TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| 皮膚および皮下組織障害 (Cont.) | | | | | | | | |
| 蕁麻疹 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 1 (2.4) | 0 | 2 (0.9) |
| 乾皮症 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 血管障害 | 6 (5.0) | 1 (3.7) | 7 (4.8) | 1 (13.9) | 0 | 0 | 1 (2.5) | 8 (3.5) |
| 深部静脈血栓症 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 高血圧 | 5 (4.2) | 1 (3.7) | 6 (4.1) | 1 (13.9) | 0 | 0 | 0 | 6 (2.6) |
| 静脈炎 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表15

[redacted]20[redacted] 12:56 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - CLINICAL/STATISTICAL


TABLE 14.3__1.3.1.1.1_J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD (N=61)<br>n (%) | UPA 15 mg QD/ UPA 30 mg QD (N=19)<br>n (%) | Total (N=61)<br>n (%) | Placebo (N=10)<br>n (%) | UPA 7.5 mg QD (N=0)<br>n (%) | UPA 15 mg QD (N=40)<br>n (%) | UPA 30 mg QD (N=49)<br>n (%) | All_UPA (N=150)<br>n (%) |
| Any adverse event | 24 (39.3) | 11 (57.9) | 34 (55.7) | 3 (30.0) | 0 | 7 (17.5) | 15 (30.6) | 56 (37.3) |
| 血液およびリンパ系障害 | 4 (6.6) | 2 (10.5) | 6 (9.8) | 0 | 0 | 3 (7.5) | 1 (2.0) | 10 (6.7) |
| 貧血 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 0 | 1 (0.7) |
| 鉄欠乏性貧血 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 0 | 1 (0.7) |
| 白血球減少症 | 2 (3.3) | 2 (10.5) | 4 (6.6) | 0 | 0 | 1 (2.5) | 1 (2.0) | 6 (4.0) |
| リンパ球減少症 | 2 (3.3) | 0 | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 好中球減少症 | 3 (4.9) | 1 (5.3) | 4 (6.6) | 0 | 0 | 0 | 1 (2.0) | 5 (3.3) |
| 耳および迷路障害 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| メニエール病 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| 眼障害 | 0 | 0 | 0 | 1 (10.0) | 0 | 0 | 0 | 0 |
| ぶどう膜炎 | 0 | 0 | 0 | 1 (10.0) | 0 | 0 | 0 | 0 |

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD (N=61)<br>n (%) | UPA 15 mg QD/ UPA 30 mg QD (N=19)<br>n (%) | Total (N=61)<br>n (%) | Placebo (N=10)<br>n (%) | UPA 7.5 mg QD (N=0)<br>n (%) | UPA 15 mg QD (N=40)<br>n (%) | UPA 30 mg QD (N=49)<br>n (%) | All UPA (N=150)<br>n (%) |
| 胃腸障害 | 3 (4.9) | 1 (5.3) | 4 (6.6) | 1 (10.0) | 0 | 1 (2.5) | 0 | 5 (3.3) |
| 下腹部痛 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 口角口唇炎 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| アフタ性潰瘍 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 潰瘍性大腸炎 | 0 | 0 | 0 | 1 (10.0) | 0 | 0 | 0 | 0 |
| 便秘 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 0 | 1 (0.7) |
| 胃炎 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 口内炎 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 一般・全身障害および投与部位の状態 | 1 (1.6) | 1 (5.3) | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 発熱 | 1 (1.6) | 1 (5.3) | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 感染症および寄生虫症 | 17 (27.9) | 8 (42.1) | 24 (39.3) | 1 (10.0) | 0 | 1 (2.5) | 5 (10.2) | 30 (20.0) |
| COVID-19 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| カンジダ感染 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | SA 1 Population<br>UPA 15 mg QD<br>(N=61)<br>n (%) | SA 1 Population<br>UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>n (%) | SA 1 Population<br>Total<br>(N=61)<br>n (%) | SA 2 Population<br>Placebo<br>(N=10)<br>n (%) | SA 2 Population<br>UPA 7.5 mg QD<br>(N=0)<br>n (%) | SA 2 Population<br>UPA 15 mg QD<br>(N=40)<br>n (%) | SA 2 Population<br>UPA 30 mg QD<br>(N=49)<br>n (%) | SA UPA<br>All UPA<br>(N=150)<br>n (%) |
|---|---|---|---|---|---|---|---|---|
| 感染症および寄生虫症 (Cont.) | | | | | | | | |
| クロストリジウム・ディフィシレ感染 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| ウイルス性結膜炎 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| サイトメガロウイルス感染 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| 爪の皮膚糸状菌症 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 歯肉炎 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| ヘルペス眼感染 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| 帯状疱疹 | 9 (14.8) | 1 (5.3) | 10 (16.4) | 1 (10.0) | 0 | 1 (2.5) | 3 (6.1) | 14 (9.3) |
| インフルエンザ | 1 (1.6) | 1 (5.3) | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 潜伏結核 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 上咽頭炎 | 3 (4.9) | 1 (5.3) | 4 (6.6) | 0 | 0 | 0 | 1 (2.0) | 5 (3.3) |
| 口腔ヘルペス | 2 (3.3) | 1 (5.3) | 3 (4.9) | 0 | 0 | 0 | 0 | 3 (2.0) |
| 咽頭炎 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>n (%) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>n (%) | Total<br>(N=61)<br>n (%) | Placebo<br>(N=10)<br>n (%) | UPA 7.5 mg QD<br>(N=0)<br>n (%) | UPA 15 mg QD<br>(N=40)<br>n (%) | UPA 30 mg QD<br>(N=49)<br>n (%) | All UPA<br>(N=150)<br>n (%) |
| 感染症および寄生虫症 (Cont.) | | | | | | | | |
| 肺炎 | 0 | 2 (10.5) | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 副鼻腔炎 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 皮膚感染 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 上気道感染 | 2 (3.3) | 1 (5.3) | 3 (4.9) | 0 | 0 | 0 | 0 | 3 (2.0) |
| 水痘 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 臨床検査 | 8 (13.1) | 4 (21.1) | 12 (19.7) | 0 | 0 | 0 | 8 (16.3) | 20 (13.3) |
| アラニンアミノトランスフェラーゼ増加 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| アスパラギン酸アミノトランスフェラーゼ増加 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| 血中クレアチンホスホキナーゼ増加 | 3 (4.9) | 3 (15.8) | 6 (9.8) | 0 | 0 | 0 | 1 (2.0) | 7 (4.7) |
| 高比重リポ蛋白増加 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| リンパ球数減少 | 1 (1.6) | 1 (5.3) | 2 (3.3) | 0 | 0 | 0 | 2 (4.1) | 4 (2.7) |
| 好中球数減少 | 2 (3.3) | 0 | 2 (3.3) | 0 | 0 | 0 | 3 (6.1) | 5 (3.3) |

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>n (%) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>n (%) | Total<br>(N=61)<br>n (%) | Placebo<br>(N=10)<br>n (%) | UPA 7.5 mg QD<br>(N=0)<br>n (%) | UPA 15 mg QD<br>(N=40)<br>n (%) | UPA 30 mg QD<br>(N=49)<br>n (%) | All UPA<br>(N=150)<br>n (%) |
| 臨床検査 (Cont.) | | | | | | | | |
| 尿中白血球エステラーゼ陽性 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 白血球数減少 | 4 (6.6) | 0 | 4 (6.6) | 0 | 0 | 0 | 2 (4.1) | 6 (4.0) |
| 代謝および栄養障害 | 5 (8.2) | 0 | 5 (8.2) | 0 | 0 | 2 (5.0) | 0 | 7 (4.7) |
| 脂質異常症 | 2 (3.3) | 0 | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 高コレステロール血症 | 2 (3.3) | 0 | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 高脂血症 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 1 (2.5) | 0 | 2 (1.3) |
| 低蛋白血症 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 0 | 1 (0.7) |
| 筋骨格系および結合組織障害 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 1 (2.5) | 0 | 2 (1.3) |
| 関節障害 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 0 | 1 (0.7) |
| 筋骨格系胸痛 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 0 | 1 (0.7) |
| 四肢痛 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 関節周囲炎 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 0 | 1 (0.7) |

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>n (%) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>n (%) | Total<br>(N=61)<br>n (%) | Placebo<br>(N=10)<br>n (%) | UPA 7.5 mg QD<br>(N=0)<br>n (%) | UPA 15 mg QD<br>(N=40)<br>n (%) | UPA 30 mg QD<br>(N=49)<br>n (%) | All UPA<br>(N=150)<br>n (%) |
| 神経系障害 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 感覚鈍麻 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 腎および尿路障害 | 2 (3.3) | 0 | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 腎機能障害 | 2 (3.3) | 0 | 2 (3.3) | 0 | 0 | 0 | 0 | 2 (1.3) |
| 皮膚および皮下組織障害 | 2 (3.3) | 2 (10.5) | 4 (6.6) | 0 | 0 | 1 (2.5) | 2 (4.1) | 7 (4.7) |
| ざ瘡 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 1 (2.5) | 0 | 2 (1.3) |
| 湿疹 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| 毛孔性角化症 | 1 (1.6) | 0 | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| そう痒症 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |
| 発疹 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (0.7) |
| 脂漏性皮膚炎 | 0 | 1 (5.3) | 1 (1.6) | 0 | 0 | 0 | 0 | 1 (0.7) |

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表16

[redacted]20[redacted] 12:56 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - CLINICAL/STATISTICAL


