discontinuation of study drug	5 (11.4)	2 (4.1)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	17 (38.6)	20 (40.8)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (6.8)	5 (10.2)
AEs leading to death	0	0
Infections	25 (56.8)	25 (51.0)
Serious infections	5 (11.4)	1 (2.0)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (2.0)
Oral candidiasis	0	0
Tuberculosis	4 (9.1)	1 (2.0)
Active tuberculosis	0	0

表 2.7.4.7-125. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes (N=44) n (%)	No (N=49) n (%)
Latent tuberculosis	4 (9.1)	1 (2.0)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	3 (6.8)	3 (6.1)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-125. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes	No
	(N=44)	(N=49)
	n (%)	n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (2.3)	0
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (2.3)	1 (2.0)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	5 (11.4)	10 (20.4)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-125. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes	No
	(N=44)	(N=49)
	n (%)	n (%)
Injection site reaction	4 (9.1)	4 (8.2)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
$ true baseline systemic corticosteroid use is displayed. Subject [redacted] was randomized in the stratum 'No', but actually has baseline systemic corticosteroid use documented.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.6

表 2.7.4.7-126.　ベースラインにおける免疫抑制剤の使用の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes (N=55) n (%)	No (N=38) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	47 (85.5)	33 (86.8)
Serious AE	15 (27.3)	11 (28.9)
Severe AE	6 (10.9)	6 (15.8)
AEs leading to discontinuation of study drug	5 (9.1)	2 (5.3)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	15 (27.3)	22 (57.9)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (3.6)	6 (15.8)
AEs leading to death	0	0
Infections	28 (50.9)	22 (57.9)
Serious infections	3 (5.5)	3 (7.9)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (2.6)
Oral candidiasis	0	0
Tuberculosis	3 (5.5)	2 (5.3)
Active tuberculosis	0	0

表 2.7.4.7-126. ベースラインにおける免疫抑制剤の使用の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes (N=55) n (%)	No (N=38) n (%)
Latent tuberculosis	3 (5.5)	2 (5.3)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	3 (5.5)	3 (7.9)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-126. ベースラインにおける免疫抑制剤の使用の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes (N=55) n (%)	No (N=38) n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (2.6)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (1.8)	1 (2.6)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	12 (21.8)	3 (7.9)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-126. ベースラインにおける免疫抑制剤の使用の有無別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes (N=55) n (%)	No (N=38) n (%)
Injection site reaction	2 (3.6)	6 (15.8)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.7

表 2.7.4.7-127. Mayo スコアに基づく疾患重症度別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9 (N=76) n (%)	> 9 (N=17) n (%)
Subjects with any treatment-emergent		
Adverse event (AE)	66 (86.8)	14 (82.4)
Serious AE	24 (31.6)	2 (11.8)
Severe AE	11 (14.5)	1 (5.9)
AEs leading to discontinuation of study drug	6 (7.9)	1 (5.9)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	33 (43.4)	4 (23.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	7 (9.2)	1 (5.9)
AEs leading to death	0	0
Infections	41 (53.9)	9 (52.9)
Serious infections	6 (7.9)	0
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	1 (1.3)	0
Oral candidiasis	0	0
Tuberculosis	5 (6.6)	0
Active tuberculosis	0	0

表 2.7.4.7-127. Mayo スコアに基づく疾患重症度別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9 (N=76) n (%)	> 9 (N=17) n (%)
Latent tuberculosis	5 (6.6)	0
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0
Allergic reactions including angioedema/anaphylaxis	5 (6.6)	1 (5.9)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0

表 2.7.4.7-127. Mayo スコアに基づく疾患重症度別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9 (N=76) n (%)	> 9 (N=17) n (%)
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (1.3)	0
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	2 (2.6)	0
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	11 (14.5)	4 (23.5)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0

表 2.7.4.7-127. Mayo スコアに基づく疾患重症度別の有害事象の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9 (N=76) n (%)	> 9 (N=17) n (%)
Injection site reaction	8 (10.5)	0
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
ADA = Adalimumab.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.1.2.8

表 2.7.4.7-128. 抗 TNF 製剤の投与経験の有無別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) (PYS=23.0) Events (E/100PY)	No (N=78) (PYS=122.0) Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	83 (360.9)	382 (313.1)
Serious AE	12 (52.2)	32 (26.2)
Severe AE	2 (8.7)	16 (13.1)
AEs leading to discontinuation of study drug	1 (4.3)	8 (6.6)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	17 (73.9)	62 (50.8)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (13.0)	7 (5.7)
AEs leading to death	0	0
Infections	27 (117.4)	90 (73.8)
Serious infections	3 (13.0)	3 (2.5)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (0.8)

表 2.7.4.7-128. 抗 TNF 製剤の投与経験の有無別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) (PYS=23.0) Events (E/100PY)	No (N=78) (PYS=122.0) Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	1 (4.3)	4 (3.3)
Active tuberculosis	0	0
Latent tuberculosis	1 (4.3)	4 (3.3)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-128. 抗 TNF 製剤の投与経験の有無別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) (PYS=23.0) Events (E/100PY)	No (N=78) (PYS=122.0) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (8.7)	5 (4.1)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (0.8)

表 2.7.4.7-128. 抗 TNF 製剤の投与経験の有無別の有害事象の 100 人年あたりの発現頻度の概要（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Prior Exposure to Anti-TNF	
	Yes (N=15) (PYS=23.0) Events (E/100PY)	No (N=78) (PYS=122.0) Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	0	2 (1.6)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	4 (17.4)	14 (11.5)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	1 (4.3)	12 (9.8)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
TNF = Tumor necrosis factor; ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.2.2.5

表 2.7.4.7-129. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes	No
	(N=44)	(N=49)
	(PYS=57.0)	(PYS=88.0)
	Events (E/100PY)	Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	251 (440.4)	214 (243.2)
Serious AE	24 (42.1)	20 (22.7)
Severe AE	10 (17.5)	8 (9.1)
AEs leading to discontinuation of study drug	7 (12.3)	2 (2.3)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	33 (57.9)	46 (52.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (5.3)	7 (8.0)
AEs leading to death	0	0
Infections	54 (94.7)	63 (71.6)
Serious infections	5 (8.8)	1 (1.1)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (1.1)

表 2.7.4.7-129. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes	No
	(N=44)	(N=49)
	(PYS=57.0)	(PYS=88.0)
	Events (E/100PY)	Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	4 (7.0)	1 (1.1)
Active tuberculosis	0	0
Latent tuberculosis	4 (7.0)	1 (1.1)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-129. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes	No
	(N=44)	(N=49)
	(PYS=57.0)	(PYS=88.0)
	Events (E/100PY)	Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	3 (5.3)	4 (4.5)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (1.8)	0

表 2.7.4.7-129. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Systemic Corticosteroid Use$	
	Yes	No
	(N=44)	(N=49)
	(PYS=57.0)	(PYS=88.0)
	Events (E/100PY)	Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (1.8)	1 (1.1)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	7 (12.3)	11 (12.5)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	8 (14.0)	5 (5.7)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

表 2.7.4.7-129. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
$ true baseline systemic corticosteroid use is displayed. Subject [redacted] was randomized in the stratum 'No', but actually has baseline systemic corticosteroid use documented.
# As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.2.2.6

表 2.7.4.7-130. ベースラインにおける免疫抑制剤の使用の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes	No
	(N=55)	(N=38)
	(PYS=104.5)	(PYS=40.5)
	Events (E/100PY)	Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	232 (222.0)	233 (575.3)
Serious AE	28 (26.8)	16 (39.5)
Severe AE	10 (9.6)	8 (19.8)
AEs leading to discontinuation of study drug	6 (5.7)	3 (7.4)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	24 (23.0)	55 (135.8)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	4 (3.8)	6 (14.8)
AEs leading to death	0	0
Infections	71 (67.9)	46 (113.6)
Serious infections	3 (2.9)	3 (7.4)
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	1 (2.5)

表 2.7.4.7-130. ベースラインにおける免疫抑制剤の使用の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes	No
	(N=55)	(N=38)
	(PYS=104.5)	(PYS=40.5)
	Events (E/100PY)	Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	3 (2.9)	2 (4.9)
Active tuberculosis	0	0
Latent tuberculosis	3 (2.9)	2 (4.9)
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-130. ベースラインにおける免疫抑制剤の使用の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes	No
	(N=55)	(N=38)
	(PYS=104.5)	(PYS=40.5)
	Events (E/100PY)	Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	4 (3.8)	3 (7.4)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	0	1 (2.5)

表 2.7.4.7-130. ベースラインにおける免疫抑制剤の使用の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Baseline Immunosuppressants (IMM) Use	
	Yes	No
	(N=55)	(N=38)
	(PYS=104.5)	(PYS=40.5)
	Events (E/100PY)	Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	1 (1.0)	1 (2.5)
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	15 (14.4)	3 (7.4)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	3 (2.9)	10 (24.7)
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

表 2.7.4.7-130.　ベースラインにおける免疫抑制剤の使用の有無別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4　1.2.2.7

表 2.7.4.7-131. Mayo スコアに基づく疾患重症度別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9	> 9
	(N=76)	(N=17)
	(PYS=115.3)	(PYS=29.7)
	Events (E/100PY)	Events (E/100PY)
Any treatment-emergent		
Adverse event (AE)	397 (344.3)	68 (229.0)
Serious AE	41 (35.6)	3 (10.1)
Severe AE	17 (14.7)	1 (3.4)
AEs leading to discontinuation of study drug	8 (6.9)	1 (3.4)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	73 (63.3)	6 (20.2)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	8 (6.9)	2 (6.7)
AEs leading to death	0	0
Infections	86 (74.6)	31 (104.4)
Serious infections	6 (5.2)	0
Legionella infections	0	0
Diverticulitis	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	1 (0.9)	0

表 2.7.4.7-131. Mayo スコアに基づく疾患重症度別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9	> 9
	(N=76)	(N=17)
	(PYS=115.3)	(PYS=29.7)
	Events (E/100PY)	Events (E/100PY)
Oral candidiasis	0	0
Tuberculosis	5 (4.3)	0
Active tuberculosis	0	0
Latent tuberculosis	5 (4.3)	0
Parasitic infections	0	0
Reactivation of Hepatitis B	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0
Malignancies	0	0
Lymphoma	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0
Non-melanoma skin cancer (NMSC)	0	0
Melanoma	0	0
Leukemia	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0

表 2.7.4.7-131. Mayo スコアに基づく疾患重症度別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9	> 9
	(N=76)	(N=17)
	(PYS=115.3)	(PYS=29.7)
	Events (E/100PY)	Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	6 (5.2)	1 (3.4)
Lupus-like reactions and systemic lupus erythematosus	0	0
Vasculitis	0	0
Cutaneous vasculitis	0	0
Non-cutaneous vasculitis	0	0
Sarcoidosis	0	0
Autoimmune Hepatitis	0	0
Myocardial infarction (MI)	0	0
Cerebrovascular accident (CVA)	0	0
Congestive heart failure (CHF)	0	0
Pulmonary embolism	0	0
Interstitial lung disease	0	0
Intestinal perforation	0	0
Pancreatitis	1 (0.9)	0

表 2.7.4.7-131. Mayo スコアに基づく疾患重症度別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

	Any Adalimumab	
	Disease Severity per Baseline Mayo Score	
	<= 9	> 9
	(N=76)	(N=17)
	(PYS=115.3)	(PYS=29.7)
	Events (E/100PY)	Events (E/100PY)
Stevens-Johnson syndrome	0	0
Erythema multiforme	0	0
Worsening or new onset of psoriasis	2 (1.7)	0
Demyelinating disorder	0	0
Amyotrophic lateral sclerosis	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0
Hematologic disorders including pancytopenia	14 (12.1)	4 (13.5)
Liver failure and other liver events	0	0
Humira administration related medication error	0	0
Injection site reaction	13 (11.3)	0
All deaths	0	0
Occurring <=70 days after last dose	0	0
Occurring >70 days after last dose	0	0

表 2.7.4.7-131.　Mayo スコアに基づく疾患重症度別の有害事象の 100 人年あたりの発現頻度の概要
（M11-290 主試験及び M10-870 主試験の併合）（続き）

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
ADA = Adalimumab; E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: G-CTD ISS Supplemental Table 2.4　1.2.2.8

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
Any adverse event	12 (80.0)	68 (87.2)
血液およびリンパ系障害	4 (26.7)	15 (19.2)
貧血	4 (26.7)	11 (14.1)
失血性貧血	0	1 (1.3)
鉄欠乏性貧血	0	2 (2.6)
リンパ節炎	0	1 (1.3)
リンパ節症	0	1 (1.3)
血小板増加症	0	1 (1.3)
心臓障害	0	1 (1.3)
心膜炎	0	1 (1.3)
耳および迷路障害	0	1 (1.3)
耳痛	0	1 (1.3)
内分泌障害	0	1 (1.3)
甲状腺腫	0	1 (1.3)
眼障害	0	2 (2.6)
角膜炎	0	1 (1.3)
非感染性結膜炎	0	1 (1.3)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
胃腸障害	7 (46.7)	40 (51.3)
腹部不快感	0	1 (1.3)
腹痛	0	6 (7.7)
上腹部痛	0	6 (7.7)
アフタ性潰瘍	0	1 (1.3)
口唇症	0	1 (1.3)
潰瘍性大腸炎	6 (40.0)	23 (29.5)
便秘	0	3 (3.8)
下痢	1 (6.7)	2 (2.6)
血性下痢	0	1 (1.3)
消化不良	0	2 (2.6)
小腸炎	0	3 (3.8)
腸炎	0	1 (1.3)
鼓腸	0	1 (1.3)
排便回数増加	0	1 (1.3)
胃炎	0	3 (3.8)
胃食道逆流性疾患	0	2 (2.6)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
胃腸障害 (Cont.)		
血便排泄	1 (6.7)	3 (3.8)
大腸ポリープ	2 (13.3)	0
悪心	0	5 (6.4)
膵炎	0	1 (1.3)
直腸出血	0	1 (1.3)
嘔吐	1 (6.7)	3 (3.8)
一般・全身障害および投与部位の状態	3 (20.0)	15 (19.2)
腋窩痛	0	1 (1.3)
胸痛	0	1 (1.3)
疲労	1 (6.7)	2 (2.6)
炎症	0	1 (1.3)
インフルエンザ様疾患	0	1 (1.3)
注射部位紅斑	0	1 (1.3)
注射部位炎症	0	1 (1.3)
注射部位浮腫	0	1 (1.3)
注射部位疼痛	0	2 (2.6)
注射部位そう痒感	1 (6.7)	0

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	0	1 (1.3)
注射部位蕁麻疹	0	2 (2.6)
倦怠感	1 (6.7)	0
末梢性浮腫	0	1 (1.3)
末梢腫脹	0	1 (1.3)
発熱	2 (13.3)	3 (3.8)
肝胆道系障害	1 (6.7)	1 (1.3)
胆嚢炎	1 (6.7)	0
高ビリルビン血症	0	1 (1.3)
免疫系障害	1 (6.7)	1 (1.3)
薬物過敏症	1 (6.7)	0
季節性アレルギー	0	1 (1.3)
感染症および寄生虫症	9 (60.0)	41 (52.6)
肛門膿瘍	0	1 (1.3)
気管支炎	1 (6.7)	4 (5.1)
クロストリジウム・ディフィシレ感染	0	1 (1.3)
サイトメガロウイルス性腸炎	0	1 (1.3)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
感染症および寄生虫症 (Cont.)		
せつ	0	1 (1.3)
胃腸炎	0	3 (3.8)
サルモネラ菌性胃腸炎	0	1 (1.3)
ウイルス性胃腸炎	1 (6.7)	1 (1.3)
帯状疱疹	0	1 (1.3)
膿痂疹	0	1 (1.3)
感染性嚢腫	1 (6.7)	0
インフルエンザ	0	1 (1.3)
喉頭炎	0	1 (1.3)
無菌性髄膜炎	1 (6.7)	0
上咽頭炎	3 (20.0)	8 (10.3)
口腔ヘルペス	1 (6.7)	2 (2.6)
中耳炎	0	1 (1.3)
咽頭炎	2 (13.3)	9 (11.5)
気道感染	1 (6.7)	1 (1.3)
ウイルス性気道感染	0	1 (1.3)
鼻炎	0	1 (1.3)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	0	1 (1.3)
レンサ球菌感染	0	1 (1.3)
癜風	0	1 (1.3)
扁桃炎	0	1 (1.3)
歯膿瘍	1 (6.7)	1 (1.3)
気管炎	0	1 (1.3)
上気道感染	1 (6.7)	13 (16.7)
尿路感染	2 (13.3)	5 (6.4)
水痘	0	2 (2.6)
ウイルス感染	0	3 (3.8)
ウイルス性上気道感染	1 (6.7)	2 (2.6)
外陰腟真菌感染	0	1 (1.3)
外陰腟炎	0	1 (1.3)
傷害、中毒および処置合併症	0	11 (14.1)
足関節部骨折	0	1 (1.3)
節足動物咬傷	0	1 (1.3)
転倒	0	1 (1.3)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	0	2 (2.6)
注入に伴う反応	0	1 (1.3)
靱帯捻挫	0	1 (1.3)
四肢損傷	0	1 (1.3)
処置による疼痛	0	1 (1.3)
上肢骨折	0	1 (1.3)
手首関節骨折	0	2 (2.6)
臨床検査	2 (13.3)	16 (20.5)
血中アルカリホスファターゼ増加	1 (6.7)	0
血中ビリルビン増加	0	2 (2.6)
血中カルシウム減少	0	1 (1.3)
血圧上昇	0	1 (1.3)
血中ナトリウム減少	0	1 (1.3)
体温上昇	0	1 (1.3)
骨密度減少	0	1 (1.3)
Ｃ－反応性蛋白増加	0	5 (6.4)
好酸球数増加	0	1 (1.3)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	0	1 (1.3)
ヘモグロビン減少	0	1 (1.3)
肝酵素上昇	0	1 (1.3)
リンパ節触知	0	1 (1.3)
結核菌群検査陽性	1 (6.7)	4 (5.1)
好中球数減少	0	1 (1.3)
体重減少	0	2 (2.6)
白血球数減少	0	1 (1.3)
筋骨格系および結合組織障害	3 (20.0)	9 (11.5)
関節痛	2 (13.3)	3 (3.8)
背部痛	0	3 (3.8)
成長不全	1 (6.7)	0
若年性特発性関節炎	0	1 (1.3)
靭帯障害	0	1 (1.3)
四肢痛	0	1 (1.3)
脊椎痛	0	1 (1.3)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
神経系障害	4 (26.7)	22 (28.2)
頭痛	3 (20.0)	20 (25.6)
感覚鈍麻	1 (6.7)	0
意識消失	0	1 (1.3)
片頭痛	0	1 (1.3)
錯感覚	1 (6.7)	1 (1.3)
傾眠	0	1 (1.3)
振戦	0	2 (2.6)
精神障害	0	4 (5.1)
うつ病	0	4 (5.1)
腎および尿路障害	1 (6.7)	3 (3.8)
糖尿	0	1 (1.3)
血尿	0	1 (1.3)
腎結石症	1 (6.7)	0
腎仙痛	0	1 (1.3)
生殖系および乳房障害	3 (20.0)	2 (2.6)
乳房痛	0	1 (1.3)
月経困難症	2 (13.3)	0

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
生殖系および乳房障害 (Cont.)		
卵巣嚢胞	1 (6.7)	1 (1.3)
呼吸器、胸郭および縦隔障害	3 (20.0)	17 (21.8)
喘息	1 (6.7)	1 (1.3)
咳嗽	2 (13.3)	2 (2.6)
鼻出血	0	3 (3.8)
鼻閉	0	2 (2.6)
鼻浮腫	0	1 (1.3)
口腔咽頭痛	1 (6.7)	6 (7.7)
アレルギー性鼻炎	0	3 (3.8)
鼻漏	0	4 (5.1)
喘鳴	0	1 (1.3)
皮膚および皮下組織障害	3 (20.0)	12 (15.4)
脱毛症	0	1 (1.3)
皮膚炎	0	2 (2.6)
乾癬様皮膚炎	0	1 (1.3)
紅斑	1 (6.7)	0
結節性紅斑	1 (6.7)	2 (2.6)

表 2.7.4.7-132. 抗 TNF 製剤の投与経験の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Prior Exposure to Anti-TNF Yes (N=15) n (%)	Any Adalimumab Prior Exposure to Anti-TNF No (N=78) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	0	1 (1.3)
乾癬	0	1 (1.3)
発疹	0	5 (6.4)
痂皮	0	1 (1.3)
脂漏	0	1 (1.3)
皮膚障害	1 (6.7)	0
皮膚病変	0	1 (1.3)
血管障害	0	1 (1.3)
高血圧	0	1 (1.3)

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.5

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）
（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
Any adverse event	37 (84.1)	43 (87.8)
血液およびリンパ系障害	7 (15.9)	12 (24.5)
貧血	5 (11.4)	10 (20.4)
失血性貧血	0	1 (2.0)
鉄欠乏性貧血	1 (2.3)	1 (2.0)
リンパ節炎	1 (2.3)	0
リンパ節症	0	1 (2.0)
血小板増加症	1 (2.3)	0
心臓障害	1 (2.3)	0
心膜炎	1 (2.3)	0
耳および迷路障害	1 (2.3)	0
耳痛	1 (2.3)	0
内分泌障害	0	1 (2.0)
甲状腺腫	0	1 (2.0)
眼障害	1 (2.3)	1 (2.0)
角膜炎	0	1 (2.0)
非感染性結膜炎	1 (2.3)	0

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
胃腸障害	25 (56.8)	22 (44.9)
腹部不快感	0	1 (2.0)
腹痛	4 (9.1)	2 (4.1)
上腹部痛	4 (9.1)	2 (4.1)
アフタ性潰瘍	1 (2.3)	0
口唇症	1 (2.3)	0
潰瘍性大腸炎	14 (31.8)	15 (30.6)
便秘	1 (2.3)	2 (4.1)
下痢	1 (2.3)	2 (4.1)
血性下痢	1 (2.3)	0
消化不良	2 (4.5)	0
小腸炎	3 (6.8)	0
腸炎	1 (2.3)	0
鼓腸	1 (2.3)	0
排便回数増加	1 (2.3)	0
胃炎	1 (2.3)	2 (4.1)
胃食道逆流性疾患	1 (2.3)	1 (2.0)

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
胃腸障害 (Cont.)		
血便排泄	3 (6.8)	1 (2.0)
大腸ポリープ	1 (2.3)	1 (2.0)
悪心	3 (6.8)	2 (4.1)
膵炎	1 (2.3)	0
直腸出血	0	1 (2.0)
嘔吐	2 (4.5)	2 (4.1)
一般・全身障害および投与部位の状態	9 (20.5)	9 (18.4)
腋窩痛	1 (2.3)	0
胸痛	1 (2.3)	0
疲労	3 (6.8)	0
炎症	1 (2.3)	0
インフルエンザ様疾患	0	1 (2.0)
注射部位紅斑	0	1 (2.0)
注射部位炎症	0	1 (2.0)
注射部位浮腫	1 (2.3)	0
注射部位疼痛	2 (4.5)	0
注射部位そう痒感	0	1 (2.0)

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	0	1 (2.0)
注射部位蕁麻疹	1 (2.3)	1 (2.0)
倦怠感	0	1 (2.0)
末梢性浮腫	0	1 (2.0)
末梢腫脹	1 (2.3)	0
発熱	1 (2.3)	4 (8.2)
肝胆道系障害	1 (2.3)	1 (2.0)
胆嚢炎	0	1 (2.0)
高ビリルビン血症	1 (2.3)	0
免疫系障害	0	2 (4.1)
薬物過敏症	0	1 (2.0)
季節性アレルギー	0	1 (2.0)
感染症および寄生虫症	25 (56.8)	25 (51.0)
肛門膿瘍	0	1 (2.0)
気管支炎	4 (9.1)	1 (2.0)
クロストリジウム・ディフィシレ感染	0	1 (2.0)
サイトメガロウイルス性腸炎	0	1 (2.0)

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
感染症および寄生虫症 (Cont.)		
せつ	0	1 (2.0)
胃腸炎	2 (4.5)	1 (2.0)
サルモネラ菌性胃腸炎	1 (2.3)	0
ウイルス性胃腸炎	0	2 (4.1)
帯状疱疹	0	1 (2.0)
膿痂疹	1 (2.3)	0
感染性嚢腫	1 (2.3)	0
インフルエンザ	0	1 (2.0)
喉頭炎	1 (2.3)	0
無菌性髄膜炎	0	1 (2.0)
上咽頭炎	6 (13.6)	5 (10.2)
口腔ヘルペス	1 (2.3)	2 (4.1)
中耳炎	1 (2.3)	0
咽頭炎	7 (15.9)	4 (8.2)
気道感染	2 (4.5)	0
ウイルス性気道感染	0	1 (2.0)
鼻炎	1 (2.3)	0

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	1 (2.3)	0
レンサ球菌感染	0	1 (2.0)
癜風	0	1 (2.0)
扁桃炎	0	1 (2.0)
歯膿瘍	1 (2.3)	1 (2.0)
気管炎	0	1 (2.0)
上気道感染	9 (20.5)	5 (10.2)
尿路感染	4 (9.1)	3 (6.1)
水痘	0	2 (4.1)
ウイルス感染	2 (4.5)	1 (2.0)
ウイルス性上気道感染	2 (4.5)	1 (2.0)
外陰腟真菌感染	0	1 (2.0)
外陰腟炎	1 (2.3)	0
傷害、中毒および処置合併症	8 (18.2)	3 (6.1)
足関節部骨折	1 (2.3)	0
節足動物咬傷	1 (2.3)	0
転倒	0	1 (2.0)

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	1 (2.3)	1 (2.0)
注入に伴う反応	0	1 (2.0)
靭帯捻挫	1 (2.3)	0
四肢損傷	1 (2.3)	0
処置による疼痛	1 (2.3)	0
上肢骨折	1 (2.3)	0
手首関節骨折	2 (4.5)	0
臨床検査	9 (20.5)	9 (18.4)
血中アルカリホスファターゼ増加	0	1 (2.0)
血中ビリルビン増加	1 (2.3)	1 (2.0)
血中カルシウム減少	0	1 (2.0)
血圧上昇	1 (2.3)	0
血中ナトリウム減少	1 (2.3)	0
体温上昇	0	1 (2.0)
骨密度減少	0	1 (2.0)
Ｃ－反応性蛋白増加	3 (6.8)	2 (4.1)
好酸球数増加	1 (2.3)	0

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	0	1 (2.0)
ヘモグロビン減少	0	1 (2.0)
肝酵素上昇	0	1 (2.0)
リンパ節触知	1 (2.3)	0
結核菌群検査陽性	4 (9.1)	1 (2.0)
好中球数減少	0	1 (2.0)
体重減少	1 (2.3)	1 (2.0)
白血球数減少	0	1 (2.0)
筋骨格系および結合組織障害	7 (15.9)	5 (10.2)
関節痛	2 (4.5)	3 (6.1)
背部痛	2 (4.5)	1 (2.0)
成長不全	1 (2.3)	0
若年性特発性関節炎	1 (2.3)	0
靭帯障害	1 (2.3)	0
四肢痛	0	1 (2.0)
脊椎痛	1 (2.3)	0

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
神経系障害	15 (34.1)	11 (22.4)
頭痛	14 (31.8)	9 (18.4)
感覚鈍麻	0	1 (2.0)
意識消失	0	1 (2.0)
片頭痛	0	1 (2.0)
錯感覚	0	2 (4.1)
傾眠	1 (2.3)	0
振戦	1 (2.3)	1 (2.0)
精神障害	2 (4.5)	2 (4.1)
うつ病	2 (4.5)	2 (4.1)
腎および尿路障害	2 (4.5)	2 (4.1)
糖尿	1 (2.3)	0
血尿	0	1 (2.0)
腎結石症	0	1 (2.0)
腎仙痛	1 (2.3)	0
生殖系および乳房障害	2 (4.5)	3 (6.1)
乳房痛	1 (2.3)	0
月経困難症	1 (2.3)	1 (2.0)

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
生殖系および乳房障害 (Cont.)		
卵巣嚢胞	0	2 (4.1)
呼吸器、胸郭および縦隔障害	14 (31.8)	6 (12.2)
喘息	1 (2.3)	1 (2.0)
咳嗽	2 (4.5)	2 (4.1)
鼻出血	3 (6.8)	0
鼻閉	1 (2.3)	1 (2.0)
鼻浮腫	0	1 (2.0)
口腔咽頭痛	5 (11.4)	2 (4.1)
アレルギー性鼻炎	3 (6.8)	0
鼻漏	3 (6.8)	1 (2.0)
喘鳴	0	1 (2.0)
皮膚および皮下組織障害	7 (15.9)	8 (16.3)
脱毛症	1 (2.3)	0
皮膚炎	2 (4.5)	0
乾癬様皮膚炎	0	1 (2.0)
紅斑	1 (2.3)	0
結節性紅斑	2 (4.5)	1 (2.0)

表 2.7.4.7-133. ベースラインにおけるコルチコステロイドの全身投与の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Systemic Corticosteroid Use$ Yes (N=44) n (%)	Any Adalimumab Baseline Systemic Corticosteroid Use$ No (N=49) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	1 (2.3)	0
乾癬	1 (2.3)	0
発疹	1 (2.3)	4 (8.2)
痂皮	1 (2.3)	0
脂漏	0	1 (2.0)
皮膚障害	0	1 (2.0)
皮膚病変	0	1 (2.0)
血管障害	1 (2.3)	0
高血圧	1 (2.3)	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.
$ true baseline systemic corticosteroid use is displayed. Subject [redacted] was randomized in the stratum 'No', but actually has baseline systemic corticosteroid use documented.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.6

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）
（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
Any adverse event	47 (85.5)	33 (86.8)
血液およびリンパ系障害	14 (25.5)	5 (13.2)
貧血	12 (21.8)	3 (7.9)
失血性貧血	1 (1.8)	0
鉄欠乏性貧血	0	2 (5.3)
リンパ節炎	1 (1.8)	0
リンパ節症	1 (1.8)	0
血小板増加症	0	1 (2.6)
心臓障害	0	1 (2.6)
心膜炎	0	1 (2.6)
耳および迷路障害	0	1 (2.6)
耳痛	0	1 (2.6)
内分泌障害	1 (1.8)	0
甲状腺腫	1 (1.8)	0
眼障害	1 (1.8)	1 (2.6)
角膜炎	1 (1.8)	0
非感染性結膜炎	0	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
胃腸障害	27 (49.1)	20 (52.6)
腹部不快感	1 (1.8)	0
腹痛	1 (1.8)	5 (13.2)
上腹部痛	3 (5.5)	3 (7.9)
アフタ性潰瘍	0	1 (2.6)
口唇症	1 (1.8)	0
潰瘍性大腸炎	17 (30.9)	12 (31.6)
便秘	0	3 (7.9)
下痢	2 (3.6)	1 (2.6)
血性下痢	1 (1.8)	0
消化不良	1 (1.8)	1 (2.6)
小腸炎	1 (1.8)	2 (5.3)
腸炎	1 (1.8)	0
鼓腸	0	1 (2.6)
排便回数増加	0	1 (2.6)
胃炎	3 (5.5)	0
胃食道逆流性疾患	1 (1.8)	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
胃腸障害 (Cont.)		
血便排泄	0	4 (10.5)
大腸ポリープ	1 (1.8)	1 (2.6)
悪心	1 (1.8)	4 (10.5)
膵炎	0	1 (2.6)
直腸出血	1 (1.8)	0
嘔吐	0	4 (10.5)
一般・全身障害および投与部位の状態	8 (14.5)	10 (26.3)
腋窩痛	1 (1.8)	0
胸痛	0	1 (2.6)
疲労	0	3 (7.9)
炎症	0	1 (2.6)
インフルエンザ様疾患	1 (1.8)	0
注射部位紅斑	1 (1.8)	0
注射部位炎症	1 (1.8)	0
注射部位浮腫	0	1 (2.6)
注射部位疼痛	0	2 (5.3)
注射部位そう痒感	0	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	0	1 (2.6)
注射部位蕁麻疹	1 (1.8)	1 (2.6)
倦怠感	0	1 (2.6)
末梢性浮腫	1 (1.8)	0
末梢腫脹	1 (1.8)	0
発熱	2 (3.6)	3 (7.9)
肝胆道系障害	0	2 (5.3)
胆嚢炎	0	1 (2.6)
高ビリルビン血症	0	1 (2.6)
免疫系障害	0	2 (5.3)
薬物過敏症	0	1 (2.6)
季節性アレルギー	0	1 (2.6)
感染症および寄生虫症	28 (50.9)	22 (57.9)
肛門膿瘍	1 (1.8)	0
気管支炎	3 (5.5)	2 (5.3)
クロストリジウム・ディフィシレ感染	0	1 (2.6)
サイトメガロウイルス性腸炎	0	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
感染症および寄生虫症 (Cont.)		
せつ	1 (1.8)	0
胃腸炎	2 (3.6)	1 (2.6)
サルモネラ菌性胃腸炎	1 (1.8)	0
ウイルス性胃腸炎	1 (1.8)	1 (2.6)
帯状疱疹	1 (1.8)	0
膿痂疹	0	1 (2.6)
感染性嚢腫	0	1 (2.6)
インフルエンザ	1 (1.8)	0
喉頭炎	0	1 (2.6)
無菌性髄膜炎	0	1 (2.6)
上咽頭炎	3 (5.5)	8 (21.1)
口腔ヘルペス	3 (5.5)	0
中耳炎	1 (1.8)	0
咽頭炎	7 (12.7)	4 (10.5)
気道感染	1 (1.8)	1 (2.6)
ウイルス性気道感染	1 (1.8)	0
鼻炎	0	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	1 (1.8)	0
レンサ球菌感染	0	1 (2.6)
癜風	1 (1.8)	0
扁桃炎	1 (1.8)	0
歯膿瘍	2 (3.6)	0
気管炎	1 (1.8)	0
上気道感染	8 (14.5)	6 (15.8)
尿路感染	4 (7.3)	3 (7.9)
水痘	2 (3.6)	0
ウイルス感染	0	3 (7.9)
ウイルス性上気道感染	3 (5.5)	0
外陰腟真菌感染	0	1 (2.6)
外陰腟炎	0	1 (2.6)
傷害、中毒および処置合併症	6 (10.9)	5 (13.2)
足関節部骨折	0	1 (2.6)
節足動物咬傷	1 (1.8)	0
転倒	1 (1.8)	0

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	1 (1.8)	1 (2.6)
注入に伴う反応	1 (1.8)	0
靭帯捻挫	0	1 (2.6)
四肢損傷	0	1 (2.6)
処置による疼痛	0	1 (2.6)
上肢骨折	1 (1.8)	0
手首関節骨折	2 (3.6)	0
臨床検査	7 (12.7)	11 (28.9)
血中アルカリホスファターゼ増加	0	1 (2.6)
血中ビリルビン増加	0	2 (5.3)
血中カルシウム減少	0	1 (2.6)
血圧上昇	1 (1.8)	0
血中ナトリウム減少	0	1 (2.6)
体温上昇	1 (1.8)	0
骨密度減少	1 (1.8)	0
Ｃ－反応性蛋白増加	0	5 (13.2)
好酸球数増加	0	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	0	1 (2.6)
ヘモグロビン減少	1 (1.8)	0
肝酵素上昇	0	1 (2.6)
リンパ節触知	0	1 (2.6)
結核菌群検査陽性	3 (5.5)	2 (5.3)
好中球数減少	0	1 (2.6)
体重減少	0	2 (5.3)
白血球数減少	0	1 (2.6)
筋骨格系および結合組織障害	6 (10.9)	6 (15.8)
関節痛	2 (3.6)	3 (7.9)
背部痛	1 (1.8)	2 (5.3)
成長不全	0	1 (2.6)
若年性特発性関節炎	1 (1.8)	0
靭帯障害	1 (1.8)	0
四肢痛	1 (1.8)	0
脊椎痛	0	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
神経系障害	13 (23.6)	13 (34.2)
頭痛	12 (21.8)	11 (28.9)
感覚鈍麻	0	1 (2.6)
意識消失	1 (1.8)	0
片頭痛	1 (1.8)	0
錯感覚	1 (1.8)	1 (2.6)
傾眠	0	1 (2.6)
振戦	1 (1.8)	1 (2.6)
精神障害	3 (5.5)	1 (2.6)
うつ病	3 (5.5)	1 (2.6)
腎および尿路障害	1 (1.8)	3 (7.9)
糖尿	0	1 (2.6)
血尿	1 (1.8)	0
腎結石症	0	1 (2.6)
腎仙痛	0	1 (2.6)
生殖系および乳房障害	4 (7.3)	1 (2.6)
乳房痛	1 (1.8)	0
月経困難症	1 (1.8)	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
生殖系および乳房障害 (Cont.)		
卵巣嚢胞	2 (3.6)	0
呼吸器、胸郭および縦隔障害	8 (14.5)	12 (31.6)
喘息	1 (1.8)	1 (2.6)
咳嗽	2 (3.6)	2 (5.3)
鼻出血	1 (1.8)	2 (5.3)
鼻閉	1 (1.8)	1 (2.6)
鼻浮腫	1 (1.8)	0
口腔咽頭痛	1 (1.8)	6 (15.8)
アレルギー性鼻炎	1 (1.8)	2 (5.3)
鼻漏	1 (1.8)	3 (7.9)
喘鳴	1 (1.8)	0
皮膚および皮下組織障害	10 (18.2)	5 (13.2)
脱毛症	1 (1.8)	0
皮膚炎	1 (1.8)	1 (2.6)
乾癬様皮膚炎	1 (1.8)	0
紅斑	0	1 (2.6)
結節性紅斑	2 (3.6)	1 (2.6)

表 2.7.4.7-134. ベースラインにおける免疫抑制剤の使用の有無別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Baseline Immunosuppressants (IMM) Use Yes (N=55) n (%)	Any Adalimumab Baseline Immunosuppressants (IMM) Use No (N=38) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	0	1 (2.6)
乾癬	0	1 (2.6)
発疹	4 (7.3)	1 (2.6)
痂皮	1 (1.8)	0
脂漏	1 (1.8)	0
皮膚障害	1 (1.8)	0
皮膚病変	1 (1.8)	0
血管障害	1 (1.8)	0
高血圧	1 (1.8)	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.7

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
Any adverse event	66 (86.8)	14 (82.4)
血液およびリンパ系障害	15 (19.7)	4 (23.5)
貧血	11 (14.5)	4 (23.5)
失血性貧血	1 (1.3)	0
鉄欠乏性貧血	2 (2.6)	0
リンパ節炎	1 (1.3)	0
リンパ節症	1 (1.3)	0
血小板増加症	1 (1.3)	0
心臓障害	1 (1.3)	0
心膜炎	1 (1.3)	0
耳および迷路障害	1 (1.3)	0
耳痛	1 (1.3)	0
内分泌障害	1 (1.3)	0
甲状腺腫	1 (1.3)	0
眼障害	2 (2.6)	0
角膜炎	1 (1.3)	0
非感染性結膜炎	1 (1.3)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
胃腸障害	39 (51.3)	8 (47.1)
腹部不快感	1 (1.3)	0
腹痛	4 (5.3)	2 (11.8)
上腹部痛	6 (7.9)	0
アフタ性潰瘍	1 (1.3)	0
口唇症	1 (1.3)	0
潰瘍性大腸炎	24 (31.6)	5 (29.4)
便秘	3 (3.9)	0
下痢	2 (2.6)	1 (5.9)
血性下痢	1 (1.3)	0
消化不良	2 (2.6)	0
小腸炎	3 (3.9)	0
腸炎	1 (1.3)	0
鼓腸	1 (1.3)	0
排便回数増加	1 (1.3)	0
胃炎	2 (2.6)	1 (5.9)
胃食道逆流性疾患	2 (2.6)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
胃腸障害 (Cont.)		
血便排泄	4 (5.3)	0
大腸ポリープ	2 (2.6)	0
悪心	5 (6.6)	0
膵炎	1 (1.3)	0
直腸出血	1 (1.3)	0
嘔吐	4 (5.3)	0
一般・全身障害および投与部位の状態	15 (19.7)	3 (17.6)
腋窩痛	1 (1.3)	0
胸痛	1 (1.3)	0
疲労	3 (3.9)	0
炎症	1 (1.3)	0
インフルエンザ様疾患	1 (1.3)	0
注射部位紅斑	1 (1.3)	0
注射部位炎症	1 (1.3)	0
注射部位浮腫	1 (1.3)	0
注射部位疼痛	2 (2.6)	0
注射部位そう痒感	1 (1.3)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
一般・全身障害および投与部位の状態 (Cont.)		
注射部位腫脹	1 (1.3)	0
注射部位蕁麻疹	2 (2.6)	0
倦怠感	1 (1.3)	0
末梢性浮腫	0	1 (5.9)
末梢腫脹	1 (1.3)	0
発熱	3 (3.9)	2 (11.8)
肝胆道系障害	2 (2.6)	0
胆嚢炎	1 (1.3)	0
高ビリルビン血症	1 (1.3)	0
免疫系障害	2 (2.6)	0
薬物過敏症	1 (1.3)	0
季節性アレルギー	1 (1.3)	0
感染症および寄生虫症	41 (53.9)	9 (52.9)
肛門膿瘍	1 (1.3)	0
気管支炎	3 (3.9)	2 (11.8)
クロストリジウム・ディフィシレ感染	1 (1.3)	0
サイトメガロウイルス性腸炎	1 (1.3)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
感染症および寄生虫症 (Cont.)		
せつ	1 (1.3)	0
胃腸炎	3 (3.9)	0
サルモネラ菌性胃腸炎	1 (1.3)	0
ウイルス性胃腸炎	1 (1.3)	1 (5.9)
帯状疱疹	1 (1.3)	0
膿痂疹	1 (1.3)	0
感染性嚢腫	1 (1.3)	0
インフルエンザ	1 (1.3)	0
喉頭炎	1 (1.3)	0
無菌性髄膜炎	1 (1.3)	0
上咽頭炎	8 (10.5)	3 (17.6)
口腔ヘルペス	2 (2.6)	1 (5.9)
中耳炎	1 (1.3)	0
咽頭炎	7 (9.2)	4 (23.5)
気道感染	1 (1.3)	1 (5.9)
ウイルス性気道感染	1 (1.3)	0
鼻炎	1 (1.3)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
感染症および寄生虫症 (Cont.)		
副鼻腔炎	1 (1.3)	0
レンサ球菌感染	1 (1.3)	0
癜風	1 (1.3)	0
扁桃炎	0	1 (5.9)
歯膿瘍	2 (2.6)	0
気管炎	1 (1.3)	0
上気道感染	13 (17.1)	1 (5.9)
尿路感染	6 (7.9)	1 (5.9)
水痘	0	2 (11.8)
ウイルス感染	3 (3.9)	0
ウイルス性上気道感染	1 (1.3)	2 (11.8)
外陰腟真菌感染	1 (1.3)	0
外陰腟炎	1 (1.3)	0
傷害、中毒および処置合併症	10 (13.2)	1 (5.9)
足関節部骨折	1 (1.3)	0
節足動物咬傷	1 (1.3)	0
転倒	1 (1.3)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
傷害、中毒および処置合併症 (Cont.)		
手骨折	2 (2.6)	0
注入に伴う反応	1 (1.3)	0
靱帯捻挫	1 (1.3)	0
四肢損傷	1 (1.3)	0
処置による疼痛	1 (1.3)	0
上肢骨折	1 (1.3)	0
手首関節骨折	1 (1.3)	1 (5.9)
臨床検査	17 (22.4)	1 (5.9)
血中アルカリホスファターゼ増加	1 (1.3)	0
血中ビリルビン増加	1 (1.3)	1 (5.9)
血中カルシウム減少	1 (1.3)	0
血圧上昇	1 (1.3)	0
血中ナトリウム減少	1 (1.3)	0
体温上昇	1 (1.3)	0
骨密度減少	1 (1.3)	0
Ｃ－反応性蛋白増加	5 (6.6)	0
好酸球数増加	1 (1.3)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
臨床検査 (Cont.)		
便中カルプロテクチン増加	1 (1.3)	0
ヘモグロビン減少	1 (1.3)	0
肝酵素上昇	1 (1.3)	0
リンパ節触知	1 (1.3)	0
結核菌群検査陽性	5 (6.6)	0
好中球数減少	1 (1.3)	0
体重減少	2 (2.6)	0
白血球数減少	1 (1.3)	0
筋骨格系および結合組織障害	12 (15.8)	0
関節痛	5 (6.6)	0
背部痛	3 (3.9)	0
成長不全	1 (1.3)	0
若年性特発性関節炎	1 (1.3)	0
靭帯障害	1 (1.3)	0
四肢痛	1 (1.3)	0
脊椎痛	1 (1.3)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
神経系障害	24 (31.6)	2 (11.8)
頭痛	21 (27.6)	2 (11.8)
感覚鈍麻	1 (1.3)	0
意識消失	1 (1.3)	0
片頭痛	1 (1.3)	0
錯感覚	2 (2.6)	0
傾眠	1 (1.3)	0
振戦	2 (2.6)	0
精神障害	4 (5.3)	0
うつ病	4 (5.3)	0
腎および尿路障害	4 (5.3)	0
糖尿	1 (1.3)	0
血尿	1 (1.3)	0
腎結石症	1 (1.3)	0
腎仙痛	1 (1.3)	0
生殖系および乳房障害	2 (2.6)	3 (17.6)
乳房痛	1 (1.3)	0
月経困難症	1 (1.3)	1 (5.9)

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
生殖系および乳房障害 (Cont.)		
卵巣嚢胞	0	2 (11.8)
呼吸器、胸郭および縦隔障害	18 (23.7)	2 (11.8)
喘息	2 (2.6)	0
咳嗽	4 (5.3)	0
鼻出血	2 (2.6)	1 (5.9)
鼻閉	2 (2.6)	0
鼻浮腫	1 (1.3)	0
口腔咽頭痛	6 (7.9)	1 (5.9)
アレルギー性鼻炎	2 (2.6)	1 (5.9)
鼻漏	4 (5.3)	0
喘鳴	1 (1.3)	0
皮膚および皮下組織障害	13 (17.1)	2 (11.8)
脱毛症	1 (1.3)	0
皮膚炎	2 (2.6)	0
乾癬様皮膚炎	1 (1.3)	0
紅斑	1 (1.3)	0
結節性紅斑	3 (3.9)	0

表 2.7.4.7-135. Mayo スコアに基づく疾患重症度別の有害事象（MedDRA SOC 及び PT 別）（M11-290 主試験及び M10-870 主試験の併合）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Any Adalimumab Disease Severity per Baseline Mayo Score <= 9 (N=76) n (%)	Any Adalimumab Disease Severity per Baseline Mayo Score > 9 (N=17) n (%)
皮膚および皮下組織障害 (Cont.)		
逆むけ	1 (1.3)	0
乾癬	1 (1.3)	0
発疹	4 (5.3)	1 (5.9)
痂皮	1 (1.3)	0
脂漏	1 (1.3)	0
皮膚障害	1 (1.3)	0
皮膚病変	0	1 (5.9)
血管障害	1 (1.3)	0
高血圧	1 (1.3)	0

Note: TEAEs are defined as any event with onset on or after the first dose of ADA treatment in Study M11-290 and up to 70 days after the last study drug injection or up to the cut-off date, whichever comes first. For subjects who received placebo during the maintenance period of Study M11-290, the TEAE collection period ends 70 days after last induction dose of ADA and re-starts with their next ADA dose, if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
ADA = Adalimumab.

Cross reference: G-CTD ISS Supplemental Table 2.4__1.4.8

表 2.7.4.7-136. 抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	I-SD (N=7) n (%)	I-HD (N=8) n (%)	I-HD-OL (N=1) n (%)	Total (N=16) n (%)	I-SD (N=25) n (%)	I-HD (N=43) n (%)	I-HD-OL (N=17) n (%)	Total (N=85) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	4 (57.1)	4 (50.0)	1 (100)	9 (56.3)	15 (60.0)	23 (53.5)	13 (76.5)	51 (60.0)
Serious AE	0	2 (25.0)	0	2 (12.5)	5 (20.0)	2 (4.7)	1 (5.9)	8 (9.4)
Severe AE	0	1 (12.5)	0	1 (6.3)	4 (16.0)	0	0	4 (4.7)
AEs leading to discontinuation of study drug	0	1 (12.5)	0	1 (6.3)	3 (12.0)	0	0	3 (3.5)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (12.5)	0	1 (6.3)	5 (20.0)	7 (16.3)	2 (11.8)	14 (16.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	2 (8.0)	1 (2.3)	1 (5.9)	4 (4.7)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	3 (42.9)	0	0	3 (18.8)	3 (12.0)	11 (25.6)	6 (35.3)	20 (23.5)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-136. 抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=7) n (%)	I-HD (N=8) n (%)	I-HD-OL (N=1) n (%)	Total (N=16) n (%)	I-SD (N=25) n (%)	I-HD (N=43) n (%)	I-HD-OL (N=17) n (%)	Total (N=85) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (2.3)	0	1 (1.2)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-136. 抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=7) n (%)	I-HD (N=8) n (%)	I-HD-OL (N=1) n (%)	Total (N=16) n (%)	I-SD (N=25) n (%)	I-HD (N=43) n (%)	I-HD-OL (N=17) n (%)	Total (N=85) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (2.3)	0	1 (1.2)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	2 (25.0)	0	2 (12.5)	3 (12.0)	1 (2.3)	1 (5.9)	5 (5.9)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-136.　抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=7) n (%)	I-HD (N=8) n (%)	I-HD-OL (N=1) n (%)	Total (N=16) n (%)	I-SD (N=25) n (%)	I-HD (N=43) n (%)	I-HD-OL (N=17) n (%)	Total (N=85) n (%)
Injection site reaction	0	0	0	0	1 (4.0)	3 (7.0)	0	4 (4.7)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.5_J

表 2.7.4.7-137. ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	I-SD (N=15) n (%)	I-HD (N=24) n (%)	I-HD-OL (N=10) n (%)	Total (N=49) n (%)	I-SD (N=17) n (%)	I-HD (N=27) n (%)	I-HD-OL (N=8) n (%)	Total (N=52) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	10 (66.7)	15 (62.5)	8 (80.0)	33 (67.3)	9 (52.9)	12 (44.4)	6 (75.0)	27 (51.9)
Serious AE	2 (13.3)	3 (12.5)	0	5 (10.2)	3 (17.6)	1 (3.7)	1 (12.5)	5 (9.6)
Severe AE	3 (20.0)	1 (4.2)	0	4 (8.2)	1 (5.9)	0	0	1 (1.9)
AEs leading to discontinuation of study drug	3 (20.0)	0	0	3 (6.1)	0	1 (3.7)	0	1 (1.9)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (20.0)	4 (16.7)	1 (10.0)	8 (16.3)	2 (11.8)	4 (14.8)	1 (12.5)	7 (13.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (6.7)	1 (4.2)	0	2 (4.1)	1 (5.9)	0	1 (12.5)	2 (3.8)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (26.7)	6 (25.0)	3 (30.0)	13 (26.5)	2 (11.8)	5 (18.5)	3 (37.5)	10 (19.2)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-137. ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=15) n (%)	I-HD (N=24) n (%)	I-HD-OL (N=10) n (%)	Total (N=49) n (%)	I-SD (N=17) n (%)	I-HD (N=27) n (%)	I-HD-OL (N=8) n (%)	Total (N=52) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	1 (4.2)	0	1 (2.0)	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-137. ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=15) n (%)	I-HD (N=24) n (%)	I-HD-OL (N=10) n (%)	Total (N=49) n (%)	I-SD (N=17) n (%)	I-HD (N=27) n (%)	I-HD-OL (N=8) n (%)	Total (N=52) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (4.2)	0	1 (2.0)	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	1 (6.7)	1 (4.2)	1 (10.0)	3 (6.1)	2 (11.8)	2 (7.4)	0	4 (7.7)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-137.　ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=15) n (%)	I-HD (N=24) n (%)	I-HD-OL (N=10) n (%)	Total (N=49) n (%)	I-SD (N=17) n (%)	I-HD (N=27) n (%)	I-HD-OL (N=8) n (%)	Total (N=52) n (%)
Injection site reaction	1 (6.7)	2 (8.3)	0	3 (6.1)	0	1 (3.7)	0	1 (1.9)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.6_J

表 2.7.4.7-138. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	I-SD (N=23) n (%)	I-HD (N=33) n (%)	I-HD-OL (N=7) n (%)	Total (N=63) n (%)	I-SD (N=9) n (%)	I-HD (N=18) n (%)	I-HD-OL (N=11) n (%)	Total (N=38) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	12 (52.2)	15 (45.5)	5 (71.4)	32 (50.8)	7 (77.8)	12 (66.7)	9 (81.8)	28 (73.7)
Serious AE	3 (13.0)	3 (9.1)	0	6 (9.5)	2 (22.2)	1 (5.6)	1 (9.1)	4 (10.5)
Severe AE	2 (8.7)	1 (3.0)	0	3 (4.8)	2 (22.2)	0	0	2 (5.3)
AEs leading to discontinuation of study drug	2 (8.7)	1 (3.0)	0	3 (4.8)	1 (11.1)	0	0	1 (2.6)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (13.0)	1 (3.0)	1 (14.3)	5 (7.9)	2 (22.2)	7 (38.9)	1 (9.1)	10 (26.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (4.3)	0	0	1 (1.6)	1 (11.1)	1 (5.6)	1 (9.1)	3 (7.9)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	3 (13.0)	8 (24.2)	0	11 (17.5)	3 (33.3)	3 (16.7)	6 (54.5)	12 (31.6)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-138. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=23) n (%)	I-HD (N=33) n (%)	I-HD-OL (N=7) n (%)	Total (N=63) n (%)	I-SD (N=9) n (%)	I-HD (N=18) n (%)	I-HD-OL (N=11) n (%)	Total (N=38) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (5.6)	0	1 (2.6)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-138. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=23) n (%)	I-HD (N=33) n (%)	I-HD-OL (N=7) n (%)	Total (N=63) n (%)	I-SD (N=9) n (%)	I-HD (N=18) n (%)	I-HD-OL (N=11) n (%)	Total (N=38) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (5.6)	0	1 (2.6)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	2 (8.7)	2 (6.1)	0	4 (6.3)	1 (11.1)	1 (5.6)	1 (9.1)	3 (7.9)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-138. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=23) n (%)	I-HD (N=33) n (%)	I-HD-OL (N=7) n (%)	Total (N=63) n (%)	I-SD (N=9) n (%)	I-HD (N=18) n (%)	I-HD-OL (N=11) n (%)	Total (N=38) n (%)
Injection site reaction	1 (4.3)	1 (3.0)	0	2 (3.2)	0	2 (11.1)	0	2 (5.3)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.7_J

表 2.7.4.7-139. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	<= 9				> 9			
	I-SD (N=27) n (%)	I-HD (N=42) n (%)	I-HD-OL (N=15) n (%)	Total (N=84) n (%)	I-SD (N=5) n (%)	I-HD (N=9) n (%)	I-HD-OL (N=3) n (%)	Total (N=17) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	17 (63.0)	23 (54.8)	13 (86.7)	53 (63.1)	2 (40.0)	4 (44.4)	1 (33.3)	7 (41.2)
Serious AE	5 (18.5)	3 (7.1)	1 (6.7)	9 (10.7)	0	1 (11.1)	0	1 (5.9)
Severe AE	4 (14.8)	0	0	4 (4.8)	0	1 (11.1)	0	1 (5.9)
AEs leading to discontinuation of study drug	3 (11.1)	1 (2.4)	0	4 (4.8)	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	5 (18.5)	8 (19.0)	2 (13.3)	15 (17.9)	0	0	0	0
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (7.4)	1 (2.4)	1 (6.7)	4 (4.8)	0	0	0	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (14.8)	9 (21.4)	5 (33.3)	18 (21.4)	2 (40.0)	2 (22.2)	1 (33.3)	5 (29.4)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-139. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	I-SD (N=27) n (%)	I-HD (N=42) n (%)	I-HD-OL (N=15) n (%)	Total (N=84) n (%)	I-SD (N=5) n (%)	I-HD (N=9) n (%)	I-HD-OL (N=3) n (%)	Total (N=17) n (%)
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	1 (2.4)	0	1 (1.2)	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-139. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	I-SD (N=27) n (%)	I-HD (N=42) n (%)	I-HD-OL (N=15) n (%)	Total (N=84) n (%)	I-SD (N=5) n (%)	I-HD (N=9) n (%)	I-HD-OL (N=3) n (%)	Total (N=17) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (2.4)	0	1 (1.2)	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (11.1)	2 (4.8)	1 (6.7)	6 (7.1)	0	1 (11.1)	0	1 (5.9)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-139. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	I-SD (N=27) n (%)	I-HD (N=42) n (%)	I-HD-OL (N=15) n (%)	Total (N=84) n (%)	I-SD (N=5) n (%)	I-HD (N=9) n (%)	I-HD-OL (N=3) n (%)	Total (N=17) n (%)
Injection site reaction	1 (3.7)	3 (7.1)	0	4 (4.8)	0	0	0	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.1.8_J

表 2.7.4.7-140. 抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	M-SD (N=2) n (%)	M-HD (N=6) n (%)	Total-ADA (N=8) n (%)	M-PL (N=2) n (%)	M-SD (N=31) n (%)	M-HD (N=30) n (%)	Total-ADA (N=61) n (%)	M-PL (N=10) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	1 (50.0)	5 (83.3)	6 (75.0)	1 (50.0)	20 (64.5)	21 (70.0)	41 (67.2)	9 (90.0)
Serious AE	0	2 (33.3)	2 (25.0)	0	5 (16.1)	3 (10.0)	8 (13.1)	1 (10.0)
Severe AE	0	1 (16.7)	1 (12.5)	0	3 (9.7)	0	3 (4.9)	0
AEs leading to discontinuation of study drug	0	0	0	0	2 (6.5)	0	2 (3.3)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	2 (33.3)	2 (25.0)	0	8 (25.8)	9 (30.0)	17 (27.9)	5 (50.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (16.7)	1 (12.5)	0	0	0	0	1 (10.0)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	1 (50.0)	4 (66.7)	5 (62.5)	1 (50.0)	10 (32.3)	12 (40.0)	22 (36.1)	4 (40.0)
Serious infections	0	2 (33.3)	2 (25.0)	0	3 (9.7)	1 (3.3)	4 (6.6)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (3.3)	1 (1.6)	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-140. 抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=2) n (%)	M-HD (N=6) n (%)	Total-ADA (N=8) n (%)	M-PL (N=2) n (%)	M-SD (N=31) n (%)	M-HD (N=30) n (%)	Total-ADA (N=61) n (%)	M-PL (N=10) n (%)
Latent tuberculosis	0	0	0	0	0	1 (3.3)	1 (1.6)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	1 (16.7)	1 (12.5)	0	1 (3.2)	1 (3.3)	2 (3.3)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-140. 抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=2) n (%)	M-HD (N=6) n (%)	Total-ADA (N=8) n (%)	M-PL (N=2) n (%)	M-SD (N=31) n (%)	M-HD (N=30) n (%)	Total-ADA (N=61) n (%)	M-PL (N=10) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (10.0)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	1 (16.7)	1 (12.5)	0	3 (9.7)	0	3 (4.9)	2 (20.0)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-140.　抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=2) n (%)	M-HD (N=6) n (%)	Total-ADA (N=8) n (%)	M-PL (N=2) n (%)	M-SD (N=31) n (%)	M-HD (N=30) n (%)	Total-ADA (N=61) n (%)	M-PL (N=10) n (%)
Injection site reaction	0	1 (16.7)	1 (12.5)	0	4 (12.9)	1 (3.3)	5 (8.2)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.5_J

表 2.7.4.7-141. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=5) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=7) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	9 (60.0)	15 (88.2)	24 (75.0)	4 (80.0)	12 (66.7)	11 (57.9)	23 (62.2)	6 (85.7)
Serious AE	4 (26.7)	4 (23.5)	8 (25.0)	1 (20.0)	1 (5.6)	1 (5.3)	2 (5.4)	0
Severe AE	2 (13.3)	0	2 (6.3)	0	1 (5.6)	1 (5.3)	2 (5.4)	0
AEs leading to discontinuation of study drug	2 (13.3)	0	2 (6.3)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (20.0)	5 (29.4)	8 (25.0)	3 (60.0)	5 (27.8)	6 (31.6)	11 (29.7)	2 (28.6)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	1 (20.0)	0	1 (5.3)	1 (2.7)	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	5 (33.3)	10 (58.8)	15 (46.9)	1 (20.0)	6 (33.3)	6 (31.6)	12 (32.4)	4 (57.1)
Serious infections	3 (20.0)	2 (11.8)	5 (15.6)	0	0	1 (5.3)	1 (2.7)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (5.9)	1 (3.1)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-141. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=5) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=7) n (%)
Latent tuberculosis	0	1 (5.9)	1 (3.1)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	1 (5.6)	2 (10.5)	3 (8.1)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-141. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=5) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=7) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (20.0)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	1 (6.7)	0	1 (3.1)	0	2 (11.1)	1 (5.3)	3 (8.1)	2 (28.6)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-141. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=15) n (%)	M-HD (N=17) n (%)	Total-ADA (N=32) n (%)	M-PL (N=5) n (%)	M-SD (N=18) n (%)	M-HD (N=19) n (%)	Total-ADA (N=37) n (%)	M-PL (N=7) n (%)
Injection site reaction	2 (13.3)	0	2 (6.3)	0	2 (11.1)	2 (10.5)	4 (10.8)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.6_J

表 2.7.4.7-142. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	M-SD (N=19) n (%)	M-HD (N=25) n (%)	Total-ADA (N=44) n (%)	M-PL (N=8) n (%)	M-SD (N=14) n (%)	M-HD (N=11) n (%)	Total-ADA (N=25) n (%)	M-PL (N=4) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	12 (63.2)	17 (68.0)	29 (65.9)	7 (87.5)	9 (64.3)	9 (81.8)	18 (72.0)	3 (75.0)
Serious AE	3 (15.8)	3 (12.0)	6 (13.6)	1 (12.5)	2 (14.3)	2 (18.2)	4 (16.0)	0
Severe AE	2 (10.5)	0	2 (4.5)	0	1 (7.1)	1 (9.1)	2 (8.0)	0
AEs leading to discontinuation of study drug	1 (5.3)	0	1 (2.3)	0	1 (7.1)	0	1 (4.0)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (15.8)	6 (24.0)	9 (20.5)	3 (37.5)	5 (35.7)	5 (45.5)	10 (40.0)	2 (50.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	1 (12.5)	0	1 (9.1)	1 (4.0)	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	7 (36.8)	11 (44.0)	18 (40.9)	4 (50.0)	4 (28.6)	5 (45.5)	9 (36.0)	1 (25.0)
Serious infections	2 (10.5)	2 (8.0)	4 (9.1)	0	1 (7.1)	1 (9.1)	2 (8.0)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (4.0)	1 (2.3)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-142. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=19) n (%)	M-HD (N=25) n (%)	Total-ADA (N=44) n (%)	M-PL (N=8) n (%)	M-SD (N=14) n (%)	M-HD (N=11) n (%)	Total-ADA (N=25) n (%)	M-PL (N=4) n (%)
Latent tuberculosis	0	1 (4.0)	1 (2.3)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	1 (5.3)	1 (4.0)	2 (4.5)	0	0	1 (9.1)	1 (4.0)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-142. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=19) n (%)	M-HD (N=25) n (%)	Total-ADA (N=44) n (%)	M-PL (N=8) n (%)	M-SD (N=14) n (%)	M-HD (N=11) n (%)	Total-ADA (N=25) n (%)	M-PL (N=4) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (12.5)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (15.8)	1 (4.0)	4 (9.1)	2 (25.0)	0	0	0	0
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-142. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=19) n (%)	M-HD (N=25) n (%)	Total-ADA (N=44) n (%)	M-PL (N=8) n (%)	M-SD (N=14) n (%)	M-HD (N=11) n (%)	Total-ADA (N=25) n (%)	M-PL (N=4) n (%)
Injection site reaction	1 (5.3)	1 (4.0)	2 (4.5)	0	3 (21.4)	1 (9.1)	4 (16.0)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.7_J

表 2.7.4.7-143. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	<= 9				> 9			
	M-SD (N=27) n (%)	M-HD (N=31) n (%)	Total-ADA (N=58) n (%)	M-PL (N=11) n (%)	M-SD (N=6) n (%)	M-HD (N=5) n (%)	Total-ADA (N=11) n (%)	M-PL (N=1) n (%)
Subjects with any treatment-emergent								
Adverse event (AE)	19 (70.4)	22 (71.0)	41 (70.7)	9 (81.8)	2 (33.3)	4 (80.0)	6 (54.5)	1 (100)
Serious AE	5 (18.5)	5 (16.1)	10 (17.2)	1 (9.1)	0	0	0	0
Severe AE	3 (11.1)	1 (3.2)	4 (6.9)	0	0	0	0	0
AEs leading to discontinuation of study drug	2 (7.4)	0	2 (3.4)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	7 (25.9)	10 (32.3)	17 (29.3)	5 (45.5)	1 (16.7)	1 (20.0)	2 (18.2)	0
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (3.2)	1 (1.7)	1 (9.1)	0	0	0	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	10 (37.0)	14 (45.2)	24 (41.4)	5 (45.5)	1 (16.7)	2 (40.0)	3 (27.3)	0
Serious infections	3 (11.1)	3 (9.7)	6 (10.3)	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (3.2)	1 (1.7)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0

