TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Day | Rx Day of Onset /Dose Escal-ation | |
|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | |
| [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | |
| | C1-3 0OL | 46 to | 816 | 861 /816 | N: [redacted]<br>R: COVID-19 PNEUMONIA INFECTION<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia |

| E | S | AE |
|---|---|---|
| E: 913<br>L: 53 Days | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: COVID-19<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-30OL | 46 to | 833 | 878 /833 | N: [redacted]<br>R: CATHETER RELATED SEPSIS<br>S: 感染症および寄生虫症<br>P: 医療機器関連敗血症<br>L: Catheter sepsis | E: 886<br>L: 9 Days | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: COVID-19 INFECTION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:9[redacted]. [redacted] kg | | | | | | | |
| | C1-15OL | 1 to 79 | 79 | N: [redacted]<br>R: ATRIAL FIBRILLATION<br>S: 心臓障害<br>P: 心房細動<br>L: Atrial fibrillation | | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: STRESS AND EXERTION WAS MOVING INTO A NEW HOME<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - PLACEBO | | | | | | | |
| [redacted] Age:5[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg | | | | | | | |
| | C2-PBO | 1 to 97 | 97 | N: [redacted]<br>R: WORSENING OF HERPES ZOSTER<br>S: 感染症および寄生虫症<br>P: 帯状疱疹<br>L: Herpes zoster | E: 169<br>L: 73 Days | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/Yes/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:4[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg | | | | | | | |
| [redacted] | C1-15OL | 1 to 1006 | 415 /-592 | N: [redacted]<br>R: REFLUX ESOPHAGITIS<br>S: 胃腸障害<br>P: 胃食道逆流性疾患<br>L: Reflux esophagitis | | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: REFLUX ESOPHAGITIS WAS OCCUERED BY DIETARY DISORDER AND ESOPHAGEAL HERNIA.THUS,IT WAS CONSIDERED TO HAVE NO RELATIONSHIP WITH THE INVESTIGATIONAL AGENT.<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted] Age:4[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-3 0OL | 1007 to | 175 | 1181 /175 | N: [redacted]<br>R: COVID-19<br>S: 感染症および寄生虫症<br>P: COVID-19<br>L: COVID-19 | E: 1224<br>L: 44 Days | S: MODERATE<br>C: Yes<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 78 | 30 30 | N: [redacted]<br>R: UC EXACBERATION<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | E: 34<br>L: 5 Days | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: HOSPITALIZATION<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: NO<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 78 | 38 | 38 | N: [redacted]<br>R: UC EXACBERATION<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | E: 63<br>L: 26 Days | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: UC EXACBERATION<br>A: NO REASONABLE POSSIBILITY<br>E: RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Rx Day of Onset /Dose Escal-ation | |
|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | |
| TRT: COHORT 2 - UPA 30 MG QD | | | | |
| [redacted]# Age:7[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg | | | | |
| | C2-3 0DB | 1 to 635 | 403 | 403 |

N: [redacted]
R: PANCREATIC ADENOCARCINOMA
S: 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)
P: 膵腺癌
L: Pancreatic adenocarcinoma

E: 434
L: 32 Days

S: SEVERE
R: NO REASONABLE POSSIBILITY
A: DRUG WITHDRAWN
O: MULTIPLE (Concomitant medication or therapy started, DISCONTINUED STUDY, Other: HOSPITALIZED FOR FURTHER TESTING)

AE: No/No/No/No/No/No
S: Yes, death of subject, hospitalization or prolonged hospitalization
O: AGE RELATED CANCER
A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | | |
| [redacted] Age:6[redacted] Sex:Male Race:BLACK OR AFRICAN AMERICAN Weight:8[redacted].[redacted] kg | | | | | | | | |
| | C2-1 5DB | 1 to | 239 239 | | N: [redacted]<br>R: COVID-19 INFECTION<br>S: 感染症および寄生虫症<br>P: COVID-19<br>L: COVID-19 | | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: COVID-19 - TESTED POSITIVE, DROP IN O2 SATS REQUIRING HOSPITALIZATION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 1501 | 1501 | N: [redacted]<br>R: COVID 19 INFECTION<br>S: 感染症および寄生虫症<br>P: COVID-19<br>L: COVID-19 | O: Yes | S: MODERATE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PER SUBI, PATIENT DEVELOPED COVID 19 DUE TO EXPOSURE TO COVID 19 INFECTION AND BEING UNVACCINATED DESPITE RECOMMENDATIONS.<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD<br>[redacted] Age:4[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | |
| | C2-1 5DB | 1 to 708 | 708 | N: [redacted]<br>R: COVID-19 PNEUMONIA<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia | E: 719<br>L: 12 Days | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: PT OBTAINING CHEST X-RAY AND APPT WITH INFECTIOUS DISEASE | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: COVID-19 INFECTION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg | | | | | | | |
| | C2-3 0DB | 1 to 368 | 154 154 | N: [redacted]<br>R: HERPES ZOSTER<br>S: 感染症および寄生虫症<br>P: 帯状疱疹<br>L: Herpes zoster | E: 202<br>L: 49 Days | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/Yes/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 160 | 83 83 | N: [redacted]<br>R: ORCHITIS<br>S: 感染症および寄生虫症<br>P: 精巣炎<br>L: Orchitis | O: Yes | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: BACTERIAL INFECTION<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| [redacted] | C1-15OL | 1 to 474 | 474 | N: [redacted]<br>R: DEPRESSION<br>S: 精神障害<br>P: うつ病<br>L: Depression | E: 500<br>L: 27 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: MEDICAL HISTORY OF PRE-EXISTING DEPRESSION<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING DEPRESSION. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to | 690 690 | N: [redacted]<br>R: DEPRESSION<br>S: 精神障害<br>P: うつ病<br>L: Depression | E: 694<br>L: 5 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: MEDICAL HISTORY OF PRE-EXISTING DEPRESSION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to | 1079 | 1079 | N: [redacted]<br>R: DEPRESSION<br>S: 精神障害<br>P: うつ病<br>L: Depression | E: 1202<br>L: 124 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: MEDICAL HISTORY OF PRE-EXISTING DEPRESSION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to | 1318 1318 | | N: [redacted]<br>R: DEPRESSION<br>S: 精神障害<br>P: うつ病<br>L: Depression | E: 1384<br>L: 67 Days<br>I: Yes | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: MEDICAL HISTORY OF PRE-EXISTING DEPRESSION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 1422 | 1422 | N: [redacted]<br>R: WORSENING ULCERATIVE COLITIS<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | E: 1437<br>L: 16 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: WORSENING OF ULCERATIVE COLITIS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | | |
| | C2-3 0DB | 1 to 530 | 422 | 422 | N: [redacted]<br>R: COVID-19 PNEUMONIA<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia | E: 452<br>L: 31 Days | S: MODERATE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: COVID- 19 INFECTION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C2-30DB | 1 to 530 | 430 | 430 | N: [redacted]<br>R: BILATERAL PULMONARY EMBOLISMS<br>S: 呼吸器、胸郭および縦隔障害<br>P: 肺塞栓症<br>L: Pulmonary embolism | E: 452<br>L: 23 Days | S: MODERATE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/Yes<br>S: Yes, hospitalization or prolonged hospitalization<br>O: COVID -19 VIRUS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term
E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?
S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken
AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | |
|---|---|---|---|---|
| INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD | | | | |
| [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg | | | | |
| [redacted] | C1-15OL | 1 to 323 | 323 | N: [redacted]<br>R: MYOCARDIAL INFARCTION<br>S: 心臓障害<br>P: 心筋梗塞<br>L: Myocardial infarction<br>E: 326<br>L: 4 Days<br>S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: CV STENT X 3<br>O: Concomitant medication or therapy started<br>AE: No/Yes/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PT HAS A H/O HTN, A. FIB, EX SMOKER X 30 YEARS, HIGH CHOLESTEROL<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg | | | | | | | |
| | C2-1 5DB | 1 to 198 | 38 38 | N: [redacted]<br>R: COVID19 PNEUMONIA<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia | O: Yes | S: MODERATE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: COVID-19<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C2-15DB | 1 to 198 | 50 | 50 | N: [redacted]<br>R: PULMONARY EMBOLISM<br>S: 呼吸器、胸郭および縦隔障害<br>P: 肺塞栓症<br>L: Pulmonary embolism | E: 59<br>L: 10 Days | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: DISCONTINUED STUDY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/Yes<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: COVID-19<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD<br>[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| | C2-3 0DB | 1 to 588 | 588 | N: [redacted]<br>R: COVID 19 PNEUMONIA - INFECTION<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia | E: 604<br>L: 17 Days | S: MODERATE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: WORSENING OF COVID 19 INFECTION. PATIENT IS HOSPTALIZED ON [redacted]20[redacted] DUE TO PNEUMONIA<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD<br>[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | | |
| | C2-1 5DB | 1 to | 559 | 559 | N: [redacted]<br>R: LEFT TIBIAL FRACTURE<br>S: 傷害、中毒および処置合併症<br>P: 脛骨骨折<br>L: Tibia fracture | E: 567<br>L: 9 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: ACCIDENTAL FALL<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg | | | | | | | |
| | C1-3 0OL | 336 to 1596 | 433 768 /433 | N: [redacted]<br>R: BACTERIAL PNEUMONIAE<br>S: 感染症および寄生虫症<br>P: 細菌性肺炎<br>L: Pneumonia bacterial | E: 782<br>L: 15 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PI DETERMINED NOT DRUG RELATED. CAUSE IS BACTERIAL PER PI ASSESSMENT<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-30OL | 336 to 1596 | 550 | 885/550 | N: [redacted]<br>R: SEVERE GASTROENTERITIS<br>S: 感染症および寄生虫症<br>P: 胃腸炎<br>L: Gastroenteritis | E: 916<br>L: 32 Days | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: ADMITTED TO HOSPITAL X2 DAYS NO MEDICATIONS GIVEN | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: SUBJECT WAS AROUND SICK FAMILY MEMBER<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Name | Epoch | Interval | Day | Rx Day of Onset /Dose Escal-ation | V/N/R/S/P/L | E/L | S/C/R/A/O | AE |
|---|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:11[redacted] kg | | | | | | | | | |
| | C1-3 0OL | 70 to 394 | 273 | 342 | /273 | N: [redacted]<br>R: SEPSIS, E. COLI<br>S: 感染症および寄生虫症<br>P: 大腸菌感染<br>L: Escherichia coli infection | E: 350<br>L: 9 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: EXACT CAUSE OF INFECTION IS UNKNOWN. THERE ARE MULTIPLE WAYS THE SUBJECT COULD HAVE GOTTEN E. COLI<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted]<br>TRT: COHORT 1 - UPA [redacted] QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:11[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-3 0OL | 70 to 394 | 273 | 342 /273 | N: [redacted]<br>R: SEPSIS, E. COLI<br>S: 感染症および寄生虫症<br>P: 敗血症<br>L: Sepsis | E: 350<br>L: 9 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: EXACT CAUSE OF INFECTION IS UNKNOWN. THERE ARE MULTIPLE WAYS THE SUBJECT COULD HAVE GOTTEN E. COLI<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted]([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:12[redacted].[redacted] kg | | | | | | | |
| [redacted] | C1-15OL | 1 to 513 | 513 | N: [redacted]<br>R: RIGHT SHOULDER IMPINGEMENT SYNDROME DIAGNOSED ON [redacted]20[redacted]<br>S: 筋骨格系および結合組織障害<br>P: 肩回旋筋腱板症候群<br>L: Impingement syndrome shoulder | | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: SURGERY WITH FOLLOW UP PHYSICAL THERAPY X12 WEEKS<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, important medical or surgical intervention<br>O: UNKNOWN<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 7.5 MG QD<br>[redacted] Age:7[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | |
| [redacted] | C2-7 .5DB | 1 to 937 | 937 | N: [redacted]<br>R: UROSEPSIS<br>S: 感染症および寄生虫症<br>P: 尿路性敗血症<br>L: Urosepsis | E: 943<br>L: 7 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: E. COLI INFECTION<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | | |
| | C1-3 0OL | 29 to 336 | 262 | 290 /262 | N: [redacted]<br>R: LEFT TESTICULAR SEMINOMA<br>S: 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)<br>P: 精巣（純粋）セミノーマ<br>L: Testicular seminoma (pure) | E: 290<br>L: 1 Day | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No/No<br>S: Yes, important medical or surgical intervention<br>O: HISTORY OF BENIGN TESTICULAR LUMP<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | | | |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted] kg | | | | | | | |
| | C1-3 0OL | 43 to 223 | 1 | 43 /1 | N: [redacted]<br>R: HYPOPHOSPHOREMIA<br>S: 代謝および栄養障害<br>P: 低リン酸血症<br>L: Hypophosphatemia | E: 50<br>L: 8 Days<br>I: Yes | S: SEVERE<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY<br>E: RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-3 0OL | 43 to 223 | 9 51 /9 | N: [redacted]<br>R: RECIDIVISM HYPOPHOSPHOREMIA<br>S: 代謝および栄養障害<br>P: 低リン酸血症<br>L: Hypophosphatemia | O: Yes | S: SEVERE<br>R: REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>E: RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted] kg | | | | | | | |
| [redacted] | C1-15OL | 1 to 45 | 14 /-32 | N: [redacted]<br>R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE<br>S: 胃腸障害<br>P: 下痢<br>L: Diarrhoea | E: 15<br>L: 2 Days | S: MODERATE<br>R: REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: MRI<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 45 | 14 | 14 /-32 | N: [redacted]<br>R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE<br>S: 一般・全身障害および投与部位の状態<br>P: 疲労<br>L: Fatigue | E: 15<br>L: 2 Days | S: MODERATE<br>R: REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: MRI<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 45 | 14 | 14 /-32 | N: [redacted]<br>R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE<br>S: 一般・全身障害および投与部位の状態<br>P: 倦怠感<br>L: Malaise | E: 15<br>L: 2 Days | S: MODERATE<br>R: REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: MRI<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to 45 | 14 /-32 | N: [redacted]<br>R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE<br>S: 胃腸障害<br>P: 嘔吐<br>L: Vomiting | E: 15<br>L: 2 Days | S: MODERATE<br>R: REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: MRI<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-30OL | 46 to 78 | 1 | 46/1 | N: [redacted]<br>R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA<br>S: 神経系障害<br>P: 健忘<br>L: Amnesia | E: 47<br>L: 2 Days<br>I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PNES<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Rx Day of Onset /Dose Escal-ation | |
|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | |
| [redacted]# | Age:3[redacted] | Sex:Female | Race:WHITE | Weight:6[redacted].[redacted] kg |
| (Cont.) | C1-3 0OL | 46 to 78 | 1 | 46 /1 |

N: [redacted]
R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA
S: 神経系障害
P: 頭痛
L: Headache

E: 47
L: 2 Days
I: Yes

S: MODERATE
R: NO REASONABLE POSSIBILITY
A: DRUG WITHDRAWN
O: DISCONTINUED STUDY

AE: No/No/No/No/No
S: Yes, hospitalization or prolonged hospitalization
O: PNES
A: NO REASONABLE POSSIBILITY
E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term
E: Rx Day Ended Ongoing at the End of Study?
L: Length
I: Interm-ittent?
S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken
AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Day | Rx Day of Onset /Dose Escal-ation | |
|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | |
| [redacted]# | Age:3[redacted] | Sex:Female | Race:WHITE | Weight:6[redacted].[redacted] kg | |
| (Cont.) | C1-3 0OL | 46 to 78 | 1 | 46 /1 | N: [redacted]<br>R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA<br>S: 胃腸障害<br>P: 悪心<br>L: Nausea |

| E: Rx Day Ended | S: Severity | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? |
|---|---|---|
| E: 47<br>L: 2 Days<br>I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PNES<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term
E: Rx Day Ended Ongoing at the End of Study?
L: Length
I: Interm-ittent?
S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken
AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Day | Rx Day of Onset /Dose Escal-ation | |
|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | |
| (Cont.) | C1-3 0OL | 46 to 78 | 1 | 46 /1 | N: [redacted]<br>R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA<br>S: 神経系障害<br>P: 発作様現象<br>L: Seizure like phenomena |