TABLE 14.3__1.3.1.1.2_J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All_UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| Any adverse event | 69 (57.8) | 23 (85.2) | 92 (62.9) | 4 (55.6) | 0 | 13 (31.2) | 22 (54.2) | 127 (55.6) |
| 血液およびリンパ系障害 | 7 (5.9) | 3 (11.1) | 10 (6.8) | 0 | 0 | 4 (9.6) | 2 (4.9) | 16 (7.0) |
| 貧血 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 鉄欠乏性貧血 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 白血球減少症 | 2 (1.7) | 2 (7.4) | 4 (2.7) | 0 | 0 | 2 (4.8) | 1 (2.5) | 7 (3.1) |
| リンパ球減少症 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 好中球減少症 | 3 (2.5) | 1 (3.7) | 4 (2.7) | 0 | 0 | 0 | 1 (2.5) | 5 (2.2) |
| 耳および迷路障害 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| メニエール病 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 眼障害 | 0 | 0 | 0 | 1 (13.9) | 0 | 0 | 0 | 0 |
| ぶどう膜炎 | 0 | 0 | 0 | 1 (13.9) | 0 | 0 | 0 | 0 |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| 胃腸障害 | 4 (3.4) | 1 (3.7) | 5 (3.4) | 1 (13.9) | 0 | 1 (2.4) | 0 | 6 (2.6) |
| 下腹部痛 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 口角口唇炎 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| アフタ性潰瘍 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 潰瘍性大腸炎 | 0 | 0 | 0 | 1 (13.9) | 0 | 0 | 0 | 0 |
| 便秘 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 胃炎 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 口内炎 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 一般・全身障害および投与部位の状態 | 1 (0.8) | 1 (3.7) | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 発熱 | 1 (0.8) | 1 (3.7) | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| 感染症および寄生虫症 | 33 (27.7) | 11 (40.7) | 44 (30.1) | 2 (27.8) | 0 | 1 (2.4) | 6 (14.8) | 51 (22.3) |
| COVID-19 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| カンジダ感染 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| クロストリジウム・ディフィシレ感染 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| ウイルス性結膜炎 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| サイトメガロウイルス感染 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 爪の皮膚糸状菌症 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 歯肉炎 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| ヘルペス眼感染 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 帯状疱疹 | 10 (8.4) | 1 (3.7) | 11 (7.5) | 2 (27.8) | 0 | 1 (2.4) | 3 (7.4) | 15 (6.6) |
| インフルエンザ | 1 (0.8) | 1 (3.7) | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 潜伏結核 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| 感染症および寄生虫症 (Cont.) | | | | | | | | |
| 上咽頭炎 | 3 (2.5) | 1 (3.7) | 4 (2.7) | 0 | 0 | 0 | 1 (2.5) | 5 (2.2) |
| 口腔ヘルペス | 8 (6.7) | 1 (3.7) | 9 (6.2) | 0 | 0 | 0 | 0 | 9 (3.9) |
| 咽頭炎 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 肺炎 | 0 | 2 (7.4) | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 副鼻腔炎 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 皮膚感染 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 上気道感染 | 3 (2.5) | 1 (3.7) | 4 (2.7) | 0 | 0 | 0 | 0 | 4 (1.8) |
| 水痘 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 臨床検査 | 14 (11.7) | 4 (14.8) | 18 (12.3) | 0 | 0 | 0 | 11 (27.1) | 29 (12.7) |
| アラニンアミノトランスフェラーゼ増加 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| アスパラギン酸アミノトランスフェラーゼ増加 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<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 | 4 (3.4) | 3 (11.1) | 7 (4.8) | 0 | 0 | 0 | 1 (2.5) | 8 (3.5) |
| 高比重リポ蛋白増加 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| リンパ球数減少 | 1 (0.8) | 1 (3.7) | 2 (1.4) | 0 | 0 | 0 | 2 (4.9) | 4 (1.8) |
| 好中球数減少 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 4 (9.9) | 6 (2.6) |
| 尿中白血球エステラーゼ陽性 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 白血球数減少 | 4 (3.4) | 0 | 4 (2.7) | 0 | 0 | 0 | 2 (4.9) | 6 (2.6) |
| 代謝および栄養障害 | 5 (4.2) | 0 | 5 (3.4) | 0 | 0 | 2 (4.8) | 0 | 7 (3.1) |
| 脂質異常症 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 高コレステロール血症 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 高脂血症 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 1 (2.4) | 0 | 2 (0.9) |
| 低蛋白血症 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs) | UPA 15 mg QD/ UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs) | Total (N=61) (PYs=146.2) Events (E/100 PYs) | Placebo (N=10) (PYs=7.2) Events (E/100 PYs) | UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs) | UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs) | UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs) | All UPA (N=150) (PYs=228.5) Events (E/100 PYs) |
| 筋骨格系および結合組織障害 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 4 (9.6) | 0 | 5 (2.2) |
| 関節障害 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 筋骨格系胸痛 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 四肢痛 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 関節周囲炎 | 0 | 0 | 0 | 0 | 0 | 2 (4.8) | 0 | 2 (0.9) |
| 神経系障害 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 感覚鈍麻 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 腎および尿路障害 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 腎機能障害 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 皮膚および皮下組織障害 | 2 (1.7) | 2 (7.4) | 4 (2.7) | 0 | 0 | 1 (2.4) | 2 (4.9) | 7 (3.1) |
| ざ瘡 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 1 (2.4) | 0 | 2 (0.9) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| 皮膚および皮下組織障害 (Cont.) | | | | | | | | |
| 湿疹 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 毛孔性角化症 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| そう痒症 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 発疹 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 脂漏性皮膚炎 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表17

[redacted]20[redacted] 12:56 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - CLINICAL/STATISTICAL


TABLE 14.3__1.3.3_J

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All_UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| Any adverse event | 3 (2.5) | 1 (3.7) | 4 (2.7) | 2 (27.8) | 0 | 1 (2.4) | 7 (17.2) | 12 (5.3) |
| 血液およびリンパ系障害 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 好中球減少症 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 心臓障害 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 完全房室ブロック | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 胃腸障害 | 0 | 0 | 0 | 1 (13.9) | 0 | 0 | 2 (4.9) | 2 (0.9) |
| 潰瘍性大腸炎 | 0 | 0 | 0 | 1 (13.9) | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 埋伏歯 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 肝胆道系障害 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 胆嚢炎 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3 J

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs) | UPA 15 mg QD/ UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs) | Total (N=61) (PYs=146.2) Events (E/100 PYs) | Placebo (N=10) (PYs=7.2) Events (E/100 PYs) | UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs) | UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs) | UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs) | All UPA (N=150) (PYs=228.5) Events (E/100 PYs) |
| 感染症および寄生虫症 | 1 (0.8) | 0 | 1 (0.7) | 1 (13.9) | 0 | 0 | 3 (7.4) | 4 (1.8) |
| 虫垂炎 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| サイトメガロウイルス感染 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 帯状疱疹 | 1 (0.8) | 0 | 1 (0.7) | 1 (13.9) | 0 | 0 | 1 (2.5) | 2 (0.9) |
| 臨床検査 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 1 (2.5) | 2 (0.9) |
| 好中球数減少 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 1 (2.5) | 2 (0.9) |
| 腎および尿路障害 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 尿管結石症 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表18

[redacted]20[redacted] 12:56 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.3.1_J

Treatment-Emergent Adverse Events Leading to Death per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All_UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| Any adverse event | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表19

[redacted]20[redacted] 12:56 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - CLINICAL/STATISTICAL


TABLE 14.3__2.1.1_J

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All_UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| Any adverse event | 16 (13.4) | 4 (14.8) | 20 (13.7) | 1 (13.9) | 0 | 2 (4.8) | 6 (14.8) | 28 (12.3) |
| 心臓障害 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 完全房室ブロック | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 胃腸障害 | 6 (5.0) | 1 (3.7) | 7 (4.8) | 0 | 0 | 0 | 2 (4.9) | 9 (3.9) |
| 腹痛 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 潰瘍性大腸炎 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 1 (2.5) | 2 (0.9) |
| 胃食道逆流性疾患 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 大腸ポリープ | 4 (3.4) | 0 | 4 (2.7) | 0 | 0 | 0 | 0 | 4 (1.8) |
| 埋伏歯 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 肝胆道系障害 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 胆嚢炎 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1 J

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| MedDRA 23.0 System Organ Class<br>Preferred Term | SA 1 Population<br>UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | SA 1 Population<br>UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | SA 1 Population<br>Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | SA 2 Population<br>Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | SA 2 Population<br>UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | SA 2 Population<br>UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | SA 2 Population<br>UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | SA UPA<br>All UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
|---|---|---|---|---|---|---|---|---|
| 感染症および寄生虫症 | 3 (2.5) | 1 (3.7) | 4 (2.7) | 1 (13.9) | 0 | 0 | 3 (7.4) | 7 (3.1) |
| 虫垂炎 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| COVID-19 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| サイトメガロウイルス感染 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 帯状疱疹 | 2 (1.7) | 0 | 2 (1.4) | 1 (13.9) | 0 | 0 | 1 (2.5) | 3 (1.3) |
| 腎盂腎炎 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 筋骨格系および結合組織障害 | 3 (2.5) | 1 (3.7) | 4 (2.7) | 0 | 0 | 0 | 0 | 4 (1.8) |
| 背部痛 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 椎間板突出 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 腰部脊柱管狭窄症 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 骨壊死 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1 J

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<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） | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 肛門性器疣贅 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 神経系障害 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 大脳障害 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 頭痛 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 腎および尿路障害 | 2 (1.7) | 1 (3.7) | 3 (2.1) | 0 | 0 | 0 | 0 | 3 (1.3) |
| 腎結石症 | 2 (1.7) | 0 | 2 (1.4) | 0 | 0 | 0 | 0 | 2 (0.9) |
| 尿管結石症 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表20

[redacted]20[redacted] 12:56 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - CLINICAL/STATISTICAL


TABLE 14.3__2.2.1_J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All_UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| Any adverse event | 3 (2.5) | 3 (11.1) | 6 (4.1) | 1 (13.9) | 0 | 2 (4.8) | 3 (7.4) | 11 (4.8) |
| 眼障害 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 網膜静脈閉塞 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 胃腸障害 | 0 | 1 (3.7) | 1 (0.7) | 1 (13.9) | 0 | 0 | 1 (2.5) | 2 (0.9) |
| 潰瘍性大腸炎 | 0 | 1 (3.7) | 1 (0.7) | 1 (13.9) | 0 | 0 | 1 (2.5) | 2 (0.9) |
| 感染症および寄生虫症 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 1 (2.4) | 1 (2.5) | 3 (1.3) |
| 虫垂炎 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 帯状疱疹 | 0 | 0 | 0 | 0 | 0 | 1 (2.4) | 0 | 1 (0.4) |
| 肺炎 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 臨床検査 | 1 (0.8) | 1 (3.7) | 2 (1.4) | 0 | 0 | 0 | 1 (2.5) | 3 (1.3) |
| γ-グルタミルトランスフェラーゼ増加 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.2.1 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

| | SA 1 Population | | | SA 2 Population | | | | SA UPA |
|---|---|---|---|---|---|---|---|---|
| MedDRA 23.0 System Organ Class<br>Preferred Term | UPA 15 mg QD<br>(N=61)<br>(PYs=119.3)<br>Events<br>(E/100 PYs) | UPA 15 mg QD/<br>UPA 30 mg QD<br>(N=19)<br>(PYs=27.0)<br>Events<br>(E/100 PYs) | Total<br>(N=61)<br>(PYs=146.2)<br>Events<br>(E/100 PYs) | Placebo<br>(N=10)<br>(PYs=7.2)<br>Events<br>(E/100 PYs) | UPA 7.5 mg QD<br>(N=0)<br>(PYs=0.0)<br>Events<br>(E/100 PYs) | UPA 15 mg QD<br>(N=40)<br>(PYs=41.7)<br>Events<br>(E/100 PYs) | UPA 30 mg QD<br>(N=49)<br>(PYs=40.6)<br>Events<br>(E/100 PYs) | All UPA<br>(N=150)<br>(PYs=228.5)<br>Events<br>(E/100 PYs) |
| 臨床検査 (Cont.) | | | | | | | | |
| リンパ球数減少 | 0 | 1 (3.7) | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 白血球数減少 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.5) | 1 (0.4) |
| 皮膚および皮下組織障害 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| ざ瘡 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 血管障害 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |
| 深部静脈血栓症 | 1 (0.8) | 0 | 1 (0.7) | 0 | 0 | 0 | 0 | 1 (0.4) |

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| エナメル上皮腫 | X | | | |
| 術後創感染 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| AENEMIA | 20[redacted] |
| ALLERGIES TO CARBAMAZEPINE | 19[redacted] |
| GASTROESOPHAGEAL REFLUX | 20[redacted] |
| HYPERACTIVITY DISORDER | 19[redacted] |
| LEFT SIDED UC | 20[redacted] |
| LUMBOSCIATALGIA | 20[redacted] |
| RIGHT MAXILLA CYST | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: LEFT MAXILLA SURGERY | 20[redacted] |
| PRIOR PROCEDURES: WRISTLE SURGERY | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 54 | 54 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted]20[redacted] / 55 | [redacted]20[redacted] / 425 | 371 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 426 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| GLUCOCORTICOIDS | NOT REPORTED | OTHER: UNK | Y-M: 20[redacted] |
| MESALAZINE | 4 mg | QD | Y-M: 20[redacted] |
| MEPREDNISONE | 5 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 3.6 g | QD | Y-M: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 3.6 g | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 150 |
| BLOOD AND RELATED PRODUCTS | UNK OTHER: UNK | OTHER: UNK | Y-M: 20[redacted] / 139 | Y-M: 20[redacted] / 169 |
| MESALAZINE | 3.6 g | QD | Y-M: 20[redacted] / 154 | Not reported |
| ACETYLSALICYLIC ACID | 100 mg | QD | Y-M: 20[redacted] / 158 | Not reported |
| TRAMADOL | 20 OTHER: DROPS | OTHER: IF PAIN | Y-M: 20[redacted] / 158 | Not reported |
| CEFALEXIN | 1 g | OTHER: EVERY 8 HOURS | Y-M: 20[redacted] / 169 | Y-M: 20[redacted] / 181 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF MAXILLARY AMELOBLASTOMA. |
| **Preferred term** | エナメル上皮腫 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 575 / 150 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