表 2.7.4.7-143. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	M-SD (N=27) n (%)	M-HD (N=31) n (%)	Total-ADA (N=58) n (%)	M-PL (N=11) n (%)	M-SD (N=6) n (%)	M-HD (N=5) n (%)	Total-ADA (N=11) n (%)	M-PL (N=1) n (%)
Latent tuberculosis	0	1 (3.2)	1 (1.7)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0
Allergic reactions including angioedema/anaphylaxis	1 (3.7)	2 (6.5)	3 (5.2)	0	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0

表 2.7.4.7-143. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	M-SD (N=27) n (%)	M-HD (N=31) n (%)	Total-ADA (N=58) n (%)	M-PL (N=11) n (%)	M-SD (N=6) n (%)	M-HD (N=5) n (%)	Total-ADA (N=11) n (%)	M-PL (N=1) n (%)
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (9.1)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	2 (7.4)	0	2 (3.4)	2 (18.2)	1 (16.7)	1 (20.0)	2 (18.2)	0
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0

表 2.7.4.7-143. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	M-SD (N=27) n (%)	M-HD (N=31) n (%)	Total-ADA (N=58) n (%)	M-PL (N=11) n (%)	M-SD (N=6) n (%)	M-HD (N=5) n (%)	Total-ADA (N=11) n (%)	M-PL (N=1) n (%)
Injection site reaction	4 (14.8)	2 (6.5)	6 (10.3)	0	0	0	0	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
Subjects are counted once in each row, regardless of the number of events they may have had.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.2.8_J

表 2.7.4.7-144.　抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	I-SD (N=7) (PYS=1.1) Events (E/100PY)	I-HD (N=8) (PYS=1.2) Events (E/100PY)	I-HD-OL (N=1) (PYS=0.2) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=25) (PYS=3.5) Events (E/100PY)	I-HD (N=43) (PYS=6.5) Events (E/100PY)	I-HD-OL (N=17) (PYS=2.5) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	7 (636.4)	8 (666.7)	3 (1500.0)	18 (750.0)	39 (1114.3)	54 (830.8)	32 (1280.0)	125 (992.1)
Serious AE	0	2 (166.7)	0	2 (83.3)	7 (200.0)	2 (30.8)	1 (40.0)	10 (79.4)
Severe AE	0	1 (83.3)	0	1 (41.7)	5 (142.9)	0	0	5 (39.7)
AEs leading to discontinuation of study drug	0	1 (83.3)	0	1 (41.7)	4 (114.3)	0	0	4 (31.7)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (83.3)	0	1 (41.7)	8 (228.6)	15 (230.8)	5 (200.0)	28 (222.2)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	3 (85.7)	1 (15.4)	1 (40.0)	5 (39.7)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (363.6)	0	0	4 (166.7)	3 (85.7)	13 (200.0)	7 (280.0)	23 (182.5)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-144. 抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=7) (PYS=1.1) Events (E/100PY)	I-HD (N=8) (PYS=1.2) Events (E/100PY)	I-HD-OL (N=1) (PYS=0.2) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=25) (PYS=3.5) Events (E/100PY)	I-HD (N=43) (PYS=6.5) Events (E/100PY)	I-HD-OL (N=17) (PYS=2.5) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-144. 抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=7) (PYS=1.1) Events (E/100PY)	I-HD (N=8) (PYS=1.2) Events (E/100PY)	I-HD-OL (N=1) (PYS=0.2) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=25) (PYS=3.5) Events (E/100PY)	I-HD (N=43) (PYS=6.5) Events (E/100PY)	I-HD-OL (N=17) (PYS=2.5) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (15.4)	0	1 (7.9)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (15.4)	0	1 (7.9)

表 2.7.4.7-144. 抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=7) (PYS=1.1) Events (E/100PY)	I-HD (N=8) (PYS=1.2) Events (E/100PY)	I-HD-OL (N=1) (PYS=0.2) Events (E/100PY)	Total (N=16) (PYS=2.4) Events (E/100PY)	I-SD (N=25) (PYS=3.5) Events (E/100PY)	I-HD (N=43) (PYS=6.5) Events (E/100PY)	I-HD-OL (N=17) (PYS=2.5) Events (E/100PY)	Total (N=85) (PYS=12.6) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	2 (166.7)	0	2 (83.3)	3 (85.7)	1 (15.4)	1 (40.0)	5 (39.7)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	0	0	0	0	1 (28.6)	5 (76.9)	0	6 (47.6)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-144.　抗 TNF 製剤の投与経験の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.5_J

表 2.7.4.7-145. ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	I-SD (N=15) (PYS=2.0) Events (E/100PY)	I-HD (N=24) (PYS=3.7) Events (E/100PY)	I-HD-OL (N=10) (PYS=1.5) Events (E/100PY)	Total (N=49) (PYS=7.2) Events (E/100PY)	I-SD (N=17) (PYS=2.6) Events (E/100PY)	I-HD (N=27) (PYS=4.1) Events (E/100PY)	I-HD-OL (N=8) (PYS=1.2) Events (E/100PY)	Total (N=52) (PYS=7.8) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	23 (1150.0)	41 (1108.1)	19 (1266.7)	83 (1152.8)	23 (884.6)	21 (512.2)	16 (1333.3)	60 (769.2)
Serious AE	3 (150.0)	3 (81.1)	0	6 (83.3)	4 (153.8)	1 (24.4)	1 (83.3)	6 (76.9)
Severe AE	4 (200.0)	1 (27.0)	0	5 (69.4)	1 (38.5)	0	0	1 (12.8)
AEs leading to discontinuation of study drug	4 (200.0)	0	0	4 (55.6)	0	1 (24.4)	0	1 (12.8)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (150.0)	9 (243.2)	3 (200.0)	15 (208.3)	5 (192.3)	7 (170.7)	2 (166.7)	14 (179.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (50.0)	1 (27.0)	0	2 (27.8)	2 (76.9)	0	1 (83.3)	3 (38.5)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (200.0)	8 (216.2)	3 (200.0)	15 (208.3)	3 (115.4)	5 (122.0)	4 (333.3)	12 (153.8)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-145. ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=15) (PYS=2.0) Events (E/100PY)	I-HD (N=24) (PYS=3.7) Events (E/100PY)	I-HD-OL (N=10) (PYS=1.5) Events (E/100PY)	Total (N=49) (PYS=7.2) Events (E/100PY)	I-SD (N=17) (PYS=2.6) Events (E/100PY)	I-HD (N=27) (PYS=4.1) Events (E/100PY)	I-HD-OL (N=8) (PYS=1.2) Events (E/100PY)	Total (N=52) (PYS=7.8) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-145. ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=15) (PYS=2.0) Events (E/100PY)	I-HD (N=24) (PYS=3.7) Events (E/100PY)	I-HD-OL (N=10) (PYS=1.5) Events (E/100PY)	Total (N=49) (PYS=7.2) Events (E/100PY)	I-SD (N=17) (PYS=2.6) Events (E/100PY)	I-HD (N=27) (PYS=4.1) Events (E/100PY)	I-HD-OL (N=8) (PYS=1.2) Events (E/100PY)	Total (N=52) (PYS=7.8) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	1 (27.0)	0	1 (13.9)	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (27.0)	0	1 (13.9)	0	0	0	0

表 2.7.4.7-145. ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=15) (PYS=2.0) Events (E/100PY)	I-HD (N=24) (PYS=3.7) Events (E/100PY)	I-HD-OL (N=10) (PYS=1.5) Events (E/100PY)	Total (N=49) (PYS=7.2) Events (E/100PY)	I-SD (N=17) (PYS=2.6) Events (E/100PY)	I-HD (N=27) (PYS=4.1) Events (E/100PY)	I-HD-OL (N=8) (PYS=1.2) Events (E/100PY)	Total (N=52) (PYS=7.8) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	1 (50.0)	1 (27.0)	1 (66.7)	3 (41.7)	2 (76.9)	2 (48.8)	0	4 (51.3)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	1 (50.0)	4 (108.1)	0	5 (69.4)	0	1 (24.4)	0	1 (12.8)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-145.　ベースラインにおけるコルチコステロイドの全身投与の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.6_J

表 2.7.4.7-146. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	I-SD (N=23) (PYS=3.4) Events (E/100PY)	I-HD (N=33) (PYS=5.0) Events (E/100PY)	I-HD-OL (N=7) (PYS=1.1) Events (E/100PY)	Total (N=63) (PYS=9.4) Events (E/100PY)	I-SD (N=9) (PYS=1.3) Events (E/100PY)	I-HD (N=18) (PYS=2.8) Events (E/100PY)	I-HD-OL (N=11) (PYS=1.6) Events (E/100PY)	Total (N=38) (PYS=5.6) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	31 (911.8)	23 (460.0)	10 (909.1)	64 (680.9)	15 (1153.8)	39 (1392.9)	25 (1562.5)	79 (1410.7)
Serious AE	4 (117.6)	3 (60.0)	0	7 (74.5)	3 (230.8)	1 (35.7)	1 (62.5)	5 (89.3)
Severe AE	2 (58.8)	1 (20.0)	0	3 (31.9)	3 (230.8)	0	0	3 (53.6)
AEs leading to discontinuation of study drug	2 (58.8)	1 (20.0)	0	3 (31.9)	2 (153.8)	0	0	2 (35.7)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	6 (176.5)	1 (20.0)	3 (272.7)	10 (106.4)	2 (153.8)	15 (535.7)	2 (125.0)	19 (339.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	2 (58.8)	0	0	2 (21.3)	1 (76.9)	1 (35.7)	1 (62.5)	3 (53.6)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (117.6)	8 (160.0)	0	12 (127.7)	3 (230.8)	5 (178.6)	7 (437.5)	15 (267.9)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-146. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=23) (PYS=3.4) Events (E/100PY)	I-HD (N=33) (PYS=5.0) Events (E/100PY)	I-HD-OL (N=7) (PYS=1.1) Events (E/100PY)	Total (N=63) (PYS=9.4) Events (E/100PY)	I-SD (N=9) (PYS=1.3) Events (E/100PY)	I-HD (N=18) (PYS=2.8) Events (E/100PY)	I-HD-OL (N=11) (PYS=1.6) Events (E/100PY)	Total (N=38) (PYS=5.6) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-146. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=23) (PYS=3.4) Events (E/100PY)	I-HD (N=33) (PYS=5.0) Events (E/100PY)	I-HD-OL (N=7) (PYS=1.1) Events (E/100PY)	Total (N=63) (PYS=9.4) Events (E/100PY)	I-SD (N=9) (PYS=1.3) Events (E/100PY)	I-HD (N=18) (PYS=2.8) Events (E/100PY)	I-HD-OL (N=11) (PYS=1.6) Events (E/100PY)	Total (N=38) (PYS=5.6) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0	1 (35.7)	0	1 (17.9)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	1 (35.7)	0	1 (17.9)

表 2.7.4.7-146. ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	I-SD (N=23) (PYS=3.4) Events (E/100PY)	I-HD (N=33) (PYS=5.0) Events (E/100PY)	I-HD-OL (N=7) (PYS=1.1) Events (E/100PY)	Total (N=63) (PYS=9.4) Events (E/100PY)	I-SD (N=9) (PYS=1.3) Events (E/100PY)	I-HD (N=18) (PYS=2.8) Events (E/100PY)	I-HD-OL (N=11) (PYS=1.6) Events (E/100PY)	Total (N=38) (PYS=5.6) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	2 (58.8)	2 (40.0)	0	4 (42.6)	1 (76.9)	1 (35.7)	1 (62.5)	3 (53.6)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	1 (29.4)	1 (20.0)	0	2 (21.3)	0	4 (142.9)	0	4 (71.4)
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-146.　ベースラインにおける免疫抑制剤の使用の有無別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.7_J

表 2.7.4.7-147. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）

	<= 9				> 9			
	I-SD (N=27) (PYS=3.9) Events (E/100PY)	I-HD (N=42) (PYS=6.4) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=84) (PYS=12.5) Events (E/100PY)	I-SD (N=5) (PYS=0.8) Events (E/100PY)	I-HD (N=9) (PYS=1.3) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.5) Events (E/100PY)	Total (N=17) (PYS=2.6) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	42 (1076.9)	57 (890.6)	33 (1500.0)	132 (1056.0)	4 (500.0)	5 (384.6)	2 (400.0)	11 (423.1)
Serious AE	7 (179.5)	3 (46.9)	1 (45.5)	11 (88.0)	0	1 (76.9)	0	1 (38.5)
Severe AE	5 (128.2)	0	0	5 (40.0)	0	1 (76.9)	0	1 (38.5)
AEs leading to discontinuation of study drug	4 (102.6)	1 (15.6)	0	5 (40.0)	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	8 (205.1)	16 (250.0)	5 (227.3)	29 (232.0)	0	0	0	0
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (76.9)	1 (15.6)	1 (45.5)	5 (40.0)	0	0	0	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	4 (102.6)	11 (171.9)	6 (272.7)	21 (168.0)	3 (375.0)	2 (153.8)	1 (200.0)	6 (230.8)
Serious infections	0	0	0	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-147. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	I-SD (N=27) (PYS=3.9) Events (E/100PY)	I-HD (N=42) (PYS=6.4) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=84) (PYS=12.5) Events (E/100PY)	I-SD (N=5) (PYS=0.8) Events (E/100PY)	I-HD (N=9) (PYS=1.3) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.5) Events (E/100PY)	Total (N=17) (PYS=2.6) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-147. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	I-SD (N=27) (PYS=3.9) Events (E/100PY)	I-HD (N=42) (PYS=6.4) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=84) (PYS=12.5) Events (E/100PY)	I-SD (N=5) (PYS=0.8) Events (E/100PY)	I-HD (N=9) (PYS=1.3) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.5) Events (E/100PY)	Total (N=17) (PYS=2.6) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	1 (15.6)	0	1 (8.0)	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	1 (15.6)	0	1 (8.0)	0	0	0	0

表 2.7.4.7-147. Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	I-SD (N=27) (PYS=3.9) Events (E/100PY)	I-HD (N=42) (PYS=6.4) Events (E/100PY)	I-HD-OL (N=15) (PYS=2.2) Events (E/100PY)	Total (N=84) (PYS=12.5) Events (E/100PY)	I-SD (N=5) (PYS=0.8) Events (E/100PY)	I-HD (N=9) (PYS=1.3) Events (E/100PY)	I-HD-OL (N=3) (PYS=0.5) Events (E/100PY)	Total (N=17) (PYS=2.6) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (76.9)	2 (31.3)	1 (45.5)	6 (48.0)	0	1 (76.9)	0	1 (38.5)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	1 (25.6)	5 (78.1)	0	6 (48.0)	0	0	0	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-147.　Mayo スコアに基づく疾患重症度別の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.3.8_J

表 2.7.4.7-148. 抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	M-SD (N=2) (PYS=1.3) Events (E/100PY)	M-HD (N=6) (PYS=3.9) Events (E/100PY)	Total-ADA (N=8) (PYS=5.2) Events (E/100PY)	M-PL (N=2) (PYS=0.9) Events (E/100PY)	M-SD (N=31) (PYS=19.2) Events (E/100PY)	M-HD (N=30) (PYS=19.9) Events (E/100PY)	Total-ADA (N=61) (PYS=39.0) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	1 (76.9)	23 (589.7)	24 (461.5)	1 (111.1)	73 (380.2)	54 (271.4)	127 (325.6)	25 (490.2)
Serious AE	0	3 (76.9)	3 (57.7)	0	10 (52.1)	3 (15.1)	13 (33.3)	1 (19.6)
Severe AE	0	1 (25.6)	1 (19.2)	0	5 (26.0)	0	5 (12.8)	0
AEs leading to discontinuation of study drug	0	0	0	0	3 (15.6)	0	3 (7.7)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	8 (205.1)	8 (153.8)	0	14 (72.9)	12 (60.3)	26 (66.7)	6 (117.6)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (25.6)	1 (19.2)	0	0	0	0	1 (19.6)
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	1 (76.9)	7 (179.5)	8 (153.8)	1 (111.1)	17 (88.5)	15 (75.4)	32 (82.1)	8 (156.9)
Serious infections	0	2 (51.3)	2 (38.5)	0	3 (15.6)	1 (5.0)	4 (10.3)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-148. 抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=2) (PYS=1.3) Events (E/100PY)	M-HD (N=6) (PYS=3.9) Events (E/100PY)	Total-ADA (N=8) (PYS=5.2) Events (E/100PY)	M-PL (N=2) (PYS=0.9) Events (E/100PY)	M-SD (N=31) (PYS=19.2) Events (E/100PY)	M-HD (N=30) (PYS=19.9) Events (E/100PY)	Total-ADA (N=61) (PYS=39.0) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	1 (5.0)	1 (2.6)	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	1 (5.0)	1 (2.6)	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-148. 抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=2) (PYS=1.3) Events (E/100PY)	M-HD (N=6) (PYS=3.9) Events (E/100PY)	Total-ADA (N=8) (PYS=5.2) Events (E/100PY)	M-PL (N=2) (PYS=0.9) Events (E/100PY)	M-SD (N=31) (PYS=19.2) Events (E/100PY)	M-HD (N=30) (PYS=19.9) Events (E/100PY)	Total-ADA (N=61) (PYS=39.0) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	1 (25.6)	1 (19.2)	0	2 (10.4)	1 (5.0)	3 (7.7)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-148. 抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=2) (PYS=1.3) Events (E/100PY)	M-HD (N=6) (PYS=3.9) Events (E/100PY)	Total-ADA (N=8) (PYS=5.2) Events (E/100PY)	M-PL (N=2) (PYS=0.9) Events (E/100PY)	M-SD (N=31) (PYS=19.2) Events (E/100PY)	M-HD (N=30) (PYS=19.9) Events (E/100PY)	Total-ADA (N=61) (PYS=39.0) Events (E/100PY)	M-PL (N=10) (PYS=5.1) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0	0	0	1 (19.6)
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	0	1 (25.6)	1 (19.2)	0	5 (26.0)	0	5 (12.8)	2 (39.2)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	0	1 (25.6)	1 (19.2)	0	6 (31.3)	2 (10.1)	8 (20.5)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-148.　抗 TNF 製剤の投与経験の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.5_J

表 2.7.4.7-149. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=11.5) Events (E/100PY)	Total-ADA (N=32) (PYS=19.7) Events (E/100PY)	M-PL (N=5) (PYS=2.3) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=12.2) Events (E/100PY)	Total-ADA (N=37) (PYS=24.5) Events (E/100PY)	M-PL (N=7) (PYS=3.8) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	36 (439.0)	48 (417.4)	84 (426.4)	13 (565.2)	38 (308.9)	29 (237.7)	67 (273.5)	13 (342.1)
Serious AE	8 (97.6)	5 (43.5)	13 (66.0)	1 (43.5)	2 (16.3)	1 (8.2)	3 (12.2)	0
Severe AE	4 (48.8)	0	4 (20.3)	0	1 (8.1)	1 (8.2)	2 (8.2)	0
AEs leading to discontinuation of study drug	3 (36.6)	0	3 (15.2)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	8 (97.6)	7 (60.9)	15 (76.1)	4 (173.9)	6 (48.8)	13 (106.6)	19 (77.6)	2 (52.6)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	1 (43.5)	0	1 (8.2)	1 (4.1)	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	8 (97.6)	13 (113.0)	21 (106.6)	2 (87.0)	10 (81.3)	9 (73.8)	19 (77.6)	7 (184.2)
Serious infections	3 (36.6)	2 (17.4)	5 (25.4)	0	0	1 (8.2)	1 (4.1)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-149. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=11.5) Events (E/100PY)	Total-ADA (N=32) (PYS=19.7) Events (E/100PY)	M-PL (N=5) (PYS=2.3) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=12.2) Events (E/100PY)	Total-ADA (N=37) (PYS=24.5) Events (E/100PY)	M-PL (N=7) (PYS=3.8) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (8.7)	1 (5.1)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	1 (8.7)	1 (5.1)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-149. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=11.5) Events (E/100PY)	Total-ADA (N=32) (PYS=19.7) Events (E/100PY)	M-PL (N=5) (PYS=2.3) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=12.2) Events (E/100PY)	Total-ADA (N=37) (PYS=24.5) Events (E/100PY)	M-PL (N=7) (PYS=3.8) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	2 (16.3)	2 (16.4)	4 (16.3)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-149. ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=15) (PYS=8.2) Events (E/100PY)	M-HD (N=17) (PYS=11.5) Events (E/100PY)	Total-ADA (N=32) (PYS=19.7) Events (E/100PY)	M-PL (N=5) (PYS=2.3) Events (E/100PY)	M-SD (N=18) (PYS=12.3) Events (E/100PY)	M-HD (N=19) (PYS=12.2) Events (E/100PY)	Total-ADA (N=37) (PYS=24.5) Events (E/100PY)	M-PL (N=7) (PYS=3.8) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (43.5)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (36.6)	0	3 (15.2)	0	2 (16.3)	1 (8.2)	3 (12.2)	2 (52.6)
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	4 (48.8)	0	4 (20.3)	0	2 (16.3)	3 (24.6)	5 (20.4)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-149.　ベースラインにおけるコルチコステロイドの全身投与の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.6_J

表 2.7.4.7-150. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）

	Yes				No			
	M-SD (N=19) (PYS=11.8) Events (E/100PY)	M-HD (N=25) (PYS=17.3) Events (E/100PY)	Total-ADA (N=44) (PYS=29.1) Events (E/100PY)	M-PL (N=8) (PYS=4.8) Events (E/100PY)	M-SD (N=14) (PYS=8.7) Events (E/100PY)	M-HD (N=11) (PYS=6.5) Events (E/100PY)	Total-ADA (N=25) (PYS=15.1) Events (E/100PY)	M-PL (N=4) (PYS=1.3) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	35 (296.6)	44 (254.3)	79 (271.5)	16 (333.3)	39 (448.3)	33 (507.7)	72 (476.8)	10 (769.2)
Serious AE	8 (67.8)	4 (23.1)	12 (41.2)	1 (20.8)	2 (23.0)	2 (30.8)	4 (26.5)	0
Severe AE	4 (33.9)	0	4 (13.7)	0	1 (11.5)	1 (15.4)	2 (13.2)	0
AEs leading to discontinuation of study drug	2 (16.9)	0	2 (6.9)	0	1 (11.5)	0	1 (6.6)	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (25.4)	8 (46.2)	11 (37.8)	3 (62.5)	11 (126.4)	12 (184.6)	23 (152.3)	3 (230.8)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	1 (20.8)	0	1 (15.4)	1 (6.6)	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	12 (101.7)	14 (80.9)	26 (89.3)	7 (145.8)	6 (69.0)	8 (123.1)	14 (92.7)	2 (153.8)
Serious infections	2 (16.9)	2 (11.6)	4 (13.7)	0	1 (11.5)	1 (15.4)	2 (13.2)	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-150. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=19) (PYS=11.8) Events (E/100PY)	M-HD (N=25) (PYS=17.3) Events (E/100PY)	Total-ADA (N=44) (PYS=29.1) Events (E/100PY)	M-PL (N=8) (PYS=4.8) Events (E/100PY)	M-SD (N=14) (PYS=8.7) Events (E/100PY)	M-HD (N=11) (PYS=6.5) Events (E/100PY)	Total-ADA (N=25) (PYS=15.1) Events (E/100PY)	M-PL (N=4) (PYS=1.3) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (5.8)	1 (3.4)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	1 (5.8)	1 (3.4)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-150. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=19) (PYS=11.8) Events (E/100PY)	M-HD (N=25) (PYS=17.3) Events (E/100PY)	Total-ADA (N=44) (PYS=29.1) Events (E/100PY)	M-PL (N=8) (PYS=4.8) Events (E/100PY)	M-SD (N=14) (PYS=8.7) Events (E/100PY)	M-HD (N=11) (PYS=6.5) Events (E/100PY)	Total-ADA (N=25) (PYS=15.1) Events (E/100PY)	M-PL (N=4) (PYS=1.3) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (16.9)	1 (5.8)	3 (10.3)	0	0	1 (15.4)	1 (6.6)	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-150. ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	Yes				No			
	M-SD (N=19) (PYS=11.8) Events (E/100PY)	M-HD (N=25) (PYS=17.3) Events (E/100PY)	Total-ADA (N=44) (PYS=29.1) Events (E/100PY)	M-PL (N=8) (PYS=4.8) Events (E/100PY)	M-SD (N=14) (PYS=8.7) Events (E/100PY)	M-HD (N=11) (PYS=6.5) Events (E/100PY)	Total-ADA (N=25) (PYS=15.1) Events (E/100PY)	M-PL (N=4) (PYS=1.3) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (20.8)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	5 (42.4)	1 (5.8)	6 (20.6)	2 (41.7)	0	0	0	0
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	1 (8.5)	2 (11.6)	3 (10.3)	0	5 (57.5)	1 (15.4)	6 (39.7)	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-150.　ベースラインにおける免疫抑制剤の使用の有無別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.7_J

表 2.7.4.7-151. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）

	<= 9				> 9			
	M-SD (N=27) (PYS=17.4) Events (E/100PY)	M-HD (N=31) (PYS=20.0) Events (E/100PY)	Total-ADA (N=58) (PYS=37.4) Events (E/100PY)	M-PL (N=11) (PYS=5.8) Events (E/100PY)	M-SD (N=6) (PYS=3.1) Events (E/100PY)	M-HD (N=5) (PYS=3.8) Events (E/100PY)	Total-ADA (N=11) (PYS=6.9) Events (E/100PY)	M-PL (N=1) (PYS=0.2) Events (E/100PY)
Any treatment-emergent								
Adverse event (AE)	70 (402.3)	66 (330.0)	136 (363.6)	24 (413.8)	4 (129.0)	11 (289.5)	15 (217.4)	2 (1000.0)
Serious AE	10 (57.5)	6 (30.0)	16 (42.8)	1 (17.2)	0	0	0	0
Severe AE	5 (28.7)	1 (5.0)	6 (16.0)	0	0	0	0	0
AEs leading to discontinuation of study drug	3 (17.2)	0	3 (8.0)	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	13 (74.7)	19 (95.0)	32 (85.6)	6 (103.4)	1 (32.3)	1 (26.3)	2 (29.0)	0
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (5.0)	1 (2.7)	1 (17.2)	0	0	0	0
AEs leading to Death	0	0	0	0	0	0	0	0
Infections	16 (92.0)	17 (85.0)	33 (88.2)	9 (155.2)	2 (64.5)	5 (131.6)	7 (101.4)	0
Serious infections	3 (17.2)	3 (15.0)	6 (16.0)	0	0	0	0	0
Legionella infections	0	0	0	0	0	0	0	0
Diverticulitis	0	0	0	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0	0	0	0

表 2.7.4.7-151. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	M-SD (N=27) (PYS=17.4) Events (E/100PY)	M-HD (N=31) (PYS=20.0) Events (E/100PY)	Total-ADA (N=58) (PYS=37.4) Events (E/100PY)	M-PL (N=11) (PYS=5.8) Events (E/100PY)	M-SD (N=6) (PYS=3.1) Events (E/100PY)	M-HD (N=5) (PYS=3.8) Events (E/100PY)	Total-ADA (N=11) (PYS=6.9) Events (E/100PY)	M-PL (N=1) (PYS=0.2) Events (E/100PY)
Oral candidiasis	0	0	0	0	0	0	0	0
Tuberculosis	0	1 (5.0)	1 (2.7)	0	0	0	0	0
Active tuberculosis	0	0	0	0	0	0	0	0
Latent tuberculosis	0	1 (5.0)	1 (2.7)	0	0	0	0	0
Parasitic infections	0	0	0	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0	0	0	0
Melanoma	0	0	0	0	0	0	0	0
Leukemia	0	0	0	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0	0	0	0

表 2.7.4.7-151. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	M-SD (N=27) (PYS=17.4) Events (E/100PY)	M-HD (N=31) (PYS=20.0) Events (E/100PY)	Total-ADA (N=58) (PYS=37.4) Events (E/100PY)	M-PL (N=11) (PYS=5.8) Events (E/100PY)	M-SD (N=6) (PYS=3.1) Events (E/100PY)	M-HD (N=5) (PYS=3.8) Events (E/100PY)	Total-ADA (N=11) (PYS=6.9) Events (E/100PY)	M-PL (N=1) (PYS=0.2) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (11.5)	2 (10.0)	4 (10.7)	0	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0	0	0	0
Vasculitis	0	0	0	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0	0	0	0
Sarcoidosis	0	0	0	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0	0	0	0
Intestinal perforation	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0

表 2.7.4.7-151. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（統合安全性解析対象集団，M11-290 試験）（続き）

	<= 9				> 9			
	M-SD (N=27) (PYS=17.4) Events (E/100PY)	M-HD (N=31) (PYS=20.0) Events (E/100PY)	Total-ADA (N=58) (PYS=37.4) Events (E/100PY)	M-PL (N=11) (PYS=5.8) Events (E/100PY)	M-SD (N=6) (PYS=3.1) Events (E/100PY)	M-HD (N=5) (PYS=3.8) Events (E/100PY)	Total-ADA (N=11) (PYS=6.9) Events (E/100PY)	M-PL (N=1) (PYS=0.2) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0	0	0	0
Erythema multiforme	0	0	0	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (17.2)	0	0	0	0
Demyelinating disorder	0	0	0	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	4 (23.0)	0	4 (10.7)	2 (34.5)	1 (32.3)	1 (26.3)	2 (29.0)	0
Liver failure and other liver events	0	0	0	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0	0	0	0
Injection site reaction	6 (34.5)	3 (15.0)	9 (24.1)	0	0	0	0	0
All deaths	0	0	0	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0	0	0	0

表 2.7.4.7-151. Mayo スコアに基づく疾患重症度別の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: 追加解析レポート JCSS TABLE 2.7.4__1.4.8_J

表 2.7.4.7-152.　最終解析の導入療法期中の治験薬の曝露期間（統合安全性解析対象集団，M11-290 試験）

	I-SD (N=32)	I-HD (N=51)	I-HD-OL (N=18)	Total (N=101)
Duration (day)				
n	32	51	18	101
Mean (SD)	52.8(9.30)	55.4(2.22)	53.8(4.92)	54.3(5.90)
Median	56.0	56.0	56.0	56.0
Min, Max	14, 59	42, 58	41, 58	14, 59
Patient-Years of exposure	4.6	7.7	2.7	15.0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: duration of induction-exposure = last induction dose date - first induction dose date + (max.*) 14 days.
* cutting before first dose of study drug in the maintenance period.

Cross reference: M11-290 CSR_Final Table 14.1__7.1_A

表 2.7.4.7-153.　最終解析の維持療法期中の治験薬の曝露期間
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

	M-PL (N=12)	M-SD (N=33)	M-HD (N=36)	ADA-Total (N=69)	Total (N=81)
Duration (day)					
n	12	33	36	69	81
Mean (SD)	184.2(123.02)	226.8(110.20)	241.0(103.25)	234.2(106.08)	226.8(109.39)
Median	196.5	307.0	308.0	308.0	307.0
Min, Max	26, 310	30, 316	28, 316	28, 316	26, 316
Patient-Years of exposure	6.1	20.5	23.8	44.2	50.3

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: duration of maintenance-exposure = last maintenance dose date (prior to potential re-randomization due to 1st disease flare) - first maintenance dose date + (max.*) 14 days. * cutting before first dose of study drug after re-randomization due to 1st disease flare, if applicable, or the first dose of study drug in M10-870, if applicable.

Cross reference: M11-290 CSR_Final Table 14.1__7.3_A

表 2.7.4.7-154. 最終解析の試験期間全体での治験薬の曝露期間（統合安全性解析対象集団，M11-290 試験）

	Any ADA								
	I-SD				I-HD/HD-OL				
	--$ (N=10)	M-PL (N=4)	M-SD (N=8)	M-HD (N=10)	--$ (N=10)	M-PL (N=8)	M-SD (N=25)	M-HD (N=26)	Total (N=101)
Duration (day)									
n	10	4	8	10	10	8	25	26	101
Mean (SD)	45.7(14.60)	145.3(133.98)	278.9(121.10)	343.2(73.94)	51.9(7.13)	168.5(118.84)	330.7(74.56)	348.3(54.90)	256.3(138.77)
Median	54.0	93.5	364.5	364.5	55.5	145.5	364.0	364.0	363.0
Min, Max	14, 56	55, 339	132, 372	133, 372	41, 58	55, 329	134, 371	112, 371	14, 372
Patient-Years of exposure	1.3	1.6	6.1	9.4	1.4	3.7	22.6	24.8	70.9

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group,
M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: subjects who are randomized to placebo at week 8 and who have not been re-randomized due to a disease flare:
Overall ADA exposure = duration of induction-exposure.

Subjects who are randomized to placebo at week 8 and are re-randomized due to at least one disease flare during maintenance:
Overall ADA exposure = duration of induction-exposure + (last adalimumab dose date in the study after re-randomization due to 1st disease flare - first dose date of adalimumab after re-randomization due to 1st disease flare + (max.*) 14 days).

Subjects who are not randomized to placebo:
Overall ADA exposure = last adalimumab dose date in the study - first dose of adalimumab + (max.*) 14 days.
* cutting before first dose of study drug in M10-870, if applicable.

$ patients who discontinued as non-responders from the study at week 8.

Cross reference: M11-290 CSR_Final Table 14.1__7.5_A

表 2.7.4.7-155.　最終解析の導入療法期中の治験薬の曝露期間（日本人安全性解析対象集団，M11-290 試験）

	I-SD (N=2)	I-HD (N=4)	I-HD-OL (N=2)	Total (N=8)
Duration (day)				
n	2	4	2	8
Mean (SD)	35.0(29.70)	55.5(1.00)	56.5(0.71)	50.6(14.82)
Median	35.0	56.0	56.5	56.0
Min, Max	14, 56	54, 56	56, 57	14, 57
Patient-Years of exposure	0.2	0.6	0.3	1.1

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: duration of induction-exposure = last induction dose date - first induction dose date + (max.*) 14 days.
* cutting before first dose of study drug in the maintenance period.

Cross reference: M11-290 CSR_Final Table 14.1__7.1_J

表 2.7.4.7-156.　最終解析の維持療法期中の治験薬の曝露期間
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）

	M-PL (N=0)	M-SD (N=2)	M-HD (N=4)	ADA-Total (N=6)	Total (N=6)
Duration (day)					
n	0	2	4	6	6
Mean (SD)		54.5(12.02)	235.3(89.44)	175.0(116.37)	175.0(116.37)
Median		54.5	252.5	162.5	162.5
Min, Max		46, 63	125, 311	46, 311	46, 311
Patient-Years of exposure		0.3	2.6	2.9	2.9

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: duration of maintenance-exposure = last maintenance dose date (prior to potential re-randomization due to 1st disease flare) - first maintenance dose date + (max.*) 14 days. * cutting before first dose of study drug after re-randomization due to 1st disease flare, if applicable, or the first dose of study drug in M10-870, if applicable.

Cross reference: M11-290 CSR_Final Table 14.1__7.3_J

表 2.7.4.7-157.　最終解析の試験期間全体での治験薬の曝露期間（日本人安全性解析対象集団，M11-290 試験）

	Any ADA								
	I-SD				I-HD/HD-OL				
	--$ (N=2)	M-PL (N=0)	M-SD (N=0)	M-HD (N=0)	--$ (N=0)	M-PL (N=0)	M-SD (N=2)	M-HD (N=4)	Total (N=8)
Duration (day)									
n	2	0	0	0	0	0	2	4	8
Mean (SD)	35.0(29.70)						315.0(69.30)	338.5(53.02)	256.8(144.41)
Median	35.0						315.0	364.0	315.0
Min, Max	14, 56						266, 364	259, 367	14, 367
Patient-Years of exposure	0.2						1.7	3.7	5.6

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group,
M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: subjects who are randomized to placebo at week 8 and who have not been re-randomized due to a disease flare:
Overall ADA exposure = duration of induction-exposure.

Subjects who are randomized to placebo at week 8 and are re-randomized due to at least one disease flare during maintenance:
Overall ADA exposure = duration of induction-exposure + (last adalimumab dose date in the study after re-randomization due to 1st disease flare - first dose date of adalimumab after re-randomization due to 1st disease flare + (max.*) 14 days).

Subjects who are not randomized to placebo:
Overall ADA exposure = last adalimumab dose date in the study - first dose of adalimumab + (max.*) 14 days.
* cutting before first dose of study drug in M10-870, if applicable.

$ patients who discontinued as non-responders from the study at week 8.

Cross reference: M11-290 CSR_Final Table 14.1__7.5_J

表 2.7.4.7-158.　最終解析の導入療法期中の有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	I-SD (N = 32) n (%)	I-HD (N = 51) n (%)	I-HD-OL (N = 18) n (%)	Total (N = 101) n (%)
有害事象	19 (59.4)	27 (52.9)	14 (77.8)	60 (59.4)
重篤な有害事象	5 (15.6)	4 (7.8)	1 (5.6)	10 (9.9)
高度の有害事象	4 (12.5)	1 (2.0)	0	5 (5.0)
治験薬投与の中止に至った有害事象	3 (9.4)	1 (2.0)	0	4 (4.0)
治験薬との因果関係が関連ありと医師により判断された有害事象	5 (15.6)	8 (15.7)	2 (11.1)	15 (14.9)
治験薬との因果関係が関連ありと医師により判断された重篤な有害事象	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
死亡に至った有害事象	0	0	0	0
死亡	0	0	0	0

I-HD = induction high dose; I-HD-OL = induction high dose open-label; I-SD = induction standard dose

Note: TEAEs are defined as events with an onset date on or after the first dose date of the study drug in the Induction period and up to 70 days after the last dose date of study drug in the Induction period and prior to the first dose date of study drug in the Maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
TEAEs with unknown relationship are counted as "reasonable possibility of being related."
TEAEs with unknown severity are counted as "severe."

Cross reference: M11-290 CSR_Final Appendix 16.1__9.5 Table 12

表 2.7.4.7-159.　最終解析の導入療法期中の有害事象の概要（日本人安全性解析対象集団，M11-290 試験）

	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
有害事象	2 (100)	4 (100)	2 (100)	8 (100)
重篤な有害事象	0	0	0	0
高度の有害事象	0	0	0	0
治験薬投与の中止に至った有害事象	1 (50.0)	0	0	1 (12.5)
治験薬との因果関係が関連ありと医師により判断された有害事象	1 (50.0)	1 (25.0)	1 (50.0)	3 (37.5)
治験薬との因果関係が関連ありと医師により判断された重篤な有害事象	0	0	0	0
死亡に至った有害事象	0	0	0	0
死亡	0	0	0	0

I-HD = induction high dose; I-HD-OL = induction high dose open-label; I-SD = induction standard dose

Note: TEAEs are defined as events with an onset date on or after the first dose date of the study drug in the Induction period and up to 70 days after the last dose date of study drug in the Induction period and prior to the first dose date of study drug in the Maintenance period if applicable.
Subjects are counted once in each row, regardless of the number of events they may have had.
TEAEs with unknown relationship are counted as "reasonable possibility of being related."
TEAEs with unknown severity are counted as "severe."

Cross reference: M11-290 CSR_Final Table 14.3__1.1.1.1_J

表 2.7.4.7-160.　最終解析の維持療法期中の有害事象の概要（統合安全性解析対象集団，M11-290 試験）

	M-SD (N = 33) n (%)	M-HD (N = 36) n (%)	Total Adalimumab (N = 69) n (%)	M-PL (N = 12) n (%)
有害事象	21 (63.6)	26 (72.2)	47 (68.1)	10 (83.3)
重篤な有害事象	5 (15.2)	5 (13.9)	10 (14.5)	1 (8.3)
高度の有害事象	3 (9.1)	1 (2.8)	4 (5.8)	0
治験薬投与の中止に至った有害事象	2 (6.1)	0	2 (2.9)	0
治験薬との因果関係が関連ありと医師により判断された有害事象	8 (24.2)	11 (30.6)	19 (27.5)	5 (41.7)
治験薬との因果関係が関連ありと医師により判断された重篤な有害事象	0	1 (2.8)	1 (1.4)	1 (8.3)
死亡に至った有害事象	0	0	0	0
死亡	0	0	0	0

M-HD = maintenance high dose; M-PL = maintenance placebo; M-SD = maintenance standard dose

Note: TEAEs are defined as events with an onset date on or after the first dose date of study drug in the Maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the Maintenance period.
Subjects are counted once in each row, regardless of the number of events they may have had.
TEAEs with unknown relationship were counted as "reasonable possibility of being related."
TEAEs with unknown severity were counted as "severe."
Data after the first disease flare for the Integrated RR population can be found in Table 14.3__1.1.1.4_A.

Cross reference: M11-290 CSR_Final Appendix 16.1__9.5 Table 13

表 2.7.4.7-161.　最終解析の維持療法期中の有害事象の概要（日本人安全性解析対象集団，M11-290 試験）

	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total Adalimumab (N=6) n (%)	M-PL (N=0) n (%)
有害事象	1 (50.0)	4 (100)	5 (83.3)	—
重篤な有害事象	1 (50.0)	0	1 (16.7)	—
高度の有害事象	0	0	0	—
治験薬投与の中止に至った有害事象	0	0	0	—
治験薬との因果関係が関連ありと医師により判断された有害事象	0	1 (25.0)	1 (16.7)	—
治験薬との因果関係が関連ありと医師により判断された重篤な有害事象	0	0	0	—
死亡に至った有害事象	0	0	0	—
死亡	0	0	0	—

M-HD = maintenance high dose; M-PL = maintenance placebo; M-SD = maintenance standard dose

Note: TEAEs are defined as events with an onset date on or after the first dose date of study drug in the Maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the Maintenance period.
Subjects are counted once in each row, regardless of the number of events they may have had.
TEAEs with unknown relationship were counted as "reasonable possibility of being related."
TEAEs with unknown severity were counted as "severe."
Data after the first disease flare for the Integrated RR population can be found in Table 14.3__1.1.1.4_A.

Cross reference: M11-290 CSR_Final Table 14.3__1.1.1.2_J

表 2.7.4.7-162. 最終解析の導入療法期中に 5%以上の被験者に発現した有害事象（MedDRA PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 PT	I-SD (N = 32) n (%)	I-HD (N = 51) n (%)	I-HD-OL (N = 18) n (%)	Total (N = 101) n (%)
Any AE	19 (59.4)	27 (52.9)	14 (77.8)	60 (59.4)
頭痛	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
貧血	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
潰瘍性大腸炎	4 (12.5)	2 (3.9)	1 (5.6)	7 (6.9)
上咽頭炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)

AE = adverse event; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group; I-SD = induction standard dose group; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term

Note: TEAEs are defined as events with an onset date on or after the first dose date of the study drug in the Induction period and up to 70 days after the last dose date of study drug in the Induction period and prior to the first dose date of study drug in the Maintenance period if applicable.

Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Appendix 16.1__9.5 Table 14

表 2.7.4.7-163.　最終解析の導入療法期中に発現したすべての有害事象（MedDRA PT 別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 Preferred Term	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
Any adverse event	2 (100)	4 (100)	2 (100)	8 (100)
上気道感染	0	2 (50.0)	0	2 (25.0)
眼瞼炎	0	1 (25.0)	0	1 (12.5)
異常感	1 (50.0)	0	0	1 (12.5)
頭痛	1 (50.0)	0	0	1 (12.5)
注射部位紅斑	0	1 (25.0)	0	1 (12.5)
注射部位疼痛	1 (50.0)	0	0	1 (12.5)
単球数減少	0	0	1 (50.0)	1 (12.5)
好中球数減少	0	0	1 (50.0)	1 (12.5)
外耳炎	0	1 (25.0)	0	1 (12.5)
末梢腫脹	0	0	1 (50.0)	1 (12.5)
白血球数減少	0	0	1 (50.0)	1 (12.5)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.2.1.1_J

表 2.7.4.7-164.　最終解析の導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	19 (59.4)	27 (52.9)	14 (77.8)	60 (59.4)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
貧血	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
血小板増加症	0	0	1 (5.6)	1 (1.0)
心臓障害	1 (3.1)	0	0	1 (1.0)
心膜炎	1 (3.1)	0	0	1 (1.0)
内分泌障害	1 (3.1)	0	0	1 (1.0)
甲状腺腫	1 (3.1)	0	0	1 (1.0)
眼障害	1 (3.1)	1 (2.0)	0	2 (2.0)
眼瞼炎	0	1 (2.0)	0	1 (1.0)
角膜炎	1 (3.1)	0	0	1 (1.0)
胃腸障害	6 (18.8)	9 (17.6)	5 (27.8)	20 (19.8)
腹痛	0	2 (3.9)	2 (11.1)	4 (4.0)
上腹部痛	1 (3.1)	2 (3.9)	0	3 (3.0)
潰瘍性大腸炎	4 (12.5)	2 (3.9)	1 (5.6)	7 (6.9)
便秘	0	0	1 (5.6)	1 (1.0)
下痢	0	0	1 (5.6)	1 (1.0)
血性下痢	1 (3.1)	0	0	1 (1.0)
小腸炎	1 (3.1)	0	0	1 (1.0)
鼓腸	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-164. 最終解析の導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
排便回数増加	0	1 (2.0)	0	1 (1.0)
胃食道逆流性疾患	0	1 (2.0)	1 (5.6)	2 (2.0)
血便排泄	0	2 (3.9)	0	2 (2.0)
悪心	0	3 (5.9)	1 (5.6)	4 (4.0)
膵炎	0	1 (2.0)	0	1 (1.0)
嘔吐	0	1 (2.0)	1 (5.6)	2 (2.0)
一般・全身障害および投与部位の状態	5 (15.6)	7 (13.7)	1 (5.6)	13 (12.9)
腋窩痛	0	1 (2.0)	0	1 (1.0)
胸痛	0	1 (2.0)	0	1 (1.0)
疲労	0	1 (2.0)	0	1 (1.0)
異常感	1 (3.1)	0	0	1 (1.0)
注射部位紅斑	0	1 (2.0)	0	1 (1.0)
注射部位疼痛	1 (3.1)	1 (2.0)	0	2 (2.0)
注射部位蕁麻疹	0	1 (2.0)	0	1 (1.0)
末梢腫脹	1 (3.1)	0	1 (5.6)	2 (2.0)
発熱	2 (6.3)	1 (2.0)	0	3 (3.0)
肝胆道系障害	1 (3.1)	0	0	1 (1.0)
高ビリルビン血症	1 (3.1)	0	0	1 (1.0)
感染症および寄生虫症	6 (18.8)	11 (21.6)	6 (33.3)	23 (22.8)
気管支炎	0	0	1 (5.6)	1 (1.0)

表 2.7.4.7-164. 最終解析の導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
せつ	0	1 (2.0)	0	1 (1.0)
サルモネラ菌性胃腸炎	1 (3.1)	0	0	1 (1.0)
上咽頭炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
口腔ヘルペス	1 (3.1)	2 (3.9)	0	3 (3.0)
外耳炎	0	1 (2.0)	0	1 (1.0)
咽頭炎	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
レンサ球菌感染	0	0	1 (5.6)	1 (1.0)
上気道感染	0	3 (5.9)	0	3 (3.0)
尿路感染	1 (3.1)	0	0	1 (1.0)
水痘	0	1 (2.0)	0	1 (1.0)
ウイルス感染	0	0	1 (5.6)	1 (1.0)
ウイルス性上気道感染	0	1 (2.0)	0	1 (1.0)
外陰腟真菌感染	0	0	1 (5.6)	1 (1.0)
傷害、中毒および処置合併症	4 (12.5)	2 (3.9)	0	6 (5.9)
節足動物咬傷	1 (3.1)	0	0	1 (1.0)
転倒	1 (3.1)	0	0	1 (1.0)
注入に伴う反応	1 (3.1)	0	0	1 (1.0)
靱帯捻挫	1 (3.1)	0	0	1 (1.0)
処置による疼痛	0	1 (2.0)	0	1 (1.0)
手首関節骨折	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-164. 最終解析の導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
臨床検査	2 (6.3)	2 (3.9)	2 (11.1)	6 (5.9)
血圧上昇	0	1 (2.0)	0	1 (1.0)
C－反応性蛋白増加	0	1 (2.0)	0	1 (1.0)
ヘモグロビン減少	1 (3.1)	0	0	1 (1.0)
肝酵素上昇	0	0	1 (5.6)	1 (1.0)
単球数減少	0	0	1 (5.6)	1 (1.0)
好中球数減少	0	0	1 (5.6)	1 (1.0)
体重減少	1 (3.1)	1 (2.0)	0	2 (2.0)
白血球数減少	0	0	1 (5.6)	1 (1.0)
筋骨格系および結合組織障害	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
関節痛	1 (3.1)	0	1 (5.6)	2 (2.0)
背部痛	0	1 (2.0)	0	1 (1.0)
靱帯障害	0	1 (2.0)	0	1 (1.0)
四肢痛	1 (3.1)	0	0	1 (1.0)
神経系障害	6 (18.8)	5 (9.8)	4 (22.2)	15 (14.9)
頭痛	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
意識消失	1 (3.1)	0	0	1 (1.0)
片頭痛	1 (3.1)	0	0	1 (1.0)
錯感覚	1 (3.1)	0	0	1 (1.0)
振戦	0	1 (2.0)	1 (5.6)	2 (2.0)

表 2.7.4.7-164. 最終解析の導入療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
腎および尿路障害	0	0	1 (5.6)	1 (1.0)
糖尿	0	0	1 (5.6)	1 (1.0)
生殖系および乳房障害	0	1 (2.0)	0	1 (1.0)
乳房痛	0	1 (2.0)	0	1 (1.0)
呼吸器、胸郭および縦隔障害	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)
咳嗽	0	1 (2.0)	0	1 (1.0)
鼻閉	0	1 (2.0)	0	1 (1.0)
口腔咽頭痛	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)
鼻漏	0	1 (2.0)	1 (5.6)	2 (2.0)
皮膚および皮下組織障害	1 (3.1)	0	1 (5.6)	2 (2.0)
結節性紅斑	1 (3.1)	0	0	1 (1.0)
発疹	0	0	1 (5.6)	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.1_A

表 2.7.4.7-165. 最終解析の維持療法期中に 5%以上の被験者に発現した有害事象（MedDRA PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 PT	M-SD (N = 33) n (%)	M-HD (N = 36) n (%)	Total Adalimumab (N = 69) n (%)	M-PL (N = 12) n (%)
Any AE	21 (63.6)	26 (72.2)	47 (68.1)	10 (83.3)
潰瘍性大腸炎	6 (18.2)	4 (11.1)	10 (14.5)	2 (16.7)
頭痛	6 (18.2)	2 (5.6)	8 (11.6)	2 (16.7)
上咽頭炎	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)
上気道感染	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)
貧血	3 (9.1)	1 (2.8)	4 (5.8)	1 (8.3)
咽頭炎	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)

AE = adverse event; M-HD = maintenance high dose group; M-PL = maintenance placebo group; M-SD = maintenance standard dose group; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term

Note: TEAEs are defined as events with an onset date on or after the first dose date of study drug in the Maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the Maintenance period. Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Appendix 16.1__9.5 Table 15

表 2.7.4.7-166.　最終解析の維持療法期中に発現したすべての有害事象（MedDRA PT 別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 Preferred Term	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
Any adverse event	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
結膜炎	0	1 (25.0)	1 (16.7)	0	1 (16.7)
感染性腸炎	1 (50.0)	0	1 (16.7)	0	1 (16.7)
眼瞼挫傷	0	1 (25.0)	1 (16.7)	0	1 (16.7)
手骨折	0	1 (25.0)	1 (16.7)	0	1 (16.7)
膿痂疹	0	1 (25.0)	1 (16.7)	0	1 (16.7)
インフルエンザ	0	1 (25.0)	1 (16.7)	0	1 (16.7)
靭帯捻挫	0	1 (25.0)	1 (16.7)	0	1 (16.7)
紫斑	0	1 (25.0)	1 (16.7)	0	1 (16.7)
上気道感染	0	1 (25.0)	1 (16.7)	0	1 (16.7)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.2.1.2_J

表 2.7.4.7-167.　最終解析の維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	21 (63.6)	26 (72.2)	47 (68.1)	10 (83.3)	57 (70.4)
血液およびリンパ系障害	4 (12.1)	1 (2.8)	5 (7.2)	2 (16.7)	7 (8.6)
貧血	3 (9.1)	1 (2.8)	4 (5.8)	1 (8.3)	5 (6.2)
リンパ節症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好中球減少症	0	0	0	1 (8.3)	1 (1.2)
耳および迷路障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
耳痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
眼障害	0	0	0	1 (8.3)	1 (1.2)
非感染性結膜炎	0	0	0	1 (8.3)	1 (1.2)
胃腸障害	9 (27.3)	10 (27.8)	19 (27.5)	3 (25.0)	22 (27.2)
腹痛	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
上腹部痛	0	2 (5.6)	2 (2.9)	0	2 (2.5)
アフタ性潰瘍	1 (3.0)	0	1 (1.4)	0	1 (1.2)
潰瘍性大腸炎	6 (18.2)	4 (11.1)	10 (14.5)	2 (16.7)	12 (14.8)
便秘	1 (3.0)	0	1 (1.4)	0	1 (1.2)
下痢	0	1 (2.8)	1 (1.4)	0	1 (1.2)
消化不良	0	1 (2.8)	1 (1.4)	0	1 (1.2)
小腸炎	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
胃食道逆流性疾患	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-167. 最終解析の維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
一般・全身障害および投与部位の状態	5 (15.2)	3 (8.3)	8 (11.6)	1 (8.3)	9 (11.1)
胸痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
疲労	2 (6.1)	0	2 (2.9)	0	2 (2.5)
炎症	0	0	0	1 (8.3)	1 (1.2)
注射部位紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位炎症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位疼痛	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位そう痒感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位腫脹	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位蕁麻疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
倦怠感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発熱	1 (3.0)	0	1 (1.4)	0	1 (1.2)
免疫系障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
薬物過敏症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染症および寄生虫症	11 (33.3)	17 (47.2)	28 (40.6)	5 (41.7)	33 (40.7)
気管支炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
膿痂疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-167. 最終解析の維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
感染性嚢腫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
インフルエンザ	0	2 (5.6)	2 (2.9)	0	2 (2.5)
喉頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
上咽頭炎	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
口腔ヘルペス	0	1 (2.8)	1 (1.4)	0	1 (1.2)
中耳炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)
気道感染	1 (3.0)	0	1 (1.4)	0	1 (1.2)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.2)
鼻炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
癜風	1 (3.0)	0	1 (1.4)	0	1 (1.2)
歯膿瘍	0	0	0	1 (8.3)	1 (1.2)
気管炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
上気道感染	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
尿路感染	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
水痘	0	1 (2.8)	1 (1.4)	0	1 (1.2)
傷害、中毒および処置合併症	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
眼瞼挫傷	0	1 (2.8)	1 (1.4)	0	1 (1.2)
手骨折	0	2 (5.6)	2 (2.9)	0	2 (2.5)

表 2.7.4.7-167. 最終解析の維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
傷害、中毒および処置合併症 (Cont.)					
関節損傷	0	0	0	1 (8.3)	1 (1.2)
靭帯捻挫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
臨床検査	5 (15.2)	3 (8.3)	8 (11.6)	0	8 (9.9)
血中ビリルビン増加	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
血中カルシウム減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
血中ナトリウム減少	0	1 (2.8)	1 (1.4)	0	1 (1.2)
骨密度減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Cー反応性蛋白増加	3 (9.1)	0	3 (4.3)	0	3 (3.7)
好酸球数増加	0	1 (2.8)	1 (1.4)	0	1 (1.2)
リンパ節触知	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結核菌群検査陽性	0	1 (2.8)	1 (1.4)	0	1 (1.2)
好中球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
白血球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
筋骨格系および結合組織障害	1 (3.0)	2 (5.6)	3 (4.3)	1 (8.3)	4 (4.9)
関節痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
背部痛	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
筋骨格痛	0	0	0	1 (8.3)	1 (1.2)
神経系障害	6 (18.2)	3 (8.3)	9 (13.0)	2 (16.7)	11 (13.6)
頭痛	6 (18.2)	2 (5.6)	8 (11.6)	2 (16.7)	10 (12.3)
感覚鈍麻	0	1 (2.8)	1 (1.4)	0	1 (1.2)
錯感覚	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-167. 最終解析の維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
精神障害	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
うつ病	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
生殖系および乳房障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
月経困難症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
呼吸器、胸郭および縦隔障害	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
喘息	1 (3.0)	0	1 (1.4)	0	1 (1.2)
咳嗽	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻出血	0	0	0	2 (16.7)	2 (2.5)
鼻浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
口腔咽頭痛	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
アレルギー性鼻炎	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
喘鳴	0	0	0	1 (8.3)	1 (1.2)
皮膚および皮下組織障害	1 (3.0)	7 (19.4)	8 (11.6)	3 (25.0)	11 (13.6)
脱毛症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
皮膚炎	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
結節性紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
逆むけ	0	0	0	1 (8.3)	1 (1.2)

表 2.7.4.7-167. 最終解析の維持療法期中に発現したすべての有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
乾癬	0	0	0	1 (8.3)	1 (1.2)
紫斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発疹	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
痂皮	0	1 (2.8)	1 (1.4)	0	1 (1.2)
脂漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
皮膚病変	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__1.2.1.1.2_A

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	19 (59.4)	27 (52.9)	14 (77.8)	60 (59.4)
No Reasonable Possibility	14 (43.8)	19 (37.3)	12 (66.7)	45 (44.6)
Reasonable Possibility	5 (15.6)	8 (15.7)	2 (11.1)	15 (14.9)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
No Reasonable Possibility	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
貧血	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
No Reasonable Possibility	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
血小板増加症	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
心臓障害	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
心膜炎	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
内分泌障害	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
甲状腺腫	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
眼障害	1 (3.1)	1 (2.0)	0	2 (2.0)
No Reasonable Possibility	1 (3.1)	1 (2.0)	0	2 (2.0)
眼瞼炎	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
角膜炎	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
胃腸障害	6 (18.8)	9 (17.6)	5 (27.8)	20 (19.8)
No Reasonable Possibility	6 (18.8)	6 (11.8)	4 (22.2)	16 (15.8)
Reasonable Possibility	0	3 (5.9)	1 (5.6)	4 (4.0)
腹痛	0	2 (3.9)	2 (11.1)	4 (4.0)
No Reasonable Possibility	0	2 (3.9)	2 (11.1)	4 (4.0)
上腹部痛	1 (3.1)	2 (3.9)	0	3 (3.0)
No Reasonable Possibility	1 (3.1)	2 (3.9)	0	3 (3.0)
潰瘍性大腸炎	4 (12.5)	2 (3.9)	1 (5.6)	7 (6.9)
No Reasonable Possibility	4 (12.5)	2 (3.9)	0	6 (5.9)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
便秘	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
下痢	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
血性下痢	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
小腸炎	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
鼓腸	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
排便回数増加	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
胃食道逆流性疾患	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)
血便排泄	0	2 (3.9)	0	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
悪心	0	3 (5.9)	1 (5.6)	4 (4.0)
No Reasonable Possibility	0	2 (3.9)	1 (5.6)	3 (3.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
膵炎	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
嘔吐	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
一般・全身障害および投与部位の状態	5 (15.6)	7 (13.7)	1 (5.6)	13 (12.9)
No Reasonable Possibility	4 (12.5)	3 (5.9)	1 (5.6)	8 (7.9)
Reasonable Possibility	1 (3.1)	4 (7.8)	0	5 (5.0)
腋窩痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
胸痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
疲労	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
異常感	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
注射部位紅斑	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
注射部位疼痛	1 (3.1)	1 (2.0)	0	2 (2.0)
Reasonable Possibility	1 (3.1)	1 (2.0)	0	2 (2.0)
注射部位蕁麻疹	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
末梢腫脹	1 (3.1)	0	1 (5.6)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.6)	2 (2.0)
発熱	2 (6.3)	1 (2.0)	0	3 (3.0)
No Reasonable Possibility	2 (6.3)	0	0	2 (2.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
肝胆道系障害	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
高ビリルビン血症	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
感染症および寄生虫症	6 (18.8)	11 (21.6)	6 (33.3)	23 (22.8)
No Reasonable Possibility	6 (18.8)	11 (21.6)	5 (27.8)	22 (21.8)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
気管支炎	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
せつ	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
サルモネラ菌性胃腸炎	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
上咽頭炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
No Reasonable Possibility	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
口腔ヘルペス	1 (3.1)	2 (3.9)	0	3 (3.0)
No Reasonable Possibility	1 (3.1)	2 (3.9)	0	3 (3.0)
外耳炎	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
咽頭炎	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
No Reasonable Possibility	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
レンサ球菌感染	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
上気道感染	0	3 (5.9)	0	3 (3.0)
No Reasonable Possibility	0	3 (5.9)	0	3 (3.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
尿路感染	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
水痘	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
ウイルス感染	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
ウイルス性上気道感染	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
外陰腟真菌感染	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
傷害、中毒および処置合併症	4 (12.5)	2 (3.9)	0	6 (5.9)
No Reasonable Possibility	4 (12.5)	2 (3.9)	0	6 (5.9)
節足動物咬傷	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
転倒	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
傷害、中毒および処置合併症 (Cont.)				
注入に伴う反応	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
靭帯捻挫	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
処置による疼痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
手首関節骨折	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
臨床検査	2 (6.3)	2 (3.9)	2 (11.1)	6 (5.9)
No Reasonable Possibility	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)
血圧上昇	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
C－反応性蛋白増加	0	1 (2.0)	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
ヘモグロビン減少	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
臨床検査 (Cont.)				
肝酵素上昇	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
単球数減少	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
好中球数減少	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
体重減少	1 (3.1)	1 (2.0)	0	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
白血球数減少	0	0	1 (5.6)	1 (1.0)
Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
筋骨格系および結合組織障害	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
No Reasonable Possibility	1 (3.1)	2 (3.9)	1 (5.6)	4 (4.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
関節痛	1 (3.1)	0	1 (5.6)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.6)	2 (2.0)
背部痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
筋骨格系および結合組織障害 (Cont.)				
靱帯障害	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
四肢痛	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
神経系障害	6 (18.8)	5 (9.8)	4 (22.2)	15 (14.9)
No Reasonable Possibility	4 (12.5)	3 (5.9)	4 (22.2)	11 (10.9)
Reasonable Possibility	2 (6.3)	2 (3.9)	0	4 (4.0)
頭痛	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
No Reasonable Possibility	4 (12.5)	3 (5.9)	4 (22.2)	11 (10.9)
Reasonable Possibility	1 (3.1)	2 (3.9)	0	3 (3.0)
意識消失	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
片頭痛	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
錯感覚	1 (3.1)	0	0	1 (1.0)
Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
振戦	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
腎および尿路障害	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
糖尿	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)
生殖系および乳房障害	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
乳房痛	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
呼吸器、胸郭および縦隔障害	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)
No Reasonable Possibility	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)
咳嗽	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
鼻閉	0	1 (2.0)	0	1 (1.0)
No Reasonable Possibility	0	1 (2.0)	0	1 (1.0)
口腔咽頭痛	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)
No Reasonable Possibility	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)

表 2.7.4.7-168. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
鼻漏	0	1 (2.0)	1 (5.6)	2 (2.0)
No Reasonable Possibility	0	1 (2.0)	1 (5.6)	2 (2.0)
皮膚および皮下組織障害	1 (3.1)	0	1 (5.6)	2 (2.0)
No Reasonable Possibility	1 (3.1)	0	1 (5.6)	2 (2.0)
結節性紅斑	1 (3.1)	0	0	1 (1.0)
No Reasonable Possibility	1 (3.1)	0	0	1 (1.0)
発疹	0	0	1 (5.6)	1 (1.0)
No Reasonable Possibility	0	0	1 (5.6)	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.1_A

表 2.7.4.7-169. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
Any adverse event	2 (100)	4 (100)	2 (100)	8 (100)
No Reasonable Possibility	1 (50.0)	3 (75.0)	1 (50.0)	5 (62.5)
Reasonable Possibility	1 (50.0)	1 (25.0)	1 (50.0)	3 (37.5)
眼障害	0	1 (25.0)	0	1 (12.5)
No Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
眼瞼炎	0	1 (25.0)	0	1 (12.5)
No Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
一般・全身障害および投与部位の状態	2 (100)	1 (25.0)	1 (50.0)	4 (50.0)
No Reasonable Possibility	1 (50.0)	0	1 (50.0)	2 (25.0)
Reasonable Possibility	1 (50.0)	1 (25.0)	0	2 (25.0)
異常感	1 (50.0)	0	0	1 (12.5)
No Reasonable Possibility	1 (50.0)	0	0	1 (12.5)
注射部位紅斑	0	1 (25.0)	0	1 (12.5)
Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
注射部位疼痛	1 (50.0)	0	0	1 (12.5)
Reasonable Possibility	1 (50.0)	0	0	1 (12.5)
末梢腫脹	0	0	1 (50.0)	1 (12.5)
No Reasonable Possibility	0	0	1 (50.0)	1 (12.5)

表 2.7.4.7-169. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（日本人安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
感染症および寄生虫症	0	3 (75.0)	0	3 (37.5)
No Reasonable Possibility	0	3 (75.0)	0	3 (37.5)
外耳炎	0	1 (25.0)	0	1 (12.5)
No Reasonable Possibility	0	1 (25.0)	0	1 (12.5)
上気道感染	0	2 (50.0)	0	2 (25.0)
No Reasonable Possibility	0	2 (50.0)	0	2 (25.0)
臨床検査	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
単球数減少	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
好中球数減少	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
白血球数減少	0	0	1 (50.0)	1 (12.5)
Reasonable Possibility	0	0	1 (50.0)	1 (12.5)
神経系障害	1 (50.0)	0	0	1 (12.5)
No Reasonable Possibility	1 (50.0)	0	0	1 (12.5)

表 2.7.4.7-169. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）（日本人安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
神経系障害 (Cont.)				
頭痛	1 (50.0)	0	0	1 (12.5)
No Reasonable Possibility	1 (50.0)	0	0	1 (12.5)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.1_J

表 2.7.4.7-170.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	21 (63.6)	26 (72.2)	47 (68.1)	10 (83.3)	57 (70.4)
No Reasonable Possibility	13 (39.4)	15 (41.7)	28 (40.6)	5 (41.7)	33 (40.7)
Reasonable Possibility	8 (24.2)	11 (30.6)	19 (27.5)	5 (41.7)	24 (29.6)
血液およびリンパ系障害	4 (12.1)	1 (2.8)	5 (7.2)	2 (16.7)	7 (8.6)
No Reasonable Possibility	3 (9.1)	1 (2.8)	4 (5.8)	0	4 (4.9)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	2 (16.7)	3 (3.7)
貧血	3 (9.1)	1 (2.8)	4 (5.8)	1 (8.3)	5 (6.2)
No Reasonable Possibility	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	1 (8.3)	2 (2.5)
リンパ節症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好中球減少症	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
耳および迷路障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
耳痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
眼障害	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
眼障害 (Cont.)					
非感染性結膜炎	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
胃腸障害	9 (27.3)	10 (27.8)	19 (27.5)	3 (25.0)	22 (27.2)
No Reasonable Possibility	7 (21.2)	7 (19.4)	14 (20.3)	3 (25.0)	17 (21.0)
Reasonable Possibility	2 (6.1)	3 (8.3)	5 (7.2)	0	5 (6.2)
腹痛	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
上腹部痛	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
アフタ性潰瘍	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
潰瘍性大腸炎	6 (18.2)	4 (11.1)	10 (14.5)	2 (16.7)	12 (14.8)
No Reasonable Possibility	5 (15.2)	2 (5.6)	7 (10.1)	2 (16.7)	9 (11.1)
Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
便秘	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
下痢	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
胃腸障害 (Cont.)					
消化不良	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
小腸炎	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
胃食道逆流性疾患	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
一般・全身障害および投与部位の状態	5 (15.2)	3 (8.3)	8 (11.6)	1 (8.3)	9 (11.1)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
Reasonable Possibility	4 (12.1)	2 (5.6)	6 (8.7)	1 (8.3)	7 (8.6)
胸痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
疲労	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
炎症	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
注射部位紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位炎症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位疼痛	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位そう痒感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位腫脹	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位蕁麻疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
倦怠感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発熱	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
免疫系障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
薬物過敏症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染症および寄生虫症	11 (33.3)	17 (47.2)	28 (40.6)	5 (41.7)	33 (40.7)
No Reasonable Possibility	11 (33.3)	15 (41.7)	26 (37.7)	5 (41.7)	31 (38.3)
Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
気管支炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
膿痂疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
感染性嚢腫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
インフルエンザ	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
喉頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
上咽頭炎	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
No Reasonable Possibility	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
口腔ヘルペス	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
中耳炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)
No Reasonable Possibility	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
気道感染	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
鼻炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
癜風	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
歯膿瘍	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
気管炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
上気道感染	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
No Reasonable Possibility	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
尿路感染	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
水痘	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
傷害、中毒および処置合併症	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
No Reasonable Possibility	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
眼瞼挫傷	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
手骨折	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
関節損傷	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
靭帯捻挫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
臨床検査	5 (15.2)	3 (8.3)	8 (11.6)	0	8 (9.9)
No Reasonable Possibility	4 (12.1)	1 (2.8)	5 (7.2)	0	5 (6.2)
Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
血中ビリルビン増加	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
臨床検査 (Cont.)					
血中カルシウム減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
血中ナトリウム減少	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
骨密度減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
C－反応性蛋白増加	3 (9.1)	0	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好酸球数増加	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
リンパ節触知	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結核菌群検査陽性	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
好中球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
臨床検査 (Cont.)					
白血球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
筋骨格系および結合組織障害	1 (3.0)	2 (5.6)	3 (4.3)	1 (8.3)	4 (4.9)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
関節痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
背部痛	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
筋骨格痛	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
神経系障害	6 (18.2)	3 (8.3)	9 (13.0)	2 (16.7)	11 (13.6)
No Reasonable Possibility	4 (12.1)	2 (5.6)	6 (8.7)	1 (8.3)	7 (8.6)
Reasonable Possibility	2 (6.1)	1 (2.8)	3 (4.3)	1 (8.3)	4 (4.9)
頭痛	6 (18.2)	2 (5.6)	8 (11.6)	2 (16.7)	10 (12.3)
No Reasonable Possibility	4 (12.1)	2 (5.6)	6 (8.7)	1 (8.3)	7 (8.6)
Reasonable Possibility	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
感覚鈍麻	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
神経系障害 (Cont.)					
錯感覚	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
精神障害	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
うつ病	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
生殖系および乳房障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
月経困難症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
呼吸器、胸郭および縦隔障害	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
No Reasonable Possibility	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
喘息	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
咳嗽	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
鼻出血	0	0	0	2 (16.7)	2 (2.5)
No Reasonable Possibility	0	0	0	2 (16.7)	2 (2.5)
鼻浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
口腔咽頭痛	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
アレルギー性鼻炎	0	2 (5.6)	2 (2.9)	0	2 (2.5)
No Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
喘鳴	0	0	0	1 (8.3)	1 (1.2)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
皮膚および皮下組織障害	1 (3.0)	7 (19.4)	8 (11.6)	3 (25.0)	11 (13.6)
No Reasonable Possibility	1 (3.0)	2 (5.6)	3 (4.3)	1 (8.3)	4 (4.9)
Reasonable Possibility	0	5 (13.9)	5 (7.2)	2 (16.7)	7 (8.6)
脱毛症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
皮膚炎	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
No Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
結節性紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
逆むけ	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
乾癬	0	0	0	1 (8.3)	1 (1.2)
Reasonable Possibility	0	0	0	1 (8.3)	1 (1.2)
紫斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発疹	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Reasonable Possibility	0	2 (5.6)	2 (2.9)	0	2 (2.5)
痂皮	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-170. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
脂漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	1 (3.0)	0	1 (1.4)	0	1 (1.2)
皮膚病変	0	1 (2.8)	1 (1.4)	0	1 (1.2)
No Reasonable Possibility	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.2_A

表 2.7.4.7-171.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
Any adverse event	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
No Reasonable Possibility	1 (50.0)	3 (75.0)	4 (66.7)	0	4 (66.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
感染症および寄生虫症	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
No Reasonable Possibility	1 (50.0)	3 (75.0)	4 (66.7)	0	4 (66.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
結膜炎	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
感染性腸炎	1 (50.0)	0	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	1 (50.0)	0	1 (16.7)	0	1 (16.7)
膿痂疹	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
インフルエンザ	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
上気道感染	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
傷害、中毒および処置合併症	0	2 (50.0)	2 (33.3)	0	2 (33.3)
No Reasonable Possibility	0	2 (50.0)	2 (33.3)	0	2 (33.3)

表 2.7.4.7-171. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，治験薬との因果関係別）
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Relationship	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
傷害、中毒および処置合併症 (Cont.)					
眼瞼挫傷	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
手骨折	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
靭帯捻挫	0	1 (25.0)	1 (16.7)	0	1 (16.7)
No Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
皮膚および皮下組織障害	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)
紫斑	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Reasonable Possibility	0	1 (25.0)	1 (16.7)	0	1 (16.7)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown relationship, then the subject will be counted in the relationship category of "unknown," unless the subject has another occurrence of the same AE with a relationship assessment of "Reasonable Possibility."