| E: Rx Day Ended | S: Severity | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? |
|---|---|---|
| E: 47<br>L: 2 Days<br>I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PNES<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-30OL | 46 to 78 | 11 /56 | N: [redacted]<br>R: ONGOING UC, NO IMPROVEMENT FROM TREATMENT<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | E: 70<br>L: 15 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: Other: THIS WAS DURING 30-DAY FU<br>O: SURGERY | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: ONGOING UC<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | | |
| | C1-3 0OL | 106 to 264 | 27 | 132 /27 | N: [redacted]<br>R: C-DIFFICILE INFECTION<br>S: 感染症および寄生虫症<br>P: クロストリジウム・ディフィシレ感染<br>L: Clostridium difficile infection | E: 142<br>L: 11 Days | S: SEVERE<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: NONE | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO RECURRENCE OF PRE-EXISTING CLOSTRIDIUM DIFFICILE INFECTION. ULCERATIVE COLITIS IS AN ADDITIONAL RISK FACTOR. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:7[redacted] kg | | | | | | | | |
| (Cont.) | C1-3 0OL | 106 to 264 | 36 | 141 /36 | N: [redacted]<br>R: L FOOT PAIN<br>S: 筋骨格系および結合組織障害<br>P: 四肢痛<br>L: Foot pain | E: 145<br>L: 5 Days<br>I: Yes | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PARTICIPANT HOSPITALIZED ON [redacted] FOR SEVERE FOOT PAIN RELATING TO ARTHRALGIA FROM ULCERATIVE COLITIS<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING OSTEOARTHRITIS AND ANKLE PAIN. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| | C1-30OL | 71 to | 412 | 482 /412 | N: [redacted]<br>R: RENAL COLIC RIGHT KIDNEY<br>S: 腎および尿路障害<br>P: 腎仙痛<br>L: Renal colic | E: 484<br>L: 3 Days | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:2[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg | | | | | | | | |
| | C1-3 0OL | 85 to 385 | 469 /385 | N: [redacted]<br>R: UC FLARE<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: UC aggravated | E: 473<br>L: 5 Days | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 606 | 563 | 563 | N: [redacted]<br>R: POSTEROLATERAL ST ELEVATION MYOCARDIAL INFARCTION<br>S: 心臓障害<br>P: 急性心筋梗塞<br>L: ST segment elevation myocardial infarction | E: 568<br>L: 6 Days | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY<br>O: Concomitant medication or therapy started | AE: No/Yes/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Rx Day of Onset /Dose Escal-ation | |
|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | |
| [redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | |
| | C1-15OL | 1 to 216 | 104 /-113 | N: [redacted]<br>R: COVID-19 PNEUMONIA INFECTION<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia<br>E: 140<br>L: 37 Days<br>I: Yes<br>S: MODERATE<br>C: Yes<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: PATIENT WAS HOSPITALIZED<br>O: Concomitant medication or therapy started<br>AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-30OL | 217 to 191 | 407 /191 | N: [redacted]<br>R: SYNCOPE<br>S: 神経系障害<br>P: 失神<br>L: Syncope | E: 407<br>L: 1 Day | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: EVALUATION OF THE NEUROLOGY TEAM, GENERAL CLINIC AND SUBMITTED TO IMAGE EXAMS | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Rx Day of Onset /Dose Escal-ation | | | |
|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | |
| [redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted] kg | | | | | | |
| (Cont.) | C1-30OL | 217 to 191 | 407 /191 | N: [redacted]<br>R: LEFT RADIUS FRACTURE<br>S: 傷害、中毒および処置合併症<br>P: 橈骨骨折<br>L: Radius fracture | O: Yes | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: OSTEOSYNTHESIS SURGERY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: SYNCOPE<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | | |
| [redacted]# Age:5[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted] kg | | | | | | | | |
| | C2-3 0DB | 1 to 291 | 168 | 168 | N: [redacted]<br>R: WORSENING OF COVID-19 INFECTION<br>S: 感染症および寄生虫症<br>P: COVID-19<br>L: COVID-19 | E: 184<br>L: 17 Days | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, death of subject, hospitalization or prolonged hospitalization<br>O: COVID-19 |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted]# Age:5[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C2-30DB | 1 to 291 | 174 | 174 | N: [redacted]<br>R: ACUTE RENAL FAILURE<br>S: 腎および尿路障害<br>P: 急性腎障害<br>L: Acute renal failure | E: 180<br>L: 7 Days | S: MODERATE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: DIALYSIS<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: COVID-19<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted]# Age:5[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted] kg | | | | | | | |
| (Cont.) | C2-30DB | 1 to 291 | 184 | N: [redacted]<br>R: PULMONARY THROMBOEMBOLISM<br>S: 呼吸器、胸郭および縦隔障害<br>P: 肺塞栓症<br>L: Pulmonary thromboembolism | E: 184<br>L: 1 Day | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: NONE | AE: No/No/No/No/No/Yes<br>S: Yes, death of subject<br>O: COVID-19<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg | | | | | | | | |
| | C1-15OL | 1 to 1632 | 337 | 337 | N: [redacted]<br>R: COLONIC POLYP<br>S: 胃腸障害<br>P: 大腸ポリープ<br>L: Colonic polyp | E: 450<br>L: 114 Days | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: COLONIC POLYPECTOMY | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: SPORADIC LESION<br>A: NO REASONABLE POSSIBILITY<br>E: RISK FACTORS INCLUDE MALE GENDER, AGE AND PRE-EXISTING ULCERATIVE COLITIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to 1632 | 589 589 | N: [redacted]<br>R: CALCULOUS PYELONEPHRITIS<br>S: 腎および尿路障害<br>P: 腎結石症<br>L: Nephrolithiasis | E: 596<br>L: 8 Days<br>I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: NEPHROLITHIASIS<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF NEPHROLITHIASIS. ADDITIONAL RISK FACTOR IS PRE-EXISTING HYPERURICEMIA. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Name | Epoch | Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted]<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | C1-1 | 1 to 1632 | 589 | 589 | N: [redacted]<br>R: CALCULOUS PYELONEPHRITIS<br>S: 感染症および寄生虫症<br>P: 腎盂腎炎<br>L: Pyelonephritis | E: 596<br>L: 8 Days<br>I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: NEPHROLITHIASIS<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF NEPHROLITHIASIS. ADDITIONAL RISK FACTOR IS PRE-EXISTING HYPERURICEMIA. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 1632 | 631 | 631 | N: [redacted]<br>R: WORSENING OF NEPHROLITHIASIS(RIGHT)<br>S: 腎および尿路障害<br>P: 腎結石症<br>L: Nephrolithiasis | E: 633<br>L: 3 Days | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: TREATMENT FOR ADVERSE EVENT "WORSENING OF NEPHROLITHIASIS(RIGHT)".<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF NEPHROLITHIASIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 163 | 2 1199 | 1199 | N: [redacted]<br>R: COLON POLYP<br>S: 胃腸障害<br>P: 大腸ポリープ<br>L: Colonic polyp | E: 1199<br>L: 1 Day | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: ENDOSCOPIC MUCOUSAL RESECTION | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: NONE<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted][redacted]kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 163 | 2 1346 | 1346 | N: [redacted]<br>R: COLON POLYP<br>S: 胃腸障害<br>P: 大腸ポリープ<br>L: Colonic polyp | E: 1346<br>L: 1 Day | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: ENDOSCOPIC MUCOUSAL RESECTION | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: NONE<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 1632 1450 1450 | | | N: [redacted]<br>R: COLON POLYP<br>S: 胃腸障害<br>P: 大腸ポリープ<br>L: Colonic polyp | E: 1517<br>L: 68 Days | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: ENDOSCOPIC SUBMUCOSAL DISSECTION | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: NONE<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted]([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted]# Age:2[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg | | | | | | | |
| | C2-3 0DB | 1 to 364 | 276 276 | N: [redacted]<br>R: BILATERALLY-BURIED THIRD MOLARS IN THE LOWER JAW<br>S: 胃腸障害<br>P: 埋伏歯<br>L: Impacted wisdom tooth | O: Yes | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PERSONALLY DENTAL MANIFESTATION DURING GROWTH-UP<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:7[redacted] Sex:Male Race:ASIAN Weight:5[redacted] kg | | | | | | | |
| | C2-1 5DB | 1 to 297 | 163 163 | N: [redacted]<br>R: COMPLETE ATRIOVENTRICULAR BLOCK<br>S: 心臓障害<br>P: 完全房室ブロック<br>L: Atrioventricular block complete | E: 172<br>L: 10 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: EXTERNAL CARDIAC PACEMAKER INSERTION,CARDIAC PACEMAKER INSERTION | AE: No/Yes/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: ARTERIOSCLERPOSIS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 43 | 38 38 | N: [redacted]<br>R: WORSENING UC<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | O: Yes | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: HOSPITALISATION + ON [redacted]20[redacted] TOTAL COLECTOMY WITH ILEOSTOMY | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: UNDERLYING DISEASE<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS CLEARLY CONSISTENT WITH PROGRESSION OR WORSENING OF THE UNDERLYING DISEASE AND IS CONSIDERED EXPECTED FOR THIS STUDY. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted]# | Age:5[redacted] | Sex:Male | Race:WHITE | Weight:6[redacted].[redacted] kg | | | | |
| | C1-3 0OL | 71 to 409 | 329 | 399 /329 | N: [redacted]<br>R: WORSENING UC<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | O: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: Other: NOT APPLICABLE<br>O: HOSPITALISATION WITH SURGERY ON [redacted]20[redacted] | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: UNDERLYING DISEASE<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:9[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 497 | 31 31 | N: [redacted]<br>R: WORSENING ULCERATIVE COLITIS<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | E: 34<br>L: 4 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: LACK OF RESPONSE TO STUDY DRUG<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| | C1-3 0OL | 49 to | 176 | 224 /176 | N: [redacted]<br>R: UROLITHIASIS<br>S: 腎および尿路障害<br>P: 尿路結石<br>L: Urolithiasis | E: 231<br>L: 8 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: INSUFFICIENT FLUID INTAKE<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | |
| | C1-3 0OL | 85 to 55 | 139 /55 | N: [redacted]<br>R: KIDNEY STONES<br>S: 腎および尿路障害<br>P: 腎結石症<br>L: Kidney stones | E: 148<br>L: 10 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: SAE DUE TO KIDNEY STONES SURGERY<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-30OL | 85 to 128 | 212 /128 | N: [redacted]<br>R: KIDNEY STONE<br>S: 腎および尿路障害<br>P: 腎結石症<br>L: Kidney stone | E: 215<br>L: 4 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/Yes/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: KIDNEY STONES (COMORBIDITY)<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | |
| [redacted] | C2-3 0DB | 1 to 405 | 405 | N: [redacted]<br>R: COVID 19 INFECTION<br>S: 感染症および寄生虫症<br>P: COVID-19<br>L: COVID-19 | E: 432<br>L: 28 Days | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: MULTIPLE (Concomitant medication or therapy started, CONCOMITANT MEDICATION OR THERAPY DISCONTINUED, Other: PATIENT IS AT INTENSIVE CARE UNIT) | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: COVID 19 VIRUS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD<br>[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted] kg | | | | | | | |
| (Cont.) | C2-30DB | 1 to 406 | 406 | N: [redacted]<br>R: COVID-19 PNEUMONIA<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia | | S: SEVERE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: OXYGEN THERAPIES<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: COVID 19-INFECTION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 18 | 8 8 | N: [redacted]<br>R: PERSISTENT ULCERATIVE COLITIS ACTIVITY<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | O: Yes | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: DEHYDRATION WEIGHT LOSS 20X BM/D<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT MORE LIKELY DUE TO PROGRESSION OF PRE-EXISTING ULCERATIVE COLITIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:11[redacted].[redacted] kg | | | | | | | |
| [redacted] | C1-15OL | 1 to 688 | 688 | N: [redacted]<br>R: PERFORATION OF SIGMOID COLON<br>S: 胃腸障害<br>P: 大腸穿孔<br>L: Perforated colon | E: 688<br>L: 1 Day | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: SURGICAL INTERVENTION | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: ACUTE ANGLE OF SIGMOID COLON<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
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TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:11[redacted] [redacted]kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to | 783 783 | N: [redacted]<br>R: VENTRICULAR TACHYCARDIA<br>S: 心臓障害<br>P: 心室性頻脈<br>L: Ventricular tachycardia | E: 785<br>L: 3 Days<br>I: Yes | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/Yes/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: ANGINA AND PREMATURE VENTRICULAR CONTRACTIONS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted]([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:11[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to 985 | 985 | N: [redacted]<br>R: VENTRICULAR TACHYCARDIA<br>S: 心臓障害<br>P: 心室性頻脈<br>L: Ventricular tachycardia | E: 989<br>L: 5 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/Yes/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: ANGINA AND PREMATURE VENTRICULAR CONTRACTIONS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:11[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to | 1089 | 1089 | N: [redacted]<br>R: VENTRICULAR TACHYCARDIA<br>S: 心臓障害<br>P: 心室性頻脈<br>L: Ventricular tachycardia | E: 1092<br>L: 4 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED<br>O: Concomitant medication or therapy started | AE: No/Yes/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: HISTORY OF VENTRICULAR TACHYCARDIA, HAD MEDICATION SWITCHED<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
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Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted] Age:2[redacted] Sex:Female Race:BLACK OR AFRICAN AMERICAN Weight:4[redacted].[redacted] kg | | | | | | | | |
| [redacted] | C1-15OL | 1 to 77 | 1 | 1 /-77 | V: [redacted]<br>N: 17093002002<br>R: PULMONARY EMBOLUS<br>S: 呼吸器、胸郭および縦隔障害<br>P: 肺塞栓症<br>L: Pulmonary embolus | E: 7<br>L: 7 Days | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/Possibly/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: WORSENING OF ULCERATIVE COLITIS |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:9[redacted] kg | | | | | | | |
| | C2-3 0DB | 1 to 239 | 168 168 | N: [redacted]<br>R: CERVICAL SPINE CORD COMPRESSION<br>S: 神経系障害<br>P: 頚髄圧迫<br>L: Cervical cord compression | E: 240<br>L: 73 Days | S: MODERATE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | | |
| [redacted]# | Age:6[redacted] | Sex:Male | Race:ASIAN | Weight:9[redacted].[redacted] kg | | | | |
| (Cont.) | C2-3 0DB | 1 to 239 | 168 | 168 | N: [redacted]<br>R: MYELOPATHY<br>S: 神経系障害<br>P: 脊髄症<br>L: Myelopathy | E: 240<br>L: 73 Days | S: MODERATE<br>R: REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:2[redacted] Sex:Female Race:ASIAN Weight:9[redacted].[redacted] kg | | | | | | | |
| | C1-3 0OL | 45 to 447 | 368 /412 /368 | N: [redacted]<br>R: SPONTANEOUS ABORTION<br>S: 妊娠、産褥および周産期の状態<br>P: 自然流産<br>L: Spontaneous abortion | O: Yes<br>I: Yes | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No/No<br>S: Yes, important medical or surgical intervention<br>O: UNKNOWN AT THIS TIME, NOT BELIEVED TO BE STUDY RELATED.<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | | |
| | C1-15OL | 1 to 338 | 29 | 29 | N: [redacted]<br>R: ACUTE LACUNAR INFARCT RIGHT THALAMUS<br>S: 神経系障害<br>P: ラクナ梗塞<br>L: Lacunar infarction | E: 31<br>L: 3 Days<br>I: Yes | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: Concomitant medication or therapy started | AE: No/No/Yes/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: INVESTIGATIONS ONGOING<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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# Subject prematurely discontinued. & Date is estimated.

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TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 1026 | 1026 | N: [redacted]<br>R: LOWER LIMBS VARICOSE VEINS<br>S: 血管障害<br>P: 静脈瘤<br>L: Varicose veins of lower extremities | E: 1120<br>L: 95 Days | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: SURGERY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: LOWER LIMBS INSUFFICIENCY<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted]([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | | |
| | C1-15OL | 1 to 1273 | 310 | 310 | N: [redacted]<br>R: WORSENING OF MIGRAINE HEADACHES<br>S: 神経系障害<br>P: 片頭痛<br>L: Migraine aggravated | E: 311<br>L: 2 Days | S: SEVERE<br>R: REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY<br>E: RISK FACTORS INCLUDE PRE-EXISTING MIGRAINE HEADACHE, FIBROMYALGIA AND OBESITY. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to 1273 1181 1181 | | N: [redacted]<br>R: OPIOD OVERDOSE<br>S: 傷害、中毒および処置合併症<br>P: 過量投与<br>L: Drug overdose | E: 1181<br>L: 1 Day | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, important medical or surgical intervention<br>O: DRUG OVERDOSE<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 1273 | 1187 | 1187 | N: [redacted]<br>R: ANOXIC BRAIN INJURY<br>S: 神経系障害<br>P: 脳損傷<br>L: Anoxic brain damage | E: 1187<br>L: 1 Day | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No/No<br>S: Yes, death of subject, hospitalization or prolonged hospitalization<br>O: ACUTE RESPIRATORY FAILURE WITH HYPOXIA<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted]# Age:2[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg | | | | | | | |
| | C2-3 0DB | 1 to 50 | 19 19 | N: [redacted]<br>R: ACUTE APPENDICITIS<br>S: 感染症および寄生虫症<br>P: 虫垂炎<br>L: Acute appendicitis | E: 33<br>L: 15 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: IN GENERAL,APPENDICITIS IS AN EVENT,WHICH REQUIRES HOSPITALIZATION.<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg | | | | | | | |
| | C2-3 0DB | 1 to 172 | 10 | 10 | N: [redacted]<br>R: PULMONARY EMBOLISM<br>S: 呼吸器、胸郭および縦隔障害<br>P: 肺塞栓症<br>L: Pulmonary embolism | E: 13<br>L: 4 Days | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/Yes<br>S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Day | Rx Day of Onset /Dose Escal-ation | | | |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 828 | 25 | 25 /-804 | N: [redacted]<br>R: OBSTRUCTIVE DISTAL LEFT URETER STONE, URETERIC OBSTRUCTION, URETEROLITHIASIS<br>S: 腎および尿路障害<br>P: 尿管閉塞<br>L: Ureteric obstruction | E: 36<br>L: 12 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: SUBJECT HAD STENT PLACED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: UNRELATED DISORDER<br>A: NO REASONABLE POSSIBILITY<br>E: WEAK TEMPORAL ASSOCIATION. KIDNEY STONE FORMATION IS UNLIKELY WITH LESS THAN 3 MONTHS OF STUDY DRUG EXPOSURE (INCLUDING PRIOR CLINICAL TRIAL). ADDITIONALLY, RENAL STONE DISEASE IS A RELATIVELY COMMON, PROBLEM WITH AN ESTIMATED 19 PERCENT OF MEN AND 9 PERCENT OF WOMEN WILL BE DIAGNOSED WITH A KIDNEY STONE BY THE AGE OF 70 YEARS. (CURHAN G. RISK FACTORS FOR CALCIUM STONES IN ADULTS. IN: UPTODATE, POS, T TW(ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted]20[redacted].)) |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted]([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 828 | 25 | 25 /-804 | N: [redacted]<br>R: OBSTRUCTIVE DISTAL LEFT URETER STONE, URETERIC OBSTRUCTION, URETEROLITHIASIS<br>S: 腎および尿路障害<br>P: 尿管結石症<br>L: Ureterolithiasis | E: 36<br>L: 12 Days | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: SUBJECT HAD STENT PLACED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: UNRELATED DISORDER<br>A: NO REASONABLE POSSIBILITY<br>E: WEAK TEMPORAL ASSOCIATION. KIDNEY STONE FORMATION IS UNLIKELY WITH LESS THAN 3 MONTHS OF STUDY DRUG EXPOSURE (INCLUDING PRIOR CLINICAL TRIAL). ADDITIONALLY, RENAL STONE DISEASE IS A RELATIVELY COMMON, PROBLEM WITH AN ESTIMATED 19 PERCENT OF MEN AND 9 PERCENT OF WOMEN WILL BE DIAGNOSED WITH A KIDNEY STONE BY THE AGE OF 70 YEARS. (CURHAN G. RISK FACTORS FOR CALCIUM STONES IN ADULTS. IN: UPTODATE, POS, T TW(ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted]20[redacted].)) |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD<br>[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 828 | 803 | 803 /-26 | N: [redacted]<br>R: ACUTE FLARE OF ULCERATIVE COLITIS<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | E: 833<br>L: 31 Days | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: COEXISTENT MEDICAL PROBLEM: KIDNEY STONES, BACK PAIN<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 225 | 225 | N: [redacted]<br>R: CERVIX CONISATION AFTER PREBIOPSIAN SUSPECT<br>S: 生殖系および乳房障害<br>P: 子宮頚部障害<br>L: Cervix disorder | E: 227<br>L: 3 Days | S: MILD<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: CERVIX CONISATION PERFORMED. | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: DUE TO SCREENING PROCEDURE, NO SYMPTOMS, PAITIENT INDICATED TO CONISATION OF CERVIX OF UTERUS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 167 | 167 | N: [redacted]<br>R: HEADACHE<br>S: 神経系障害<br>P: 頭痛<br>L: Headache | E: 169<br>L: 3 Days<br>I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: SHE HAS A HISTORY OF SEVERE HEADACHE WITH VOMITING. IN ADDITION, TIME HAS PASSED SINCE THE START OF THE INVESTIGATIONAL AGENT. SO I THINK THAT THE SYMPTOMS ARE NOT DUE TO INVESTIGATIONAL AGENT.<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF MIGRAINE HEADACHE. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 M | | | | | | | |
| [redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to 838 | 838 | N: [redacted]<br>R: HERPES ZOSTER<br>S: 感染症および寄生虫症<br>P: 帯状疱疹<br>L: Herpes zoster | E: 851<br>L: 14 Days<br>I: Yes | S: MODERATE<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/Yes/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

| Subject Number | Epoch Name | Interval | Rx Day of Onset /Dose Escal-ation | | | |
|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted]) | | | | | | |
| TRT: COHORT 1 - UPA 15 MG QD | | | | | | |
| [redacted]# Age:2[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg | | | | | | |
| | C1-15OL | 1 to 357 | 321 | 321 | N: [redacted]<br>R: ABDOMINAL PAIN<br>S: 胃腸障害<br>P: 腹痛<br>L: Abdominal pain | E: 334<br>L: 14 Days | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: MEDICAL HISTORY OF PRIMARY SCLEROSING CHDANGITIS AND GALLBLADDER ENLARGEMENT WAS FOUND.<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS AND PRIMARY SCLEROSING CHOLANGITIS. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted] kg | | | | | | | |
| | C1-3 0OL | 160 to 50 | 209 /50 | N: [redacted]<br>R: EXACERBATION OF ULCERATIVE COLITIS<br>S: 胃腸障害<br>P: 潰瘍性大腸炎<br>L: Colitis ulcerative aggravated | E: 211<br>L: 3 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: LACK OF EFFECTIVENESS OF THE STUDY DRUG<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | | |
| [redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg | | | | | | | | |
| | C1-15OL | 1 to 203 | 104 | 104 /-100 | N: [redacted]<br>R: FOLLICULAR ADENOMA OF THE LEFT LOBE OF THE THYROID GLAND<br>S: 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)<br>P: 甲状腺腺腫<br>L: Thyroid adenoma | E: 105<br>L: 2 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: LEFT HEMITHYROIDECTOMY PERFORMED [redacted]20[redacted] | AE: Yes/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: DIFFUSE NODULAR GOITER<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | |
| [redacted] Age:4[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | |
| | C2-3 0DB | 1 to 43 | 43 | N: [redacted]<br>R: COVID-19 PNEUMONIA<br>S: 感染症および寄生虫症<br>P: COVID-19肺炎<br>L: COVID-19 pneumonia | E: 53<br>L: 11 Days | S: MODERATE<br>C: Yes<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: COVID-19 INFECTION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 39 | 39 | N: [redacted]<br>R: PNEUMONIA<br>S: 感染症および寄生虫症<br>P: 肺炎<br>L: Pneumonia | E: 48<br>L: 10 Days | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: PNEUMONIA<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