NOT REPORTED

| | |
|---|---|
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 575 / 150 |
| **Duration of AE** | 1 DAY |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | CEBACEOUS CYST |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #2: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | INFECTION IN THE AREA OF EXTRACTION OF THE LEFT FIBULAR SURGICAL FLAP |
| **Preferred term** | 術後創感染 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 589 / 164 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 606 / 181 |
| **Duration of AE** | 18 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | THE PATIENT UNDERWENT MAXILLARY SURGERY ON [redacted]- [redacted] FOR WHICH HE REQUIRED A SURGICAL FLAP THAT WAS OBTAINED FROM THE LEFT FIBULA AT THE SITE OF THE CURRENT INFECTION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は，アルゼンチンの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，上顎エナメル上皮腫の悪化及び左腓骨皮弁の摘出領域での感染の事象を発現した。関連する病歴は，多動性障害，左上顎手術，右上顎嚢胞，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 及び 2 の臨床経過：**

投与575日後＊ ，被験者は上顎エナメル上皮腫の悪化を発現し，同日回復した。投与 589日後＊，被験者は左腓骨皮弁の摘出領域での感染を発現し，投与606日後＊，消失した。

これらの事象の発現前に，被験者は投与の約4年前＊に右上顎皮脂腺嚢胞手術を行い，投与の約9ヵ月後＊に非重篤な上顎エナメル上皮腫を発現していた。

投与575日後＊ ，被験者は顎骨エナメル上皮腫を含む右上顎領域増大のために入院し，同日上顎エナメル上皮腫の切除に成功した。投与583日後＊，退院した。

投与589日後＊ ，被験者は疼痛及び発熱のため救急治療室を受診した。同日，被験者は顎顔面外科手術による左腓骨の感染により再入院した。治験責任医師によると，顎顔面外科手術には，左腓骨から得られた外科的皮弁が必要であった。被験者は診断により，左腓骨の外科的皮弁の摘出領域の外科的洗浄を提案された。投与590日後＊ ，提案された外科的創傷洗浄が行われた。投与594日後＊，退院した。

被験者には輸血が行われ，投与された薬剤は salysilic acetyl acid，トラマドール及び cefalexina であった。

**The patient's past medications include:**

MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

GLUCOCORTICOID for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MEPREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Ameloblastoma (10066796) (Ameloblastoma (10066796) ) [v.24.0] [10066796]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

2) Surgical site infection (10078408) (Postoperative wound infection (10036410) ) [v.24.0] [10078408]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of WORSENING OF MAXILLARY AMELOBLASTOMA

**- Investigator:** CEBACEOUS CYST

**- AbbVie:** Ameloblastoma is a rare, benign odontogenic tumor whose etiology remains unknown at this time in the medical literature. Additional risk factor is pre-existing right maxillary cyst.

Event of INFECTION IN THE AREA OF EXTRACTION OF THE LEFT FIBULAR SURGICAL FLAP

**- Investigator:** THE PATIENT UNDERWENT MAXILLARY SURGERY ON [redacted] FOR WHICH HE REQUIRED A SURGICAL FLAP THAT WAS OBTAINED FROM THE LEFT FIBULA AT THE SITE OF THE CURRENT INFECTION

**- AbbVie:** Event is more likely a complication from surgical procedure performed on [redacted] 20[redacted], as reported by the investigator

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BIOPSY:** Not reported

[redacted] **20[redacted] BLOOD CULTURE:** Positive: STAPHYLOCOCCUS AURUS METHYL SENSITIVE

[redacted] **20[redacted] WEIGHT:** 6[redacted] KG

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| 前立腺癌 | X | X | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: ANXIETY | NOT REPORTED |
| OTHER: HEMORRHOIDS | 20[redacted] |
| OTHER: LOW VITAMIN D | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 15 | 19[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 54 | 54 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted]20[redacted] / 55 | [redacted]20[redacted] / 418 | 364 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 419 | [redacted]20[redacted] / 1110 | 692 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 4.8 g | QD | Y-M: 20[redacted] |
| BUDESONIDE | 3 mg | QD | Y-M: 20[redacted] |
| MERCAPTOPURINE | 12.5 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: 8 WEEKLY | Y-M: 20[redacted] |
| INFLIXIMAB | 500 mg/kg | OTHER: 8 WEEKLY | Y-M: 20[redacted] |
| MAGNESIUM | 1 OTHER: TABLETS | QD | Y-M: 20[redacted] |
| VITAMIN D NOS | 1000 IU | QD | Y-M: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 4.8 g | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 147 |
| MAGNESIUM | 1 OTHER: TABLETS | QD | Y-M: 20[redacted] | ONGOING |
| VITAMIN D NOS | 1000 IU | QD | Y-M: 20[redacted] | ONGOING |
| MESALAZINE | 2.4 mg | QD | Y-M: 20[redacted] / 148 | Y-M: 20[redacted] / 251 |
| DOXYCYCLINE | 50 mg | QD | Y-M: 20[redacted] / 657 | Y-M: 20[redacted] / 668 |
| ISOTRETINOIN | 10 mg | QD | Y-M: 20[redacted] / 694 | ONGOING |

**Event #1: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | ELEVATED CK |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / InitialRx Day / Rx Day** | [redacted]20[redacted] / 15 / -404 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 1090 / 672 |
| **Duration of AE** | 1076 DAYS |
| **Severity** | MILD |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC**

| | |
|---|---|
| **Event Description** | PROSTATE CANCER |
| **Preferred term** | 前立腺癌 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1014 / 596 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 539): NPTST265-PSA: 6.3 [0.3 - 4.5] UG/L;
[redacted]20[redacted] (RX DAY 547): NPTST265-PSA: 11.45 [0.3 - 4.5] UG/L;
[redacted]20[redacted] (RX DAY 706): NPTST265-PSA: 5.43 [0.3 - 4.5] UG/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | FAMILY HISTORY - BROTHER ALSO HAD RADICAL PROSTATECTOMY |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストラリアの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，前立腺癌の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 15 年間），潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

**Event 2 の臨床経過：**

投与1014日後＊，被験者は前立腺癌を発現した。

本事象により，治験薬の投与は完全に中止された。

治験責任医師によると，投与の約32ヵ月後＊からの PSA 上昇（11.34 ug/L）の病歴が本事象と関連のある危険因子であった。

**The patient's past medications include:**

MEZAVANT for ULCERATIVE COLITIS ([redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted])

6 MERCAPTOPURINE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

---

1) Prostate cancer (10060862) (Prostate cancer (10060862) ) [v.24.0] [10060862]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of PROSTATE CANCER

**- Investigator:** Family history - Brother also had radical prostatectomy

**- AbbVie:** Approximately 12.1 percent of men will be diagnosed with prostate cancer at some point during their lifetime. The highest incidence is in the age group greater than 50 years and older. Additional risk factors include age and family history.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] MRI PROSTATE:** PI-RADS 5 lesion, prostate base transition zone on the right, with likely microscopic extra capsular extension

[redacted] **20[redacted] PET CT:** The 18F-DCFPyl PET demonstrates a focus of intensely avid tracer uptake in the right anterior aspect of the prostatic base extending into the mid to involving the transition zone. This is most suspicious for a primary tumour. The remainder of the gland has heterogeneous mildly to moderately increased activity suggesting inflammatory change. No evidence for tracer avid local regional or distant metastatic disease.

[redacted] **20[redacted] PROSTATE BIOPSY:** Transperineal prostate core biopsies. Prostate adenocarcinoma, involving two sites (3 cores), Gleason score 3+3=6 (Grade Group 1).

[redacted] **20[redacted] PSA:** 6.3 ug/L (normal 0.30 to 4.5)

[redacted] **20[redacted] PSA:** 11.45 ug/L (normal 0.3 to 4.5)

[redacted] **20[redacted] PSA:** 5.43 ug/L (normal 0.3 to 4.5)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 滑液包炎 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 4[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| OTHER: KIDNEY STONES (SELF-RESOLVED) | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: INGUINAL HERNIA REPAIR | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 59 | 59 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 60 | [redacted]20[redacted] / 423 | 364 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted]20[redacted] / 424 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 2 g | OTHER: DAILY | Y: 20[redacted] |
| MESALAZINE | 4.8 g | OTHER: DAILY | Y: 20[redacted] |
| BUDESONIDE | 1.2 g | OTHER: DAILY | Y: 20[redacted] |
| BUDESONIDE | 2016 mg | QD | Y: 20[redacted] |
| PREDNISOLONE | 5 mg | OTHER: DAILY | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| CEFALEXIN | 500 mg | QID | Y-M: 20[redacted] / 392 | Y-M: 20[redacted] / 392 |
| FLUCLOXACILLIN | 2 g | OTHER: 6/24 | Y-M: 20[redacted] / 392 | Y-M: 20[redacted] / 396 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 393 | Y-M: 20[redacted] / 395 |
| OXYCODONE | 2.5 mg | PRN | Y-M: 20[redacted] / 393 | Y-M: 20[redacted] / 393 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 393 | Y-M: 20[redacted] / 395 |
| LORATADINE | 10 mg | PRN | Y-M: 20[redacted] / 394 | Y-M: 20[redacted] / 394 |
| FLUCLOXACILLIN | 1 g | TID | Y-M: 20[redacted] / 396 | Y-M: 20[redacted] / 413 |
| MESALAZINE | 4.8 g | OTHER: DAILY | Y: 20[redacted] | Not reported |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | BURSITIS RIGHT ELBOW |
| **Preferred term** | 滑液包炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 752 / 329 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 392): Lymphocytes/Leukocytes: 25 [45 - 75] %; Monocytes/Leukocytes: 0 [2 - 8] %; NPTST204-LEUCOCYTES: 11400 [0 - 203] U/L; Neutrophils/Leukocytes: 75 [55 - 70] %

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | PT LIFTS WEIGHTS AND HAS HAD PREVIOUS TENNIS ELBOW |

| | |
|---|---|
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

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Program Source Code:[redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストラリアの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右肘の滑液包炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，腎結石，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与752日後＊，被験者は右肘の滑液包炎を発現した。

投与813日後＊　の朝，被験者は肘に痛みを感じ始めた。午後からは，被験者は肘周辺の腫脹に気づき始めた。投与814日後＊　，被験者は紅斑を発現した。被験者は医師の診察を受け，実際に熱は出ておらず，セファレキシンを投与された。被験者は自宅で 2 回分を既に服用していた。医師は関節穿刺を行い，数ミリリットルの透明な黄色の液体を吸引した。午後 6 時頃，被験者の体温は摂氏 37.8°C 及び 38°C を記録し，ふらつきを感じた。医師は，被験者に救急科を受診するよう助言した。投与815日後＊　，被験者は入院した。肘部位への直接の損傷はなく，他の感染性の症状もなく，他の関節にも痛みはなかった。肘に氷を当てたところ，痛みが悪化した。被験者は肘に体重をかけることはできるが，痛みを感じていた。フルクロキサシリンの静脈内投与が開始された。投与816日後＊　，超音波検査が実施された。投与819日後＊　　，被験者は，フルクロキサシリンを経口投与され，退院した。

治験責任医師によると，被験者はテニス肘の病歴があった。

投与された薬剤は，エノキサパリン，セファレキシン，フルクロキサシリン，paracetamol，オキシコドン及びロラタジンであった。

**The patient's past medications include:**

SALOFALK for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

BUDENOFALK for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

CORTIMENT for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Elbow bursitis (10073532) (Bursitis (10006811) ) [v.23.0] [10073532]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of BURSITIS RIGHT ELBOW

**- Investigator:** PT LIFTS WEIGHTS AND HAS HAD PREVIOUS TENNIS ELBOW

**- AbbVie:** Risk factors include frequent exercise involving the elbow as well as prior history of tennis elbow as noted by PI.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] RIGHT ELBOW ASPIRATE LEUKOCYTES:** 11400 U/L (normal 0 to 203)

[redacted] **20[redacted] RIGHT ELBOW ASPIRATE LYMPHOCYTES:** 25 % (normal 45 to 75)

[redacted] **20[redacted] RIGHT ELBOW ASPIRATE MONOCYTES:** 0 % (normal 2 to 8)