Cross reference: M11-290 CSR_Final Table 14.3__1.3.1.2_J

表 2.7.4.7-172.　最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	19 (59.4)	27 (52.9)	14 (77.8)	60 (59.4)
Mild	12 (37.5)	19 (37.3)	12 (66.7)	43 (42.6)
Moderate	3 (9.4)	7 (13.7)	2 (11.1)	12 (11.9)
Severe	4 (12.5)	1 (2.0)	0	5 (5.0)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
Mild	1 (3.1)	1 (2.0)	1 (5.6)	3 (3.0)
Moderate	1 (3.1)	2 (3.9)	0	3 (3.0)
Severe	1 (3.1)	0	0	1 (1.0)
貧血	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
Mild	1 (3.1)	1 (2.0)	1 (5.6)	3 (3.0)
Moderate	1 (3.1)	2 (3.9)	0	3 (3.0)
Severe	1 (3.1)	0	0	1 (1.0)
血小板増加症	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
心臓障害	1 (3.1)	0	0	1 (1.0)
Severe	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
心臓障害 (Cont.)				
心膜炎	1 (3.1)	0	0	1 (1.0)
Severe	1 (3.1)	0	0	1 (1.0)
内分泌障害	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
甲状腺腫	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
眼障害	1 (3.1)	1 (2.0)	0	2 (2.0)
Mild	1 (3.1)	1 (2.0)	0	2 (2.0)
眼瞼炎	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
眼障害 (Cont.)				
角膜炎	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
胃腸障害	6 (18.8)	9 (17.6)	5 (27.8)	20 (19.8)
Mild	2 (6.3)	4 (7.8)	4 (22.2)	10 (9.9)
Moderate	2 (6.3)	4 (7.8)	1 (5.6)	7 (6.9)
Severe	2 (6.3)	1 (2.0)	0	3 (3.0)
腹痛	0	2 (3.9)	2 (11.1)	4 (4.0)
Mild	0	2 (3.9)	2 (11.1)	4 (4.0)
上腹部痛	1 (3.1)	2 (3.9)	0	3 (3.0)
Mild	1 (3.1)	1 (2.0)	0	2 (2.0)
Moderate	0	1 (2.0)	0	1 (1.0)
潰瘍性大腸炎	4 (12.5)	2 (3.9)	1 (5.6)	7 (6.9)
Mild	0	0	1 (5.6)	1 (1.0)
Moderate	2 (6.3)	1 (2.0)	0	3 (3.0)
Severe	2 (6.3)	1 (2.0)	0	3 (3.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
便秘	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
下痢	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
血性下痢	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
小腸炎	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
鼓腸	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
排便回数増加	0	1 (2.0)	0	1 (1.0)
Moderate	0	1 (2.0)	0	1 (1.0)
胃食道逆流性疾患	0	1 (2.0)	1 (5.6)	2 (2.0)
Mild	0	1 (2.0)	1 (5.6)	2 (2.0)
血便排泄	0	2 (3.9)	0	2 (2.0)
Mild	0	1 (2.0)	0	1 (1.0)
Moderate	0	1 (2.0)	0	1 (1.0)
悪心	0	3 (5.9)	1 (5.6)	4 (4.0)
Mild	0	3 (5.9)	1 (5.6)	4 (4.0)
膵炎	0	1 (2.0)	0	1 (1.0)
Moderate	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
胃腸障害 (Cont.)				
嘔吐	0	1 (2.0)	1 (5.6)	2 (2.0)
Mild	0	1 (2.0)	0	1 (1.0)
Moderate	0	0	1 (5.6)	1 (1.0)
一般・全身障害および投与部位の状態	5 (15.6)	7 (13.7)	1 (5.6)	13 (12.9)
Mild	3 (9.4)	6 (11.8)	1 (5.6)	10 (9.9)
Moderate	2 (6.3)	1 (2.0)	0	3 (3.0)
腋窩痛	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
胸痛	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
疲労	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
異常感	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
注射部位紅斑	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
注射部位疼痛	1 (3.1)	1 (2.0)	0	2 (2.0)
Moderate	1 (3.1)	1 (2.0)	0	2 (2.0)
注射部位蕁麻疹	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
末梢腫脹	1 (3.1)	0	1 (5.6)	2 (2.0)
Mild	1 (3.1)	0	1 (5.6)	2 (2.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
発熱	2 (6.3)	1 (2.0)	0	3 (3.0)
Mild	1 (3.1)	1 (2.0)	0	2 (2.0)
Moderate	1 (3.1)	0	0	1 (1.0)
肝胆道系障害	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
高ビリルビン血症	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
感染症および寄生虫症	6 (18.8)	11 (21.6)	6 (33.3)	23 (22.8)
Mild	5 (15.6)	11 (21.6)	5 (27.8)	21 (20.8)
Moderate	0	0	1 (5.6)	1 (1.0)
Severe	1 (3.1)	0	0	1 (1.0)
気管支炎	0	0	1 (5.6)	1 (1.0)
Moderate	0	0	1 (5.6)	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
せつ	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
サルモネラ菌性胃腸炎	1 (3.1)	0	0	1 (1.0)
Severe	1 (3.1)	0	0	1 (1.0)
上咽頭炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
Mild	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
口腔ヘルペス	1 (3.1)	2 (3.9)	0	3 (3.0)
Mild	1 (3.1)	2 (3.9)	0	3 (3.0)
外耳炎	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
咽頭炎	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
Mild	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
レンサ球菌感染	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
上気道感染	0	3 (5.9)	0	3 (3.0)
Mild	0	3 (5.9)	0	3 (3.0)
尿路感染	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
水痘	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
感染症および寄生虫症 (Cont.)				
ウイルス感染	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
ウイルス性上気道感染	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
外陰膣真菌感染	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
傷害、中毒および処置合併症	4 (12.5)	2 (3.9)	0	6 (5.9)
Mild	4 (12.5)	1 (2.0)	0	5 (5.0)
Moderate	0	1 (2.0)	0	1 (1.0)
節足動物咬傷	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
傷害、中毒および処置合併症 (Cont.)				
転倒	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
注入に伴う反応	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
靭帯捻挫	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
処置による疼痛	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
手首関節骨折	0	1 (2.0)	0	1 (1.0)
Moderate	0	1 (2.0)	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
臨床検査	2 (6.3)	2 (3.9)	2 (11.1)	6 (5.9)
Mild	2 (6.3)	1 (2.0)	2 (11.1)	5 (5.0)
Moderate	0	1 (2.0)	0	1 (1.0)
血圧上昇	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
C－反応性蛋白増加	0	1 (2.0)	0	1 (1.0)
Moderate	0	1 (2.0)	0	1 (1.0)
ヘモグロビン減少	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
肝酵素上昇	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
臨床検査 (Cont.)				
単球数減少	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
好中球数減少	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
体重減少	1 (3.1)	1 (2.0)	0	2 (2.0)
Mild	1 (3.1)	0	0	1 (1.0)
Moderate	0	1 (2.0)	0	1 (1.0)
白血球数減少	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
筋骨格系および結合組織障害	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
Mild	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
筋骨格系および結合組織障害 (Cont.)				
関節痛	1 (3.1)	0	1 (5.6)	2 (2.0)
Mild	1 (3.1)	0	1 (5.6)	2 (2.0)
背部痛	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
靭帯障害	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
四肢痛	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
神経系障害	6 (18.8)	5 (9.8)	4 (22.2)	15 (14.9)
Mild	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
Moderate	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
神経系障害 (Cont.)				
頭痛	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
Mild	5 (15.6)	5 (9.8)	4 (22.2)	14 (13.9)
意識消失	1 (3.1)	0	0	1 (1.0)
Mild	1 (3.1)	0	0	1 (1.0)
片頭痛	1 (3.1)	0	0	1 (1.0)
Moderate	1 (3.1)	0	0	1 (1.0)
錯感覚	1 (3.1)	0	0	1 (1.0)
Moderate	1 (3.1)	0	0	1 (1.0)
振戦	0	1 (2.0)	1 (5.6)	2 (2.0)
Mild	0	1 (2.0)	1 (5.6)	2 (2.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
腎および尿路障害	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
糖尿	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)
生殖系および乳房障害	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
乳房痛	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
呼吸器、胸郭および縦隔障害	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)
Mild	1 (3.1)	3 (5.9)	3 (16.7)	7 (6.9)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
咳嗽	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
鼻閉	0	1 (2.0)	0	1 (1.0)
Mild	0	1 (2.0)	0	1 (1.0)
口腔咽頭痛	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)
Mild	1 (3.1)	1 (2.0)	2 (11.1)	4 (4.0)
鼻漏	0	1 (2.0)	1 (5.6)	2 (2.0)
Mild	0	1 (2.0)	1 (5.6)	2 (2.0)
皮膚および皮下組織障害	1 (3.1)	0	1 (5.6)	2 (2.0)
Mild	0	0	1 (5.6)	1 (1.0)
Moderate	1 (3.1)	0	0	1 (1.0)

表 2.7.4.7-172. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（統合安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
皮膚および皮下組織障害 (Cont.)				
結節性紅斑	1 (3.1)	0	0	1 (1.0)
Moderate	1 (3.1)	0	0	1 (1.0)
発疹	0	0	1 (5.6)	1 (1.0)
Mild	0	0	1 (5.6)	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Table depicts the most servere adverse event for each preferred term as assessed for each subject. Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown severity, then the subject will be counted in the severity category of "unknown,"even if the subject has another occurrence of the same event with a severity present. The only exception is if the subject has another occurrence of the same AE with the most extreme severity - "Severe." In this case, the subject will be counted under the "Severe" category.

Cross reference: M11-290 CSR_Final Table 14.3__1.3.2.1_A

表 2.7.4.7-173.　最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
Any adverse event	2 (100)	4 (100)	2 (100)	8 (100)
Mild	1 (50.0)	4 (100)	2 (100)	7 (87.5)
Moderate	1 (50.0)	0	0	1 (12.5)
眼障害	0	1 (25.0)	0	1 (12.5)
Mild	0	1 (25.0)	0	1 (12.5)
眼瞼炎	0	1 (25.0)	0	1 (12.5)
Mild	0	1 (25.0)	0	1 (12.5)
一般・全身障害および投与部位の状態	2 (100)	1 (25.0)	1 (50.0)	4 (50.0)
Mild	1 (50.0)	1 (25.0)	1 (50.0)	3 (37.5)
Moderate	1 (50.0)	0	0	1 (12.5)
異常感	1 (50.0)	0	0	1 (12.5)
Mild	1 (50.0)	0	0	1 (12.5)
注射部位紅斑	0	1 (25.0)	0	1 (12.5)
Mild	0	1 (25.0)	0	1 (12.5)
注射部位疼痛	1 (50.0)	0	0	1 (12.5)
Moderate	1 (50.0)	0	0	1 (12.5)

表 2.7.4.7-173. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（日本人安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
末梢腫脹	0	0	1 (50.0)	1 (12.5)
Mild	0	0	1 (50.0)	1 (12.5)
感染症および寄生虫症	0	3 (75.0)	0	3 (37.5)
Mild	0	3 (75.0)	0	3 (37.5)
外耳炎	0	1 (25.0)	0	1 (12.5)
Mild	0	1 (25.0)	0	1 (12.5)
上気道感染	0	2 (50.0)	0	2 (25.0)
Mild	0	2 (50.0)	0	2 (25.0)
臨床検査	0	0	1 (50.0)	1 (12.5)
Mild	0	0	1 (50.0)	1 (12.5)
単球数減少	0	0	1 (50.0)	1 (12.5)
Mild	0	0	1 (50.0)	1 (12.5)
好中球数減少	0	0	1 (50.0)	1 (12.5)
Mild	0	0	1 (50.0)	1 (12.5)

表 2.7.4.7-173. 最終解析の導入療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）（日本人安全性解析対象集団，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
臨床検査 (Cont.)				
白血球数減少	0	0	1 (50.0)	1 (12.5)
Mild	0	0	1 (50.0)	1 (12.5)
神経系障害	1 (50.0)	0	0	1 (12.5)
Mild	1 (50.0)	0	0	1 (12.5)
頭痛	1 (50.0)	0	0	1 (12.5)
Mild	1 (50.0)	0	0	1 (12.5)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Table depicts the most servere adverse event for each preferred term as assessed for each subject. Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown severity, then the subject will be counted in the severity category of "unknown,"even if the subject has another occurrence of the same event with a severity present. The only exception is if the subject has another occurrence of the same AE with the most extreme severity - "Severe." In this case, the subject will be counted under the "Severe" category.

Cross reference: M11-290 CSR_Final Table 14.3__1.3.2.1_J

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	21 (63.6)	26 (72.2)	47 (68.1)	10 (83.3)	57 (70.4)
Mild	7 (21.2)	18 (50.0)	25 (36.2)	8 (66.7)	33 (40.7)
Moderate	11 (33.3)	7 (19.4)	18 (26.1)	2 (16.7)	20 (24.7)
Severe	3 (9.1)	1 (2.8)	4 (5.8)	0	4 (4.9)
血液およびリンパ系障害	4 (12.1)	1 (2.8)	5 (7.2)	2 (16.7)	7 (8.6)
Mild	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
Moderate	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
Severe	1 (3.0)	0	1 (1.4)	0	1 (1.2)
貧血	3 (9.1)	1 (2.8)	4 (5.8)	1 (8.3)	5 (6.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Moderate	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
Severe	1 (3.0)	0	1 (1.4)	0	1 (1.2)
リンパ節症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好中球減少症	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)

表 2.7.4.7-174. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
耳および迷路障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
耳痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
眼障害	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
非感染性結膜炎	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
胃腸障害	9 (27.3)	10 (27.8)	19 (27.5)	3 (25.0)	22 (27.2)
Mild	3 (9.1)	6 (16.7)	9 (13.0)	2 (16.7)	11 (13.6)
Moderate	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
Severe	3 (9.1)	0	3 (4.3)	0	3 (3.7)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
胃腸障害 (Cont.)					
腹痛	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
Mild	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
上腹部痛	0	2 (5.6)	2 (2.9)	0	2 (2.5)
Mild	0	2 (5.6)	2 (2.9)	0	2 (2.5)
アフタ性潰瘍	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
潰瘍性大腸炎	6 (18.2)	4 (11.1)	10 (14.5)	2 (16.7)	12 (14.8)
Mild	1 (3.0)	0	1 (1.4)	1 (8.3)	2 (2.5)
Moderate	2 (6.1)	4 (11.1)	6 (8.7)	1 (8.3)	7 (8.6)
Severe	3 (9.1)	0	3 (4.3)	0	3 (3.7)
便秘	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
胃腸障害 (Cont.)					
下痢	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
消化不良	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
小腸炎	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Moderate	2 (6.1)	0	2 (2.9)	0	2 (2.5)
胃食道逆流性疾患	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
一般・全身障害および投与部位の状態	5 (15.2)	3 (8.3)	8 (11.6)	1 (8.3)	9 (11.1)
Mild	3 (9.1)	2 (5.6)	5 (7.2)	1 (8.3)	6 (7.4)
Moderate	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
胸痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
疲労	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Mild	2 (6.1)	0	2 (2.9)	0	2 (2.5)
炎症	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
注射部位紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位炎症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位疼痛	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位そう痒感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位腫脹	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位蕁麻疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
一般・全身障害および投与部位の状態 (Cont.)					
倦怠感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発熱	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	1 (3.0)	0	1 (1.4)	0	1 (1.2)
免疫系障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
薬物過敏症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染症および寄生虫症	11 (33.3)	17 (47.2)	28 (40.6)	5 (41.7)	33 (40.7)
Mild	5 (15.2)	14 (38.9)	19 (27.5)	5 (41.7)	24 (29.6)
Moderate	6 (18.2)	2 (5.6)	8 (11.6)	0	8 (9.9)
Severe	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
気管支炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	1 (3.0)	0	1 (1.4)	0	1 (1.2)
結膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
Mild	0	0	0	1 (8.3)	1 (1.2)
Moderate	2 (6.1)	0	2 (2.9)	0	2 (2.5)
膿痂疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
感染性嚢腫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
インフルエンザ	0	2 (5.6)	2 (2.9)	0	2 (2.5)
Mild	0	2 (5.6)	2 (2.9)	0	2 (2.5)
喉頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Severe	0	1 (2.8)	1 (1.4)	0	1 (1.2)
上咽頭炎	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
Mild	1 (3.0)	4 (11.1)	5 (7.2)	1 (8.3)	6 (7.4)
Moderate	2 (6.1)	0	2 (2.9)	0	2 (2.5)

表 2.7.4.7-174. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
中耳炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)
Mild	2 (6.1)	1 (2.8)	3 (4.3)	1 (8.3)	4 (4.9)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
気道感染	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	1 (3.0)	0	1 (1.4)	0	1 (1.2)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)

表 2.7.4.7-174. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
鼻炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
癜風	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
歯膿瘍	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
気管炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	1 (3.0)	0	1 (1.4)	0	1 (1.2)
上気道感染	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
Mild	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
尿路感染	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
Mild	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
水痘	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
傷害、中毒および処置合併症	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
Mild	0	3 (8.3)	3 (4.3)	1 (8.3)	4 (4.9)
眼瞼挫傷	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
手骨折	0	2 (5.6)	2 (2.9)	0	2 (2.5)
Mild	0	2 (5.6)	2 (2.9)	0	2 (2.5)

表 2.7.4.7-174. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
傷害、中毒および処置合併症 (Cont.)					
関節損傷	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
靭帯捻挫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
臨床検査	5 (15.2)	3 (8.3)	8 (11.6)	0	8 (9.9)
Mild	3 (9.1)	3 (8.3)	6 (8.7)	0	6 (7.4)
Moderate	2 (6.1)	0	2 (2.9)	0	2 (2.5)
血中ビリルビン増加	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
Mild	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
血中カルシウム減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
臨床検査 (Cont.)					
血中ナトリウム減少	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
骨密度減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
C一反応性蛋白増加	3 (9.1)	0	3 (4.3)	0	3 (3.7)
Mild	2 (6.1)	0	2 (2.9)	0	2 (2.5)
Moderate	1 (3.0)	0	1 (1.4)	0	1 (1.2)
好酸球数増加	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
リンパ節触知	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
臨床検査 (Cont.)					
結核菌群検査陽性	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
好中球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
白血球数減少	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	1 (3.0)	0	1 (1.4)	0	1 (1.2)
筋骨格系および結合組織障害	1 (3.0)	2 (5.6)	3 (4.3)	1 (8.3)	4 (4.9)
Mild	1 (3.0)	1 (2.8)	2 (2.9)	1 (8.3)	3 (3.7)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
関節痛	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
筋骨格系および結合組織障害 (Cont.)					
背部痛	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
Mild	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
筋骨格痛	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
神経系障害	6 (18.2)	3 (8.3)	9 (13.0)	2 (16.7)	11 (13.6)
Mild	4 (12.1)	2 (5.6)	6 (8.7)	2 (16.7)	8 (9.9)
Moderate	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
頭痛	6 (18.2)	2 (5.6)	8 (11.6)	2 (16.7)	10 (12.3)
Mild	4 (12.1)	2 (5.6)	6 (8.7)	2 (16.7)	8 (9.9)
Moderate	2 (6.1)	0	2 (2.9)	0	2 (2.5)
感覚鈍麻	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
神経系障害 (Cont.)					
錯感覚	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
精神障害	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
うつ病	1 (3.0)	1 (2.8)	2 (2.9)	0	2 (2.5)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
生殖系および乳房障害	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
月経困難症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
呼吸器、胸郭および縦隔障害	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
Mild	4 (12.1)	5 (13.9)	9 (13.0)	3 (25.0)	12 (14.8)
喘息	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
咳嗽	0	2 (5.6)	2 (2.9)	0	2 (2.5)
Mild	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻出血	0	0	0	2 (16.7)	2 (2.5)
Mild	0	0	0	2 (16.7)	2 (2.5)
鼻浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)					
口腔咽頭痛	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
Mild	2 (6.1)	1 (2.8)	3 (4.3)	0	3 (3.7)
アレルギー性鼻炎	0	2 (5.6)	2 (2.9)	0	2 (2.5)
Mild	0	2 (5.6)	2 (2.9)	0	2 (2.5)
鼻漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)
喘鳴	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
皮膚および皮下組織障害	1 (3.0)	7 (19.4)	8 (11.6)	3 (25.0)	11 (13.6)
Mild	1 (3.0)	6 (16.7)	7 (10.1)	3 (25.0)	10 (12.3)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
脱毛症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
皮膚炎	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
Mild	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
結節性紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Moderate	0	1 (2.8)	1 (1.4)	0	1 (1.2)
逆むけ	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)

表 2.7.4.7-174. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
乾癬	0	0	0	1 (8.3)	1 (1.2)
Mild	0	0	0	1 (8.3)	1 (1.2)
紫斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
発疹	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
Mild	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
痂皮	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)
脂漏	1 (3.0)	0	1 (1.4)	0	1 (1.2)
Mild	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-174.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
皮膚および皮下組織障害 (Cont.)					
皮膚病変	0	1 (2.8)	1 (1.4)	0	1 (1.2)
Mild	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Table depicts the most servere adverse event for each preferred term as assessed for each subject. Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown severity, then the subject will be counted in the severity category of "unknown,"even if the subject has another occurrence of the same event with a severity present. The only exception is if the subject has another occurrence of the same AE with the most extreme severity - "Severe." In this case, the subject will be counted under the "Severe" category.

Cross reference: M11-290 CSR_Final Table 14.3__1.3.2.2_A

表 2.7.4.7-175.　最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
Any adverse event	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
Mild	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
感染症および寄生虫症	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
Mild	1 (50.0)	4 (100)	5 (83.3)	0	5 (83.3)
結膜炎	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)
感染性腸炎	1 (50.0)	0	1 (16.7)	0	1 (16.7)
Mild	1 (50.0)	0	1 (16.7)	0	1 (16.7)
膿痂疹	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)
インフルエンザ	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)
上気道感染	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)

表 2.7.4.7-175. 最終解析の維持療法期中に発現した有害事象（MedDRA SOC 及び PT 別，重症度別）
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term Severity	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
傷害、中毒および処置合併症	0	2 (50.0)	2 (33.3)	0	2 (33.3)
Mild	0	2 (50.0)	2 (33.3)	0	2 (33.3)
眼瞼挫傷	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)
手骨折	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)
靭帯捻挫	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)
皮膚および皮下組織障害	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)
紫斑	0	1 (25.0)	1 (16.7)	0	1 (16.7)
Mild	0	1 (25.0)	1 (16.7)	0	1 (16.7)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Table depicts the most servere adverse event for each preferred term as assessed for each subject. Subjects are counted once in each row, regardless of the number of events they may have had.
If a subject has an AE with unknown severity, then the subject will be counted in the severity category of "unknown,"even if the subject has another occurrence of the same event with a severity present. The only exception is if the subject has another occurrence of the same AE with the most extreme severity - "Severe." In this case, the subject will be counted under the "Severe" category.

Cross reference: M11-290 CSR_Final Table 14.3__1.3.2.2_J

表 2.7.4.7-176.　最終解析の導入療法期中に発現した重篤な有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	5 (15.6)	4 (7.8)	1 (5.6)	10 (9.9)
血液およびリンパ系障害	2 (6.3)	0	0	2 (2.0)
貧血	2 (6.3)	0	0	2 (2.0)
心臓障害	1 (3.1)	0	0	1 (1.0)
心膜炎	1 (3.1)	0	0	1 (1.0)
胃腸障害	2 (6.3)	3 (5.9)	1 (5.6)	6 (5.9)
潰瘍性大腸炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
膵炎	0	1 (2.0)	0	1 (1.0)
傷害、中毒および処置合併症	0	1 (2.0)	0	1 (1.0)
手首関節骨折	0	1 (2.0)	0	1 (1.0)
神経系障害	1 (3.1)	0	0	1 (1.0)
頭痛	1 (3.1)	0	0	1 (1.0)
意識消失	1 (3.1)	0	0	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.1.1.1.1_A

表 2.7.4.7-177.　最終解析の導入療法期中に発現した重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）
（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) (PYS=4.6) Events (E/100PY)	I-HD (N=51) (PYS=7.7) Events (E/100PY)	I-HD-OL (N=18) (PYS=2.7) Events (E/100PY)	Total (N=101) (PYS=15.0) Events (E/100PY)
Any adverse event	7 (152.2)	4 (51.9)	1 (37.0)	12 (80.0)
血液およびリンパ系障害	2 (43.5)	0	0	2 (13.3)
貧血	2 (43.5)	0	0	2 (13.3)
心臓障害	1 (21.7)	0	0	1 (6.7)
心膜炎	1 (21.7)	0	0	1 (6.7)
胃腸障害	2 (43.5)	3 (39.0)	1 (37.0)	6 (40.0)
潰瘍性大腸炎	2 (43.5)	2 (26.0)	1 (37.0)	5 (33.3)
膵炎	0	1 (13.0)	0	1 (6.7)
傷害、中毒および処置合併症	0	1 (13.0)	0	1 (6.7)
手首関節骨折	0	1 (13.0)	0	1 (6.7)
神経系障害	2 (43.5)	0	0	2 (13.3)
頭痛	1 (21.7)	0	0	1 (6.7)
意識消失	1 (21.7)	0	0	1 (6.7)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: E/100PY = Events per 100 patient-years.

Cross reference: M11-290 CSR_Final Table 14.3__2.1.1.2.1_A

表 2.7.4.7-178.　最終解析の導入療法期中に発現した治験薬と関連ありの重篤な有害事象（MedDRA SOC 及び PT 別）
（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
心臓障害	1 (3.1)	0	0	1 (1.0)
心膜炎	1 (3.1)	0	0	1 (1.0)
胃腸障害	0	1 (2.0)	1 (5.6)	2 (2.0)
潰瘍性大腸炎	0	0	1 (5.6)	1 (1.0)
膵炎	0	1 (2.0)	0	1 (1.0)
神経系障害	1 (3.1)	0	0	1 (1.0)
頭痛	1 (3.1)	0	0	1 (1.0)
意識消失	1 (3.1)	0	0	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.1.2.1.1_A

表 2.7.4.7-179.　最終解析の維持療法期中に発現した重篤な有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	5 (15.2)	5 (13.9)	10 (14.5)	1 (8.3)	11 (13.6)
血液およびリンパ系障害	1 (3.0)	0	1 (1.4)	0	1 (1.2)
貧血	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸障害	3 (9.1)	1 (2.8)	4 (5.8)	0	4 (4.9)
潰瘍性大腸炎	3 (9.1)	0	3 (4.3)	0	3 (3.7)
消化不良	0	1 (2.8)	1 (1.4)	0	1 (1.2)
小腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
感染症および寄生虫症	3 (9.1)	3 (8.3)	6 (8.7)	0	6 (7.4)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	0	2 (2.5)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
尿路感染	0	1 (2.8)	1 (1.4)	0	1 (1.2)
傷害、中毒および処置合併症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
手骨折	0	1 (2.8)	1 (1.4)	0	1 (1.2)
皮膚および皮下組織障害	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
結節性紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
乾癬	0	0	0	1 (8.3)	1 (1.2)

表 2.7.4.7-179.　最終解析の維持療法期中に発現した重篤な有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.1.1.1.2_A

表 2.7.4.7-180. 最終解析の維持療法期中に発現した重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) (PYS=20.5) Events (E/100PY)	M-HD (N=36) (PYS=23.8) Events (E/100PY)	Total-ADA (N=69) (PYS=44.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=81) (PYS=50.3) Events (E/100PY)
Any adverse event	10 (48.8)	6 (25.2)	16 (36.2)	1 (16.4)	17 (33.8)
血液およびリンパ系障害	2 (9.8)	0	2 (4.5)	0	2 (4.0)
貧血	2 (9.8)	0	2 (4.5)	0	2 (4.0)
胃腸障害	5 (24.4)	1 (4.2)	6 (13.6)	0	6 (11.9)
潰瘍性大腸炎	4 (19.5)	0	4 (9.0)	0	4 (8.0)
消化不良	0	1 (4.2)	1 (2.3)	0	1 (2.0)
小腸炎	1 (4.9)	0	1 (2.3)	0	1 (2.0)
感染症および寄生虫症	3 (14.6)	3 (12.6)	6 (13.6)	0	6 (11.9)
感染性腸炎	1 (4.9)	0	1 (2.3)	0	1 (2.0)
胃腸炎	2 (9.8)	0	2 (4.5)	0	2 (4.0)
無菌性髄膜炎	0	1 (4.2)	1 (2.3)	0	1 (2.0)
咽頭炎	0	1 (4.2)	1 (2.3)	0	1 (2.0)
尿路感染	0	1 (4.2)	1 (2.3)	0	1 (2.0)
傷害、中毒および処置合併症	0	1 (4.2)	1 (2.3)	0	1 (2.0)
手骨折	0	1 (4.2)	1 (2.3)	0	1 (2.0)
皮膚および皮下組織障害	0	1 (4.2)	1 (2.3)	1 (16.4)	2 (4.0)
結節性紅斑	0	1 (4.2)	1 (2.3)	0	1 (2.0)
乾癬	0	0	0	1 (16.4)	1 (2.0)

表 2.7.4.7-180.　最終解析の維持療法期中に発現した重篤な有害事象の 100 人年あたりの発現頻度（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: E/100PY = Events per 100 patient-years.

Cross reference: M11-290 CSR_Final Table 14.3__2.1.1.2.2_A

表 2.7.4.7-181.　最終解析の維持療法期中に発現した治験薬と関連ありの重篤な有害事象（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	0	1 (2.8)	1 (1.4)	1 (8.3)	2 (2.5)
感染症および寄生虫症	0	1 (2.8)	1 (1.4)	0	1 (1.2)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
皮膚および皮下組織障害	0	0	0	1 (8.3)	1 (1.2)
乾癬	0	0	0	1 (8.3)	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.1.2.1.2_A

表 2.7.4.7-182. 最終解析の AESI の概要（試験期別，用量群別）
（統合安全性解析対象集団，日本人安全性解析対象集団及び統合再無作為化集団，M11-290 試験）

	n (%) of Subjects						
	Safety					RR	Safety
	Induction[a]			Maintenance Up to First Disease Flare[b]		After First Disease Flare with Re-Induction[c]	Any Adalimumab[d]
AESI Category	I-SD	I-HD	I-HD-OL	M-SD	M-HD		
Integrated population	N = 32	N = 51	N = 18	N = 33	N =36	N = 8	N = 101
Infection	6 (18.8)	11 (21.6)	6 (33.3)	11 (33.3)	16 (44.4)	4 (50.0)	49 (48.5)
Serious infection	0	0	0	3 (9.1)	3 (8.3)	0	6 (5.9)
Opportunistic infection excluding oral candidiasis and TB	0	0	0	0	0	1 (12.5)[e]	1 (1.0)
Latent TB	0	0	0	0	1 (2.8)	0	1 (1.0)
Allergic reactions including angioedema/ anaphylaxis	0	1 (2.0)	0	1 (3.0)	2 (5.6)	0	4 (4.0)
Pancreatitis	0	1 (2.0)	0	0	0	0	1 (1.0)
Worsening or new onset of psoriasis	0	0	0	0	0	0	0
Hematologic disorders including pancytopenia	3 (9.4)	3 (5.9)	1 (5.6)	3 (9.1)	1 (2.8)	0	12 (11.9)
Injection site reaction	1 (3.1)	3 (5.9)	0	4 (12.1)	2 (5.6)	0	10 (9.9)

表 2.7.4.7-182. 最終解析の AESI の概要（試験期別，用量群別）
（統合安全性解析対象集団，日本人安全性解析対象集団及び統合再無作為化集団，M11-290 試験）（続き）

	n (%) of Subjects						
	Safety					RR	Safety
	Induction[a]			Maintenance Up to First Disease Flare[b]		After First Disease Flare with Re-Induction[c]	Any Adalimumab[d]
AESI Category	I-SD	I-HD	I-HD-OL	M-SD	M-HD		
Japan population	N = 2	N = 4	N = 2	N = 2	N = 4	—	N = 8
Infection	0	3 (75.0)	0	1 (50.0)	3 (75.0)	—	5 (62.5)
Serious infection	0	0	0	1 (50.0)	0	—	1 (12.5)
Latent TB	0	0	0	0	0	—	0
Allergic reactions including angioedema/ anaphylaxis	0	0	0	0	0	—	0
Pancreatitis	0	0	0	0	0	—	0
Worsening or new onset of psoriasis	0	0	0	0	0	—	0
Hematologic disorders including pancytopenia	0	0	0	0	0	—	0
Injection site reaction	1 (50.0)	1 (25.0)	0	0	0	—	2 (25.0)

AESI = adverse event of special interest; I-HD = induction high dose; I-HD-OL = induction high dose open-label; I-SD = induction standard dose; M-HD = maintenance high dose; M-SD = maintenance standard dose; RR = re-randomized population; TB = tuberculosis

a. Integrated Safety population; TEAEs are defined as events with an onset date on or after the date of the first dose of study drug in the Induction period and prior to the first dose date of study drug in the Maintenance period (if applicable).

b. Integrated Safety population – subjects with at least 1 dose of study drug during Maintenance period; TEAEs are defined as events with an onset date on or after the first dose date of study drug in the Maintenance period and prior to re-randomization due to the first disease flare (if applicable) and up to 70 days after the last dose date of study drug in the Maintenance period.

表 2.7.4.7-182.　最終解析の AESI の概要（試験期別，用量群別）
（統合安全性解析対象集団，日本人安全性解析対象集団及び統合再無作為化集団，M11-290 試験）（続き）

c. Integrated RR population with re-induction dose (shown as the total of M-SD and M-HD): TEAEs are defined as events with an onset date on or after the first dose date of study drug after re-randomization due to first disease flare and up to 70 days after the last dose date of study drug.

d. Subjects in the Any Adalimumab population may also be counted under the individual dose groups per study period, so the Any Adalimumab group is not the sum of subjects in the individual period dose groups.

e. Subject had previously received adalimumab during Induction (I-HD-OL group) and during Maintenance up to the first disease flare (M-SD group).

Note: TEAEs are defined as events with an onset date on or after the first dose date of adalimumab and up to 70 days after the last date of adalimumab in this study. For subjects randomized to placebo at Week 8 without disease flare, AEs with an onset date on or after the first dose date of placebo are excluded. For subjects randomized to placebo at Week 8 and were re-randomized due to disease flare, AEs with an onset date within the first dose date of placebo and last dose date of placebo are excluded. Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Appendix 16.1__9.5 Table 16

表 2.7.4.7-183. 最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）

	I-SD (N=32) (PYS=4.6) Events (E/100PY)	I-HD (N=51) (PYS=7.7) Events (E/100PY)	I-HD-OL (N=18) (PYS=2.7) Events (E/100PY)	Total (N=101) (PYS=15.0) Events (E/100PY)
Any treatment-emergent				
Adverse event (AE)	46 (1000.0)	62 (805.2)	35 (1296.3)	143 (953.3)
Serious AE	7 (152.2)	4 (51.9)	1 (37.0)	12 (80.0)
Severe AE	5 (108.7)	1 (13.0)	0	6 (40.0)
AEs leading to discontinuation of study drug	4 (87.0)	1 (13.0)	0	5 (33.3)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	8 (173.9)	16 (207.8)	5 (185.2)	29 (193.3)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	3 (65.2)	1 (13.0)	1 (37.0)	5 (33.3)
AEs leading to Death	0	0	0	0
Infections	7 (152.2)	13 (168.8)	7 (259.3)	27 (180.0)
Serious infections	0	0	0	0
Legionella infections	0	0	0	0
Diverticulitis	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0

表 2.7.4.7-183.　最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=32) (PYS=4.6) Events (E/100PY)	I-HD (N=51) (PYS=7.7) Events (E/100PY)	I-HD-OL (N=18) (PYS=2.7) Events (E/100PY)	Total (N=101) (PYS=15.0) Events (E/100PY)
Oral candidiasis	0	0	0	0
Tuberculosis	0	0	0	0
Active tuberculosis	0	0	0	0
Latent tuberculosis	0	0	0	0
Parasitic infections	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0
Malignancies	0	0	0	0
Lymphoma	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0
Melanoma	0	0	0	0
Leukemia	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0

表 2.7.4.7-183.　最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=32) (PYS=4.6) Events (E/100PY)	I-HD (N=51) (PYS=7.7) Events (E/100PY)	I-HD-OL (N=18) (PYS=2.7) Events (E/100PY)	Total (N=101) (PYS=15.0) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	1 (13.0)	0	1 (6.7)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0
Vasculitis	0	0	0	0
Cutaneous vasculitis	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0
Sarcoidosis	0	0	0	0
Autoimmune Hepatitis	0	0	0	0
Myocardial infarction (MI)	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0
Pulmonary embolism	0	0	0	0
Interstitial lung disease	0	0	0	0
Intestinal perforation	0	0	0	0
Pancreatitis	0	1 (13.0)	0	1 (6.7)

表 2.7.4.7-183.　最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（統合安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=32) (PYS=4.6) Events (E/100PY)	I-HD (N=51) (PYS=7.7) Events (E/100PY)	I-HD-OL (N=18) (PYS=2.7) Events (E/100PY)	Total (N=101) (PYS=15.0) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0
Erythema multiforme	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0
Demyelinating disorder	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0
Hematologic disorders including pancytopenia	3 (65.2)	3 (39.0)	1 (37.0)	7 (46.7)
Liver failure and other liver events	0	0	0	0
Humira administration related medication error	0	0	0	0
Injection site reaction	1 (21.7)	5 (64.9)	0	6 (40.0)
All deaths	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0
Occurring >70 days after last dose	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: M11-290 CSR_Final Table 14.3__1.1.2.1_A

表 2.7.4.7-184. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

	M-SD (N=33) (PYS=20.5) Events (E/100PY)	M-HD (N=36) (PYS=23.8) Events (E/100PY)	Total-ADA (N=69) (PYS=44.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=81) (PYS=50.3) Events (E/100PY)
Any treatment-emergent					
Adverse event (AE)	74 (361.0)	77 (323.5)	151 (341.6)	26 (426.2)	177 (351.9)
Serious AE	10 (48.8)	6 (25.2)	16 (36.2)	1 (16.4)	17 (33.8)
Severe AE	5 (24.4)	1 (4.2)	6 (13.6)	0	6 (11.9)
AEs leading to discontinuation of study drug	3 (14.6)	0	3 (6.8)	0	3 (6.0)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	14 (68.3)	20 (84.0)	34 (76.9)	6 (98.4)	40 (79.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	1 (4.2)	1 (2.3)	1 (16.4)	2 (4.0)
AEs leading to Death	0	0	0	0	0
Infections	18 (87.8)	22 (92.4)	40 (90.5)	9 (147.5)	49 (97.4)
Serious infections	3 (14.6)	3 (12.6)	6 (13.6)	0	6 (11.9)
Legionella infections	0	0	0	0	0
Diverticulitis	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0

表 2.7.4.7-184. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=33) (PYS=20.5) Events (E/100PY)	M-HD (N=36) (PYS=23.8) Events (E/100PY)	Total-ADA (N=69) (PYS=44.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=81) (PYS=50.3) Events (E/100PY)
Oral candidiasis	0	0	0	0	0
Tuberculosis	0	1 (4.2)	1 (2.3)	0	1 (2.0)
Active tuberculosis	0	0	0	0	0
Latent tuberculosis	0	1 (4.2)	1 (2.3)	0	1 (2.0)
Parasitic infections	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0
Malignancies	0	0	0	0	0
Lymphoma	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0
Melanoma	0	0	0	0	0
Leukemia	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0

表 2.7.4.7-184. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=33) (PYS=20.5) Events (E/100PY)	M-HD (N=36) (PYS=23.8) Events (E/100PY)	Total-ADA (N=69) (PYS=44.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=81) (PYS=50.3) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	2 (9.8)	2 (8.4)	4 (9.0)	0	4 (8.0)
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0
Vasculitis	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0
Sarcoidosis	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0
Intestinal perforation	0	0	0	0	0
Pancreatitis	0	0	0	0	0

表 2.7.4.7-184. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=33) (PYS=20.5) Events (E/100PY)	M-HD (N=36) (PYS=23.8) Events (E/100PY)	Total-ADA (N=69) (PYS=44.2) Events (E/100PY)	M-PL (N=12) (PYS=6.1) Events (E/100PY)	Total (N=81) (PYS=50.3) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0
Erythema multiforme	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	1 (16.4)	1 (2.0)
Demyelinating disorder	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0
Hematologic disorders including pancytopenia	5 (24.4)	1 (4.2)	6 (13.6)	2 (32.8)	8 (15.9)
Liver failure and other liver events	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0
Injection site reaction	6 (29.3)	3 (12.6)	9 (20.4)	0	9 (17.9)
All deaths	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0

表 2.7.4.7-184.　最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: M11-290 CSR_Final Table 14.3__1.1.2.2_A

表 2.7.4.7-185.　最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（日本人安全性解析対象集団，M11-290 試験）

	I-SD (N=2) (PYS=0.2) Events (E/100PY)	I-HD (N=4) (PYS=0.6) Events (E/100PY)	I-HD-OL (N=2) (PYS=0.3) Events (E/100PY)	Total (N=8) (PYS=1.1) Events (E/100PY)
Any treatment-emergent				
Adverse event (AE)	3 (1500.0)	5 (833.3)	4 (1333.3)	12 (1090.9)
Serious AE	0	0	0	0
Severe AE	0	0	0	0
AEs leading to discontinuation of study drug	1 (500.0)	0	0	1 (90.9)
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	1 (500.0)	1 (166.7)	3 (1000.0)	5 (454.5)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0
AEs leading to Death	0	0	0	0
Infections	0	3 (500.0)	0	3 (272.7)
Serious infections	0	0	0	0
Legionella infections	0	0	0	0
Diverticulitis	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0

表 2.7.4.7-185. 最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（日本人安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=2) (PYS=0.2) Events (E/100PY)	I-HD (N=4) (PYS=0.6) Events (E/100PY)	I-HD-OL (N=2) (PYS=0.3) Events (E/100PY)	Total (N=8) (PYS=1.1) Events (E/100PY)
Oral candidiasis	0	0	0	0
Tuberculosis	0	0	0	0
Active tuberculosis	0	0	0	0
Latent tuberculosis	0	0	0	0
Parasitic infections	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0
Malignancies	0	0	0	0
Lymphoma	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0
Melanoma	0	0	0	0
Leukemia	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0

表 2.7.4.7-185. 最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（日本人安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=2) (PYS=0.2) Events (E/100PY)	I-HD (N=4) (PYS=0.6) Events (E/100PY)	I-HD-OL (N=2) (PYS=0.3) Events (E/100PY)	Total (N=8) (PYS=1.1) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0
Vasculitis	0	0	0	0
Cutaneous vasculitis	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0
Sarcoidosis	0	0	0	0
Autoimmune Hepatitis	0	0	0	0
Myocardial infarction (MI)	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0
Pulmonary embolism	0	0	0	0
Interstitial lung disease	0	0	0	0
Intestinal perforation	0	0	0	0
Pancreatitis	0	0	0	0

表 2.7.4.7-185. 最終解析の導入療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要（日本人安全性解析対象集団，M11-290 試験）（続き）

	I-SD (N=2) (PYS=0.2) Events (E/100PY)	I-HD (N=4) (PYS=0.6) Events (E/100PY)	I-HD-OL (N=2) (PYS=0.3) Events (E/100PY)	Total (N=8) (PYS=1.1) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0
Erythema multiforme	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0
Demyelinating disorder	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0
Hematologic disorders including pancytopenia	0	0	0	0
Liver failure and other liver events	0	0	0	0
Humira administration related medication error	0	0	0	0
Injection site reaction	1 (500.0)	1 (166.7)	0	2 (181.8)
All deaths	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0
Occurring >70 days after last dose	0	0	0	0

I-SD = induction standard dose group, I-HD = induction high dose group, I-HD-OL = induction high dose open-label group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the induction period and up to 70 days after the last dose date of the study drug in the induction period and prior to the first dose date of the study drug in the maintenance period if applicable.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: M11-290 CSR_Final Table 14.3__1.1.2.1_J

表 2.7.4.7-186. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）

	M-SD (N=2) (PYS=0.3) Events (E/100PY)	M-HD (N=4) (PYS=2.6) Events (E/100PY)	Total-ADA (N=6) (PYS=2.9) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	Total (N=6) (PYS=2.9) Events (E/100PY)
Any treatment-emergent					
Adverse event (AE)	1 (333.3)	8 (307.7)	9 (310.3)	0	9 (310.3)
Serious AE	1 (333.3)	0	1 (34.5)	0	1 (34.5)
Severe AE	0	0	0	0	0
AEs leading to discontinuation of study drug	0	0	0	0	0
AEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	2 (76.9)	2 (69.0)	0	2 (69.0)
SAEs rated as possibly related to study drug by the investigator (reasonable possibility)#	0	0	0	0	0
AEs leading to Death	0	0	0	0	0
Infections	1 (333.3)	3 (115.4)	4 (137.9)	0	4 (137.9)
Serious infections	1 (333.3)	0	1 (34.5)	0	1 (34.5)
Legionella infections	0	0	0	0	0
Diverticulitis	0	0	0	0	0
Opportunistic infections excluding oral candidiasis and tuberculosis (TB)	0	0	0	0	0

表 2.7.4.7-186. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=2) (PYS=0.3) Events (E/100PY)	M-HD (N=4) (PYS=2.6) Events (E/100PY)	Total-ADA (N=6) (PYS=2.9) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	Total (N=6) (PYS=2.9) Events (E/100PY)
Oral candidiasis	0	0	0	0	0
Tuberculosis	0	0	0	0	0
Active tuberculosis	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0
Parasitic infections	0	0	0	0	0
Reactivation of Hepatitis B	0	0	0	0	0
Progressive multifocal leukoencephalopathy (PML)	0	0	0	0	0
Malignancies	0	0	0	0	0
Lymphoma	0	0	0	0	0
Hepatosplenic T-cell lymphoma (HSTCL)	0	0	0	0	0
Non-melanoma skin cancer (NMSC)	0	0	0	0	0
Melanoma	0	0	0	0	0
Leukemia	0	0	0	0	0
Malignancy other than lymphoma, HSTCL, leukemia, NMSC or melanoma	0	0	0	0	0

表 2.7.4.7-186. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=2) (PYS=0.3) Events (E/100PY)	M-HD (N=4) (PYS=2.6) Events (E/100PY)	Total-ADA (N=6) (PYS=2.9) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	Total (N=6) (PYS=2.9) Events (E/100PY)
Allergic reactions including angioedema/anaphylaxis	0	0	0	0	0
Lupus-like reactions and systemic lupus erythematosus	0	0	0	0	0
Vasculitis	0	0	0	0	0
Cutaneous vasculitis	0	0	0	0	0
Non-cutaneous vasculitis	0	0	0	0	0
Sarcoidosis	0	0	0	0	0
Autoimmune Hepatitis	0	0	0	0	0
Myocardial infarction (MI)	0	0	0	0	0
Cerebrovascular accident (CVA)	0	0	0	0	0
Congestive heart failure (CHF)	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0
Interstitial lung disease	0	0	0	0	0
Intestinal perforation	0	0	0	0	0
Pancreatitis	0	0	0	0	0

表 2.7.4.7-186. 最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）（続き）

	M-SD (N=2) (PYS=0.3) Events (E/100PY)	M-HD (N=4) (PYS=2.6) Events (E/100PY)	Total-ADA (N=6) (PYS=2.9) Events (E/100PY)	M-PL (N=0) (PYS=0.0) Events (E/100PY)	Total (N=6) (PYS=2.9) Events (E/100PY)
Stevens-Johnson syndrome	0	0	0	0	0
Erythema multiforme	0	0	0	0	0
Worsening or new onset of psoriasis	0	0	0	0	0
Demyelinating disorder	0	0	0	0	0
Amyotrophic lateral sclerosis	0	0	0	0	0
Reversible posterior leukoencephalopathy syndrome (RPLS)	0	0	0	0	0
Hematologic disorders including pancytopenia	0	0	0	0	0
Liver failure and other liver events	0	0	0	0	0
Humira administration related medication error	0	0	0	0	0
Injection site reaction	0	0	0	0	0
All deaths	0	0	0	0	0
Occurring <=70 days after last dose	0	0	0	0	0
Occurring >70 days after last dose	0	0	0	0	0

表 2.7.4.7-186.　最終解析の維持療法期中に発現した有害事象の 100 人年あたりの発現頻度の概要
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）（続き）

M-PL = maintenance placebo group, M-SD = maintenance standard dose group, M-HD = maintenance high dose group.
Note: Treatment-emergent adverse events are defined as events with an onset date on or after the first dose date of the study drug in the maintenance period and prior to re-randomization due to first disease flare if applicable and up to 70 days after the last dose date of the study drug in the maintenance period. The events with an onset date on or after the first dose date in M10-870 are excluded.
E/100PY = Events per 100 patient-years.
AEs with unknown relationship were counted as 'reasonable possibility of being related'.
AEs with unknown severity were counted as 'severe'.
As assessed by investigator.