INV: [redacted] ([redacted])
TRT: COHORT 1 - UPA 15 MG QD

[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| (Cont.) | C1-15OL | 1 to 76 | 76 | N: [redacted]<br>R: ENLARGEMENT OF PULMONARY NODULE IN RIGHT LUNG FROM 3 TO 4 MM<br>S: 呼吸器、胸郭および縦隔障害<br>P: 肺腫瘤<br>L: Lung nodule | O: Yes | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: BRONCHOSCOPY WITH BIOPSY | AE: No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: UNKNOWN<br>A: NO REASONABLE POSSIBILITY<br>E: EVENT IS MORE LIKELY RELATED TO PRIOR PNEUMONIA. |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg | | | | | | | | |
| | C1-15OL | 1 to 719 | 658 | 658 | N: [redacted]<br>R: MALIGNANT TESTICULAR TUMOR (LEFT SIDED)<br>S: 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)<br>P: 精巣癌<br>L: Malignant neoplasm of testis | O: Yes | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG WITHDRAWN<br>O: DISCONTINUED STUDY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: UNKNOWN<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg | | | | | | | |
| [redacted] | C1-15OL | 1 to 483 | 483 | N: [redacted]<br>R: LUMBAGO<br>S: 筋骨格系および結合組織障害<br>P: 背部痛<br>L: Lumbago | I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: EXERCISE<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity<br>O: MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 671 | 671 | | N: [redacted]<br>R: LUMBAR SPINAL CANAL STENOSIS<br>S: 筋骨格系および結合組織障害<br>P: 腰部脊柱管狭窄症<br>L: Lumbar spinal stenosis | I: Yes | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: SURGICAL OPERATION | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION.<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to | 788 | 788 | N: [redacted]<br>R: EXACERBATION OF LUMBAR DISC HERNIATION<br>S: 筋骨格系および結合組織障害<br>P: 椎間板突出<br>L: Lumbar disc herniation | I: Yes | S: MODERATE<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: SURGICAL OPERATION | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention<br>O: MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION.<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 30 MG QD | | | | | | | | |
| [redacted] Age:3[redacted] Sex:Male Race:ASIAN Weight:9[redacted].[redacted] kg | | | | | | | | |
| | C2-3 0DB | 1 to | 81 | 81 | N: [redacted]<br>R: CHOLECYSTITIS<br>S: 肝胆道系障害<br>P: 胆嚢炎<br>L: Cholecystitis | E: 90<br>L: 10 Days<br>I: Yes | S: SEVERE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: UC NASH<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | |
| [redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted] kg | | | | | | | |
| | C1-15OL | 1 to 647 | 647 | N: [redacted]<br>R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA<br>S: 傷害、中毒および処置合併症<br>P: 挫傷<br>L: Contusion | E: 649<br>L: 3 Days | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: TRAFFIC ACCIDENT<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD | | | | | | | | |
| [redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to | 647 | 647 | N: [redacted]<br>R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA<br>S: 傷害、中毒および処置合併症<br>P: 挫傷<br>L: Contusion of knee | E: 649<br>L: 3 Days | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: TRAFFIC ACCIDENT<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C1-15OL | 1 to 647 | 647 | N: [redacted]<br>R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA<br>S: 筋骨格系および結合組織障害<br>P: 椎間板障害<br>L: Intervertebral disc disorder | E: 649<br>L: 3 Days | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: TRAFFIC ACCIDENT<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD<br>[redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted] kg | | | | | | | | |
| (Cont.) | C1-15OL | 1 to 647 | 647 | | N: [redacted]<br>R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA<br>S: 筋骨格系および結合組織障害<br>P: 脊柱変形<br>L: Spinal deformity | E: 649<br>L: 3 Days | S: MILD<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: TRAFFIC ACCIDENT<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escal-ation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted]([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | | |
| [redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg | | | | | | | | |
| | C2-1 5DB | 1 to | 212 212 | | N: [redacted]<br>R: ENDOMETRIOSIS<br>S: 生殖系および乳房障害<br>P: 子宮内膜症<br>L: Endometriosis | E: 215<br>L: 4 Days | S: MODERATE<br>C: No<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>O: OVARIAN CYSTS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Day | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 1 QD | | | | | | | | |
| [redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg | | | | | | | | |
| | C1-15OL | 1 to | 871 | 871 | N: [redacted]<br>R: HERPES ZOSTER<br>S: 感染症および寄生虫症<br>P: 帯状疱疹<br>L: Herpes zoster | O: Yes<br>I: Yes | S: SEVERE<br>C: No<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: OCULAR SURGERY<br>O: Concomitant medication or therapy started | AE: No/No/No/No/Yes/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted]([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | |
| | C2-1 5DB | 1 to 591 | 66 66 | N: [redacted]<br>R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION<br>S: 精神障害<br>P: 不安<br>L: Anxiety aggravated | E: 73<br>L: 8 Days<br>I: Yes | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C2-15DB | 1 to 591 | 66 66 | N: [redacted]<br>R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION<br>S: 精神障害<br>P: うつ病<br>L: Depression aggravated | E: 73<br>L: 8 Days<br>I: Yes | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | |
| (Cont.) | C2-15DB | 1 to 591 | 66 66 | N: [redacted]<br>R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION<br>S: 傷害、中毒および処置合併症<br>P: 企図的過量投与<br>L: Intentional overdose | E: 73<br>L: 8 Days<br>I: Yes | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Name | Epoch | Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 2 - UPA 15 MG QD | | | | | | | | |
| [redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg | | | | | | | | |
| (Cont.) | C2-1 5DB | 1 to 591 | 66 | 66 | N: [redacted]<br>R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION<br>S: 精神障害<br>P: 自殺念慮<br>L: Active suicidal ideation | E: 73<br>L: 8 Days<br>I: Yes | S: SEVERE<br>R: NO REASONABLE POSSIBILITY<br>A: DOSE NOT CHANGED<br>O: NONE | AE: No/No/No/No/No/No<br>S: Yes, life threatening, hospitalization or prolonged hospitalization<br>O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

| Subject Number | Epoch Name | Epoch Interval | Rx Day of Onset /Dose Escalation | V: AE Serial Number in Previous Study<br>N: AE Serial Number<br>R: Reported Term<br>S: System Organ Class<br>P: MedDRA 23.0 Preferred Term<br>L: Lower Level Term | E: Rx Day Ended<br>O: Ongoing at the End of Study?<br>L: Length<br>I: Interm-ittent? | S: Severity<br>C: AE Related to COVID-19 Infection<br>R: Relationship to Study Treatment<br>A: Action Taken with Study Treatment<br>O: Other Actions Taken | AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?<br>S: Serious AE?<br>O: Other Cause of Event<br>A: AbbVie Opinion of Causality<br>E: Sponsor Alternate Etiology |
|---|---|---|---|---|---|---|---|
| INV: [redacted] ([redacted])<br>TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD | | | | | | | |
| [redacted]# Age:2[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted].[redacted] kg | | | | | | | |
| | C1-3 0OL | 770 to 933 | 47 816 /47 | N: [redacted]<br>R: SEPSIS DUE TO UNSPECIFIED ORGANISM<br>S: 感染症および寄生虫症<br>P: 敗血症<br>L: Sepsis | E: 820<br>L: 5 Days | S: MODERATE<br>R: REASONABLE POSSIBILITY<br>A: DRUG INTERRUPTED<br>O: Concomitant medication or therapy started | AE: No/No/No/No/No/No<br>S: Yes, hospitalization or prolonged hospitalization<br>A: NO REASONABLE POSSIBILITY |

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

表 2.7.4.7-112.

[redacted]20[redacted]08:55 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted]
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 5 (25.4) | 8 (93.9) | 6 (7.6) |
| 心臓障害 | 0 | 0 | 0 |
| 完全房室ブロック | 0 | 0 | 0 |
| 胃腸障害 | 2 (10.2) | 4 (46.9) | 2 (2.5) |
| 腹痛 | 0 | 0 | 1 (1.3) |
| 潰瘍性大腸炎 | 2 (10.2) | 0 | 1 (1.3) |
| 胃食道逆流性疾患 | 0 | 0 | 0 |
| 大腸ポリープ | 0 | 4 (46.9) | 0 |
| 膵炎 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=16)<br>(PYs=2.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=41)<br>(PYs=82.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=49)<br>(PYs=110.9)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=54)<br>(PYs=100.9)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=193)<br>(PYs=355.3)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 4 (163.2) | 11 (13.3) | 9 (8.1) | 13 (12.9) | 45 (12.7) |
| 心臓障害 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 完全房室ブロック | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 胃腸障害 | 2 (81.6) | 3 (3.6) | 0 | 3 (3.0) | 11 (3.1) |
| 腹痛 | 0 | 0 | 0 | 0 | 1 (0.3) |
| 潰瘍性大腸炎 | 2 (81.6) | 2 (2.4) | 0 | 1 (1.0) | 4 (1.1) |
| 胃食道逆流性疾患 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 大腸ポリープ | 0 | 0 | 0 | 0 | 4 (1.1) |
| 膵炎 | 0 | 1 (1.2) | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 埋伏歯 | 0 | 0 | 0 |
| 一般・全身障害および投与部位の状態 | 0 | 0 | 0 |
| 胸痛 | 0 | 0 | 0 |
| 発熱 | 0 | 0 | 0 |
| 肝胆道系障害 | 0 | 0 | 0 |
| 胆嚢炎 | 0 | 0 | 0 |
| 感染症および寄生虫症 | 0 | 2 (23.5) | 1 (1.3) |
| 虫垂炎 | 0 | 0 | 0 |
| 細菌性関節炎 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=16)<br>(PYs=2.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=41)<br>(PYs=82.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=49)<br>(PYs=110.9)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=54)<br>(PYs=100.9)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=193)<br>(PYs=355.3)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 胃腸障害 (Cont.) | | | | | |
| 埋伏歯 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 一般・全身障害および投与部位の状態 | 1 (40.8) | 0 | 0 | 1 (1.0) | 2 (0.6) |
| 胸痛 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 発熱 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 肝胆道系障害 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 胆嚢炎 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 感染症および寄生虫症 | 1 (40.8) | 3 (3.6) | 4 (3.6) | 6 (5.9) | 14 (3.9) |
| 虫垂炎 | 0 | 0 | 1 (0.9) | 1 (1.0) | 2 (0.6) |
| 細菌性関節炎 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| COVID-19 | 0 | 0 | 0 |
| サイトメガロウイルス感染 | 0 | 0 | 0 |
| 帯状疱疹 | 0 | 1 (11.7) | 1 (1.3) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 |
| 大腸感染 | 0 | 0 | 0 |
| ニューモシスチス・イロベチイ肺炎 | 0 | 0 | 0 |
| 肺炎 | 0 | 0 | 0 |
| 腎盂腎炎 | 0 | 1 (11.7) | 0 |
| ウイルス感染 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs) | UPA 45 mg/ PBO (N=41) (PYs=82.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs) | Any UPA (N=193) (PYs=355.3) Events (E/100 PYs) |
| 感染症および寄生虫症 (Cont.) | | | | | |
| COVID-19 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| サイトメガロウイルス感染 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 帯状疱疹 | 0 | 1 (1.2) | 0 | 2 (2.0) | 4 (1.1) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 大腸感染 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| ニューモシスチス・イロベチイ肺炎 | 0 | 1 (1.2) | 0 | 0 | 0 |
| 肺炎 | 0 | 1 (1.2) | 0 | 1 (1.0) | 1 (0.3) |
| 腎盂腎炎 | 0 | 0 | 0 | 0 | 1 (0.3) |
| ウイルス感染 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 傷害、中毒および処置合併症 | 0 | 0 | 0 |
| 肺挫傷 | 0 | 0 | 0 |
| 胸椎骨折 | 0 | 0 | 0 |
| 代謝および栄養障害 | 1 (5.1) | 0 | 0 |
| 低アルブミン血症 | 1 (5.1) | 0 | 0 |
| 栄養障害 | 0 | 0 | 0 |
| 筋骨格系および結合組織障害 | 0 | 0 | 1 (1.3) |
| 背部痛 | 0 | 0 | 0 |
| 椎間板突出 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs) | UPA 45 mg/ PBO (N=41) (PYs=82.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs) | Any UPA (N=193) (PYs=355.3) Events (E/100 PYs) |
| 傷害、中毒および処置合併症 | 0 | 0 | 2 (1.8) | 0 | 2 (0.6) |
| 肺挫傷 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 胸椎骨折 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 代謝および栄養障害 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 低アルブミン血症 | 0 | 0 | 0 | 0 | 0 |
| 栄養障害 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 筋骨格系および結合組織障害 | 0 | 3 (3.6) | 0 | 0 | 4 (1.1) |
| 背部痛 | 0 | 1 (1.2) | 0 | 0 | 1 (0.3) |
| 椎間板突出 | 0 | 1 (1.2) | 0 | 0 | 1 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | |
| 腰部脊柱管狭窄症 | 0 | 0 | 0 |
| 骨壊死 | 0 | 0 | 1 (1.3) |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 0 | 0 | 0 |
| 結腸腺癌 | 0 | 0 | 0 |
| 肛門性器疣贅 | 0 | 0 | 0 |
| 神経系障害 | 1 (5.1) | 0 | 1 (1.3) |
| 手根管症候群 | 1 (5.1) | 0 | 0 |
| 大脳障害 | 0 | 0 | 0 |
| 頭痛 | 0 | 0 | 1 (1.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=16)<br>(PYs=2.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=41)<br>(PYs=82.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=49)<br>(PYs=110.9)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=54)<br>(PYs=100.9)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=193)<br>(PYs=355.3)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | | | |
| 腰部脊柱管狭窄症 | 0 | 1 (1.2) | 0 | 0 | 1 (0.3) |
| 骨壊死 | 0 | 0 | 0 | 0 | 1 (0.3) |
| 良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む) | 0 | 1 (1.2) | 0 | 1 (1.0) | 2 (0.6) |
| 結腸腺癌 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 肛門性器疣贅 | 0 | 1 (1.2) | 0 | 0 | 1 (0.3) |
| 神経系障害 | 0 | 1 (1.2) | 0 | 1 (1.0) | 3 (0.8) |
| 手根管症候群 | 0 | 0 | 0 | 0 | 0 |
| 大脳障害 | 0 | 1 (1.2) | 0 | 0 | 1 (0.3) |
| 頭痛 | 0 | 0 | 0 | 0 | 1 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| くも膜下出血 | 0 | 0 | 0 |
| 腎および尿路障害 | 0 | 2 (23.5) | 1 (1.3) |
| 腎結石症 | 0 | 2 (23.5) | 0 |
| 尿管結石症 | 0 | 0 | 1 (1.3) |
| 皮膚および皮下組織障害 | 1 (5.1) | 0 | 0 |
| 脂肪織炎 | 0 | 0 | 0 |
| 壊疽性膿皮症 | 1 (5.1) | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=16)<br>(PYs=2.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=41)<br>(PYs=82.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=49)<br>(PYs=110.9)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=54)<br>(PYs=100.9)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=193)<br>(PYs=355.3)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 神経系障害 (Cont.) | | | | | |
| くも膜下出血 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 腎および尿路障害 | 0 | 0 | 0 | 0 | 3 (0.8) |
| 腎結石症 | 0 | 0 | 0 | 0 | 2 (0.6) |
| 尿管結石症 | 0 | 0 | 0 | 0 | 1 (0.3) |
| 皮膚および皮下組織障害 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 脂肪織炎 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 壊疽性膿皮症 | 0 | 0 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-113.

[redacted]20[redacted] 09:30 [redacted]



TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 43 (32.7) | 6 (4.8) | 61 (8.7) |
| 血液およびリンパ系障害 | 0 | 0 | 0 |
| リンパ球減少症 | 0 | 0 | 0 |
| 小球性貧血 | 0 | 0 | 0 |
| 心臓障害 | 0 | 0 | 0 |
| 急性心筋梗塞 | 0 | 0 | 0 |
| 耳および迷路障害 | 0 | 0 | 0 |
| 耳鳴 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| Any adverse event | 34 (141.2) | 28 (5.9) | 32 (5.1) | 43 (7.3) | 183 (7.8) |
| 血液およびリンパ系障害 | 1 (4.2) | 0 | 2 (0.3) | 1 (0.2) | 4 (0.2) |
| リンパ球減少症 | 1 (4.2) | 0 | 1 (0.2) | 1 (0.2) | 3 (0.1) |
| 小球性貧血 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 心臓障害 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |
| 急性心筋梗塞 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |
| 耳および迷路障害 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 耳鳴 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 眼障害 | 0 | 0 | 1 (0.1) |
| 網膜静脈閉塞 | 0 | 0 | 0 |
| 霧視 | 0 | 0 | 0 |
| 視力障害 | 0 | 0 | 1 (0.1) |
| 胃腸障害 | 29 (22.1) | 1 (0.8) | 29 (4.1) |
| 腹部膨満 | 1 (0.8) | 0 | 0 |
| 腹痛 | 0 | 0 | 2 (0.3) |
| 上腹部痛 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 眼障害 | 1 (4.2) | 0 | 1 (0.2) | 0 | 3 (0.1) |
| 網膜静脈閉塞 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 霧視 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 視力障害 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 胃腸障害 | 14 (58.1) | 12 (2.5) | 11 (1.8) | 7 (1.2) | 65 (2.8) |
| 腹部膨満 | 0 | 0 | 0 | 0 | 0 |
| 腹痛 | 0 | 0 | 0 | 0 | 2 (<0.1) |
| 上腹部痛 | 0 | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 肛門潰瘍 | 0 | 0 | 0 |
| 大腸炎 | 2 (1.5) | 0 | 0 |
| 潰瘍性大腸炎 | 25 (19.0) | 1 (0.8) | 19 (2.7) |
| 結腸異形成 | 0 | 0 | 2 (0.3) |
| クローン病 | 0 | 0 | 1 (0.1) |
| イレウス | 0 | 0 | 0 |
| 腸閉塞 | 0 | 0 | 0 |
| 大腸穿孔 | 1 (0.8) | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 胃腸障害 (Cont.) | | | | | |
| 肛門潰瘍 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 大腸炎 | 0 | 0 | 0 | 0 | 0 |
| 潰瘍性大腸炎 | 12 (49.8) | 10 (2.1) | 8 (1.3) | 5 (0.8) | 48 (2.0) |
| 結腸異形成 | 0 | 0 | 1 (0.2) | 0 | 3 (0.1) |
| クローン病 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| イレウス | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 腸閉塞 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 大腸穿孔 | 0 | 1 (0.2) | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 胃腸障害 (Cont.) | | | |
| 大腸ポリープ | 0 | 0 | 1 (0.1) |
| 悪心 | 0 | 0 | 2 (0.3) |
| 膵炎 | 0 | 0 | 0 |
| 直腸異形成 | 0 | 0 | 0 |
| 直腸出血 | 0 | 0 | 1 (0.1) |
| 一般・全身障害および投与部位の状態 | 2 (1.5) | 0 | 3 (0.4) |
| 無力症 | 1 (0.8) | 0 | 0 |
| 悪寒 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| 胃腸障害 (Cont.) | | | | | |
| 大腸ポリープ | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 悪心 | 0 | 0 | 0 | 0 | 2 (<0.1) |
| 膵炎 | 0 | 1 (0.2) | 0 | 1 (0.2) | 1 (<0.1) |
| 直腸異形成 | 1 (4.2) | 0 | 1 (0.2) | 0 | 2 (<0.1) |
| 直腸出血 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 一般・全身障害および投与部位の状態 | 2 (8.3) | 1 (0.2) | 1 (0.2) | 0 | 6 (0.3) |
| 無力症 | 0 | 0 | 0 | 0 | 0 |
| 悪寒 | 0 | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 一般・全身障害および投与部位の状態 (Cont.) | | | |
| 異形成 | 0 | 0 | 1 (0.1) |
| 疲労 | 1 (0.8) | 0 | 0 |
| 発熱 | 0 | 0 | 1 (0.1) |
| 肝胆道系障害 | 0 | 0 | 1 (0.1) |
| 硬化性胆管炎 | 0 | 0 | 0 |
| 薬物性肝障害 | 0 | 0 | 0 |
| 肝機能異常 | 0 | 0 | 0 |
| 肝炎 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 一般・全身障害および投与部位の状態 (Cont.) | | | | | |
| 異形成 | 0 | 0 | 1 (0.2) | 0 | 2 (<0.1) |
| 疲労 | 0 | 0 | 0 | 0 | 0 |
| 発熱 | 2 (8.3) | 1 (0.2) | 0 | 0 | 3 (0.1) |
| 肝胆道系障害 | 0 | 0 | 0 | 3 (0.5) | 4 (0.2) |
| 硬化性胆管炎 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 薬物性肝障害 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 肝機能異常 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 肝炎 | 0 | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 | 3 (2.3) | 0 | 4 (0.6) |
| 腹部膿瘍 | 0 | 0 | 0 |
| 急性心内膜炎 | 0 | 0 | 0 |
| 虫垂炎 | 0 | 0 | 0 |
| 細菌性関節炎 | 0 | 0 | 0 |
| COVID-19 | 0 | 0 | 0 |
| COVID-19肺炎 | 0 | 0 | 0 |
| クロストリジウム・ディフィシレ感染 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| 感染症および寄生虫症 | 5 (20.8) | 4 (0.8) | 4 (0.6) | 10 (1.7) | 24 (1.0) |
| 腹部膿瘍 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |
| 急性心内膜炎 | 0 | 1 (0.2) | 0 | 0 | 0 |
| 虫垂炎 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 細菌性関節炎 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| COVID-19 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| COVID-19肺炎 | 0 | 0 | 1 (0.2) | 1 (0.2) | 2 (<0.1) |
| クロストリジウム・ディフィシレ感染 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 腸球菌感染 | 1 (0.8) | 0 | 0 |
| 大腸菌感染 | 1 (0.8) | 0 | 0 |
| 真菌性性器感染 | 0 | 0 | 0 |
| 帯状疱疹 | 0 | 0 | 2 (0.3) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 |
| 筋膿瘍 | 1 (0.8) | 0 | 0 |
| 肺炎 | 0 | 0 | 1 (0.1) |
| クリプトコッカス性肺炎 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| 感染症および寄生虫症 (Cont.) | | | | | |
| 腸球菌感染 | 0 | 0 | 0 | 0 | 0 |
| 大腸菌感染 | 0 | 0 | 0 | 0 | 0 |
| 真菌性性器感染 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 帯状疱疹 | 3 (12.5) | 0 | 1 (0.2) | 2 (0.3) | 8 (0.3) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 筋膿瘍 | 0 | 0 | 0 | 0 | 0 |
| 肺炎 | 0 | 1 (0.2) | 0 | 1 (0.2) | 2 (<0.1) |
| クリプトコッカス性肺炎 | 0 | 0 | 0 | 2 (0.3) | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | |
| 結核 | 0 | 0 | 1 (0.1) |
| ウイルス感染 | 0 | 0 | 0 |
| ウイルス性咽頭炎 | 0 | 0 | 0 |
| 傷害、中毒および処置合併症 | 1 (0.8) | 0 | 2 (0.3) |
| 消化管ストーマ壊死 | 1 (0.8) | 0 | 0 |
| 過量投与 | 0 | 0 | 0 |
| 処置による腸管穿孔 | 0 | 0 | 1 (0.1) |
| 子宮穿孔 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | | | |
| 結核 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| ウイルス感染 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| ウイルス性咽頭炎 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 傷害、中毒および処置合併症 | 1 (4.2) | 0 | 0 | 0 | 3 (0.1) |
| 消化管ストーマ壊死 | 0 | 0 | 0 | 0 | 0 |
| 過量投与 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 処置による腸管穿孔 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 子宮穿孔 | 0 | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 | 2 (1.5) | 0 | 7 (1.0) |
| アラニンアミノトランスフェラーゼ増加 | 0 | 0 | 2 (0.3) |
| アスパラギン酸アミノトランスフェラーゼ増加 | 0 | 0 | 2 (0.3) |
| 血中クレアチンホスホキナーゼ増加 | 0 | 0 | 0 |
| γ-グルタミルトランスフェラーゼ増加 | 0 | 0 | 1 (0.1) |
| ヘモグロビン減少 | 1 (0.8) | 0 | 0 |
| 肝酵素上昇 | 0 | 0 | 1 (0.1) |
| B型肝炎DNA測定陽性 | 1 (0.8) | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| 臨床検査 | 2 (8.3) | 0 | 3 (0.5) | 5 (0.8) | 17 (0.7) |
| アラニンアミノトランスフェラーゼ増加 | 0 | 0 | 0 | 1 (0.2) | 3 (0.1) |
| 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 | 2 (<0.1) |
| 血中クレアチンホスホキナーゼ増加 | 1 (4.2) | 0 | 1 (0.2) | 1 (0.2) | 3 (0.1) |
| γ-グルタミルトランスフェラーゼ増加 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| ヘモグロビン減少 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 肝酵素上昇 | 0 | 0 | 1 (0.2) | 0 | 2 (<0.1) |
| B型肝炎DNA測定陽性 | 0 | 0 | 0 | 1 (0.2) | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| リンパ球数減少 | 0 | 0 | 0 |
| 好中球数減少 | 0 | 0 | 0 |
| 白血球数減少 | 0 | 0 | 0 |
| 代謝および栄養障害 | 1 (0.8) | 0 | 0 |
| 高ナトリウム血症 | 0 | 0 | 0 |
| 低リン酸血症 | 1 (0.8) | 0 | 0 |
| 筋骨格系および結合組織障害 | 0 | 0 | 2 (0.3) |
| 関節痛 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
| 臨床検査 (Cont.) | | | | | |
| リンパ球数減少 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 好中球数減少 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 白血球数減少 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 代謝および栄養障害 | 0 | 0 | 0 | 2 (0.3) | 2 (<0.1) |
| 高ナトリウム血症 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 低リン酸血症 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 筋骨格系および結合組織障害 | 3 (12.5) | 0 | 1 (0.2) | 0 | 6 (0.3) |
| 関節痛 | 1 (4.2) | 0 | 0 | 0 | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 筋骨格系および結合組織障害 (Cont.) | | | |
| 関節炎 | 0 | 0 | 0 |
| 筋肉痛 | 0 | 0 | 1 (0.1) |
| 横紋筋融解症 | 0 | 0 | 0 |
| 弾発指 | 0 | 0 | 0 |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 0 | 2 (1.6) | 3 (0.4) |
| 結腸腺癌 | 0 | 1 (0.8) | 0 |
| 膵腺癌 | 0 | 0 | 1 (0.1) |
| 血管肉腫 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| 筋骨格系および結合組織障害 (Cont.) | | | | | |
| 関節炎 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 筋肉痛 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 横紋筋融解症 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 弾発指 | 1 (4.2) | 0 | 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) | 0 | 3 (0.6) | 2 (0.3) | 5 (0.8) | 14 (0.6) |
| 結腸腺癌 | 0 | 0 | 0 | 1 (0.2) | 2 (<0.1) |
| 膵腺癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 血管肉腫 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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)<br>(Cont.) | | | |
| 乳癌 | 0 | 0 | 1 (0.1) |
| 浸潤性乳癌 | 0 | 0 | 0 |
| 喉頭扁平上皮癌 | 0 | 1 (0.8) | 0 |
| 悪性黒色腫 | 0 | 0 | 1 (0.1) |
| 髄膜腫 | 0 | 0 | 0 |
| 前立腺癌 | 0 | 0 | 0 |
| 小細胞癌 | 0 | 0 | 0 |
| 子宮頚部扁平上皮癌 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 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）<br>(Cont.) | | | | | |
| 乳癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 浸潤性乳癌 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |
| 喉頭扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 悪性黒色腫 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 髄膜腫 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 前立腺癌 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 小細胞癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 子宮頚部扁平上皮癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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）<br>(Cont.) | | | |
| 精巣（純粋）セミノーマ | 0 | 0 | 0 |
| 精巣癌 | 0 | 0 | 0 |
| 神経系障害 | 2 (1.5) | 0 | 4 (0.6) |
| 健忘 | 0 | 0 | 1 (0.1) |
| 脳損傷 | 0 | 0 | 0 |
| 灼熱感 | 0 | 0 | 0 |
| 頚髄圧迫 | 0 | 0 | 0 |
| 頭痛 | 1 (0.8) | 0 | 2 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| 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.) | | | | | |
| 精巣（純粋）セミノーマ | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 精巣癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 神経系障害 | 1 (4.2) | 0 | 1 (0.2) | 3 (0.5) | 9 (0.4) |
| 健忘 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 脳損傷 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 灼熱感 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 頚髄圧迫 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 頭痛 | 0 | 0 | 0 | 0 | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| ラクナ梗塞 | 0 | 0 | 0 |
| 片頭痛 | 1 (0.8) | 0 | 0 |
| 脊髄症 | 0 | 0 | 0 |
| 発作様現象 | 0 | 0 | 1 (0.1) |
| 妊娠、産褥および周産期の状態 | 0 | 0 | 0 |
| 自然流産 | 0 | 0 | 0 |
| 精神障害 | 0 | 0 | 2 (0.3) |
| 抑うつ気分 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 神経系障害 (Cont.) | | | | | |
| ラクナ梗塞 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 片頭痛 | 0 | 0 | 0 | 0 | 0 |
| 脊髄症 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 発作様現象 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 妊娠、産褥および周産期の状態 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 自然流産 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 精神障害 | 0 | 0 | 0 | 0 | 2 (<0.1) |
| 抑うつ気分 | 0 | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 精神障害 (Cont.) | | | |
| 易刺激性 | 0 | 0 | 1 (0.1) |
| 腎および尿路障害 | 0 | 0 | 0 |
| 慢性腎臓病 | 0 | 0 | 0 |
| 腎機能障害 | 0 | 0 | 0 |
| 呼吸器、胸郭および縦隔障害 | 1 (0.8) | 0 | 1 (0.1) |
| 胞隔炎 | 0 | 0 | 0 |
| 間質性肺疾患 | 0 | 0 | 0 |
| 肺浸潤 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 精神障害 (Cont.) | | | | | |
| 易刺激性 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 腎および尿路障害 | 1 (4.2) | 0 | 1 (0.2) | 0 | 2 (<0.1) |
| 慢性腎臓病 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 腎機能障害 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 呼吸器、胸郭および縦隔障害 | 1 (4.2) | 1 (0.2) | 0 | 4 (0.7) | 6 (0.3) |
| 胞隔炎 | 1 (4.2) | 0 | 0 | 0 | 1 (<0.1) |
| 間質性肺疾患 | 0 | 1 (0.2) | 0 | 0 | 0 |
| 肺浸潤 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 呼吸器、胸郭および縦隔障害 (Cont.) | | | |
| 肺塞栓症 | 1 (0.8) | 0 | 1 (0.1) |
| 皮膚および皮下組織障害 | 1 (0.8) | 1 (0.8) | 0 |
| ざ瘡 | 0 | 0 | 0 |
| 紅斑 | 0 | 0 | 0 |
| 結節性紅斑 | 0 | 0 | 0 |
| 脂肪織炎 | 0 | 0 | 0 |
| そう痒症 | 1 (0.8) | 0 | 0 |
| 発疹 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 呼吸器、胸郭および縦隔障害 (Cont.) | | | | | |
| 肺塞栓症 | 0 | 0 | 0 | 3 (0.5) | 4 (0.2) |
| 皮膚および皮下組織障害 | 1 (4.2) | 4 (0.8) | 2 (0.3) | 1 (0.2) | 6 (0.3) |
| ざ瘡 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 紅斑 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 結節性紅斑 | 0 | 1 (0.2) | 0 | 0 | 0 |
| 脂肪織炎 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| そう痒症 | 0 | 1 (0.2) | 0 | 0 | 0 |
| 発疹 | 1 (4.2) | 1 (0.2) | 0 | 0 | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 皮膚および皮下組織障害 (Cont.) | | | |
| 斑状丘疹状皮疹 | 0 | 1 (0.8) | 0 |
| 脂漏性皮膚炎 | 0 | 0 | 0 |
| 外科および内科処置 | 0 | 0 | 1 (0.1) |
| 人工流産 | 0 | 0 | 1 (0.1) |
| 血管障害 | 1 (0.8) | 2 (1.6) | 1 (0.1) |
| 深部静脈血栓症 | 0 | 1 (0.8) | 1 (0.1) |
| 高血圧 | 0 | 0 | 0 |
| 骨盤静脈血栓症 | 1 (0.8) | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 皮膚および皮下組織障害 (Cont.) | | | | | |
| 斑状丘疹状皮疹 | 0 | 0 | 0 | 0 | 0 |
| 脂漏性皮膚炎 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 外科および内科処置 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 人工流産 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 血管障害 | 0 | 2 (0.4) | 1 (0.2) | 2 (0.3) | 6 (0.3) |
| 深部静脈血栓症 | 0 | 0 | 0 | 2 (0.3) | 4 (0.2) |
| 高血圧 | 0 | 1 (0.2) | 0 | 0 | 0 |
| 骨盤静脈血栓症 | 0 | 0 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 血管障害 (Cont.) | | | |
| 末梢静脈疾患 | 0 | 1 (0.8) | 0 |
| 静脈血栓症 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
| 血管障害 (Cont.) | | | | | |
| 末梢静脈疾患 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 静脈血栓症 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-114.

[redacted]20[redacted] 08:55 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 5 (25.4) | 1 (11.7) | 6 (7.6) |
| 眼障害 | 0 | 0 | 0 |
| 網膜静脈閉塞 | 0 | 0 | 0 |
| 胃腸障害 | 5 (25.4) | 0 | 2 (2.5) |
| 潰瘍性大腸炎 | 5 (25.4) | 0 | 2 (2.5) |
| 膵炎 | 0 | 0 | 0 |
| 一般・全身障害および投与部位の状態 | 0 | 0 | 0 |
| 発熱 | 0 | 0 | 0 |
| 肝胆道系障害 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs) | UPA 45 mg/ PBO (N=41) (PYs=82.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs) | Any UPA (N=193) (PYs=355.3) Events (E/100 PYs) |
| Any adverse event | 10 (408.1) | 5 (6.1) | 4 (3.6) | 10 (9.9) | 32 (9.0) |
| 眼障害 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 網膜静脈閉塞 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 胃腸障害 | 3 (122.4) | 3 (3.6) | 0 | 1 (1.0) | 6 (1.7) |
| 潰瘍性大腸炎 | 3 (122.4) | 2 (2.4) | 0 | 1 (1.0) | 6 (1.7) |
| 膵炎 | 0 | 1 (1.2) | 0 | 0 | 0 |
| 一般・全身障害および投与部位の状態 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 発熱 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 肝胆道系障害 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 肝胆道系障害 (Cont.) | | | |
| 肝機能異常 | 0 | 0 | 0 |
| 感染症および寄生虫症 | 0 | 0 | 2 (2.5) |
| 虫垂炎 | 0 | 0 | 0 |
| 細菌性関節炎 | 0 | 0 | 0 |
| 帯状疱疹 | 0 | 0 | 1 (1.3) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 |
| 肺炎 | 0 | 0 | 1 (1.3) |
| ウイルス感染 | 0 | 0 | 0 |
| 臨床検査 | 0 | 0 | 1 (1.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=16)<br>(PYs=2.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=41)<br>(PYs=82.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=49)<br>(PYs=110.9)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=54)<br>(PYs=100.9)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=193)<br>(PYs=355.3)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 肝胆道系障害 (Cont.) | | | | | |
| 肝機能異常 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 感染症および寄生虫症 | 3 (122.4) | 0 | 1 (0.9) | 5 (5.0) | 11 (3.1) |
| 虫垂炎 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 細菌性関節炎 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 帯状疱疹 | 2 (81.6) | 0 | 0 | 2 (2.0) | 5 (1.4) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 肺炎 | 0 | 0 | 0 | 1 (1.0) | 2 (0.6) |
| ウイルス感染 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 臨床検査 | 0 | 0 | 1 (0.9) | 2 (2.0) | 4 (1.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| 血中クレアチンホスホキナーゼ増加 | 0 | 0 | 0 |
| γ-グルタミルトランスフェラーゼ増加 | 0 | 0 | 1 (1.3) |
| リンパ球数減少 | 0 | 0 | 0 |
| 白血球数減少 | 0 | 0 | 0 |
| 筋骨格系および結合組織障害 | 0 | 0 | 0 |
| 関節炎 | 0 | 0 | 0 |
| 弾発指 | 0 | 0 | 0 |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 0 | 0 | 0 |
| 結腸腺癌 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=16)<br>(PYs=2.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=41)<br>(PYs=82.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=49)<br>(PYs=110.9)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=54)<br>(PYs=100.9)<br>Events<br>(E/100 PYs) | <br><br>Any UPA<br>(N=193)<br>(PYs=355.3)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 臨床検査 (Cont.) | | | | | |
| 血中クレアチンホスホキナーゼ増加 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| γ-グルタミルトランスフェラーゼ増加 | 0 | 0 | 0 | 0 | 1 (0.3) |
| リンパ球数減少 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 白血球数減少 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 筋骨格系および結合組織障害 | 2 (81.6) | 0 | 0 | 0 | 2 (0.6) |
| 関節炎 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 弾発指 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む) | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |
| 結腸腺癌 | 0 | 0 | 0 | 1 (1.0) | 1 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 | 0 | 0 | 1 (1.3) |
| 頭痛 | 0 | 0 | 1 (1.3) |
| 腎および尿路障害 | 0 | 0 | 0 |
| 慢性腎臓病 | 0 | 0 | 0 |
| 皮膚および皮下組織障害 | 0 | 0 | 0 |
| ざ瘡 | 0 | 0 | 0 |
| 脂肪織炎 | 0 | 0 | 0 |
| 血管障害 | 0 | 1 (11.7) | 0 |
| 深部静脈血栓症 | 0 | 1 (11.7) | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=16)<br>(PYs=2.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=41)<br>(PYs=82.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=49)<br>(PYs=110.9)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=54)<br>(PYs=100.9)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=193)<br>(PYs=355.3)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 神経系障害 | 0 | 0 | 0 | 0 | 1 (0.3) |
| 頭痛 | 0 | 0 | 0 | 0 | 1 (0.3) |
| 腎および尿路障害 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 慢性腎臓病 | 1 (40.8) | 0 | 0 | 0 | 1 (0.3) |
| 皮膚および皮下組織障害 | 0 | 1 (1.2) | 1 (0.9) | 0 | 2 (0.6) |
| ざ瘡 | 0 | 1 (1.2) | 0 | 0 | 1 (0.3) |
| 脂肪織炎 | 0 | 0 | 1 (0.9) | 0 | 1 (0.3) |
| 血管障害 | 0 | 1 (1.2) | 0 | 0 | 1 (0.3) |
| 深部静脈血栓症 | 0 | 0 | 0 | 0 | 1 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=56)<br>(PYs=19.7)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=3)<br>(PYs=8.5)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=30)<br>(PYs=78.6)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 血管障害 (Cont.) | | | |
| 静脈血栓症 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs) | UPA 45 mg/ PBO (N=41) (PYs=82.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs) | Any UPA (N=193) (PYs=355.3) Events (E/100 PYs) |
| 血管障害 (Cont.) | | | | | |
| 静脈血栓症 | 0 | 1 (1.2) | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

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表 2.7.4.7-115.