[redacted] **20[redacted] RIGHT ELBOW ASPIRATE NEUTROPHILS:** 75 % (normal 55 to 70)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 貧血 | | | | X |
| ニューモシスチス・イロベチイ感染 | | | | X |
| 肺炎 | X | | | X |
| 肺腫瘤 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ASTHMA | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| PNEUMONIA | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 59 | 59 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 60 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| BECLOMETASONE;FORMOTEROL | 1 DF | BID | Y-M: 20[redacted] |
| LECITHIN | 1 DF | TID | Y-M: 20[redacted] / -337 |
| MESALAZINE | 1 DF | QD | Y-M: 20[redacted] / -306 |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] / -306 |
| INFLIXIMAB | 10 g | OTHER: EVERY 8 WEKS | Y-M: 20[redacted] / -241 |
| TIOTROPIUM | 18 OTHER: MCG | QD | Y-M: 20[redacted] / -155 |
| MAGNESIUM CARBONATE;MAGNESIUM OXIDE | 1 DF | OTHER: TWICE PER WEEK | Y-M: 20[redacted] / -60 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| BECLOMETASONE;FORMOTEROL | 1 DF | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 39 |
| LECITHIN | 1 DF | TID | Y-M: 20[redacted] / -337 | Y-M: 20[redacted] / 179 |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] / -306 | Y-M: 20[redacted] / 140 |
| TIOTROPIUM | 18 OTHER: MCG | QD | Y-M: 20[redacted] / -155 | Y-M: 20[redacted] / 39 |
| MAGNESIUM CARBONATE;MAGNESIUM OXIDE | 1 DF | OTHER: TWICE PER WEEK | Y-M: 20[redacted] / -60 | Y-M: 20[redacted] / 26 |
| BECLOMETASONE;FORMOTEROL | 2 DF | BID | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 144 |
| MOXIFLOXACIN | 400 mg | QD | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 42 |
| TIOTROPIUM | 5 OTHER: MCG | QD | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 144 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 41 | Y-M: 20[redacted] / 49 |
| AZITHROMYCIN | 1.5 g | QD | Y-M: 20[redacted] / 42 | Y-M: 20[redacted] / 42 |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 42 | Y-M: 20[redacted] / 48 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 42 | Y-M: 20[redacted] / 50 |
| DEXIBUPROFEN | 400 mg | TID | Y-M: 20[redacted] / 81 | Y-M: 20[redacted] / 87 |
| AZELASTINE;FLUTICASONE | 1 OTHER: PUFF | BID | Y-M: 20[redacted] / 83 | Y-M: 20[redacted] / 112 |
| PROBIOTICS [UMBRELLA TERM] | 1 DF | BID | Y-M: 20[redacted] / 137 | Y-M: 20[redacted] / 303 |
| SULFAMETROLE;TRIMETHOPRIM | 1 DF | TID | Y-M: 20[redacted] / 137 | Y-M: 20[redacted] / 303 |
| TIOTROPIUM | 2.5 OTHER: MCG | QD | Y-M: 20[redacted] / 145 | Y-M: 20[redacted] / 180 |

| | | | | |
|---|---|---|---|---|
| LECITHIN | 1 DF | BID | Y-M: 20[redacted] / 180 | Y-M: 20[redacted] / 348 |
| PROBIOTICS [UMBRELLA TERM] | 1 DF | PRN | Y-M: 20[redacted] / 304 | ONGOING |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 330 | Y-M: 20[redacted] / 330 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 362 | Y-M: 20[redacted] / 362 |
| LACTOBACILLUS ACIDOPHILUS | 2 DF | TID | Y-M: 20[redacted] / 605 | Y-M: 20[redacted] / 607 |
| SACCHAROMYCES BOULARDII | 2 DF | TID | Y-M: 20[redacted] / 605 | Y-M: 20[redacted] / 607 |
| BECLOMETASONE;FORMOTEROL | 100/6 ug | BID | Y-M: 20[redacted] / 709 | Y-M: 20[redacted] / 809 |
| FENOTEROL;IPRATROPIUM | 1 DF | PRN | Y-M: 20[redacted] / 709 | ONGOING |
| INFLUENZA VACCINE | 1 DF | OTHER: ONCE | Y-M: 20[redacted] / 729 | Y-M: 20[redacted] / 729 |
| BECLOMETASONE;FORMOTEROL | 200/12 ug | BID | Y-M: 20[redacted] / 810 | ONGOING |
| MONTELUKAST | 10 mg | QD | Y-M: 20[redacted] / 810 | Y-M: 20[redacted] / 911 |
| SODIUM PHOSPHATE | 1 DF | QD | Y-M: 20[redacted] / 1016 | Y-M: 20[redacted] / 1016 |
| INFLUENZA VACCINE | 0.5 mL | QD | Y-M: 20[redacted] / 1068 | Y-M: 20[redacted] / 1068 |
| MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 4000 mL | OTHER: ONCE | Y-M: 20[redacted] / 1354 | Y-M: 20[redacted] / 1354 |
| PROPOFOL | 260 mg | OTHER: ONCE | Y-M: 20[redacted] / 1355 | Y-M: 20[redacted] / 1355 |
| INFLUENZA VACCINE | 0.5 mL | OTHER: ONCE | Y-M: 20[redacted] / 1485 | Y-M: 20[redacted] / 1485 |

**Event #1: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 81 / 22 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 142 / 83 |
| **Duration of AE** | 62 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | PNEUMONIA |
| **Preferred term** | 肺炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 98 / 39 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

[redacted]20[redacted] (RX DAY 41): BLOOD NPTST035-ANTIGEN OF ASPERGILLUS SPP.: Negative; BLOOD NPTST036-ANTIGEN OF CRYPTOCOCCUS NEOFORM: Negative; SPUTUM NPTST043-BACTERIAL AND FUNGAL CULTURE: Negative; URINE NPTST290-S. PNEUMONIAE AND L. PNEUMOPHIL: Negative; [redacted]20[redacted] (RX DAY 42): BLOOD NPTST109-CULTURE: Negative

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 107 / 48 |
| **Duration of AE** | 10 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | PNEUMONIA |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zoster**

| | |
|---|---|
| **Event Description** | PRESENCE IF PNEUMOCYSTIS JIROVECII IN LUNG |
| **Preferred term** | ニューモシスチス・イロベチイ感染 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 102 / 43 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

NOT APPLICABLE

| | |
|---|---|
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 362 / 303 |
| **Duration of AE** | 261 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #4: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | ENLARGEMENT OF PULMONARY NODULE IN RIGHT LUNG FROM 3 TO 4 MM |
| **Preferred term** | 肺腫瘤 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 135 / 76 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| [redacted]20[redacted] (RX DAY 124): OTHER BRONCHOALVEOLAR LAVAGE NPTST109-CULTURE: Positive-MORAXELLA CATARRHALIS 10E4 CBU/ML | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | UNKNOWN |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

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Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストリアの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，喘息，肺炎，非喫煙者及び非飲酒者であった。

**Event 2 の臨床経過：**

投与98日後＊，被験者は肺炎を発現した。投与107日後＊，肺炎は消失した。

投与98日後＊　　，被験者は発熱及び咳嗽があり，入院した。投与99日後＊　，胸部 CT 検査で右肺の上葉に肺炎を認めた。被験者は抗生物質で治療された。投与109日後＊　，被験者は退院した。

投与された薬剤は pantoloc，アベロックス，セフトリアキソン，zithromax 及び lovenox であった。

**The patient's past medications include:**

SALOFALK KLYSMEN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK SUPP for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IFX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

---

1)　Pneumonia (10035664)　(Pneumonia (10035664) )　[v.20.1]　[10035664]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of PNEUMONIA

**- Investigator:** Pneumonia.

**- AbbVie:** Not applicable.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ANTIGEN OF ASPERGILLUS SPP.:** Negative.

[redacted] **20[redacted] ANTIGEN OF CRYPTOCOCCUS NEOFORMANS:** Negative.

[redacted] **20[redacted] BLOOD CULTURE:** Negative.

[redacted] **20[redacted] BRONCHOSCOPY:** Reddening of mucosa.

[redacted] **20[redacted] CHEST X RAY:** Consolidation in right upper part of the lung.

[redacted] **20[redacted] CHEST X RAY:** Compared to chest x ray of [redacted] 20[redacted] consolidation almost completely gone.

[redacted] **20[redacted] CT OF THORAX:** Pneumonia in right upper lobe

[redacted] **20[redacted] SPUTUM-BACTERIAL AND FUNGAL CULTURE:** Negative.

[redacted] **20[redacted] URINE- S. PNEUMONIAE AND L. PNEUMOPHILA:** Negative.
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストリアの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，右肺の肺結節の腫大（3 mm から 4 mm）の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 4 の臨床経過：**

投与135日後＊，被験者は右肺の肺結節の腫大（3 mm から 4 mm）を発現した。

被験者は，臨床的な徴候及び症状はなかった。投与182日後＊，被験者は小さな肺結節があるため，入院した。投与183日後＊，被験者は気管支鏡検査及び生検を受け，肺炎が発見されたが，結節の組織検査及び組織培養では原因不明であった。同日，被験者は退院した。

Causality for UPADACITINIB (Open Label)

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1) Lung nodule (10049498) (Pulmonary mass (10056342) ) [v.24.0] [10049498]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of ENLARGEMENT OF PULMONARY NODULE IN RIGHT LUNG FROM 3 TO 4 MM

**- Investigator:** Unknown

**- AbbVie:** Event is more likely related to prior pneumonia.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BRONCHOALVEOLAR CULTURE: Positive:** Moraxella catarrhalis; 10E4 CBU/ml

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| COVID-19 | X | | | X |
| COVID-19 肺炎 | X | | | X |
| 前立腺特異性抗原増加 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA | 20[redacted] |
| APPENDICITIS | 20[redacted] |
| AXIAL HIATUS HERNIA | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| FRACTURED RIBS | 20[redacted] |
| INTOLERANCE TO AZATHIOPRIN | 20[redacted] |
| NODULI HEMORRHOIDALES GRAD III | 20[redacted] |
| SEPTOPLASTY | 20[redacted] |
| STATUS POST CYTOMEGALOVIRUS | NOT REPORTED |
| STATUS POST EPSTEIN BARR VIRUS | NOT REPORTED |
| TURBINOPLASTY | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: APPENDECTOMY | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1.5 PACK | 29 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 60 | 60 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted] / 61 | [redacted] / 109 | 49 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted] / 110 | [redacted] / 472 | 363 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted] / 473 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 3000 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: EVERY WEEK | Y-M: 20[redacted] |
| MESALAZINE | 1000 mg | QD | Y-M: 20[redacted] |
| SULTAMICILLIN | 1 g | TID | Y-M: 20[redacted] |
| SULTAMICILLIN | 3 g | TID | Y-M: 20[redacted] |
| BUDESONIDE | 9 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1000 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] |
| PREDNISOLONE | 10 mg | QD | Y-M: 20[redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] |
| METAMIZOLE | 20 gtt | PRN | Y-M: 20[redacted] |
| COLECALCIFEROL-CHOLESTERIN | 5 gtt | QD | Y-M: 20[redacted] / -301 |
| MESALAZINE | 1000 mg | OTHER: 2 TIMES A WEEK | Y-M: 20[redacted] / -111 |
| MESALAZINE | 4 g | OTHER: 5 TIMES A WEEK | Y-M: 20[redacted] / -111 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 3000 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 405 |
| METAMIZOLE | 20 gtt | PRN | Y-M: 20[redacted] | Not reported |
| COLECALCIFEROL-CHOLESTERIN | 5 gtt | QD | Y-M: 20[redacted] / -301 | Y-M: 20[redacted] / 405 |
| MESALAZINE | 1000 mg | OTHER: 2 TIMES A WEEK | Y-M: 20[redacted] / -111 | Y-M: 20[redacted] / 405 |
| MESALAZINE | 4 g | OTHER: 5 TIMES A WEEK | Y-M: 20[redacted] / -111 | Not reported |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] / 246 | Y-M: 20[redacted] / 281 |
| ATORVASTATIN | 20 mg | OTHER: EVERY OTHER DAY | Y-M: 20[redacted] / 282 | Y-M: 20[redacted] / 405 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: BAG | QD | Y-M: 20[redacted] / 315 | Y-M: 20[redacted] / 316 |
| PROPOFOL | 180 mg | QD | Y-M: 20[redacted] / 316 | Y-M: 20[redacted] / 316 |
| ATROPINE | UNK | OTHER: UNKNOWN | Y-M: 20[redacted] / 406 | Y-M: 20[redacted] / 406 |
| DOBUTAMINE | UNKNOWN | OTHER: UNKNOWN | Y-M: 20[redacted] / 406 | Y-M: 20[redacted] / 406 |
| SULTAMICILLIN | UNKNOWN | OTHER: UNKNOWN | Y-M: 20[redacted] / 406 | Y-M: 20[redacted] / 413 |
| CEFEPIME | UNKNOWN | OTHER: UNKNOWN | Y-M: 20[redacted] / 414 | Y-M: 20[redacted] / 446 |
| DEXAMETHASONE | 4 mg | BID | Y-M: 20[redacted] / 433 | Y-M: 20[redacted] / 438 |
| BUDESONIDE | 9 mg | QD | Y-M: 20[redacted] / 439 | Y-M: 20[redacted] / 442 |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] / 446 | Not reported |
| COLECALCIFEROL-CHOLESTERIN | 5 gtt | QD | Y-M: 20[redacted] / 446 | Not reported |
| MESALAZINE | 1000 mg | PRN | Y-M: 20[redacted] / 446 | Not reported |
| MESALAZINE | 3000 mg | QD | Y-M: 20[redacted] / 446 | Not reported |