Cross reference: M11-290 CSR_Final Table 14.3__1.1.2.2_J

表 2.7.4.7-187.　最終解析の導入療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	6 (18.8)	11 (21.6)	6 (33.3)	23 (22.8)
感染症および寄生虫症	6 (18.8)	11 (21.6)	6 (33.3)	23 (22.8)
気管支炎	0	0	1 (5.6)	1 (1.0)
せつ	0	1 (2.0)	0	1 (1.0)
サルモネラ菌性胃腸炎	1 (3.1)	0	0	1 (1.0)
上咽頭炎	2 (6.3)	2 (3.9)	1 (5.6)	5 (5.0)
口腔ヘルペス	1 (3.1)	2 (3.9)	0	3 (3.0)
外耳炎	0	1 (2.0)	0	1 (1.0)
咽頭炎	2 (6.3)	1 (2.0)	1 (5.6)	4 (4.0)
レンサ球菌感染	0	0	1 (5.6)	1 (1.0)
上気道感染	0	3 (5.9)	0	3 (3.0)
尿路感染	1 (3.1)	0	0	1 (1.0)
水痘	0	1 (2.0)	0	1 (1.0)
ウイルス感染	0	0	1 (5.6)	1 (1.0)
ウイルス性上気道感染	0	1 (2.0)	0	1 (1.0)
外陰腟真菌感染	0	0	1 (5.6)	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.1.1_A

表 2.7.4.7-188.　最終解析の導入療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
Any adverse event	0	3 (75.0)	0	3 (37.5)
感染症および寄生虫症	0	3 (75.0)	0	3 (37.5)
外耳炎	0	1 (25.0)	0	1 (12.5)
上気道感染	0	2 (50.0)	0	2 (25.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.1.1_J

表 2.7.4.7-189.　最終解析の維持療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	11 (33.3)	16 (44.4)	27 (39.1)	5 (41.7)	32 (39.5)
感染症および寄生虫症	11 (33.3)	16 (44.4)	27 (39.1)	5 (41.7)	32 (39.5)
気管支炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	1 (8.3)	3 (3.7)
膿痂疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)
感染性嚢腫	0	1 (2.8)	1 (1.4)	0	1 (1.2)
インフルエンザ	0	2 (5.6)	2 (2.9)	0	2 (2.5)
喉頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
上咽頭炎	3 (9.1)	4 (11.1)	7 (10.1)	1 (8.3)	8 (9.9)
口腔ヘルペス	0	1 (2.8)	1 (1.4)	0	1 (1.2)
中耳炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	2 (6.1)	2 (5.6)	4 (5.8)	1 (8.3)	5 (6.2)
気道感染	1 (3.0)	0	1 (1.4)	0	1 (1.2)
ウイルス性気道感染	0	0	0	1 (8.3)	1 (1.2)
鼻炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
癜風	1 (3.0)	0	1 (1.4)	0	1 (1.2)
歯膿瘍	0	0	0	1 (8.3)	1 (1.2)
気管炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)

表 2.7.4.7-189. 最終解析の維持療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
感染症および寄生虫症 (Cont.)					
上気道感染	2 (6.1)	4 (11.1)	6 (8.7)	2 (16.7)	8 (9.9)
尿路感染	1 (3.0)	2 (5.6)	3 (4.3)	0	3 (3.7)
水痘	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.1.2_A

表 2.7.4.7-190.　最終解析の維持療法期中に発現したすべての感染症（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた日本人安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=2) n (%)	M-HD (N=4) n (%)	Total-ADA (N=6) n (%)	M-PL (N=0) n (%)	Total (N=6) n (%)
Any adverse event	1 (50.0)	3 (75.0)	4 (66.7)	0	4 (66.7)
感染症および寄生虫症	1 (50.0)	3 (75.0)	4 (66.7)	0	4 (66.7)
感染性腸炎	1 (50.0)	0	1 (16.7)	0	1 (16.7)
膿痂疹	0	1 (25.0)	1 (16.7)	0	1 (16.7)
インフルエンザ	0	1 (25.0)	1 (16.7)	0	1 (16.7)
上気道感染	0	1 (25.0)	1 (16.7)	0	1 (16.7)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.1.2_J

表 2.7.4.7-191.　最終解析の維持療法期中に発現した重篤な感染症（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	3 (9.1)	3 (8.3)	6 (8.7)	0	6 (7.4)
感染症および寄生虫症	3 (9.1)	3 (8.3)	6 (8.7)	0	6 (7.4)
感染性腸炎	1 (3.0)	0	1 (1.4)	0	1 (1.2)
胃腸炎	2 (6.1)	0	2 (2.9)	0	2 (2.5)
無菌性髄膜炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
咽頭炎	0	1 (2.8)	1 (1.4)	0	1 (1.2)
尿路感染	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.2.2_A

表 2.7.4.7-192.　最終解析の導入療法期中に発現した汎血球減少症を含む血液障害（MedDRA SOC 及び PT 別）
（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
血液およびリンパ系障害	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)
貧血	3 (9.4)	3 (5.9)	1 (5.6)	7 (6.9)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.40.1_A

表 2.7.4.7-193.　最終解析の維持療法期中に発現した汎血球減少症を含む血液障害（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	3 (9.1)	1 (2.8)	4 (5.8)	2 (16.7)	6 (7.4)
血液およびリンパ系障害	3 (9.1)	1 (2.8)	4 (5.8)	2 (16.7)	6 (7.4)
貧血	3 (9.1)	1 (2.8)	4 (5.8)	1 (8.3)	5 (6.2)
好中球減少症	0	0	0	1 (8.3)	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.40.2_A

表 2.7.4.7-194.　最終解析の導入療法期中に発現した注射部位反応（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=32) n (%)	I-HD (N=51) n (%)	I-HD-OL (N=18) n (%)	Total (N=101) n (%)
Any adverse event	1 (3.1)	3 (5.9)	0	4 (4.0)
一般・全身障害および投与部位の状態	1 (3.1)	3 (5.9)	0	4 (4.0)
注射部位紅斑	0	1 (2.0)	0	1 (1.0)
注射部位疼痛	1 (3.1)	1 (2.0)	0	2 (2.0)
注射部位蕁麻疹	0	1 (2.0)	0	1 (1.0)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.43.1_A

表 2.7.4.7-195.　最終解析の導入療法期中に発現した注射部位反応（MedDRA SOC 及び PT 別）（日本人安全性解析対象集団，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	I-SD (N=2) n (%)	I-HD (N=4) n (%)	I-HD-OL (N=2) n (%)	Total (N=8) n (%)
Any adverse event	1 (50.0)	1 (25.0)	0	2 (25.0)
一般・全身障害および投与部位の状態	1 (50.0)	1 (25.0)	0	2 (25.0)
注射部位紅斑	0	1 (25.0)	0	1 (12.5)
注射部位疼痛	1 (50.0)	0	0	1 (12.5)

I-SD = induction standard dose group; I-HD = induction high dose group; I-HD-OL = induction high dose open-label group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.43.1_J

表 2.7.4.7-196.　最終解析の維持療法期中に発現した注射部位反応（MedDRA SOC 及び PT 別）
（維持療法期中に治験薬の投与を 1 回以上受けた統合安全性解析対象集団の被験者，M11-290 試験）

MedDRA 22.0 System Organ Class Preferred Term	M-SD (N=33) n (%)	M-HD (N=36) n (%)	Total-ADA (N=69) n (%)	M-PL (N=12) n (%)	Total (N=81) n (%)
Any adverse event	4 (12.1)	2 (5.6)	6 (8.7)	0	6 (7.4)
一般・全身障害および投与部位の状態	4 (12.1)	2 (5.6)	6 (8.7)	0	6 (7.4)
注射部位紅斑	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位炎症	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位浮腫	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位疼痛	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位そう痒感	0	1 (2.8)	1 (1.4)	0	1 (1.2)
注射部位腫脹	1 (3.0)	0	1 (1.4)	0	1 (1.2)
注射部位蕁麻疹	0	1 (2.8)	1 (1.4)	0	1 (1.2)

M-PL = maintenance placebo group; M-SD = maintenance standard dose group; M-HD = maintenance high dose group;
Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Cross reference: M11-290 CSR_Final Table 14.3__2.4.43.2_A

2.7.5 参考文献

参考文献は，各セクションの末尾に記載した。

M14-033 試験（薬物動態）

治験の標題： Pharmacokinetic and Immunogenicity Assessments from the Phase 3 Trial: A Double-Blind, Randomized, Multicenter Study of Higher Versus Standard Adalimumab Dosing Regimens for Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis	
施設数 / 実施国名： 主試験：120 施設 / 世界各国，日本サブ試験：22 施設 / 日本	
治験期間： 最初の被験者の初回来院日：2014 年 3 月 27 日 最終被験者の最終来院日：2019 年 11 月 11 日	開発のフェーズ： 第 III 相
目的： 本試験の目的は，中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者に，高用量での導入療法及び維持療法を行ったときの有効性及び安全性を検討することであった。 本報告書では，UC 患者（日本人及び日本人以外）にアダリムマブを投与したときの薬物動態及び免疫原性に関して報告する。	
治験方法： 本試験は，中等症から重症の活動性 UC 患者を対象に，アダリムマブの高用量及び標準用量での導入療法及び維持療法を比較する第 III 相多施設共同無作為化二重盲検比較試験である。本試験は 8 週間の二重盲検導入療法試験及び 44 週間の維持用量試験により構成されている。被験者は，ベースライン（Week 0）において，高用量導入療法群又は標準用量導入療法群のいずれかの群に 3:2 の割合で無作為に割付けられた。高用量導入療法では，投与 0，1，2 及び 3 週時にアダリムマブ 160 mg，投与 4 及び 6 週時にアダリムマブ 40 mg を投与することで，8 週間の合計投与量は標準用量（320 mg）の約 2 倍の 720 mg となる。 維持用量試験では，被験者は，投与 8 週時において，40 mg 週 1 回群，40 mg 隔週群又は薬物治療モニタリング（以下「TDM」）群のいずれかに 2：2：1 の割合で再度無作為に割付けられた。なお，日本人被験者は TDM 群には割付けなかった。 血清中アダリムマブ濃度及び血清中抗アダリムマブ抗体（以下「AAA」）濃度測定のための血液検体は以下の時点で採取した。 ● アダリムマブ：ベースライン（投与 0 週時），投与 2，4，8，10，12，16，22，24，29，35，37，42，48，52 週時又は早期中止時，若しくは，予定外の来院時（適宜） ● AAA：ベースライン（投与 0 週時），投与 4，8，12，24，37，52 又は早期中止時，若しくは，予定外の来院時（適宜） また，インフリキシマブ及びヒト抗キメラ抗体（以下「HACA」）測定用検体もベースラインで採取した。 アダリムマブ及び AAA の検体は，アッヴィの濃度測定部門（AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany）で測定された。未希釈のヒト血清中アダリムマブ濃度の定量下限（以下「LLOQ」）は酵素結合免疫吸着測定（ELISA）法で 31.3 ng/mL，電気化学発光免疫測定（ECL）法で 50 ng/mL であった。未希釈のヒト血清中の AAA の LLOQ は 10.3 ng/mL であった。	
被験者数 (計画時と解析時) ： 計画時：840 例，同意取得例数：952 例，薬物動態解析に含めた例数：952 例（日本人 100 例，日本人以外 852 例）	

診断と主要な組入れ基準：

主な選択基準：

- ベースライン時の年齢が 18 歳以上 75 歳以下の男女。
- ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中の内視鏡検査（全大腸内視鏡検査又は S 状結腸鏡検査）で診断が確認されると共に，現在の感染症，上皮異形成及び / 又は悪性腫瘍が除外されている患者。
- 治験実施計画書で規定した副腎皮質ステロイドの経口剤又は免疫抑制剤による現在の治療，あるいは医師の判断で十分かつ適切な過去の治療にもかかわらず，ベースラインの Mayo スコア（以下「FMS」）が 6～12 ポイント，かつ内視鏡所見サブスコアが 2～3 ポイント（中央判定による評価）である活動性の UC 患者。

被験薬，用量，投与方法及びバッチ番号：

アダリムマブ プレフィルドシリンジ 40 mg / 0.8 mL（皮下注射用）

治療期間：52 週間

評価基準：

薬物動態：

導入療法試験及び維持療法試験において，各時点における血清中アダリムマブ濃度を用量及び集団（日本人及び日本人以外）で層別し要約した。また，導入療法試験及び維持療法試験において，用量及び集団（日本人及び日本人以外）で層別した平均アダリムマブ濃度推移を図示した。更に，投与 8 週時及び投与 52 週時における non-responder imputation（NRI）による寛解の有無で層別したときの平均アダリムマブ濃度の比較を行った。導入療法試験においては，インフリキシマブ投与経験の有無，ベースラインにおける HACA の有無及び投与量で層別した平均アダリムマブ濃度も示した。アダリムマブの個別データに関しては，その一覧表を作成した。要約統計量の算出及び作図においては，LLOQ 未満の濃度値は 0 として取り扱った。

免疫原性：

血清中 AAA 濃度は一覧表として示した。アダリムマブ投与後 30 日以内に採取された検体において，1 検体以上で AAA 濃度が 20 ng/mL 超（確認試験［confirmatory assay］で確認）であった被験者を AAA 陽性被験者として取り扱うこととした。AAA 陽性被験者に関しては，導入療法試験及び維持療法試験における投与量で層別して，その例数及び陽性率を算出し，AAA の有無が血清中アダリムマブ濃度，有効性及び安全性に及ぼす影響を検討した。

また，導入療法試験においては，ベースラインにおける HACA の有無が血清中アダリムマブ濃度に与える影響を導入用量で層別して検討した。

結果及び考察：

導入療法試験における薬物動態

導入療法試験において，標準用量が投与された被験者の投与 8 週時における平均アダリムマブ濃度は 8.0 µg/mL（N=379）であり，一方，高用量が投与された被験者では 19.2 µg/mL（N=573）であった。投与 8 週時において臨床的寛解に達した被験者の平均アダリムマブ濃度は，臨床的寛解に達しなかった被験者と比較して，投与量にかかわらず，わずかに高い傾向が認められた。インフリキシマブ投与経験の有無及びベースラインにおける HACA の有無は，アダリムマブ濃度に対して影響を与えなかった。日本人及び日本人以外の平均血清中アダリムマブ濃度はおおむね類似していた。

維持療法試験における薬物動態

44 週間の維持療法試験において，40 mg 週 1 回投与された被験者の定常状態における平均血清中アダリムマブ濃度は，導入用量にかかわらず，40 mg 隔週投与された被験者より高い傾向を示した。投与 52 週時において臨床的寛解に達した被験者の定常状態における平均血清中アダリムマブ濃度は，いずれの維持用量においても，臨床的寛解に達しなかった被験者より，わずかながら高い傾向を示した。44 週間の維持療法試験において，日本人及び日本人以外の平均血清中アダリムマブ濃度推移はおおむね類似していた。

免疫原性

本試験において AAA 陽性となった被験者は計 24 例（日本人被験者 4 例，日本人以外の被験者 20 例）であり，AAA 陽性率は 2.5%（24/952 例）であった。AAA 陽性被験者の血清中アダリムマブ濃度は概して AAA 陰性被験者より低い傾向を示した。投与 52 週時に Mayo スコア（以下「FMS」）で寛解に達した被験者の割合は，AAA 陰性被験者（24.5%）と比較して，AAA 陽性被験者（17.4%）では低い傾向が認められた。本試験において新たな安全性シグナルは認められなかった。成人 UC 患者におけるアダリムマブの安全性に対して，免疫原性は大きな影響を与えないと考えられた。

結論：

導入療法試験の投与 8 週時において，高用量が投与された被験者のアダリムマブの平均トラフ濃度は 19.2 µg/mL であり，標準用量が投与された被験者では 8.0 µg/mL であった。44 週間の維持療法試験において，40 mg 週 1 回投与された被験者の定常状態における平均血清中アダリムマブ濃度は，導入用量にかかわらず，40 mg 隔週投与された被験者より高い傾向を示した。

投与 8 週及び 52 週時において臨床的寛解に達した被験者の定常状態における平均血清中アダリムマブ濃度は，臨床的寛解に達しなかった被験者より，わずかながら高い傾向を示した。

日本人及び日本人以外の平均血清中アダリムマブ濃度推移は，導入療法期間及び維持療法期間のいずれにおいても，おおむね類似していた。

本試験における AAA 陽性率は 2.5%（24/952 例）であった。全体として，成人 UC 患者におけるアダリムマブの安全性に対して，免疫原性は大きな影響を与えないと考えられた。

M11-290 試験（薬物動態）

治験の標題： Pharmacokinetic and Immunogenicity Assessments of: A Multicenter, Randomized, Double-Blind Study of the Human Anti-TNF Monoclonal Antibody Adalimumab in Pediatric Subjects with Moderate to Severe Ulcerative Colitis	
治験期間： 最初の被験者の初回来院日：2014 年 12 月 22 日（日本人被験者） 最終被験者の最終来院日：2020 年 2 月 ■ 日（日本人被験者）	開発のフェーズ： 第 III 相
目的： 本試験の目的は，中等症から重症の小児潰瘍性大腸炎（以下「UC」）患者に対するアダリムマブの有効性及び安全性，並びにアダリムマブ皮下投与後の薬物動態について検討することである。 本報告書では，中等症から重症の小児 UC 患者にアダリムマブを投与したときの薬物動態及び免疫原性に関して報告する。	
治験方法： 本試験は，中等症から重症の小児 UC 患者を対象に，アダリムマブの有効性及び安全性を評価する第 III 相多施設共同無作為化二重盲検比較試験である。本試験は，日本以外の施設で登録された被験者を対象とする主試験と，日本の施設で登録された被験者を対象とする日本サブ試験で構成される。 治験実施計画書の改訂 4 版より前に登録された被験者は，ベースライン時に 3：2 の比率でアダリムマブの導入療法期二重盲検治療群（導入療法期高用量又は導入療法期標準用量）のいずれかに無作為に割付けられた。投与 8 週時に部分的 Mayo スコア（以下「PMS」）による臨床的改善（PMS がベースラインから 2 ポイント以上かつ 30%以上減少）が認められた被験者を，2：2：1 の比率で維持療法期高用量，維持療法期標準用量又は維持療法期プラセボのいずれかに無作為に割り付けた。維持療法期の被験者は，投与 52 週時まで盲検下で投与を継続することとした。 治験実施計画書の改訂 4 版以降に登録された被験者には，アダリムマブ導入療法期高用量を非盲検下で投与した（導入療法期非盲検高用量）。投与 8 週時に PMS による臨床的改善が認められた被験者を，投与 8 週時の PMS による寛解状態（PMS が 2 ポイント以下，かつ，いずれのサブスコアも 1 ポイントを超えない）を因子として層別し，1：1 の比率でアダリムマブの維持療法期治療群のいずれかに無作為に割り付けた。維持療法期の被験者は，投与 52 週時まで盲検下で投与を継続することとした。 血清中アダリムマブ濃度測定のための血液検体は投与 0 週時（ベースライン），投与 2，4，8，12，26，34，52 週時又は早期中止時，若しくは，用量を変更する際の予定外の来院時に採取した。血清中抗アダリムマブ抗体（以下「AAA」）濃度測定のための血液検体は投与 0 週時（ベースライン），投与 4，8， 26，52 週時又は早期中止時に採取した。	
治療期間：52 週間	
被験者数 (計画時と解析時) ： 同意取得例数：101 例，薬物動態解析に含めた例数：101 例（日本人 8 例を含む） 被験者 101 例の平均年齢は 14 歳，平均体重は 55.4 kg，49.5%が男性，50.5%が女性であった。	

診断と主要な組入れ基準： ベースラインでの治験薬投与前に，少なくともスクリーニングの 12 週間前に生体組織採取検査を含めた内視鏡検査で UC の診断が確認された年齢が 4～17 歳の患者で，活動性 UC（Mayo スコア［以下「FMS」］が 6～12 ポイント，かつ内視鏡所見サブスコアが 2～3 ポイント）を有している患者
被験薬，用量，投与方法及びバッチ番号： アダリムマブ バイアル 40 mg / 0.8 mL 及びマッチングプラセボ（皮下注射用）
評価基準： 薬物動態： 各時点における血清中アダリムマブ濃度は要約統計量を用いて要約した。導入療法期間においては，血清中アダリムマブ濃度を，導入用量，抗 TNF（anti-tumor necrosis factor）製剤投与経験の有無，ヒト抗キメラ抗体（HACA）の有無及び投与 8 週時での PMS による寛解到達の有無で層別した。維持療法期間においては，投与 8 週時での PMS による臨床反応が得られている患者における血清中アダリムマブ濃度を，維持用量及び投与 52 週時での FMS による寛解到達の有無で層別し，比較した。個別データに関しては，その一覧表を作成した。要約統計量の算出及び作図においては，LLOQ 未満の濃度値は 0 として取り扱った。 免疫原性： アダリムマブ投与後 30 日以内に採取された検体において，1 検体以上で酵素結合免疫吸着測定（ELISA）法による AAA 濃度が 20 ng/mL 超（確認試験［confirmatory assay］で確認）であった被験者を AAA 陽性被験者として取り扱うこととした。AAA 陽性被験者に関しては，AAA 陽性被験者数及びその割合を示した。また，AAA の有無が血清中アダリムマブ濃度，有効性及び安全性に及ぼす影響を検討した。血清中 AAA 濃度は一覧表として示した。
結果及び結論： 本試験において，導入療法期高用量が投与された被験者の投与 2 及び 4 週時における平均アダリムマブ濃度はそれぞれ 23.9 µg/mL 及び 17.1 µg/mL であり，導入療法期標準用量が投与された被験者ではそれぞれ 9.83 µg/mL 及び 10.5 µg/mL であった。投与 26 週以降，維持療法期高用量及び維持療法期標準用量が投与された被験者の定常状態における平均アダリムマブ濃度はそれぞれ約 15 - 17 µg/mL 及び 4 - 6 µg/mL であった。 本試験における AAA 陽性率は 3%（3/101 例）であり，日本人において AAA 陽性被験者は認められなかった。AAA 陽性被験者の血清中アダリムマブ濃度は概して AAA 陰性被験者より低い傾向を示した。有効性に対する AAA の影響に関しては，本試験における AAA 陽性被験者の例数が少なかったため（N = 3），明確な結論を導くことは困難であった。小児 UC 患者におけるアダリムマブの安全性に対して，免疫原性は大きな影響は与えないと考えられた。 本試験において日本人被験者は少なかったものの，全体として，日本人と日本人以外のアダリムマブ濃度は導入療法期及び維持療法期で類似していた。

M14-033 主試験 導入療法試験

治験の標題： A Double-Blind, Randomized, Multicenter Study of Higher Versus Standard Adalimumab Dosing Regimens for Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis	
施設数 / 実施国名： 120 施設 / オーストリア，ベルギー，カナダ，チェコ共和国，デンマーク，フランス，ドイツ，ハンガリー，イスラエル，イタリア，オランダ，ポーランド，ルーマニア，スロバキア，スペイン，スイス，ウクライナ，英国及び米国	
治験責任医師： [redacted] MD 他	
公表文献 (参考資料) ： Panes J, Colombel JF, D'Haens GR, et al. OP216 High versus standard adalimumab induction dosing regimens in patients with moderately to severely active ulcerative colitis: Results from the SERENE-UC induction study. United European Gastroenterol J. 2019;7 (Suppl 8S):118.	
治験期間： 治験開始日（最初の被験者の初回来院日）： 2014 年 3 月 27 日 治験終了日（最後の被験者の追跡調査終了日）： 20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ： 第 III 相
治験の種類： 第 III 相，多施設共同，無作為化，二重盲検試験	
目的： 本試験の目的は，中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者に，高用量での導入療法及び維持療法を行ったときの有効性及び安全性を検討することであった。	
被験者数 (計画時と解析時) ： 計画時： 840 例 組入れ時： 852 例 解析時： 852 例	
診断と主要な組入れ基準： M14-033 試験の主要な選択基準は以下のとおりであった：ベースライン時の年齢が 18 歳以上 75 歳以下の男女。ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中の内視鏡検査（全大腸内視鏡検査又は S 状結腸鏡検査）で診断が確認されると共に，現在の感染症，上皮異形成及び / 又は悪性腫瘍が除外されている患者。治験実施計画書で規定した副腎皮質ステロイドの経口剤又は免疫抑制剤による現在の治療，あるいは医師の判断で十分かつ適切な過去の治療にもかかわらず，ベースラインの Mayo スコア（以下，「FMS」）が 6～12 ポイント，かつ内視鏡所見サブスコアが 2～3 ポイント（中央判定による評価）である活動性の UC 患者。インフリキシマブの投与で以前に UC の治療効果が認められ，その後効果消失又は不耐容となったため，インフリキシマブの投与を中止した患者を，本試験に組み入れることができる（効果消失又は不耐容を示す記録を確認すること）。女性患者の場合は，本試験への参加から 1 年以上前に閉経した，又は不妊手術（両側卵管結紮術，両側卵巣摘出術，及び / 又は子宮摘出術）を行ったことで，妊娠の可能性がないこと。妊娠の可能性がある女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，治験実施計画書で規定した方法で避妊すること。女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，授乳しないこと。結核スクリーニング検査が陰性の患者。既往歴やスクリーニング期間中に実施する臨床検査，身体的所見，胸部 X 線検査，12 誘導心電図検査の結果から，治験責任医師が健康状態にその他の問題がないと判断した患者。 M14-033 試験の主要な除外基準は以下のとおりであった：クローン病と診断されている，若しくは既往がある，又は indeterminate colitis と診断されている患者。劇症の大腸炎又は中毒性巨大結腸症と診断されている患者。ス	

クリーニング時の内視鏡検査で，病変が直腸のみに限局している患者（潰瘍性直腸炎）。回腸直腸瘻造設を伴う結腸亜全摘術，若しくは回腸嚢，Koch パウチ，回腸ストマ造設を伴う結腸切除術の既往がある患者。又は腸管の手術を予定している患者。
治験方法： M14-033 試験は，導入療法試験と維持療法試験で構成される。M14-033 試験では，高用量の導入療法及び維持療法を，承認されている標準用量の導入療法及び維持療法と比較した。また，薬物治療モニタリング戦略を用いた探索的な維持療法も実施した。すべての選択基準を満たし，いずれの除外基準にも抵触しない中等症から重症の成人活動性 UC 患者を本試験の参加に適格とした。 本報告では，日本以外の治験実施医療機関で登録されたすべての被験者（主試験集団）を対象とした，M14-033 導入療法試験の解析結果を示す。本報告には，導入療法試験を中止し，中止後に市販のアダリムマブの使用を開始しなかった被験者に関して，最終投与 70 日後の追跡調査までに得られたデータを含める（追跡調査終了日：20[redacted] 年[redacted] 月[redacted] 日）。本報告は，導入療法試験の組織学検査データ，及び前版からの最終的なデータの変更を反映した治験総括報告書の最終版（データベースロック日：20[redacted] 年[redacted] 月[redacted] 日）に基づいている。
被験薬，用量，投与方法及びバッチ番号： 8 週間の二重盲検導入療法試験では，無作為化時にインフリキシマブによる治療歴及びベースラインでの副腎皮質ステロイドの投与を因子として被験者を層別化した。治験薬は毎回ほぼ同じ時刻に自己皮下投与した。高用量の導入療法では，投与 0，1，2 及び 3 週時にアダリムマブ 160 mg，投与 4 及び 6 週時にアダリムマブ 40 mg を投与することで，8 週間の合計投与量は標準用量（320 mg）の約 2 倍の 720 mg となる。 高用量群に割り付けられた被験者には，投与 0，1，2 及び 3 週時にアダリムマブ 160 mg（4 シリンジ），投与 4 及び 6 週時にアダリムマブ 40 mg（1 シリンジ）を投与した。標準療法群に割り付けられた被験者には，ベースライン（投与 0 週時）にアダリムマブ 160 mg（4 シリンジ），投与 1 週時にプラセボ（4 シリンジ），投与 2 週時にアダリムマブ 80 mg（2 シリンジ）及びプラセボ（2 シリンジ），投与 3 週時にプラセボ（4 シリンジ），投与 4 及び 6 週時にアダリムマブ 40 mg（1 シリンジ）を投与した。 ロット番号： アダリムマブ　：[redacted], [redacted], [redacted], [redacted], [redacted], [redacted], [redacted] プラセボ　：[redacted], [redacted], [redacted], [redacted], [redacted] 治療期間：8 週間
対照薬，用量，投与方法及びバッチ番号： なし

評価基準：

有効性：

導入療法試験の主要評価項目は，投与 8 週時に FMS で寛解（FMS が 2 以下で，かついずれのサブスコアも 1 を超えない）を達成した被験者の割合であった。

導入療法試験における順位付き副次評価項目（昇順に順位を階層化）は以下のとおりであった。

1. 投与 8 週時に内視鏡検査で改善（内視鏡所見サブスコアが 0 又は 1）が認められた被験者の割合
2. 投与 8 週時に便中カルプロテクチン値が 150 mg/kg 未満となった被験者の割合
3. 投与 8 週時に Inflammatory Bowel Disease Questionnaire（以下「IBDQ」）で改善（ベースラインと比較して IBDQ スコアの 16 以上の増加）が認められた被験者の割合
4. 投与 8 週時に FMS で改善例となった被験者の割合
5. 投与 8 週時に内視鏡検査で寛解（内視鏡所見サブスコアが 0）が認められた被験者の割合
6. 投与 8 週時に IBDQ の腸症状ドメインで改善（ベースラインと比較して IBDQ の腸症状ドメインスコアの 6 以上の増加）が認められた被験者の割合
7. 投与 8 週時に IBDQ の疲労に関する項目で改善（ベースラインと比較して IBDQ の疲労に関する項目のスコアの 1 以上の増加）が認められた被験者の割合

薬物動態：

別途報告書に記載することとした。

安全性：

治験期間中の有害事象，バイタルサインの変化，身体的所見，及び臨床検査値を評価した。

統計手法：

有効性：

主試験の導入療法試験では，有効性の主解析は主試験 Intent-to-treat（以下「ITT」）集団を対象に実施した。導入療法試験の有効性の解析では，投与 8 週時の欠測値の補完に，欠測値を「非反応」としてデータ補完する統計手法を用いた。解析では，主試験 ITT 集団を対象に，高用量の導入療法と標準用量の導入療法を比較した。投与 8 週時に寛解を達成した被験者の割合の群間差を，インフリキシマブによる治療歴及びベースラインでの副腎皮質ステロイドの投与の有無で調整した Cochran-Mantel-Haenszel（以下「CMH」）検定を用いて評価した。CMH 検定に基づき，割合の群間差の両側 95%信頼区間を算出した。

薬物動態：

別途報告書に記載することとした。

安全性：

主試験の導入療法試験では，安全性の解析は主試験安全性解析対象集団を対象に実施した。被験者が実際に受けた治療に基づき，治療群ごとに安全性評価項目を要約した。安全性評価項目の群間差は，有意水準 0.05 の両側検定を用いて評価した。

特に断らない限り，連続変数の安全性評価項目（例：臨床検査値のベースラインから最終測定時までの変化量）の群間差は，治療を因子とした分散分析モデルを用いて評価した。また，カテゴリカル変数の安全性評価項目の群間差は，Fisher の正確確率検定を用いて評価した。

要約 / 結論：

有効性：

投与 8 週時に FMS で寛解を達成した被験者の割合について，高用量群と標準用量群の間で統計学的に有意な差は認められなかった。部分集団解析の結果は，主解析の結果とおおむね一致していた。

事前に規定した固定順序による多重検定手順に基づき，順位付き副次評価項目に関して，高用量群と標準用量群

の間で統計学的に有意な差はなかった。
薬物動態： 別途報告書に記載することとした。
安全性： アダリムマブの安全性プロファイルは高用量群と標準用量群で同様であり，アダリムマブの既知の安全性プロファイルと一致していた。新たな安全性シグナル又は予期しない傾向は認められなかった。 各導入療法を受けた被験者の約半数に 1 件以上の有害事象が発現した。導入療法試験中，2 例が死亡した（術後腹膜炎及び心停止）。いずれも高用量群の被験者であり，治験薬との因果関係は関連なしと判断された。全体での重篤な有害事象及び治験薬投与の中止に至った有害事象の発現割合は低く，高用量群と標準用量群で同程度であった。最も多く報告された器官別大分類（以下「SOC」）は，いずれの投与群でも胃腸障害であった（高用量群：18.0%，標準用量群：22.1%）。最も多く（被験者の 5%以上）報告された基本語（以下「PT」）は，いずれの投与群でも潰瘍性大腸炎及び頭痛であった。有害事象の大部分は重症度が軽度又は中等度で，治験薬と関連なしと判断された。特に注目すべき有害事象（以下「AESI」）の発現割合は，感染症，注射部位反応，血液障害及びアレルギー反応を除き，全般的に低かった（1%未満）。いずれの AESI も発現割合は投与群間でおおむね同程度であった。ただし，注射部位反応の発現割合は高用量群（12.1%）の方が標準用量群（3.8%）よりも高かった。 臨床検査（血液学的検査，血液生化学検査及び尿検査）の平均値にベースラインからの顕著な変化は認められなかった。血液学的検査，血液生化学検査値及び尿検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，及びベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者は少数であり，臨床的に重要ではないと判断された。 バイタルサインの平均値にベースラインからの顕著な変化は認められなかった。 導入療法試験中，妊娠又は製品の安全性部品に係る苦情は報告されなかった。 治験期間中，予期しない機器の問題は認められなかった。
結論： 投与 8 週時に FMS で寛解を達成した被験者の割合に関して，標準用量のアダリムマブ導入療法に対する高用量のアダリムマブ導入療法の統計学的に有意な優越性は認められなかった。したがって，中等症から重症の活動性 UC 患者において，高用量のアダリムマブ導入療法による追加のベネフィットは得られず，現在承認されているアダリムマブ導入療法（160 mg / 80 mg）が中等症から重症の活動性 UC 患者に対する適切な導入療法であることが示された。安全性プロファイルは高用量群と標準用量群で同様であり，アダリムマブの全般的な安全性プロファイルと一致していた。新たな安全性のシグナル又は傾向は認められなかった。全体として，本試験の対象集団における標準用量のアダリムマブ導入療法のベネフィット・リスクプロファイルは不変であった。

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
ANY ADVERSE EVENT	184 (54.1)	271 (52.9)	455 (53.4)
血液およびリンパ系障害			
貧血	13 (3.8)	16 (3.1)	29 (3.4)
鉄欠乏性貧血	1 (0.3)	0	1 (0.1)
白血球減少症	1 (0.3)	3 (0.6)	4 (0.5)
リンパ節症	2 (0.6)	2 (0.4)	4 (0.5)
リンパ球減少症	1 (0.3)	1 (0.2)	2 (0.2)
好中球減少症	1 (0.3)	0	1 (0.1)
血小板減少症	0	2 (0.4)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	19 (5.6)	24 (4.7)	43 (5.0)
心臓障害			
心停止	0	1 (0.2)	1 (0.1)
動悸	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	1 (0.3)	2 (0.4)	3 (0.4)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
先天性、家族性および遺伝性障害			
エーラース・ダンロス症候群	0	1 (0.2)	1 (0.1)
包皮小帯	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	2 (0.4)	2 (0.2)
耳および迷路障害			
聴力低下	0	1 (0.2)	1 (0.1)
耳鳴	1 (0.3)	0	1 (0.1)
回転性めまい	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	2 (0.6)	1 (0.2)	3 (0.4)
内分泌障害			
ステロイド離脱症候群	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
眼障害			
眼瞼痙攣	0	1 (0.2)	1 (0.1)
後天性涙道狭窄	0	1 (0.2)	1 (0.1)
ドライアイ	2 (0.6)	1 (0.2)	3 (0.4)
眼瞼湿疹	1 (0.3)	0	1 (0.1)
上強膜炎	0	1 (0.2)	1 (0.1)
眼の障害	1 (0.3)	1 (0.2)	2 (0.2)
眼痛	1 (0.3)	0	1 (0.1)
眼部腫脹	0	1 (0.2)	1 (0.1)
眼瞼浮腫	1 (0.3)	0	1 (0.1)
羞明	0	2 (0.4)	2 (0.2)
視力低下	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	7 (2.1)	8 (1.6)	15 (1.8)
胃腸障害			
腹部不快感	1 (0.3)	1 (0.2)	2 (0.2)
腹部膨満	3 (0.9)	1 (0.2)	4 (0.5)
腹痛	6 (1.8)	11 (2.1)	17 (2.0)
上腹部痛	3 (0.9)	4 (0.8)	7 (0.8)
腹部圧痛	0	2 (0.4)	2 (0.2)
裂肛	1 (0.3)	1 (0.2)	2 (0.2)
アフタ性潰瘍	3 (0.9)	1 (0.2)	4 (0.5)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
胃腸障害 (Cont.)			
根尖肉芽腫	0	1 (0.2)	1 (0.1)
大腸炎	3 (0.9)	2 (0.4)	5 (0.6)
潰瘍性大腸炎	30 (8.8)	29 (5.7)	59 (6.9)
便秘	1 (0.3)	2 (0.4)	3 (0.4)
便意切迫	1 (0.3)	0	1 (0.1)
下痢	5 (1.5)	12 (2.3)	17 (2.0)
消化不良	8 (2.4)	2 (0.4)	10 (1.2)
心窩部不快感	0	1 (0.2)	1 (0.1)
鼓腸	1 (0.3)	8 (1.6)	9 (1.1)
食中毒	1 (0.3)	1 (0.2)	2 (0.2)
胃食道逆流性疾患	1 (0.3)	3 (0.6)	4 (0.5)
歯肉出血	0	1 (0.2)	1 (0.1)
歯肉痛	0	1 (0.2)	1 (0.1)
血便排泄	1 (0.3)	0	1 (0.1)
痔核	2 (0.6)	5 (1.0)	7 (0.8)
血栓性痔核	1 (0.3)	3 (0.6)	4 (0.5)
歯の知覚過敏	1 (0.3)	0	1 (0.1)
大腸狭窄	0	1 (0.2)	1 (0.1)
悪心	9 (2.6)	17 (3.3)	26 (3.1)
嚥下痛	0	1 (0.2)	1 (0.1)
急性膵炎	0	1 (0.2)	1 (0.1)
肛門周囲痛	3 (0.9)	1 (0.2)	4 (0.5)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
胃腸障害 (Cont.)			
直腸出血	1 (0.3)	0	1 (0.1)
直腸しぶり	0	1 (0.2)	1 (0.1)
脂肪便	0	1 (0.2)	1 (0.1)
歯の障害	1 (0.3)	1 (0.2)	2 (0.2)
歯痛	1 (0.3)	2 (0.4)	3 (0.4)
臍ヘルニア	1 (0.3)	0	1 (0.1)
嘔吐	4 (1.2)	9 (1.8)	13 (1.5)
SUBJECTS WITH ONE OR MORE EVENTS	75 (22.1)	92 (18.0)	167 (19.6)
一般・全身障害および投与部位の状態			
投与部位疼痛	1 (0.3)	0	1 (0.1)
適用部位そう痒感	0	1 (0.2)	1 (0.1)
適用部位反応	0	1 (0.2)	1 (0.1)
無力症	6 (1.8)	8 (1.6)	14 (1.6)
腋窩痛	0	1 (0.2)	1 (0.1)
胸部不快感	1 (0.3)	0	1 (0.1)
胸痛	3 (0.9)	1 (0.2)	4 (0.5)
悪寒	2 (0.6)	1 (0.2)	3 (0.4)
不快感	0	1 (0.2)	1 (0.1)
疲労	9 (2.6)	13 (2.5)	22 (2.6)
異常感	2 (0.6)	0	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
冷感	1 (0.3)	1 (0.2)	2 (0.2)
体温変動感	0	1 (0.2)	1 (0.1)
炎症	1 (0.3)	0	1 (0.1)
インフルエンザ様疾患	2 (0.6)	0	2 (0.2)
注射部位内出血	3 (0.9)	4 (0.8)	7 (0.8)
注射部位紅斑	2 (0.6)	14 (2.7)	16 (1.9)
注射部位血腫	0	1 (0.2)	1 (0.1)
注射部位過敏反応	0	3 (0.6)	3 (0.4)
注射部位硬結	0	1 (0.2)	1 (0.1)
注射部位炎症	0	2 (0.4)	2 (0.2)
注射部位腫瘤	0	1 (0.2)	1 (0.1)
注射部位浮腫	0	1 (0.2)	1 (0.1)
注射部位疼痛	3 (0.9)	6 (1.2)	9 (1.1)
注射部位そう痒感	2 (0.6)	13 (2.5)	15 (1.8)
注射部位発疹	1 (0.3)	4 (0.8)	5 (0.6)
注射部位反応	1 (0.3)	19 (3.7)	20 (2.3)
注射部位腫脹	2 (0.6)	9 (1.8)	11 (1.3)
注射部位蕁麻疹	1 (0.3)	1 (0.2)	2 (0.2)
倦怠感	1 (0.3)	1 (0.2)	2 (0.2)
非心臓性胸痛	1 (0.3)	0	1 (0.1)
末梢性浮腫	0	2 (0.4)	2 (0.2)
疼痛	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
末梢腫脹	1 (0.3)	1 (0.2)	2 (0.2)
発熱	5 (1.5)	7 (1.4)	12 (1.4)
腫脹	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	39 (11.5)	89 (17.4)	128 (15.0)
肝胆道系障害			
肝病変	1 (0.3)	0	1 (0.1)
脂肪肝	0	1 (0.2)	1 (0.1)
肝炎	0	1 (0.2)	1 (0.1)
高トランスアミナーゼ血症	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (0.3)	3 (0.6)	4 (0.5)
免疫系障害			
薬物過敏症	1 (0.3)	1 (0.2)	2 (0.2)
過敏症	1 (0.3)	2 (0.4)	3 (0.4)
季節性アレルギー	0	3 (0.6)	3 (0.4)
SUBJECTS WITH ONE OR MORE EVENTS	2 (0.6)	6 (1.2)	8 (0.9)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症			
膿瘍	1 (0.3)	0	1 (0.1)
四肢膿瘍	1 (0.3)	1 (0.2)	2 (0.2)
肛門膿瘍	0	1 (0.2)	1 (0.1)
ブラストシスティス感染	0	1 (0.2)	1 (0.1)
気管支炎	1 (0.3)	1 (0.2)	2 (0.2)
ウイルス性気管支炎	1 (0.3)	0	1 (0.1)
カンジダ感染	0	1 (0.2)	1 (0.1)
蜂巣炎	1 (0.3)	0	1 (0.1)
クロストリジウム・ディフィシレ感染	0	2 (0.4)	2 (0.2)
結膜炎	1 (0.3)	1 (0.2)	2 (0.2)
膀胱炎	0	1 (0.2)	1 (0.1)
サイトメガロウイルス性大腸炎	0	1 (0.2)	1 (0.1)
耳感染	1 (0.3)	2 (0.4)	3 (0.4)
丹毒	1 (0.3)	0	1 (0.1)
毛包炎	0	1 (0.2)	1 (0.1)
真菌感染	0	1 (0.2)	1 (0.1)
胃腸炎	0	1 (0.2)	1 (0.1)
ウイルス性胃腸炎	1 (0.3)	2 (0.4)	3 (0.4)
ヘルペスウイルス感染	0	1 (0.2)	1 (0.1)
帯状疱疹	2 (0.6)	0	2 (0.2)
麦粒腫	0	1 (0.2)	1 (0.1)
膿痂疹	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症 (Cont.)			
感染性嚢腫	0	1 (0.2)	1 (0.1)
感染	0	1 (0.2)	1 (0.1)
インフルエンザ	6 (1.8)	1 (0.2)	7 (0.8)
喉頭炎	1 (0.3)	0	1 (0.1)
限局性感染	0	1 (0.2)	1 (0.1)
上咽頭炎	14 (4.1)	19 (3.7)	33 (3.9)
食道カンジダ症	1 (0.3)	0	1 (0.1)
爪真菌症	0	1 (0.2)	1 (0.1)
口腔ヘルペス	2 (0.6)	2 (0.4)	4 (0.5)
中耳炎	1 (0.3)	0	1 (0.1)
咽頭炎	5 (1.5)	3 (0.6)	8 (0.9)
細菌性咽頭炎	1 (0.3)	0	1 (0.1)
レンサ球菌性咽頭炎	0	1 (0.2)	1 (0.1)
肺炎	2 (0.6)	1 (0.2)	3 (0.4)
腎盂腎炎	1 (0.3)	0	1 (0.1)
膿疱性皮疹	2 (0.6)	1 (0.2)	3 (0.4)
気道感染	0	1 (0.2)	1 (0.1)
鼻炎	3 (0.9)	2 (0.4)	5 (0.6)
副鼻腔炎	4 (1.2)	5 (1.0)	9 (1.1)
皮膚感染	0	1 (0.2)	1 (0.1)
白癬感染	0	2 (0.4)	2 (0.2)
歯感染	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症 (Cont.)			
結核	0	1 (0.2)	1 (0.1)
上気道感染	3 (0.9)	6 (1.2)	9 (1.1)
尿路感染	5 (1.5)	6 (1.2)	11 (1.3)
腟感染	1 (0.3)	0	1 (0.1)
ウイルス感染	0	3 (0.6)	3 (0.4)
ウイルス性上気道感染	1 (0.3)	0	1 (0.1)
外陰部腟カンジダ症	1 (0.3)	2 (0.4)	3 (0.4)
外陰腟真菌感染	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	59 (17.4)	70 (13.7)	129 (15.1)
傷害、中毒および処置合併症			
動物による引っかき傷	0	1 (0.2)	1 (0.1)
節足動物咬傷	1 (0.3)	0	1 (0.1)
挫傷	2 (0.6)	4 (0.8)	6 (0.7)
角膜擦過傷	0	1 (0.2)	1 (0.1)
転倒	0	1 (0.2)	1 (0.1)
注入に伴う反応	1 (0.3)	0	1 (0.1)
注射に伴う反応	0	1 (0.2)	1 (0.1)
関節損傷	0	1 (0.2)	1 (0.1)
靭帯捻挫	0	1 (0.2)	1 (0.1)
四肢損傷	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
傷害、中毒および処置合併症 (Cont.)			
肉離れ	0	1 (0.2)	1 (0.1)
処置による疼痛	1 (0.3)	0	1 (0.1)
交通事故	1 (0.3)	1 (0.2)	2 (0.2)
皮膚擦過傷	0	1 (0.2)	1 (0.1)
脊柱損傷	0	1 (0.2)	1 (0.1)
スポーツ損傷	1 (0.3)	0	1 (0.1)
舌損傷	0	1 (0.2)	1 (0.1)
尺骨神経損傷	0	1 (0.2)	1 (0.1)
上肢骨折	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	6 (1.8)	16 (3.1)	22 (2.6)
臨床検査			
アラニンアミノトランスフェラーゼ増加	1 (0.3)	2 (0.4)	3 (0.4)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.6)	1 (0.2)	3 (0.4)
細菌検査陽性	0	1 (0.2)	1 (0.1)
血中ビリルビン増加	1 (0.3)	2 (0.4)	3 (0.4)
血中コレステロール増加	1 (0.3)	1 (0.2)	2 (0.2)
血中クレアチニン増加	0	1 (0.2)	1 (0.1)
血中ブドウ糖増加	0	1 (0.2)	1 (0.1)
血中リン減少	1 (0.3)	0	1 (0.1)
血圧上昇	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
臨床検査 (Cont.)			
血中トリグリセリド増加	1 (0.3)	2 (0.4)	3 (0.4)
血中尿素増加	1 (0.3)	1 (0.2)	2 (0.2)
血中尿素窒素／クレアチニン比増加	0	1 (0.2)	1 (0.1)
呼吸音異常	1 (0.3)	0	1 (0.1)
C－反応性蛋白増加	2 (0.6)	0	2 (0.2)
クロストリジウム検査陽性	0	1 (0.2)	1 (0.1)
ヘマトクリット減少	0	1 (0.2)	1 (0.1)
ヘモグロビン減少	1 (0.3)	0	1 (0.1)
好中球数増加	0	1 (0.2)	1 (0.1)
血小板数増加	0	2 (0.4)	2 (0.2)
尿中赤血球陽性	1 (0.3)	1 (0.2)	2 (0.2)
皮膚ツルゴール低下	0	1 (0.2)	1 (0.1)
体重減少	1 (0.3)	1 (0.2)	2 (0.2)
白血球数減少	1 (0.3)	1 (0.2)	2 (0.2)
白血球数増加	0	1 (0.2)	1 (0.1)
尿中白血球陽性	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	14 (4.1)	19 (3.7)	33 (3.9)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
代謝および栄養障害			
食欲減退	1 (0.3)	1 (0.2)	2 (0.2)
脱水	1 (0.3)	2 (0.4)	3 (0.4)
高コレステロール血症	1 (0.3)	1 (0.2)	2 (0.2)
高血糖	1 (0.3)	2 (0.4)	3 (0.4)
高トリグリセリド血症	1 (0.3)	0	1 (0.1)
低アルブミン血症	1 (0.3)	0	1 (0.1)
低カリウム血症	3 (0.9)	0	3 (0.4)
血液量減少症	0	1 (0.2)	1 (0.1)
空腹時血中ブドウ糖不良	1 (0.3)	0	1 (0.1)
食欲亢進	0	1 (0.2)	1 (0.1)
代謝性アシドーシス	1 (0.3)	0	1 (0.1)
ビタミンD欠乏	2 (0.6)	0	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	10 (2.9)	7 (1.4)	17 (2.0)
筋骨格系および結合組織障害			
関節痛	9 (2.6)	17 (3.3)	26 (3.1)
軸性脊椎関節炎	1 (0.3)	0	1 (0.1)
背部痛	3 (0.9)	12 (2.3)	15 (1.8)
滑液包炎	2 (0.6)	0	2 (0.2)
側腹部痛	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
筋骨格系および結合組織障害 (Cont.)			
尺骨部痛	0	1 (0.2)	1 (0.1)
関節雑音	0	1 (0.2)	1 (0.1)
関節可動域低下	1 (0.3)	0	1 (0.1)
関節腫脹	2 (0.6)	0	2 (0.2)
筋痙縮	1 (0.3)	3 (0.6)	4 (0.5)
筋緊張	0	1 (0.2)	1 (0.1)
筋骨格痛	0	1 (0.2)	1 (0.1)
筋骨格硬直	2 (0.6)	1 (0.2)	3 (0.4)
筋肉痛	1 (0.3)	2 (0.4)	3 (0.4)
頚部痛	0	1 (0.2)	1 (0.1)
変形性関節症	1 (0.3)	0	1 (0.1)
四肢痛	1 (0.3)	1 (0.2)	2 (0.2)
顎痛	0	1 (0.2)	1 (0.1)
肩回旋筋腱板症候群	0	1 (0.2)	1 (0.1)
仙腸骨炎	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	23 (6.8)	41 (8.0)	64 (7.5)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) 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）			
肛門性器疣贅	0	1 (0.2)	1 (0.1)
基底細胞癌	1 (0.3)	0	1 (0.1)
表皮内悪性黒色腫	1 (0.3)	0	1 (0.1)
子宮頚部扁平上皮癌	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	3 (0.9)	1 (0.2)	4 (0.5)
神経系障害			
浮動性めまい	4 (1.2)	12 (2.3)	16 (1.9)
蟻走感	1 (0.3)	0	1 (0.1)
頭痛	23 (6.8)	47 (9.2)	70 (8.2)
感覚鈍麻	1 (0.3)	3 (0.6)	4 (0.5)
嗜眠	2 (0.6)	1 (0.2)	3 (0.4)
片頭痛	2 (0.6)	4 (0.8)	6 (0.7)
神経痛	0	1 (0.2)	1 (0.1)
錯感覚	1 (0.3)	4 (0.8)	5 (0.6)
失神寸前の状態	2 (0.6)	2 (0.4)	4 (0.5)
神経根障害	0	1 (0.2)	1 (0.1)
痙攣発作	0	1 (0.2)	1 (0.1)
失神	1 (0.3)	1 (0.2)	2 (0.2)
振戦	1 (0.3)	1 (0.2)	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
神経系障害 (Cont.)			
SUBJECTS WITH ONE OR MORE EVENTS	34 (10.0)	67 (13.1)	101 (11.9)
精神障害			
不安	1 (0.3)	1 (0.2)	2 (0.2)
抑うつ気分	0	1 (0.2)	1 (0.1)
不眠症	2 (0.6)	2 (0.4)	4 (0.5)
パニック発作	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	3 (0.9)	5 (1.0)	8 (0.9)
腎および尿路障害			
急性腎障害	1 (0.3)	0	1 (0.1)
着色尿	0	1 (0.2)	1 (0.1)
排尿困難	1 (0.3)	1 (0.2)	2 (0.2)
血尿	1 (0.3)	2 (0.4)	3 (0.4)
高シュウ酸尿症	0	1 (0.2)	1 (0.1)
腎結石症	1 (0.3)	1 (0.2)	2 (0.2)
夜間頻尿	0	1 (0.2)	1 (0.1)
多尿	1 (0.3)	0	1 (0.1)
腎仙痛	0	1 (0.2)	1 (0.1)
腎不全	1 (0.3)	1 (0.2)	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
腎および尿路障害 (Cont.)			
SUBJECTS WITH ONE OR MORE EVENTS	5 (1.5)	7 (1.4)	12 (1.4)
生殖系および乳房障害			
バルトリン嚢腫	0	1 (0.2)	1 (0.1)
不正子宮出血	1 (0.3)	0	1 (0.1)
卵巣嚢胞	1 (0.3)	0	1 (0.1)
骨盤痛	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	2 (0.6)	1 (0.2)	3 (0.4)
呼吸器、胸郭および縦隔障害			
喘息	0	2 (0.4)	2 (0.2)
咳嗽	6 (1.8)	9 (1.8)	15 (1.8)
発声障害	0	1 (0.2)	1 (0.1)
呼吸困難	1 (0.3)	2 (0.4)	3 (0.4)
鼻出血	0	3 (0.6)	3 (0.4)
鼻閉	1 (0.3)	0	1 (0.1)
口腔咽頭痛	5 (1.5)	15 (2.9)	20 (2.3)
咽頭障害	0	1 (0.2)	1 (0.1)
湿性咳嗽	0	1 (0.2)	1 (0.1)
鼻漏	0	2 (0.4)	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
副鼻腔うっ血	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	13 (3.8)	28 (5.5)	41 (4.8)
皮膚および皮下組織障害			
ざ瘡	3 (0.9)	1 (0.2)	4 (0.5)
脱毛症	7 (2.1)	4 (0.8)	11 (1.3)
血管浮腫	0	1 (0.2)	1 (0.1)
冷汗	0	1 (0.2)	1 (0.1)
頭部粃糠疹	1 (0.3)	1 (0.2)	2 (0.2)
皮膚炎	1 (0.3)	3 (0.6)	4 (0.5)
アトピー性皮膚炎	0	1 (0.2)	1 (0.1)
接触皮膚炎	0	1 (0.2)	1 (0.1)
乾癬様皮膚炎	1 (0.3)	0	1 (0.1)
皮膚乾燥	1 (0.3)	1 (0.2)	2 (0.2)
湿疹	2 (0.6)	1 (0.2)	3 (0.4)
紅斑	1 (0.3)	5 (1.0)	6 (0.7)
結節性紅斑	0	1 (0.2)	1 (0.1)
男性型多毛症	1 (0.3)	0	1 (0.1)
多汗症	1 (0.3)	0	1 (0.1)
多毛症	1 (0.3)	0	1 (0.1)
寝汗	1 (0.3)	1 (0.2)	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
皮膚および皮下組織障害 (Cont.)			
そう痒症	3 (0.9)	3 (0.6)	6 (0.7)
全身性そう痒症	0	1 (0.2)	1 (0.1)
乾癬	1 (0.3)	1 (0.2)	2 (0.2)
発疹	8 (2.4)	10 (2.0)	18 (2.1)
紅斑性皮疹	2 (0.6)	1 (0.2)	3 (0.4)
斑状丘疹状皮疹	0	1 (0.2)	1 (0.1)
丘疹性皮疹	0	1 (0.2)	1 (0.1)
顔面腫脹	0	1 (0.2)	1 (0.1)
蕁麻疹	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	31 (9.1)	38 (7.4)	69 (8.1)
外科および内科処置			
創部ドレナージ	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
血管障害			
血腫	1 (0.3)	3 (0.6)	4 (0.5)
出血	0	1 (0.2)	1 (0.1)
高血圧	2 (0.6)	1 (0.2)	3 (0.4)
低血圧	1 (0.3)	1 (0.2)	2 (0.2)
蒼白	1 (0.3)	0	1 (0.1)
末梢静脈疾患	0	1 (0.2)	1 (0.1)
表在性静脈炎	2 (0.6)	0	2 (0.2)
血栓性静脈炎	0	1 (0.2)	1 (0.1)
静脈血栓症	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	8 (2.4)	7 (1.4)	15 (1.8)

NOTE: THE SUM OF THE TOTAL NUMBER OF SUBJECTS REPORTING EACH OF THE PREFERRED TERMS SHOULD BE GREATER THAN OR EQUAL TO THE SYSTEM ORGAN CLASS TOTAL. A SUBJECT WHO REPORTS TWO OR MORE DIFFERENT PREFERRED TERMS WHICH ARE IN THE SAME SYSTEM ORGAN CLASS IS COUNTED ONLY ONCE IN THE SYSTEM ORGAN CLASS TOTAL.
TREATMENT-EMERGENT ADVERSE EVENTS DURING INDUCTION STUDY ARE DEFINED AS EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY MEDICATION AND UP TO THE FIRST DOSE OF THE STUDY MEDICATION IN MAINTENANCE STUDY FOR THOSE WHO ARE RE-RANDOMIZED AT WEEK 8, OR EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY DRUG AND WITHIN 70 DAYS AFTER THE LAST DOSE OF THE STUDY MEDICATION IN THE INDUCTION STUDY FOR SUBJECTS WHO ARE NOT RE-RANDOMIZED.

Cross Reference: M14-033 Induction Main-study Final CSR_Table 14.3__1.2.1

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）

	ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD INDUCTION DOSE (N=340) n (%)	HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
ANY ADVERSE EVENT	75 (22.1)	138 (27.0)	213 (25.0)
血液およびリンパ系障害			
貧血	0	1 (0.2)	1 (0.1)
白血球減少症	0	1 (0.2)	1 (0.1)
リンパ節症	1 (0.3)	0	1 (0.1)
好中球減少症	1 (0.3)	0	1 (0.1)
血小板減少症	0	2 (0.4)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	2 (0.6)	4 (0.8)	6 (0.7)
心臓障害			
動悸	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	1 (0.3)	1 (0.2)	2 (0.2)
先天性、家族性および遺伝性障害			
エーラース・ダンロス症候群	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
眼障害			
眼瞼痙攣	0	1 (0.2)	1 (0.1)
ドライアイ	1 (0.3)	1 (0.2)	2 (0.2)
眼瞼湿疹	1 (0.3)	0	1 (0.1)
眼痛	1 (0.3)	0	1 (0.1)
眼瞼浮腫	1 (0.3)	0	1 (0.1)
羞明	0	2 (0.4)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	4 (1.2)	4 (0.8)	8 (0.9)
胃腸障害			
腹痛	0	2 (0.4)	2 (0.2)
上腹部痛	1 (0.3)	1 (0.2)	2 (0.2)
根尖肉芽腫	0	1 (0.2)	1 (0.1)
潰瘍性大腸炎	0	1 (0.2)	1 (0.1)
下痢	0	1 (0.2)	1 (0.1)
鼓腸	1 (0.3)	3 (0.6)	4 (0.5)
歯肉出血	0	1 (0.2)	1 (0.1)
歯肉痛	0	1 (0.2)	1 (0.1)
血栓性痔核	1 (0.3)	0	1 (0.1)
悪心	6 (1.8)	7 (1.4)	13 (1.5)
嚥下痛	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
胃腸障害 (Cont.)			
直腸しぶり	0	1 (0.2)	1 (0.1)
嘔吐	2 (0.6)	3 (0.6)	5 (0.6)
SUBJECTS WITH ONE OR MORE EVENTS	10 (2.9)	16 (3.1)	26 (3.1)
一般・全身障害および投与部位の状態			
投与部位疼痛	1 (0.3)	0	1 (0.1)
適用部位そう痒感	0	1 (0.2)	1 (0.1)
適用部位反応	0	1 (0.2)	1 (0.1)
無力症	3 (0.9)	3 (0.6)	6 (0.7)
胸痛	2 (0.6)	0	2 (0.2)
悪寒	1 (0.3)	1 (0.2)	2 (0.2)
疲労	5 (1.5)	9 (1.8)	14 (1.6)
冷感	1 (0.3)	1 (0.2)	2 (0.2)
インフルエンザ様疾患	1 (0.3)	0	1 (0.1)
注射部位内出血	1 (0.3)	3 (0.6)	4 (0.5)
注射部位紅斑	2 (0.6)	14 (2.7)	16 (1.9)
注射部位過敏反応	0	3 (0.6)	3 (0.4)
注射部位硬結	0	1 (0.2)	1 (0.1)
注射部位炎症	0	2 (0.4)	2 (0.2)
注射部位腫瘤	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
注射部位浮腫	0	1 (0.2)	1 (0.1)
注射部位疼痛	3 (0.9)	6 (1.2)	9 (1.1)
注射部位そう痒感	2 (0.6)	13 (2.5)	15 (1.8)
注射部位発疹	1 (0.3)	4 (0.8)	5 (0.6)
注射部位反応	1 (0.3)	19 (3.7)	20 (2.3)
注射部位腫脹	2 (0.6)	9 (1.8)	11 (1.3)
注射部位蕁麻疹	1 (0.3)	1 (0.2)	2 (0.2)
末梢性浮腫	0	1 (0.2)	1 (0.1)
疼痛	1 (0.3)	0	1 (0.1)
発熱	3 (0.9)	0	3 (0.4)
腫脹	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	21 (6.2)	71 (13.9)	92 (10.8)
肝胆道系障害			
高トランスアミナーゼ血症	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
免疫系障害			
薬物過敏症	0	1 (0.2)	1 (0.1)
過敏症	1 (0.3)	2 (0.4)	3 (0.4)
SUBJECTS WITH ONE OR MORE EVENTS	1 (0.3)	3 (0.6)	4 (0.5)
感染症および寄生虫症			
四肢膿瘍	0	1 (0.2)	1 (0.1)
ブラストシスティス感染	0	1 (0.2)	1 (0.1)
ウイルス性気管支炎	1 (0.3)	0	1 (0.1)
カンジダ感染	0	1 (0.2)	1 (0.1)
クロストリジウム・ディフィシレ感染	0	1 (0.2)	1 (0.1)
結膜炎	1 (0.3)	0	1 (0.1)
膀胱炎	0	1 (0.2)	1 (0.1)
毛包炎	0	1 (0.2)	1 (0.1)
真菌感染	0	1 (0.2)	1 (0.1)
胃腸炎	0	1 (0.2)	1 (0.1)
ヘルペスウイルス感染	0	1 (0.2)	1 (0.1)
帯状疱疹	1 (0.3)	0	1 (0.1)
麦粒腫	0	1 (0.2)	1 (0.1)
感染性嚢腫	0	1 (0.2)	1 (0.1)
インフルエンザ	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症 (Cont.)			
喉頭炎	1 (0.3)	0	1 (0.1)
上咽頭炎	3 (0.9)	3 (0.6)	6 (0.7)
食道カンジダ症	1 (0.3)	0	1 (0.1)
口腔ヘルペス	1 (0.3)	1 (0.2)	2 (0.2)
咽頭炎	2 (0.6)	0	2 (0.2)
肺炎	1 (0.3)	1 (0.2)	2 (0.2)
膿疱性皮疹	2 (0.6)	1 (0.2)	3 (0.4)
副鼻腔炎	1 (0.3)	1 (0.2)	2 (0.2)
白癬感染	0	1 (0.2)	1 (0.1)
歯感染	0	1 (0.2)	1 (0.1)
結核	0	1 (0.2)	1 (0.1)
上気道感染	1 (0.3)	1 (0.2)	2 (0.2)
尿路感染	1 (0.3)	2 (0.4)	3 (0.4)
ウイルス性上気道感染	1 (0.3)	0	1 (0.1)
外陰部腟カンジダ症	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	17 (5.0)	23 (4.5)	40 (4.7)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
傷害、中毒および処置合併症			
挫傷	0	1 (0.2)	1 (0.1)
注射に伴う反応	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	2 (0.4)	2 (0.2)
臨床検査			
アラニンアミノトランスフェラーゼ増加	0	2 (0.4)	2 (0.2)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.2)	1 (0.1)
血中ビリルビン増加	1 (0.3)	2 (0.4)	3 (0.4)
血中コレステロール増加	1 (0.3)	0	1 (0.1)
血中リン減少	1 (0.3)	0	1 (0.1)
血圧上昇	1 (0.3)	0	1 (0.1)
血中トリグリセリド増加	0	1 (0.2)	1 (0.1)
呼吸音異常	1 (0.3)	0	1 (0.1)
C－反応性蛋白増加	1 (0.3)	0	1 (0.1)
クロストリジウム検査陽性	0	1 (0.2)	1 (0.1)
白血球数減少	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	6 (1.8)	7 (1.4)	13 (1.5)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
代謝および栄養障害			
高コレステロール血症	1 (0.3)	1 (0.2)	2 (0.2)
高血糖	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (0.3)	2 (0.4)	3 (0.4)
筋骨格系および結合組織障害			
関節痛	5 (1.5)	5 (1.0)	10 (1.2)
背部痛	0	2 (0.4)	2 (0.2)
側腹部痛	1 (0.3)	0	1 (0.1)
関節雑音	0	1 (0.2)	1 (0.1)
関節可動域低下	1 (0.3)	0	1 (0.1)
関節腫脹	1 (0.3)	0	1 (0.1)
筋痙縮	1 (0.3)	1 (0.2)	2 (0.2)
筋骨格痛	0	1 (0.2)	1 (0.1)
筋肉痛	1 (0.3)	0	1 (0.1)
顎痛	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	8 (2.4)	11 (2.1)	19 (2.2)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) 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）			
肛門性器疣贅	0	1 (0.2)	1 (0.1)
表皮内悪性黒色腫	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (0.3)	1 (0.2)	2 (0.2)
神経系障害			
浮動性めまい	1 (0.3)	3 (0.6)	4 (0.5)
蟻走感	1 (0.3)	0	1 (0.1)
頭痛	12 (3.5)	12 (2.3)	24 (2.8)
片頭痛	0	3 (0.6)	3 (0.4)
神経痛	0	1 (0.2)	1 (0.1)
痙攣発作	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	13 (3.8)	20 (3.9)	33 (3.9)
精神障害			
不安	1 (0.3)	0	1 (0.1)
不眠症	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	2 (0.6)	0	2 (0.2)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
腎および尿路障害			
着色尿	0	1 (0.2)	1 (0.1)
排尿困難	0	1 (0.2)	1 (0.1)
血尿	0	1 (0.2)	1 (0.1)
高シュウ酸尿症	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	2 (0.4)	2 (0.2)
生殖系および乳房障害			
バルトリン嚢腫	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (0.2)	1 (0.1)
呼吸器、胸郭および縦隔障害			
咳嗽	4 (1.2)	5 (1.0)	9 (1.1)
呼吸困難	1 (0.3)	0	1 (0.1)
鼻出血	0	1 (0.2)	1 (0.1)
鼻閉	1 (0.3)	0	1 (0.1)
口腔咽頭痛	0	4 (0.8)	4 (0.5)
咽頭障害	0	1 (0.2)	1 (0.1)
鼻漏	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
副鼻腔うっ血	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	7 (2.1)	10 (2.0)	17 (2.0)
皮膚および皮下組織障害			
脱毛症	3 (0.9)	4 (0.8)	7 (0.8)
血管浮腫	0	1 (0.2)	1 (0.1)
冷汗	0	1 (0.2)	1 (0.1)
皮膚炎	1 (0.3)	2 (0.4)	3 (0.4)
アトピー性皮膚炎	0	1 (0.2)	1 (0.1)
乾癬様皮膚炎	1 (0.3)	0	1 (0.1)
皮膚乾燥	1 (0.3)	0	1 (0.1)
湿疹	1 (0.3)	1 (0.2)	2 (0.2)
紅斑	0	4 (0.8)	4 (0.5)
多汗症	1 (0.3)	0	1 (0.1)
寝汗	0	1 (0.2)	1 (0.1)
そう痒症	3 (0.9)	1 (0.2)	4 (0.5)
全身性そう痒症	0	1 (0.2)	1 (0.1)
乾癬	1 (0.3)	1 (0.2)	2 (0.2)
発疹	4 (1.2)	3 (0.6)	7 (0.8)
紅斑性皮疹	2 (0.6)	1 (0.2)	3 (0.4)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の導入療法試験）（続き）

SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	ADALIMUMAB STANDARD INDUCTION DOSE (N=340) n (%)	ADALIMUMAB HIGHER INDUCTION DOSE (N=512) n (%)	TOTAL (N=852) n (%)
皮膚および皮下組織障害 (Cont.)			
丘疹性皮疹	0	1 (0.2)	1 (0.1)
蕁麻疹	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	18 (5.3)	23 (4.5)	41 (4.8)
血管障害			
血腫	1 (0.3)	1 (0.2)	2 (0.2)
低血圧	1 (0.3)	0	1 (0.1)
末梢静脈疾患	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	2 (0.6)	2 (0.4)	4 (0.5)

NOTE: THE SUM OF THE TOTAL NUMBER OF SUBJECTS REPORTING EACH OF THE PREFERRED TERMS SHOULD BE GREATER THAN OR EQUAL TO THE SYSTEM ORGAN CLASS TOTAL. A SUBJECT WHO REPORTS TWO OR MORE DIFFERENT PREFERRED TERMS WHICH ARE IN THE SAME SYSTEM ORGAN CLASS IS COUNTED ONLY ONCE IN THE SYSTEM ORGAN CLASS TOTAL.
TREATMENT-EMERGENT ADVERSE EVENTS DURING INDUCTION STUDY ARE DEFINED AS EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY MEDICATION AND UP TO THE FIRST DOSE OF THE STUDY MEDICATION IN MAINTENANCE STUDY FOR THOSE WHO ARE RE-RANDOMIZED AT WEEK 8, OR EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY DRUG AND WITHIN 70 DAYS AFTER THE LAST DOSE OF THE STUDY MEDICATION IN THE INDUCTION STUDY FOR SUBJECTS WHO ARE NOT RE-RANDOMIZED.
EVENT WITH UNKNOWN RELATIONSHIP TO STUDY DRUG IS BEING COUNTED AS DRUG-RELATED.