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TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=245) | UPA 15 mg QD (N=250) | UPA 30 mg QD (N=251) | UPA 15 mg QD (N=285) | UPA 30 mg QD (N=291) |
| Subgroup: 0 - < 3 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=53.4) Events (E/100PYs) [95% CI] | (PYs=59.1) Events (E/100PYs) [95% CI] | (PYs=60.7) Events (E/100PYs) [95% CI] | (PYs=70.6) Events (E/100PYs) [95% CI] | (PYs=70.1) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 3 (5.6) [1.2, 16.4] | 3 (5.1) [1.0, 14.8] | 1 (1.6) [0.0, 9.2] | 3 (4.3) [0.9, 12.4] | 2 (2.9) [0.3, 10.3] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 2 (3.7) [0.5, 13.5] | 2 (3.4) [0.4, 12.2] | 0 | 2 (2.8) [0.3, 10.2] | 0 |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 2 (3.4) [0.4, 12.2] | 4 (6.6) [1.8, 16.9] | 2 (2.8) [0.3, 10.2] | 4 (5.7) [1.6, 14.6] |
| Any adjudicated gastrointestinal perforations | 1 (1.9) [0.0, 10.4] | 1 (1.7) [0.0, 9.4] | 0 | 1 (1.4) [0.0, 7.9] | 0 |
| Any anemia | 10 (18.7) [9.0, 34.4] | 8 (13.5) [5.8, 26.7] | 6 (9.9) [3.6, 21.5] | 11 (15.6) [7.8, 27.9] | 9 (12.8) [5.9, 24.4] |
| Any neutropenia | 4 (7.5) [2.0, 19.2] | 7 (11.8) [4.8, 24.4] | 12 (19.8) [10.2, 34.5] | 7 (9.9) [4.0, 20.4] | 14 (20.0) [10.9, 33.5] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=245) | UPA 15 mg QD (N=250) | UPA 30 mg QD (N=251) | UPA 15 mg QD (N=285) | UPA 30 mg QD (N=291) |
| Subgroup: 0 - < 3 Month (Cont.) | | | | | |
| Any lymphopenia | 5 (9.4) [3.0, 21.8] | 5 (8.5) [2.7, 19.7] | 3 (4.9) [1.0, 14.4] | 5 (7.1) [2.3, 16.5] | 3 (4.3) [0.9, 12.5] |
| Any creatine phosphokinase (CPK) elevation | 2 (3.7) [0.5, 13.5] | 10 (16.9) [8.1, 31.1] | 10 (16.5) [7.9, 30.3] | 11 (15.6) [7.8, 27.9] | 11 (15.7) [7.8, 28.1] |
| Any hepatic disorder | 4 (7.5) [2.0, 19.2] | 13 (22.0) [11.7, 37.6] | 9 (14.8) [6.8, 28.2] | 14 (19.8) [10.8, 33.3] | 14 (20.0) [10.9, 33.5] |
| Any renal dysfunction | 1 (1.9) [0.0, 10.4] | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=168) | UPA 15 mg QD (N=221) | UPA 30 mg QD (N=232) | UPA 15 mg QD (N=279) | UPA 30 mg QD (N=267) |
| Subgroup: >= 3 - < 6 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=35.0) Events (E/100PYs) [95% CI] | (PYs=52.2) Events (E/100PYs) [95% CI] | (PYs=55.6) Events (E/100PYs) [95% CI] | (PYs=66.2) Events (E/100PYs) [95% CI] | (PYs=63.8) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 3 (8.6) [1.8, 25.0] | 4 (7.7) [2.1, 19.6] | 4 (7.2) [2.0, 18.4] | 4 (6.0) [1.6, 15.5] | 4 (6.3) [1.7, 16.0] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 1 (1.8) [0.0, 10.0] | 0 | 1 (1.6) [0.0, 8.7] |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 5 (9.6) [3.1, 22.3] | 4 (7.2) [2.0, 18.4] | 6 (9.1) [3.3, 19.7] | 5 (7.8) [2.5, 18.3] |
| Any adjudicated gastrointestinal perforations | 0 | 1 (1.9) [0.0, 10.7] | 1 (1.8) [0.0, 10.0] | 2 (3.0) [0.4, 10.9] | 1 (1.6) [0.0, 8.7] |
| Any anemia | 1 (2.9) [0.1, 15.9] | 1 (1.9) [0.0, 10.7] | 0 | 1 (1.5) [0.0, 8.4] | 1 (1.6) [0.0, 8.7] |
| Any neutropenia | 1 (2.9) [0.1, 15.9] | 3 (5.7) [1.2, 16.8] | 2 (3.6) [0.4, 13.0] | 4 (6.0) [1.6, 15.5] | 2 (3.1) [0.4, 11.3] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=168) | UPA 15 mg QD (N=221) | UPA 30 mg QD (N=232) | UPA 15 mg QD (N=279) | UPA 30 mg QD (N=267) |
| Subgroup: >= 3 - < 6 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 1 (1.9) [0.0, 10.7] | 2 (3.6) [0.4, 13.0] | 2 (3.0) [0.4, 10.9] | 2 (3.1) [0.4, 11.3] |
| Any creatine phosphokinase (CPK) elevation | 1 (2.9) [0.1, 15.9] | 1 (1.9) [0.0, 10.7] | 7 (12.6) [5.1, 26.0] | 1 (1.5) [0.0, 8.4] | 7 (11.0) [4.4, 22.6] |
| Any hepatic disorder | 0 | 5 (9.6) [3.1, 22.3] | 2 (3.6) [0.4, 13.0] | 5 (7.6) [2.5, 17.6] | 2 (3.1) [0.4, 11.3] |
| Any renal dysfunction | 0 | 0 | 1 (1.8) [0.0, 10.0] | 0 | 1 (1.6) [0.0, 8.7] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=119) | UPA 15 mg QD (N=196) | UPA 30 mg QD (N=216) | UPA 15 mg QD (N=253) | UPA 30 mg QD (N=249) |
| Subgroup: >= 6 - < 9 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=26.1) Events (E/100PYs) [95% CI] | (PYs=46.5) Events (E/100PYs) [95% CI] | (PYs=52.8) Events (E/100PYs) [95% CI] | (PYs=60.3) Events (E/100PYs) [95% CI] | (PYs=60.9) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 2 (7.7) [0.9, 27.7] | 2 (4.3) [0.5, 15.5] | 2 (3.8) [0.5, 13.7] | 3 (5.0) [1.0, 14.5] | 3 (4.9) [1.0, 14.4] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 1 (1.9) [0.0, 10.5] | 0 | 1 (1.6) [0.0, 9.1] |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 3 (6.5) [1.3, 18.9] | 4 (7.6) [2.1, 19.4] | 3 (5.0) [1.0, 14.5] | 5 (8.2) [2.7, 19.2] |
| Any adjudicated gastrointestinal perforations | 0 | 0 | 1 (1.9) [0.0, 10.5] | 0 | 1 (1.6) [0.0, 9.1] |
| Any anemia | 7 (26.8) [10.8, 55.2] | 3 (6.5) [1.3, 18.9] | 1 (1.9) [0.0, 10.5] | 4 (6.6) [1.8, 17.0] | 2 (3.3) [0.4, 11.9] |
| Any neutropenia | 2 (7.7) [0.9, 27.7] | 2 (4.3) [0.5, 15.5] | 3 (5.7) [1.2, 16.6] | 2 (3.3) [0.4, 12.0] | 3 (4.9) [1.0, 14.4] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=119) | UPA 15 mg QD (N=196) | UPA 30 mg QD (N=216) | UPA 15 mg QD (N=253) | UPA 30 mg QD (N=249) |
| Subgroup: >= 6 - < 9 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 3 (6.5) [1.3, 18.9] | 1 (1.9) [0.0, 10.5] | 3 (5.0) [1.0, 14.5] | 1 (1.6) [0.0, 9.1] |
| Any creatine phosphokinase (CPK) elevation | 2 (7.7) [0.9, 27.7] | 4 (8.6) [2.3, 22.0] | 3 (5.7) [1.2, 16.6] | 6 (9.9) [3.7, 21.7] | 5 (8.2) [2.7, 19.2] |
| Any hepatic disorder | 3 (11.5) [2.4, 33.6] | 11 (23.7) [11.8, 42.3] | 4 (7.6) [2.1, 19.4] | 12 (19.9) [10.3, 34.8] | 4 (6.6) [1.8, 16.8] |
| Any renal dysfunction | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=89) | UPA 15 mg QD (N=178) | UPA 30 mg QD (N=206) | UPA 15 mg QD (N=232) | UPA 30 mg QD (N=237) |
| Subgroup: >= 9 - < 12 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=19.9) Events (E/100PYs) [95% CI] | (PYs=40.8) Events (E/100PYs) [95% CI] | (PYs=47.8) Events (E/100PYs) [95% CI] | (PYs=55.6) Events (E/100PYs) [95% CI] | (PYs=56.1) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 0 | 1 (2.5) [0.1, 13.7] | 0 | 1 (1.8) [0.0, 10.0] | 0 |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 0 | 0 | 0 |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 2 (4.9) [0.6, 17.7] | 3 (6.3) [1.3, 18.4] | 3 (5.4) [1.1, 15.8] | 4 (7.1) [1.9, 18.3] |
| Any adjudicated gastrointestinal perforations | 0 | 0 | 1 (2.1) [0.1, 11.7] | 0 | 1 (1.8) [0.0, 9.9] |
| Any anemia | 1 (5.0) [0.1, 28.1] | 0 | 3 (6.3) [1.3, 18.4] | 0 | 3 (5.3) [1.1, 15.6] |
| Any neutropenia | 0 | 0 | 2 (4.2) [0.5, 15.1] | 0 | 2 (3.6) [0.4, 12.9] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=89) | UPA 15 mg QD (N=178) | UPA 30 mg QD (N=206) | UPA 15 mg QD (N=232) | UPA 30 mg QD (N=237) |
| Subgroup: >= 9 - < 12 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 0 | 1 (2.1) [0.1, 11.7] | 1 (1.8) [0.0, 10.0] | 2 (3.6) [0.4, 12.9] |
| Any creatine phosphokinase (CPK) elevation | 0 | 1 (2.5) [0.1, 13.7] | 2 (4.2) [0.5, 15.1] | 2 (3.6) [0.4, 13.0] | 4 (7.1) [1.9, 18.3] |
| Any hepatic disorder | 1 (5.0) [0.1, 28.1] | 5 (12.3) [4.0, 28.6] | 5 (10.5) [3.4, 24.4] | 5 (9.0) [2.9, 21.0] | 6 (10.7) [3.9, 23.3] |
| Any renal dysfunction | 0 | 1 (2.5) [0.1, 13.7] | 0 | 1 (1.8) [0.0, 10.0] | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=30) | UPA 15 mg QD (N=65) | UPA 30 mg QD (N=82) | UPA 15 mg QD (N=178) | UPA 30 mg QD (N=212) |
| Subgroup: >= 12 - < 15 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=0.5) Events (E/100PYs) [95% CI] | (PYs=0.8) Events (E/100PYs) [95% CI] | (PYs=1.7) Events (E/100PYs) [95% CI] | (PYs=36.1) Events (E/100PYs) [95% CI] | (PYs=48.2) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 0 | 0 | 0 | 2 (5.5) [0.7, 20.0] | 2 (4.2) [0.5, 15.0] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 0 | 0 | 1 (2.1) [0.1, 11.6] |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 0 | 1 (60.6) [1.5, 337.5] | 4 (11.1) [3.0, 28.4] | 2 (4.2) [0.5, 15.0] |
| Any adjudicated gastrointestinal perforations | 0 | 0 | 0 | 1 (2.8) [0.1, 15.4] | 0 |
| Any anemia | 0 | 0 | 1 (60.6) [1.5, 337.5] | 1 (2.8) [0.1, 15.4] | 6 (12.5) [4.6, 27.1] |
| Any neutropenia | 0 | 0 | 0 | 3 (8.3) [1.7, 24.3] | 6 (12.5) [4.6, 27.1] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=30) | UPA 15 mg QD (N=65) | UPA 30 mg QD (N=82) | UPA 15 mg QD (N=178) | UPA 30 mg QD (N=212) |
| Subgroup: >= 12 - < 15 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 0 | 0 | 1 (2.8) [0.1, 15.4] | 3 (6.2) [1.3, 18.2] |
| Any creatine phosphokinase (CPK) elevation | 0 | 0 | 0 | 3 (8.3) [1.7, 24.3] | 9 (18.7) [8.5, 35.5] |
| Any hepatic disorder | 0 | 0 | 0 | 4 (11.1) [3.0, 28.4] | 13 (27.0) [14.4, 46.2] |
| Any renal dysfunction | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=128) | UPA 30 mg QD (N=172) |
| Subgroup: >= 15 - < 18 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=29.4) Events (E/100PYs) [95% CI] | (PYs=39.1) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 0 | 0 | 0 | 2 (6.8) [0.8, 24.6] | 3 (7.7) [1.6, 22.4] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 0 | 0 | 0 |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 0 | 0 | 0 | 1 (2.6) [0.1, 14.3] |
| Any adjudicated gastrointestinal perforations | 0 | 0 | 0 | 0 | 1 (2.6) [0.1, 14.3] |
| Any anemia | 0 | 0 | 0 | 2 (6.8) [0.8, 24.6] | 0 |
| Any neutropenia | 0 | 0 | 0 | 0 | 3 (7.7) [1.6, 22.4] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=128) | UPA 30 mg QD (N=172) |
| Subgroup: >= 15 - < 18 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 0 | 0 | 0 | 0 |
| Any creatine phosphokinase (CPK) elevation | 0 | 0 | 0 | 0 | 3 (7.7) [1.6, 22.4] |
| Any hepatic disorder | 0 | 0 | 0 | 2 (6.8) [0.8, 24.6] | 0 |
| Any renal dysfunction | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=109) | UPA 30 mg QD (N=140) |
| Subgroup: >= 18 - < 21 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=25.0) Events (E/100PYs) [95% CI] | (PYs=30.6) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 0 | 0 | 0 | 2 (8.0) [1.0, 28.8] | 2 (6.5) [0.8, 23.6] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 0 | 0 | 0 |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 0 | 0 | 2 (8.0) [1.0, 28.8] | 3 (9.8) [2.0, 28.7] |
| Any adjudicated gastrointestinal perforations | 0 | 0 | 0 | 0 | 0 |
| Any anemia | 0 | 0 | 0 | 1 (4.0) [0.1, 22.2] | 0 |
| Any neutropenia | 0 | 0 | 0 | 0 | 1 (3.3) [0.1, 18.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=109) | UPA 30 mg QD (N=140) |
| Subgroup: >= 18 - < 21 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 0 | 0 | 0 | 0 |
| Any creatine phosphokinase (CPK) elevation | 0 | 0 | 0 | 0 | 0 |
| Any hepatic disorder | 0 | 0 | 0 | 0 | 0 |
| Any renal dysfunction | 0 | 0 | 0 | 0 | 1 (3.3) [0.1, 18.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=90) | UPA 30 mg QD (N=109) |
| Subgroup: >= 21 - < 24 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=0.0) | (PYs=0.0) | (PYs=0.0) | (PYs=19.4) | (PYs=23.4) |
| | Events (E/100PYs) [95% CI] | Events (E/100PYs) [95% CI] | Events (E/100PYs) [95% CI] | Events (E/100PYs) [95% CI] | Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 0 | 0 | 0 | 1 (5.2) [0.1, 28.7] | 2 (8.5) [1.0, 30.9] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 0 | 0 | 0 |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 0 | 0 | 2 (10.3) [1.2, 37.2] | 4 (17.1) [4.7, 43.8] |
| Any adjudicated gastrointestinal perforations | 0 | 0 | 0 | 0 | 0 |
| Any anemia | 0 | 0 | 0 | 0 | 0 |
| Any neutropenia | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=90) | UPA 30 mg QD (N=109) |
| Subgroup: >= 21 - < 24 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 0 | 0 | 0 | 0 |
| Any creatine phosphokinase (CPK) elevation | 0 | 0 | 0 | 1 (5.2) [0.1, 28.7] | 1 (4.3) [0.1, 23.8] |
| Any hepatic disorder | 0 | 0 | 0 | 2 (10.3) [1.2, 37.2] | 0 |
| Any renal dysfunction | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=67) | UPA 30 mg QD (N=77) |
| Subgroup: >= 24 Month | | | | | |
| Exposure-adjusted event rate: | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=0.0) Events (E/100PYs) [95% CI] | (PYs=51.2) Events (E/100PYs) [95% CI] | (PYs=33.1) Events (E/100PYs) [95% CI] |
| Subjects with any treatment-emergent | | | | | |
| Any serious infections | 0 | 0 | 0 | 0 | 1 (3.0) [0.1, 16.9] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0 | 0 | 0 | 0 | 0 |
| Any active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| Any herpes zoster | 0 | 0 | 0 | 0 | 0 |
| Any adjudicated gastrointestinal perforations | 0 | 0 | 0 | 0 | 0 |
| Any anemia | 0 | 0 | 0 | 4 (7.8) [2.1, 20.0] | 0 |
| Any neutropenia | 0 | 0 | 0 | 1 (2.0) [0.0, 10.9] | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=0) | UPA 15 mg QD (N=0) | UPA 30 mg QD (N=0) | UPA 15 mg QD (N=67) | UPA 30 mg QD (N=77) |
| Subgroup: >= 24 Month (Cont.) | | | | | |
| Any lymphopenia | 0 | 0 | 0 | 2 (3.9) [0.5, 14.1] | 1 (3.0) [0.1, 16.9] |
| Any creatine phosphokinase (CPK) elevation | 0 | 0 | 0 | 0 | 1 (3.0) [0.1, 16.9] |
| Any hepatic disorder | 0 | 0 | 0 | 4 (7.8) [2.1, 20.0] | 0 |
| Any renal dysfunction | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

表 2.7.4.7-116.

[redacted]20[redacted] 10:10 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL



TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | |
|---|---|---|---|
| | Placebo QD (N=245) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 15 mg QD (N=250) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=251) n/PYs (n/100 PYs) [SSA n/100 PYs] |
| Any serious infections | 8/132.7 (6.0) [6.0] | 9/195.2 (4.6) [4.6] | 7/217.3 (3.2) [3.2] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 2/134.0 (1.5) [1.7] | 2/199.1 (1.0) [0.9] | 2/218.5 (0.9) [0.9] |
| Any active tuberculosis | 0/135.0 | 0/199.4 | 0/218.5 |
| Any herpes zoster | 0/135.0 | 12/194.7 (6.2) [6.0] | 14/212.9 (6.6) [6.6] |
| Any adjudicated gastrointestinal perforations | 1/135.0 (0.7) [0.8] | 0/199.4 | 0/218.5 |
| Any anemia | 15/128.0 (11.7) [11.4] | 11/192.0 (5.7) [5.8] | 10/213.8 (4.7) [4.7] |
| Any neutropenia | 5/132.2 (3.8) [3.7] | 8/193.9 (4.1) [4.1] | 15/208.6 (7.2) [7.2] |
| Any lymphopenia | 4/133.0 (3.0) [2.8] | 6/195.6 (3.1) [3.1] | 5/216.6 (2.3) [2.3] |
| Any creatine phosphokinase (CPK) elevation | 5/133.2 (3.8) [4.0] | 15/190.2 (7.9) [8.0] | 19/206.3 (9.2) [9.3] |
| Any hepatic disorder | 6/131.8 (4.6) [4.7] | 18/189.0 (9.5) [9.7] | 13/212.0 (6.1) [6.1] |
| Any renal dysfunction | 1/135.0 (0.7) [0.8] | 1/199.4 (0.5) [0.5] | 1/218.5 (0.5) [0.5] |
| Any malignancy | 1/135.0 (0.7) [0.8] | 1/199.4 (0.5) [0.5] | 5/217.3 (2.3) [2.3] |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 1/135.0 (0.7) [0.8] | 1/199.4 (0.5) [0.5] | 2/218.4 (0.9) [0.9] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

[C] Study-size adjusted risk differences between treatment groups.

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

| | ---M14-234 Substudy 3 (Cohorts 1 and 3) [B]--- UPA 15 mg QD (N=285) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=291) n/PYs (n/100 PYs) [SSA n/100 PYs] | Differences [C] Cohort 1 15 mg - PBO RD (95% CI) | 30 mg - PBO RD (95% CI) |
|---|---|---|---|---|
| Any serious infections | 17/399.4 (4.3) [4.4] | 19/416.2 (4.6) [4.4] | -1.4 (-6.6, 3.7) | -2.8 (-7.6, 2.0) |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 2/412.8 (0.5) [0.5] | 3/424.8 (0.7) [0.7] | -0.7 (-3.4, 1.9) | -0.7 (-3.4, 1.9) |
| Any active tuberculosis | 0/413.8 | 0/425.2 | 0.0 | 0.0 |
| Any herpes zoster | 22/381.8 (5.8) [5.7] | 25/404.6 (6.2) [6.1] | 6.0 (2.6, 9.4) | 6.6 (3.1, 10.0) |
| Any adjudicated gastrointestinal perforations | 0/413.8 | 0/425.2 | -0.8 (-2.4, 0.8) | -0.8 (-2.4, 0.8) |
| Any anemia | 21/393.5 (5.3) [5.6] | 17/406.6 (4.2) [4.3] | -5.6 (-12.3, 1.2) | -6.7 (-13.2, -0.2) |
| Any neutropenia | 13/397.5 (3.3) [3.3] | 21/399.6 (5.3) [5.1] | 0.4 (-3.9, 4.8) | 3.5 (-1.4, 8.4) |
| Any lymphopenia | 10/404.9 (2.5) [2.5] | 8/419.1 (1.9) [2.2] | 0.3 (-3.4, 4.0) | -0.5 (-3.9, 2.9) |
| Any creatine phosphokinase (CPK) elevation | 19/382.3 (5.0) [5.0] | 34/391.1 (8.7) [8.4] | 4.0 (-1.3, 9.4) | 5.3 (-0.1, 10.8) |
| Any hepatic disorder | 25/381.2 (6.6) [6.7] | 21/406.4 (5.2) [5.2] | 5.0 (-0.8, 10.8) | 1.5 (-3.6, 6.5) |
| Any renal dysfunction | 1/413.8 (0.2) [0.2] | 2/425.2 (0.5) [0.4] | -0.3 (-2.2, 1.5) | -0.4 (-2.2, 1.5) |
| Any malignancy | 1/413.8 (0.2) [0.3] | 9/418.5 (2.2) [2.2] | -0.3 (-2.2, 1.6) | 1.5 (-1.1, 4.1) |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 1/413.8 (0.2) [0.3] | 3/425.1 (0.7) [0.8] | -0.3 (-2.2, 1.6) | 0.1 (-1.9, 2.2) |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

[C] Study-size adjusted risk differences between treatment groups.

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | |
|---|---|---|---|
| | Placebo QD (N=245) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 15 mg QD (N=250) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=251) n/PYs (n/100 PYs) [SSA n/100 PYs] |
| Any NMSC | 0/135.0 | 0/199.4 | 3/217.4 (1.4) [1.4] |
| Any lymphoma | 0/135.0 | 0/199.4 | 0/218.5 |
| Any adjudicated MACE * | 1/135.0 (0.7) [0.7] | 0/199.4 | 1/217.7 (0.5) [0.5] |
| Any adjudicated VTE ** | 0/135.0 | 2/199.1 (1.0) [1.0] | 2/218.5 (0.9) [0.9] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

| | ---M14-234 Substudy 3 (Cohorts 1 and 3) [B]--- | | Differences [C] Cohort 1 | |
|---|---|---|---|---|
| | UPA 15 mg QD (N=285) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=291) n/PYs (n/100 PYs) [SSA n/100 PYs] | 15 mg - PBO RD (95% CI) | 30 mg - PBO RD (95% CI) |
| Any NMSC | 0/413.8 | 6/418.6 (1.4) [1.3] | 0.0 | 1.4 (-0.2, 3.0) |
| Any lymphoma | 0/413.8 | 0/425.2 | 0.0 | 0.0 |
| Any adjudicated MACE * | 0/413.8 | 2/422.1 (0.5) [0.5] | -0.7 (-2.0, 0.6) | -0.2 (-1.8, 1.4) |
| Any adjudicated VTE ** | 4/410.3 (1.0) [0.9] | 3/425.1 (0.7) [0.7] | 1.0 (-0.4, 2.4) | 0.9 (-0.4, 2.2) |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

[C] Study-size adjusted risk differences between treatment groups.

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-117.