**Event #1: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | INCREASED CREATINKINASE LAB VALUE |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 305 / -168 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 5[redacted] |

| | |
|---|---|
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 753 / 281 |
| **Duration of AE** | 449 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Event of Interest - Possible Malignancies**

| | |
|---|---|
| **Event Description** | ELEVATED LAB PSA VALUE |
| **Preferred term** | 前立腺特異性抗原増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 452 / -21 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #3: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | INCREASED CREATINKINASE LAB VALUE |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 753 / 281 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #4: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | COVID 19 INFECTION |
| **Preferred term** | COVID-19 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 877 / 405 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 405): NPTST108-CRP: 13.8 [0 - 0.6] MG/DL; NPTST190-INTERLEUKIN 6: 153 [0 - 7] 099,PG/ML; [redacted]20[redacted] (RX DAY 409): NPTST190-INTERLEUKIN 6: 1870 [0 - 7] 099,PG/ML; [redacted]20[redacted] (RX DAY 410): NPTST108-CRP: 29 [0 - 0.6] MG/DL; [redacted]20[redacted] (RX DAY 421): NPTST190-INTERLEUKIN 6: 73.2 [0 - 7] 099,PG/ML; [redacted]20[redacted] (RX DAY 432): NPTST108-CRP: 2.5 [0 - 0.6] MG/DL

**Microbiology**

[redacted]20[redacted](RX DAY 408): SPUTUM NPTST309-STAPHYLOCOCCUS EPIDERMIS: Positive-BACTERIAL SUPERINFECTION BY COVID-19 INFECTION; [redacted]20[redacted] (RX DAY 414): SPUTUM NPTST127-ENTEROBACTER AEROGENES: Positive-BACTERIAL SUPERINFECTION BY COVID-19 INFECTION

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 904 / 432 |
| **Duration of AE** | 28 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | COVID 19 VIRUS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING |

**Event #5: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | COVID-19 PNEUMONIA |

| | |
|---|---|
| **Preferred term** | COVID-19 肺炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 878 / 406 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted] (RX DAY 405): NPTST108-CRP: 13.8 [0 - 0.6] MG/DL; NPTST190-INTERLEUKIN 6: 153 [0 - 7] 099,PG/ML; [redacted]20[redacted] (RX DAY 409): NPTST190-INTERLEUKIN 6: 1870 [0 - 7] 099,PG/ML; [redacted]20[redacted] (RX DAY 410): NPTST108-CRP: 29 [0 - 0.6] MG/DL; [redacted]20[redacted] (RX DAY 421): NPTST190-INTERLEUKIN 6: 73.2 [0 - 7] 099,PG/ML; [redacted]20[redacted] (RX DAY 432): NPTST108-CRP: 2.5 [0 - 0.6] MG/DL | |
| **Microbiology** | |
| [redacted]20[redacted] (RX DAY 408): SPUTUM NPTST309-STAPHYLOCOCCUS EPIDERMIS: Positive-BACTERIAL SUPERINFECTION BY COVID-19 INFECTION; [redacted]20[redacted] (RX DAY 414): SPUTUM NPTST127-ENTEROBACTER AEROGENES: Positive-BACTERIAL SUPERINFECTION BY COVID-19 INFECTION | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | COVID 19-INFECTION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストリアの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化した治験薬が投与され，COVID-19 感染症と COVID-19 肺炎を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 29 年間），潰瘍性大腸炎，サイトメガロウイルス感染後，エプスタイン・バーウイルス感染後及び元飲酒者（1 日 2 杯未満）であった。

**Event 4 及び 5 の臨床経過：**

投与877日後＊　　，被験者は COVID-19 に感染し，投与878日後＊　　に COVID-19 肺炎を発現した。投与904日後＊に COVID-19 感染症は消失した。



＊新薬承認情報提供時に置き換え

投与877日後＊　　，被験者は食欲不振，5 日間の水分摂取減少及び呼吸困難を訴えて救急車で救急治療室を受診した。被験者は自宅でトイレに行く途中で倒れ，搬送中に非侵襲的換気を必要とした。同日，被験者の酸素飽和度が低下し挿管された。投与878日後＊　　，換気はチューブ付き Cpap モードに変更された。投与890日後＊　　，抜管されマスクを介して酸素が供給された。被験者の酸素圧が変化し，オプトフローに切り替えられた。その後，被験者は再び非侵襲的換気を必要とした。投与891日後＊　　，非侵襲的酸素サポートは不要になり，オプトフローのみとなった。投与893日後＊，被験者は集中治療室から肺科に移された。投与910日後＊　　，被験者は在宅で酸素療法を行うことで退院した。

被験者は免疫抑制薬服用により発現した事象に関連した危険因子を有しており，COVID-19 のワクチン接種を受けていなかった。

投与された薬剤は，atropin，dobutrex，unasyn，fortecortin, leovit 及び酸素であった。

**The patient's past medications include:**

APREDNISLON for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

ANAEROBEX for ULCERATIVE COLITIS ([redacted])

CIPROFLOXACIN for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

---

1)　COVID-19 (10084268)　(COVID-19 (10084268) )　[v.24.1]　[10084268]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

2)　COVID-19 pneumonia (10084380)　(COVID-19 pneumonia (10084380) )　[v.24.1]　[10084380]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of COVID 19 INFECTION

**- Investigator:** COVID 19 VIRUS

**- AbbVie:** Event is more likely related to the COVID-19 pandemic outbreak.

Event of COVID PNEUMONIA

**- Investigator:** COVID 19-INFECTION

**- AbbVie:** Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BMI:** 29.6 kg/m2

[redacted] **20[redacted] BODY TEMPERATURE:** 37.5 Degrees C

[redacted] **20[redacted] COVID TEST:** PCR: Positive LINEAGE B.1.617.2, CT VALUE WAS 11.10

[redacted] **20[redacted] COVID TEST:** Positive

[redacted] **20[redacted] COVID TEST:** Negative

[redacted] **20[redacted] CRP:** 13.8 mg/dL (normal 0 to 0.6)

[redacted] **20[redacted] CRP:** 29 mg/dL (normal 0 to 0.6)

[redacted] **20[redacted] CRP:** 2.5 mg/dL (normal 0 to 0.6)

[redacted] **20[redacted] ENTEROBACTER AEROGENES:** Sputum: Positive BACTERIAL SUPERINFECTION BY COVID-19 INFECTION

[redacted] **20[redacted] INTERLEUKIN 6:** 153 PG/ML (normal 0 to 7.0)

[redacted] **20[redacted] INTERLEUKIN 6:** 1870 PG/ML (normal 0 to 7.0)

[redacted] **20[redacted] INTERLEUKIN 6:** 73.2 PG/ML (normal 0 to 7.0)

[redacted] **20[redacted] OXYGEN SATURATION:** Dropped

[redacted] **20[redacted] SPO2:** 89 %

[redacted] **20[redacted] STAPHYLOCOCCUS EPIDERMIS:** Sputum: Positive BACTERIAL SUPERINFECTION BY COVID-19 INFECTION

[redacted] **20[redacted] THORAX RONTGEN:** INFECTIOUS INFILTRATES ON BOTH LUNGS

[redacted] **20[redacted] THORAX RONTGEN:** CONDITION IMPROVING

[redacted] **20[redacted] THORAX RONTGEN:** PNEUMONIA, NO RELEVANT CHANGES

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: ALLERGY OF HOUSE DUST AND CAT HAIR | 20[redacted] |
| OTHER: BROKEN ARM | 20[redacted] |
| OTHER: EXANTHEMA WHOLE BODY | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: ADENECTOMY | 19[redacted] |
| SURGERY: TONSILLECTOMY | 19[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 55 | 55 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 56 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| AZATHIOPRINE | 225 mg | QD | Y-M: 20[redacted] |
| GOLIMUMAB | 50 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 100 mg | OTHER: EVERY 4 WEEKS | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] / -358 |
| SULFAMETROLE;TRIMETHOPRIM | 400 mg | QD | Y-M: 20[redacted] / -280 |
| AZATHIOPRINE | 100 mg | QD | Y-M: 20[redacted] / -150 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PREDNISOLONE | 50 mg | QD | Y-M: 20[redacted] / 242 | Y-M: 20[redacted] / 242 |
| ELECTROLYTES NOS | 500 mL | QD | Y-M: 20[redacted] / 243 | Y-M: 20[redacted] / 243 |
| ELECTROLYTES NOS | 500 mL | BID | Y-M: 20[redacted] / 244 | Y-M: 20[redacted] / 244 |
| ELECTROLYTES NOS | 500 mL | QD | Y-M: 20[redacted] / 245 | Y-M: 20[redacted] / 245 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF COLITIS ULCEROSA |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 298 / 243 |
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 243): Alkaline Phosphatase: 69 [30 - 120] U/L; Bilirubin: 14.880384 [0 - 20.524668] UMOL/L; Calcium: 2.4 [2.2 - 2.6] MMOL/L; Creatinine: 89.287293 [61.882282 - 106.083912] UMOL/L; NPTST071-CALPROTECTIN: 1000 [0 - 50] ?G/G; NPTST108-CRP: 0.84 [0 - 0.5] MG/DL; NPTST201-LDH: 217 [0 - 248] U/L; Potassium: 3.85 [3.6 - 4.8] MMOL/L; Sodium: 143 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 244): NPTST071-CALPROTECTIN: >1000 [0 - 50] ?G/G

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 301 / 246 |
| **Duration of AE** | 4 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | SUSPECTED FLARE OF STUDY DISEASE OR DUE TO INFECTION, |

| | |
|---|---|
| | FURTHER INVESTIGATIONS HAVE TO BE DONE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code:[redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストリアの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

**Event 1 の臨床経過：**

投与298日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与301日後＊　，潰瘍性大腸炎の悪化は消失した。

投与298日後＊　，被験者は治療のために入院した。被験者は 1 日に 8–10 回の排便と共に血便を経験した。被験者は prednisolon を 1 日 5 mg から 1 日 50 mg に増量し，治療を受けた。入院中に合併症は報告されず，手術も行われなかった。投与301日後＊，被験者は退院した。

投与された薬剤は，elomel 及び prednisolon であった。

**The patient's past medications include:**

SIMPONI for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900) )　[v.23.1]　[10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of WORSENING OF COLITIS ULCEROSA