Cross reference: M14-033 Induction Main-study Final CSR_Table 14.3__1.6

M14-033 日本サブ試験 導入療法試験

治験の標題： A Double-Blind, Randomized, Multicenter Study of Higher Versus Standard Adalimumab Dosing Regimens for Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis	
施設数 / 実施国名： 主試験：120 施設 / オーストリア，ベルギー，カナダ，チェコ共和国，デンマーク，フランス，ドイツ，ハンガリー，イスラエル，イタリア，オランダ，ポーランド，ルーマニア，スロバキア，スペイン，スイス，ウクライナ，英国及び米国 日本サブ試験：22 施設 / 日本	
治験責任医師： [redacted], MD 他	
公表文献 (参考資料) ： Panes J, Colombel JF, D'Haens GR, et al. OP216 High versus standard adalimumab induction dosing regimens in patients with moderately to severely active ulcerative colitis: Results from the SERENE UC induction study. United European Gastroenterol J. 2019;7 (Suppl 8S):118.	
治験期間： 治験開始日（最初の被験者の初回来院日）： 主試験： 2014 年 3 月 27 日 日本サブ試験： 20[redacted] 年 [redacted] 月 [redacted] 日 治験終了日 （最後の被験者の追跡調査終了日）： 主試験： 20[redacted] 年 [redacted] 月 [redacted] 日 日本サブ試験： 20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ： 第 III 相
治験の種類： 第 III 相，多施設共同，無作為化，二重盲検試験	
目的： 本試験の目的は，中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者に，高用量での導入療法及び維持療法を行ったときの有効性及び安全性を検討すること，並びに日本人集団と統合集団（日本及び日本以外の治験実施医療機関で登録されたすべての被験者）の間での有効性の一貫性を示すことであった。	
被験者数 (計画時と解析時) ： 計画時： 940 例（主試験：840 例，日本サブ試験：100 例） 組入れ時： 952 例（主試験：852 例，日本サブ試験：100 例） 解析時： 952 例（主試験：852 例，日本サブ試験：100 例）	

診断と主要な組入れ基準：

M14-033 試験の主要な選択基準は以下のとおりであった：ベースライン時の年齢が 18 歳以上 75 歳以下の男女。ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中の内視鏡検査（全大腸内視鏡検査又は S 状結腸鏡検査）で診断が確認されると共に，現在の感染症，上皮異形成及び / 又は悪性腫瘍が除外されている患者。治験実施計画書で規定した副腎皮質ステロイドの経口剤又は免疫抑制剤による現在の治療，あるいは医師の判断で十分かつ適切な過去の治療にもかかわらず，ベースラインの Mayo スコア（以下，「FMS」）が 6～12 ポイント，かつ内視鏡所見サブスコアが 2～3 ポイント（中央判定による評価）である活動性の UC 患者。インフリキシマブの投与で以前に UC の治療効果が認められ，その後効果消失又は不耐容となったため，インフリキシマブの投与を中止した患者を，本試験に組み入れることができる（効果消失又は不耐容を示す記録を確認すること）。女性患者の場合は，本試験への参加から 1 年以上前に閉経した，又は不妊手術（両側卵管結紮術，両側卵巣摘出術，及び / 又は子宮摘出術）を行ったことで，妊娠の可能性がないこと。妊娠の可能性がある女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，治験実施計画書で規定した方法で避妊すること。女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，授乳しないこと。結核スクリーニング検査が陰性の患者。既往歴やスクリーニング期間中に実施する臨床検査，身体的所見，胸部 X 線検査，12 誘導心電図検査の結果から，治験責任医師が健康状態にその他の問題がないと判断した患者。

M14-033 試験の主要な除外基準は以下のとおりであった：クローン病と診断されている，若しくは既往がある，又は indeterminate colitis と診断されている患者。劇症の大腸炎又は中毒性巨大結腸症と診断されている患者。スクリーニング時の内視鏡検査で，病変が直腸のみに限局している患者（潰瘍性直腸炎）。回腸直腸瘻造設を伴う結腸亜全摘術，若しくは回腸嚢，Koch パウチ，回腸ストマ造設を伴う結腸切除術の既往がある患者。又は腸管の手術を予定している患者。

治験方法：

M14-033 試験は，導入療法試験と維持療法試験で構成される。また，日本以外の他国の治験実施医療機関で登録された被験者を対象とした主試験と，日本の治験実施医療機関で登録された被験者を対象とした日本サブ試験で構成される。M14-033 試験では，高用量の導入療法及び維持療法を，承認されている標準用量の導入療法及び維持療法と比較した。すべての選択基準を満たし，いずれの除外基準にも抵触しない中等症から重症の成人活動性 UC 患者を本試験の参加に適格とした。

本報告では，日本及び日本以外の治験実施医療機関で登録されたすべての被験者（統合集団）並びに日本の治験実施医療機関で登録されたすべての被験者（日本人集団）を対象とした，M14-033 導入療法試験の解析結果を示す。本報告には，導入療法試験を中止し，中止後に市販のアダリムマブの使用を開始しなかった被験者に関して，最終投与 70 日後の追跡調査までに得られたデータを含める（追跡調査終了日：20[redacted] 年[redacted] 月[redacted] 日）。本報告は，導入療法試験（主試験及び日本サブ試験）の組織学検査データ，及び前版からの最終的なデータの変更を反映した治験総括報告書の最終版（データベースロック日：20[redacted] 年[redacted] 月[redacted] 日）に基づいている。

被験薬，用量，投与方法及びバッチ番号：

8 週間の二重盲検導入療法試験では，無作為化時にインフリキシマブによる治療歴及びベースラインでの副腎皮質ステロイドの投与を因子として被験者を層別化した。高用量の導入療法では，投与 0，1，2 及び 3 週時にアダリムマブ 160 mg，投与 4 及び 6 週時にアダリムマブ 40 mg を投与することで，8 週間の合計投与量は標準療法（320 mg）の約 2 倍の 720 mg となる。

高用量群に割り付けられた被験者には，投与 0，1，2 及び 3 週時にアダリムマブ 160 mg（4 シリンジ），投与 4 及び 6 週時にアダリムマブ 40 mg（1 シリンジ）を投与した。標準療法群に割り付けられた被験者には，ベースライン（投与 0 週時）にアダリムマブ 160 mg（4 シリンジ），投与 1 週時にプラセボ（4 シリンジ），投与 2 週時にアダリムマブ 80 mg（2 シリンジ）及びプラセボ（2 シリンジ），投与 3 週時にプラセボ（4 シリンジ），投与 4 及び 6 週時にアダリムマブ 40 mg（1 シリンジ）を投与した。

ロット番号：

アダリムマブ： [redacted]，[redacted]，[redacted]，[redacted]，[redacted]，[redacted]，[redacted]（主試験）
[redacted]，[redacted]，[redacted]（日本サブ試験）

プラセボ： [redacted]，[redacted]，[redacted]，[redacted]，[redacted]（主試験）
[redacted]，[redacted]（日本サブ試験）

治療期間：8 週間

対照薬，用量，投与方法及びバッチ番号：

なし

評価基準：

有効性：

導入療法試験の主要評価項目は，投与 8 週時に FMS で寛解（FMS が 2 以下で，かついずれのサブスコアも 1 を超えない）を達成した被験者の割合であった。

導入療法試験における順位付き副次評価項目（昇順に順位を階層化）は以下のとおりであった。

1. 投与 8 週時に内視鏡検査で改善（内視鏡所見サブスコアが 0 又は 1）が認められた被験者の割合
2. 投与 8 週時に便中カルプロテクチン値が 150 mg/kg 未満となった被験者の割合
3. 投与 8 週時に Inflammatory Bowel Disease Questionnaire（以下「IBDQ」）で改善（ベースラインと比較して IBDQ スコアの 16 以上の増加）が認められた被験者の割合
4. 投与 8 週時に FMS で改善例となった被験者の割合
5. 投与 8 週時に内視鏡検査で寛解（内視鏡所見サブスコアが 0）が認められた被験者の割合
6. 投与 8 週時に IBDQ の腸症状ドメインで改善（ベースラインと比較して IBDQ の腸症状ドメインスコアの 6 以上の増加）が認められた被験者の割合
7. 投与 8 週時に IBDQ の疲労に関する項目で改善（ベースラインと比較して IBDQ の疲労に関する項目のスコアの 1 以上の増加）が認められた被験者の割合

薬物動態：

別途報告書に記載することとした。

安全性：

治験期間中の有害事象，バイタルサインの変化，身体的所見，及び臨床検査値を評価した。

統計手法：

有効性：

日本サブ試験の導入療法試験では，有効性の主解析は統合 Intent-to-treat（以下「ITT」）集団及び日本人 ITT 集団を対象に実施した。導入療法試験の有効性の解析では，投与 8 週時の欠測値の補完に，欠測値を「非反応」としてデータ補完する統計手法を用いた。解析では，統合 ITT 集団及び日本人 ITT 集団を対象に，高用量の導入療法と標準用量の導入療法を比較した。投与 8 週時に寛解を達成した被験者の割合の群間差を，インフリキシマブによる治療歴及びベースラインでの副腎皮質ステロイドの投与の有無で調整した Cochran-Mantel-Haenszel（以下「CMH」）検定を用いて評価した。CMH 検定に基づき，割合の群間差の両側 95%信頼区間を算出した。また，主要評価項目の感度分析として，無作為化時の層別因子，ベースライン時点における免疫抑制剤の使用，C 反応性たん白値及び重症度，並びに地域（統合 ITT 集団のみ）の効果について調整したロジスティック回帰分析を実施した。

薬物動態：

別途報告書に記載することとした。

安全性：

日本サブ試験の導入療法試験では，安全性の解析は統合安全性解析対象集団及び日本人安全性解析対象集団を対象に実施した。被験者が実際に受けた治療に基づき，治療群ごとに安全性評価項目を要約した。安全性評価項目の群間差は，有意水準 0.05 の両側検定を用いて評価した。

特に断らない限り，連続変数の安全性評価項目（例：臨床検査値のベースラインから最終測定時までの変化量）の群間差は，治療を因子とした分散分析モデルを用いて評価した。また，カテゴリカル変数の安全性評価項目の群間差は，Fisher の正確確率検定を用いて評価した。

要約 / 結論：

有効性：

統合 ITT 集団及び日本人 ITT 集団のいずれにおいても，投与 8 週時に FMS で寛解を達成した被験者の割合について，高用量群と標準用量群の間で統計学的に有意な差は認められなかった。部分集団解析の結果は，主解析の結果とおおむね一致していた。

順位付き副次評価項目に関しては，日本人 ITT 集団における IBDQ に基づく評価項目を除き，高用量群の方が標準用量群よりも割合が数値的に高かった。

統合 ITT 集団と日本人 ITT 集団の間で，有効性の結果はおおむね一貫していた。

薬物動態：

別途報告書に記載することとした。

安全性：

アダリムマブの安全性プロファイルは高用量群と標準用量群で同様であり，アダリムマブの既知の安全性プロファイルと一致していた。新たな安全性シグナル又は予期しない傾向は認められなかった。

統合安全性解析対象集団では，各導入療法を受けた被験者の約半数に 1 件以上の有害事象が発現した。導入療法試験中，2 例が死亡した（術後腹膜炎及び心停止）。いずれも主試験の高用量群の被験者であり，治験薬との因果関係は関連なしと判断された。全体での重篤な有害事象及び治験薬投与の中止に至った有害事象の発現割合は低く，高用量群と標準用量群で同程度であった。最も多く報告された器官別大分類（以下「SOC」）は，いずれの投与群でも胃腸障害であった（高用量群：17.8%，標準用量群：20.6%）。最も多く（被験者の 5%以上）報告された基本語（以下「PT」）は，いずれの投与群でも潰瘍性大腸炎及び頭痛であった。有害事象の大部分は重症度が軽度又は中等度で，治験薬と関連なしと判断された。特に注目すべき有害事象（以下「AESI」）の発現割合は，感染症，注射部位反応，血液障害及びアレルギー反応を除き，全般的に低かった（1%未満）。いずれの AESI も発現割合は投与群間でおおむね同程度であった。ただし，注射部位反応の発現割合は高用量群（12.0%）の方が標準用量群（4.2%）よりも高かった。

日本人安全性解析対象集団では，被験者の 50.0%に 1 件以上の有害事象が発現した。死亡は認められなかった。全体での重篤な有害事象及び治験薬投与の中止に至った有害事象の発現割合は低く（5 例［5.0%］以下），高用量群と標準用量群で同程度であった。最も多く報告された SOC は，感染症および寄生虫症であった。最も多く

（被験者の 5%以上）報告された PT は，上咽頭炎，注射部位反応及び発熱であった。標準療法群ではこれらの他に発疹，貧血，関節痛及び潰瘍性大腸炎が 5%以上に発現したが，高用量群ではこれらの他に 5%以上に発現した有害事象はなかった。有害事象の大部分は重症度が軽度又は中等度で，治験薬と関連なしと判断された。特に注目すべき有害事象（以下「AESI」）に関して，感染症の発現割合は高用量群で 23.0%，標準療法群で 10.3%であった。他の AESI の発現割合は全般的に低く，投与群間でおおむね同程度であった。

臨床検査（血液学的検査，血液生化学検査及び尿検査）の平均値にベースラインからの顕著な変化は認められなかった。血液学的検査，血液生化学検査値及び尿検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，及びベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者は少数であり，臨床的に重要ではないと判断された。治験薬投与の中止に至った臨床検査値の上昇は認められず，Hy's law の基準に該当した被験者も認められなかった。

バイタルサインの平均値にベースラインからの顕著な変化は認められなかった。

導入療法試験では，主試験及び日本サブ試験のいずれにおいても，治験薬が投与されなかった 70 日間の追跡調査期間も含めて，妊娠又は製品の安全性部品に係る苦情は報告されなかった。

結論：

日本サブ試験の導入療法試験において，投与 8 週時に FMS で寛解を達成した被験者の割合に関して，標準用量のアダリムマブ導入療法に対する高用量のアダリムマブ導入療法の統計学的に有意な優越性は認められなかった。したがって，中等症から重症の活動性 UC 患者において，高用量のアダリムマブ導入療法による追加のベネフィットは得られず，現在承認されているアダリムマブ導入療法（160 mg / 80 mg）が中等症から重症の活動性 UC 患者に対する適切な導入療法であることが示された。投与 8 週時に FMS で寛解を達成した被験者の割合は，日本人集団，主試験集団及び統合集団で一貫していた。安全性プロファイルは高用量群と標準用量群で同様であり，統合集団（日本及び日本以外の治験実施医療機関で登録された被験者）における安全性プロファイル，並びに UC 及び他の疾患を対象とした，数十年間にわたる国際共同治験及び市販後調査のデータに基づくアダリムマブの安全性プロファイルとも一致していた。新たな安全性のシグナル又は傾向は認められなかった。全体として，本試験の対象集団における標準用量のアダリムマブ導入療法のベネフィット・リスクプロファイルは不変であった。

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
ANY ADVERSE EVENT	16 (41.0)	34 (55.7)	50 (50.0)	200 (52.8)	305 (53.2)	505 (53.0)	184 (54.1)	271 (52.9)	455 (53.4)
血液およびリンパ系障害									
貧血	2 (5.1)	2 (3.3)	4 (4.0)	15 (4.0)	18 (3.1)	33 (3.5)	13 (3.8)	16 (3.1)	29 (3.4)
大球性貧血	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
鉄欠乏性貧血	0	1 (1.6)	1 (1.0)	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	0	1 (0.1)
白血球減少症	0	1 (1.6)	1 (1.0)	1 (0.3)	4 (0.7)	5 (0.5)	1 (0.3)	3 (0.6)	4 (0.5)
リンパ節症	0	0	0	2 (0.5)	2 (0.3)	4 (0.4)	2 (0.6)	2 (0.4)	4 (0.5)
リンパ球減少症	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
好中球減少症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
血小板減少症	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	2 (5.1)	4 (6.6)	6 (6.0)	21 (5.5)	28 (4.9)	49 (5.1)	19 (5.6)	24 (4.7)	43 (5.0)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
心臓障害									
心停止	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
動悸	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
先天性、家族性および遺伝性障害									
エーラース・ダンロス症候群	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
包皮小帯	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
耳および迷路障害									
聴力低下	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
耳鳴	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
回転性めまい	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
内分泌障害									
ステロイド離脱症候群	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
眼障害									
アレルギー性眼瞼炎	1 (2.6)	0	1 (1.0)	1 (0.3)	0	1 (0.1)	0	0	0
眼瞼痙攣	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
アレルギー性結膜炎	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
後天性涙道狭窄	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ドライアイ	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
眼瞼湿疹	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
上強膜炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
眼の障害	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
眼痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
眼部腫脹	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
眼瞼浮腫	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
緑内障	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
羞明	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
眼障害 (Cont.)									
視力低下	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (2.6)	2 (3.3)	3 (3.0)	8 (2.1)	10 (1.7)	18 (1.9)	7 (2.1)	8 (1.6)	15 (1.8)
胃腸障害									
腹部不快感	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
腹部膨満	1 (2.6)	0	1 (1.0)	4 (1.1)	1 (0.2)	5 (0.5)	3 (0.9)	1 (0.2)	4 (0.5)
腹痛	0	2 (3.3)	2 (2.0)	6 (1.6)	13 (2.3)	19 (2.0)	6 (1.8)	11 (2.1)	17 (2.0)
上腹部痛	0	0	0	3 (0.8)	4 (0.7)	7 (0.7)	3 (0.9)	4 (0.8)	7 (0.8)
腹部圧痛	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
裂肛	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
アフタ性潰瘍	0	1 (1.6)	1 (1.0)	3 (0.8)	2 (0.3)	5 (0.5)	3 (0.9)	1 (0.2)	4 (0.5)
根尖肉芽腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
大腸炎	0	0	0	3 (0.8)	2 (0.3)	5 (0.5)	3 (0.9)	2 (0.4)	5 (0.6)
潰瘍性大腸炎	2 (5.1)	2 (3.3)	4 (4.0)	32 (8.4)	31 (5.4)	63 (6.6)	30 (8.8)	29 (5.7)	59 (6.9)
便秘	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
便意切迫	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
齲歯	1 (2.6)	1 (1.6)	2 (2.0)	1 (0.3)	1 (0.2)	2 (0.2)	0	0	0

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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
胃腸障害 (Cont.)									
下痢	0	0	0	5 (1.3)	12 (2.1)	17 (1.8)	5 (1.5)	12 (2.3)	17 (2.0)
消化不良	0	1 (1.6)	1 (1.0)	8 (2.1)	3 (0.5)	11 (1.2)	8 (2.4)	2 (0.4)	10 (1.2)
心窩部不快感	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
鼓腸	0	0	0	1 (0.3)	8 (1.4)	9 (0.9)	1 (0.3)	8 (1.6)	9 (1.1)
食中毒	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
胃食道逆流性疾患	0	1 (1.6)	1 (1.0)	1 (0.3)	4 (0.7)	5 (0.5)	1 (0.3)	3 (0.6)	4 (0.5)
歯肉出血	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
歯肉痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
血便排泄	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
痔核	0	0	0	2 (0.5)	5 (0.9)	7 (0.7)	2 (0.6)	5 (1.0)	7 (0.8)
血栓性痔核	0	0	0	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	3 (0.6)	4 (0.5)
歯の知覚過敏	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
大腸狭窄	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
悪心	1 (2.6)	1 (1.6)	2 (2.0)	10 (2.6)	18 (3.1)	28 (2.9)	9 (2.6)	17 (3.3)	26 (3.1)
嚥下痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
急性膵炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
肛門周囲痛	0	0	0	3 (0.8)	1 (0.2)	4 (0.4)	3 (0.9)	1 (0.2)	4 (0.5)
直腸出血	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
直腸しぶり	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
胃腸障害 (Cont.)									
脂肪便	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
歯の障害	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
歯痛	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
臍ヘルニア	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
嘔吐	1 (2.6)	2 (3.3)	3 (3.0)	5 (1.3)	11 (1.9)	16 (1.7)	4 (1.2)	9 (1.8)	13 (1.5)
SUBJECTS WITH ONE OR MORE EVENTS	3 (7.7)	10 (16.4)	13 (13.0)	78 (20.6)	102 (17.8)	180 (18.9)	75 (22.1)	92 (18.0)	167 (19.6)
一般・全身障害および投与部位の状態									
投与部位疼痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
適用部位そう痒感	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
適用部位反応	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
無力症	0	0	0	6 (1.6)	8 (1.4)	14 (1.5)	6 (1.8)	8 (1.6)	14 (1.6)
腋窩痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
胸部不快感	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
胸痛	1 (2.6)	0	1 (1.0)	4 (1.1)	1 (0.2)	5 (0.5)	3 (0.9)	1 (0.2)	4 (0.5)
悪寒	0	1 (1.6)	1 (1.0)	2 (0.5)	2 (0.3)	4 (0.4)	2 (0.6)	1 (0.2)	3 (0.4)
不快感	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
一般・全身障害および投与部位の状態 (Cont.)									
疲労	0	0	0	9 (2.4)	13 (2.3)	22 (2.3)	9 (2.6)	13 (2.5)	22 (2.6)
異常感	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
冷感	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
体温変動感	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
炎症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
インフルエンザ様疾患	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
注射部位内出血	0	0	0	3 (0.8)	4 (0.7)	7 (0.7)	3 (0.9)	4 (0.8)	7 (0.8)
注射部位紅斑	1 (2.6)	0	1 (1.0)	3 (0.8)	14 (2.4)	17 (1.8)	2 (0.6)	14 (2.7)	16 (1.9)
注射部位血腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射部位過敏反応	0	0	0	0	3 (0.5)	3 (0.3)	0	3 (0.6)	3 (0.4)
注射部位硬結	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射部位炎症	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
注射部位腫瘤	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射部位浮腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射部位疼痛	0	0	0	3 (0.8)	6 (1.0)	9 (0.9)	3 (0.9)	6 (1.2)	9 (1.1)
注射部位そう痒感	0	0	0	2 (0.5)	13 (2.3)	15 (1.6)	2 (0.6)	13 (2.5)	15 (1.8)
注射部位発疹	0	0	0	1 (0.3)	4 (0.7)	5 (0.5)	1 (0.3)	4 (0.8)	5 (0.6)
注射部位反応	2 (5.1)	6 (9.8)	8 (8.0)	3 (0.8)	25 (4.4)	28 (2.9)	1 (0.3)	19 (3.7)	20 (2.3)

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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
一般・全身障害および投与部位の状態 (Cont.)									
注射部位腫脹	0	0	0	2 (0.5)	9 (1.6)	11 (1.2)	2 (0.6)	9 (1.8)	11 (1.3)
注射部位蕁麻疹	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
倦怠感	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
非心臓性胸痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
浮腫	1 (2.6)	0	1 (1.0)	1 (0.3)	0	1 (0.1)	0	0	0
末梢性浮腫	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
疼痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
末梢腫脹	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
発熱	2 (5.1)	3 (4.9)	5 (5.0)	7 (1.8)	10 (1.7)	17 (1.8)	5 (1.5)	7 (1.4)	12 (1.4)
腫脹	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	5 (12.8)	10 (16.4)	15 (15.0)	44 (11.6)	99 (17.3)	143 (15.0)	39 (11.5)	89 (17.4)	128 (15.0)
肝胆道系障害									
肝病変	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
脂肪肝	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
肝炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
高トランスアミナーゼ血症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
肝胆道系障害 (Cont.)									
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	3 (0.6)	4 (0.5)
免疫系障害									
薬物過敏症	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
過敏症	0	1 (1.6)	1 (1.0)	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	2 (0.4)	3 (0.4)
季節性アレルギー	0	0	0	0	3 (0.5)	3 (0.3)	0	3 (0.6)	3 (0.4)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (1.6)	1 (1.0)	2 (0.5)	7 (1.2)	9 (0.9)	2 (0.6)	6 (1.2)	8 (0.9)
感染症および寄生虫症									
膿瘍	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
四肢膿瘍	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
肛門膿瘍	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ブラストシスティス感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
気管支炎	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
ウイルス性気管支炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
カンジダ感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症 (Cont.)									
蜂巣炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
クロストリジウム・ディフィシレ感染	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
結膜炎	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
膀胱炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
サイトメガロウイルス性大腸炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
サイトメガロウイルス感染	1 (2.6)	0	1 (1.0)	1 (0.3)	0	1 (0.1)	0	0	0
耳感染	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
丹毒	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
毛包炎	0	1 (1.6)	1 (1.0)	0	2 (0.3)	2 (0.2)	0	1 (0.2)	1 (0.1)
真菌感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
胃腸炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ウイルス性胃腸炎	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
消化管感染	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
単純ヘルペス	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
ヘルペスウイルス感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
帯状疱疹	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
麦粒腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
膿痂疹	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症 (Cont.)									
感染性嚢腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
インフルエンザ	0	1 (1.6)	1 (1.0)	6 (1.6)	2 (0.3)	8 (0.8)	6 (1.8)	1 (0.2)	7 (0.8)
喉頭炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
限局性感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
上咽頭炎	2 (5.1)	10 (16.4)	12 (12.0)	16 (4.2)	29 (5.1)	45 (4.7)	14 (4.1)	19 (3.7)	33 (3.9)
食道カンジダ症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
爪真菌症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
口腔ヘルペス	0	0	0	2 (0.5)	2 (0.3)	4 (0.4)	2 (0.6)	2 (0.4)	4 (0.5)
中耳炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
咽頭炎	0	0	0	5 (1.3)	3 (0.5)	8 (0.8)	5 (1.5)	3 (0.6)	8 (0.9)
細菌性咽頭炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
レンサ球菌性咽頭炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
肺炎	1 (2.6)	0	1 (1.0)	3 (0.8)	1 (0.2)	4 (0.4)	2 (0.6)	1 (0.2)	3 (0.4)
腎盂腎炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
膿疱性皮疹	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
気道感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
鼻炎	0	0	0	3 (0.8)	2 (0.3)	5 (0.5)	3 (0.9)	2 (0.4)	5 (0.6)

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症 (Cont.)									
副鼻腔炎	0	0	0	4 (1.1)	5 (0.9)	9 (0.9)	4 (1.2)	5 (1.0)	9 (1.1)
皮膚感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
白癬感染	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
歯感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
結核	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
上気道感染	0	0	0	3 (0.8)	6 (1.0)	9 (0.9)	3 (0.9)	6 (1.2)	9 (1.1)
尿路感染	0	0	0	5 (1.3)	6 (1.0)	11 (1.2)	5 (1.5)	6 (1.2)	11 (1.3)
腟感染	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
水痘	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
ウイルス感染	0	0	0	0	3 (0.5)	3 (0.3)	0	3 (0.6)	3 (0.4)
ウイルス性上気道感染	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
外陰部腟カンジダ症	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
外陰腟真菌感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	4 (10.3)	14 (23.0)	18 (18.0)	63 (16.6)	84 (14.7)	147 (15.4)	59 (17.4)	70 (13.7)	129 (15.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
傷害、中毒および処置合併症									
動物による引っかき傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
節足動物咬傷	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
挫傷	1 (2.6)	1 (1.6)	2 (2.0)	3 (0.8)	5 (0.9)	8 (0.8)	2 (0.6)	4 (0.8)	6 (0.7)
角膜擦過傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
転倒	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注入に伴う反応	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
注射に伴う反応	0	1 (1.6)	1 (1.0)	0	2 (0.3)	2 (0.2)	0	1 (0.2)	1 (0.1)
関節損傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
靱帯捻挫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
四肢損傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
肉離れ	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
処置による疼痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
交通事故	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
皮膚擦過傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
脊柱損傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
脊椎圧迫骨折	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
スポーツ損傷	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
舌損傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
傷害、中毒および処置合併症 (Cont.)									
尺骨神経損傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
上肢骨折	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (2.6)	3 (4.9)	4 (4.0)	7 (1.8)	19 (3.3)	26 (2.7)	6 (1.8)	16 (3.1)	22 (2.6)
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 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
アスパラギン酸アミノトランスフェラーゼ増加	1 (2.6)	0	1 (1.0)	3 (0.8)	1 (0.2)	4 (0.4)	2 (0.6)	1 (0.2)	3 (0.4)
細菌検査陽性	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
血中ビリルビン増加	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
血中コレステロール増加	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
血中クレアチニン増加	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
血中ブドウ糖増加	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
血中リン減少	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
血圧上昇	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
血中トリグリセリド増加	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
血中尿素増加	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)

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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
臨床検査 (Cont.)									
血中尿素窒素／クレアチニン比増加	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
呼吸音異常	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
C－反応性蛋白増加	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
クロストリジウム検査陽性	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ヘマトクリット減少	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ヘモグロビン減少	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
好中球数増加	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
膵酵素増加	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
血小板数増加	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
尿中赤血球陽性	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
皮膚ツルゴール低下	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
体重減少	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
白血球数減少	1 (2.6)	1 (1.6)	2 (2.0)	2 (0.5)	2 (0.3)	4 (0.4)	1 (0.3)	1 (0.2)	2 (0.2)
白血球数増加	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
尿中白血球陽性	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	2 (5.1)	2 (3.3)	4 (4.0)	16 (4.2)	21 (3.7)	37 (3.9)	14 (4.1)	19 (3.7)	33 (3.9)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
代謝および栄養障害									
食欲減退	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
脱水	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
高コレステロール血症	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
高血糖	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
高トリグリセリド血症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
低アルブミン血症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
低カリウム血症	0	0	0	3 (0.8)	0	3 (0.3)	3 (0.9)	0	3 (0.4)
血液量減少症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
空腹時血中ブドウ糖不良	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
食欲亢進	0	1 (1.6)	1 (1.0)	0	2 (0.3)	2 (0.2)	0	1 (0.2)	1 (0.1)
代謝性アシドーシス	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
ビタミンD欠乏	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (1.6)	1 (1.0)	10 (2.6)	8 (1.4)	18 (1.9)	10 (2.9)	7 (1.4)	17 (2.0)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
筋骨格系および結合組織障害									
関節痛	2 (5.1)	1 (1.6)	3 (3.0)	11 (2.9)	18 (3.1)	29 (3.0)	9 (2.6)	17 (3.3)	26 (3.1)
関節炎	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
軸性脊椎関節炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
背部痛	1 (2.6)	2 (3.3)	3 (3.0)	4 (1.1)	14 (2.4)	18 (1.9)	3 (0.9)	12 (2.3)	15 (1.8)
滑液包炎	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
側腹部痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
尺骨部痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
関節雑音	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
関節可動域低下	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
関節腫脹	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
筋痙縮	0	0	0	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	3 (0.6)	4 (0.5)
筋緊張	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
筋骨格痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
筋骨格硬直	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
筋肉痛	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
頚部痛	1 (2.6)	0	1 (1.0)	1 (0.3)	1 (0.2)	2 (0.2)	0	1 (0.2)	1 (0.1)
変形性関節症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
四肢痛	1 (2.6)	1 (1.6)	2 (2.0)	2 (0.5)	2 (0.3)	4 (0.4)	1 (0.3)	1 (0.2)	2 (0.2)

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
筋骨格系および結合組織障害 (Cont.)									
顎痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
肩回旋筋腱板症候群	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
仙腸骨炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	3 (7.7)	4 (6.6)	7 (7.0)	26 (6.9)	45 (7.9)	71 (7.5)	23 (6.8)	41 (8.0)	64 (7.5)
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）									
肛門性器疣贅	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
基底細胞癌	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
表皮内悪性黒色腫	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
メラノサイト性母斑	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
子宮頚部扁平上皮癌	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (1.6)	1 (1.0)	3 (0.8)	2 (0.3)	5 (0.5)	3 (0.9)	1 (0.2)	4 (0.5)

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
神経系障害									
浮動性めまい	0	2 (3.3)	2 (2.0)	4 (1.1)	14 (2.4)	18 (1.9)	4 (1.2)	12 (2.3)	16 (1.9)
蟻走感	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
頭痛	0	1 (1.6)	1 (1.0)	23 (6.1)	48 (8.4)	71 (7.5)	23 (6.8)	47 (9.2)	70 (8.2)
感覚鈍麻	1 (2.6)	0	1 (1.0)	2 (0.5)	3 (0.5)	5 (0.5)	1 (0.3)	3 (0.6)	4 (0.5)
嗜眠	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
片頭痛	0	0	0	2 (0.5)	4 (0.7)	6 (0.6)	2 (0.6)	4 (0.8)	6 (0.7)
神経痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
錯感覚	0	0	0	1 (0.3)	4 (0.7)	5 (0.5)	1 (0.3)	4 (0.8)	5 (0.6)
失神寸前の状態	0	0	0	2 (0.5)	2 (0.3)	4 (0.4)	2 (0.6)	2 (0.4)	4 (0.5)
神経根障害	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
痙攣発作	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
傾眠	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
失神	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
振戦	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	1 (2.6)	3 (4.9)	4 (4.0)	35 (9.2)	70 (12.2)	105 (11.0)	34 (10.0)	67 (13.1)	101 (11.9)

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
精神障害									
不安	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
抑うつ気分	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
不眠症	0	1 (1.6)	1 (1.0)	2 (0.5)	3 (0.5)	5 (0.5)	2 (0.6)	2 (0.4)	4 (0.5)
パニック発作	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (1.6)	1 (1.0)	3 (0.8)	6 (1.0)	9 (0.9)	3 (0.9)	5 (1.0)	8 (0.9)
腎および尿路障害									
急性腎障害	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
着色尿	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
排尿困難	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
血尿	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
高シュウ酸尿症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
腎結石症	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
夜間頻尿	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
多尿	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
腎仙痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
腎不全	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
腎および尿路障害 (Cont.)									
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	5 (1.3)	7 (1.2)	12 (1.3)	5 (1.5)	7 (1.4)	12 (1.4)
生殖系および乳房障害									
バルトリン嚢腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
不正子宮出血	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
卵巣嚢胞	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
骨盤痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
呼吸器、胸郭および縦隔障害									
喘息	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
咳嗽	0	0	0	6 (1.6)	9 (1.6)	15 (1.6)	6 (1.8)	9 (1.8)	15 (1.8)
発声障害	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
呼吸困難	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
鼻出血	0	0	0	0	3 (0.5)	3 (0.3)	0	3 (0.6)	3 (0.4)
鼻閉	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)									
口腔咽頭痛	1 (2.6)	2 (3.3)	3 (3.0)	6 (1.6)	17 (3.0)	23 (2.4)	5 (1.5)	15 (2.9)	20 (2.3)
咽頭障害	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
湿性咳嗽	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
鼻漏	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
副鼻腔うっ血	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (2.6)	2 (3.3)	3 (3.0)	14 (3.7)	30 (5.2)	44 (4.6)	13 (3.8)	28 (5.5)	41 (4.8)
皮膚および皮下組織障害									
ざ瘡	0	1 (1.6)	1 (1.0)	3 (0.8)	2 (0.3)	5 (0.5)	3 (0.9)	1 (0.2)	4 (0.5)
脱毛症	1 (2.6)	1 (1.6)	2 (2.0)	8 (2.1)	5 (0.9)	13 (1.4)	7 (2.1)	4 (0.8)	11 (1.3)
血管浮腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
冷汗	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
頭部粃糠疹	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
皮膚炎	0	0	0	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	3 (0.6)	4 (0.5)
アトピー性皮膚炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
接触皮膚炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
乾癬様皮膚炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
皮膚および皮下組織障害 (Cont.)									
皮膚乾燥	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
湿疹	0	1 (1.6)	1 (1.0)	2 (0.5)	2 (0.3)	4 (0.4)	2 (0.6)	1 (0.2)	3 (0.4)
紅斑	1 (2.6)	0	1 (1.0)	2 (0.5)	5 (0.9)	7 (0.7)	1 (0.3)	5 (1.0)	6 (0.7)
結節性紅斑	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
男性型多毛症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
多汗症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
多毛症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
寝汗	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
そう痒症	0	0	0	3 (0.8)	3 (0.5)	6 (0.6)	3 (0.9)	3 (0.6)	6 (0.7)
全身性そう痒症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
乾癬	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
発疹	3 (7.7)	0	3 (3.0)	11 (2.9)	10 (1.7)	21 (2.2)	8 (2.4)	10 (2.0)	18 (2.1)
紅斑性皮疹	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
斑状丘疹状皮疹	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
丘疹性皮疹	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
顔面腫脹	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
蕁麻疹	1 (2.6)	0	1 (1.0)	2 (0.5)	1 (0.2)	3 (0.3)	1 (0.3)	1 (0.2)	2 (0.2)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
皮膚および皮下組織障害 (Cont.)									
SUBJECTS WITH ONE OR MORE EVENTS	5 (12.8)	3 (4.9)	8 (8.0)	36 (9.5)	41 (7.2)	77 (8.1)	31 (9.1)	38 (7.4)	69 (8.1)
外科および内科処置									
創部ドレナージ	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
血管障害									
血腫	0	0	0	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	3 (0.6)	4 (0.5)
出血	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
高血圧	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
低血圧	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
蒼白	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
末梢静脈疾患	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
表在性静脈炎	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
血栓性静脈炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，
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	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
血管障害 (Cont.)									
静脈血栓症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	8 (2.1)	7 (1.2)	15 (1.6)	8 (2.4)	7 (1.4)	15 (1.8)

NOTE: THE SUM OF THE TOTAL NUMBER OF SUBJECTS REPORTING EACH OF THE PREFERRED TERMS SHOULD BE GREATER THAN OR EQUAL TO THE SYSTEM ORGAN CLASS TOTAL. A SUBJECT WHO REPORTS TWO OR MORE DIFFERENT PREFERRED TERMS WHICH ARE IN THE SAME SYSTEM ORGAN CLASS IS COUNTED ONLY ONCE IN THE SYSTEM ORGAN CLASS TOTAL.
TREATMENT-EMERGENT ADVERSE EVENTS DURING INDUCTION STUDY ARE DEFINED AS EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY MEDICATION AND UP TO THE FIRST DOSE OF THE STUDY MEDICATION IN MAINTENANCE STUDY FOR THOSE WHO ARE RE-RANDOMIZED AT WEEK 8, OR EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY DRUG AND WITHIN 70 DAYS AFTER THE LAST DOSE OF THE STUDY MEDICATION IN THE INDUCTION STUDY FOR SUBJECTS WHO ARE NOT RE-RANDOMIZED.

Cross Reference: M14-033 Induction Japan Sub-study Final CSR Table 14.3__1.2_J

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
ANY ADVERSE EVENT	8 (20.5)	11 (18.0)	19 (19.0)	83 (21.9)	149 (26.0)	232 (24.4)	75 (22.1)	138 (27.0)	213 (25.0)
血液およびリンパ系障害									
貧血	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
白血球減少症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
リンパ節症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
好中球減少症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
血小板減少症	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	2 (0.5)	4 (0.7)	6 (0.6)	2 (0.6)	4 (0.8)	6 (0.7)
心臓障害									
動悸	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET / ADALIMUMAB			INTEGRATED SAFETY SET / ADALIMUMAB			SAFETY SET / ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
先天性、家族性および遺伝性障害									
エーラース・ダンロス症候群	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
眼障害									
眼瞼痙攣	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ドライアイ	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
眼瞼湿疹	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
眼痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
眼瞼浮腫	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
羞明	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	4 (1.1)	4 (0.7)	8 (0.8)	4 (1.2)	4 (0.8)	8 (0.9)
胃腸障害									
腹部膨満	1 (2.6)	0	1 (1.0)	1 (0.3)	0	1 (0.1)	0	0	0
腹痛	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
胃腸障害 (Cont.)									
上腹部痛	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
根尖肉芽腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
潰瘍性大腸炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
下痢	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
鼓腸	0	0	0	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	3 (0.6)	4 (0.5)
歯肉出血	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
歯肉痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
血栓性痔核	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
悪心	0	0	0	6 (1.6)	7 (1.2)	13 (1.4)	6 (1.8)	7 (1.4)	13 (1.5)
嚥下痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
直腸しぶり	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
嘔吐	0	1 (1.6)	1 (1.0)	2 (0.5)	4 (0.7)	6 (0.6)	2 (0.6)	3 (0.6)	5 (0.6)
SUBJECTS WITH ONE OR MORE EVENTS	1 (2.6)	1 (1.6)	2 (2.0)	11 (2.9)	17 (3.0)	28 (2.9)	10 (2.9)	16 (3.1)	26 (3.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
一般・全身障害および投与部位の状態									
投与部位疼痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
適用部位そう痒感	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
適用部位反応	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
無力症	0	0	0	3 (0.8)	3 (0.5)	6 (0.6)	3 (0.9)	3 (0.6)	6 (0.7)
胸痛	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
悪寒	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
疲労	0	0	0	5 (1.3)	9 (1.6)	14 (1.5)	5 (1.5)	9 (1.8)	14 (1.6)
冷感	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
インフルエンザ様疾患	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
注射部位内出血	0	0	0	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	3 (0.6)	4 (0.5)
注射部位紅斑	1 (2.6)	0	1 (1.0)	3 (0.8)	14 (2.4)	17 (1.8)	2 (0.6)	14 (2.7)	16 (1.9)
注射部位過敏反応	0	0	0	0	3 (0.5)	3 (0.3)	0	3 (0.6)	3 (0.4)
注射部位硬結	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射部位炎症	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
注射部位腫瘤	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射部位浮腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射部位疼痛	0	0	0	3 (0.8)	6 (1.0)	9 (0.9)	3 (0.9)	6 (1.2)	9 (1.1)
注射部位そう痒感	0	0	0	2 (0.5)	13 (2.3)	15 (1.6)	2 (0.6)	13 (2.5)	15 (1.8)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

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一般・全身障害および投与部位の状態 (Cont.)									
注射部位発疹	0	0	0	1 (0.3)	4 (0.7)	5 (0.5)	1 (0.3)	4 (0.8)	5 (0.6)
注射部位反応	2 (5.1)	5 (8.2)	7 (7.0)	3 (0.8)	24 (4.2)	27 (2.8)	1 (0.3)	19 (3.7)	20 (2.3)
注射部位腫脹	0	0	0	2 (0.5)	9 (1.6)	11 (1.2)	2 (0.6)	9 (1.8)	11 (1.3)
注射部位蕁麻疹	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
末梢性浮腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
疼痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
発熱	0	1 (1.6)	1 (1.0)	3 (0.8)	1 (0.2)	4 (0.4)	3 (0.9)	0	3 (0.4)
腫脹	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	3 (7.7)	6 (9.8)	9 (9.0)	24 (6.3)	77 (13.4)	101 (10.6)	21 (6.2)	71 (13.9)	92 (10.8)
肝胆道系障害									
高トランスアミナーゼ血症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
免疫系障害									
薬物過敏症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
過敏症	0	1 (1.6)	1 (1.0)	1 (0.3)	3 (0.5)	4 (0.4)	1 (0.3)	2 (0.4)	3 (0.4)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (1.6)	1 (1.0)	1 (0.3)	4 (0.7)	5 (0.5)	1 (0.3)	3 (0.6)	4 (0.5)
感染症および寄生虫症									
四肢膿瘍	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ブラストシスティス感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
ウイルス性気管支炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
カンジダ感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
クロストリジウム・ディフィシレ感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
結膜炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
膀胱炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
サイトメガロウイルス感染	1 (2.6)	0	1 (1.0)	1 (0.3)	0	1 (0.1)	0	0	0
毛包炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
真菌感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
胃腸炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
感染症および寄生虫症 (Cont.)									
消化管感染	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
単純ヘルペス	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
ヘルペスウイルス感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
帯状疱疹	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
麦粒腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
感染性嚢腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
インフルエンザ	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
喉頭炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
上咽頭炎	0	1 (1.6)	1 (1.0)	3 (0.8)	4 (0.7)	7 (0.7)	3 (0.9)	3 (0.6)	6 (0.7)
食道カンジダ症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
口腔ヘルペス	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
咽頭炎	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
肺炎	1 (2.6)	0	1 (1.0)	2 (0.5)	1 (0.2)	3 (0.3)	1 (0.3)	1 (0.2)	2 (0.2)
膿疱性皮疹	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
副鼻腔炎	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
白癬感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
歯感染	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
結核	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

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感染症および寄生虫症 (Cont.)									
上気道感染	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
尿路感染	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
ウイルス性上気道感染	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
外陰部腟カンジダ症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	2 (5.1)	3 (4.9)	5 (5.0)	19 (5.0)	26 (4.5)	45 (4.7)	17 (5.0)	23 (4.5)	40 (4.7)
傷害、中毒および処置合併症									
挫傷	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
注射に伴う反応	0	1 (1.6)	1 (1.0)	0	2 (0.3)	2 (0.2)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (1.6)	1 (1.0)	0	3 (0.5)	3 (0.3)	0	2 (0.4)	2 (0.2)
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	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (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	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

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SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
臨床検査 (Cont.)									
血中ビリルビン増加	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
血中コレステロール増加	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
血中リン減少	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
血圧上昇	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
血中トリグリセリド増加	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
呼吸音異常	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
C－反応性蛋白増加	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
クロストリジウム検査陽性	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
白血球数減少	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	6 (1.6)	7 (1.2)	13 (1.4)	6 (1.8)	7 (1.4)	13 (1.5)
代謝および栄養障害									
高コレステロール血症	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
高血糖	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)

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筋骨格系および結合組織障害									
関節痛	0	1 (1.6)	1 (1.0)	5 (1.3)	6 (1.0)	11 (1.2)	5 (1.5)	5 (1.0)	10 (1.2)
背部痛	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
側腹部痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
関節雑音	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
関節可動域低下	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
関節腫脹	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
筋痙縮	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
筋骨格痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
筋肉痛	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
頚部痛	1 (2.6)	0	1 (1.0)	1 (0.3)	0	1 (0.1)	0	0	0
四肢痛	0	1 (1.6)	1 (1.0)	0	1 (0.2)	1 (0.1)	0	0	0
顎痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (2.6)	1 (1.6)	2 (2.0)	9 (2.4)	12 (2.1)	21 (2.2)	8 (2.4)	11 (2.1)	19 (2.2)

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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）									
肛門性器疣贅	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
表皮内悪性黒色腫	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
神経系障害									
浮動性めまい	0	1 (1.6)	1 (1.0)	1 (0.3)	4 (0.7)	5 (0.5)	1 (0.3)	3 (0.6)	4 (0.5)
蟻走感	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
頭痛	0	0	0	12 (3.2)	12 (2.1)	24 (2.5)	12 (3.5)	12 (2.3)	24 (2.8)
片頭痛	0	0	0	0	3 (0.5)	3 (0.3)	0	3 (0.6)	3 (0.4)
神経痛	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
痙攣発作	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	1 (1.6)	1 (1.0)	13 (3.4)	21 (3.7)	34 (3.6)	13 (3.8)	20 (3.9)	33 (3.9)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
精神障害									
不安	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
不眠症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	2 (0.5)	0	2 (0.2)	2 (0.6)	0	2 (0.2)
腎および尿路障害									
着色尿	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
排尿困難	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
血尿	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
高シュウ酸尿症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	0	2 (0.3)	2 (0.2)	0	2 (0.4)	2 (0.2)
生殖系および乳房障害									
バルトリン嚢腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
呼吸器、胸郭および縦隔障害									
咳嗽	0	0	0	4 (1.1)	5 (0.9)	9 (0.9)	4 (1.2)	5 (1.0)	9 (1.1)
呼吸困難	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
鼻出血	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
鼻閉	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
口腔咽頭痛	1 (2.6)	1 (1.6)	2 (2.0)	1 (0.3)	5 (0.9)	6 (0.6)	0	4 (0.8)	4 (0.5)
咽頭障害	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
鼻漏	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
副鼻腔うっ血	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	1 (2.6)	1 (1.6)	2 (2.0)	8 (2.1)	11 (1.9)	19 (2.0)	7 (2.1)	10 (2.0)	17 (2.0)
皮膚および皮下組織障害									
脱毛症	1 (2.6)	0	1 (1.0)	4 (1.1)	4 (0.7)	8 (0.8)	3 (0.9)	4 (0.8)	7 (0.8)
血管浮腫	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
冷汗	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
皮膚炎	0	0	0	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	2 (0.4)	3 (0.4)
アトピー性皮膚炎	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET ADALIMUMAB			INTEGRATED SAFETY SET ADALIMUMAB			SAFETY SET ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
皮膚および皮下組織障害 (Cont.)									
乾癬様皮膚炎	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
皮膚乾燥	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
湿疹	0	1 (1.6)	1 (1.0)	1 (0.3)	2 (0.3)	3 (0.3)	1 (0.3)	1 (0.2)	2 (0.2)
紅斑	0	0	0	0	4 (0.7)	4 (0.4)	0	4 (0.8)	4 (0.5)
多汗症	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
寝汗	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
そう痒症	0	0	0	3 (0.8)	1 (0.2)	4 (0.4)	3 (0.9)	1 (0.2)	4 (0.5)
全身性そう痒症	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
乾癬	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
発疹	2 (5.1)	0	2 (2.0)	6 (1.6)	3 (0.5)	9 (0.9)	4 (1.2)	3 (0.6)	7 (0.8)
紅斑性皮疹	0	0	0	2 (0.5)	1 (0.2)	3 (0.3)	2 (0.6)	1 (0.2)	3 (0.4)
丘疹性皮疹	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
蕁麻疹	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	3 (7.7)	1 (1.6)	4 (4.0)	21 (5.5)	24 (4.2)	45 (4.7)	18 (5.3)	23 (4.5)	41 (4.8)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（統合安全性解析対象集団，日本人安全性解析対象集団及び主試験安全性解析対象集団，M14-033 日本サブ試験の導入療法試験）（続き）

	JAPAN SAFETY SET / ADALIMUMAB			INTEGRATED SAFETY SET / ADALIMUMAB			SAFETY SET / ADALIMUMAB		
SYSTEM ORGAN CLASS MEDDRA 22.0 PREFERRED TERM	STANDARD DOSE (N=39) n (%)	HIGHER DOSE (N=61) n (%)	TOTAL (N=100) n (%)	STANDARD DOSE (N=379) n (%)	HIGHER DOSE (N=573) n (%)	TOTAL (N=952) n (%)	STANDARD DOSE (N=340) n (%)	HIGHER DOSE (N=512) n (%)	TOTAL (N=852) n (%)
血管障害									
血腫	0	0	0	1 (0.3)	1 (0.2)	2 (0.2)	1 (0.3)	1 (0.2)	2 (0.2)
低血圧	0	0	0	1 (0.3)	0	1 (0.1)	1 (0.3)	0	1 (0.1)
末梢静脈疾患	0	0	0	0	1 (0.2)	1 (0.1)	0	1 (0.2)	1 (0.1)
SUBJECTS WITH ONE OR MORE EVENTS	0	0	0	2 (0.5)	2 (0.3)	4 (0.4)	2 (0.6)	2 (0.4)	4 (0.5)

NOTE: THE SUM OF THE TOTAL NUMBER OF SUBJECTS REPORTING EACH OF THE PREFERRED TERMS SHOULD BE GREATER THAN OR EQUAL TO THE SYSTEM ORGAN CLASS TOTAL. A SUBJECT WHO REPORTS TWO OR MORE DIFFERENT PREFERRED TERMS WHICH ARE IN THE SAME SYSTEM ORGAN CLASS IS COUNTED ONLY ONCE IN THE SYSTEM ORGAN CLASS TOTAL.
TREATMENT-EMERGENT ADVERSE EVENTS DURING INDUCTION STUDY ARE DEFINED AS EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY MEDICATION AND UP TO THE FIRST DOSE OF THE STUDY MEDICATION IN MAINTENANCE STUDY FOR THOSE WHO ARE RE-RANDOMIZED AT WEEK 8, OR EVENTS THAT BEGIN OR WORSEN EITHER ON OR AFTER THE FIRST DOSE OF THE STUDY DRUG AND WITHIN 70 DAYS AFTER THE LAST DOSE OF THE STUDY MEDICATION IN THE INDUCTION STUDY FOR SUBJECTS WHO ARE NOT RE-RANDOMIZED.
EVENT WITH UNKNOWN RELATIONSHIP TO STUDY DRUG IS BEING COUNTED AS DRUG-RELATED.

Cross reference: M14-033 Induction Japan Sub-study Final CSR Table 14.3__1.5_J

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
四肢痛	X			
創部ドレナージ	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	6[redacted]	MALE	White

Medical History*	Onset Date
CORONARY ARTERY DISEASE: TRIPLE BY PASS SURGERY	[redacted]20[redacted]
DEPRESSION: ANXIETY	[redacted]20[redacted]
DIABETES MELLITUS	[redacted]19[redacted]
HYPERLIPIDEMIA: HIGH CHOLESTEROL	[redacted]19[redacted]
HYPERTENSION	[redacted]19[redacted]
MYOCARDIAL INFARCTION	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ATOPIC DERMATITIS	[redacted]20[redacted]
OTHER: DEEP VEIN THROMBOSIS	[redacted]20[redacted]
OTHER: THROMBOCYTOPENIA	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
				[redacted]20[redacted] / 57	[redacted]20[redacted] / 189	133

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
VITAMINS NOS	1 TAB	QD	Y: 20[redacted]	ONGOING
METOPROLOL	100 mg (milligram(s))	QD	-344	ONGOING
RANOLAZINE	500 mg (milligram(s))	QD	-344	ONGOING
SIMVASTATIN	10 mg (milligram(s))	QD	-344	ONGOING
SIMVASTATIN	10 mg (milligram(s))	QD	-344	ONGOING
MESALAZINE	1.2 g (gram(s))	QD	-275	ONGOING
INSULIN GLARGINE	30 mg/kg (milligram(s)/kilogram)	QD	-253	ONGOING
METFORMIN	500 mg (milligram(s))	QD	-253	ONGOING
GLIPIZIDE	10 mg (milligram(s))	QD	-132	ONGOING
PREDNISONE	40 mg (milligram(s))	QD	-83	28
MERCAPTOPURINE	50 mg (milligram(s))	QD	-70	ONGOING
BACTRIM	2 TABS	BID	21	30
PREDNISONE	30 mg (milligram(s))	QD	29	35
PREDNISONE	20 mg (milligram(s))	QD	36	42
GLUCOSE	15 g (gram(s))	PRN	43	44
MORPHINE	2 mg (milligram(s))	PRN	43	45
MAGNESIUM HYDROXIDE	30 mL (millilitre(s))	PRN	43	47
ONDANSETRON	4 mg (milligram(s))	PRN	43	48
PREDNISONE	10 mg (milligram(s))	QD	43	49
VICODIN	2 TABS	PRN	43	56
ACETYLSALICYLIC ACID	81 mg (milligram(s))	QD	43	ONGOING
PARACETAMOL	650 mg (milligram(s))	PRN	43	ONGOING

Event #1: Serious Adverse Event*

Event Description	SEVERE LEG PAIN DRAINING WOUND
Preferred term	四肢痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	6[redacted]
AE Stopped Rx Day	49
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ACTIVE DIABETES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION, IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Event #2: Serious Adverse Event*

Event Description	SEVERE LEG PAIN DRAINING WOUND
Preferred term	創部ドレナージ
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	6[redacted]
AE Stopped Rx Day	49
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ACTIVE DIABETES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION, IMPORTANT MEDICAL OR SURGICAL INTERVENTION

* Information presented verbatim as provided by the investigator.

Investigator No.:[redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（米国）であり，重篤な有害事象の排液性創傷による高度の下肢痛を発現した。関連する病歴は，高血圧，糖尿病，コレステロール高値，血小板減少症，三枝血管バイパス術，深部静脈血栓症，心筋梗塞，アトピー性皮膚炎及び潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，排液性創傷による高度の下肢痛が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，排液性創傷による高度の下肢痛は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，下肢の擦傷（非重篤）が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，左ふくらはぎに有痛性の排液性創傷が認められ，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，外科的治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてモルヒネ，Zosyn（タゾバクタム／ピペラシリン水和物），hydrocodone／アセトアミノフェン，テトラサイクリン，Bactrim（スルファメトキサゾール／トリメトプリム）及びTylenol（アセトアミノフェン）が投与された。

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Wound drainage (10050325) (Wound drainage (10050325)) [v.20.1] [10050325]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Leg pain (10024130) (Pain in extremity (10033425)) [v.20.1] [10024130]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of SEVERE LEG PAIN DRAINING WOUND

- Investigator: Active Diabetes

- AbbVie: Event is more likely related to preceding abrasion. Additional risk factors include diabetes mellitus and obesity.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	3[redacted]	MALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: ATTENTION DEFICIT HYPERACTIVITY DISORDER	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
				[redacted]20[redacted] / 60	[redacted]20[redacted] / 165	106

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
OBETROL	10 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
MESALAZINE	2400 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
AXOTAL	50/325/40 mg (milligram(s))	QD	29	60
METHYLPREDNISOLONE	125 mg (milligram(s))	Other	47	47
MORPHINE	4 mg (milligram(s))	Other	47	47
ONDANSETRON	4 mg (milligram(s))	Other	47	47
PARACETAMOL	650 mg (milligram(s))	Other	47	47

Event #1: Serious Adverse Event*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 47
Age at AE Onset	3[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	WORSENING OF ULCERATIVE COLITIS; NOT RESPONDING TO HUMIRA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。

被験者に発熱，悪寒，嘔吐，血性下痢及び左側腹痛が認められた。

入院記録に基づく情報：20[redacted]年[redacted]月[redacted]日，被験者は入院した。腹痛が4日間認められていた。過去数ヵ月間に潰瘍性大腸炎の再燃はみられなかったが，4 日前にクリームチーズを摂取した後，腹痛が発現した。被験者によると，被験者には以前から乳製品による重大な問題が認められていた。下痢及び黒色の液状便のため，被験者は一晩中起きていた。翌日，ほうれん草を摂取した後に高度の下痢が認められ，このときを除いて便は鮮紅色であった。母親が医師に電話したところ，Augmentin（クラブラン酸カリウム／アモキシシリン水和物）の服用を勧められた。被験者は Augmentin（クラブラン酸カリウム／アモキシシリン水和物）1 g を 1 日 2 回服用したが改善せず，医師は救急科を受診するよう勧めた。被験者によると，痛みは高度で，主に左下腹部に認められた。被験者が過去に経験したことがない最大の腹痛であり，これまでの再燃時の痛みよりも高度であった。また，38.3°C の発熱及び発汗が認められた。咳嗽，悪寒，胸痛又は排尿困難はみられなかった。20[redacted]年[redacted]月[redacted]日，被験者は退院した。
治療薬として Augmentin（クラブラン酸カリウム／アモキシシリン水和物），モルヒネ，Fioricet，prednisone，Lomotil，Tylenol（アセトアミノフェン），Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び Zofran（オンダンセトロン塩酸塩水和物）が投与された。

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Worsening of ulcerative colitis; not responding to Humira.

- AbbVie: The worsening of UC was possibly related to a viral infection

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] aspartate aminotrans: 85 U/L (normal 14 to 59)

[redacted] 20[redacted] Blood pressure: 114/53 mmHg

[redacted] 20[redacted] body temperature: 101.9F

Unknown date body temperature: 37.7 Degrees C

[redacted] 20[redacted] Chest x-ray PA/Lat:

Worsening intestinal process which may represent atypical infection. Developing interstitial lung disease difficult to exclude.

[redacted] 20[redacted] CT abdomen/pelvis/w contrast:

Impression: diffuse wall thickening in the descending and rectosigmoid colon likely colitis. 2. No evidence of obstruction or free fluid. 3. Enlarged mesenteric lymph nodes, nonspecific.

[redacted] 20[redacted] hematocrit: 42.2 % (normal 41 to 53)

[redacted] 20[redacted] hemoglobin: 14.2 G/DL (normal 13.9 to 16.3)

[redacted] 20[redacted] white blood cell count: 9.51 (normal 4.5 to 11.0)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		
血液量減少症	X			
腎不全	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	5[redacted]	MALE	Black

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: ABDOMINAL PAIN	[redacted]20[redacted]
SURGERY: LEFT KNEE ARTHROSCOPY	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]0[redacted] / 15	15

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
PREDNISONE	30 mg (milligram(s))	QD	Y:	ONGOING
TRAMADOL	50 mg (milligram(s))	PRN	-10	36
MOVIPREP	UNK mL (millilitre(s))	QD	-8	-8
PROPOFOL	400 mg (milligram(s))	Other	-7	-7
DOXEPIN	10 mg (milligram(s))	QD	8	18
SODIUM CHLORIDE	1 L (litre(s))	Other	8	8
SODIUM CHLORIDE	2 L (litre(s))	Other	11	11
SODIUM CHLORIDE	1 L (litre(s))	Other	18	18
LOPERAMIDE	2 mg (milligram(s))	PRN	18	34
COLESTYRAMINE	4 g (gram(s))	QD	18	ONGOING
DIAZEPAM	2.5 mg (milligram(s))	QD	18	ONGOING
PREDNISONE	30 mg (milligram(s))	QD	21	36
METHYLPREDNISOLONE	100 mg (milligram(s))	Other	22	22
SODIUM CHLORIDE	2 L (litre(s))	Other	22	22
HYDROMORPHONE	1 mg (milligram(s))	Other	24	24
SODIUM CHLORIDE	1000 mL (millilitre(s))	Other	24	24
ONDANSETRON	4 mg (milligram(s))	Other	24	35

Event #1: AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 21 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	23 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	NOT APPLICABLE
Other Cause of Event	
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event*

Event Description	ULCERATIVE COLITIS EXACERBATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 24 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	36 (21 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	DISEASE UNDER STUDY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #3: Serious Adverse Event*

Event Description	RENAL INSUFFICIENCY WITH VOLUME DEPLETION
Preferred term	血液量減少症
AE Onset Date / Rx Day	[redacted]20[redacted] / 24 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	36 (21 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS EXACERBATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎の増悪及び体液量減少を伴う腎機能障害を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪及び体液量減少を伴う腎機能障害が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は血性下痢，悪心の悪化及び脱力の症状を呈し，救急治療室を受診した。潰瘍性大腸炎の増悪及び体液量減少を伴う腎機能障害と診断され，被験者は入院した。薬剤投与によって被験者の状態は改善し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪及び体液量減少を伴う腎機能障害は回復した。

治療薬として塩化カリウム，Levaquin（レボフロキサシン水和物），Zofran（オンダンセトロン塩酸塩水和物），硫酸マグネシウム，Pepcid（ファモチジン），5%ブドウ糖，Cortenema（ヒドロコルチゾン），Imodium（ロペラミド塩酸塩），prednisone，モルヒネ硫酸塩水和物，ヒドロモルフォン，Sol-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び Tylenol（アセトアミノフェン）が投与された。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Renal insufficiency (10038474) (Renal failure (10038435)) [v.19.0] [10038474]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

3) Volume depletion (10047691) (Hypovolaemia (10021137)) [v.19.0] [10047691]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS EXACERBATION

- Investigator: Disease under study.

- AbbVie: Disease severity and activity. The patient with severe ulcerative colitis (Baseline Mayo Score 12), without no improvement in stool frequency up to week two of study treatment.

Event of RENAL INSUFFICIENCY WITH VOLUME DEPLETION

- Investigator: Ulcerative colitis exacerbation.