[redacted]20[redacted] 10:10 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | |
|---|---|---|---|
| | Placebo QD (N=41) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 15 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs] |
| Any serious infections | 2/22.8 (8.8) [8.6] | 2/40.4 (5.0) [5.8] | 1/40.3 (2.5) [2.6] |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 1/23.2 (4.3) [4.5] | 0/41.3 | 0/40.3 |
| Any active tuberculosis | 0/23.2 | 0/41.3 | 0/40.3 |
| Any herpes zoster | 0/23.2 | 4/40.3 (9.9) [9.7] | 5/39.2 (12.8) [13.3] |
| Any adjudicated gastrointestinal perforations | 0/23.2 | 0/41.3 | 0/40.3 |
| Any anemia | 4/21.9 (18.3) [17.9] | 1/40.4 (2.5) [2.9] | 3/38.3 (7.8) [7.9] |
| Any neutropenia | 2/22.1 (9.1) [8.8] | 1/40.7 (2.5) [2.8] | 8/35.2 (22.7) [22.8] |
| Any lymphopenia | 1/22.9 (4.4) [4.0] | 0/41.3 | 2/40.2 (5.0) [5.0] |
| Any creatine phosphokinase (CPK) elevation | 1/22.9 (4.4) [3.9] | 5/37.7 (13.3) [14.0] | 6/36.2 (16.6) [16.7] |
| Any hepatic disorder | 2/22.3 (9.0) [13.0] | 5/38.3 (13.1) [14.2] | 4/38.1 (10.5) [10.8] |
| Any renal dysfunction | 0/23.2 | 0/41.3 | 1/40.3 (2.5) [2.3] |
| Any malignancy | 0/23.2 | 0/41.3 | 1/40.3 (2.5) [2.3] |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 0/23.2 | 0/41.3 | 1/40.3 (2.5) [2.3] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

| | ---M14-234 Substudy 3 (Cohorts 1 and 3) [B]--- UPA 15 mg QD (N=46) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=54) n/PYs (n/100 PYs) [SSA n/100 PYs] | Differences [C] Cohort 1 15 mg - PBO RD (95% CI) | 30 mg - PBO RD (95% CI) |
|---|---|---|---|---|
| Any serious infections | 2/81.1 (2.5) [3.0] | 5/80.9 (6.2) [5.9] | -2.8 (-17.2, 11.5) | -5.9 (-18.9, 7.0) |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0/82.0 | 0/82.9 | -4.5 (-13.4, 4.4) | -4.5 (-13.4, 4.4) |
| Any active tuberculosis | 0/82.0 | 0/82.9 | 0.0 | 0.0 |
| Any herpes zoster | 5/70.8 (7.1) [6.6] | 9/77.7 (11.6) [11.2] | 9.7 (0.2, 19.3) | 13.3 (1.6, 25.0) |
| Any adjudicated gastrointestinal perforations | 0/82.0 | 0/82.9 | 0.0 | 0.0 |
| Any anemia | 2/78.9 (2.5) [3.3] | 3/77.3 (3.9) [5.0] | -15.0 (-33.4, 3.4) | -10.0 (-29.7, 9.7) |
| Any neutropenia | 3/78.2 (3.8) [4.6] | 12/69.5 (17.3) [15.6] | -6.0 (-19.5, 7.4) | 13.9 (-6.1, 34.0) |
| Any lymphopenia | 0/82.0 | 4/80.5 (5.0) [5.6] | -4.0 (-11.8, 3.8) | 1.0 (-9.4, 11.4) |
| Any creatine phosphokinase (CPK) elevation | 5/67.1 (7.4) [7.6] | 10/72.5 (13.8) [14.3] | 10.1 (-4.5, 24.7) | 12.8 (-2.7, 28.3) |
| Any hepatic disorder | 6/70.3 (8.5) [9.2] | 6/76.6 (7.8) [7.5] | 1.3 (-21.2, 23.7) | -2.1 (-23.5, 19.3) |
| Any renal dysfunction | 0/82.0 | 1/82.9 (1.2) [1.0] | 0.0 | 2.3 (-2.2, 6.9) |
| Any malignancy | 0/82.0 | 1/82.9 (1.2) [1.0] | 0.0 | 2.3 (-2.2, 6.9) |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 0/82.0 | 1/82.9 (1.2) [1.0] | 0.0 | 2.3 (-2.2, 6.9) |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | |
|---|---|---|---|
| | Placebo QD (N=41) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 15 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs] |
| Any NMSC | 0/23.2 | 0/41.3 | 0/40.3 |
| Any lymphoma | 0/23.2 | 0/41.3 | 0/40.3 |
| Any adjudicated MACE * | 0/23.2 | 0/41.3 | 1/39.5 (2.5) [2.7] |
| Any adjudicated VTE ** | 0/23.2 | 0/41.3 | 0/40.3 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

| | ---M14-234 Substudy 3 (Cohorts 1 and 3) [B]--- | | Differences [C] Cohort 1 | |
|---|---|---|---|---|
| | UPA 15 mg QD (N=46) n/PYs (n/100 PYs) [SSA n/100 PYs] | UPA 30 mg QD (N=54) n/PYs (n/100 PYs) [SSA n/100 PYs] | 15 mg - PBO RD (95% CI) | 30 mg - PBO RD (95% CI) |
| Any NMSC | 0/82.0 | 0/82.9 | 0.0 | 0.0 |
| Any lymphoma | 0/82.0 | 0/82.9 | 0.0 | 0.0 |
| Any adjudicated MACE * | 0/82.0 | 1/82.1 (1.2) [1.3] | 0.0 | 2.7 (-2.6, 8.0) |
| Any adjudicated VTE ** | 0/82.0 | 0/82.9 | 0.0 | 0.0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
n/100PYs = Number of subjects per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-118.

[redacted]20[redacted] 09:21 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

| | Induction = PBO [A] PBO (N=378) n/PYs (n/100 PYs) | Induction Dose < 45 mg QD [B] UPA 15-30 mg / PBO (N=36) n/PYs (n/100 PYs) | Induction Dose < 45 mg QD [B] UPA < 45 mg / <= 30 mg (N=285) n/PYs (n/100 PYs) |
|---|---|---|---|
| Any serious infections | 8/127.9 (6.3) | 2/121.8 (1.6) | 24/656.8 (3.7) |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 1/131.5 (0.8) | 0/125.2 | 2/692.2 (0.3) |
| Any active tuberculosis | 0/131.5 | 0/125.2 | 1/699.5 (0.1) |
| Any herpes zoster | 0/131.5 | 3/117.4 (2.6) | 24/663.4 (3.6) |
| Any adjudicated gastrointestinal perforations | 1/131.5 (0.8) | 0/125.2 | 1/698.0 (0.1) |
| Any anemia | 29/125.5 (23.1) | 7/103.7 (6.7) | 27/653.3 (4.1) |
| Any neutropenia | 2/130.3 (1.5) | 1/122.5 (0.8) | 11/682.4 (1.6) |
| Any lymphopenia | 4/130.5 (3.1) | 1/122.1 (0.8) | 16/671.4 (2.4) |
| Any creatine phosphokinase (CPK) elevation | 6/128.8 (4.7) | 10/98.4 (10.2) | 29/648.5 (4.5) |
| Any hepatic disorder | 13/123.1 (10.6) | 4/112.9 (3.5) | 29/643.2 (4.5) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| | UPA 45 mg / NM (N=129) | UPA 45 mg / PBO (N=245) | UPA 45 mg / 15 mg (N=306) | UPA 45 mg / 30 mg (N=307) | Any UPA (N=1308) |
| | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) |
| Any serious infections | 3/23.8 (12.6) | 15/466.0 (3.2) | 31/594.1 (5.2) | 26/574.3 (4.5) | 93/2256.8 (4.1) |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 2/23.8 (8.4) | 2/477.5 (0.4) | 3/618.9 (0.5) | 4/590.2 (0.7) | 11/2337.6 (0.5) |
| Any active tuberculosis | 0/24.1 | 0/478.5 | 0/622.4 | 0/591.7 | 1/2350.2 (<0.1) |
| Any herpes zoster | 7/23.7 (29.5) | 11/464.2 (2.4) | 31/576.4 (5.4) | 29/564.4 (5.1) | 104/2225.5 (4.7) |
| Any adjudicated gastrointestinal perforations | 0/24.1 | 1/478.5 (0.2) | 1/622.4 (0.2) | 0/591.7 | 2/2348.7 (<0.1) |
| Any anemia | 17/22.3 (76.4) | 28/439.2 (6.4) | 36/573.9 (6.3) | 27/559.0 (4.8) | 129/2189.3 (5.9) |
| Any neutropenia | 4/23.7 (16.9) | 17/449.8 (3.8) | 28/575.8 (4.9) | 30/546.4 (5.5) | 90/2224.9 (4.0) |
| Any lymphopenia | 3/24.1 (12.5) | 12/453.0 (2.6) | 18/590.5 (3.0) | 16/569.6 (2.8) | 63/2251.9 (2.8) |
| Any creatine phosphokinase (CPK) elevation | 8/23.5 (34.0) | 26/442.2 (5.9) | 42/553.0 (7.6) | 54/508.0 (10.6) | 163/2110.6 (7.7) |
| Any hepatic disorder | 4/23.5 (17.0) | 18/453.0 (4.0) | 39/559.8 (7.0) | 32/540.0 (5.9) | 120/2160.2 (5.6) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

| | Induction = PBO [A] | Induction Dose < 45 mg QD [B] | |
|---|---|---|---|
| | PBO (N=378) n/PYs (n/100 PYs) | UPA 15-30 mg / PBO (N=36) n/PYs (n/100 PYs) | UPA < 45 mg / <= 30 mg (N=285) n/PYs (n/100 PYs) |
| Any renal dysfunction | 0/131.5 | 0/125.2 | 1/696.4 (0.1) |
| Any malignancy | 0/131.5 | 4/122.5 (3.3) | 6/694.9 (0.9) |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 0/131.5 | 2/125.1 (1.6) | 4/697.2 (0.6) |
| Any NMSC | 0/131.5 | 3/122.5 (2.4) | 3/696.3 (0.4) |
| Any lymphoma | 0/131.5 | 0/125.2 | 0/699.5 |
| Any adjudicated MACE * | 0/131.5 | 0/125.2 | 1/698.4 (0.1) |
| Any adjudicated VTE ** | 1/131.5 (0.8) | 2/124.3 (1.6) | 4/695.1 (0.6) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| | UPA 45 mg / NM (N=129) | UPA 45 mg / PBO (N=245) | UPA 45 mg / 15 mg (N=306) | UPA 45 mg / 30 mg (N=307) | Any UPA (N=1308) |
| | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) |
| Any renal dysfunction | 0/24.1 | 1/478.5 (0.2) | 4/617.9 (0.6) | 2/591.8 (0.3) | 7/2342.7 (0.3) |
| Any malignancy | 0/24.1 | 6/472.7 (1.3) | 2/622.4 (0.3) | 10/585.1 (1.7) | 27/2333.0 (1.2) |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 0/24.1 | 3/478.2 (0.6) | 2/622.4 (0.3) | 4/591.6 (0.7) | 14/2349.0 (0.6) |
| Any NMSC | 0/24.1 | 3/473.0 (0.6) | 0/622.4 | 6/585.2 (1.0) | 15/2333.5 (0.6) |
| Any lymphoma | 0/24.1 | 0/478.5 | 0/622.4 | 0/591.7 | 0/2350.2 |
| Any adjudicated MACE * | 0/24.1 | 1/478.5 (0.2) | 1/622.3 (0.2) | 3/588.6 (0.5) | 5/2345.9 (0.2) |
| Any adjudicated VTE ** | 1/24.1 (4.1) | 0/478.5 | 4/618.8 (0.6) | 3/591.7 (0.5) | 14/2341.9 (0.6) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-119.

[redacted]20[redacted] 08:55 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL



TABLE 2.4 6.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | ----Induction Dose = 45 mg QD [A]---- UPA 45 mg / 15 mg - 30 mg (N=103) (PYs=211.8) Events (E/100 PYs) |
|---|---|
| Any serious infections | 10 (4.7) |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 2 (0.9) |
| Any active tuberculosis | 0 |
| Any herpes zoster | 18 (8.5) |
| Any adjudicated gastrointestinal perforations | 0 |
| Any anemia | 10 (4.7) |
| Any neutropenia | 35 (16.5) |
| Any lymphopenia | 9 (4.2) |
| Any creatine phosphokinase (CPK) elevation | 29 (13.7) |
| Any hepatic disorder | 34 (16.1) |
| Any renal dysfunction | 2 (0.9) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100 PYs = Events per 100 patient-years.
UPA = Upadacitinib.

[A] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-120.

[redacted]20[redacted] 09:21 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL



TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction = PBO [A] PBO (N=56) n/PYs (n/100 PYs) | Induction Dose < 45 mg QD [B] UPA 15-30 mg / PBO (N=3) n/PYs (n/100 PYs) | Induction Dose < 45 mg QD [B] UPA < 45 mg / <= 30 mg (N=30) n/PYs (n/100 PYs) |
|---|---|---|---|
| Any serious infections | 0/19.7 | 2/5.1 (39.1) | 1/76.8 (1.3) |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0/19.7 | 0/8.5 | 0/78.6 |
| Any active tuberculosis | 0/19.7 | 0/8.5 | 0/78.6 |
| Any herpes zoster | 0/19.7 | 1/5.6 (18.0) | 6/74.1 (8.1) |
| Any adjudicated gastrointestinal perforations | 0/19.7 | 0/8.5 | 0/78.6 |
| Any anemia | 4/19.5 (20.5) | 1/4.1 (24.3) | 1/77.9 (1.3) |
| Any neutropenia | 0/19.7 | 0/8.5 | 2/72.0 (2.8) |
| Any lymphopenia | 1/19.4 (5.1) | 0/8.5 | 2/73.9 (2.7) |
| Any creatine phosphokinase (CPK) elevation | 0/19.7 | 2/1.6 (121.8) | 3/73.5 (4.1) |
| Any hepatic disorder | 1/19.6 (5.1) | 0/8.5 | 6/65.0 (9.2) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| | UPA 45 mg / NM (N=16) | UPA 45 mg / PBO (N=41) | UPA 45 mg / 15 mg (N=49) | UPA 45 mg / 30 mg (N=54) | Any UPA (N=193) |
| | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) |
| Any serious infections | 1/2.5 (40.8) | 4/79.2 (5.1) | 4/108.7 (3.7) | 6/98.3 (6.1) | 15/346.7 (4.3) |
| Any opportunistic infection excluding tuberculosis and herpes zoster | 0/2.5 | 1/82.4 (1.2) | 1/110.3 (0.9) | 1/99.7 (1.0) | 2/353.5 (0.6) |
| Any active tuberculosis | 0/2.5 | 0/82.5 | 0/110.9 | 0/100.9 | 0/355.3 |
| Any herpes zoster | 3/2.5 (120.8) | 3/81.0 (3.7) | 6/96.5 (6.2) | 10/95.6 (10.5) | 28/328.8 (8.5) |
| Any adjudicated gastrointestinal perforations | 0/2.5 | 0/82.5 | 0/110.9 | 0/100.9 | 0/355.3 |
| Any anemia | 1/2.5 (40.2) | 5/76.7 (6.5) | 6/100.9 (5.9) | 4/94.9 (4.2) | 15/333.5 (4.5) |
| Any neutropenia | 2/2.2 (92.1) | 5/72.6 (6.9) | 8/94.6 (8.5) | 16/77.2 (20.7) | 33/302.2 (10.9) |
| Any lymphopenia | 1/2.4 (41.1) | 4/74.0 (5.4) | 3/102.5 (2.9) | 6/96.3 (6.2) | 15/333.5 (4.5) |
| Any creatine phosphokinase (CPK) elevation | 2/2.3 (85.7) | 3/78.1 (3.8) | 11/86.2 (12.8) | 11/86.0 (12.8) | 32/302.5 (10.6) |
| Any hepatic disorder | 1/2.4 (41.6) | 4/75.7 (5.3) | 9/92.2 (9.8) | 8/88.9 (9.0) | 27/306.3 (8.8) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction = PBO [A] | Induction Dose < 45 mg QD [B] | |
|---|---|---|---|
| | PBO (N=56) n/PYs (n/100 PYs) | UPA 15-30 mg / PBO (N=3) n/PYs (n/100 PYs) | UPA < 45 mg / <= 30 mg (N=30) n/PYs (n/100 PYs) |
| Any renal dysfunction | 0/19.7 | 0/8.5 | 1/75.5 (1.3) |
| Any malignancy | 0/19.7 | 0/8.5 | 0/78.6 |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 0/19.7 | 0/8.5 | 0/78.6 |
| Any NMSC | 0/19.7 | 0/8.5 | 0/78.6 |
| Any lymphoma | 0/19.7 | 0/8.5 | 0/78.6 |
| Any adjudicated MACE * | 0/19.7 | 0/8.5 | 0/78.6 |
| Any adjudicated VTE ** | 0/19.7 | 1/8.5 (11.7) | 0/78.6 |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| | UPA 45 mg / NM (N=16) | UPA 45 mg / PBO (N=41) | UPA 45 mg / 15 mg (N=49) | UPA 45 mg / 30 mg (N=54) | Any UPA (N=193) |
| | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) | n/PYs (n/100 PYs) |
| Any renal dysfunction | 0/2.5 | 0/82.5 | 1/108.1 (0.9) | 1/100.9 (1.0) | 3/349.4 (0.9) |
| Any malignancy | 0/2.5 | 0/82.5 | 0/110.9 | 1/100.9 (1.0) | 1/355.3 (0.3) |
| Any malignancies excluding non-melanoma skin cancer (NMSC) | 0/2.5 | 0/82.5 | 0/110.9 | 1/100.9 (1.0) | 1/355.3 (0.3) |
| Any NMSC | 0/2.5 | 0/82.5 | 0/110.9 | 0/100.9 | 0/355.3 |
| Any lymphoma | 0/2.5 | 0/82.5 | 0/110.9 | 0/100.9 | 0/355.3 |
| Any adjudicated MACE * | 0/2.5 | 0/82.5 | 0/110.9 | 1/100.1 (1.0) | 1/354.5 (0.3) |
| Any adjudicated VTE ** | 0/2.5 | 0/82.5 | 0/110.9 | 0/100.9 | 1/355.6 (0.3) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-121.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.2

Treatment-Emergent Opportunistic Infections Excluding Tuberculosis and Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 1 (0.8) | 0 | 2 (0.3) |
| 感染症および寄生虫症 | 1 (0.8) | 0 | 2 (0.3) |
| サイトメガロウイルス性大腸炎 | 0 | 0 | 0 |
| サイトメガロウイルス感染 | 1 (0.8) | 0 | 0 |
| 食道カンジダ症 | 0 | 0 | 0 |
| 口腔真菌感染 | 0 | 0 | 1 (0.1) |
| ニューモシスチス・イロベチイ感染 | 0 | 0 | 1 (0.1) |
| ニューモシスチス・イロベチイ肺炎 | 0 | 0 | 0 |
| クリプトコッカス性肺炎 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.2

Treatment-Emergent Opportunistic Infections Excluding Tuberculosis and Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 2 (8.3) | 2 (0.4) | 3 (0.5) | 4 (0.7) | 11 (0.5) |
| 感染症および寄生虫症 | 2 (8.3) | 2 (0.4) | 3 (0.5) | 4 (0.7) | 11 (0.5) |
| サイトメガロウイルス性大腸炎 | 0 | 0 | 0 | 2 (0.3) | 2 (<0.1) |
| サイトメガロウイルス感染 | 1 (4.2) | 1 (0.2) | 2 (0.3) | 0 | 3 (0.1) |
| 食道カンジダ症 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 口腔真菌感染 | 1 (4.2) | 0 | 0 | 0 | 2 (<0.1) |
| ニューモシスチス・イロベチイ感染 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| ニューモシスチス・イロベチイ肺炎 | 0 | 1 (0.2) | 0 | 0 | 0 |
| クリプトコッカス性肺炎 | 0 | 0 | 0 | 2 (0.3) | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-122.

[redacted]20[redacted] 10:10 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.4.1.8

Treatment-Emergent Herpes Zoster in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=245) (PYs=135.0) | UPA 15 mg QD (N=250) (PYs=199.4) | UPA 30 mg QD (N=251) (PYs=218.5) | UPA 15 mg QD (N=285) (PYs=413.8) | UPA 30 mg QD (N=291) (PYs=425.2) |
| MedDRA 23.0 System Organ Class<br>Preferred Term | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] |
| Any adverse event | 0 | 12 (6.0) [5.8] | 16 (7.3) [7.3] | 22 (5.3) [5.3] | 28 (6.6) [6.4] |
| 感染症および寄生虫症 | 0 | 12 (6.0) [5.8] | 16 (7.3) [7.3] | 22 (5.3) [5.3] | 27 (6.4) [6.2] |
| 帯状疱疹 | 0 | 11 (5.5) [5.4] | 15 (6.9) [6.9] | 20 (4.8) [4.8] | 26 (6.1) [6.0] |
| 帯状疱疹性髄膜炎 | 0 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] |
| 耳帯状疱疹 | 0 | 0 | 0 | 1 (0.2) [0.3] | 0 |
| 水痘帯状疱疹ウイルス感染 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] | 0 |
| 神経系障害 | 0 | 0 | 0 | 0 | 1 (0.2) [0.2] |
| ヘルペス後神経痛 | 0 | 0 | 0 | 0 | 1 (0.2) [0.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-123.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.4

Treatment-Emergent Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 0 | 4 (3.2) | 25 (3.6) |
| 感染症および寄生虫症 | 0 | 4 (3.2) | 25 (3.6) |
| 帯状疱疹 | 0 | 4 (3.2) | 24 (3.4) |
| 播種性帯状疱疹 | 0 | 0 | 0 |
| 神経合併症を伴う帯状疱疹感染 | 0 | 0 | 1 (0.1) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 |
| 耳帯状疱疹 | 0 | 0 | 0 |
| 水痘帯状疱疹ウイルス感染 | 0 | 0 | 0 |
| 神経系障害 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.4

Treatment-Emergent Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 8 (33.2) | 12 (2.5) | 34 (5.5) | 33 (5.6) | 114 (4.9) |
| 感染症および寄生虫症 | 7 (29.1) | 12 (2.5) | 34 (5.5) | 32 (5.4) | 112 (4.8) |
| 帯状疱疹 | 7 (29.1) | 11 (2.3) | 32 (5.1) | 31 (5.2) | 107 (4.6) |
| 播種性帯状疱疹 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 神経合併症を伴う帯状疱疹感染 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 帯状疱疹性髄膜炎 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 耳帯状疱疹 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 水痘帯状疱疹ウイルス感染 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 神経系障害 | 1 (4.2) | 0 | 0 | 1 (0.2) | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.4

Treatment-Emergent Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 神経系障害 (Cont.) | | | |
| ヘルペス後神経痛 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.4

Treatment-Emergent Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 神経系障害 (Cont.) | | | | | |
| ヘルペス後神経痛 | 1 (4.2) | 0 | 0 | 1 (0.2) | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-124.