**- Investigator:** Suspected flare of study disease or due to infection, further investigations have to be done.

**- AbbVie:** Event is more likely related to flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 69 U/L (normal 30 to 120)

[redacted] **20[redacted] BILIRUBIN TEST:** 0.87 mg/dL (normal 0 to 1.20)

[redacted] **20[redacted] CALCIUM:** 2.40 MCMOL/L (normal 2.20 to 2.60)

[redacted] **20[redacted] CREATININE:** 1.01 mg/dL (normal 0.7 to 1.2)

[redacted] **20[redacted] CRP:** 0.84 mg/dL (normal 0 to 0.50)

[redacted] **20[redacted] ENDOSCOPY:** Mayo score 1-3

[redacted] **20[redacted] LDH:** 217 U/L (normal 0 to 248)

[redacted] **20[redacted] POTASSIUM:** 3.85 MMOL/L (normal 3.60 to 4.80)

[redacted] **20[redacted] SODIUM:** 143 MMOL/L (normal 135 to 145)

[redacted] **20[redacted] STOOL CALPROTECTIN:** 1000 ug/dL (normal 0 to 50)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 胸痛 | X | | | |
| 帯状疱疹 | | | | X |
| 腱断裂 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| COGNITIVE OR PSYCHIATRIC DISORDER: INSOMNIA | 20[redacted] |
| HEARING DISORDER: TINNITUS | NOT REPORTED |
| HYPOTHYROIDISM | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.14 PACK | 8 | 19[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 7.5 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 59 | 59 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 60 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| CALCIUM CARBONATE;ERGOCALCIFEROL | 500 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1000 mg | OTHER: 3 TIMES WEEKLY | Y-M: 20[redacted] |
| MESALAZINE | 3000 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 4 g | OTHER: 2 TIMES PER WEEK | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| CEFUROXIME | 500 mg | BID | Y-M: 20[redacted] |
| COLECALCIFEROL-CHOLESTERIN | 30 gtt | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 300 mg | OTHER: EVERY 4 WEEKS | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 4 WEEKS | Y-M: 20[redacted] |
| MOXIFLOXACIN | 400 mg | BID | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| LEVOTHYROXINE | 88 ug | QD | Y-M: 20[redacted] / -184 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / -16 |
| TRIAZOLAM | 0,25 mg | OTHER: AS NEEDED | Y: 20[redacted] |
| METAMIZOLE | 30 mg | OTHER: AS NEEDED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| CALCIUM CARBONATE;ERGOCALCIFEROL | 500 mg | QD | Y-M: 20[redacted] | Not reported |
| MESALAZINE | 3000 mg | QD | Y-M: 20[redacted] | Not reported |
| COLECALCIFEROL-CHOLESTERIN | 30 gtt | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 600 |
| LEVOTHYROXINE | 88 ug | QD | Y-M: 20[redacted] / -184 | Not reported |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / -16 | Y-M: 20[redacted] / 509 |
| PRAMIPEXOLE | 0.18 mg | PRN | Y-M: 20[redacted] / 250 | Not reported |
| PANTOPRAZOLE | 20 mg | QD | Y-M: 20[redacted] / 510 | ONGOING |
| AMLODIPINE | 5 mg | OTHER: AS NEEDED | Y-M: 20[redacted] / 794 | Y-M: 20[redacted] / 876 |
| CANDESARTAN | 8 mg | BID | Y-M: 20[redacted] / 794 | Not reported |
| AMLODIPINE;CANDE | 8/5 mg | OTHER: ONCE A DAY | Y-M: 20[redacted] / 846 | Not reported |

| | | | | |
|---|---|---|---|---|
| SARTAN | | | | |
| CARBOMER;HYALURONIC ACID;XANTHAN GUM | 3 OTHER: TABLETTS | TID | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 936 |
| MOMETASONE | 1 OTHER: HUB | BID | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 936 |
| COLECALCIFEROL-CHOLESTERIN | 30 gtt | QD | Y-M: 20[redacted] / 1090 | Not reported |
| TRIAMCINOLONE | 10 mg | OTHER: ONCE | Y-M: 20[redacted] / 1091 | ONGOING |
| MAGNESIUM | NA mg | OTHER: ONE CAPSULE TWICE A DAY | Y-M: 20[redacted] / 1093 | Y-M: 20[redacted] / 1114 |
| LIDOCAINE | 5 mL | OTHER: ONCE | Y-M: 20[redacted] / 1170 | Y-M: 20[redacted] / 1170 |
| TRIAMCINOLONE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 1170 | Y-M: 20[redacted] / 1170 |
| METAMIZOLE | 500 mg | QD | Y-M: 20[redacted] / 1265 | Y-M: 20[redacted] / 1301 |
| METAMIZOLE | 500 MG mg | OTHER: 3X2 | Y-M: 20[redacted] / 1267 | Y-M: 20[redacted] / 1301 |
| TRAMADOL | 15 GTT gtt | OTHER: UP TO MAX. 3X DAILY | Y-M: 20[redacted] / 1267 | Not reported |
| TRAMADOL | 2X 100 MG mg | OTHER: AS LONG AS SEVERE PAIN | Y-M: 20[redacted] / 1267 | Not reported |
| OTHER VIRAL VACCINES | 0.3 mL | QD | Y-M: 20[redacted] / 1295 | Y-M: 20[redacted] / 1295 |
| OTHER VIRAL VACCINES | 0.3 mL | QD | Y-M: 20[redacted] / 1317 | Y-M: 20[redacted] / 1317 |
| CLARITHROMYCIN | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 1438 | Y-M: 20[redacted] / 1444 |
| SALBUTAMOL | 3 OTHER: SPRAYS | BID | Y-M: 20[redacted] / 1438 | Y-M: 20[redacted] / 1440 |
| ACETYLCYSTEINE | 600 mg | QD | Y-M: 20[redacted] / 1443 | Y-M: 20[redacted] / 1469 |
| CYANOCOBALAMIN; DEXAMETHASONE;KEBUZONE;LIDOCAINE;SALAMIDACETIC ACID | 3 mL | QD | Y-M: 20[redacted] / 1443 | Y-M: 20[redacted] / 1469 |
| TRIAZOLAM | 0,25 mg | OTHER: AS NEEDED | Y: 20[redacted] | ONGOING |
| METAMIZOLE | 30 mg | OTHER: AS NEEDED | Y: 20[redacted] | ONGOING |

**Event #1: Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 280 / 221 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 479 / 420 |
| **Duration of AE** | 200 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | CHEST PAIN |
| **Preferred term** | 胸痛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 923 / 864 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 794): NPTST329-TROPONIN-I HS (ABBOTT): 3 [0 - 26] NG/L;[redacted]20[redacted] (RX DAY 864): NPTST058-BRAIN NATRIURETIC PEPTIDE: 26 [0 - 120] PG/ML

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 1240 / 1181 |
| **Duration of AE** | 318 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | CHEST PAIN WITH MUSCULAR SKELETAL ORIGIN |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | PARTIAL TENDON RUPTURE RIGHT SHOULDER |
| **Preferred term** | 腱断裂 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1087 / 1028 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | RUPTURE OF THE SHOULDER |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストリアの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，胸痛の事象を発現した。関連する病歴は，元喫煙者（1 日 0.14 箱を 8 年間），甲状腺機能低下症，潰瘍性大腸炎，認知障害又は精神障害（不眠症）及び非飲酒者であった。

**Event 2 の臨床経過：**

投与923日後＊，被験者は胸痛を発現した。投与の約41ヵ月後＊，胸痛は消失した。

投与923日後＊　，被験者は胸痛があり，入院した。被験者は，この数ヶ月間続く，運動と無関係に発現する左胸部の刺すような痛みを繰り返し経験していた。被験者は動脈性高血圧で，高血圧のエピソードを繰り返しており，カンデサルタンを増量した。被験者の血圧は上昇したままであった。24 時間血圧測定検査の結果，日中に特に血圧値が上昇することが判明した。被験者はさらにアムロジピンを投与された。冠動脈疾患イベントを除外するために冠血管造影 CT 検査を受けたところ，軽度の硬化が認められたが，著しい狭窄は認められなかった。所見及び痛みの種類から，心疾患の可能性は極めて低いと判断された。投与925日後＊　，被験者は退院した。

**The patient's past medications include:**

SALOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK KLYSMEN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted]r 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACINIB (Open Label)

---

1) Chest pain (10008479) (Chest pain (10008479) ) [v.24.0] [10008479]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of CHEST PAIN

**- Investigator:** Chest pain with muscular skeletal origin

**- AbbVie:** Event is common in the general population. The mean annual prevalence of non-cardiac chest pain in 6 population-based studies was approximately 25%.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BLOOD PRESSURE:** Systolic blood pressure increased during the day

[redacted] **20[redacted] BNP:** 26 PG/ML (normal 0 to 120)

[redacted] **20[redacted] CHEST X-RAY:** Normal.

[redacted] 20[redacted] **CHOLESTEROL TOTAL:** 233 mg/dL (normal 100 to 200)

[redacted] 20[redacted] **CT CORONARY ANGIOGRAPHY:** Slight calcifications in coronary artery. No significant stenosis

[redacted] 20[redacted] **DOPPLER ULTRASOUND:** Color Doppler: Mild aortic insufficiency. Left ventricle function sustained with mild septal left ventricular hypertrophy, no evidence of regional wall movement disorders. Mild aortic insufficiency. No increase of pressure in the pulmonary circulation. Diastolic function normal for patient's age.

[redacted] 20[redacted] **ECG:** Findings: Ventricular rate: 53 BPM, P-R interval: 160 ms, QRS duration: 82 ms, QT/QTc: 402/377 ms, Sinus bradycardia, Left axis deviation

[redacted] 20[redacted] **ECHOCARDIOGRAM:** Ultrasound examination visibility: satisfactory from apical and parasternal, examination in sinus rhythm. Left ventricular EDD: 41mm, Right ventricular EDD: 28mm, Left atrium: 32mm, right atrium: 33mm. The left ventricular is of normal size with low basal septal hypertrophy. Right ventricle normal size, normal function. Atria not enlarged. No pericardial effusion. HEART VALVES: Aortic valve: tricuspid, delicate. Mitral valve: inconspicuous in ultrasound examination. Tricuspid valve: inconspicuous

[redacted] 20[redacted] **ELECTROCARDIOGRAM:** Normal

[redacted] 20[redacted] **HDL:** 44.0 mg/dL (normal 40 to 100)

[redacted] 20[redacted] **LDL:** 130.4 mg/dL (normal <160)

[redacted] 20[redacted] **POTASSIUM:** 4.0 MMOL/L (normal 3.2 to 5.2)

[redacted] 20[redacted] **SODIUM:** 138 MMOL/L (normal 135 to 150)

[redacted] 20[redacted] **TRIGLYCERIDES:** 293 mg/dL (normal 25 to 180)

[redacted] 20[redacted] **TROPONIN 1 HS:** 3 NG/L (normal 0 to 26)
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はオーストリアの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，右肩部の部分的な腱断裂の事象を発現した。関連する病歴は，元喫煙者（1 日 0.14 箱を 8 年間），潰瘍性大腸炎及び非飲酒者であった。

**Event 3 の臨床経過：**

投与1087日後＊，被験者は右肩部の部分的な腱断裂を発現した。

投与1323日後＊，被験者は，右肩部の部分的な腱断裂の外科的修復のために予定された手術のため，入院した。手術では，合併症は認められなかった。投与1326日後＊，被験者は良好な全身状態で退院した。

投与された薬剤は，xyloneural 及び volon a であった。

**The patient's past medications include:**

SALOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK KLYSMEN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLON HNP for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

APREDNISOLON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLON NYC for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AVELOX for PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Tendon rupture (10043248) (Tendon rupture (10043248) ) [v.24.0] [10043248]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of PARTIAL TENDON RUPTURE RIGHT SHOULDER

**- Investigator:** Rupture of the shoulder

**- AbbVie:** Rotator cuff injuries are common in the general population with age being the single most important risk factor for rotator cuff tears with a prevalence of 10.7% in subjects whose age was in the 50's.