- AbbVie: The patient with severe ulcerative colitis (Baseline Mayo Score 12), and no improvement in stool frequency up to week two of study, which may have contributed to the dehydration and elevation of creatinine levels. Baseline creatinine levels were in the upper limit since baseline, and dehydration was observed early in the study.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] colonoscopy:

showed severe disease (spontaneous bleeding and ulceration to the rectum, sigmoid and descending colon), marked erythema, absent vascular pattern, friability, and erosions to the transverse colon, erythema, decreased vascular pattern and mild friability in the ascending colon and cecum.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	5[redacted]	FEMALE	White

Medical History*	Onset Date
DRUG ALLERGIES/REACTIONS: SULFASALAZINE ALLERGY	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: CHRONIC TENSION HEADACHES	19[redacted]
OTHER: DILATION AND CURETTAGE	19[redacted]
OTHER: OSTEOPENIA	[redacted]20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
SURGERY: LEFT PHOTOREFRACTIVE KERATECTOMY	19[redacted]
SURGERY: RIGHT BENIGN BREAST BIOPSY	19[redacted]
SURGERY: RIGHT PHOTOREFRACTIVE KERATECTOMY	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
				[redacted]20[redacted] / 59	[redacted]20[redacted] / 79	21

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
PARACETAMOL	325 mg (milligram(s))	PRN	Y: 20[redacted]	ONGOING
LORATADINE	10 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
AXOTAL	1 TABLET	PRN	Y: 20[redacted]	ONGOING
CILEST	1 TABLET	QD	Y: 20[redacted]	ONGOING
PREDNISONE	20 mg (milligram(s))	QD	-21	29
TRAMADOL	50 mg (milligram(s))	PRN	14	ONGOING
VITAMINS, OTHER COMBINATIONS	1 TABLET	QD	23	ONGOING
PREDNISONE	15 mg (milligram(s))	QD	30	36
PREDNISONE	10 mg (milligram(s))	QD	37	43
PREDNISONE	7.5 mg (milligram(s))	QD	44	50
PREDNISONE	5 mg (milligram(s))	QD	51	57
DIAZEPAM	5 mg (milligram(s))	QD	52	ONGOING
FENTANYL	50 mcg (microgram(s))	Other	55	55
ONDANSETRON	4 mg (milligram(s))	Other	55	55
MORPHINE	2 mg (milligram(s))	Other	55	56

Event #1: Serious Adverse Event*

Event Description	ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 55
Age at AE Onset	5[redacted]
AE Stopped Rx Day	56
Duration of AE	2 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	DISEASE UNDER STUDY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: [redacted]

本被験者は，5[redacted] 歳の女性（米国）であり，重篤な有害事象の潰瘍性大腸炎を発現した。関連する病歴は，活動性潰瘍性大腸炎：左側潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎が発現した。
20[redacted] 年 [redacted] 月 [redacted] 日，高度かつ広範囲にわたる腹痛が認められ，被験者は救急治療室を受診した。フェンタニルが静脈内投与された。疼痛及び潰瘍性大腸炎の再燃のため，一晩被験者を入院させ，疼痛が消失するまで麻酔剤を静脈内投与することが決定された。このため，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院した。症状の経過／持続期間は一定していた。増悪因子又は緩和因子は認められなかった。過去には慢性的及び偶発的なエピソードがみられた。腹部の身体診察所見は柔軟で圧痛はなく，膨満も認められなかった。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎は回復した。

治療薬として Zofran（オンダンセトロン塩酸塩水和物），モルヒネ，Norco，プロポフォール，Fleet enema 及びフェンタニルが投与された。

The patient's past medications include:

APRISO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Ulcerative colitis (10045365) (Colitis ulcerative (10009900)) [v.18.1] [10045365]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS

- Investigator: Disease under study

- AbbVie: The subject has persistent sever disease activity after 4 of treatment with adalimumab

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	4[redacted]	MALE	White

Medical History*	Onset Date
ANEMIA: SECONDARY TO UC	[redacted]20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
NEPHROLITHIASIS: USUALLY OCCURS EVERY 2 - 3 YEARS.	19[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ANXIETY	20[redacted]
OTHER: HIP PAIN SECONDARY TO UC	[redacted]20[redacted]
OTHER: INSOMNIA SECONDARY TO PREDNISONE.	[redacted]20[redacted]
OTHER: SKIN PUSTULES LIKELY ERYTHEMA NODOSUM, SECONDARY TO UC	[redacted]20[redacted]
SURGERY: TONSILLECTOMY	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Former (5 YEARS, 0.5 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
				[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
ALPRAZOLAM	0.5 mg (milligram(s))	PRN	Y: 20[redacted]	ONGOING
OMEPRAZOLE	40 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
BALSALAZIDE	750 mg (milligram(s))	TID	-300	ONGOING
PREDNISONE	40 mg (milligram(s))	QD	-300	ONGOING
IRON	65 mg (milligram(s))	QD	-234	ONGOING
OXYCODONE	5 mg (milligram(s))	PRN	-45	ONGOING
CIPROFLOXACIN	500 mg (milligram(s))	BID	30	33
ATROPA BELLADONNA	1 SUPPOSITORY	PRN	33	36
DIAZEPAM	2.5 mg (milligram(s))	PRN	33	36
HYDROMORPHONE	1 mg (milligram(s))	PRN	33	36
ONDANSETRON	4 mg (milligram(s))	PRN	33	36
POTASSIUM	40 mg (milligram(s))	BID	33	36
SODIUM CHLORIDE	1000 mL (millilitre(s))	PRN	33	37
VANCOMYCIN	UNK UNK	Other	34	35
POTASSIUM	40 mg (milligram(s))	TID	34	37
TAMSULOSIN	0.4 mg (milligram(s))	QD	34	ONGOING
CIPROFLOXACIN	500 mg (milligram(s))	BID	37	54
METHYLPREDNISOLONE	40 mg (milligram(s))	BID	42	43
UNACID	UNK UNKOWN	QID	42	43

Event #1: Serious Adverse Event*

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 29
Age at AE Onset	4[redacted]
AE Stopped Rx Day	37
Duration of AE	9 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	WORSENING OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event*

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted]/ 42
Age at AE Onset	4[redacted]
AE Stopped Rx Day	43
Duration of AE	2 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	WORSENING OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted]歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎の増悪が 2 回（20[redacted]年[redacted]月[redacted]日及び 20[redacted]年[redacted]月[redacted]日）認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎及び潰瘍性大腸炎に伴う貧血であった。

20[redacted]年[redacted]月[redacted]日及び 20[redacted]年[redacted]月[redacted]日，潰瘍性大腸炎の増悪が認められた。被験者には腹痛及び腎機能障害が認められた。疼痛の増加が 2 日間にわたって認められ，疼痛は増し，耐え難いものとなっていた。被験者は，直腸痛のため，トラック運転手としての勤務中に座ることが困難であると訴えた。被験者には腎結石の病歴があり，20[redacted]年[redacted]月に腎結石のため入院したことがあった。被験者は救急治療室を受診し，膀胱の超音波検査を受けたところ，膀胱に 999 mL を超える尿が認められた。被験者によると，直腸痛及び痙縮の症状が発現した際に排尿困難となった。被験者は 20[redacted]年[redacted]月[redacted]日に入院した。フォーリーカテーテルが留置され，Flomax（タムスロシン塩酸塩）及びバンコマイシンの投与が開始された。被験者は 20[redacted]年[redacted]月[redacted]日に退院した。20[redacted]年[redacted]月[redacted]日，腹痛及び直腸痛の症状のため，被験者は入院した。被験者は，少し前に入院し，抑制剤及び抗生剤の投与が開始されたことから，状態は徐々に悪化していると感じた。被験者の症状の原因となっているおそれのある他の二次感染の可能性を除外するため，クロストリジウム・ディフィシレに対する便培養及び便検体が採取された。新たな感染がみられなけれ

ば，被験者に認められている再燃の緩和のための治療を実施し，かかりつけの消化器内科医によるフォローアップを受ける予定であった。抗生剤の投与及びステロイド剤の静脈内投与が行われ，被験者は20[redacted]年[redacted]月[redacted]日に退院した。20[redacted]年[redacted]月[redacted]日，潰瘍性大腸炎の増悪は回復した。

治療薬としてCipro（シプロフロキサシン），Sol-medrol（メチルプレドニゾロンコハク酸エステルナトリウム），Unasyn（アンピシリンナトリウム／スルバクタムナトリウム），生理食塩水，バンコマイシン，Valium（ジアゼパム），Dilaudid（ヒドロモルフォン塩酸塩），Flomax（タムスロシン塩酸塩），オキシコドン及びZofran（オンダンセトロン塩酸塩水和物）が投与された。

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし
Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: Worsening of ulcerative colitis

- AbbVie: The patient presented with severe abdominal and rectal pain, which led to hospitalization.

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: Worsening of ulcerative colitis

- AbbVie: Hospitalization due to severe abdominal pain, possibly due to worsening of the baseline disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] C Difficile Stool: Negative

[redacted] 20[redacted] Chest X-ray:

VAGUE ILL-DEFINED LOWER LUNG OPACITIES ARE NONSPECIFIC AND MAY SIMPLY RELATE TO

HYPOAERATION CHANGES WITH MILD INFILTRATE NOT EXCLUDED.

[redacted] 20[redacted] CT abdomen and Pelvis:

KIDNEYS: BILATERAL NEPHROLITHIASIS WITH 2 SMALL CALCULI WITHIN THE RENAL SINUS COLLECTING SYSTEMS. BOWEL: INCOMPLETELY OPACIFIED, NO BOWEL

OBSTRUCTION. PERSISTENT CIRCUMFERENTIAL THICKENING OF THE WALL OF THE DISTAL COLON, DESCENDING COLON THROUGH THE RECTUM.

[redacted] 20[redacted] CT of Abdomen and pelvis:

Examination of the inferior chest shows no lung consolidation. Examination of the abdomen and pelvis shows the liver, gallbladder, right adrenal gland, left adrenal gland, spleen and pancreas to appear unremarkable. There is bowl wall thickening of the descending colon and sigmoid. This represents findings of edema and probably inflammation. There is also some stranding of the mesentery around the distal sigmoid colon and rectum suggesting findings of inflammation.

[redacted] 20[redacted] Girdia/ Cryptosporidium: Negative

[redacted] 20[redacted] Yersinis Culture: Negative

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
脱毛症		X		
貧血	X	X		
潰瘍性大腸炎		X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	2[redacted]	FEMALE	White

Medical History*	Onset Date
ANEMIA: SECONDARY TO ULCERATIVE COLITIS	[redacted]20[redacted]
MIGRAINE HEADACHE	20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 42	42

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
DICYCLOVERINE	20 mg (milligram(s))	PRN	-268	ONGOING
MESALAZINE	2.4 g (gram(s))	QD	-268	ONGOING
BACILLUS COAGULANS	1 CAPSULE	QD	-41	ONGOING
VITAMINS NOS	1 TABLET	QD	-41	ONGOING
IBUPROFEN	400 mg (milligram(s))	PRN	-11	-11
MACROGOL 3350	238 g (gram(s))	Other	-9	-9
PROPOFOL	20 mg (milligram(s))	Other	-8	-8
IRON	500 mg (milligram(s))	Other	14	14
RED BLOOD CELLS	1 UNIT	Other	15	15

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 6
Age at AE Onset	2[redacted]
AE Stopped Rx Day	33
Duration of AE	28 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	NORMAL DISEASE FLARE OF UC
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug*

Event Description	ULCERATIVE COLITIS EXACERBATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 6
Age at AE Onset	2[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	NOT APPLICABLE
Other Cause of Event	
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #3: AE Leading to Discontinuation of Study Drug*

Event Description	HAIR LOSS
Preferred term	脱毛症
AE Onset Date / Rx Day	[redacted]20[redacted] / 21
Age at AE Onset	2[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	NOT APPLICABLE
Other Cause of Event	
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（米国）であり，重篤な有害事象の貧血を発現した。関連する病歴は，潰瘍性大腸炎に伴う貧血及び潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，貧血が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。過去 1 週間ほど，被験者の体調は優れず，悪心の悪化（嘔吐はみられず）及び血性軟便が 1 日 8～10 回認められた。脱水，頻脈及び貧血の兆候及び症状がみられた。熱感及び若干の悪寒が認められたが，報告当時には温感が認められるのみであった。浮動性めまい，頭痛，視力の変化，胸痛，動悸，息切れ，咳嗽及び泌尿器症状はみられなかった。20[redacted] 年 [redacted] 月 [redacted] 日，非重篤な有害事象の潰瘍性大腸炎の増悪が認められ，持続していた。

治療として濃厚赤血球の輸血，並びに含糖酸化鉄及び静脈内輸液の投与が行われた。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Anemia (10002272) (Anaemia (10002034)) [v.21.1] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of ANEMIA

- Investigator: Normal Disease Flare of UC

- AbbVie: THE SUBJECT HAS KNOWN MEDICAL HISTORY OF ANEMIA RELATED TO UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Colonoscopy: Rectum/descending colon/transverse colon/ascending colon/cecum: 2 = moderate disease (marked erythema, absent vascular pattern, friability, erosion)

Sigmoid: 3 = severe disease (spontaneous bleeding, ulceration).

Presence of friability = yes

Subscore = 3

[redacted] 20[redacted] Colonoscopy:

Colonoscopy: Rectum= 2= Moderate disease (marked erythema, absent vascular

pattern, friability, erosions).

Sigmoid/descending/transverse/ascending colon/cecum = 3 = severe disease (spontaneous bleeding, ulceration).

Presence of friability - yes

Subscore = 3

[redacted] 20[redacted] Hematocrit: 32.2 % (normal 36 to 46)

[redacted] 20[redacted] Hematocrit: 30.6 % (normal 36 to 46)

[redacted] 20[redacted] Hematocrit: 25.0 % (normal 36 to 46)

[redacted] 20[redacted] Hemoglobin: 10.0 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] Hemoglobin: 7.7 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] Hemoglobin: 9.5 G/DL (normal 12.0 to 16.0)

Subject [redacted](Investigator[redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	3[redacted]	MALE	White

Medical History*	Onset Date
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 29	29

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	2.4 g (gram(s))	QD	Y: 20[redacted]	34
BUDESONIDE	9 mg (milligram(s))	QD	-42	30
LOPERAMIDE	2 mg (milligram(s))	PRN	-5	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 29
Age at AE Onset	3[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（米国）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，潰瘍性大腸炎（左側）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，過去 3 日間下痢の悪化が認められたため，被験者は入院した。1 日最高 12～15 回の排便，4／10 の程度で間欠性及び痙攣性の腹痛，悪心並びに嘔吐を伴っていた。被験者は潰瘍性大腸炎の増悪と診断された。Sol-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）の静脈内投与，静脈内輸液及び Flagyl（メトロニダゾール）の静脈内投与による治療が行われた。軟性 S 状結腸鏡検査が実施され，活動性の大腸炎（40 cm）と判明した。被験者は prednisone 及び Flagyl（メトロニダゾール）の経口投与の処方を受け，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。その他の家庭薬は中止された。

治療薬として Entyvio（ベドリズマブ），モルヒネ，Zofran（オンダンセトロン塩酸塩水和物），prednisone，Flagyl（メトロニダゾール），硫酸鉄，メトロニダゾール，Sol-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及びファモチジンが投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし
Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: Ulcerative colitis.

- AbbVie: The event is exacerbation of underlying UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ALBUMIN: 3.3 G/DL (normal 3.4 to 5.0)

[redacted] 20[redacted] FLEXIBLE SIGMOIDOSCOPY: Severe Ulcerative colitis found in the rectum and sigmoid colon, 40 cm form the entry site. the mucosa appeared erythematous, granular, and ulcerated.

[redacted] 20[redacted] HEMATOCRIT: 32.2 % (normal 40.1 to 51.0)

[redacted] 20[redacted] HEMOGLOBIN: 9.1 G/DL (normal 13.7 to 17.5)

[redacted] 20[redacted] MCH: 22.0 PG (normal 25.6 to 32.2)

[redacted] 20[redacted] MCHC: 28.3 G/DL (normal 32.0 to 36.0)

[redacted] 20[redacted] MCV: 77.8 FL (normal 80.0 to 96.1)

[redacted] 20[redacted] PLATELET COUNT: 486 X10**9/L (normal 140 to 450)

[redacted] 20[redacted] SIGMOIDOSCOPY: active colitis - 40 cm

[redacted] 20[redacted] STOOL C.DIFFICILE: not detected

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
感染	X			
発熱	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	5[redacted]	MALE	White

Medical History*	Onset Date
MYOCARDIAL INFARCTION	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: EXANTHEMA WHOLE BODY	NOT REPORTED
OTHER: HYPERTENSION	NOT REPORTED
OTHER: HYPERURICEMIA	NOT REPORTED

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Former (15 YEARS, 1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
				[redacted]20[redacted] / 56	[redacted]20[redacted] / 61	6

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
LEKOVIT CA	1 DF (dosage form)	QD	Y: 20[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	100 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
ATORVASTATIN	80 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
BISOPROLOL	2.5 mg (milligram(s))	BID	Y: 20[redacted]	ONGOING
RAMIPRIL	10 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
AKTIFERRIN COMP	1 DF (dosage form)	QD	Y: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	-186	ONGOING
CYANOCOBALAMIN	1000 mcg (microgram(s))	QD	-94	ONGOING
FUROSEMIDE	40 mg (milligram(s))	PRN	-94	ONGOING
HOMEOPATHIC PREPARATION	5 gtt (drop(s))	BID	-94	ONGOING
ASCORBIC ACID	1000 mg (milligram(s))	QD	-57	ONGOING
ALLOPURINOL	150 mg (milligram(s))	Other	-33	ONGOING
BUDESONIDE	3 mg (milligram(s))	TID	-21	26
LISINOPRIL	10 mg (milligram(s))	QD	-9	28
BUDESONIDE	3 mg (milligram(s))	BID	27	34
BUDESONIDE	3 mg (milligram(s))	QD	35	40

Event #1: Serious Adverse Event*

Event Description	FEVERISH INFECTION
Preferred term	感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 44
Age at AE Onset	5[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	WITHDRAWAL OF STEROIDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event*

Event Description	FEVERISH INFECTION
Preferred term	発熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 44
Age at AE Onset	5[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	WITHDRAWAL OF STEROIDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（オーストリア）であり，重篤な有害事象の発熱性感染を発現した。
20[redacted] 年 [redacted] 月 [redacted] 日，発熱性感染が発現した。
20[redacted] 年 [redacted] 月 [redacted] 日（投与 8 週時），予定されていた内視鏡検査が実施され，直腸に異形成（非重篤）が認められた。被験者は試験を中止した。ほぼ同時期に発熱及び痛みの増強が認められ，インフルエンザ感染が疑われた。症状は持続した。
20[redacted] 年 [redacted] 月 [redacted] 日，夜間の発熱，悪心，食欲不振，脱力及び低ナトリウム血症のため，被験者は入院した。副腎機能不全の疑いによる入院であった。20[redacted] 年 [redacted] 月 [redacted] 日，直腸鏡検査が実施され，直腸内に偽ポリープが認められた。治験責任医師によると，症状は被験者が数年間使用していたステロイド剤の用量を漸減した直後に認められていたことが後に分かった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。ステロイド剤の投与が再開され，症状は消失した。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Fever (10016558) (Pyrexia (10037660)) [v.21.1] [10016558]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Infection (10021789) (Infection (10021789)) [v.21.1] [10021789]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of FEVERISH INFECTION

- Investigator: Withdrawal of steroids

- AbbVie: Risk factor includes pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CT abdomen:

Evidence of Crohns disease in duodenum , jejunum, terminal Ileum, colon sigmoideum and rectum. Simple cyst in right kidney.

[redacted] 20[redacted] EGFR (cdk): 61 ML/MIN (normal <60)

[redacted] 20[redacted] EGFR (CKD): 85 No Units

[redacted] 20[redacted] ESR 1H: 75 MMHG (normal <20)

[redacted] 20[redacted] ESR 2H: 117 MMHG (normal <20)

[redacted] 20[redacted] Flexible sigmoidoscopy:

Colonoscopy lab results for:

Rectum - severe disease (spontaneous bleeding, ulceration)

Sigmoid - moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Descending colon - moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Transverse colon - normal or inactive disease

Ascending colon/cecum - normal or inactive disease

[redacted] 20[redacted] free t 3: 4.22 pg/ml (normal 2 to 4.4)

[redacted] 20[redacted] GGT: 144 U/L (normal <60)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 0.8 MG/L (normal <5)

[redacted] 20[redacted] Monocytes: 1.5 X10**9/L (normal 0 to 1.2)

[redacted] 20[redacted] Platelet Count: 441 X10**9/L (normal 150 to 350)

[redacted] 20[redacted] Platelets: 466 X10**9/L (normal 150 to 350)

[redacted] 20[redacted] POTASSIUM: 3.9 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] SGOT/ALT: 37 U/L (normal 10 to 50)

[redacted] 20[redacted] SODIUM: 140 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] stool calprotectin: >6000 mg/kg (normal >50)

[redacted] 20[redacted] TOTAL BILIRUBIN: 0.3 mg/dL (normal <1.2)

[redacted] 20[redacted] URIC ACID: 11.8 mg/dL (normal 3.4 to 7)

[redacted] 20[redacted] URINE NITRITE: NEGATIVE

[redacted] 20[redacted] URINE PROTEIN: 25 mg/dL (normal <10)

[redacted] 20[redacted] UROBILINOGEN: <1 mg/dL (normal <1)

[redacted] 20[redacted] WBC: 8.5 G/L (normal 4 to 10)

[redacted] 20[redacted] WBC (Hemotology): 500 X10**9/L (normal <10)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
痔核	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	3[redacted]	FEMALE	White

Medical History*	Onset Date
HYPOTHYROIDISM	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ACNE	[redacted]20[redacted]
OTHER: ECZEMA	20[redacted]
OTHER: HAEMORRHOIDS	NOT REPORTED
OTHER: INTOLERANCE TO LACTOSIS	[redacted]20[redacted]
OTHER: LESION ON RIGHT HAND PLANTAR	[redacted]20[redacted]
OTHER: UNSPECIFIC HEADACHE	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
				[redacted]20[redacted] / 56	[redacted]20[redacted] / 358	303

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
LEVOTHYROXINE	50 mcg (microgram(s))	QD	Y: 20[redacted]	ONGOING
MESALAZINE	4 g (gram(s))	QD	Y: 20[redacted]	ONGOING
AZATHIOPRINE	50 mg (milligram(s))	QD	-165	18
AMITRIPTYLINE	75 mg (milligram(s))	QD	-84	82
ISONIAZID	300 mg (milligram(s))	QD	-14	260
NEUROBION FORTE	1 DF (dosage form)	TID	1	260

Event #1: Serious Adverse Event*

Event Description	WORSENING OF HAEMORRHOIDS
Preferred term	痔核
AE Onset Date / Rx Day	[redacted]20[redacted] / 47
Age at AE Onset	3[redacted]
AE Stopped Rx Day	97
Duration of AE	51 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	HAMORROIDS ALREADY EXISTED PRIOR TO STUDY ENTRY (MED HISTORY!)
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（オーストリア）であり，重篤な有害事象の痔核の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側）及び痔核であった。

20[redacted] 年 [redacted] 月，痔核の悪化が認められた。

被験者には潰瘍性大腸炎の改善による症候性の痔核が数年間認められていたが，この点を除いては健康そのものであった。痔核のため，排便時の疼痛及び出血もみられた。便の硬さの改

善に一致して痔核はより症候性となり，出血がみられるようになったため，被験者は外科医の評価を受けるために搬送された。20[redacted] 年 [redacted] 月 [redacted] 日，ミリガンモルガン手術が実施され，合併症は認められなかった。

治療薬として Prospan，Tantum verde pastilles，Ciprocin（シプロフロキサシン），Anaerobex（メトロニダゾール），Lovenox（エノキサパリンナトリウム），Xylocaine（リドカイン）5%，パンテノール及び Antiflat が投与された。

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Haemorrhoids aggravated (10048363) (Haemorrhoids (10019022)) [v.20.0] [10048363]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of WORSENING OF HAEMORRHOIDS

- Investigator: Hamorroids already existed prior to study entry (med history)

- AbbVie: Subject has known medical history of haemorrhoids.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ENDOSCOPY: Rectum: 1 Mild disease, Sigmoid: 1 Mild disease, Descending Colon: 2 Moderate disease, Transverse Colon: Normal or inactive disease, Ascending colon/cecum: 1 Mild disease.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	2[redacted]	MALE	White

Medical History*	Onset Date
MIGRAINE HEADACHE	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Former (9 YEARS, 1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 22	22

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	4000 mg (milligram(s))	QD	Y: 20[redacted]	35
HYOSCINE	10 mg (milligram(s))	PRN	-50	42
METAMIZOLE	500 mg (milligram(s))	PRN	-33	ONGOING
LEKOVIT CA	1 DF (dosage form)	BID	-29	ONGOING
PREDNISOLONE	10 mg (milligram(s))	QD	-29	ONGOING
CIPROFLOXACIN	400 mg (milligram(s))	BID	12	18
METRONIDAZOLE	1.5 g (gram(s))	QD	12	18
ENOXAPARIN	40 mg (milligram(s))	QD	14	18
FLEBOBAG RING LACT	1000 mL (millilitre(s))	BID	14	18
FLEBOBAG RING LACT	1000 mL (millilitre(s))	QD	25	25
CICLOSPORIN	192 mg (milligram(s))	Other	25	37
ENOXAPARIN	40 mg (milligram(s))	QD	25	41

Event #1: Serious Adverse Event*

Event Description	WORSENING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 12
Age at AE Onset	2[redacted]
AE Stopped Rx Day	24 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	13 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	DISEASE UNDER STUDY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 25 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
AE Stopped Rx Day	83 (61 DAYS AFTER LAST TREATMENT)
Duration of AE	59 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted]歳の男性（オーストリア）であり，重篤な有害事象の潰瘍性大腸炎の悪化が 2 回認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。被験者は元喫煙者（1 日 1 箱を 9 年間）及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，全身健康状態低下及び発熱のため，被験者は入院した。高頻度の排便，直腸出血及び腹痛も認められ，抗生剤が投与された。便培養及び尿培養が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，全身健康状態低下及び発熱の持続のため，被験者は入院した。付随する兆候及び症状として，高頻度の排便，直腸出血，発熱及び腹痛が認められた。C 反応性たん白値の上昇も認められたが低下し，被験者の状態は改善した。Entyvio（ベドリズマブ）及びシクロスポリンの投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてシクロスポリン，Entyvio（ベドリズマブ），Fresubin，シクロスポリン A，Anaerobex（メトロニダゾール），Novalgin，Ciproxin（シプロフロキサシン），Lovenox（エノキサパリンナトリウム），Konakion（フィトナジオン），Mesagran，Sandimmun（シクロスポリ

ン），Perfalgan（アセトアミノフェン），Salofalk（メサラジン），Folsan，乳酸リンゲル液及びCiprofloxacin Kabi（シプロフロキサシン）が投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of WORSENING OF UC

- Investigator: DISEASE UNDER STUDY

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Ulcerative Colitis

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD CULTURE: negative

[redacted] 20[redacted] BLOOD CULTURE: negative

[redacted] 20[redacted] BLOOD CULTURE: negative

[redacted] 20[redacted] CATHETER CULTURE: tip of central venous catheter- negative

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 10.78 mg/dL (normal 0 to 0.5)

[redacted] 20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN: 5.47 mg/dL (normal 0 to 0.5)

[redacted] 20[redacted] SEPTIFAST PCR: negative

[redacted] 20[redacted] STOOL - CLOSTRIDIUM DIFFICILE: negative

[redacted] 20[redacted] STOOL CULTURE: negative

[redacted] 20[redacted] URINE: Positive for Group B - Hemolytic Streptococcus 10E3 KBE/ml

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	6[redacted]	MALE	White

Medical History*	Onset Date
ANEMIA: ANEMIA SECONDARY TO ULCERATIVE COLITIS	20[redacted]
ARTHRITIS: FINGERS, WRISTS, ELBOWS, ANKLES AND KNEES	[redacted]20[redacted]
DRUG ALLERGIES/REACTIONS: AZATHIOPRINE INTOLERANCE	[redacted]20[redacted]
ERYTHEMA NODOSUM: INTERMITTENT	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ADRENAL ADENOMA	20[redacted]
OTHER: INTERMITTENT "ACNE-LIKE" RASH	20[redacted]
OTHER: INTERMITTENT APTHOUS STOMATITIS	20[redacted]
OTHER: LOSS OF TASTE	[redacted]20[redacted]
OTHER: RENAL CYST	20[redacted]
OTHER: THROAT PAIN ON SWALLOWING	[redacted]20[redacted]
OTHER: TINNITUS	20[redacted]
SURGERY: BILATERAL INGUINAL HERNIA REPAIR	19[redacted]
SURGERY: ORCHIECTOMY	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Former (14 YEARS, 1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 27	27

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	1600 mg (milligram(s))	BID	Y: 20[redacted]	ONGOING
PARACETAMOL	1 TABLET	PRN	-282	ONGOING
LOPERAMIDE	2 mg (milligram(s))	PRN	-101	ONGOING
PARACETAMOL	1 TABLET	PRN	-17	ONGOING
FENTANYL	125 mcg (microgram(s))	Other	-4	-4
MIDAZOLAM	6 mg (milligram(s))	Other	-4	-4

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 27
Age at AE Onset	6[redacted]
AE Stopped Rx Day	50 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	24 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（カナダ）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側），潰瘍性大腸炎に伴う貧血及びアザチオプリン不耐症であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。血性下痢，腹痛，体重減少，アルブミン低値及び薬物治療に抵抗性を有する貧血のため，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院した。ステロイド剤の静脈内投与が開始され，胃内視鏡検査を実施したところ，カンジダ性食道炎の所見が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，用手補助腹腔鏡下腹式結腸全摘除及び終末型回腸瘻造設が実施された。術後回復期に問題はなく，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

治療薬として prednisone，カルシウム，ビタミン D，硫酸鉄，Cortifoam enema（ヒドロコルチゾン酢酸エステル），塩化カリウム，sodium phosphate，パントプラゾール，炭酸カルシウム，フマル酸第一鉄，ダルテパリン，Tylenol #3，メトクロプラミド，アセトアミノフェン，モルヒネ，ヒドロモルフォン，ヒドロコルチゾン，Asacol（メサラジン）及びフルコナゾールが投与された。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CORTIFOAM RECTAL 10% ENEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IMODIUM for DIARRHEA and ULCERATIVE COLITIS (Started [redacted] 20[redacted])

CODEINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Ulcerative Colitis

- AbbVie: Event is more likely related to pre-existing ulcerative colitis.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
心停止	X	X	X	

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	3[redacted]	MALE	White

Medical History*	Onset Date
ANEMIA: IRON DEFICIENT	20[redacted]
DEPRESSION: DEPRESSION	20[redacted]
DIABETES MELLITUS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	[redacted]20[redacted]
HYPERTENSION	20[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
SLEEP APNEA	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ANXIETY	20[redacted]
OTHER: ENVIRONMENTAL ALLERGIES	20[redacted]
OTHER: LEFT VENTRICULAR HYPERTROPHY	NOT REPORTED
OTHER: SLEEP DISTURBANCE	20[redacted]
OTHER: STRIAE ON ARMS, LEGS, ABDOMEN	20[redacted]
OTHER: VITAMIN D DEFICIENCY	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Former
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 17	17

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
KARVEA HCT	300/12.5 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
CIPROFLOXACIN	20 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
INSULIN GLARGINE	30-40 UNITS	QD	Y: 20[redacted]	ONGOING
INSULIN LISPRO	15-20 UNITS	TID	Y: 20[redacted]	ONGOING
METFORMIN	1000 mg (milligram(s))	BID	Y: 20[redacted]	ONGOING
CETIRIZINE	10 mg (milligram(s))	PRN	Y: 20[redacted]	ONGOING
ERGOCALCIFEROL	1000 IU (international unit(s))	QD	Y: 20[redacted]	ONGOING
VITAMINS NOS	1 TABLET	QD	Y: 20[redacted]	ONGOING
AMLODIPINE	10 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
CODEINE	30 mg (milligram(s))	PRN	Y: 20[redacted]	ONGOING
LOMOTIL	5 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
MESALAZINE	2 g (gram(s))	BID	Y: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	BID	Y: 20[redacted]	ONGOING
TEMAZEPAM	30 mg (milligram(s))	PRN	Y: 20[redacted]	ONGOING
PREDNISONE	25 mg (milligram(s))	QD	-14	ONGOING
FENTANYL	200 mcg (microgram(s))	Other	-5	-5
FLEET	1 APPLICATION	Other	-5	-5
MIDAZOLAM	10 mg (milligram(s))	Other	-5	-5
DIPHTHERIA VACCINE TOXOID W/PERTUSS	0.5 mL (millilitre(s))	Other	20	20
HYDROMORPHONE	2 mg (milligram(s))	Other	20	20
KETOROLAC	3 mg (milligram(s))	Other	20	20
ONDANSETRON	8 mg (milligram(s))	Other	20	20
POTASSIUM	40 mEq (milliequivalent(s))	Other	20	20

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Death*

Event Description	CARDIAC ARREST
Preferred term	心停止
AE Onset Date / Rx Day	[redacted]20[redacted] / 20 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
AE Stopped Rx Day	20 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	NO KNOWN AT THIS TIME
Discontinued Study Drug Due to the Event	YES
SAE Criteria	LIFE THREATENING, DEATH OF SUBJECT

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（カナダ）であり，致死的な有害事象の心停止を発現した。関連する病歴は，高血圧，睡眠障害，糖尿病，睡眠時無呼吸及び左室肥大であった。被験者は元アルコール摂取者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，心停止が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は心停止と報告された。剖検が実施されたかどうかは不明であった。

20[redacted] 年 [redacted] 月 [redacted] 日 0 時 32 分，被験者は失神（非重篤）が認められた後に階段から 14 段落ち，救急治療室（以下「ER」）を受診した。ER において，Zofran（オンダンセトロン塩酸塩水和物），Toradol，Dilaudid（ヒドロモルフォン塩酸塩），ジフテリア・破傷風・百日咳三種混合ワクチン及び K-dur（塩化カリウム）が投与された。心電図及び頭部コンピュータ断層撮影検査が実施され，被験者は 6 時 17 分に自宅に退院した。

同日，ER からの退院 11 時間後，被験者はベッドで無反応となっているところを発見された。救急医療サービスに出動要請をし，二次救命処置（以下「ACLS」）が開始された。ER の医師の記録によると，被験者は，被験者の妻によって無反応となっているところを発見された（無反応であった時間は不明だが 2 時間超）。ACLS は継続されたが，失敗に終わった。

心停止のリスク因子：高血圧，インスリン依存性糖尿病及び左室肥大。
治療薬として Zofran（オンダンセトロン塩酸塩水和物），Toradol，Dilaudid（ヒドロモルフォン塩酸塩），ジフテリア・破傷風・百日咳三種混合ワクチン及び K-dur（塩化カリウム）が投与された。

Causality for HUMIRA (Open Label)

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1) Cardiac arrest (10007515) (Cardiac arrest (10007515)) [v.18.0] [10007515]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of CARDIAC ARREST

- Investigator: No known at this time

- AbbVie: Patient has known medical history that could lead to this event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CK (17:44): 275 U/L (normal <250)

[redacted] 20[redacted] CT head: normal brain

[redacted] 20[redacted] EKG:

Normal

[redacted] 20[redacted] glucose (17:44): 16.6 MMOL/L (normal 3.3 to 11.0)

[redacted] 20[redacted] HBG (17:44): 107 G/L

[redacted] 20[redacted] HCT (17:44): 0.39

[redacted] 20[redacted] MAGNESIUM (17:44): 1.63 MMOL/L (normal 0.70 to 1.00)

[redacted] 20[redacted] PLATELETS (17:44): 37 X10**9/L

[redacted] 20[redacted] potassium (17:44): 7.2 MMOL/L (normal 3.3 to 4.8)

[redacted] 20[redacted] sodium (17:44): 151 MCMOL/L (normal 133 to 146)

[redacted] 20[redacted] Troponin: 0.67 (normal <0.15)

[redacted] 20[redacted] TROPONIN (17:44): 0.67 (normal 0 to 15)

[redacted] 20[redacted] WBC (17:44): 20.1 X10**9/L

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	5[redacted]	MALE	White

Medical History*	Onset Date
ANEMIA: ANEMIA	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ABRASIONS TO L2 TO L4 THORACIC AREA; ABRASIONS TO RIGHT ARM	[redacted]20[redacted]
OTHER: LIGHTHEADEDNESS	20[redacted]
OTHER: MIGRAINES	20[redacted]
OTHER: PALMAR ERYTHEMA	[redacted]20[redacted]
OTHER: PITTING EDEMA BILATERAL LOWER LEGS	[redacted]20[redacted]
OTHER: RAYNAUDS DISEASE	20[redacted]
SURGERY: CHOLECYCSTECTOMY	NOT REPORTED

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	45

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
AZATHIOPRINE	150 mg (milligram(s))	QD	-96	ONGOING
IRON	300 mg (milligram(s))	QD	-96	ONGOING
PREDNISONE	20 mg (milligram(s))	QD	22	48
PREDNISONE	30 mg (milligram(s))	QD	49	55
PREDNISONE	35 mg (milligram(s))	QD	56	62
PREDNISONE	40 mg (milligram(s))	QD	63	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 64 (19 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	71 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	PT. DID NOT RESPOND TO STUDY MEDICATION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（カナダ）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院した。鋭く刺すような腹痛の悪化の兆候及び症状が認められた。わずかな血液の混入を伴う水様便が 1

日に 6～7 回認められた。被験者は，経口摂取減少を伴う悪心も訴えた。発熱，悪寒又は抗生剤の使用は報告されなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，一連の腹部 X 線検査が行われ，閉塞が疑われる小腸拡張が示された。20[redacted] 年 [redacted] 月 [redacted] 日に腹部コンピュータ断層撮影検査も実施され，回腸の短く堅い狭窄による小腸高遠位部の閉塞が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，クローン病の可能性を除外するため，結腸内視鏡検査及び生検が実施された。病理学的所見は潰瘍性大腸炎と考えられるものであった。メチルプレドニゾロンが静脈内投与され，被験者の状態が改善し経口摂取が可能となるまで完全静脈栄養法（以下「TPN」）が行われた。被験者の状態は改善し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

治療薬としてフェンタニル，メチルプレドニゾロン，ミダゾラム及び Peglyte が投与され，TPN による治療が行われた。

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Patient did not respond to study medication

- AbbVie: Underlying ulcerative colitis disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] abdominal CT:

High distal small bowel obstruction due to short tight stricture in the ileum.

[redacted] 20[redacted] abdominal xray:

Inicated distended small bowel, possibly an obstruction.

[redacted] 20[redacted] Colonoscopy:

Rectum 1 = mild disease (erythema, decreased vascular pattern, mild friability)

Sigmoid 2= Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Transverse colon 2= Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Ascending colon/cecum 2= Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

With presence of friability. Sub score of 2.

[redacted] 20[redacted] Colonoscopy: pathology consistent w/ ulcerative colitis

[redacted] 20[redacted] Electrocardiogram:

Abnormal- not clinically significant; ST segment; elevated >=1 mm; possible digitalis effect

Subject [redacted] (Investigator [redacted])Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
**腺癌	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	5[redacted]	MALE	Asian

Medical History*	Onset Date
ANEMIA: IRON DEFICIENCY	20[redacted]
BENIGN PROSTATIC HYPERPLASIA	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: H PYLORI	20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
				[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	2.4 g (gram(s))	QD	Y: 20[redacted]	ONGOING

* Information presented verbatim as provided by the investigator.

Subject Number: [redacted]

本被験者は，5[redacted] 歳の男性（カナダ）であり，重篤な有害事象の腺癌を発現した。関連する病歴は，潰瘍性大腸炎及びヘリコバクター・ピロリ感染であった。被験者は非喫煙者及びアルコール摂取者（1 日 2 杯未満）であった。

被験者は腺癌を発現した（発現日不明）。20[redacted] 年[redacted] 月[redacted] 日，投与 8 週時に所定の軟性 S 状結腸鏡検査が実施され，脆弱化が認められた。本事象の兆候又は症状は認められなかった。20[redacted] 年[redacted] 月，組織生検の結果，腺癌に対して陽性と判定された。その後に実施された結腸内視鏡検査（実施日不明）の結果は，癌に対して陰性であった。後に検体評価を実施した理由は不明であった。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Adenocarcinoma (10001141) (Adenocarcinoma (10001141)) [v.23.0] [10001141]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of ADENOCARCINOMA

- Investigator: Unknown at this time as limited details provided.
- AbbVie: weak temporal association with less than one year of study drug exposure. Pre-existing ulcerative colitis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BIOPSY TISSUE ANALYSIS: Adenocarcinoma

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腹痛	X			
下痢	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	3[redacted]	MALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
SURGERY: RUPTURE OF NERVUS PERINEUS	20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 29	29

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	800 mg (milligram(s))	BID	-254	5
AZATHIOPRINE	100 mg (milligram(s))	QD	-254	ONGOING
PREDNISONE	20 mg (milligram(s))	QD	-75	ONGOING
DOCUSATE	62.5 mL (millilitre(s))	Other	-8	-8
METOCLOPRAMIDE	10 mg (milligram(s))	QD	3	3

Event #1: Serious Adverse Event*

Event Description	ABDOMINAL PAIN WITH DIARRHOE
Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 3
Age at AE Onset	3[redacted]
AE Stopped Rx Day	6
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	PATIENT HOSPITALIZED ON [redacted] 20[redacted] FOR ABDOMINAL PAIN WITH DIARRHOE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event*

Event Description	ABDOMINAL PAIN WITH DIARRHOE
Preferred term	下痢
AE Onset Date / Rx Day	[redacted]20[redacted] / 3
Age at AE Onset	3[redacted]
AE Stopped Rx Day	6
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	PATIENT HOSPITALIZED ON [redacted] 20[redacted] FOR ABDOMINAL PAIN WITH DIARRHOE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，男性（チェコ共和国）であり，重篤な有害事象の下痢を伴う腹痛を発現した。
20[redacted] 年 [redacted] 月 [redacted] 日，下痢を伴う腹痛が発現した。同日，腹痛，下痢，嘔吐及び脱水のため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，下痢を伴う腹痛は回復し，被験者は同日に退院した。
治療薬として Degan（メトクロプラミド）が投与された。

Causality for HUMIRA (Open Label)

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1) Abdominal pain (10000081) (Abdominal pain (10000081)) [v.18.0] [10000081]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

2) Diarrhea (10012727) (Diarrhoea (10012735)) [v.18.0] [10012727]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ABDOMINAL PAIN WITH DIARRHOE

- Investigator: The subject evolved with worsening of UC, leading to hospitalization. The event happened 5dys after baseline visit. Mayo score reflects severe disease.

- AbbVie: Patient hospitalized on [redacted] 20[redacted] for abdominal pain with diarrhea

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Electrocardiogram: Normal

[redacted] 20[redacted] Flexible sigmoidoscopy:

mild disease rectum/sigmoid, moderate descending colon

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
帯状疱疹	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	5[redacted]	FEMALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: MECANIC CONTRACEPTION	20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 16	16

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
INTRAVAGINAL CONTRACEPTIVES	NOT APPLICABLE NOT APPLICABLE	Other	Y: 20[redacted]	ONGOING
MESALAZINE	2 g (gram(s))	BID	-362	ONGOING
SPASFON	2 DF (dosage form)	TID	-66	20
PARACETAMOL	1 g (gram(s))	TID	13	20

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	CUTANEOUS ZONA
Preferred term	帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 17 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Relation to Study Drug by AbbVie	Reasonable possibility
Other Cause of Event	
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.:[redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の女性（フランス）であり，重篤な有害事象の皮膚の帯状疱疹を発現した。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，皮膚の帯状疱疹が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。帯状疱疹の症状が認められ，治療を受けたところ，皮膚症状はみられなくなった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてZona（クロナゼパム），Contramal（トラマドール塩酸塩），Acupan及びZovirax（アシクロビル）が投与された。
The patient's past medications include:

IMUREL for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Zona (10067526) (Herpes zoster (10019974)) [v.19.0] [10067526]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: No

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of CUTANEOUS ZONA

- Investigator: N/A

- AbbVie: N/A

Subject [redacted] (Investigator[redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	5[redacted]	FEMALE	White

Medical History*	Onset Date
DEPRESSION: DEPRESSIVE SYNDROME	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: MENOPAUSE	20[redacted]
SURGERY: ANAL FISTULA	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 20	20

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
AMISULPRIDE	50 mg (milligram(s))	BID	Y: 20[redacted]	ONGOING
FLUOXETINE	50 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
MESALAZINE	1600 mg (milligram(s))	BID	Y: 20[redacted]	36
METHYLPREDNISOLONE	120 mg (milligram(s))	Other	34	36
PREDNISOLONE	40 mg (milligram(s))	QD	37	46
AZATHIOPRINE	150 mg (milligram(s))	QD	37	ONGOING
GLUCOSE	250 mL (millilitre(s))	QD	39	39
HYDROCORTISONE	200 mg (milligram(s))	QD	39	39
INFLIXIMAB	5 mg/kg (milligram(s)/kilogram)	QD	39	39
ESOMEPRAZOLE	40 mg (milligram(s))	QD	39	ONGOING
DEXCHLORPHENIRAMINE	5 mg (milligram(s))	QD	47	47
MORPHINE	5 mg (milligram(s))	QD	47	47
NEFOPAM	20 mg (milligram(s))	QD	47	47
PARACETAMOL	1 g (gram(s))	QD	47	47
PREDNISOLONE	30 mg (milligram(s))	QD	47	47
TRAMADOL	100 mg (milligram(s))	QD	47	47
METHYLPREDNISOLONE	120 mg (milligram(s))	Other	47	49

Event #1: Serious Adverse Event*

Event Description	FLARE UP OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 34 (14 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	40 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	EVOLUTION OF THE ULCERATIVE COLITIS AND STUDY TREATMENT FAILURE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event*

Event Description	FLARE OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 47 (27 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	54 (34 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	FLARE OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の女性（フランス）であり，重篤な有害事象の潰瘍性大腸炎の再燃が 2 回認められた。関連する病歴は，潰瘍性大腸炎（左側）及び痔瘻であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は潰瘍性大腸炎の再燃のため入院した。腰痛，腹痛及び血性下痢の兆候及び症状が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，高度の腹痛のため，被験者は入院した。被験者はインフリキシマブにアレルギー反応を示したため，ベドリズマブに変更された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として 5%ブドウ糖，Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム），Imurel（アザチオプリン），Inexium（エソメプラゾールマグネシウム水和物），インフリキシマブ，ベドリズマブ，Solupred（プレドニゾロン），Polaramine（d-クロルフェニラミンマレイン酸塩），モルヒネ，Perfalgan（アセトアミノフェン），Contramal（トラマドール塩酸塩），Hudrocortisone，ヒドロコルチゾン及び Acupan が投与された。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CORTANCYL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DIFFU K for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of FLARE UP OF ULCERATIVE COLITIS

- Investigator: EVOLUTION OF THE ULCERATIVE COLITIS AND STUDY TREATMENT FAILURE

- AbbVie: THE EVENT IS EXACERBATION OF THE UC UNDERLYING DISEASE.

Event of FLARE OF ULCERATIVE COLITIS

- Investigator: Flare

- AbbVie: THE EVENT IS EXACERBATION OF THE UC UNDERLYING DISEASE.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	4[redacted]	MALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: ANOREXIA	[redacted]20[redacted]
SURGERY: LEFT THUMB PARONYCHIA	[redacted]20[redacted]
SURGERY: RIGHT AND LEFT MENISCECTOMY	NOT REPORTED

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Unknown	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 1	1

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
PREDNISOLONE	20 mg (milligram(s))	QD	-33	-11
MOVIPREP	1 L (litre(s))	QD	-16	-15
PREDNISOLONE	40 mg (milligram(s))	QD	-10	1
CEFTRIAXONE	2 g (gram(s))	QD	1	3
METRONIDAZOLE	500 mg (milligram(s))	TID	1	3

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	ACUTE SEVERE COLITIS
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 1
Age at AE Onset	4[redacted]
AE Stopped Rx Day	9 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（フランス）であり，重篤な有害事象の高度の急性大腸炎を発現した。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，高度の急性大腸炎が発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，非高度の敗血症，高熱及び頻脈のため入院した。抗生剤及びコルチコステロイドが投与され，「速やかな臨床経過の改善がみられ」」奏効した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，高度の急性大腸炎は回復した。

治療薬として Rocephin（セフトリアキソンナトリウム水和物），Flagyl（メトロニダゾール），メチルプレドニゾロン，アザチオプリン，プレドニゾロン及び Lovenox（エノキサパリンナトリウム）が投与された。

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1)　Colitis (10009887)　(Colitis (10009887))　[v.21.0]　[10009887]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of ACUTE SEVERE COLITIS

- Investigator: Ulcerative colitis

- AbbVie: Pre-existing ulcerative colitis is a potential risk factor

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL SCAN: no intravital peritoneal fluid effusion. parietal thickening with contrast enhancement and infiltration of peri-colonic fat in favor of colitis

[redacted] 20[redacted] CLOSTRIDIUM: NEGATIVE

[redacted] 20[redacted] CRP: 140 MG/L (normal 0 to 6)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	4[redacted]	MALE	White

Medical History*	Onset Date
HYPOTHYROIDISM	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: NICKEL ALLERGY	20[redacted]
OTHER: PLASTER ALLERGY	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
				[redacted]20[redacted] / 57	[redacted]20[redacted] / 167	111

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
LEVOTHYROXINE	150 mcg (microgram(s))	QD	Y: 20[redacted]	ONGOING
MESALAZINE	1.2 g (gram(s))	QD	Y: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
MIDAZOLAM	5 mg (milligram(s))	QD	-14	-14
PROPOFOL	80 mg (milligram(s))	QD	-14	-14

Event #1: Serious Adverse Event*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 17
Age at AE Onset	4[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（ドイツ）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側）及び結腸内視鏡検査であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。潰瘍性大腸炎の再燃及び下痢による脱水が認められた。腹痛，直腸出血及び下痢の兆候及び症状がみられた。20[redacted] 年 [redacted] 月 [redacted] 日，内視鏡検査が実施された。

治療としてリンゲル液，ミダゾラム及びプロポフォールの投与，並びに静脈栄養法が行われた。

The patient's past medications include:

INFLIXIMAB for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Ulcerative colitis

- AbbVie: Subject with severe UC, without any improvement after 2 weeks of dosing.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ENDOSCOPY:

Flexible sigmoidoscopy

RECTUM: Moderate disease

SIGMOID: Moderate disease

DESCENDING COLON: Moderate disease

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		
サイトメガロウイルス性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	5[redacted]	MALE	White

Medical History*	Onset Date
ASTHMA: ALLERGIC BRONCHIAL ASTHMA	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: FRUCTOSE MALABSORPTION	20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Former (34 YEARS, 1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
IRON	1 TABLET	QD	Y: 20[redacted]	ONGOING
MESALAZINE	1.2 g (gram(s))	BID	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF ULCERATIVE COLITIS DUE TO CMV-COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 40
Age at AE Onset	5[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF ULCERATIVE COLITIS DUE TO CMV-COLITIS
Preferred term	サイトメガロウイルス性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 40
Age at AE Onset	5[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（ドイツ）であり，サイトメガロウイルス（以下「CMV」）性大腸炎による潰瘍性大腸炎の悪化が認められた。関連する病歴は，左側潰瘍性大腸炎，フルクトース吸収不良及び結腸内視鏡検査であった。被験者は元紙巻タバコ喫煙者（1 日 1 箱を 34 年間）及び軽度のアルコール摂取者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，CMV 性大腸炎による潰瘍性大腸炎の悪化が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，S 状結腸鏡検査が実施され，Mayo スコアが 3 の潰瘍性大腸炎が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，体重減少，直腸出血及び CMV 性大腸炎による排便回数の増加の症状のため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Prednisolon（プレドニゾロン），シプロフロキサシン，メトロニダゾール，プロポフォール，ミダゾラム及び Nutriflex peri（完全静脈栄養製剤）が投与された。

The patient's past medications include:

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MIDAZOLAM for ENDOSCOPY and SEDATION ([redacted] 20[redacted] - [redacted] 20[redacted])

PROPOFOL for ENDOSCOPY and SEDATION ([redacted] 20[redacted] - [redacted] 20[redacted])

freka klyss for ENDOSCOPY PREP and ENDOSCOPY PREP ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) CMV colitis (10051359) (Cytomegalovirus colitis (10048983)) [v.18.1] [10051359]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

2) Colitis ulcerative aggravated (10009901)(Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS DUE TO CMV COLITIS

- Investigator: Ulcerative colitis.

- AbbVie: The event is likely related to underlying illness of ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] biopsy Sigmoid:

histological result: cmv-colitis

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	3[redacted]	FEMALE	White

Medical History*	Onset Date
ANEMIA: IRON DEFICIENCY ANEMIA	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: NICKEL ALLERGIE	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Former (12 YEARS, 0.3 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 7	7

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	4 g (gram(s))	BID	Y: 20[redacted]	12
AZATHIOPRINE	150 mg (milligram(s))	BID	Y: 20[redacted]	12
PREDNISOLONE	30 mg (milligram(s))	QD	-113	11
IRON	100 mg (milligram(s))	QD	-113	ONGOING
NUVARING	0,120 mg (milligram(s))	Other	-113	ONGOING
PANTOPRAZOLE	40 mg (milligram(s))	QD	-113	ONGOING
COLECALCIFEROL	1000 IU (international unit(s))	BID	-54	ONGOING
IRON	500 mg (milligram(s))	PRN	-43	ONGOING
TRANSIPEG	69 g (gram(s))	Other	-12	-12
MESALAZINE	1500 mg (milligram(s))	TID	12	ONGOING
MESALAZINE	4 g (gram(s))	BID	12	ONGOING
PREDNISOLONE	50 mg (milligram(s))	QD	12	ONGOING

Event #1: Serious Adverse Event*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 12 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
AE Stopped Rx Day	19 (12 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	PRIMARY DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（ドイツ）であり，潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側）であった。
20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年[redacted] 月[redacted] 日，被験者は急性の疾患再燃のため入院した。39°C の発熱，血便及び全身状態低下の兆候及び症状が認められた。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎の悪化は回復した。
治療薬として Salofalk（メサラジン），プレドニゾロン及び Claversal（メサラジン）が投与された。

The patient's past medications include:

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

KLEANPREP for ENDOSCOPY PREP and ENDOSCOPY PREP ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.18.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Primary disease.

- AbbVie: The patient has severe ulcerative colitis, with worsening right after randomization.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	2[redacted]	MALE	White

Medical History*	Onset Date
HYPERTENSION	20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Unknown	Unknown
Cigarettes: Unknown	
Cigars: Unknown	
Pipes: Unknown	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 44	44

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
AZATHIOPRINE	150 mg (milligram(s))	BID	-109	53
MESALAZINE	3 g (gram(s))	TID	-109	53
LOPERAMIDE	4 mg (milligram(s))	PRN	8	71
CICLOSPORIN	600 mg (milligram(s))	BID	51	ONGOING
JELLIPROCT	0.25/50.0 mg (milligram(s))	TID	51	ONGOING
PAPAVER SOMNIFERUM	0.6 mL (millilitre(s))	TID	51	ONGOING
PREDNISOLONE	110 mg (milligram(s))	QD	53	59

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF COLITIS ULCEROSA DISEASE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 53 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
AE Stopped Rx Day	71 (27 DAYS AFTER LAST TREATMENT)
Duration of AE	19 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	THE ULCERATIVE COLITIS DISEASE IS DEGRADED.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY, IMPORTANT MEDICAL OR SURGICAL INTERVENTION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（ドイツ）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

被験者は，血性下痢，心窩部痛及び嘔吐の症状のため入院した。入院中，下痢は軽快し，血便は減少した。嘔吐及び心窩部痛も回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Structucabiven（静脈栄養製剤），ロペラミド，シクロスポリン，Prednisolon（プレドニゾロン），Jelliproct（リドカイン塩酸塩），Novaminsulfon，Pantozol（パントプラゾールナトリウム水和物）及び Tincture opii（アヘンチンキ）が投与された。

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: The ulcerative colitis disease is degraded.

- AbbVie: Patient with worsening of ulcerative colitis and increase in stool frequency and rectal bleeding leading to hospitalization.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Rectum-3= Severe disease (spontaneous bleeding, ulceration)

Sigmoid -2= Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Descending colon 1= Mild disease (erythema, decreased vascular pattern, mild friability

Transverse colon- 0 = Normal or inactive disease

Ascending colon/cecum - Normal or inactive disease

With Presence of friability; Subscore 3

[redacted] 20[redacted] ECG: Normal

[redacted] 20[redacted] GASTROSCOPY: Erthematose Pangastritis

[redacted] 20[redacted] psych council: Suspected psycho vegetative dysregulation

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	2[redacted]	FEMALE	White

Medical History*	Onset Date
ARTHRALGIA: FEET AND KNEES	20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Current (8 YEARS, 0.1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 22	22

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	4 g (gram(s))	QD	-215	72
ASCORBIC ACID	200 IU (international unit(s))	QD	-126	ONGOING
PREDNISONE	30 mg (milligram(s))	QD	-20	45

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	UC EXACERBATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 31 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	EXACERBATION OF THE DISEASE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（イスラエル）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，関節痛（両足及び膝）及び潰瘍性大腸炎であった。被験者は喫煙者（1 日 0.1 箱を 8 年間）及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。

入院する前の週に，血性下痢，腹痛及び直腸しぶりの症状が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。血性下痢，直腸しぶり，体重減少及び手関節の関節痛の兆候及び症状が認められ，ステロイドが静脈内投与された。20[redacted] 年 [redacted] 月 [redacted] 日，ステロイドの経口投与の処方を受け，被験者は退院した。

治療薬として prednisone 及びヒドロコルチゾンが投与された。

The patient's past medications include:

CIPRODEX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.22.0] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of UC EXACERBATION

- Investigator: Exacerbation of the disease.

- AbbVie: Event more likely related to pre-existing Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

Unknown date CRP: 12 - units not provided.

Unknown date HB: 12 - units not provided.

[redacted] 20[redacted] WEIGHT: 54 KG

[redacted] 20[redacted] WEIGHT: 56.2 KG

[redacted] 20[redacted] WEIGHT: 56.6 KG

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	3[redacted]	MALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: AMOXICILLIN ALLERGY	[redacted]19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 22	22

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
BECLOMETASONE	5 mg (milligram(s))	QD	-49	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	UC WORSENING
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 25 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
AE Stopped Rx Day	39 (17 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS SEVERE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（イタリア）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，腹痛，直腸出血，体重減少及び液状便の頻度増加のため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted]20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PENTACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of UC WORSENING

- Investigator: Ulcerative colitis severe

- AbbVie: Worsening underlying disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL X-RAY: Mild intestinal lobe relaxation

[redacted] 20[redacted] CRP: 75.30 MG/L (normal 0 to 6)

[redacted] 20[redacted] CRP: 2.90 MG/L (normal 0 to 6)

[redacted] 20[redacted] HEMOGLOBIN: 135 G/L (normal 140 to 175)

[redacted] 20[redacted] INR: 1.23 % (normal 0.88 to 1.13)

[redacted] 20[redacted] LYMPHOCYTES: 5.22 X10**9/L (normal 1.10 to 4.80)

[redacted] 20[redacted] MONOCYTES: 1.23 X10**9/L (normal 0.20 to 0.96)

[redacted] 20[redacted] NEUTROPHILS: 12.53 X10**9/L (normal 1.80 to 7.80)

[redacted] 20[redacted] PLATELET COUNT: 467 X10**9/L (normal 150 to 450)

[redacted] 20[redacted] PLATELET COUNT: 550 X10**9/L (normal 150 to 450)

[redacted] 20[redacted] POTASSIUM: 4.8 MMOL/L (normal 3.4 to 4.5)

[redacted] 20[redacted] POTASSIUM: 5.3 MMOL/L (normal 3.4 to 4.5)

[redacted] 20[redacted] PROTHROMBIN ACTIVITY: 71 % (normal 75 to 112)

[redacted] 20[redacted] PT: 1.23 % (normal 0.90 to 1.20)

[redacted] 20[redacted] SGPT/ALT: 53 U/L (normal 10 to 50)

[redacted] 20[redacted] UNCONJUGATED BILIRUBIN: 2.3 UMOL/L (normal 3.4 to 13.7)

[redacted] 20[redacted] WBC: 12.86 X10**9/L (normal 4.40 to 11.00)

[redacted] 20[redacted] WBC: 18.98 X10**9/L (normal 4.40 to 11.00)

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
表皮内悪性黒色腫	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	4[redacted]	FEMALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: EUTHYROID SICK SYNDROME	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
No information.				

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	MELANOMA IN SITU (BRESLOW 0.4 MM)
Preferred term	表皮内悪性黒色腫
AE Onset Date / Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	4[redacted]
AE Stopped Rx Day	29
Duration of AE	15 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（イタリア）であり，重篤な有害事象の表皮内黒色腫（ブレスローの腫瘍深達度：0.4 mm）を発現した。関連する病歴は，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，表皮内悪性黒色腫（ブレスローの腫瘍深達度：0.4 mm）が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，メラノサイト性病変の切除が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，表皮内悪性黒色腫（ブレスローの腫瘍深達度：0.4 mm）は回復した。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Melanoma in situ (10027148) (Malignant melanoma in situ (10025652)) [v.19.1] [10027148]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of MELANOMA IN SITU (BRESLOW 0.4MM)

- Investigator: Not reported.

- AbbVie: The event was reported at week 2 of the study. Based on currently limited information reported by the site, the event could started prior to the study drug treatment initiation.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肝炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	2[redacted]	FEMALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: EASY BRUISING	20[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Current (8 YEARS, 1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 51	51
				[redacted]20[redacted] / 52	[redacted]20[redacted] / 362	311

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
FISH OIL	1 CAPSULE	QD	Y: 20[redacted]	28
TRYPTOPHAN, L-	1 CAPSULE	QD	Y: 20[redacted]	28
VITAMINS NOS	1 TABLET	QD	Y: 20[redacted]	28
MESALAZINE	4.8 g (gram(s))	QD	-259	ONGOING
SPIRULINA SPP.	1 CAPSULE	QD	-209	28
NUTRIENTS NOS	125 mL (millilitre(s))	BID	-8	10
BISACODYL	5 mg (milligram(s))	BID	-7	-7
MOVIPREP	2 L (litre(s))	QD	-6	-5
FENTANYL	125 mcg (microgram(s))	QD	-5	-5
MIDAZOLAM	5 mg (milligram(s))	QD	-5	-5
PARACETAMOL	1000 mg (milligram(s))	QID	-2	3
ACETYLCYSTEINE	UNKNOWN UNKNOWN	Other	-2	6

Event #1: Serious Adverse Event*

Event Description	HEPATITIS OF UNKNOWN ETIOLOGY
Preferred term	肝炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 1
Age at AE Onset	2[redacted]
AE Stopped Rx Day	28
Duration of AE	28 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	USE OF MELANOTAN, A COMPOUND THAT INDUCES SKIN PIGMENTATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（オランダ）であり，重篤な有害事象の原因不明の肝炎を発現した。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，原因不明の肝炎が発現した。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。入院時の記録及び診察記録によると，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に潰瘍性大腸炎の再燃のため入院した。トランスアミナーゼ値は正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，アダリムマブの初回投与が行われた。初回投与前に血液検体が採取され，ベースライン来院時の臨床検査の結果，アラニンアミノトランスフェラーゼ（以下「ALT」）増加（基準範囲上限の 10 倍）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日に再実施された臨床検査では ALT は 5241 U/L であった。本事象の臨床経過として，アセチルシステインの投与が開始され，アセトアミノフェンは中止された。また，肝炎ウイルスの血清検査のため，血液検体が採取された。20[redacted] 年 [redacted] 月 [redacted] 日，トランスアミナーゼ値は大幅に低下していた（ALT 3511 U/L）。潰瘍性大腸炎の症状は週末明けにほぼ完全に消失しており，トランスアミナーゼ値が着実に低下していたことから，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。20[redacted] 年 [redacted] 月 [redacted] 日，原因不明の肝炎は回復した。

治療薬として硫酸マグネシウム，塩化カリウム，Fluimicil（アセチルシステイン），メトクロプラミド，Duspatal，Flaxiparin（ヘパリンカルシウム），アセトアミノフェン及びオンダンセトロンが投与された。

Causality for HUMIRA (Open Label)

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1) Hepatitis (10019717) (Hepatitis (10019717)) [v.18.1] [10019717]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of HEPATITIS OF UNKNOWN ETIOLOGY

- Investigator: Use of Melanotan, a compound that induces skin pigmentation.

- AbbVie: The subject has very elevated ALT and AST on the baseline visit. The PI reported that the subject is taking melatonin, a supplement for skin protection.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Endoscopy at screening:

RECTUM - 1 = Mild disease (erythema, decreased vascular pattern, mild friability)

SIDMOID, DESCENCING COLON, TRANVERSE COLON, ASCENDING COLON/CECUM - 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Presence of friability – yes

Subscore- 2

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	3[redacted]	FEMALE	White

Medical History*	Onset Date
DIABETES MELLITUS: DURING CORTICOSTEROID THERAPY	[redacted]20[redacted]
HYPERTHYROIDISM	19[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ABDOMINAL PAIN	[redacted]20[redacted]
OTHER: AGENESIS OF THE LEFT KIDNEY	[redacted]19[redacted]
OTHER: ASYMPTOMATIC ELEVATION OF TRANSAMINASES, PROBABLY DUE TO FORMER HBV INFECTION	[redacted]20[redacted]
OTHER: BREAST CYST 7 MM	[redacted]20[redacted]
OTHER: CLOSTRIDIUM DIFFICILE INFECTION	20[redacted]
OTHER: CORTICOSTEROID-INDUCED ACNE	[redacted]20[redacted]
OTHER: OVARIAN CYST	20[redacted]
OTHER: SPONTANEOUS ABORTION	[redacted]20[redacted]
OTHER: UTERINE MYOMA	[redacted]20[redacted]
OTHER: VESICOURTERAL REFLUX	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
				[redacted]20[redacted] / 60	[redacted]20[redacted] / 256	197

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MERCAPTOPURINE	50 mg (milligram(s))	QD	-195	125
MESALAZINE	1500 mg (milligram(s))	BID	-130	17
LOPERAMIDE	2 mg (milligram(s))	PRN	-18	ONGOING
FORTRANS	111 g (gram(s))	QD	-15	-14
ETOMIDATE	4 mg (milligram(s))	QD	-14	-14
MIDAZOLAM	1 mg (milligram(s))	QD	-14	-14
PROPOFOL	40 mg (milligram(s))	QD	-14	-14
SUFENTANIL	10 mcg (microgram(s))	QD	-14	-14
PANTOPRAZOLE	40 mg (milligram(s))	QD	-11	-2
PARACETAMOL	500 mg (milligram(s))	PRN	2	2
PANTOPRAZOLE	20 mg (milligram(s))	PRN	9	12
PARACETAMOL	500 mg (milligram(s))	PRN	9	9
CALCIUM CARBONATE	1000 mg (milligram(s))	QD	11	190
POTASSIUM	391 mg (milligram(s))	BID	11	190
PREDNISONE	40 mg (milligram(s))	Other	11	25
ALBUMIN HUMAN	UNK mL (millilitre(s))	QD	11	41
COLECALCIFEROL	UNK IU (international unit(s))	QD	11	41
ENOXAPARIN	UNK mg (milligram(s))	QD	11	41
IRON	UNK mg (milligram(s))	QD	11	41
PANTOPRAZOLE	20 mg (milligram(s))	QD	11	41
FLURBIPROFEN	8.75 mg (milligram(s))	QID	12	13
FLUTICASONE	1 DF (dosage form)	BID	13	174

Event #1: Serious Adverse Event*

Event Description	ULCERATIVE COLITIS AGGRAVATED
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	3[redacted]
AE Stopped Rx Day	25
Duration of AE	11 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS WITH SEVERE COURSE WITHIN LAST 2-3 YRS, GRADUALLY WORSENING DISEASE AFTER CORTICOSTEROIDS HAD BEEN STOPPED.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者には粘液性の血性下痢の悪化が認められ，排便回数は 1 日最高 6 回であった。発熱（38°C），「高度」の貧血，めまい，脱力及び乾性咳嗽もみられた。コルチコステロイドの投与及び濃厚赤血球 4 単位の輸血が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

治療として Monover，20%アルブミン，Kalipoz prolongatum（塩化カリウム），Encorton，Controloc（パントプラゾールナトリウム水和物），Clexane（エノキサパリンナトリウム），ferric isomaltose，アルブミン，メサラジン及びメルカプトプリンの投与，並びに濃厚赤血球の輸

血が行われた。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for HUMIRA (Open Label)

Event of ULCERATIVE COLITIS AGGRAVATED

- Investigator: Ulcerative colitis with severe course within last 2-3 years, gradually worsening disease after corticosteroids had been stopped.