[redacted]20[redacted] 10:10 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.4.1.20

Treatment-Emergent Hepatic Disorders in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=245) (PYs=135.0) | UPA 15 mg QD (N=250) (PYs=199.4) | UPA 30 mg QD (N=251) (PYs=218.5) | UPA 15 mg QD (N=285) (PYs=413.8) | UPA 30 mg QD (N=291) (PYs=425.2) |
| MedDRA 23.0 System Organ Class<br>Preferred Term | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] |
| Any adverse event | 8 (5.9) [5.9] | 34 (17.0) [17.4] | 20 (9.2) [9.1] | 48 (11.6) [12.1] | 39 (9.2) [9.0] |
| 肝胆道系障害 | 4 (3.0) [2.9] | 7 (3.5) [3.4] | 2 (0.9) [0.9] | 10 (2.4) [2.4] | 3 (0.7) [0.8] |
| 薬物性肝障害 | 0 | 1 (0.5) [0.5] | 1 (0.5) [0.5] | 1 (0.2) [0.2] | 1 (0.2) [0.2] |
| 肝機能異常 | 3 (2.2) [2.1] | 2 (1.0) [0.9] | 0 | 3 (0.7) [0.7] | 1 (0.2) [0.2] |
| 脂肪肝 | 0 | 2 (1.0) [1.0] | 0 | 4 (1.0) [1.0] | 0 |
| 高トランスアミナーゼ血症 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] | 0 |
| 肝障害 | 0 | 0 | 1 (0.5) [0.4] | 0 | 1 (0.2) [0.4] |
| 肝損傷 | 1 (0.7) [0.8] | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.4.1.20

Treatment-Emergent Hepatic Disorders in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=245) (PYs=135.0) | UPA 15 mg QD (N=250) (PYs=199.4) | UPA 30 mg QD (N=251) (PYs=218.5) | UPA 15 mg QD (N=285) (PYs=413.8) | UPA 30 mg QD (N=291) (PYs=425.2) |
| MedDRA 23.0 System Organ Class<br>Preferred Term | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] |
| 臨床検査 | 4 (3.0) [3.0] | 27 (13.5) [14.0] | 18 (8.2) [8.2] | 38 (9.2) [9.7] | 36 (8.5) [8.2] |
| アラニンアミノトランスフェラーゼ増加 | 1 (0.7) [0.7] | 9 (4.5) [4.7] | 7 (3.2) [3.2] | 12 (2.9) [3.0] | 12 (2.8) [2.7] |
| アスパラギン酸アミノトランスフェラーゼ増加 | 2 (1.5) [1.5] | 9 (4.5) [4.8] | 5 (2.3) [2.3] | 10 (2.4) [2.6] | 10 (2.4) [2.2] |
| 血中ビリルビン増加 | 0 | 3 (1.5) [1.5] | 3 (1.4) [1.4] | 3 (0.7) [0.8] | 5 (1.2) [1.2] |
| γ-グルタミルトランスフェラーゼ増加 | 1 (0.7) [0.8] | 5 (2.5) [2.6] | 1 (0.5) [0.5] | 10 (2.4) [2.6] | 4 (0.9) [0.9] |
| 肝酵素上昇 | 0 | 1 (0.5) [0.5] | 1 (0.5) [0.5] | 2 (0.5) [0.4] | 2 (0.5) [0.4] |
| 肝機能検査値上昇 | 0 | 0 | 1 (0.5) [0.5] | 0 | 2 (0.5) [0.4] |
| トランスアミナーゼ上昇 | 0 | 0 | 0 | 1 (0.2) [0.3] | 1 (0.2) [0.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-125.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 25 (19.0) | 9 (7.2) | 51 (7.3) |
| 肝胆道系障害 | 5 (3.8) | 2 (1.6) | 12 (1.7) |
| 胆汁うっ滞 | 1 (0.8) | 0 | 0 |
| 薬物性肝障害 | 0 | 0 | 0 |
| 肝嚢胞 | 0 | 0 | 1 (0.1) |
| 肝機能異常 | 0 | 0 | 3 (0.4) |
| 脂肪肝 | 0 | 2 (1.6) | 4 (0.6) |
| 肝炎 | 0 | 0 | 1 (0.1) |
| 肝細胞損傷 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 6 (24.9) | 36 (7.5) | 80 (12.9) | 64 (10.8) | 236 (10.0) |
| 肝胆道系障害 | 1 (4.2) | 10 (2.1) | 13 (2.1) | 5 (0.8) | 39 (1.7) |
| 胆汁うっ滞 | 0 | 0 | 0 | 0 | 0 |
| 薬物性肝障害 | 0 | 1 (0.2) | 1 (0.2) | 1 (0.2) | 3 (0.1) |
| 肝嚢胞 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 肝機能異常 | 0 | 3 (0.6) | 5 (0.8) | 3 (0.5) | 11 (0.5) |
| 脂肪肝 | 0 | 1 (0.2) | 4 (0.6) | 0 | 11 (0.5) |
| 肝炎 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 肝細胞損傷 | 0 | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 肝胆道系障害 (Cont.) | | | |
| 肝腫大 | 0 | 0 | 0 |
| 高ビリルビン血症 | 2 (1.5) | 0 | 0 |
| 高トランスアミナーゼ血症 | 0 | 0 | 0 |
| 肝障害 | 1 (0.8) | 0 | 0 |
| 肝損傷 | 1 (0.8) | 0 | 0 |
| 非アルコール性脂肪性肝炎 | 0 | 0 | 1 (0.1) |
| 非アルコール性脂肪性肝疾患 | 0 | 0 | 1 (0.1) |
| 臨床検査 | 20 (15.2) | 7 (5.6) | 39 (5.6) |
| アラニンアミノトランスフェラーゼ増加 | 6 (4.6) | 2 (1.6) | 10 (1.4) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 肝胆道系障害 (Cont.) | | | | | |
| 肝腫大 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 高ビリルビン血症 | 0 | 0 | 0 | 0 | 0 |
| 高トランスアミナーゼ血症 | 1 (4.2) | 0 | 1 (0.2) | 0 | 2 (<0.1) |
| 肝障害 | 0 | 2 (0.4) | 1 (0.2) | 1 (0.2) | 4 (0.2) |
| 肝損傷 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |
| 非アルコール性脂肪性肝炎 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 非アルコール性脂肪性肝疾患 | 0 | 1 (0.2) | 0 | 0 | 2 (<0.1) |
| 臨床検査 | 5 (20.8) | 26 (5.4) | 67 (10.8) | 59 (10.0) | 197 (8.4) |
| アラニンアミノトランスフェラーゼ増加 | 0 | 8 (1.7) | 17 (2.7) | 19 (3.2) | 54 (2.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| アスパラギン酸アミノトランスフェラーゼ増加 | 7 (5.3) | 2 (1.6) | 10 (1.4) |
| 血中ビリルビン増加 | 0 | 0 | 2 (0.3) |
| 血中非抱合ビリルビン増加 | 0 | 0 | 0 |
| γ-グルタミルトランスフェラーゼ増加 | 6 (4.6) | 2 (1.6) | 5 (0.7) |
| 肝酵素上昇 | 0 | 0 | 10 (1.4) |
| 肝機能検査異常 | 0 | 1 (0.8) | 0 |
| 肝機能検査値上昇 | 1 (0.8) | 0 | 2 (0.3) |
| トランスアミナーゼ上昇 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 臨床検査 (Cont.) | | | | | |
| アスパラギン酸アミノトランスフェラーゼ増加 | 1 (4.2) | 10 (2.1) | 18 (2.9) | 17 (2.9) | 56 (2.4) |
| 血中ビリルビン増加 | 0 | 0 | 9 (1.4) | 8 (1.4) | 19 (0.8) |
| 血中非抱合ビリルビン増加 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| γ-グルタミルトランスフェラーゼ増加 | 0 | 5 (1.0) | 12 (1.9) | 6 (1.0) | 28 (1.2) |
| 肝酵素上昇 | 4 (16.6) | 1 (0.2) | 7 (1.1) | 5 (0.8) | 27 (1.1) |
| 肝機能検査異常 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 肝機能検査値上昇 | 0 | 1 (0.2) | 0 | 2 (0.3) | 5 (0.2) |
| トランスアミナーゼ上昇 | 0 | 1 (0.2) | 4 (0.6) | 1 (0.2) | 6 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-126.

[redacted]20[redacted] 10:10 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL



TABLE 2.4 3.4.1.12

Treatment-Emergent Anemia in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | M14-234 Substudy 3 (Cohort 1) [A]<br>Placebo QD<br>(N=245)<br>(PYs=135.0)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 15 mg QD<br>(N=250)<br>(PYs=199.4)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 30 mg QD<br>(N=251)<br>(PYs=218.5)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 15 mg QD<br>(N=285)<br>(PYs=413.8)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 30 mg QD<br>(N=291)<br>(PYs=425.2)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] |
|---|---|---|---|---|---|
| Any adverse event | 19 (14.1) [13.8] | 12 (6.0) [6.1] | 11 (5.0) [5.0] | 24 (5.8) [5.9] | 21 (4.9) [4.9] |
| 血液およびリンパ系障害 | 18 (13.3) [13.0] | 10 (5.0) [5.1] | 10 (4.6) [4.6] | 18 (4.3) [4.6] | 14 (3.3) [3.3] |
| 貧血 | 13 (9.6) [9.2] | 10 (5.0) [5.1] | 9 (4.1) [4.1] | 16 (3.9) [4.0] | 12 (2.8) [2.7] |
| 鉄欠乏性貧血 | 5 (3.7) [3.8] | 0 | 0 | 1 (0.2) [0.3] | 1 (0.2) [0.2] |
| 小球性貧血 | 0 | 0 | 1 (0.5) [0.4] | 1 (0.2) [0.3] | 1 (0.2) [0.4] |
| 臨床検査 | 1 (0.7) [0.8] | 2 (1.0) [0.9] | 1 (0.5) [0.5] | 6 (1.4) [1.4] | 7 (1.6) [1.7] |
| ヘマトクリット減少 | 0 | 0 | 0 | 1 (0.2) [0.2] | 0 |
| ヘモグロビン減少 | 1 (0.7) [0.8] | 2 (1.0) [0.9] | 1 (0.5) [0.5] | 4 (1.0) [0.9] | 5 (1.2) [1.2] |
| 平均赤血球容積異常 | 0 | 0 | 0 | 0 | 1 (0.2) [0.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.4.1.12

Treatment-Emergent Anemia in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | M14-234 Substudy 3 (Cohort 1) [A]<br>Placebo QD<br>(N=245)<br>(PYs=135.0)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 15 mg QD<br>(N=250)<br>(PYs=199.4)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 30 mg QD<br>(N=251)<br>(PYs=218.5)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 15 mg QD<br>(N=285)<br>(PYs=413.8)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 30 mg QD<br>(N=291)<br>(PYs=425.2)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] |
|---|---|---|---|---|---|
| 臨床検査 (Cont.) | | | | | |
| 平均赤血球容積増加 | 0 | 0 | 0 | 1 (0.2) [0.3] | 1 (0.2) [0.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-127.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 32 (24.3) | 9 (7.2) | 34 (4.9) |
| 血液およびリンパ系障害 | 28 (21.3) | 8 (6.4) | 28 (4.0) |
| 貧血 | 26 (19.8) | 8 (6.4) | 24 (3.4) |
| 大球性貧血 | 0 | 0 | 0 |
| 失血性貧血 | 0 | 0 | 0 |
| 鉄欠乏性貧血 | 1 (0.8) | 0 | 4 (0.6) |
| 小球性貧血 | 0 | 0 | 0 |
| 正球性貧血 | 1 (0.8) | 0 | 0 |
| 臨床検査 | 4 (3.0) | 1 (0.8) | 6 (0.9) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 19 (78.9) | 36 (7.5) | 47 (7.6) | 35 (5.9) | 159 (6.8) |
| 血液およびリンパ系障害 | 18 (74.8) | 33 (6.9) | 38 (6.1) | 28 (4.7) | 133 (5.7) |
| 貧血 | 17 (70.6) | 24 (5.0) | 30 (4.8) | 21 (3.5) | 109 (4.6) |
| 大球性貧血 | 0 | 0 | 2 (0.3) | 0 | 2 (<0.1) |
| 失血性貧血 | 0 | 0 | 0 | 2 (0.3) | 2 (<0.1) |
| 鉄欠乏性貧血 | 1 (4.2) | 8 (1.7) | 4 (0.6) | 4 (0.7) | 16 (0.7) |
| 小球性貧血 | 0 | 1 (0.2) | 2 (0.3) | 1 (0.2) | 4 (0.2) |
| 正球性貧血 | 0 | 0 | 0 | 0 | 0 |
| 臨床検査 | 1 (4.2) | 3 (0.6) | 9 (1.4) | 7 (1.2) | 26 (1.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 臨床検査 (Cont.) | | | |
| ヘマトクリット減少 | 0 | 0 | 1 (0.1) |
| ヘモグロビン減少 | 4 (3.0) | 1 (0.8) | 5 (0.7) |
| 平均赤血球容積異常 | 0 | 0 | 0 |
| 平均赤血球容積増加 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 臨床検査 (Cont.) | | | | | |
| ヘマトクリット減少 | 0 | 0 | 1 (0.2) | 0 | 2 (<0.1) |
| ヘモグロビン減少 | 1 (4.2) | 3 (0.6) | 7 (1.1) | 5 (0.8) | 21 (0.9) |
| 平均赤血球容積異常 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 平均赤血球容積増加 | 0 | 0 | 1 (0.2) | 1 (0.2) | 2 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-128.

[redacted]20[redacted] 10:10 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.4.1.14

Treatment-Emergent Neutropenia in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | M14-234 Substudy 3 (Cohort 1) [A]<br>Placebo QD<br>(N=245)<br>(PYs=135.0)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 15 mg QD<br>(N=250)<br>(PYs=199.4)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 30 mg QD<br>(N=251)<br>(PYs=218.5)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 15 mg QD<br>(N=285)<br>(PYs=413.8)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 30 mg QD<br>(N=291)<br>(PYs=425.2)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] |
|---|---|---|---|---|---|
| Any adverse event | 7 (5.2) [5.1] | 12 (6.0) [6.0] | 19 (8.7) [8.7] | 17 (4.1) [4.2] | 31 (7.3) [7.0] |
| 血液およびリンパ系障害 | 3 (2.2) [2.1] | 7 (3.5) [3.4] | 6 (2.7) [2.8] | 7 (1.7) [1.8] | 11 (2.6) [2.4] |
| 好中球減少症 | 3 (2.2) [2.1] | 7 (3.5) [3.4] | 6 (2.7) [2.8] | 7 (1.7) [1.8] | 11 (2.6) [2.4] |
| 臨床検査 | 4 (3.0) [3.0] | 5 (2.5) [2.5] | 13 (5.9) [6.0] | 10 (2.4) [2.4] | 20 (4.7) [4.6] |
| 顆粒球数減少 | 0 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] |
| 好中球数減少 | 4 (3.0) [3.0] | 5 (2.5) [2.5] | 12 (5.5) [5.5] | 10 (2.4) [2.4] | 19 (4.5) [4.4] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-129.

[redacted]20[redacted] 09:30 [redacted]
UPADACI IB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.7

Treatment-Emergent Neutropenia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 3 (2.3) | 1 (0.8) | 13 (1.9) |
| 血液およびリンパ系障害 | 3 (2.3) | 0 | 8 (1.1) |
| 周期性好中球減少症 | 0 | 0 | 0 |
| 顆粒球減少症 | 0 | 0 | 0 |
| 好中球減少症 | 3 (2.3) | 0 | 8 (1.1) |
| 臨床検査 | 0 | 1 (0.8) | 5 (0.7) |
| 顆粒球数減少 | 0 | 0 | 0 |
| 好中球数減少 | 0 | 1 (0.8) | 5 (0.7) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.7

Treatment-Emergent Neutropenia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 5 (20.8) | 33 (6.9) | 44 (7.1) | 46 (7.8) | 135 (5.7) |
| 血液およびリンパ系障害 | 1 (4.2) | 15 (3.1) | 21 (3.4) | 18 (3.0) | 60 (2.6) |
| 周期性好中球減少症 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 顆粒球減少症 | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 好中球減少症 | 1 (4.2) | 14 (2.9) | 20 (3.2) | 18 (3.0) | 58 (2.5) |
| 臨床検査 | 4 (16.6) | 18 (3.8) | 23 (3.7) | 28 (4.7) | 75 (3.2) |
| 顆粒球数減少 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 好中球数減少 | 4 (16.6) | 18 (3.8) | 23 (3.7) | 27 (4.6) | 74 (3.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-130.

[redacted]20[redacted] 10:10 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.4.1.16

Treatment-Emergent Lymphopenia in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | M14-234 Substudy 3 (Cohort 1) [A]<br>Placebo QD<br>(N=245)<br>(PYs=135.0)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 15 mg QD<br>(N=250)<br>(PYs=199.4)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 30 mg QD<br>(N=251)<br>(PYs=218.5)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 15 mg QD<br>(N=285)<br>(PYs=413.8)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 30 mg QD<br>(N=291)<br>(PYs=425.2)<br>Events(E/100 PYs)<br>[SSA E/100 PYs] |
|---|---|---|---|---|---|
| Any adverse event | 5 (3.7) [3.4] | 9 (4.5) [4.5] | 7 (3.2) [3.2] | 14 (3.4) [3.3] | 12 (2.8) [3.2] |
| 血液およびリンパ系障害 | 3 (2.2) [2.0] | 3 (1.5) [1.5] | 1 (0.5) [0.5] | 5 (1.2) [1.3] | 3 (0.7) [0.6] |
| リンパ球減少症 | 3 (2.2) [2.0] | 3 (1.5) [1.5] | 1 (0.5) [0.5] | 5 (1.2) [1.3] | 3 (0.7) [0.6] |
| 臨床検査 | 2 (1.5) [1.4] | 6 (3.0) [3.0] | 6 (2.7) [2.7] | 9 (2.2) [2.1] | 9 (2.1) [2.5] |
| リンパ球数減少 | 2 (1.5) [1.4] | 5 (2.5) [2.5] | 5 (2.3) [2.3] | 8 (1.9) [1.8] | 8 (1.9) [2.3] |
| リンパ球百分率減少 | 0 | 1 (0.5) [0.5] | 1 (0.5) [0.5] | 1 (0.2) [0.2] | 1 (0.2) [0.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-131.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.8

Treatment-Emergent Lymphopenia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 5 (3.8) | 1 (0.8) | 20 (2.9) |
| 血液およびリンパ系障害 | 4 (3.0) | 1 (0.8) | 9 (1.3) |
| リンパ球減少症 | 4 (3.0) | 1 (0.8) | 9 (1.3) |
| 臨床検査 | 1 (0.8) | 0 | 11 (1.6) |
| リンパ球数減少 | 1 (0.8) | 0 | 11 (1.6) |
| リンパ球百分率減少 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.8

Treatment-Emergent Lymphopenia
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| Any adverse event | 3 (12.5) | 16 (3.3) | 32 (5.1) | 22 (3.7) | 89 (3.8) |
| 血液およびリンパ系障害 | 3 (12.5) | 10 (2.1) | 10 (1.6) | 9 (1.5) | 39 (1.7) |
| リンパ球減少症 | 3 (12.5) | 10 (2.1) | 10 (1.6) | 9 (1.5) | 39 (1.7) |
| 臨床検査 | 0 | 6 (1.3) | 22 (3.5) | 13 (2.2) | 50 (2.1) |
| リンパ球数減少 | 0 | 6 (1.3) | 16 (2.6) | 11 (1.9) | 42 (1.8) |
| リンパ球百分率減少 | 0 | 0 | 6 (1.0) | 2 (0.3) | 8 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-132.