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Herpes zoster: One dermatome.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 貧血 | | | | X |
| 裂肛 | X | | | |
| 胃腸炎 | X | | | X |
| 伝染性単核症 | X | | | X |
| 腎仙痛 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: ARTRALGIA | 20[redacted] |
| OTHER: BACK PAIN | 20[redacted] |
| OTHER: CRAMPS CALF | 20[redacted] |
| OTHER: CUSHINGOID FACE | 20[redacted] |
| OTHER: FATIGUE | 20[redacted] |
| OTHER: FEMOROACETABULAR (TYPE PINCER) IMPINGEMENT SYNDROME | 20[redacted] |
| OTHER: MUSCULAR ATROPHY | 20[redacted] |
| OTHER: PRECORDIALGY | 20[redacted] |
| OTHER: PYROSIS AND RETROSTERNAL BURNING | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 30 mg | ORAL | QD | [redacted] / 1 | [redacted] / 50 | 50 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted] / 51 | [redacted] / 97 | 47 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 98 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 2 g | BID | Y-M: [redacted] |
| AZATHIOPRINE | 150 mg | QD | Y-M: [redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EVERY 4 WEEKS | Y-M: [redacted] |
| BECLOMETASONE | 5 mg | BID | Y-M: [redacted] |
| MESALAZINE | 1 OTHER: SUPPO | QD | Y-M: [redacted] |
| MESALAZINE | 2 g | BID | Y-M: [redacted] |
| ADALIMUMAB | 40 mg | OTHER: EVERY WEEK | Y-M: [redacted] |
| MESALAZINE | 1 OTHER: APPLICATION | QD | Y-M: [redacted] |
| MESALAZINE | 2 g | BID | Y-M: [redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: [redacted] |
| BLINDED THERAPY | NOT REPORTED | NOT REPORTED | Y-M: [redacted] |
| ETROLIZUMAB | 105 mg | OTHER: Q4W | Y-M: [redacted] |
| USTEKINUMAB | NOT REPORTED | NOT REPORTED | Y-M: [redacted] |
| MESALAZINE | 4 g | QD | Y-M: [redacted] / -228 |
| BECLOMETASONE | 5 mg | QD | Y-M: [redacted] / -210 |
| BECLOMETASONE | 5 mg | BID | Y-M: [redacted] / -174 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / Stop Year-Month / RX Day | |
|---|---|---|---|---|
| MESALAZINE | 2 g | BID | Y-M: 20[redacted] | Not reported |
| CODEINE;PARACETAMOL | 1 OTHER: TABLET | PRN | Y-M: 20[redacted] / 15 | Y-M: 20[redacted] / 27 |
| GLYCERYL TRINITRATE | 1 OTHER: FNIGERTIP | QD | Y-M: 20[redacted] / 2 | Y-M: 20[redacted] / 90 |
| SODIUM CHLORIDE | 10 mL | BID | Y-M: 20[redacted] / 27 | Y-M: 20[redacted] / 27 |
| TRAMADOL | 50 mg | PRN | Y-M: 20[redacted] / 27 | Y-M: 20[redacted] / 28 |
| ALIZAPRIDE | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 28 | Y-M: 20[redacted] / 28 |
| ELECTROLYTES NOS | 1000 mL | QD | Y-M: 20[redacted] / 28 | Y-M: 20[redacted] / 28 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 28 | Y-M: 20[redacted] / 28 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 28 | Y-M: 20[redacted] / 29 |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 39 | Y-M: 20[redacted] / 65 |
| IRON | 500 mg | OTHER: ONCE | Y-M: 20[redacted] / 53 | Y-M: 20[redacted] / 53 |
| LOPERAMIDE | 2 mg | PRN | Y-M: 20[redacted] / 170 | Not reported |
| CHLORHEXIDINE;LIDOCAINE | 1 DF | OTHER: 6 TIMES / DAY | Y-M: 20[redacted] / 284 | Y-M: 20[redacted] / 288 |
| PELARGONIUM SIDOIDES | 20 mg | TID | Y-M: 20[redacted] / 284 | Y-M: 20[redacted] / 288 |
| SODIUM CHLORIDE | 10 mL | OTHER: ONCE | Y-M: 20[redacted] / 286 | Y-M: 20[redacted] / 287 |
| CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 1000 mL | OTHER: ONCE | Y-M: 20[redacted] / 287 | Y-M: 20[redacted] / 287 |
| PARACETAMOL | 1 g | TID | Y-M: 20[redacted] / 287 | Y-M: 20[redacted] / 287 |
| ALIZAPRIDE | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 288 | Y-M: 20[redacted] / 288 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 288 | Y-M: 20[redacted] / 330 |

| | | | | |
|---|---|---|---|---|
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 921 | Not reported |
| IRON | 1000 mg | OTHER: ONCE | Y-M: 20[redacted] / 1101 | Y-M: 20[redacted] / 1101 |
| HAMAMELIS VIRGINIANA;ICHTHAMMOL;TITANIC HYDROXIDE;TITANIUM DIOXIDE;ZINC | 1 DF | PRN | Y-M: 20[redacted] / 1120 | Y-M: 20[redacted] / 1214 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 1121 | Y-M: 20[redacted] / 1133 |
| METHYLPREDNISOLONE | 12 mg | QD | Y-M: 20[redacted] / 1134 | Y-M: 20[redacted] / 1165 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 1166 | Y-M: 20[redacted] / 1184 |
| METHYLPREDNISOLONE | 4 mg | OTHER: EOD | Y-M: 20[redacted] / 1185 | Y-M: 20[redacted] / 1199 |
| METHYLPREDNISOLONE | 8 mg | OTHER: EVERY OTHER DAY | Y-M: 20[redacted] / 1186 | Y-M: 20[redacted] / 1199 |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / 1200 | Y-M: 20[redacted] / 1252 |
| METHYLPREDNISOLONE | 2 mg | QD | Y-M: 20[redacted] / 1253 | Y-M: 20[redacted] / 1316 |
| AMOXICILLIN | 500 mg | TID | Y-M: 20[redacted] / 1261 | Y-M: 20[redacted] / 1264 |
| ALIZAPRIDE | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 1264 | Y-M: 20[redacted] / 1264 |
| CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 1000 mL | OTHER: 1X / 12HOURS | Y-M: 20[redacted] / 1264 | Y-M: 20[redacted] / 1267 |
| IBUPROFEN | 600 mg | OTHER: ONCE | Y-M: 20[redacted] / 1264 | Y-M: 20[redacted] / 1264 |
| METHYLPREDNISOLONE | 125 mg | OTHER: ONCE | Y-M: 20[redacted] / 1264 | Y-M: 20[redacted] / 1264 |
| PARACETAMOL | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 1264 | Y-M: 20[redacted] / 1264 |
| SODIUM CHLORIDE;TRAMADOL | 100 mg | OTHER: ONCE | Y-M: 20[redacted] / 1264 | Y-M: 20[redacted] / 1264 |
| AMOXICILLIN | 1000 mg | BID | Y-M: 20[redacted] / 1265 | Y-M: 20[redacted] / 1265 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 1265 | Y-M: 20[redacted] / 1268 |

| | | | | |
|---|---|---|---|---|
| TRAMADOL | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 1265 | Y-M: 20[redacted] / 1265 |
| MAGALDRATE | 800 mg | OTHER: ONCE | Y-M: 20[redacted] / 1266 | Y-M: 20[redacted] / 1266 |
| PARACETAMOL | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 1266 | Y-M: 20[redacted] / 1266 |
| SERTRALINE | 50 mg | QD | Y-M: 20[redacted] / 1333 | Y-M: 20[redacted] / 1334 |
| CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE | 1 OTHER: SACHET | QD | Y-M: 20[redacted] / 1336 | Y-M: 20[redacted] / 1337 |
| PANTOPRAZOLE | 20 mg | QD | Y-M: 20[redacted] / 1337 | Not reported |
| PROPOFOL | 2 mg/kg | OTHER: ONCE | 20[redacted] / 1337 | 20[redacted] / 1337 |
| LIDOCAINE;METHYLPREDNISOLONE | 1 mL | OTHER: ONCE | 20[redacted] / 1338 | 20[redacted] / 1338 |
| FOLIC ACID | 4 mg | QD | Y-M: 20[redacted] / 1464 | Not reported |
| IRON | 80 mg | QD | Y-M: 20[redacted] / 1464 | Not repored |
| MEPIVACAINE | 23 mL | OTHER: ONCE | Y-M: 20[redacted] / 1551 | Y-M: 20[redacted] / 1551 |
| MIDAZOLAM | 1 mg | OTHER: ONCE | Y-M: 20[redacted] / 1551 | Y-M: 20[redacted] / 1551 |
| SUFENTANIL | 5 ug | OTHER: ONCE | Y-M: 20[redacted] / 1551 | Y-M: 20[redacted] / 1551 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | RENAL COLIC |
| **Preferred term** | 腎仙痛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 124 / 27 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 27): NPTST135-ERYTHROCYTES: 290 [0 - 25] /UL;
[redacted]20[redacted] (RX DAY 28): NPTST221-MRSA: NEGATIVE [NOT REPORTED - NOT REPORTED] NA

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 126 / 29 |
| **Duration of AE** | 3 DAYS |
| **Severity** | MODERATE |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NO CLEAR CAUSE OF EVENT |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 150 / 53 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 183 / 86 |
| **Duration of AE** | 34 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #3: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | PERIANAL FISSURE |
| **Preferred term** | 裂肛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 188 / 91 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 189 / 92 |
| **Duration of AE** | 2 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | COLITIS ULCEROSA |

| | |
|---|---|
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #4: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | GASTROENTERITIS |
| **Preferred term** | 胃腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 383 / 286 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |

[redacted]20[redacted] (RX DAY 286): NPTST108-CRP: 97 [0 - 7] MG/L; [redacted]20[redacted] (RX DAY 287): NPTST108-CRP: 73 [0 - 7] MG/L; NPTST221-MRSA: NEGATIVE [NOT REPORTED - NOT REPORTED] NA

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 385 / 288 |
| **Duration of AE** | 3 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | VIRAL INFECTION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #5: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1186 / 1089 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the** | NO |

| | |
|---|---|
| **Event** | |
| **SAE Criteria** | NONE |

**Event #6: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | INFECTIOUS MONONUCLEOSIS |
| **Preferred term** | 伝染性単核症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1355 / 1258 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 1264): NPTST108-CRP: 18.7 [0 - 5] MG/L;
20[redacted] (RX DAY 1266): Leukocytes: 11.2 [4.2 - 9.8] 10^9/L; NPTST108-CRP: 7.4 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 1267): Leukocytes: 7.33 [4.2 - 9.8] 10^9/L; NPTST108-CRP: 4.1 [0 - 5] MG/L

**Microbiology**

[redacted]20[redacted] (RX DAY 1264): BLOOD NPTST130-EPSTEIN BARR IGG: Negative; BLOOD NPTST131-EPSTEIN BARR IGM: Positive-STRONG POSITIVE TEST; BLOOD NPTST218-MONONUCLEOSE QUICKTEST: Positive-POSITIVE TEST ==> VIRAL CAUSE OF TONSILLITIS

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腎仙痛の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

**Event 1 の臨床経過：**

投与124日後＊，被験者は腎仙痛を発現した。

投与124日後＊　，被験者は入院した。被験者は，投与123日後＊　　から右側腹部及び恥骨上の部分へ放散する右季肋部付近の激しい腹痛を呈していた。また，被験者は排尿時にも痛みを経験していた。投与124日後＊　，被験者は血尿が出たが，発熱はなかった。徴候及び症状には，激しい腹痛，悪心及び血尿が含まれた。臨床経過には，腎臓結石の通過によると思われる右側腹部及び右季肋部の激しい痛みが含まれた。腹部 CT 検査では，結石は確認されなかった。尿検査では，顕微鏡的血尿が認められた。投与126日後＊，被験者は退院した。

投与された薬剤は，paracetamol fresenius，mini-plasco 塩化ナトリウム 0.9%，dafalgan forte，sterofundin b，litican 及び tradonal odis であった。

**The patient's past medications include:**

AZATHIOPRINE for ULCERATIVE COLITIS (Started[redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COLITOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1)　Renal colic (10038419)　(Renal colic (10038419) )　[v.20.0]　[10038419]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** NotApplicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of RENAL COLIC

**- Investigator:** Not reported.

**- AbbVie:** No plausible mechanism to implicate study drug

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] CT ABDOMEN:** No arguments for urolithiasis, low accentuation of the pyelocalicial sytem and of the right ureter to distal compared with contralateral: stone passage?