- AbbVie: This report was initially submitted as a respiratory infection with hospitalization. Updated information was sent and the reason for the hospitalization was worsening of ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Albumin: 2.6 G/DL

[redacted] 20[redacted] body temperature: 38 Degrees C

[redacted] 20[redacted] C-reactive protein: 2.6 mg/dL

[redacted] 20[redacted] Clostridium difficile toxin: Negative

[redacted] 20[redacted] cmv igm: negative

[redacted] 20[redacted] EBV IgM: negative

[redacted] 20[redacted] hemoglobin: 6.8 G/DL

[redacted] 20[redacted] stool OVA & CYSTS: Negative

[redacted] 20[redacted] WBC (hematology): 5.34 X10**3/MCL

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血	X			
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	3[redacted]	MALE	White

Medical History*	Onset Date
ANEMIA: SECONDARY	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 63	63
				[redacted]20[redacted] / 64	[redacted]20[redacted] / 358	295

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
FERRO-FOLSAN	1 TABLET	BID	Y: 20[redacted]	424
MESALAZINE	1 g (gram(s))	TID	Y: 20[redacted]	424
AZATHIOPRINE	100 mg (milligram(s))	QD	Y: 20[redacted]	424
METHYLPREDNISOLONE	8 mg (milligram(s))	BID	-200	27
METHYLPREDNISOLONE	14 mg (milligram(s))	QD	28	34
METHYLPREDNISOLONE	12 mg (milligram(s))	QD	35	41
METHYLPREDNISOLONE	10 mg (milligram(s))	QD	42	48
METHYLPREDNISOLONE	8 mg (milligram(s))	QD	49	55
HYDROCORTISONE	UNK		56	63
IRON	UNK		56	63
METRONIDAZOLE	UNK		56	63
RED BLOOD CELLS	3 DF (dosage form)	QD	56	63

Event #1: Serious Adverse Event*

Event Description	SECONDARY ANEMIA INCREASING, ULCERATIVE COLITIS FLARE
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 56
Age at AE Onset	3[redacted]
AE Stopped Rx Day	63
Duration of AE	8 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	SYMPTOMATIC SECONDARY ANEMIA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event*

Event Description	SECONDARY ANEMIA INCREASING, ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 56
Age at AE Onset	3[redacted]
AE Stopped Rx Day	63
Duration of AE	8 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	SYMPTOMATIC SECONDARY ANEMIA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の再燃による二次性貧血の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側潰瘍性大腸炎）及び二次性貧血であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃による二次性貧血の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃による二次性貧血の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。疲労及び回転性めまいが認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。治験責任医師によると，二次性貧血は潰瘍性大腸炎の再燃のため悪化した。

治療として Corhydrone（ヒドロコルチゾン），Ferinject（カルボキシマルトース第二鉄），Cipronex（シプロフロキサシン），Metypred（メチルプレドニゾロン），メトロニダゾール及び Ferrum（フマル酸第一鉄）の投与，並びに濃厚赤血球の輸血が行われた。

Causality for HUMIRA (Open Label)

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1) Secondary anemia (10054606) (Anaemia (10002034)) [v.19.0] [10054606]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of SECONDARY ANEMIA INCREASING, ULCERATVE COLITIS FLARE

- Investigator: Symptomatic secondary anemia.

- AbbVie: The patient has known medical history of anemia that was present at the study enrollment. The event has no reasonable possibility to be caused by study drug. It is exacerbation of preexisting condition.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Abdomen RTG: No signs of megacolon toxicum

[redacted] 20[redacted] Hematocrit: 25.3 %

[redacted] 20[redacted] Hematocrit: 30.9 %

[redacted] 20[redacted] Hemoglobin: 7.8 G/DL

[redacted] 20[redacted] Hemoglobin: 9.8 G/DL

[redacted] 20[redacted] High-sensitivity C-reactive protein: 132.8 MG/L (normal 0 to 5)

[redacted] 20[redacted] Platelet count: 1095 X10**3/MCL

[redacted] 20[redacted] Platelet count: 760 X10**3/MCL

[redacted] 20[redacted] WBC (hematology): 6.21

[redacted] 20[redacted] WBC (hematology): 4.05

Subject [redacted] (Investigator[redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血	X			
クロストリジウム・ディフィシレ感染	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	2[redacted]	FEMALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: HYPOTHYROIDISM	[redacted]20[redacted]
OTHER: MENSTRUAL DISORDERS	[redacted]20[redacted]
OTHER: RIGHT KIDNEY CYST	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
				[redacted]20[redacted] / 60	[redacted]20[redacted] / 165	106

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
LEVOTHYROXINE	25 mcg (microgram(s))	Other	-313	ONGOING
DROTAVERINE	40 mg (milligram(s))	BID	-130	ONGOING
ESOMEPRAZOLE	20 mg (milligram(s))	QD	-130	ONGOING
AZATHIOPRINE	100 mg (milligram(s))	QD	-113	ONGOING
MESALAZINE	4,5 g (gram(s))	QD	-113	ONGOING
RED BLOOD CELLS	UNK mL (millilitre(s))	QD	36	36
ETAMSILATE	4 mL (millilitre(s))	BID	36	39
GLUCOSE	500 mL (millilitre(s))	QD	36	39
PANTOPRAZOLE	40 mg (milligram(s))	QD	36	39
PAPAVERINE	40 mg (milligram(s))	BID	36	39
SODIUM CHLORIDE	500 mL (millilitre(s))	BID	36	39
TRAMADOL	100 mg (milligram(s))	QD	36	39

Event #1: Serious Adverse Event*

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 36
Age at AE Onset	2[redacted]
AE Stopped Rx Day	37
Duration of AE	2 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	Reasonable possibility
Other Cause of Event	CLOSTRIDIUM DIFFICILE INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event*

Event Description	CLOSTRIDIUM DIFFICILE INFECTION
Preferred term	クロストリジウム・ディフィシレ感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 36
Age at AE Onset	2[redacted]
AE Stopped Rx Day	41
Duration of AE	6 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の女性（ポーランド）であり，重篤な有害事象のクロストリジウム・ディフィシレ感染及び貧血を発現した。関連する病歴は，潰瘍性大腸炎及び月経障害であった。被験者は非喫煙者及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，クロストリジウム・ディフィシレ感染及び貧血が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，クロストリジウム・ディフィシレ感染は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者には腹痛，悪心，血性下痢，食欲減退，発熱，安静時の息切れ，血色不良，頻脈及び高度の脱力の症状が認められた。薬剤，静脈内輸液及び完全静脈栄養法による治療を 2 日間受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療として Paraverinum，5%ブドウ糖，Cosmofer，Kabiven TPN，Cyclonamine 12.5%，Hemofer prolongatum（硫酸鉄水和物），Eziclen，Encorton，Asamax（メサラジン），Controloc（パントプラゾールナトリウム水和物），メトロニダゾール，トラマドール，Corhydrone（ヒドロコルチゾン），アセトアミノフェン及び 0.9%塩化ナトリウムの投与，並びに輸血剤（濃厚赤血球）及び濃厚赤血球の輸血が行われた。

The patient's past medications include:

EZICLEN for ENDOSCOPY [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Clostridium difficile infection (10054236) (Clostridium difficile infection (10054236)) [v.22.0] [10054236]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Anemia (10002272) (Anaemia (10002034)) [v.22.0] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of CLOSTRIDIUM DIFFICILE INFECTION

- Investigator: Not reported

- AbbVie: Clostridium difficile infection is relatively common in ulcerative colitis and associated immunosuppression. The subject is also using immunomodulators.

Event of ANEMIA

- Investigator: Clostridium difficile infection.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] C-reactive protein: 51.9 MG/L (normal >0)

[redacted] 20[redacted] C-reactive protein: 9.1 MG/L (normal 0 to 5)

[redacted] 20[redacted] Electrocardiogram: Normal

[redacted] 20[redacted] Hemoglobin: 7.0 G/DL (normal 11.0 to 15.0)

[redacted] 20[redacted] Hemoglobin: 9.5 G/DL (normal 11 to 15)

[redacted] 20[redacted] HISTOPATHOLOGY: Colitis Ulcerosa in stadio activa

[redacted] 20[redacted] PANENDOSCOPY: Normal

[redacted] 20[redacted] RECTOSCOPY: Mayo 2

[redacted] 20[redacted] TOXIN A AND B OF CLOSTRIDIUM DIFFICILE (STOOL): Positive

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	2[redacted]	MALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Current (10 YEARS, 0.5 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
				[redacted]20[redacted] / 59	[redacted]20[redacted] / 358	300

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	2500 mg (milligram(s))	BID	Y: 20[redacted]	ONGOING
BUDESONIDE	9 mg (milligram(s))	QD	-50	31
HYDROCORTISONE	100 mg (milligram(s))	QID	35	42
IRON	mg (milligram(s))	QD	35	42
METAMIZOLE	mg (milligram(s))	QD	35	42
OMEPRAZOLE	mg (milligram(s))	QD	35	42
PARACETAMOL	MG/ML	QD	35	42
HYDROCORTISONE	100 mg (milligram(s))	QID	35	44

Event #1: Serious Adverse Event*

Event Description	EXACERBATION OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 35
Age at AE Onset	2[redacted]
AE Stopped Rx Day	42
Duration of AE	8 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	THE PATIENT WAS ADMITTED TO THE HOSPITAL DUE INFLAMMATION OF ULCERATIVE COLITIS. THE PATIENT STOPPED SMOKING.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（ポーランド）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，左側潰瘍性大腸炎であった。被験者は喫煙者（10 年間）及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が発現し，腹痛及び 1 日最高 15 回の血便量増加の兆候及び症状が認められた。同日，潰瘍性大腸炎の増悪のため，被験者は入院した。被験者が禁煙したため，本事象が疑われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬として Corhydron（ヒドロコルチゾン），Polprazol（オメプラゾール），Perfalgan（アセトアミノフェン），Monover，Pyralgina（スルピリン水和物），ヒドロコルチゾン及びロペラミドが投与された。

The patient's past medications include:

Sulfasalazyna for ULCERATIVE COLITIS [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA (Blinded)

Event of EXACERBATION OF UC

- Investigator: THE PATIENT WAS ADMITTED TO THE HOSPITAL DUE INFLAMMATION OF ULCERATIVE COLITIS. THE PATIENT STOPPED SMOKING.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL XRAY: no obstruction or perforation has been demonstrated within the abdominal cavity

[redacted] 20[redacted] WBC: 18.56 tys/ul

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血	X	X		
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	2[redacted]	MALE	White

Medical History*	Onset Date
ANEMIA: POST-HAEMORRHAGIC ANEMIA+ CHRONIC INFLAMMATORY DISEASE	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 49	49

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
COLECALCIFEROL	500 IU (international unit(s))	QD	Y: 20[redacted]	ONGOING
FISH OIL	1 CAPSULE	QD	Y: 20[redacted]	ONGOING
SUPRADYN	1 CAPSULE	QD	Y: 20[redacted]	ONGOING
METHYLPREDNISOLONE	32 mg (milligram(s))	BID	-61	ONGOING
BLOOD AND RELATED PRODUCTS	1 UNIT/DAY 1 UNIT PER DAY	QD	21	23

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	UC FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 35
Age at AE Onset	2[redacted]
AE Stopped Rx Day	56 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	22 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	LACK OF RESPONSE TO INVESTIGATIONAL THERAPY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	SEVERE ANEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 49
Age at AE Onset	2[redacted]
AE Stopped Rx Day	52 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	SEVERE ULCERATIVE COLITIS, UNCONTROLLED BY THE SUDY MEDICATION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY, IMPORTANT MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（ルーマニア）であり，重篤な有害事象の高度の貧血を発現した。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎，貧血（出血後貧血及び慢性炎症性疾患）及び胃腸障害であった。

20[redacted] 年 [redacted] 月 [redacted] 日，高度の貧血が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，高度の貧血は回復した。

治験責任医師によると，試験開始時（20[redacted] 年 [redacted] 月 [redacted] 日）からヘモグロビン値 7.7 g/dL の中等度の貧血が認められていた。試験中，本事象は徐々に悪化した（治験薬の投与によるコントロールが不能な高度の潰瘍性大腸炎）。非重篤な貧血に対し，20[redacted] 年 [redacted] 月 [redacted] 日，[redacted] 日及び [redacted] 日に輸血が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。重篤な本事象に伴う兆候及び症状として，100 回/分の頻脈が認められた。被験者は輸血を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

本事象に関連するリスク因子には高度の貧血があった。本事象の原因は，治験薬投与によるコントロールが不能な高度の潰瘍性大腸炎であった。
治療として輸血が行われた。
The patient's past medications include:

IMURAN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOL for INDICATION UNKNOWN ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) Anemia (10002272) (Anaemia (10002034)) [v.22.0] [10002272]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of SEVERE ANEMIA

- Investigator: SEVERE ULCERATIVE COLITIS, UNCONTROLLED BY THE STUDY MEDICATION

- AbbVie: SUBJECT HAS KNOWN MEDICAL HISTORY OF ANEMIA

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（ルーマニア）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎及び出血後貧血であった。被験者は非喫煙者及び非アルコール摂取者であった。
20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。
試験開始時から，治験薬投与によるコントロールが不能な高度の潰瘍性大腸炎による中等度の貧血（非重篤）が認められていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は血性下痢の症状を伴う潰瘍性大腸炎の再燃と診断され，入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は高度の貧血と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化のため，直腸結腸全切除が実施された。回腸嚢を造設したことから，術後の被験者の状態は良好であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
本事象のため，治験薬の投与は中止された。

The patient's past medications include:

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.22.0] [10045283]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of UC FLARE

- Investigator: Lack of response to investigational therapy.

- AbbVie: Event more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COLONOSCOPY: Extensive UC/pancolitis

[redacted] 20[redacted] HEART RATE: 100 /min

20[redacted] HEMOGLOBIN: 7.7 G/DL

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	4[redacted]	MALE	White

Medical History*	Onset Date
DEPRESSION: POST TRAUMATIC REACTION AFTER A CAR ACCIDENT , IN WHICH THE WIFE DIED	[redacted]20[redacted]
OSTEOPOROSIS	20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Former
Cigarettes: Former (20 YEARS, 2 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 45	45

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	4000 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
METAMIZOLE	500 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
ESCITALOPRAM	20 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
LEKOVIT CA	1 TABLET	QD	Y: 20[redacted]	ONGOING
QUETIAPINE	200 mg (milligram(s))	BID	Y: 20[redacted]	ONGOING
PREDNISONE	30 mg (milligram(s))	QD	-47	13
PARACETAMOL	1 g (gram(s))	QD	13	13
CEFTRIAXONE	2 g (gram(s))	QD	13	22
DALTEPARIN	5000 IU (international unit(s))	QD	13	22
METHYLPREDNISOLONE	60 mg (milligram(s))	QD	13	22
METRONIDAZOLE	500 mg (milligram(s))	TID	13	22
RINGERS LACTAT	1000 mL (millilitre(s))	QD	13	22
STEROFUNDIN ISO	1000 mL (millilitre(s))	QD	13	22
PREDNISONE	30 mg (milligram(s))	QD	22	58

Event #1: Serious Adverse Event*

Event Description	WORSENING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 13
Age at AE Onset	4[redacted]
AE Stopped Rx Day	22
Duration of AE	10 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ACUTE FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION, IMPORTANT MEDICAL OR SURGICAL INTERVENTION

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	4[redacted]
AE Stopped Rx Day	67 (22 DAYS AFTER LAST TREATMENT)
Duration of AE	25 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	WORSENING OF UC
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（スイス）であり，潰瘍性大腸炎の悪化が認められた。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化，排便回数 1 日 15 回，血便が 50%超，腹痛，寝汗及び関節痛のため，被験者は入院した。発熱は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師によると，本事象に関連するリスク因子として潰瘍性大腸炎があった。本事象に関連する家族歴はなかった。

治療薬として Flagyl（メトロニダゾール），セフトリアキソン，アセトアミノフェン，Ringerlakat，Ringerfundin（等張電解質液），Solu-medrol（メチルプレドニゾロンコハク酸エステルナトリウム）及び Fragmin（ダルテパリンナトリウム）が投与された。

The patient's past medications include:

CICLOSPORIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDENOFALK FOAM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK FOAM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.21.0]　[10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of WORSENING OF UC

- Investigator: Acute flare.

- AbbVie: RECURRING EXACERBATION OF A PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] RECTOSIGMOSCOPY: Severe UC.
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（スイス）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（広範囲の潰瘍性大腸炎／汎大腸炎）及びうつ病（妻が死亡した交通事故後の外傷後反応）であった。被験者は元紙巻タバコ喫煙者（1 日 2 箱を 20 年間）及び元アルコール摂取者（1 日 2～4 杯）であった。
20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎の悪化，15 回を超える血便及び関節痛が認められた。
20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎の悪化は回復した。
20[redacted] 年[redacted] 月[redacted] 日，裂肛（非重篤）が発現した。20[redacted] 年[redacted] 月[redacted] 日，被験者は入院し，静脈内治療を受けた。中等度の腹痛が認められた。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。
治療薬として Factu cream 50/10 mg，Sandimmun neoral（シクロスポリン），Escitalopram mepha（エスシタロプラム），Vi de 3（コレカルシフェロール），Esomep mups（エソメプラゾールマグネシウム水和物），Imurek（アザチオプリン），Fragmin（ダルテパリンナトリウム），Xylocain gel（リドカイン），Nitroglycerin-salbe 0.2%（ニトログリセリン），シクロスポリン，アセトアミノフェン，シプロフロキサシン，Flagyl（メトロニダゾール）及び Bactrim forte（スルファメトキサゾール／トリメトプリム）が投与された。

The patient's past medications include:

CICLOSPORIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDENOFALK FOAM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PARACETAMOL for PAIN RELEASE BY DISEASE WORSENING and PAIN RELEASE BY DISEASE WORSENING ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.1] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of WORSENING OF UC

- Investigator: Worsening of ulcerative colitis.

- AbbVie: Event is more likely related to pre-existing ulcerative colitis.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
子宮頚部扁平上皮癌	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	3[redacted]	FEMALE	White

Medical History*	Onset Date
ARTHRITIS: RIGHT KNEE MONO ARTHRITIS	[redacted]20[redacted]
CONGENITAL HEART DISEASE: VENTRICULAR SEPTIAL DEFECT	[redacted]19[redacted]
OSTEOPOROSIS: OSTEOPENIA	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: MECHANICAL BACK PAIN	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Former (19 YEARS, 1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 28	28

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	4.8 g (gram(s))	QD	Y: 20[redacted]	ONGOING
PARACETAMOL	500 mg (milligram(s))	PRN	Y: 20[redacted]	ONGOING
LEKOVIT CA	1250 mg (milligram(s))	Other	Y: 20[redacted]	ONGOING
MESALAZINE	4.8 g (gram(s))	QD	Y: 20[redacted]	ONGOING
FOLIC ACID	5 mg (milligram(s))	Other	Y: 20[redacted]	ONGOING
METHOTREXATE	25 mg (milligram(s))	Other	Y: 20[redacted]	ONGOING
BECLOMETASONE	5 mg (milligram(s))	QD	-67	28

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	SQUAMUS CARCINOMA OF CERVIX, FIGO STAGE 1A1&CIN3
Preferred term	子宮頚部扁平上皮癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 39 (11 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
AE Stopped Rx Day	
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ABNORMAL SMEAR
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL OR SURGICAL INTERVENTION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，3[redacted] 歳の女性（イギリス）であり，重篤な有害事象の子宮頚部扁平上皮癌，FIGO 分類 IA1 及び CIN3 を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，子宮頚部扁平上皮癌，FIGO 分類 IA1 及び CIN3 が発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，腹痛及び手術を受けるため，被験者は入院した。被験者は 20[redacted] 年 [redacted] 月に子宮頚部扁平上皮癌，FIGO 分類 IA1 及び CIN3 と診断されていた。腹腔鏡下根治的子宮摘出，両側卵管摘除及び両側骨盤リンパ節郭清が実施され，被験者は手術から回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for HUMIRA (Blinded)

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1) Squamous cell carcinoma of the cervix (10041848) (Squamous cell carcinoma of the cervix (10041848)) [v.21.1] [10041848]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA (Blinded)

Event of SQUAMUS CARCINOMA OF CERVIX, FIGO STAGE 1A1&CIN3

- Investigator: Abnormal smear.

- AbbVie: Weak temporal association with only a little over one month of study drug exposure prior to onset of the event. Event was likely pre-existing.

Subject [redacted] (Investigator [redacted]

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	5[redacted]	MALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: ALLERGIC RHINITIS	NOT REPORTED
SURGERY: TONSILLECTOMY	19[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Former (19 YEARS, 1 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 31	31

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
SALBUTAMOL	PRN PUFFS	PRN	Y: 19[redacted]	ONGOING
MESALAZINE	4.8 g (gram(s))	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	FLARE OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 39 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	40 (9 DAYS AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	FLARE OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（イギリス）であり，重篤な有害事象の潰瘍性大腸炎の再燃が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の再燃は回復した。

投与 4 週時の来院時（20[redacted] 年 [redacted] 月 [redacted] 日），持続する再燃の症状のため，被験者は治験実施施設に連絡を取った。被験者は治験分担医師との話し合いの後に治験薬の投与を中止し，潰瘍性大腸炎の管理に関する外科医の意見を聞くため，地域の病院に入院することが決定された。治験分担医師によって紹介の手続きが行われた。20[redacted] 年 [redacted] 月 [redacted] 日，症状の悪化（1 日 8 回の便通，直腸出血及び腹痛）のため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，結腸亜全摘及び回腸瘻造設が行われ，被験者は手術から回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治療薬としてプレドニゾロンが投与された。

The patient's past medications include:

TACROLIMUS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.21.1]　[10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA (Blinded)

Event of FLARE OF ULRATIVE COLITIS

- Investigator: FLare of ulcerative colitis

- AbbVie: This patient has severe disease activity and was hospitalized due to a disease flare.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
大腸狭窄	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	5[redacted]	MALE	White

Medical History*	Onset Date
HYPERTENSION: ESSENTIAL HYPERTENSION	[redacted]20[redacted]
KIDNEY DISORDER: CHRONIC PYELONEPHRITIS KIDNEY CYSTS	[redacted]20[redacted]
PANCREATITIS: CHRONIC PANCREATITIS WITH EXOCRINE PANCREATIC INSUFFICIENCY	[redacted]20[redacted]
PEPTIC ULCER DISEASE: DUODENAL ULCER DISEASE	20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ACUTE MIOCARDITIS	[redacted]20[redacted]
SURGERY: APPENDECTOMY	20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	1 g (gram(s))	QID	-67	ONGOING
PREDNISOLONE	40 mg (milligram(s))	QD	-23	29
PREDNISOLONE	35 mg (milligram(s))	QD	30	36
PREDNISOLONE	30 mg (milligram(s))	QD	37	43
PREDNISOLONE	25 mg (milligram(s))	QD	44	50
PREDNISOLONE	20 mg (milligram(s))	QD	51	ONGOING
MOVIPREP	2 L (litre(s))	PRN	56	56

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	COLONIC STENOSIS
Preferred term	大腸狭窄
AE Onset Date / Rx Day	[redacted]20[redacted] / 57 (14 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	102 (59 DAYS AFTER LAST TREATMENT)
Duration of AE	46 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	COMPLICATION OF THE MAIN DISEASE, DESCENDING COLON STRICTURE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY, IMPORTANT MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（ウクライナ）であり，致死的な有害事象の外科手術後の腹膜炎及び結腸狭窄が発現した。関連する病歴は，消化性潰瘍疾患，十二指腸潰瘍疾患，膵外分泌機能不全を伴う慢性膵炎，本態性高血圧及び潰瘍性大腸炎であった。被験者は非喫煙者及び非アルコール摂取者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，結腸狭窄が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，結腸狭窄は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，外科手術後腹膜炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は外科手術後腹膜炎と報告された。剖検が実施されたかどうかは不明であった。

20[redacted] 年 [redacted] 月 [redacted] 日，周期性腹痛，腹部膨満感，1 日 2～5 回の下痢，全身の脱力，結腸の部分閉塞を伴う下行結腸及び S 状結腸狭窄と診断された低タンパク血症の症状のため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，開腹，横行結腸，下行結腸及び S 状結腸の 2/3 の切除，上行及び S 状結腸切除術，並びに腹部ドレナージが実施された。手術後，一般的な局所治療を実施している間に中程度に良好な動態が認められたが，20[redacted] 年 [redacted] 月 [redacted] 日には左後腹膜にフレグモーネを伴う結腸内外における不完全及び不定形の瘻孔の形成を伴い，被験者の状態は著しく悪化した。術後の内因性中毒症状は悪化し，左切開部からの膿汁の分泌が認められた。局所療法が行われ，腹膜腔のドレナージ及び後腹膜腔の洗浄が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は更なる治療を断固として拒否し，クリニックから退院した。

治験実施施設は，電話にて被験者が 20[redacted] 年 [redacted] 月 [redacted] 日に死亡したと連絡を受けた。死因は外科手術後腹膜炎であった。死亡時，被験者は入院していなかった。更なる詳細情報は提供されなかった。

Causality for HUMIRA (Blinded)

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1) Peritonitis (10034674) (Peritonitis (10034674)) [v.21.1] [10034674]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

2) Colonic stenosis (10010004) (Large intestinal stenosis (10074061)) [v.21.1] [10010004]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA (Blinded)

Event of POST SURGICAL OPERATION PERITONITIS

- Investigator: The site was informed about this event on [redacted] 20[redacted] via phone.

- AbbVie: Event is more likely related to a surgical complication.

Event of COLONIC STENOSIS

- Investigator: Complication of the main disease

- AbbVie: Event is more likely related to pre-existing ulcerative colitis

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] FLEXIBLE SIGMOIDOSCOPY: Descending colon- severe disease (spontaneous bleeding, ulceration)

[redacted] 20[redacted] HISTOLOGY: Histological analysis of biopsy specimens: mucosa of the colon with uneven folding, here and there with the hyperplasia of the foveolar epithelium, atrophy and small ulceration. Submucosa - edema, partially sclerosis, hemorrhage.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
丹毒	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	5[redacted]	MALE	White

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: INTERNAL HEMOROIDS	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Former
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	4 mg (milligram(s))	QD	-36	ONGOING
PREDNISOLONE	30 mg (milligram(s))	QD	-9	29
PREDNISOLONE	25 mg (milligram(s))	QD	30	36
PREDNISOLONE	20 mg (milligram(s))	QD	37	43
PREDNISOLONE	15 mg (milligram(s))	QD	44	50
PREDNISOLONE	10 mg (milligram(s))	QD	51	57
LEVOFLOXACIN	500 mg (milligram(s))	QD	51	63
METRONIDAZOLE	500 mg (milligram(s))	TID	51	63
PENTOXIFYLLINE	100 mg (milligram(s))	QD	51	63

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	ERYTHEMATOUS ERYSIPELAS LOWER THIRD OF THE RIGHT TIBIA AND ANKLE JOINT.
Preferred term	丹毒
AE Onset Date / Rx Day	[redacted]20[redacted] / 51 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
AE Stopped Rx Day	107 (64 DAYS AFTER LAST TREATMENT)
Duration of AE	57 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	PATIENT HOSPITALISED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，5[redacted] 歳の男性（ウクライナ）であり，重篤な有害事象の右脛骨下 3 分の 1 領域及び足関節の紅斑性丹毒を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，右脛骨下 3 分の 1 領域及び足関節の紅斑性丹毒が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右脛骨下 3 分の 1 領域及び足関節の紅斑性丹毒は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，右下肢の腫脹及び紅斑の症状のため，被験者は緊急入院した。充血，脛骨下部の浮腫の兆候及び症状が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，外来で治療を受けるため，被験者は退院した。
治療薬としてメトロニダゾール，Latren，プレドニゾロン及びレボフロキサシンが投与された。

Causality for HUMIRA (Open Label)

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1) Erysipelas (10015145) (Erysipelas (10015145)) [v.18.1] [10015145]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of ERYTHEMATOUS ERYSIPELAS LOWER THIRD OF THE RIGHT TIBIA AND ANKLE JOINT

- Investigator: The patient was hospitalized.

- AbbVie: The event is likely related to concurrent disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Rectum, sigmoid and descending colon was grade 3 severe. Presence of friability existed and sub score was 3.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	4[redacted]	MALE	White

Medical History*	Onset Date
ANEMIA: SECONDARY ANEMIA	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
No information.	

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
				[redacted]20[redacted] / 57	[redacted]20[redacted] / 358	302

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
PREDNISOLONE	15 mg (milligram(s))	QD	-54	28
MOVIPREP	200 g (gram(s))	Other	-9	-9

Event #1: Serious Adverse Event*

Event Description	ANAEMIA
Preferred term	貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 3
Age at AE Onset	4[redacted]
AE Stopped Rx Day	10
Duration of AE	8 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	PLANNED HAEMOTRANSFUSION FOR SECONDARY ANAEMIA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の男性（ウクライナ）であり，重篤な有害事象の貧血を発現した。関連する病歴は，二次性貧血及び左側潰瘍性大腸炎であった。
20[redacted] 年 [redacted] 月 [redacted] 日，貧血が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，貧血は回復した。
20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。ヘモグロビン低値が認められた。措置として輸血が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。
治療として輸血及び Sorbifer の投与が行われた。

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Anaemia (10002034) (Anaemia (10002034)) [v.19.1] [10002034]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of ANAEMIA

- Investigator: Planned haemotransfusion for secondary anaemia.

- AbbVie: The subject has known medical history of anemia since 20[redacted].

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			
水痘	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	2[redacted]	MALE	Asian

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: FOLLICULITIS	NOT REPORTED
OTHER: HEADACHE	NOT REPORTED

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 29	29

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
MESALAZINE	1200 mg (milligram(s))	TID	-96	ONGOING
PREDNISOLONE	5 mg (milligram(s))	QD	-15	29
PREDNISOLONE	10 mg (milligram(s))	QD	-15	29
BETAMETHASONE	APPLICATION APPLICATION	PRN	-6	ONGOING
LOPERAMIDE	1 mg (milligram(s))	PRN	29	30
PREDNISOLONE	7 mg (milligram(s))	BID	30	ONGOING
COLYTE	0.25 PACKAGE	QD	32	32
DIMETICONE	5 mL (millilitre(s))	QD	32	32
LACTULOSE	90 mL (millilitre(s))	QD	32	32
VALACICLOVIR	500 mg (milligram(s))	BID	51	53

Event #1: Serious Adverse Event*

Event Description	ULCERATIVE COLITIS DEVELOPMENT
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 30 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
AE Stopped Rx Day	73 (44 DAYS AFTER LAST TREATMENT)
Duration of AE	44 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	ULCERATIVE COLITIS DEVELOPMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY

Event #2: Serious Adverse Event*

Event Description	VARICELLA
Preferred term	水痘
AE Onset Date / Rx Day	[redacted]20[redacted] / 51 (22 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
AE Stopped Rx Day	61 (32 DAYS AFTER LAST TREATMENT)
Duration of AE	11 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	TACROLIMUS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（日本）であり，重篤な有害事象の潰瘍性大腸炎の発現及び水痘を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の発現が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，水痘が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，水痘は回復した。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の発現は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の発現が原因で血便を伴う反復性の下痢及び腹痛の症状が認められ，被験者は入院した。治験薬の投与期間中に潰瘍性大腸炎の増悪が認められたため，治験薬の投与は中止された。その後，タクロリムス及び強化顆粒球単球吸着療法が開始されたが，排便及び血便の改善は認められなかった。絶食及び安静による治療が行われた。

20[redacted] 年 [redacted] 月 [redacted] 日，結腸全摘除及びストーマ造設が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，術後の経過が良好になった後，被験者は退院した。

顔面，両腕及び背部の単純ヘルペス感染発現時の体重は 74.0 kg であった。顔面，両腕及び背部に多数の発疹の兆候及び症状が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，発疹が発現し，悪化した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，皮膚科医によって顔面，両腕及び背部の単純ヘルペス感染と診断された。タクロリムス及びプレドニゾロンの用量は漸減され，中止された。20[redacted] 年 [redacted] 月 [redacted] 日，水痘と考えられるいくつかの発疹が認められた。最終的に被験者は水痘帯状疱疹感染と診

断された。アシクロビルが静脈内投与された。20[redacted] 年 [redacted] 月 [redacted] 日，水痘帯状疱疹は完全に消失し，改善した。
治療薬として Gascon drop（ジメチコン），Monilac（ラクツロース），Niflec for endoscopy prep（塩化カリウム／塩化ナトリウム／炭酸水素ナトリウム／無水硫酸ナトリウム），Prograf（タクロリムス水和物）及び Valtrex（バラシクロビル塩酸塩）が投与された。

Causality for HUMIRA (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Varicella (10046980) (Varicella (10046980)) [v.21.0] [10046980]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for HUMIRA (Blinded)

Event of ULCERATIVE COLITIS DEVELOPMENT

- Investigator: Ulcerative colitis development.

- AbbVie: The event is exacerbation of underlying disease.

Event of VARICELLA

- Investigator: Not reported

- AbbVie: POSSIBLY RELATED TO LONG TERM IMMUNOMODULARY TREATMENT FOR UNDERLYING DISEASE AND NOT RELATED TO STUDY PARTICIPATION FROM [redacted] 20[redacted].

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] Colonoscopy:

Endoscopy at screening -Rectum, sigmoid, descending colon, transverse colon and ascending colon/cecum: 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions): Presence of Friability Yes; Subscore 2

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	2[redacted]	MALE	Asian

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: ANTERIOR CRUCIATE LIGAMENT RUPTURE	[redacted]20[redacted]
OTHER: HEMORRHOID	[redacted]20[redacted]
SURGERY: ANTERIOR CRUCIATE LIGAMENT RUPTURE	[redacted]20[redacted]
SURGERY: HEMORRHOID	[redacted]20[redacted]
SURGERY: HEMORRHOID	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Current
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 23	23

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
BIFIDOBACTERIUM LACTIS	1 g (gram(s))	TID	-90	ONGOING
MESALAZINE	1200 mg (milligram(s))	TID	-90	ONGOING
TIQUIZIUM	10 mg (milligram(s))	TID	-38	ONGOING
PREDNISOLONE	5 mg (milligram(s))	QD	-37	55
HYDROCORTISONE	200 mg (milligram(s))	QD	29	29
INFLIXIMAB	500 mg (milligram(s))	QD	29	29

Event #1: Serious Adverse Event*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 43 (20 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
AE Stopped Rx Day	63 (40 DAYS AFTER LAST TREATMENT)
Duration of AE	21 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	NATURAL COUSE OF UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（日本）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎（左側潰瘍性大腸炎）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 4 週時），有効性の欠如のため，医師はアダリムマブの投与を中止した。Solu-cortef（ヒドロコルチゾンコハク酸エステルナトリウム）200 mg 及び Remicade（インフリキシマブ）500 mg が 20[redacted] 年 [redacted] 月 [redacted] 日に投与された。20[redacted] 年 [redacted] 月 [redacted] 日，排便回数増加，腹痛の増悪及び有効性の欠如のため，Remicade（インフリキシマブ）の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，重篤な有害事象である潰瘍性大腸炎の悪化のため，X 線検査及び治療法の変更を目的とし，被験者は入院した。本事象に伴う兆候及び症状として，排便回数の増加及び腹痛が認められた。20[redacted] 年 [redacted] 月 [redacted] 日に絶食が開始され，20[redacted] 年 [redacted] 月 [redacted] 日まで継続された。Bfluid（ビタミン B1・糖・電解質・アミノ酸液），Solacet（ブドウ糖加酢酸リンゲル液），Fesin（含糖酸化鉄）／5%ブドウ糖，タクロリムス及びプレドニゾロンが投与された。20[redacted] 年 [redacted] 月 [redacted] 日，改善が認められ始めた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。
治療薬として 5%ブドウ糖，Fesin（含糖酸化鉄），タクロリムス，Solacet（ブドウ糖加酢酸リンゲル液），Bfluid（ビタミン B1・糖・電解質・アミノ酸液）及びプレドニゾロンが投与された。

The patient's past medications include:

SOL-MELCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA ENEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: natural course of UC

- AbbVie: THE EVENT IS EXACERBATION OF UNDERLYING DISEASE

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] C-REACTIVE PROTEIN: 0.92 mg/dL (normal >=0.0 to <=0.0)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 0.25 mg/dL (normal >=0.0 to <=0.0)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 0.13 mg/dL (normal >=0.0 to <=0.0)

[redacted] 20[redacted] Colonoscopy:

Rectum:

2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Sigmoid:

2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)

Descending colon:

1 = Mild disease (erythema, decreased vascular pattern, mild friability)

Transverse colon:

1 = Mild disease (erythema, decreased vascular pattern, mild friability)

Ascending colon/cecum:

0+Normal or inactive disease

Presence of friability – yes

Subscore – 2

[redacted] 20[redacted] Electrocardiogram:

- Abnormal-not clinically significant

T-waves – abnormal

Counterclockwise torn

[redacted] 20[redacted] Hemoglobin: 9.4 G/DL (normal >=12.6 to <=16.5)

[redacted] 20[redacted] Hemoglobin: 9.7

[redacted] 20[redacted] Hemoglobin: 10.4

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		
肺炎	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	2[redacted]	MALE	Asian

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: EDEMA	[redacted]20[redacted]
OTHER: HABITUAL TONSILLITIS	[redacted]20[redacted]
SURGERY: ADENOTOMY	19[redacted]
SURGERY: BOTH FAUCIAL TONSILS ENUCLEATION	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Former
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 43	43

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
CLOSTRIDIUM BUTYRICUM	40 mg (milligram(s))	TID	Y: 20[redacted]	70
MESALAZINE	2000 mg (milligram(s))	BID	-346	70
ALENDRONIC ACID	35 mg (milligram(s))	Other	-315	70
URSODEOXYCHOLIC ACID	300 mg (milligram(s))	TID	-134	ONGOING
ASPHAGEN	40 mL (millilitre(s))	Other	-6	5
FEXOFENADINE	60 mg (milligram(s))	BID	15	70
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL (millilitre(s))	QD	49	49

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 33
Age at AE Onset	2[redacted]
AE Stopped Rx Day	127 (84 DAYS AFTER LAST TREATMENT)
Duration of AE	95 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	NATURAL COURSE OF UC
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

Event #2: Serious Adverse Event*

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 67 (24 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
AE Stopped Rx Day	144 (101 DAYS AFTER LAST TREATMENT)
Duration of AE	78 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable possibility
Relation to Study Drug by AbbVie	Reasonable possibility
Other Cause of Event	
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（日本）であり，重篤な有害事象の肺炎を発現した。関連する病歴は，広範囲の潰瘍性大腸炎／汎大腸炎であった。被験者は元アルコール摂取者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，肺炎が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，胸痛（非重篤と判断された）が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，仕事中に胸痛が悪化し，救急車にて病院へ搬送された。病院において，38.4°C の発熱及び呼吸苦が認められた。心電図，血液及びコンピュータ断層撮影（以下「CT」）検査が実施された。Soldem 1（ブドウ糖-電解質液［開始液］）500 mL が静脈内投与された。血液検査の結果，白血球数は 12400/mL，C 反応性たん白は 2.72 mg/dL であった。CT 画像において肺の異常所見が示された。同日，被験者は入院した。入院後，Firstcin 1 g（セフォゾプラン塩酸塩）及び Bfluid（ビタミン B1・糖・電解質・アミノ酸液）1000 mL の静脈内投与が開始され，胸痛及び絶食のため，Acelio（アセトアミノフェン）600 mg が導入された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は呼吸器科医の診察を受けた。Solacet（ブドウ糖加酢酸リンゲル液）500 mL の静脈内投与が開始された。胸痛を改善するため，Acelio（アセトアミノフェン）600 mg の投与及び Ropion（フルルビプロフェン　アキセチル）50 mg の静脈内投与が行われていた。20[redacted] 年 [redacted] 月 [redacted] 日，Firstcin 1 g（セフォゾプラン塩

酸塩）の静脈内投与は中止され，Pasil（パズフロキサシンメシル酸塩）500 mg の静脈内投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，CT，胸部 X 線及び呼吸機能検査が実施された。治験責任医師によると，再考の結果，事象名は肺炎に，重症度は高度に変更された。

20[redacted] 年 [redacted] 月 [redacted] 日，胸痛は消失した。20[redacted] 年 [redacted] 月 [redacted] 日に左胸水の増加及び左中下肺野の悪化が認められ，気管支鏡検査が実施された。20[redacted] 年 [redacted] 月 [redacted] 日，気管支鏡検査の結果は正常であった。Pasil（パズフロキサシンメシル酸塩）及び Solacet（ブドウ糖加酢酸リンゲル液）の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，胸部 CT 検査が実施された。20[redacted] 年 [redacted] 月 [redacted] 日の 4 時 50 分に前胸部痛が認められ，心電図検査が実施された。Calonal（アセトアミノフェン）200 mg が投与され，14 時 33 分に前胸部痛は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，呼吸器科の診察が行われ，呼吸器科医は，肺炎の原因を特定することは困難と判断した。被験者の症状は軽減し，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は呼吸器科を受診し，胸部 CT 検査が実施された。肺陰影は完全に消失していた。

本事象に関連するリスク因子又は家族歴はなかった。過去に本事象が発現したことはなかった。

治療薬として Pasil（パズフロキサシンメシル酸塩），Soldem 1（ブドウ糖-電解質液［開始液］），Acelio（アセトアミノフェン），Solacet（ブドウ糖加酢酸リンゲル液），Ropion（フルルビプロフェン　アキセチル），Firstcin（セフォゾプラン塩酸塩）及び Bfluid（ビタミン B1・糖・電解質・アミノ酸液）が投与された。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PASIL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Blinded)

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1)　Pneumonia (10035664)　(Pneumonia (10035664))　[v.20.0]　[10035664]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連あり

治験依頼者による因果関係判定（薬剤／ワクチン）：関連あり

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Blinded)

Event of PNEUMONIA

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BODY TEMPERATURE: 38.4 Degrees C

[redacted] 20[redacted] BRONCHOSCOPY: Normal

[redacted] 20[redacted] C-REACTIVE PROTEIN: 2.72 mg/dL (normal 0 to 0.3)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 8.76 mg/dL(normal 0 to 0.3)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 5.29 mg/dL (normal 0 to 0.3)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 0.88 mg/dL (normal 0 to 0.3)

[redacted] 20[redacted] CHEST X-RAY: Abnormal

[redacted] 20[redacted] CHEST X-RAY: Abnormal

[redacted] 20[redacted] CRP: 0.53 mg/dL (normal 0.0 to 0.3)

[redacted] 20[redacted] CRP: 0.21 mg/dL (normal 0.0 to 0.3)

[redacted] 20[redacted] CRP: 0.38 mg/dL (normal 0.0 to 0.3)

[redacted] 20[redacted] CT SCAN: Abnormal findings

[redacted] 20[redacted] CT SCAN: Abnormal

[redacted] 20[redacted] CT SCAN: Abnormal

[redacted] 20[redacted] ELECTROCARDIOGRAM: Normal

[redacted] 20[redacted] ELECTROCARDIOGRAM: Abnormal

[redacted] 20[redacted] PULMONARY FUNCTION TEST: Abnormal

[redacted] 20[redacted] WBC: 12.4 X10**3/MCL (normal 3.6 to 9)

[redacted] 20[redacted] WBC: 14.1 X10**3/MCL (normal 3.6 to 9)

[redacted] 20[redacted] WBC: 6.5 X10**3/MCL (normal 3.6 to 9)

[redacted] 20[redacted] WBC: 6.0 X10**3/MCL (normal 3.6 to 9)

[redacted] 20[redacted] WBC (HEMATOLOGY): 6.3 X10**3/MCL (normal 3.6 to 9.0)

[redacted] 20[redacted] WBC (HEMATOLOGY): 6.1 X10**3/MCL (normal 3.6 to 9.0)

[redacted] 20[redacted] WBC (HEMATOLOGY): 4.6 X10**3/MCL (normal3.6 to 9.0)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，2[redacted] 歳の男性（日本）であり，重篤な有害事象の潰瘍性大腸炎の悪化が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎の悪化が認められた。20[redacted] 年[redacted] 月[redacted] 日，潰瘍性大腸炎の悪化は回復した。

20[redacted] 年[redacted] 月[redacted] 日，排便回数及び血便の増加が認められ（20[redacted] 年[redacted] 月[redacted] 日から増加，1 日 3～6 回），被験者はその後病院を受診した。治験責任医師は，治験薬の効果はないと判断し，治験薬の投与を中止した。Soldem 3A（ブドウ糖-電解質液［維持液］）500 mL が静脈内投与された。新規の治療を受けるため，被験者は入院の予約を取った。20[redacted] 年[redacted] 月[redacted] 日，被験者は肺炎のため入院した。29[redacted] 年[redacted] 月[redacted] 日に肺炎の治療が終了したため，20[redacted] 年[redacted] 月[redacted] 日に術前検査が開始された。被験者は外来にて外科を受診し，手術の予約を取った。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。被験者は 20[redacted] 年[redacted] 月[redacted] 日に予定されている手術のため，20[redacted] 年[redacted] 月[redacted] 日に入院した。20[redacted] 年[redacted] 月[redacted] 日，腹腔鏡下結腸切除及び回腸肛門吻合が実施され，合併症はみられなかった。20[redacted] 年[redacted] 月[redacted] 日，イレウスが疑われたため，腹部 CT 検査が実施された。腹部膨満感が認められたため，食事の開始は延期された。20[redacted] 年[redacted] 月[redacted] 日，食事が開始された。20[redacted] 年[redacted] 月[redacted] 日，術後の状態は安定していたため，被験者は退院した。

治療薬として Firstcin（セフォゾプラン塩酸塩），Bfluid（ビタミン B1・糖・電解質・アミノ酸液），Solacet（ブドウ糖加酢酸リンゲル液），Acelio（アセトアミノフェン），Calonal（アセトアミノフェン），フェンタニル，Popscaine（レボブピバカイン塩酸塩），Soldem 3A（ブドウ糖-電解質液［維持液］），Solacetd，セフメタゾールナトリウム，Soldem 1（ブドウ糖-電解質液［開始液］），Ropion（フルルビプロフェン　アキセチル）及び Pasil（パズフロキサシンメシル酸塩）が投与された。

The patient's past medications include:

AZANIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BFLUID for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PASIL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SOLACET for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ROPION for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: No

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: NATURAL COURSE OF ULCERATIVE COLITIS.

- AbbVie: The event is exacerbation of underlying UV.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL CT: Normal

[redacted] 20[redacted] ABDOMINAL X-P: Normal

[redacted] 20[redacted] CHEST X-P: Normal

[redacted] 20[redacted] COLONOSCOPY: Abnormal

[redacted] 20[redacted] ELECTROCARDIOGRAM: normal

[redacted] 20[redacted] GASTROSCOPY: Abnormal

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB STANDARD INDUCTION DOSE	4[redacted]	FEMALE	Asian

Medical History*	Onset Date
No information.	

Other Medical History / Surgery*	Onset Date
OTHER: INSOMNIA	[redacted]20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Never
Cigarettes: Never	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	STANDARD/	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 16	16

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
ETIZOLAM	10 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
LANSOPRAZOLE	30 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
MESALAZINE	1200 mg (milligram(s))	TID	Y: 20[redacted]	ONGOING
ZOLPIDEM	10 mg (milligram(s))	QD	Y: 20[redacted]	ONGOING
PREDNISOLONE	10 mg (milligram(s))	QD	-41	30
PARACETAMOL	400 mg (milligram(s))	PRN	1	ONGOING
TIMEPIDIUM	30 mg (milligram(s))	TID	1	ONGOING
LOXOPROFEN	60 mg (milligram(s))	PRN	16	ONGOING
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL (millilitre(s))	QD	25	25
PENTAZOCINE	15 mg (milligram(s))	Other	25	25
VITAMEDIN	1 VIAL	QD	25	34
DEXTROSE IN LACTATED RINGER'S	500 mL (millilitre(s))	QD	25	39

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug*

Event Description	UC AGGRAVATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 25 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
AE Stopped Rx Day	56 (40 DAYS AFTER LAST TREATMENT)
Duration of AE	32 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	NATURAL PROGRESS OF THE UNDERLYING DISEASE,INSUFFICIENCY EFFICACY OF STUDY DRUG
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，4[redacted] 歳の女性（日本）であり，重篤な有害事象の潰瘍性大腸炎の増悪が認められた。関連する病歴は，潰瘍性大腸炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，潰瘍性大腸炎の増悪は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 3 週時），腹痛の悪化及び腹痛による食欲減退の症状が認められ，被験者は同日に入院した。20[redacted] 年 [redacted] 月 [redacted] 日，ステロイド剤の投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日に 6-メルカプトプリン及びメサラジン坐剤の投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日にはステロイド浣腸（dnedonema）が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，症状は改善し，被験者は退院した。被験者は試験を中止した。

治療薬として，内視鏡検査の準備のため Kenei g enema（グリセリン），Xylocaine（リドカイン），Buscopan（ブチルスコポラミン臭化物）及びナロキソン塩酸塩，栄養補助のため Bfluid iv（ビタミン B1・糖・電解質・アミノ酸液），ブドウ糖，Lactec d injection（5%ブドウ糖加乳酸リンゲル液），Ascorbic acid injection（アスコルビン酸）及び Vitamedin（リン酸チアミンジスルフィド／ピリドキシン塩酸塩／シアノコバラミン），潰瘍性大腸炎による腹痛のため Sosegon（ペンタゾシン），貧血の予防のため Fesin（含糖酸化鉄），並びに Leukerin（メルカプトプリン水和物）及び Predonema enema（プレドニゾロンリン酸エステルナトリウム）が投与された。

The patient's past medications include:

BUSCOPAN for ENDSCOPY PREP and ENDSCOPY PREP ([redacted] 20[redacted] - [redacted] 20[redacted])

MOVIPREP for ENDOSCOPY PREP and ENDOSCOPY PREP ([redacted] 20[redacted] - [redacted] 20[redacted])

NALOXONE for ENDOSCOPY PREP and ENDOSCOPY PREP ([redacted] 20[redacted] - [redacted] 20[redacted])

OPYSTAN for ENDOSCOPY PREP and ENDOSCOPY PREP ([redacted] 20[redacted] - [redacted] 20[redacted])

XYLOCAINE for ENDOSCOPY PREP and ENDOSCOPY PREP ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for HUMIRA (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.19.0] [10009901]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Yes

Rechallenge: Not Applicable

Alternative Etiology for HUMIRA (Open Label)

Event of UC AGGRAVATION

- Investigator: Natural progress of the underlying disease, insufficiency efficacy of study drug.

- AbbVie: The event is exacerbation of underlying disease of ulcerative colitis.

Subject [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腹痛	X			

Treatment Group	Age at Study Start	Sex	Race
ADALIMUMAB HIGHER INDUCTION DOSE	6[redacted]	MALE	Asian

Medical History*	Onset Date
BENIGN PROSTATIC HYPERPLASIA	[redacted]20[redacted]
DIABETES MELLITUS	[redacted]20[redacted]
DRUG ALLERGIES/REACTIONS: SIDE EFFECT OF IMURAN	[redacted]20[redacted]

Other Medical History / Surgery*	Onset Date
OTHER: ANXIETY DISORDER	[redacted]20[redacted]
OTHER: CATARACT	[redacted]20[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	[redacted]20[redacted]
OTHER: OVERACTIVE BLADDER	[redacted]20[redacted]
OTHER: POLLINOSIS	20[redacted]

Tobacco Use*	Alcohol Use
Chewing tobacco: Never	Former
Cigarettes: Former (8 YEARS, 0.5 PACKS PER PER DAY)	
Cigars: Never	
Pipes: Never	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADALIMUMAB	HIGHER/ IN	DOSE		[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
				[redacted]20[redacted] / 58	[redacted]20[redacted] / 358	301

Other Medications - Medications taken within 30 days prior to each narrative event

Medication Name (WHO Drug)	Dose/Units	Frequency	Start RX Day or Year	Stop RX Day
LOPERAMIDE	1 mg (milligram(s))	TID	Y: 20[redacted]	55
ALBUMIN TANNATE	1 g (gram(s))	TID	Y: 20[redacted]	55
SULFASALAZINE	1000 mg (milligram(s))	TID	Y: 20[redacted]	55
HERBAL POLLEN NOS	126 mg (milligram(s))	TID	Y: 20[redacted]	55
TANDOSPIRONE	20 mg (milligram(s))	TID	Y: 20[redacted]	55
CLOTIAZEPAM	5 mg (milligram(s))	BID	-315	55
POLYCARBOPHIL	1000 mg (milligram(s))	TID	-206	55
SILODOSIN	4 mg (milligram(s))	BID	-206	55
NUTRIENTS NOS	250 mL (millilitre(s))	QD	-150	55
RAMOSETRON	10 mcg (microgram(s))	QD	-108	55
MIRABEGRON	50 mg (milligram(s))	QD	-24	55
BISACODYL	10 mg (milligram(s))	QD	56	56
GLYCEROL	120 mL (millilitre(s))	QD	56	56
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL (millilitre(s))	QD	56	57
CEFMETAZOLE	1 g (gram(s))	BID	56	57
SOLACET F	500 mL (millilitre(s))	QD	56	57

Event #1: Serious Adverse Event*

Event Description	ABDOMINAL PAIN
Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 56
Age at AE Onset	6[redacted]
AE Stopped Rx Day	61
Duration of AE	6 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No reasonable possibility
Relation to Study Drug by AbbVie	No reasonable possibility
Other Cause of Event	COLON BIOPSY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION

* Information presented verbatim as provided by the investigator.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-033

本被験者は，6[redacted] 歳の男性（日本）であり，重篤な有害事象の腹痛を発現した。関連する病歴は，潰瘍性大腸炎，過敏性腸症候群及び糖尿病であった。被験者は元紙巻タバコ喫煙者（1 日 0.5 箱を 8 年間）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，腹痛が発現した。20[redacted] 年 [redacted] 月 [redacted] 日，腹痛は回復した。

20[redacted] 年 [redacted] 月 [redacted] 日，投与 8 週時の評価のため，被験者は治験実施施設に来院した。S 状結腸鏡検査が実施された。治験責任医師の臨床判断によると，改善が認められ，視覚化された部分について潰瘍性大腸炎は寛解と判断された。しかし，生検が深部まで実施されたため，クリップによる縫縮が行われた。治験責任医師は，滲出液を確認することができなかった。コンピュータ断層撮影が実施され，腹部に遊離ガスが認められたが，確認はされなかった。20[redacted] 年 [redacted] 月 [redacted] 日，フォローアップのため，被験者は入院した。

20[redacted] 年 [redacted] 月 [redacted] 日，絶食が継続され，抗菌薬が静脈内投与された。腹痛は徐々に軽快した。メレナ又は発熱は認められなかった。夜には水分の経口摂取が開始されたが，著しい変化はみられなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，血液検査の結果，C 反応性たん白（以下「CRP」）は 0.87 mg/dL，体温は 36.9°C，血圧は 125/53 mmHg であった。その他の臨床症状は以下のとおりであった：貧血，腹部症状の増悪又はメレナは認められなかった。被験者に改善がみられたため，午前中に食物摂取（三分粥）が開始された。食後に潰瘍性大腸炎の治療薬及び併用薬の経口投与が再開された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，CRP は 0.18 mg/dL，体温は 36.6°C であった。腹痛又はメレナは認められず，食欲は良好であった。治験責任医師によると，限局性腹膜炎はみられなかった。

治療薬として Rize（クロチアゼパム），Sediel（タンドスピロンクエン酸塩），Tannalbin（タンニン酸アルブミン），Lopemin（ロペラミド塩酸塩），Irribow（ラモセトロン塩酸塩），Polyful（ポリカルボフィルカルシウム），Salazopyrin（サラゾスルファピリジン），Urief（シロドシン），Cernilton（セルニチンポーレンエキス），Betanis（ミラベグロン），Ensure liquid（経腸成分栄養剤），Teleminsoft（ビサコジル），グリセリン，Flivas（ナフトピジル），セフメタゾールナトリウム及び Soldem 3A（ブドウ糖-電解質液［維持液］）が投与された。

Causality for HUMIRA 40MG/0.8ML (Open Label)

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1) Abdominal pain (10000081) (Abdominal pain (10000081)) [v.19.1] [10000081]

治験責任医師による因果関係判定（薬剤／ワクチン）：関連なし

治験依頼者による因果関係判定（薬剤／ワクチン）：関連なし

Dechallenge: Not Applicable

Alternative Etiology for HUMIRA 40MG/0.8ML (Open Label)

Event of ABDOMINAL PAIN

- Investigator: Colon biopsy.

- AbbVie: The Event is likely related to the underlying study disease (UC).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BLOOD PRESSURE: 125/53mmhg

[redacted] 20[redacted] BODY TEMPERATURE: 36.9 Degrees C

[redacted] 20[redacted] BODY TEMPERATURE: 36.6 Degrees C

[redacted] 20[redacted] CRP: 0.87 mg/dL (normal <0.30)

[redacted] 20[redacted] HIGH SENSITIVITY CRP: 0.18 mg/dL (normal <0.30)

[redacted] 20[redacted] CT SCAN: unconfirmed free air and exudate.