[redacted]20[redacted] 10:10 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.4.1.18

Treatment-Emergent Creatine Phosphokinase (CPK) Elevations in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| | M14-234 Substudy 3 (Cohort 1) [A] | | | M14-234 Substudy 3 (Cohorts 1 and 3) [B] | |
|---|---|---|---|---|---|
| | Placebo QD (N=245) (PYs=135.0) | UPA 15 mg QD (N=250) (PYs=199.4) | UPA 30 mg QD (N=251) (PYs=218.5) | UPA 15 mg QD (N=285) (PYs=413.8) | UPA 30 mg QD (N=291) (PYs=425.2) |
| MedDRA 23.0 System Organ Class<br>Preferred Term | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] |
| Any adverse event | 5 (3.7) [3.9] | 16 (8.0) [8.1] | 22 (10.1) [10.1] | 24 (5.8) [5.8] | 41 (9.6) [9.2] |
| 臨床検査 | 5 (3.7) [3.9] | 16 (8.0) [8.1] | 22 (10.1) [10.1] | 24 (5.8) [5.8] | 41 (9.6) [9.2] |
| 血中クレアチンホスホキナーゼ増加 | 5 (3.7) [3.9] | 16 (8.0) [8.1] | 22 (10.1) [10.1] | 24 (5.8) [5.8] | 41 (9.6) [9.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-133.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.9

Treatment-Emergent Creatine Phosphokinase (CPK) Elevations
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 6 (4.6) | 12 (9.6) | 40 (5.7) |
| 臨床検査 | 6 (4.6) | 12 (9.6) | 40 (5.7) |
| 血中クレアチンホスホキナーゼ増加 | 6 (4.6) | 12 (9.6) | 40 (5.7) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.9

Treatment-Emergent Creatine Phosphokinase (CPK) Elevations
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| Any adverse event | 8 (33.2) | 33 (6.9) | 56 (9.0) | 72 (12.2) | 213 (9.1) |
| 臨床検査 | 8 (33.2) | 33 (6.9) | 56 (9.0) | 72 (12.2) | 213 (9.1) |
| 血中クレアチンホスホキナーゼ増加 | 8 (33.2) | 33 (6.9) | 56 (9.0) | 72 (12.2) | 213 (9.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-134.

[redacted]20[redacted] 10:10 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.4.1.22

Treatment-Emergent Renal Dysfunction in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | M14-234 Substudy 3 (Cohort 1) [A]<br>Placebo QD<br>(N=245)<br>(PYs=135.0)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 15 mg QD<br>(N=250)<br>(PYs=199.4)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 30 mg QD<br>(N=251)<br>(PYs=218.5)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 15 mg QD<br>(N=285)<br>(PYs=413.8)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 30 mg QD<br>(N=291)<br>(PYs=425.2)<br>Events (E/100 PYs)<br>[SSA E/100 PYs] |
|---|---|---|---|---|---|
| Any adverse event | 1 (0.7) [0.8] | 1 (0.5) [0.5] | 1 (0.5) [0.5] | 1 (0.2) [0.2] | 2 (0.5) [0.4] |
| 腎および尿路障害 | 1 (0.7) [0.8] | 1 (0.5) [0.5] | 1 (0.5) [0.5] | 1 (0.2) [0.2] | 2 (0.5) [0.4] |
| 急性腎障害 | 1 (0.7) [0.8] | 0 | 1 (0.5) [0.5] | 0 | 2 (0.5) [0.4] |
| 腎機能障害 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-135.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.11

Treatment-Emergent Renal Dysfunction
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 0 | 0 | 1 (0.1) |
| 腎および尿路障害 | 0 | 0 | 1 (0.1) |
| 急性腎障害 | 0 | 0 | 0 |
| 腎機能障害 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.11

Treatment-Emergent Renal Dysfunction
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 0 | 1 (0.2) | 4 (0.6) | 2 (0.3) | 7 (0.3) |
| 腎および尿路障害 | 0 | 1 (0.2) | 4 (0.6) | 2 (0.3) | 7 (0.3) |
| 急性腎障害 | 0 | 1 (0.2) | 1 (0.2) | 2 (0.3) | 3 (0.1) |
| 腎機能障害 | 0 | 0 | 3 (0.5) | 0 | 4 (0.2) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-136.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.5

Treatment-Emergent Adjudicated Gastrointestinal Perforations
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 1 (0.8) | 0 | 1 (0.1) |
| 胃腸障害 | 1 (0.8) | 0 | 1 (0.1) |
| 大腸穿孔 | 1 (0.8) | 0 | 1 (0.1) |
| 感染症および寄生虫症 | 0 | 0 | 0 |
| 腹部膿瘍 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.5

Treatment-Emergent Adjudicated Gastrointestinal Perforations
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 0 | 2 (0.4) | 1 (0.2) | 0 | 2 (<0.1) |
| 胃腸障害 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 大腸穿孔 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 感染症および寄生虫症 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |
| 腹部膿瘍 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-137.

[redacted]20[redacted] 10:10 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL



TABLE 2.4 3.4.1.24

Treatment-Emergent Malignancies in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

| | --- M14-234 Substudy 3 (Cohort 1) [A] --- | | | --- M14-234 Substudy 3 (Cohorts 1 and 3) [B] --- | |
|---|---|---|---|---|---|
| | Placebo QD (N=245) (PYs=135.0) | UPA 15 mg QD (N=250) (PYs=199.4) | UPA 30 mg QD (N=251) (PYs=218.5) | UPA 15 mg QD (N=285) (PYs=413.8) | UPA 30 mg QD (N=291) (PYs=425.2) |
| MedDRA 23.0 System Organ Class<br>Preferred Term | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] | Events (E/100 PYs)<br>[SSA E/100 PYs] |
| Any adverse event | 1 (0.7) [0.8] | 1 (0.5) [0.5] | 5 (2.3) [2.3] | 1 (0.2) [0.3] | 12 (2.8) [2.8] |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 1 (0.7) [0.8] | 1 (0.5) [0.5] | 5 (2.3) [2.3] | 1 (0.2) [0.3] | 12 (2.8) [2.8] |
| 結腸腺癌 | 0 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] |
| 基底細胞癌 | 0 | 0 | 3 (1.4) [1.4] | 0 | 7 (1.6) [1.5] |
| ボーエン病 | 0 | 0 | 0 | 0 | 1 (0.2) [0.2] |
| 浸潤性乳癌 | 1 (0.7) [0.8] | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.3] | 0 |
| 小細胞癌 | 0 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] |
| 皮膚有棘細胞癌 | 0 | 0 | 0 | 0 | 1 (0.2) [0.2] |
| 子宮頚部扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (0.2) [0.4] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-138.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 0 | 6 (4.8) | 9 (1.3) |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 0 | 6 (4.8) | 9 (1.3) |
| 結腸腺癌 | 0 | 1 (0.8) | 0 |
| 膵腺癌 | 0 | 0 | 1 (0.1) |
| 血管肉腫 | 0 | 0 | 0 |
| 基底細胞癌 | 0 | 3 (2.4) | 1 (0.1) |
| ボーエン病 | 0 | 1 (0.8) | 1 (0.1) |
| 乳癌 | 0 | 0 | 1 (0.1) |
| 浸潤性乳癌 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 0 | 6 (1.3) | 2 (0.3) | 13 (2.2) | 35 (1.5) |
| 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) | 0 | 6 (1.3) | 2 (0.3) | 13 (2.2) | 35 (1.5) |
| 結腸腺癌 | 0 | 0 | 0 | 1 (0.2) | 2 (<0.1) |
| 膵腺癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 血管肉腫 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 基底細胞癌 | 0 | 2 (0.4) | 0 | 7 (1.2) | 13 (0.6) |
| ボーエン病 | 0 | 0 | 0 | 1 (0.2) | 3 (0.1) |
| 乳癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 浸潤性乳癌 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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）<br>(Cont.) | | | |
| 喉頭扁平上皮癌 | 0 | 1 (0.8) | 0 |
| 悪性黒色腫 | 0 | 0 | 1 (0.1) |
| 前立腺癌 | 0 | 0 | 0 |
| 小細胞癌 | 0 | 0 | 0 |
| 扁平上皮癌 | 0 | 0 | 1 (0.1) |
| 皮膚有棘細胞癌 | 0 | 0 | 2 (0.3) |
| 子宮頚部扁平上皮癌 | 0 | 0 | 0 |
| 舌扁平上皮癌 | 0 | 0 | 1 (0.1) |
| 精巣（純粋）セミノーマ | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 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）<br>(Cont.) | | | | | |
| 喉頭扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 悪性黒色腫 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 前立腺癌 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 小細胞癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 皮膚有棘細胞癌 | 0 | 1 (0.2) | 0 | 1 (0.2) | 4 (0.2) |
| 子宮頚部扁平上皮癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 舌扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 精巣（純粋）セミノーマ | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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）<br>(Cont.)<br>精巣癌 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| 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）<br>(Cont.)<br>精巣癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-139.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 0 | 2 (1.6) | 5 (0.7) |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 0 | 2 (1.6) | 5 (0.7) |
| 結腸腺癌 | 0 | 1 (0.8) | 0 |
| 膵腺癌 | 0 | 0 | 1 (0.1) |
| 血管肉腫 | 0 | 0 | 0 |
| 乳癌 | 0 | 0 | 1 (0.1) |
| 浸潤性乳癌 | 0 | 0 | 0 |
| 喉頭扁平上皮癌 | 0 | 1 (0.8) | 0 |
| 悪性黒色腫 | 0 | 0 | 1 (0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| Any adverse event | 0 | 3 (0.6) | 2 (0.3) | 4 (0.7) | 15 (0.6) |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 0 | 3 (0.6) | 2 (0.3) | 4 (0.7) | 15 (0.6) |
| 結腸腺癌 | 0 | 0 | 0 | 1 (0.2) | 2 (<0.1) |
| 膵腺癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 血管肉腫 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 乳癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 浸潤性乳癌 | 0 | 1 (0.2) | 1 (0.2) | 0 | 1 (<0.1) |
| 喉頭扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 悪性黒色腫 | 0 | 0 | 0 | 0 | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| 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）<br>(Cont.) | | | |
| 前立腺癌 | 0 | 0 | 0 |
| 小細胞癌 | 0 | 0 | 0 |
| 扁平上皮癌 | 0 | 0 | 1 (0.1) |
| 子宮頚部扁平上皮癌 | 0 | 0 | 0 |
| 舌扁平上皮癌 | 0 | 0 | 1 (0.1) |
| 精巣（純粋）セミノーマ | 0 | 0 | 0 |
| 精巣癌 | 0 | 0 | 0 |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| | Induction Dose = 45 mg QD [C] | | | | |
|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs) | UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs) | UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs) | UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs) | Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs) |
| 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）<br>(Cont.) | | | | | |
| 前立腺癌 | 0 | 1 (0.2) | 0 | 0 | 1 (<0.1) |
| 小細胞癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 子宮頚部扁平上皮癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |
| 舌扁平上皮癌 | 0 | 0 | 0 | 0 | 1 (<0.1) |
| 精巣（純粋）セミノーマ | 0 | 0 | 1 (0.2) | 0 | 1 (<0.1) |
| 精巣癌 | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-140.

[redacted]20[redacted] 09:30 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL



TABLE 2.4 4.4.1.14

Treatment-Emergent NMSC
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 0 | 4 (3.2) | 4 (0.6) |
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 0 | 4 (3.2) | 4 (0.6) |
| 基底細胞癌 | 0 | 3 (2.4) | 1 (0.1) |
| ボーエン病 | 0 | 1 (0.8) | 1 (0.1) |
| 皮膚有棘細胞癌 | 0 | 0 | 2 (0.3) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.14

Treatment-Emergent NMSC
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | <br>UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | <br>Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 0 | 3 (0.6) | 0 | 9 (1.5) | 20 (0.9) |
| 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 | 3 (0.6) | 0 | 9 (1.5) | 20 (0.9) |
| 基底細胞癌 | 0 | 2 (0.4) | 0 | 7 (1.2) | 13 (0.6) |
| ボーエン病 | 0 | 0 | 0 | 1 (0.2) | 3 (0.1) |
| 皮膚有棘細胞癌 | 0 | 1 (0.2) | 0 | 1 (0.2) | 4 (0.2) |

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-141.

[redacted]20[redacted] 08:54 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL



TABLE 2.4__4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 0 | 2 (1.6) | 2 (0.3) |
| MACE * | 0 | 0 | 1 (0.1) |
| Cardiovascular death | 0 | 0 | 0 |
| Fatal acute myocardial infarction | 0 | 0 | 0 |
| Sudden cardiac death | 0 | 0 | 0 |
| Heart failure | 0 | 0 | 0 |
| Cardiovascular procedure-related death | 0 | 0 | 0 |
| Death due to cardiovascular hemorrhage | 0 | 0 | 0 |
| Fatal stroke | 0 | 0 | 0 |
| Pulmonary embolism ** | 0 | 0 | 0 |
| Venous thrombosis ** | 0 | 0 | 0 |
| Non-cardiac/Non-neurologic arterial thrombosis | 0 | 0 | 0 |
| Other | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 0 | 2 (0.4) | 1 (0.2) | 3 (0.5) | 8 (0.3) |
| MACE * | 0 | 1 (0.2) | 1 (0.2) | 3 (0.5) | 5 (0.2) |
| Cardiovascular death | 0 | 0 | 0 | 0 | 0 |
| Fatal acute myocardial infarction | 0 | 0 | 0 | 0 | 0 |
| Sudden cardiac death | 0 | 0 | 0 | 0 | 0 |
| Heart failure | 0 | 0 | 0 | 0 | 0 |
| Cardiovascular procedure-related death | 0 | 0 | 0 | 0 | 0 |
| Death due to cardiovascular hemorrhage | 0 | 0 | 0 | 0 | 0 |
| Fatal stroke | 0 | 0 | 0 | 0 | 0 |
| Pulmonary embolism ** | 0 | 0 | 0 | 0 | 0 |
| Venous thrombosis ** | 0 | 0 | 0 | 0 | 0 |
| Non-cardiac/Non-neurologic arterial thrombosis | 0 | 0 | 0 | 0 | 0 |
| Other | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| MACE * (Cont.) | | | |
| Non-fatal myocardial infarction | 0 | 0 | 1 (0.1) |
| Non-fatal stroke | 0 | 0 | 0 |
| Undetermined/UNK cause of death | 0 | 0 | 0 |
| Other cardiovascular events (non-fatal) | 0 | 2 (1.6) | 1 (0.1) |
| Cardiovascular procedures | 0 | 1 (0.8) | 1 (0.1) |
| Unstable angina requiring hospitalization | 0 | 1 (0.8) | 0 |
| Hospital based treatment for heart failure | 0 | 0 | 0 |
| Transient ischemic attack | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| MACE * (Cont.) | | | | | |
| Non-fatal myocardial infarction | 0 | 1 (0.2) | 1 (0.2) | 0 | 2 (<0.1) |
| Non-fatal stroke | 0 | 0 | 0 | 3 (0.5) | 3 (0.1) |
| Undetermined/UNK cause of death | 0 | 0 | 0 | 0 | 0 |
| Other cardiovascular events (non-fatal) | 0 | 1 (0.2) | 0 | 0 | 3 (0.1) |
| Cardiovascular procedures | 0 | 0 | 0 | 0 | 2 (<0.1) |
| Unstable angina requiring hospitalization | 0 | 0 | 0 | 0 | 1 (<0.1) |
| Hospital based treatment for heart failure | 0 | 1 (0.2) | 0 | 0 | 0 |
| Transient ischemic attack | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

Program Source Code: [redacted]

表 2.7.4.7-142.

[redacted]20[redacted] 10:01 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 3.4.1.34

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term (Responders Maintenance Analysis Set)

| Event Category<br>Adjudicated Term | M14-234 Substudy 3 (Cohort 1) [A]<br>Placebo QD (N=245) (PYs=135.0)<br>Events (E/100 PYs) [SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 15 mg QD (N=250) (PYs=199.4)<br>Events (E/100 PYs) [SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 30 mg QD (N=251) (PYs=218.5)<br>Events (E/100 PYs) [SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 15 mg QD (N=285) (PYs=413.8)<br>Events (E/100 PYs) [SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 30 mg QD (N=291) (PYs=425.2)<br>Events (E/100 PYs) [SSA E/100 PYs] |
|---|---|---|---|---|---|
| Any adverse event | 1 (0.7) [0.8] | 2 (1.0) [1.0] | 3 (1.4) [1.4] | 4 (1.0) [0.9] | 4 (0.9) [0.9] |
| Venous thromboembolic events (fatal and non-fatal) | 0 | 2 (1.0) [1.0] | 2 (0.9) [0.9] | 4 (1.0) [0.9] | 3 (0.7) [0.7] |
| Venous thromboembolic events (fatal) * | 0 | 0 | 0 | 0 | 0 |
| Pulmonary embolism | 0 | 0 | 0 | 0 | 0 |
| Venous thrombosis | 0 | 0 | 0 | 0 | 0 |
| Venous thromboembolic events (non-fatal) ** | 0 | 2 (1.0) [1.0] | 2 (0.9) [0.9] | 4 (1.0) [0.9] | 3 (0.7) [0.7] |
| Deep vein thrombosis (DVT) | 0 | 0 | 2 (0.9) [0.9] | 1 (0.2) [0.3] | 2 (0.5) [0.5] |
| Pulmonary embolism (PE) | 0 | 2 (1.0) [1.0] | 0 | 3 (0.7) [0.6] | 1 (0.2) [0.2] |
| DVT and PE (concurrent) | 0 | 0 | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

TABLE 2.4 3.4.1.34

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(Responders Maintenance Analysis Set)

| Event Category<br>Adjudicated Term | M14-234 Substudy 3 (Cohort 1) [A]<br>Placebo QD<br>(N=245)<br>(PYs=135.0)<br>Events<br>(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 15 mg QD<br>(N=250)<br>(PYs=199.4)<br>Events<br>(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohort 1) [A]<br>UPA 30 mg QD<br>(N=251)<br>(PYs=218.5)<br>Events<br>(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 15 mg QD<br>(N=285)<br>(PYs=413.8)<br>Events<br>(E/100 PYs)<br>[SSA E/100 PYs] | M14-234 Substudy 3 (Cohorts 1 and 3) [B]<br>UPA 30 mg QD<br>(N=291)<br>(PYs=425.2)<br>Events<br>(E/100 PYs)<br>[SSA E/100 PYs] |
|---|---|---|---|---|---|
| Other venous thrombosis (non-fatal) | 1 (0.7) [0.8] | 0 | 0 | 0 | 0 |
| Arterial thromboembolic events (non-cardiac, non-neurologic)(non-fatal) | 0 | 0 | 1 (0.5) [0.5] | 0 | 1 (0.2) [0.2] |

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

表 2.7.4.7-143.

[redacted]20[redacted] 08:54 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL


TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate
per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Any adverse event | 1 (0.8) | 2 (1.6) | 4 (0.6) |
| Venous thromboembolic events (fatal and non-fatal) | 1 (0.8) | 2 (1.6) | 4 (0.6) |
| Venous thromboembolic events (fatal) * | 0 | 0 | 0 |
| Pulmonary embolism | 0 | 0 | 0 |
| Venous thrombosis | 0 | 0 | 0 |
| Venous thromboembolic events (non-fatal) ** | 1 (0.8) | 2 (1.6) | 4 (0.6) |
| Deep vein thrombosis (DVT) | 1 (0.8) | 2 (1.6) | 2 (0.3) |
| Pulmonary embolism (PE) | 1 (0.8) | 0 | 3 (0.4) |
| DVT and PE (concurrent) | 1 (0.8) | 0 | 1 (0.1) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Any adverse event | 1 (4.2) | 1 (0.2) | 4 (0.6) | 4 (0.7) | 15 (0.6) |
| Venous thromboembolic events (fatal and non-fatal) | 1 (4.2) | 0 | 4 (0.6) | 3 (0.5) | 14 (0.6) |
| Venous thromboembolic events (fatal) * | 0 | 0 | 0 | 0 | 0 |
| Pulmonary embolism | 0 | 0 | 0 | 0 | 0 |
| Venous thrombosis | 0 | 0 | 0 | 0 | 0 |
| Venous thromboembolic events (non-fatal) ** | 1 (4.2) | 0 | 4 (0.6) | 3 (0.5) | 14 (0.6) |
| Deep vein thrombosis (DVT) | 1 (4.2) | 0 | 1 (0.2) | 2 (0.3) | 8 (0.3) |
| Pulmonary embolism (PE) | 1 (4.2) | 0 | 3 (0.5) | 1 (0.2) | 8 (0.3) |
| DVT and PE (concurrent) | 1 (4.2) | 0 | 0 | 0 | 2 (<0.1) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

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TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction = PBO [A]<br>PBO<br>(N=378)<br>(PYs=131.5)<br>Events<br>(E/100 PYs) | ------ Induction Dose < 45 mg QD [B] -------<br>UPA 15-30 mg/<br>PBO<br>(N=36)<br>(PYs=125.2)<br>Events<br>(E/100 PYs) | <br>UPA < 45 mg/<br><= 30 mg<br>(N=285)<br>(PYs=699.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|
| Other venous thrombosis (non-fatal) | 0 | 0 | 0 |
| Arterial thromboembolic events (non-cardiac, non-neurologic)(non-fatal) | 0 | 0 | 0 |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

| Event Category<br>Adjudicated Term | Induction Dose = 45 mg QD [C]<br>UPA 45 mg/ NM<br>(N=129)<br>(PYs=24.1)<br>Events<br>(E/100 PYs) | UPA 45 mg/ PBO<br>(N=245)<br>(PYs=478.5)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 15 mg<br>(N=306)<br>(PYs=622.4)<br>Events<br>(E/100 PYs) | UPA 45 mg/ 30 mg<br>(N=307)<br>(PYs=591.7)<br>Events<br>(E/100 PYs) | Any UPA<br>(N=1308)<br>(PYs=2350.2)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|
| Other venous thrombosis (non-fatal) | 0 | 1 (0.2) | 0 | 0 | 0 |
| Arterial thromboembolic events (non-cardiac, non-neurologic)(non-fatal) | 0 | 0 | 0 | 1 (0.2) | 1 (<0.1) |

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

## 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。