0M14-033 主試験 維持療法試験

治験の標題： A Double-Blind, Randomized, Multicenter Study of Higher Versus Standard Adalimumab Dosing Regimens for Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis	
施設数 / 実施国名： 115 施設 / オーストリア，ベルギー，カナダ，チェコ共和国，デンマーク，フランス，ドイツ，ハンガリー，イスラエル，イタリア，オランダ，ポーランド，ルーマニア，スロバキア，スペイン，スイス，ウクライナ，英国及び米国	
治験責任医師： [redacted], MD 他	
公表文献 (参考資料) ： Panes J, Colombel JF, D'Haens GR, et al. OP216 High versus standard adalimumab induction dosing regimens in patients with moderately to severely active ulcerative colitis: Results from the SERENE UC induction study. United European Gastroenterol J. 2019;7 (Suppl 8S):118. Panes J, Colombel JF, D'Haens GR, et al. OP01 High vs. standard adalimumab maintenance regimens in patients with moderately to severely active ulcerative colitis: Results from the SERENE-UC maintenance study. J Crohns Colitis. 2020;14 (Suppl 1):S001.	
治験期間： 治験開始日（最初の被験者の初回来院日）： 2014 年 3 月 27 日（導入療法試験） 20[redacted] 年 [redacted] 月 [redacted] 日（維持療法試験への組入れ時） 治験終了日（最後の被験者の追跡調査終了日）： 2019 年 11 月 11 日	開発のフェーズ： 第 III 相
治験の種類： 第 III 相，多施設共同，無作為化，二重盲検試験	
目的： 本試験の目的は，中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者に，高用量での導入療法及び維持療法を行ったときの有効性及び安全性を検討することであった。	
被験者数 (計画時と解析時) ： 計画時（導入療法試験）　：840 例 組入れ時（導入療法試験）　：852 例 組入れ時（維持療法試験）　：757 例 解析時（維持療法試験）　：757 例	

診断と主要な組入れ基準：

M14-033 試験の主要な選択基準は以下のとおりであった：ベースライン時の年齢が 18 歳以上 75 歳以下の男女。ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中の内視鏡検査（全大腸内視鏡検査又は S 状結腸鏡検査）で診断が確認されると共に，現在の感染症，上皮異形成及び / 又は悪性腫瘍が除外されている患者。治験実施計画書で規定した副腎皮質ステロイドの経口剤又は免疫抑制剤による現在の治療，あるいは医師の判断で十分かつ適切な過去の治療にもかかわらず，ベースラインの Mayo スコア（以下，「FMS」）が 6～12 ポイント，かつ内視鏡所見サブスコアが 2～3 ポイント（中央判定による評価）である活動性の UC 患者。インフリキシマブの投与で以前に UC の治療効果が認められ，その後効果消失又は不耐容となったため，インフリキシマブの投与を中止した患者を，本試験に組み入れることができる（効果消失又は不耐容を示す記録を確認すること）。女性患者の場合は，本試験への参加から 1 年以上前に閉経した，又は不妊手術（両側卵管結紮術，両側卵巣摘出術，及び / 又は子宮摘出術）を行ったことで，妊娠の可能性がないこと。妊娠の可能性がある女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，治験実施計画書で規定した方法で避妊すること。女性患者の場合は，治験期間中及び治験薬の最終投与日の 150 日後まで，授乳しないこと。結核スクリーニング検査が陰性の患者。既往歴やスクリーニング期間中に実施する臨床検査，身体的所見，胸部 X 線検査，12 誘導心電図検査の結果から，治験責任医師が健康状態にその他の問題がないと判断した患者。

M14-033 試験の主要な除外基準は以下のとおりであった：クローン病と診断されている，若しくは既往がある，又は indeterminate colitis と診断されている患者。劇症の大腸炎又は中毒性巨大結腸症と診断されている患者。スクリーニング時の内視鏡検査で，病変が直腸のみに限局している患者（潰瘍性直腸炎）。回腸直腸瘻造設を伴う結腸亜全摘術，若しくは回腸嚢，Koch パウチ，回腸ストマ造設を伴う結腸切除術の既往がある患者。又は腸管の手術を予定している患者。

治験方法：

M14-033 試験は，導入療法試験と維持療法試験で構成される。M14-033 試験では，高用量の導入療法及び維持療法を，承認されている標準用量の導入療法及び維持療法と比較した。また，薬物治療モニタリング（以下「TDM」）戦略を用いた探索的な維持療法も実施した。すべての選択基準を満たし，いずれの除外基準にも抵触しない中等症から重症の成人活動性 UC 患者を本試験の参加に適格とした。

本報告では，日本以外の治験実施医療機関で登録されたすべての被験者（主試験集団）を対象とした，M14-033 維持療法試験の解析結果を示す。本報告には，最後の被験者の最終投与 70 日後の追跡調査までに得られたデータを含める（追跡調査終了日：2019 年 11 月 11 日）。本報告は，維持療法試験の組織学検査データ，及び前版からの最終的なデータの変更を反映した治験総括報告書の最終版（データベースロック日：20[redacted] 年 [redacted] 月 [redacted] 日）に基づいている。

被験薬，用量，投与方法及びバッチ番号：

投与 8 週時に，被験者を 40 mg 週 1 回投与群，40 mg 隔週投与群又は TDM 群のいずれかに 2：2：1 の比率で再無作為化した。投与 8 週時の再無作為化では，導入療法試験での治療，及び投与 8 週時における改善の有無（治験実施医療機関から提供された投与 8 週時の内視鏡サブスコアを用いた FMS に基づく）を因子として被験者を再度層別化した。投与 8 週時の改善例では，再割付け時に，投与 8 週時の寛解の有無（治験実施医療機関から提供された投与 8 週時の内視鏡サブスコアを用いた FMS に基づく）で更に層別化した。

40 mg 隔週投与群の被験者は，本試験の終了までアダリムマブ 40 mg の隔週投与を継続した。40 mg 週 1 回投与群の被験者は，投与 8 週時にアダリムマブ 40 mg の週 1 回投与を開始し，本試験の終了まで継続した。

TDM 群の被験者は，投与 8 及び 10 週時にアダリムマブ 40 mg の隔週投与を受けた。また，投与 12，24 及び 37 週時に，直前の来院時（それぞれ投与 10，22 及び 35 週時）に盲検下でアダリムマブの血清中濃度を評価した結果，並びに直前及び当該来院時の直腸出血サブスコアに基づき，アダリムマブの用量を調整できることとした。

ロット番号：

アダリムマブ　：[redacted], [redacted], [redacted], [redacted], [redacted], [redacted], [redacted]

プラセボ　　：[redacted], [redacted], [redacted], [redacted], [redacted]

治療期間：44 週間

対照薬，用量，投与方法及びバッチ番号：
なし

評価基準：
有効性：
維持療法試験の主要評価項目は，投与 8 週時に FMS で改善例（ベースラインからの FMS の減少が 3 以上かつ 30%以上，更に直腸出血サブスコアの減少が 1 以上あるいは直腸出血サブスコアが 0 又は 1）となり，かつ投与 52 週時に FMS で寛解（FMS が 2 以下で，かついずれのサブスコアも 1 を超えない）を達成した被験者の割合であった。
維持療法試験における順位付き副次評価項目（昇順に順位を階層化）は以下のとおりであった。

1. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に内視鏡検査で改善（内視鏡所見サブスコアが 0 又は 1）が認められた被験者の割合
2. ベースラインで副腎皮質ステロイドを投与しており，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱できた被験者の割合
3. ベースラインで副腎皮質ステロイドを投与しており，投与 8 週時に FMS で改善例となり，かつ投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱でき，更に FMS で寛解を達成した被験者の割合
4. 投与 8 週時，投与 52 週時にいずれも FMS で寛解例となった被験者の割合
5. 投与 8 週時に FMS で寛解例となり，かつ投与 52 週時に内視鏡検査で改善（内視鏡所見サブスコアが 0 又は 1）が認められた被験者の割合
6. ベースラインで副腎皮質ステロイドを投与していた被験者で，投与 8 週時に FMS で寛解例となり，かつ投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱できた被験者の割合
7. ベースラインで副腎皮質ステロイドを投与していた被験者で，投与 8 週時に FMS で寛解例となり，かつ投与 52 週時に副腎皮質ステロイドを 90 日間以上離脱でき，更に FMS で寛解を達成した被験者の割合
8. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に Inflammatory Bowel Disease Questionnaire（以下「IBDQ」）で改善（ベースラインと比較して IBDQ スコアの 16 以上の増加）が認められた被験者の割合
9. 投与 8 週時に FMS で非改善例であった被験者のうち，投与 52 週時に FMS で寛解を達成した被験者の割合
10. 投与 8 週時に FMS で非寛解例であった被験者のうち，投与 52 週時に FMS で寛解を達成した被験者の割合
11. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に内視鏡所見サブスコアが 0 ポイントになった被験者の割合
12. 投与 8 週時に FMS で寛解例となり，かつ投与 52 週時に内視鏡所見サブスコアが 0 ポイントになった被験者の割合
13. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に IBDQ の腸症状ドメインで改善（ベースラインと比較して IBDQ の腸症状ドメインのスコアの 6 以上の増加）が認められた被験者の割合
14. 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に IBDQ の疲労に関する項目で改善（ベースライ

ンと比較して IBDQ の疲労に関する項目のスコアの 1 以上の増加）が認められた被験者の割合
薬物動態： 別途報告書に記載することとした。 安全性： 治験期間中の有害事象，バイタルサインの変化，身体的所見，及び臨床検査値を評価した。
統計手法： 有効性： 主試験の維持療法試験では，主試験 Intent-to-treat 集団（維持療法試験に移行するため投与 8 週時に再度無作為割付けを行ったすべての被験者）を対象に，アダリムマブ 40 mg の週 1 回投与とアダリムマブ 40 mg の隔週投与を比較した。欠測値の補完には，欠測値を「非反応」としてデータ補完する統計手法を用いた（以下「NRI」）。カテゴリカル変数である投与 52 週時の副次価項目については，導入療法試験での治療，及び投与 8 週時における改善 / 寛解の有無で調整した両側 Cochran-Mantel-Haenszel（以下「CMH」）検定を用いて解析した。また，CMH 検定に基づき，割合の群間差の両側 95%信頼区間を算出した。主要評価項目の感度分析として，治療群，層別化割付け因子及びベースライン時点における免疫抑制剤の使用，ベースライン時の高感度 CRP 値，ベースライン時の重症度などの臨床的に重要な因子を用いた Logistic 回帰分析を実施した。 投与 52 週時のすべての主要評価項目及び順位付き副次評価項目について，TDM 群とアダリムマブ 40 mg 週 1 回投与群を比較する解析，及び TDM 群とアダリムマブ 40 mg 隔週投与群を比較する解析を同様に実施した。 薬物動態： 別途報告書に記載することとした。 安全性： 主試験の維持療法試験では，安全性の解析はすべて主試験安全性解析対象集団を対象に実施した。被験者が実際に受けた治療に基づき，治療群ごとに安全性評価項目を要約した。安全性評価項目の 40 mg 週 1 回投与群と 40 mg 隔週投与群の群間差は，有意水準 0.05 の両側検定を用いて評価した。 特に断らない限り，連続変数の安全性評価項目（例：臨床検査値のベースラインから最終測定時までの変化量）の群間差は，治療を因子とした分散分析モデルを用いて評価した。また，カテゴリカル変数の安全性評価項目の群間差は，Fisher の正確確率検定を用いて評価した。
要約 / 結論： 有効性： 投与 8 週時に FMS で改善例となり，かつ投与 52 週時に FMS で寛解を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも数値的に高かった。部分集団解析の結果は，主解析の結果とおおむね一致していた。 各順位付き副次評価項目を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも数値的に高かった。
薬物動態： 別途報告書に記載することとした。

安全性：

アダリムマブの安全性プロファイルは，40 mg 週 1 回投与群，40 mg 隔週投与群及び TDM 群で同様であり，アダリムマブの既知の安全性プロファイルと一致していた。新たな安全性シグナル又は予期しない傾向は認められなかった。

各投与群の被験者の大部分に 1 件以上の有害事象が発現した。維持療法試験中，4 例が死亡した。うち 2 例は 40 mg 週 1 回投与群の被験者であり，2 例は 40 mg 隔週投与群の被験者であった。いずれの死亡も治験薬との因果関係は関連なしと判断された。有害事象及び重篤な有害事象の発現割合は投与群間で同程度であった。重篤な有害事象が 97 例に発現し，治験薬投与の中止に至った有害事象が 85 例に発現した。最も多く報告された器官別大分類（以下「SOC」）は，いずれの投与群でも胃腸障害（40 mg 週 1 回投与群：33.9%，40 mg 隔週投与群：42.4%，TDM 群：29.8%）及び感染症および寄生虫症（40 mg 週 1 回投与群：34.9%，40 mg 隔週投与群：37.7%，TDM 群：34.4%）であった。最も多く（被験者の 5%以上）報告された基本語（以下「PT」）は，潰瘍性大腸炎，上咽頭炎，関節痛，上気道感染及び頭痛であった。特に注目すべき有害事象（以下「AESI」）の発現割合は，感染症及び血液障害を除き，全般的に低かった（5%未満）。いずれの AESI も発現割合は投与群間でおおむね同程度であった。

臨床検査（血液学的検査，血液生化学検査及び尿検査）の平均値にベースラインからの顕著な変化は認められなかった。血液学的検査，血液生化学検査値及び尿検査値に関して，ベースラインが正常値若しくは異常高値であった検査値が最終測定時に異常低値に変動した被験者，及びベースラインが異常低値若しくは正常値であった検査値が最終測定時に異常高値に変動した被験者は少数であり，臨床的に重要ではないと判断された。

バイタルサインの平均値にベースラインからの顕著な変化は認められなかった。

維持療法試験中，5 例の妊娠が報告された。妊娠の転帰は，先天性異常なしの出産が 4 例，妊娠前期での自然流産が 1 例であった。

治験期間中，予期しない治験薬又は機器の問題は認められなかった。

結論：

投与 8 週時に FMS で改善例となり，かつ投与 52 週時に FMS で寛解を達成した被験者の割合は，40 mg 週 1 回投与群の方が 40 mg 隔週投与群よりも数値的に高かった。

アダリムマブの安全性プロファイルは，40 mg 週 1 回投与群，40 mg 隔週投与群及び TDM 群で同様であり，アダリムマブの既知の安全性プロファイルと一致していた。新たな安全性のシグナル又は予期しない傾向は認められなかった。全体として，本試験の対象集団における標準用量のアダリムマブ維持療法のベネフィット・リスクプロファイルは不変であった。

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
Any Adverse Event	220 (72.8)	222 (73.0)	96 (63.6)	538 (71.1)
血液およびリンパ系障害	17 (5.6)	26 (8.6)	9 (6.0)	52 (6.9)
貧血	12 (4.0)	13 (4.3)	5 (3.3)	30 (4.0)
内出血発生の増加傾向	0	1 (0.3)	0	1 (0.1)
鉄欠乏性貧血	2 (0.7)	2 (0.7)	0	4 (0.5)
白血球増加症	1 (0.3)	2 (0.7)	0	3 (0.4)
白血球減少症	1 (0.3)	4 (1.3)	0	5 (0.7)
リンパ節症	0	2 (0.7)	1 (0.7)	3 (0.4)
リンパ球減少症	0	0	1 (0.7)	1 (0.1)
好中球減少症	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
血小板減少症	1 (0.3)	0	1 (0.7)	2 (0.3)
血小板増加症	1 (0.3)	3 (1.0)	0	4 (0.5)
心臓障害	6 (2.0)	4 (1.3)	1 (0.7)	11 (1.5)
急性心筋梗塞	1 (0.3)	0	0	1 (0.1)
心房細動	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
うっ血性心不全	1 (0.3)	0	0	1 (0.1)
冠動脈疾患	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
心臓障害 (Cont.)				
心筋虚血	1 (0.3)	0	0	1 (0.1)
動悸	2 (0.7)	2 (0.7)	0	4 (0.5)
洞性徐脈	0	1 (0.3)	0	1 (0.1)
頻脈	1 (0.3)	0	0	1 (0.1)
耳および迷路障害	5 (1.7)	3 (1.0)	1 (0.7)	9 (1.2)
外耳道狭窄	1 (0.3)	0	0	1 (0.1)
耳痛	0	1 (0.3)	0	1 (0.1)
耳鳴	2 (0.7)	2 (0.7)	1 (0.7)	5 (0.7)
回転性めまい	2 (0.7)	0	0	2 (0.3)
内分泌障害	3 (1.0)	3 (1.0)	0	6 (0.8)
クッシング様症状	2 (0.7)	0	0	2 (0.3)
甲状腺腫	0	1 (0.3)	0	1 (0.1)
甲状腺機能低下症	1 (0.3)	2 (0.7)	0	3 (0.4)
眼障害	9 (3.0)	16 (5.3)	2 (1.3)	27 (3.6)
閉塞隅角緑内障	0	1 (0.3)	0	1 (0.1)
乱視	0	1 (0.3)	0	1 (0.1)
眼瞼炎	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
眼障害 (Cont.)				
眼瞼痙攣	0	2 (0.7)	0	2 (0.3)
白内障	1 (0.3)	1 (0.3)	0	2 (0.3)
複視	0	1 (0.3)	0	1 (0.1)
ドライアイ	1 (0.3)	1 (0.3)	0	2 (0.3)
眼瞼紅斑	1 (0.3)	0	0	1 (0.1)
眼の炎症	0	1 (0.3)	0	1 (0.1)
眼刺激	0	1 (0.3)	0	1 (0.1)
眼痛	1 (0.3)	0	0	1 (0.1)
眼瞼縁痂皮	0	1 (0.3)	0	1 (0.1)
眼瞼下垂	0	2 (0.7)	0	2 (0.3)
眼瞼そう痒症	1 (0.3)	0	0	1 (0.1)
緑内障	1 (0.3)	0	0	1 (0.1)
眼充血	0	1 (0.3)	1 (0.7)	2 (0.3)
眼酒さ	0	1 (0.3)	0	1 (0.1)
視神経萎縮	1 (0.3)	0	0	1 (0.1)
老視	0	1 (0.3)	0	1 (0.1)
網膜剥離	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
眼障害 (Cont.)				
眼瞼腫脹	0	3 (1.0)	0	3 (0.4)
霧視	0	1 (0.3)	1 (0.7)	2 (0.3)
視力低下	1 (0.3)	0	0	1 (0.1)
視力障害	1 (0.3)	0	0	1 (0.1)
胃腸障害	128 (42.4)	103 (33.9)	45 (29.8)	276 (36.5)
腹部不快感	1 (0.3)	2 (0.7)	0	3 (0.4)
腹部膨満	5 (1.7)	1 (0.3)	1 (0.7)	7 (0.9)
腹部ヘルニア	1 (0.3)	0	0	1 (0.1)
腹痛	7 (2.3)	6 (2.0)	1 (0.7)	14 (1.8)
下腹部痛	2 (0.7)	2 (0.7)	0	4 (0.5)
上腹部痛	3 (1.0)	6 (2.0)	1 (0.7)	10 (1.3)
腹部圧痛	2 (0.7)	0	1 (0.7)	3 (0.4)
後天性食道ウエッブ	0	1 (0.3)	0	1 (0.1)
裂肛	0	4 (1.3)	0	4 (0.5)
肛門出血	1 (0.3)	1 (0.3)	0	2 (0.3)
肛門失禁	0	1 (0.3)	0	1 (0.1)
肛門そう痒症	0	0	1 (0.7)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
胃腸障害 (Cont.)				
肛門性器異形成	0	2 (0.7)	0	2 (0.3)
アフタ性潰瘍	0	0	1 (0.7)	1 (0.1)
呼気臭	1 (0.3)	0	0	1 (0.1)
口唇のひび割れ	1 (0.3)	0	0	1 (0.1)
口唇炎	0	0	1 (0.7)	1 (0.1)
大腸炎	6 (2.0)	1 (0.3)	1 (0.7)	8 (1.1)
潰瘍性大腸炎	74 (24.5)	60 (19.7)	29 (19.2)	163 (21.5)
結腸異形成	1 (0.3)	0	0	1 (0.1)
便秘	3 (1.0)	5 (1.6)	1 (0.7)	9 (1.2)
クローン病	0	1 (0.3)	0	1 (0.1)
便意切迫	0	1 (0.3)	0	1 (0.1)
齲歯	2 (0.7)	1 (0.3)	0	3 (0.4)
歯嚢胞	1 (0.3)	0	0	1 (0.1)
下痢	10 (3.3)	7 (2.3)	1 (0.7)	18 (2.4)
憩室	0	2 (0.7)	0	2 (0.3)
口内乾燥	0	1 (0.3)	1 (0.7)	2 (0.3)
穿孔性十二指腸潰瘍	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
胃腸障害 (Cont.)				
十二指腸炎	0	1 (0.3)	0	1 (0.1)
十二指腸胃逆流	0	0	1 (0.7)	1 (0.1)
排便困難	0	1 (0.3)	0	1 (0.1)
消化不良	3 (1.0)	4 (1.3)	3 (2.0)	10 (1.3)
嚥下障害	0	3 (1.0)	0	3 (0.4)
小腸炎	0	1 (0.3)	0	1 (0.1)
鼓腸	3 (1.0)	1 (0.3)	4 (2.6)	8 (1.1)
排便回数増加	1 (0.3)	2 (0.7)	0	3 (0.4)
胃炎	1 (0.3)	0	1 (0.7)	2 (0.3)
びらん性胃炎	0	2 (0.7)	1 (0.7)	3 (0.4)
胃腸障害	1 (0.3)	0	0	1 (0.1)
胃腸の炎症	1 (0.3)	0	0	1 (0.1)
胃食道逆流性疾患	0	7 (2.3)	1 (0.7)	8 (1.1)
歯肉出血	0	1 (0.3)	0	1 (0.1)
歯肉障害	1 (0.3)	0	0	1 (0.1)
舌炎	1 (0.3)	0	0	1 (0.1)
血便排泄	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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胃腸障害 (Cont.)				
痔出血	1 (0.3)	1 (0.3)	0	2 (0.3)
痔核	7 (2.3)	6 (2.0)	1 (0.7)	14 (1.8)
裂孔ヘルニア	0	1 (0.3)	0	1 (0.1)
大腸ポリープ	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
マロリー・ワイス症候群	0	0	1 (0.7)	1 (0.1)
口腔内潰瘍形成	1 (0.3)	1 (0.3)	0	2 (0.3)
粘液便	1 (0.3)	0	0	1 (0.1)
悪心	13 (4.3)	6 (2.0)	3 (2.0)	22 (2.9)
口腔障害	0	0	1 (0.7)	1 (0.1)
膵不全	1 (0.3)	0	0	1 (0.1)
急性膵炎	1 (0.3)	0	0	1 (0.1)
肛門周囲痛	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
直腸炎	0	1 (0.3)	0	1 (0.1)
偽性ポリポーシス	1 (0.3)	0	0	1 (0.1)
直腸出血	2 (0.7)	4 (1.3)	0	6 (0.8)
直腸ポリープ	1 (0.3)	0	0	1 (0.1)
唾液腺障害	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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胃腸障害 (Cont.)				
小腸閉塞	0	0	1 (0.7)	1 (0.1)
口内炎	1 (0.3)	0	0	1 (0.1)
歯の障害	0	2 (0.7)	1 (0.7)	3 (0.4)
埋伏歯	1 (0.3)	0	0	1 (0.1)
歯痛	4 (1.3)	6 (2.0)	1 (0.7)	11 (1.5)
上部消化管出血	0	0	1 (0.7)	1 (0.1)
嘔吐	7 (2.3)	8 (2.6)	2 (1.3)	17 (2.2)
一般・全身障害および投与部位の状態	40 (13.2)	51 (16.8)	12 (7.9)	103 (13.6)
医薬品副作用	0	1 (0.3)	0	1 (0.1)
無力症	4 (1.3)	7 (2.3)	2 (1.3)	13 (1.7)
胸部不快感	0	1 (0.3)	0	1 (0.1)
胸痛	6 (2.0)	2 (0.7)	0	8 (1.1)
悪寒	2 (0.7)	1 (0.3)	0	3 (0.4)
嚢胞	1 (0.3)	1 (0.3)	0	2 (0.3)
不快感	1 (0.3)	0	0	1 (0.1)
薬物相互作用	0	1 (0.3)	0	1 (0.1)
異形成	1 (0.3)	0	2 (1.3)	3 (0.4)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
早期満腹	1 (0.3)	0	0	1 (0.1)
疲労	4 (1.3)	6 (2.0)	0	10 (1.3)
歩行障害	1 (0.3)	0	0	1 (0.1)
異常高熱	0	1 (0.3)	0	1 (0.1)
高熱	0	0	1 (0.7)	1 (0.1)
インフルエンザ様疾患	2 (0.7)	4 (1.3)	0	6 (0.8)
注入部位紅斑	0	1 (0.3)	0	1 (0.1)
注入部位血腫	0	0	1 (0.7)	1 (0.1)
注入部位そう痒感	0	1 (0.3)	0	1 (0.1)
注射部位紅斑	3 (1.0)	2 (0.7)	1 (0.7)	6 (0.8)
注射部位過敏反応	0	1 (0.3)	0	1 (0.1)
注射部位硬結	1 (0.3)	0	0	1 (0.1)
注射部位炎症	0	2 (0.7)	0	2 (0.3)
注射部位結節	1 (0.3)	0	0	1 (0.1)
注射部位疼痛	2 (0.7)	2 (0.7)	0	4 (0.5)
注射部位そう痒感	0	2 (0.7)	1 (0.7)	3 (0.4)
注射部位発疹	1 (0.3)	2 (0.7)	0	3 (0.4)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
注射部位反応	2 (0.7)	2 (0.7)	3 (2.0)	7 (0.9)
注射部位腫脹	1 (0.3)	2 (0.7)	0	3 (0.4)
限局性浮腫	1 (0.3)	0	0	1 (0.1)
小結節	0	1 (0.3)	0	1 (0.1)
非心臓性胸痛	1 (0.3)	0	0	1 (0.1)
末梢性浮腫	4 (1.3)	2 (0.7)	0	6 (0.8)
疼痛	2 (0.7)	4 (1.3)	0	6 (0.8)
末梢腫脹	2 (0.7)	1 (0.3)	0	3 (0.4)
ポリープ	0	0	1 (0.7)	1 (0.1)
偽ポリープ	0	1 (0.3)	0	1 (0.1)
発熱	8 (2.6)	12 (3.9)	1 (0.7)	21 (2.8)
腫脹	1 (0.3)	3 (1.0)	0	4 (0.5)
圧痛	1 (0.3)	2 (0.7)	0	3 (0.4)
組織変色	0	0	1 (0.7)	1 (0.1)
血管穿刺部位血腫	0	1 (0.3)	0	1 (0.1)
肝胆道系障害	3 (1.0)	4 (1.3)	7 (4.6)	14 (1.8)
胆管結石	0	1 (0.3)	1 (0.7)	2 (0.3)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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肝胆道系障害 (Cont.)				
胆石症	1 (0.3)	0	0	1 (0.1)
胆嚢ポリープ	1 (0.3)	0	1 (0.7)	2 (0.3)
脂肪肝	0	1 (0.3)	0	1 (0.1)
高ビリルビン血症	0	1 (0.3)	0	1 (0.1)
高トランスアミナーゼ血症	1 (0.3)	1 (0.3)	4 (2.6)	6 (0.8)
非アルコール性脂肪性肝炎	1 (0.3)	0	0	1 (0.1)
門脈脾静脈腸間膜静脈血栓症	0	0	1 (0.7)	1 (0.1)
免疫系障害	2 (0.7)	4 (1.3)	1 (0.7)	7 (0.9)
節足動物刺傷アレルギー	0	1 (0.3)	0	1 (0.1)
薬物過敏症	1 (0.3)	0	0	1 (0.1)
過敏症	0	1 (0.3)	0	1 (0.1)
複合アレルギー	0	1 (0.3)	0	1 (0.1)
季節性アレルギー	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
感染症および寄生虫症	114 (37.7)	106 (34.9)	52 (34.4)	272 (35.9)
四肢膿瘍	0	2 (0.7)	0	2 (0.3)
急性副鼻腔炎	0	2 (0.7)	0	2 (0.3)
肛門膿瘍	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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感染症および寄生虫症 (Cont.)				
虫垂炎	0	1 (0.3)	0	1 (0.1)
無症候性細菌尿	0	1 (0.3)	0	1 (0.1)
細菌感染	1 (0.3)	0	0	1 (0.1)
細菌性膣症	0	1 (0.3)	0	1 (0.1)
気管支炎	4 (1.3)	1 (0.3)	3 (2.0)	8 (1.1)
カンジダ感染	1 (0.3)	2 (0.7)	1 (0.7)	4 (0.5)
蜂巣炎	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
クロストリジウム・ディフィシレ感染	4 (1.3)	2 (0.7)	0	6 (0.8)
結膜炎	5 (1.7)	2 (0.7)	3 (2.0)	10 (1.3)
膀胱炎	1 (0.3)	0	2 (1.3)	3 (0.4)
サイトメガロウイルス感染	1 (0.3)	0	0	1 (0.1)
憩室炎	0	1 (0.3)	0	1 (0.1)
耳感染	3 (1.0)	2 (0.7)	3 (2.0)	8 (1.1)
蟯虫症	0	2 (0.7)	0	2 (0.3)
エプスタイン・バーウイルス感染	2 (0.7)	0	0	2 (0.3)
外耳蜂巣炎	1 (0.3)	0	0	1 (0.1)
眼瞼感染	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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感染症および寄生虫症 (Cont.)				
毛包炎	0	4 (1.3)	1 (0.7)	5 (0.7)
真菌感染	1 (0.3)	0	0	1 (0.1)
皮膚真菌感染	1 (0.3)	0	1 (0.7)	2 (0.3)
せつ	1 (0.3)	0	0	1 (0.1)
胃腸炎	5 (1.7)	5 (1.6)	2 (1.3)	12 (1.6)
ウイルス性胃腸炎	1 (0.3)	2 (0.7)	0	3 (0.4)
消化管感染	1 (0.3)	0	0	1 (0.1)
性器カンジダ症	1 (0.3)	1 (0.3)	0	2 (0.3)
歯肉膿瘍	0	1 (0.3)	0	1 (0.1)
ヘリコバクター感染	1 (0.3)	0	0	1 (0.1)
ヘルペス眼感染	0	1 (0.3)	0	1 (0.1)
単純ヘルペス	2 (0.7)	0	0	2 (0.3)
帯状疱疹	3 (1.0)	3 (1.0)	1 (0.7)	7 (0.9)
麦粒腫	1 (0.3)	2 (0.7)	0	3 (0.4)
膿痂疹	1 (0.3)	1 (0.3)	0	2 (0.3)
インフルエンザ	13 (4.3)	11 (3.6)	5 (3.3)	29 (3.8)
喉頭炎	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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感染症および寄生虫症 (Cont.)				
限局性感染	1 (0.3)	1 (0.3)	0	2 (0.3)
下気道感染	0	1 (0.3)	1 (0.7)	2 (0.3)
ライム病	1 (0.3)	0	0	1 (0.1)
伝染性軟属腫	0	1 (0.3)	0	1 (0.1)
鼓膜炎	0	0	1 (0.7)	1 (0.1)
鼻ヘルペス	1 (0.3)	0	0	1 (0.1)
上咽頭炎	31 (10.3)	30 (9.9)	11 (7.3)	72 (9.5)
口腔カンジダ症	1 (0.3)	0	1 (0.7)	2 (0.3)
口腔真菌感染	0	1 (0.3)	0	1 (0.1)
口腔ヘルペス	2 (0.7)	3 (1.0)	1 (0.7)	6 (0.8)
外耳炎	1 (0.3)	2 (0.7)	0	3 (0.4)
中耳炎	0	0	1 (0.7)	1 (0.1)
急性中耳炎	1 (0.3)	0	0	1 (0.1)
寄生虫性胃腸炎	0	0	1 (0.7)	1 (0.1)
爪囲炎	1 (0.3)	1 (0.3)	0	2 (0.3)
骨盤膿瘍	0	1 (0.3)	0	1 (0.1)
骨盤内感染	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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感染症および寄生虫症 (Cont.)				
骨盤内炎症性疾患	0	1 (0.3)	0	1 (0.1)
会陰膿瘍	1 (0.3)	0	0	1 (0.1)
歯周炎	1 (0.3)	0	0	1 (0.1)
扁桃周囲膿瘍	0	1 (0.3)	0	1 (0.1)
咽頭炎	3 (1.0)	6 (2.0)	6 (4.0)	15 (2.0)
レンサ球菌性咽頭炎	4 (1.3)	0	1 (0.7)	5 (0.7)
咽頭扁桃炎	0	1 (0.3)	0	1 (0.1)
肺炎	3 (1.0)	7 (2.3)	1 (0.7)	11 (1.5)
マイコプラズマ性肺炎	0	0	1 (0.7)	1 (0.1)
処置後感染	0	1 (0.3)	0	1 (0.1)
腎盂腎炎	0	0	1 (0.7)	1 (0.1)
急性腎盂腎炎	0	1 (0.3)	0	1 (0.1)
膿疱性皮疹	2 (0.7)	0	0	2 (0.3)
気道感染	0	0	1 (0.7)	1 (0.1)
ウイルス性気道感染	1 (0.3)	0	0	1 (0.1)
鼻炎	3 (1.0)	3 (1.0)	0	6 (0.8)
敗血症	0	0	1 (0.7)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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感染症および寄生虫症 (Cont.)				
副鼻腔炎	13 (4.3)	9 (3.0)	7 (4.6)	29 (3.8)
皮膚カンジダ	0	1 (0.3)	0	1 (0.1)
皮膚感染	0	2 (0.7)	0	2 (0.3)
ブドウ球菌感染	0	1 (0.3)	0	1 (0.1)
胸骨炎	1 (0.3)	0	0	1 (0.1)
レンサ球菌感染	1 (0.3)	0	0	1 (0.1)
頭部白癬	1 (0.3)	0	0	1 (0.1)
癜風	1 (0.3)	0	1 (0.7)	2 (0.3)
扁桃炎	2 (0.7)	3 (1.0)	2 (1.3)	7 (0.9)
歯膿瘍	2 (0.7)	0	2 (1.3)	4 (0.5)
歯感染	2 (0.7)	4 (1.3)	0	6 (0.8)
結核	0	1 (0.3)	1 (0.7)	2 (0.3)
胸腔内リンパ節結核	0	1 (0.3)	0	1 (0.1)
上気道感染	21 (7.0)	17 (5.6)	9 (6.0)	47 (6.2)
尿路感染	8 (2.6)	4 (1.3)	4 (2.6)	16 (2.1)
腟感染	1 (0.3)	0	0	1 (0.1)
ウイルス感染	1 (0.3)	2 (0.7)	1 (0.7)	4 (0.5)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
感染症および寄生虫症 (Cont.)				
ウイルス性咽頭炎	0	2 (0.7)	0	2 (0.3)
外陰部腟カンジダ症	0	3 (1.0)	0	3 (0.4)
外陰腟真菌感染	1 (0.3)	2 (0.7)	1 (0.7)	4 (0.5)
外陰腟炎	0	0	1 (0.7)	1 (0.1)
エルシニア感染	1 (0.3)	1 (0.3)	0	2 (0.3)
傷害、中毒および処置合併症	17 (5.6)	16 (5.3)	8 (5.3)	41 (5.4)
動物咬傷	2 (0.7)	0	0	2 (0.3)
節足動物咬傷	0	0	1 (0.7)	1 (0.1)
節足動物刺傷	1 (0.3)	0	0	1 (0.1)
第2度熱傷	0	0	1 (0.7)	1 (0.1)
術後錯乱	0	1 (0.3)	0	1 (0.1)
挫傷	0	1 (0.3)	0	1 (0.1)
転倒	0	1 (0.3)	0	1 (0.1)
尾骨骨折	0	0	1 (0.7)	1 (0.1)
仙骨骨折	0	1 (0.3)	0	1 (0.1)
上腕骨骨折	1 (0.3)	1 (0.3)	0	2 (0.3)
注射に伴う反応	0	0	1 (0.7)	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
傷害、中毒および処置合併症 (Cont.)				
関節脱臼	1 (0.3)	1 (0.3)	0	2 (0.3)
関節損傷	1 (0.3)	0	0	1 (0.1)
靭帯捻挫	2 (0.7)	0	0	2 (0.3)
四肢損傷	0	0	1 (0.7)	1 (0.1)
半月板損傷	1 (0.3)	1 (0.3)	0	2 (0.3)
肉離れ	1 (0.3)	0	0	1 (0.1)
膝蓋骨骨折	0	1 (0.3)	0	1 (0.1)
処置後出血	0	1 (0.3)	1 (0.7)	2 (0.3)
術後高血圧	0	1 (0.3)	0	1 (0.1)
処置による疼痛	2 (0.7)	1 (0.3)	0	3 (0.4)
橈骨骨折	0	1 (0.3)	0	1 (0.1)
肋骨骨折	1 (0.3)	0	0	1 (0.1)
交通事故	1 (0.3)	0	0	1 (0.1)
瘢痕	0	1 (0.3)	0	1 (0.1)
皮膚裂傷	2 (0.7)	0	1 (0.7)	3 (0.4)
ストーマ合併症	0	0	1 (0.7)	1 (0.1)
熱傷	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
傷害、中毒および処置合併症 (Cont.)				
脛骨骨折	0	1 (0.3)	0	1 (0.1)
上肢骨折	1 (0.3)	0	0	1 (0.1)
創傷	0	1 (0.3)	1 (0.7)	2 (0.3)
臨床検査	21 (7.0)	23 (7.6)	12 (7.9)	56 (7.4)
アラニンアミノトランスフェラーゼ増加	2 (0.7)	4 (1.3)	0	6 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	4 (1.3)	6 (2.0)	1 (0.7)	11 (1.5)
抱合ビリルビン増加	1 (0.3)	1 (0.3)	0	2 (0.3)
血中ビリルビン増加	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
血中コレステロール増加	0	0	3 (2.0)	3 (0.4)
血中クレアチニン増加	1 (0.3)	1 (0.3)	0	2 (0.3)
血中ブドウ糖増加	1 (0.3)	0	0	1 (0.1)
血中鉄減少	1 (0.3)	1 (0.3)	0	2 (0.3)
血圧上昇	0	1 (0.3)	1 (0.7)	2 (0.3)
血中甲状腺刺激ホルモン正常	1 (0.3)	0	0	1 (0.1)
血中トリグリセリド増加	0	1 (0.3)	2 (1.3)	3 (0.4)
体温上昇	0	0	1 (0.7)	1 (0.1)
C－反応性蛋白増加	4 (1.3)	2 (0.7)	0	6 (0.8)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
臨床検査 (Cont.)				
心雑音	0	0	1 (0.7)	1 (0.1)
クロストリジウム検査陽性	1 (0.3)	0	0	1 (0.1)
尿中結晶陽性	0	0	1 (0.7)	1 (0.1)
ヘマトクリット減少	1 (0.3)	0	0	1 (0.1)
ヘモグロビン減少	2 (0.7)	1 (0.3)	0	3 (0.4)
心拍数不整	1 (0.3)	0	0	1 (0.1)
肝酵素上昇	0	1 (0.3)	1 (0.7)	2 (0.3)
HIV検査陽性	0	0	1 (0.7)	1 (0.1)
リパーゼ増加	1 (0.3)	0	0	1 (0.1)
肝機能検査値上昇	3 (1.0)	2 (0.7)	0	5 (0.7)
リンパ球数増加	1 (0.3)	0	0	1 (0.1)
好中球数減少	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
血小板数増加	0	1 (0.3)	0	1 (0.1)
赤血球数減少	1 (0.3)	0	0	1 (0.1)
サイロキシン増加	1 (0.3)	0	0	1 (0.1)
トランスアミナーゼ上昇	0	0	1 (0.7)	1 (0.1)
トリヨードチロニン正常	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
臨床検査 (Cont.)				
尿検査異常	0	1 (0.3)	0	1 (0.1)
体重減少	0	1 (0.3)	0	1 (0.1)
白血球数減少	1 (0.3)	3 (1.0)	3 (2.0)	7 (0.9)
白血球数増加	0	1 (0.3)	0	1 (0.1)
尿中白血球陽性	0	0	1 (0.7)	1 (0.1)
代謝および栄養障害	14 (4.6)	15 (4.9)	4 (2.6)	33 (4.4)
食欲減退	2 (0.7)	2 (0.7)	0	4 (0.5)
脱水	1 (0.3)	2 (0.7)	0	3 (0.4)
糖尿病	1 (0.3)	2 (0.7)	0	3 (0.4)
コントロール不良の糖尿病	1 (0.3)	0	0	1 (0.1)
痛風	0	1 (0.3)	0	1 (0.1)
高カルシウム血症	1 (0.3)	0	0	1 (0.1)
高コレステロール血症	6 (2.0)	2 (0.7)	1 (0.7)	9 (1.2)
高脂血症	1 (0.3)	1 (0.3)	0	2 (0.3)
高トリグリセリド血症	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
低アルブミン血症	0	1 (0.3)	0	1 (0.1)
低カリウム血症	1 (0.3)	4 (1.3)	1 (0.7)	6 (0.8)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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代謝および栄養障害 (Cont.)				
低ナトリウム血症	0	1 (0.3)	0	1 (0.1)
低リン酸血症	1 (0.3)	0	1 (0.7)	2 (0.3)
ビタミン欠乏症	0	1 (0.3)	0	1 (0.1)
血液量減少症	0	0	1 (0.7)	1 (0.1)
空腹時血中ブドウ糖不良	0	0	1 (0.7)	1 (0.1)
鉄欠乏	1 (0.3)	2 (0.7)	1 (0.7)	4 (0.5)
栄養障害	0	1 (0.3)	0	1 (0.1)
代謝性アルカローシス	0	0	1 (0.7)	1 (0.1)
ビタミンB12欠乏	1 (0.3)	0	0	1 (0.1)
ビタミンD欠乏	1 (0.3)	0	1 (0.7)	2 (0.3)
筋骨格系および結合組織障害	45 (14.9)	52 (17.1)	14 (9.3)	111 (14.7)
関節痛	24 (7.9)	24 (7.9)	5 (3.3)	53 (7.0)
関節炎	2 (0.7)	1 (0.3)	2 (1.3)	5 (0.7)
関節障害	0	0	1 (0.7)	1 (0.1)
腋窩腫瘤	0	1 (0.3)	0	1 (0.1)
背部痛	6 (2.0)	9 (3.0)	3 (2.0)	18 (2.4)
尾骨痛	2 (0.7)	0	0	2 (0.3)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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筋骨格系および結合組織障害 (Cont.)				
デュプイトラン拘縮	0	1 (0.3)	0	1 (0.1)
瘻孔	0	1 (0.3)	0	1 (0.1)
側腹部痛	0	0	1 (0.7)	1 (0.1)
帙径部痛	1 (0.3)	0	0	1 (0.1)
椎間板変性症	0	2 (0.7)	0	2 (0.3)
椎間板突出	0	1 (0.3)	0	1 (0.1)
関節硬直	1 (0.3)	0	0	1 (0.1)
関節腫脹	0	1 (0.3)	0	1 (0.1)
運動性低下	1 (0.3)	0	0	1 (0.1)
筋痙縮	4 (1.3)	2 (0.7)	1 (0.7)	7 (0.9)
筋力低下	1 (0.3)	0	0	1 (0.1)
筋骨格系胸痛	0	2 (0.7)	0	2 (0.3)
筋骨格痛	0	3 (1.0)	1 (0.7)	4 (0.5)
筋肉痛	6 (2.0)	4 (1.3)	1 (0.7)	11 (1.5)
筋炎	1 (0.3)	0	0	1 (0.1)
頚部痛	0	2 (0.7)	0	2 (0.3)
変形性関節症	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
筋骨格系および結合組織障害 (Cont.)				
骨減少症	0	3 (1.0)	0	3 (0.4)
四肢痛	2 (0.7)	9 (3.0)	1 (0.7)	12 (1.6)
顎痛	0	0	1 (0.7)	1 (0.1)
肩回旋筋腱板症候群	1 (0.3)	0	0	1 (0.1)
仙腸骨炎	0	2 (0.7)	0	2 (0.3)
脊椎痛	0	1 (0.3)	0	1 (0.1)
滑液嚢腫	1 (0.3)	0	1 (0.7)	2 (0.3)
滑膜炎	0	1 (0.3)	0	1 (0.1)
顎関節症候群	0	1 (0.3)	0	1 (0.1)
腱痛	0	1 (0.3)	0	1 (0.1)
腱炎	1 (0.3)	1 (0.3)	0	2 (0.3)
斜頚	1 (0.3)	0	0	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）	5 (1.7)	11 (3.6)	3 (2.0)	19 (2.5)
アクロコルドン	0	2 (0.7)	0	2 (0.3)
肛門性器疣贅	0	1 (0.3)	0	1 (0.1)
基底細胞癌	1 (0.3)	1 (0.3)	0	2 (0.3)
膀胱癌	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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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） (Cont.)				
線維腫症	0	1 (0.3)	0	1 (0.1)
胃腸管腺腫	0	1 (0.3)	1 (0.7)	2 (0.3)
脂肪腫	0	1 (0.3)	1 (0.7)	2 (0.3)
悪性黒色腫	0	1 (0.3)	0	1 (0.1)
メラノサイト性母斑	3 (1.0)	0	1 (0.7)	4 (0.5)
新生物	0	1 (0.3)	0	1 (0.1)
非小細胞肺癌	1 (0.3)	0	0	1 (0.1)
食道腺癌	0	1 (0.3)	0	1 (0.1)
子宮平滑筋腫	0	1 (0.3)	0	1 (0.1)
神経系障害	27 (8.9)	40 (13.2)	13 (8.6)	80 (10.6)
健忘	0	0	1 (0.7)	1 (0.1)
脳血管障害	0	0	1 (0.7)	1 (0.1)
慢性炎症性脱髄性多発根ニューロパチー	0	0	1 (0.7)	1 (0.1)
注意力障害	0	1 (0.3)	0	1 (0.1)
浮動性めまい	5 (1.7)	5 (1.6)	2 (1.3)	12 (1.6)
体位性めまい	0	1 (0.3)	0	1 (0.1)
頭部不快感	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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神経系障害 (Cont.)				
頭痛	16 (5.3)	20 (6.6)	8 (5.3)	44 (5.8)
知覚過敏	0	1 (0.3)	0	1 (0.1)
感覚鈍麻	0	4 (1.3)	0	4 (0.5)
虚血性脳卒中	0	0	1 (0.7)	1 (0.1)
腰仙部神経根障害	0	1 (0.3)	0	1 (0.1)
片頭痛	2 (0.7)	5 (1.6)	0	7 (0.9)
単ニューロパチー	0	1 (0.3)	0	1 (0.1)
末梢性ニューロパチー	0	1 (0.3)	0	1 (0.1)
錯感覚	4 (1.3)	2 (0.7)	2 (1.3)	8 (1.1)
坐骨神経痛	3 (1.0)	2 (0.7)	0	5 (0.7)
視野欠損	0	2 (0.7)	0	2 (0.3)
精神障害	9 (3.0)	10 (3.3)	6 (4.0)	25 (3.3)
抑うつ気分を伴う適応障害	0	1 (0.3)	0	1 (0.1)
激越	0	1 (0.3)	0	1 (0.1)
不安	5 (1.7)	1 (0.3)	2 (1.3)	8 (1.1)
むちゃ飲み	0	0	1 (0.7)	1 (0.1)
双極性障害	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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精神障害 (Cont.)				
抑うつ気分	1 (0.3)	0	2 (1.3)	3 (0.4)
うつ病	2 (0.7)	2 (0.7)	1 (0.7)	5 (0.7)
感情的苦悩	0	0	1 (0.7)	1 (0.1)
疾病恐怖	0	0	1 (0.7)	1 (0.1)
不眠症	2 (0.7)	1 (0.3)	1 (0.7)	4 (0.5)
精神疲労	0	0	1 (0.7)	1 (0.1)
落ち着きのなさ	0	1 (0.3)	0	1 (0.1)
睡眠障害	0	1 (0.3)	0	1 (0.1)
ストレス	0	1 (0.3)	0	1 (0.1)
自殺念慮	0	1 (0.3)	0	1 (0.1)
腎および尿路障害	9 (3.0)	7 (2.3)	3 (2.0)	19 (2.5)
尿路結石	1 (0.3)	0	0	1 (0.1)
排尿困難	1 (0.3)	1 (0.3)	0	2 (0.3)
血尿	1 (0.3)	2 (0.7)	0	3 (0.4)
腎結石症	3 (1.0)	1 (0.3)	2 (1.3)	6 (0.8)
ネフローゼ症候群	1 (0.3)	0	0	1 (0.1)
夜間頻尿	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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腎および尿路障害 (Cont.)				
頻尿	0	1 (0.3)	0	1 (0.1)
腎前性腎不全	0	1 (0.3)	0	1 (0.1)
腎仙痛	2 (0.7)	0	0	2 (0.3)
腎嚢胞	0	0	1 (0.7)	1 (0.1)
尿失禁	1 (0.3)	1 (0.3)	0	2 (0.3)
尿閉	0	1 (0.3)	1 (0.7)	2 (0.3)
生殖系および乳房障害	7 (2.3)	5 (1.6)	1 (0.7)	13 (1.7)
無月経	0	1 (0.3)	0	1 (0.1)
バルトリン嚢腫	1 (0.3)	0	0	1 (0.1)
乳房腫瘤	0	1 (0.3)	0	1 (0.1)
月経困難症	3 (1.0)	0	1 (0.7)	4 (0.5)
卵管障害	1 (0.3)	0	0	1 (0.1)
卵巣嚢胞	1 (0.3)	0	0	1 (0.1)
多嚢胞性卵巣	0	1 (0.3)	0	1 (0.1)
前立腺炎	0	1 (0.3)	0	1 (0.1)
前立腺腫大	1 (0.3)	0	0	1 (0.1)
精索静脈瘤	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
呼吸器、胸郭および縦隔障害	30 (9.9)	40 (13.2)	9 (6.0)	79 (10.4)
喘息	1 (0.3)	0	0	1 (0.1)
咳嗽	8 (2.6)	11 (3.6)	2 (1.3)	21 (2.8)
発声障害	0	1 (0.3)	0	1 (0.1)
呼吸困難	4 (1.3)	2 (0.7)	0	6 (0.8)
肺気腫	0	1 (0.3)	0	1 (0.1)
鼻出血	1 (0.3)	2 (0.7)	0	3 (0.4)
喀血	0	1 (0.3)	0	1 (0.1)
鼻閉	4 (1.3)	4 (1.3)	1 (0.7)	9 (1.2)
鼻汁変色	1 (0.3)	0	0	1 (0.1)
鼻の炎症	0	1 (0.3)	0	1 (0.1)
鼻粘膜潰瘍	0	1 (0.3)	0	1 (0.1)
鼻茸	1 (0.3)	0	0	1 (0.1)
鼻中隔弯曲	0	1 (0.3)	0	1 (0.1)
鼻潰瘍	0	1 (0.3)	0	1 (0.1)
口腔咽頭痛	5 (1.7)	11 (3.6)	5 (3.3)	21 (2.8)
咽頭の炎症	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
胸膜炎	1 (0.3)	0	0	1 (0.1)
湿性咳嗽	0	1 (0.3)	0	1 (0.1)
肺塞栓症	1 (0.3)	3 (1.0)	0	4 (0.5)
ラ音	1 (0.3)	0	0	1 (0.1)
気道うっ血	1 (0.3)	0	0	1 (0.1)
鼻痛	1 (0.3)	0	0	1 (0.1)
アレルギー性鼻炎	1 (0.3)	3 (1.0)	0	4 (0.5)
鼻漏	1 (0.3)	2 (0.7)	1 (0.7)	4 (0.5)
副鼻腔うっ血	3 (1.0)	3 (1.0)	0	6 (0.8)
副鼻腔ポリープ	1 (0.3)	0	0	1 (0.1)
睡眠時無呼吸症候群	2 (0.7)	0	0	2 (0.3)
上気道咳症候群	4 (1.3)	1 (0.3)	0	5 (0.7)
喘鳴	0	1 (0.3)	0	1 (0.1)
皮膚および皮下組織障害	44 (14.6)	59 (19.4)	19 (12.6)	122 (16.1)
ざ瘡	7 (2.3)	4 (1.3)	3 (2.0)	14 (1.8)
脱毛症	4 (1.3)	7 (2.3)	3 (2.0)	14 (1.8)
血管浮腫	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
皮膚および皮下組織障害 (Cont.)				
水疱	0	1 (0.3)	0	1 (0.1)
頭部粃糠疹	0	1 (0.3)	0	1 (0.1)
皮膚嚢腫	1 (0.3)	0	0	1 (0.1)
皮膚炎	1 (0.3)	3 (1.0)	0	4 (0.5)
アレルギー性皮膚炎	1 (0.3)	0	1 (0.7)	2 (0.3)
アトピー性皮膚炎	0	1 (0.3)	0	1 (0.1)
接触皮膚炎	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
薬疹	0	1 (0.3)	0	1 (0.1)
皮膚乾燥	2 (0.7)	3 (1.0)	0	5 (0.7)
斑状出血	1 (0.3)	0	0	1 (0.1)
湿疹	1 (0.3)	3 (1.0)	2 (1.3)	6 (0.8)
紅斑	3 (1.0)	7 (2.3)	2 (1.3)	12 (1.6)
結節性紅斑	2 (0.7)	1 (0.3)	1 (0.7)	4 (0.5)
過剰皮膚	0	1 (0.3)	0	1 (0.1)
剥脱性発疹	1 (0.3)	1 (0.3)	0	2 (0.3)
過敏性血管炎	0	0	1 (0.7)	1 (0.1)
間擦疹	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
皮膚および皮下組織障害 (Cont.)				
扁平苔癬	0	0	1 (0.7)	1 (0.1)
リニアIgA病	1 (0.3)	0	0	1 (0.1)
爪の障害	0	1 (0.3)	0	1 (0.1)
寝汗	2 (0.7)	2 (0.7)	0	4 (0.5)
類天疱瘡	0	0	1 (0.7)	1 (0.1)
色素沈着障害	0	0	1 (0.7)	1 (0.1)
そう痒症	6 (2.0)	8 (2.6)	1 (0.7)	15 (2.0)
乾癬	2 (0.7)	1 (0.3)	1 (0.7)	4 (0.5)
発疹	10 (3.3)	19 (6.3)	4 (2.6)	33 (4.4)
紅斑性皮疹	1 (0.3)	1 (0.3)	0	2 (0.3)
斑状皮疹	0	1 (0.3)	0	1 (0.1)
丘疹性皮疹	2 (0.7)	2 (0.7)	1 (0.7)	5 (0.7)
酒さ	0	1 (0.3)	0	1 (0.1)
脂漏性皮膚炎	0	0	1 (0.7)	1 (0.1)
皮膚灼熱感	1 (0.3)	0	0	1 (0.1)
皮膚病変	2 (0.7)	2 (0.7)	1 (0.7)	5 (0.7)
皮膚線条	0	1 (0.3)	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
皮膚および皮下組織障害 (Cont.)				
角層下膿疱性皮膚症	0	1 (0.3)	0	1 (0.1)
顔面腫脹	0	1 (0.3)	0	1 (0.1)
蕁麻疹	1 (0.3)	2 (0.7)	0	3 (0.4)
社会環境	1 (0.3)	0	0	1 (0.1)
閉経	1 (0.3)	0	0	1 (0.1)
血管障害	9 (3.0)	12 (3.9)	3 (2.0)	24 (3.2)
大動脈瘤	0	1 (0.3)	0	1 (0.1)
大動脈硬化症	0	1 (0.3)	0	1 (0.1)
動脈炎	0	1 (0.3)	0	1 (0.1)
本態性高血圧症	0	0	1 (0.7)	1 (0.1)
潮紅	0	1 (0.3)	0	1 (0.1)
血腫	0	1 (0.3)	0	1 (0.1)
高血圧	6 (2.0)	6 (2.0)	1 (0.7)	13 (1.7)
高血圧性血管障害	0	1 (0.3)	0	1 (0.1)
高血圧クリーゼ	1 (0.3)	0	0	1 (0.1)
起立性低血圧	0	0	1 (0.7)	1 (0.1)
蒼白	1 (0.3)	0	0	1 (0.1)

表 1. すべての有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
血管障害 (Cont.)				
静脈炎	0	1 (0.3)	0	1 (0.1)
血栓性静脈炎	1 (0.3)	0	0	1 (0.1)
血栓症	1 (0.3)	0	0	1 (0.1)

Note: The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Treatment-emergent adverse events during the maintenance study are defined as events that begin or worsen either on or after the first dose of the study drug in the maintenance study and within 70 days after the last dose of the study drug.

Cross reference: M14-033 Maintenance Main-study Final CSR_Table 14.3__1.2.1

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
Any Adverse Event	82 (27.2)	104 (34.2)	49 (32.5)	235 (31.0)
血液およびリンパ系障害	3 (1.0)	6 (2.0)	4 (2.6)	13 (1.7)
貧血	0	1 (0.3)	0	1 (0.1)
白血球減少症	1 (0.3)	2 (0.7)	0	3 (0.4)
リンパ節症	0	2 (0.7)	1 (0.7)	3 (0.4)
リンパ球減少症	0	0	1 (0.7)	1 (0.1)
好中球減少症	1 (0.3)	1 (0.3)	1 (0.7)	3 (0.4)
血小板減少症	1 (0.3)	0	1 (0.7)	2 (0.3)
血小板増加症	1 (0.3)	0	0	1 (0.1)
耳および迷路障害	4 (1.3)	0	0	4 (0.5)
耳鳴	2 (0.7)	0	0	2 (0.3)
回転性めまい	2 (0.7)	0	0	2 (0.3)
眼障害	3 (1.0)	3 (1.0)	0	6 (0.8)
ドライアイ	0	1 (0.3)	0	1 (0.1)
眼の炎症	0	1 (0.3)	0	1 (0.1)
眼痛	1 (0.3)	0	0	1 (0.1)
眼瞼縁痂皮	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
眼障害 (Cont.)				
眼瞼下垂	0	1 (0.3)	0	1 (0.1)
視神経萎縮	1 (0.3)	0	0	1 (0.1)
視力障害	1 (0.3)	0	0	1 (0.1)
胃腸障害	9 (3.0)	13 (4.3)	7 (4.6)	29 (3.8)
腹部膨満	2 (0.7)	0	0	2 (0.3)
腹痛	0	1 (0.3)	0	1 (0.1)
上腹部痛	1 (0.3)	0	0	1 (0.1)
裂肛	0	1 (0.3)	0	1 (0.1)
肛門そう痒症	0	0	1 (0.7)	1 (0.1)
アフタ性潰瘍	0	0	1 (0.7)	1 (0.1)
潰瘍性大腸炎	3 (1.0)	6 (2.0)	3 (2.0)	12 (1.6)
クローン病	0	1 (0.3)	0	1 (0.1)
下痢	2 (0.7)	0	0	2 (0.3)
口内乾燥	0	1 (0.3)	0	1 (0.1)
鼓腸	0	0	1 (0.7)	1 (0.1)
歯肉出血	0	1 (0.3)	0	1 (0.1)
血便排泄	1 (0.3)	0	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
胃腸障害 (Cont.)				
痔核	0	1 (0.3)	0	1 (0.1)
粘液便	1 (0.3)	0	0	1 (0.1)
悪心	2 (0.7)	1 (0.3)	1 (0.7)	4 (0.5)
急性膵炎	1 (0.3)	0	0	1 (0.1)
肛門周囲痛	1 (0.3)	0	0	1 (0.1)
直腸出血	1 (0.3)	0	0	1 (0.1)
歯痛	0	2 (0.7)	0	2 (0.3)
一般・全身障害および投与部位の状態	14 (4.6)	26 (8.6)	6 (4.0)	46 (6.1)
無力症	3 (1.0)	4 (1.3)	0	7 (0.9)
嚢胞	1 (0.3)	0	0	1 (0.1)
薬物相互作用	0	1 (0.3)	0	1 (0.1)
異形成	0	0	1 (0.7)	1 (0.1)
疲労	2 (0.7)	2 (0.7)	0	4 (0.5)
高熱	0	0	1 (0.7)	1 (0.1)
インフルエンザ様疾患	0	2 (0.7)	0	2 (0.3)
注入部位紅斑	0	1 (0.3)	0	1 (0.1)
注入部位そう痒感	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
注射部位紅斑	3 (1.0)	2 (0.7)	1 (0.7)	6 (0.8)
注射部位過敏反応	0	1 (0.3)	0	1 (0.1)
注射部位硬結	1 (0.3)	0	0	1 (0.1)
注射部位炎症	0	2 (0.7)	0	2 (0.3)
注射部位結節	1 (0.3)	0	0	1 (0.1)
注射部位疼痛	2 (0.7)	1 (0.3)	0	3 (0.4)
注射部位そう痒感	0	2 (0.7)	1 (0.7)	3 (0.4)
注射部位発疹	1 (0.3)	2 (0.7)	0	3 (0.4)
注射部位反応	2 (0.7)	2 (0.7)	3 (2.0)	7 (0.9)
注射部位腫脹	1 (0.3)	2 (0.7)	0	3 (0.4)
限局性浮腫	1 (0.3)	0	0	1 (0.1)
末梢腫脹	0	1 (0.3)	0	1 (0.1)
発熱	0	4 (1.3)	0	4 (0.5)
腫脹	0	1 (0.3)	0	1 (0.1)
肝胆道系障害	2 (0.7)	1 (0.3)	4 (2.6)	7 (0.9)
高トランスアミナーゼ血症	1 (0.3)	1 (0.3)	4 (2.6)	6 (0.8)
非アルコール性脂肪性肝炎	1 (0.3)	0	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
感染症および寄生虫症	31 (10.3)	36 (11.8)	20 (13.2)	87 (11.5)
四肢膿瘍	0	2 (0.7)	0	2 (0.3)
急性副鼻腔炎	0	1 (0.3)	0	1 (0.1)
細菌性膣症	0	1 (0.3)	0	1 (0.1)
カンジダ感染	0	1 (0.3)	0	1 (0.1)
蜂巣炎	0	0	1 (0.7)	1 (0.1)
クロストリジウム・ディフィシレ感染	1 (0.3)	2 (0.7)	0	3 (0.4)
結膜炎	0	0	2 (1.3)	2 (0.3)
膀胱炎	1 (0.3)	0	2 (1.3)	3 (0.4)
サイトメガロウイルス感染	1 (0.3)	0	0	1 (0.1)
耳感染	2 (0.7)	0	0	2 (0.3)
エプスタイン・バーウイルス感染	1 (0.3)	0	0	1 (0.1)
外耳蜂巣炎	1 (0.3)	0	0	1 (0.1)
毛包炎	0	1 (0.3)	0	1 (0.1)
真菌感染	1 (0.3)	0	0	1 (0.1)
皮膚真菌感染	1 (0.3)	0	1 (0.7)	2 (0.3)
胃腸炎	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
感染症および寄生虫症 (Cont.)				
性器カンジダ症	0	1 (0.3)	0	1 (0.1)
歯肉膿瘍	0	1 (0.3)	0	1 (0.1)
ヘルペス眼感染	0	1 (0.3)	0	1 (0.1)
帯状疱疹	3 (1.0)	2 (0.7)	1 (0.7)	6 (0.8)
麦粒腫	0	1 (0.3)	0	1 (0.1)
インフルエンザ	1 (0.3)	5 (1.6)	1 (0.7)	7 (0.9)
下気道感染	0	0	1 (0.7)	1 (0.1)
鼓膜炎	0	0	1 (0.7)	1 (0.1)
上咽頭炎	6 (2.0)	9 (3.0)	5 (3.3)	20 (2.6)
口腔カンジダ症	1 (0.3)	0	0	1 (0.1)
口腔真菌感染	0	1 (0.3)	0	1 (0.1)
口腔ヘルペス	0	2 (0.7)	0	2 (0.3)
外耳炎	1 (0.3)	1 (0.3)	0	2 (0.3)
急性中耳炎	1 (0.3)	0	0	1 (0.1)
咽頭炎	0	1 (0.3)	1 (0.7)	2 (0.3)
レンサ球菌性咽頭炎	1 (0.3)	0	0	1 (0.1)
肺炎	1 (0.3)	3 (1.0)	1 (0.7)	5 (0.7)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
感染症および寄生虫症 (Cont.)				
腎盂腎炎	0	0	1 (0.7)	1 (0.1)
急性腎盂腎炎	0	1 (0.3)	0	1 (0.1)
膿疱性皮疹	2 (0.7)	0	0	2 (0.3)
鼻炎	1 (0.3)	0	0	1 (0.1)
敗血症	0	0	1 (0.7)	1 (0.1)
副鼻腔炎	1 (0.3)	2 (0.7)	2 (1.3)	5 (0.7)
皮膚感染	0	1 (0.3)	0	1 (0.1)
扁桃炎	0	3 (1.0)	1 (0.7)	4 (0.5)
歯膿瘍	1 (0.3)	0	0	1 (0.1)
歯感染	0	1 (0.3)	0	1 (0.1)
結核	0	1 (0.3)	0	1 (0.1)
上気道感染	7 (2.3)	4 (1.3)	3 (2.0)	14 (1.8)
尿路感染	1 (0.3)	1 (0.3)	2 (1.3)	4 (0.5)
腟感染	1 (0.3)	0	0	1 (0.1)
ウイルス感染	0	1 (0.3)	0	1 (0.1)
ウイルス性咽頭炎	0	2 (0.7)	0	2 (0.3)
外陰部腟カンジダ症	0	1 (0.3)	0	1 (0.1)

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感染症および寄生虫症 (Cont.)				
外陰膣真菌感染	0	1 (0.3)	0	1 (0.1)
外陰膣炎	0	0	1 (0.7)	1 (0.1)
傷害、中毒および処置合併症	0	0	1 (0.7)	1 (0.1)
注射に伴う反応	0	0	1 (0.7)	1 (0.1)
臨床検査	5 (1.7)	8 (2.6)	3 (2.0)	16 (2.1)
アラニンアミノトランスフェラーゼ増加	0	3 (1.0)	0	3 (0.4)
アスパラギン酸アミノトランスフェラーゼ増加	0	4 (1.3)	0	4 (0.5)
抱合ビリルビン増加	0	1 (0.3)	0	1 (0.1)
血中ビリルビン増加	0	1 (0.3)	0	1 (0.1)
血中コレステロール増加	0	0	1 (0.7)	1 (0.1)
血中クレアチニン増加	1 (0.3)	0	0	1 (0.1)
血中トリグリセリド増加	0	0	1 (0.7)	1 (0.1)
肝機能検査値上昇	2 (0.7)	0	0	2 (0.3)
好中球数減少	1 (0.3)	1 (0.3)	0	2 (0.3)
白血球数減少	1 (0.3)	3 (1.0)	2 (1.3)	6 (0.8)
代謝および栄養障害	5 (1.7)	1 (0.3)	0	6 (0.8)
食欲減退	1 (0.3)	0	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

MedDRA 22.0 System Organ Class Preferred Term	Adalimumab 40mg EOW (N=302) n (%)	Adalimumab 40mg EW (N=304) n (%)	Adalimumab TDM Regimen (N=151) n (%)	Total (N=757) n (%)
代謝および栄養障害 (Cont.)				
コントロール不良の糖尿病	1 (0.3)	0	0	1 (0.1)
高コレステロール血症	1 (0.3)	0	0	1 (0.1)
高トリグリセリド血症	1 (0.3)	0	0	1 (0.1)
低カリウム血症	0	1 (0.3)	0	1 (0.1)
低リン酸血症	1 (0.3)	0	0	1 (0.1)
筋骨格系および結合組織障害	11 (3.6)	16 (5.3)	3 (2.0)	30 (4.0)
関節痛	9 (3.0)	10 (3.3)	2 (1.3)	21 (2.8)
関節炎	0	1 (0.3)	0	1 (0.1)
デュプイトラン拘縮	0	1 (0.3)	0	1 (0.1)
関節硬直	1 (0.3)	0	0	1 (0.1)
関節腫脹	0	1 (0.3)	0	1 (0.1)
筋痙縮	0	1 (0.3)	0	1 (0.1)
筋骨格系胸痛	0	1 (0.3)	0	1 (0.1)
筋肉痛	0	1 (0.3)	1 (0.7)	2 (0.3)
筋炎	1 (0.3)	0	0	1 (0.1)
骨減少症	0	1 (0.3)	0	1 (0.1)
四肢痛	2 (0.7)	3 (1.0)	0	5 (0.7)
腱痛	0	1 (0.3)	0	1 (0.1)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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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	5 (1.6)	0	5 (0.7)
アクロコルドン	0	2 (0.7)	0	2 (0.3)
肛門性器疣贅	0	1 (0.3)	0	1 (0.1)
基底細胞癌	0	1 (0.3)	0	1 (0.1)
線維腫症	0	1 (0.3)	0	1 (0.1)
神経系障害	3 (1.0)	12 (3.9)	6 (4.0)	21 (2.8)
健忘	0	0	1 (0.7)	1 (0.1)
慢性炎症性脱髄性多発根ニューロパチー	0	0	1 (0.7)	1 (0.1)
注意力障害	0	1 (0.3)	0	1 (0.1)
浮動性めまい	2 (0.7)	2 (0.7)	1 (0.7)	5 (0.7)
体位性めまい	0	1 (0.3)	0	1 (0.1)
頭部不快感	0	1 (0.3)	0	1 (0.1)
頭痛	0	8 (2.6)	3 (2.0)	11 (1.5)
感覚鈍麻	0	2 (0.7)	0	2 (0.3)
単ニューロパチー	0	1 (0.3)	0	1 (0.1)
錯感覚	1 (0.3)	1 (0.3)	0	2 (0.3)

表 2. 治験薬と関連ありの有害事象（MedDRA SOC 及び PT 別）（主試験安全性解析対象集団，M14-033 主試験の維持療法試験）（続き）

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精神障害	0	2 (0.7)	0	2 (0.3)
激越	0	1 (0.3)	0	1 (0.1)
うつ病	0	1 (0.3)	0	1 (0.1)
腎および尿路障害	2 (0.7)	0	1 (0.7)	3 (0.4)
腎結石症	1 (0.3)	0	0	1 (0.1)
ネフローゼ症候群	1 (0.3)	0	0	1 (0.1)
尿閉	0	0	1 (0.7)	1 (0.1)
生殖系および乳房障害	1 (0.3)	0	0	1 (0.1)
バルトリン嚢腫	1 (0.3)	0	0	1 (0.1)
呼吸器、胸郭および縦隔障害	5 (1.7)	11 (3.6)	5 (3.3)	21 (2.8)
咳嗽	3 (1.0)	4 (1.3)	0	7 (0.9)
呼吸困難	1 (0.3)	1 (0.3)	0	2 (0.3)
肺気腫	0	1 (0.3)	0	1 (0.1)
鼻出血	0	1 (0.3)	0	1 (0.1)
鼻閉	0	0	1 (0.7)	1 (0.1)
口腔咽頭痛	0	3 (1.0)	3 (2.0)	6 (0.8)
湿性咳嗽	0	1 (0.3)	0	1 (0.1)

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呼吸器、胸郭および縦隔障害 (Cont.)				
鼻痛	1 (0.3)	0	0	1 (0.1)
鼻漏	0	1 (0.3)	1 (0.7)	2 (0.3)
喘鳴	0	1 (0.3)	0	1 (0.1)
皮膚および皮下組織障害	20 (6.6)	31 (10.2)	13 (8.6)	64 (8.5)
ざ瘡	2 (0.7)	2 (0.7)	2 (1.3)	6 (0.8)
脱毛症	2 (0.7)	6 (2.0)	3 (2.0)	11 (1.5)
皮膚炎	0	1 (0.3)	0	1 (0.1)
アトピー性皮膚炎	0	1 (0.3)	0	1 (0.1)
接触皮膚炎	0	1 (0.3)	0	1 (0.1)
薬疹	0	1 (0.3)	0	1 (0.1)
皮膚乾燥	1 (0.3)	2 (0.7)	0	3 (0.4)
湿疹	1 (0.3)	3 (1.0)	1 (0.7)	5 (0.7)
紅斑	2 (0.7)	2 (0.7)	2 (1.3)	6 (0.8)
結節性紅斑	1 (0.3)	0	0	1 (0.1)
剥脱性発疹	1 (0.3)	0	0	1 (0.1)
扁平苔癬	0	0	1 (0.7)	1 (0.1)
リニアIgA病	1 (0.3)	0	0	1 (0.1)