[redacted] **20[redacted] MRSA NASAL SWAB:** negative

[redacted] **20[redacted] RX THORAX:** no findings

[redacted] **20[redacted] URINE ERYTHROCYTES:** 290 uL (normal 0 to 25)
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，肛門周囲の裂傷の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 3 の臨床経過：**
投与188日後＊，被験者は肛門周囲の裂傷を発現した。投与189日後＊　　，肛門周囲の裂傷は消失した。

本事象発現前に，投与98日後＊から 投与187日後＊　　まで，被験者は肛門周囲の裂傷（非重篤）を経験し，悪化し続けていた。そのため，手術が推奨された。

投与188日後＊　，被験者は手術のため入院した。被験者は疼痛を経験していた。同日，内側側面の括約筋切開術が行われた。手術中，肛門鏡検査が行われ，肛門ポリープも切除された。手術後，スポンゴスタンが所定の位置に装着された。手術中又は手術後に，合併症は確認されなかった。投与189日後＊，被験者は良好な状態で退院した。

**The patient's past medications include:**

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], Stopped [redacted] 20[redacted])

DAFALGAN CODEINE for PERIANAL FISSURE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

---

1) Anal fissure (10002153) (Anal fissure (10002153) ) [v.20.1] [10002153]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of PERIANAL FISSURE

**- Investigator:** Colitis ulcerosa.

**- AbbVie:** Event more likely a complication of underlying ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] PATHOLOGY:** BENIGN DISCRETE TRAUMATIZED ANAL POLYP. NO EVIDENCE FOR KOILOCYTOTIC ATYPIA, DYSPLASIA OR MALIGNANCY
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，胃腸炎の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），結腸内視鏡検査，非喫煙者及び非飲酒者であった。

**Event 4 の臨床経過：**

投与383日後＊，被験者は胃腸炎を発現した。投与385日後＊，胃腸炎は消失した。

投与383日後＊，被験者は腹痛，下痢，嘔吐及び発熱感があり，救急科を受診し，入院した。被験者は，1 週間前からこれらの症状を患っていた。一般開業医により，ウイルス症候群の疑い

で支持療法が既に開始されていた。被験者は排便時に多少の出血があった。一般開業医での 2 日前の血液検査では，CRP が 60 mg/dL であった。身体検査では，腹部及び右窩を押すと痛みがあった。胃腸炎が疑われた。CRP の上昇（97 mg/dL）が認められた。被験者は発熱がなかった。支持療法の方針が継続され，炎症性パラメータのフォローアップが行われた。　投与384日後＊，腹部超音波検査が実施された。投与385日後＊　，被験者は退院した。治験責任医師によると，被験者には本事象に関連する危険因子はなかった。

投与された薬剤は，paracetamol，塩化ナトリウム，alizapride 及び stereofundin・ブドウ糖合剤であった。

**The patient's past medications include:**

PENTASA for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

COLITOFALK for ULCERATIVE COLITIS ([redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

ETROLIZUMAB OR PLACEBO for ULCERATIVE COLITIS ([redacted])

ETROLIZUMAB for ULCERATIVE COLITIS [redacted])

STELARA OR PLACEBO for ULCERATIVE COLITIS [redacted])

Causality for ABT-494 (Open Label)

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1)　Gastroenteritis (10017888)　(Gastroenteritis (10017888) )　[v.21.0]　[10017888]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of GASTROENTERITIS

**- Investigator:** VIRAL INFECTION

**- AbbVie:** EVENT IS COMMON IN THE GENERALPOPULATION. ADDITIONAL RISK FACTOR INCLUDES PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CRP:** 97 mg/dL (normal 0.0 to 7.0)

[redacted] **20[redacted] CRP:** 73 mg/dL (normal 0.0 to 7.0)

[redacted] **20[redacted] ULTRASOUND ABDOMEN:** Normal, viral gastroenteritis
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブを投与され，伝染性単核症の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 6 の臨床経過：**

投与1355日後＊，被験者は伝染性単核症を発現した。

投与1355日後＊　　，被験者は発熱，咽頭痛，脱力感及び頭痛を経験していた。投与1358日後＊，一般開業医を受診し，COVID-19 検査を受けたが結果は陰性であった。アモキシシリンで治療されたが，改善しなかった。その後も咽頭痛が続き，飲食も困難であった。

投与1361日後＊　，咽頭痛，白い点が散らばった扁桃腺の大きな腫脹，左右対称の腫脹，口蓋垂の偏りなし，膿瘍の徴候なし，頭痛，熱っぽさ，脱力感，会話や飲食が困難，といった症状



＊新薬承認情報提供時に置き換え

があり，救急治療室を受診した。単核症の迅速診断テストの結果は陽性であった。投与1363日後＊，エプスタイン・バーウイルスによる扁桃腺炎の経過は，臨床的に良好であった。被験者 は全身倦怠感があり，飲食が困難であったが，大幅な回復が認められた。投与1365日後＊，被験者は退院した。

投与された薬剤は，paracetamol，トラマドール，methylprednisolon，litican，riopan，オーグメンチン，イブプロフェン，sterofundin・ブドウ糖合剤及びアモキシシリンであった。

**The patient's past medications include:**

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

COLITOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CLAVERSAL for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COLITOFALK ENEMA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Infectious mononucleosis (10021914) (Infectious mononucleosis (10021914) ) [v.23.1] [10021914]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of INFECTIOUS MONONUCLEOSIS

**- Investigator:** Not applicable.

**- AbbVie:** Event is common in the general population. Worldwide seropositive prevalence is estimated to be 90 to 95 percent. Primary Epstein-Barr virus (EBV) infection during childhood is usually subclinical, whereas infection of adolescents or adults results in infectious mononucleosis (IM) in 30 to 70% of cases and can prove severe.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] COVID 19 TEST:** Negative

[redacted] **20[redacted] CRP:** 18.7 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 7.4 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 4.1 MG/L (normal 0 to 5)

[redacted] **20[redacted] EPSTEIN BARR IGG:** Negative

[redacted] **20[redacted] EPSTEIN BARR IGM:** STRONG POSITIVE TEST

[redacted] **20[redacted] MONONUCLEOSE QUICKTEST:** POSITIVE TEST VIRAL CAUSE OF TONSILLITIS

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.20 X10**3/MCL (normal 4.2 to 9.8)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.33 X10**3/MCL (normal 4.2 to 9.8)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| ヘリコバクター性胃炎 | X | | | X |
| 帯状疱疹 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 4[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| DRUG ALLERGIES/REACTIONS: ALLERGY IMURAN | 20[redacted] |
| DRUG ALLERGIES/REACTIONS: REMICADE ALLERGIC REACTION | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| OTHER: ANXIETY DISORDER | NOT REPORTED |
| OTHER: ARTHRALGIA | NOT REPORTED |
| OTHER: CHRONIC SINUSITIS | 20[redacted] |
| OTHER: CRAMPS | NOT REPORTED |
| OTHER: FIBROMYALGIA | 20[redacted] |
| OTHER: HARD STOOL | 20[redacted] |
| OTHER: RESECTION ENDO-ANAL POLYP (APO: TROMBOSED HEMORRHOID) | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SAE SUPPLEMENTAL PROCEDURE: ABDOMINAL ULTRASOUND | 20[redacted] |
| SAE SUPPLEMENTAL PROCEDURE: CT ABDOMEN | 20[redacted] |
| SAE SUPPLEMENTAL PROCEDURE: RX ABDOMEN | 20[redacted] |
| SURGERY: CESARIAN SECTION | 19[redacted] |
| SURGERY: FISTULA RESECTION | 20[redacted] |
| SURGERY: HAEMORRHOIDECETOMY | 20[redacted] |
| SURGERY: SINUS SURGERY | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 25 | 20[redacted] |

| | |
|---|---|
| CIGARS | NEVER |
| PIPES | NEVER |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 50 | 50 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 51 | [redacted] / 91 | 41 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 93 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 250 mg | BID | Y-M: [redacted] |
| MESALAZINE | 1 DF | QD | Y-M: [redacted] |
| MESALAZINE | 500 mg | QD | Y-M: [redacted] |
| AZATHIOPRINE | 50 mg | QD | Y-M: [redacted] |
| BECLOMETASONE | 5 mg | QD | Y-M: [redacted] |
| BUDESONIDE | 2 mg | OTHER: 2 TIMES A WEEK | Y-M: [redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: [redacted] |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: [redacted] |
| INFLIXIMAB | 325 mg | OTHER: WEEK 0 AND WEEK 2 | Y-M: [redacted] |
| ADALIMUMAB | 40 mg | OTHER: EVERY WEEK | Y-M: [redacted] |
| BECLOMETASONE | 5 mg | OTHER: EVERY OTHER DAY | Y-M: [redacted] |
| MESALAZINE | 500 mg | QD | Y-M: [redacted] |
| BECLOMETASONE | 3 mg | OTHER: EVERY OTHER DAY | Y-M: [redacted] / -337 |

| | | | |
|---|---|---|---|
| BUDESONIDE | 2 mg | OTHER: EVERY OTHER DAY | Y-M: 20[redacted] / -337 |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 4 WEEKS | Y-M: 20[redacted] / -317 |
| BECLOMETASONE | 5 mg | BID | Y-M: 20[redacted] / -323 |
| METHYLPREDNISOLONE | 8 mg | OTHER: EVERY 2 DAYS | Y-M: 20[redacted] / -242 |
| MAGNESIUM SULFATE | 450 mg | QD | Y-M: 20[redacted] / -202 |
| INFLIXIMAB | 375 mg | OTHER: ONCE | Y-M: 20[redacted] / -170 |
| ANTIDEPRESSANTS IN COMBINATION WITH PSYCHOLEPTICS | 1 DF | QD | Y-M: 20[redacted] / -172 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / -92 |
| CYSTEINE;DL-METHIONINE;HESPERIDIN;MINERALS NOS;PHOSPHORUS;VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -63 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / -78 |
| ENOXAPARIN | 100 mg | QD | Y-M: 20[redacted] / -1 |
| MOMETASONE | 1 DF | BID | Y-M: 20[redacted] / -19 |
| AMOXICILLIN;CLAVULANIC ACID | 1 OTHER: TABLET | TID | Y-M: 20[redacted] / -3 |
| DIHYDROCODEINE | 10 mg | TID | Y-M: 20[redacted] / -3 |
| ETHINYLESTRADIOL;LEVONORGESTREL | 1 OTHER: TABLET | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / Stop Year-Month / RX Day | RX Day |
|---|---|---|---|---|
| MAGNESIUM SULFATE | 450 mg | QD | Y-M: 20[redacted] / -202 | Not reported |
| ANTIDEPRESSANTS IN COMBINATION WITH PSYCHOLEPTICS | 1 DF | QD | Y-M: 20[redacted] / -172 | Not reported |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / -92 | Not reported |
| CYSTEINE;DL-METHIONINE;HESPERIDIN;MINE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / | Not reported |

| | | | | |
|---|---|---|---|---|
| RALS NOS;PHOSPHORUS;VITAMINS NOS | | | -63 | |
| MACROGOL 4000 | 1 OTHER: SACHET | PRN | Y-M: 20[redacted] / 63 | Not reported |
| PARAFFIN, LIQUID | 1 OTHER: TEASPOON | PRN | Y-M: 20[redacted] / 225 | Y-M: 20[redacted] / 1260 |
| MOMETASONE | 1 OTHER: PUFF | PRN | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 894 |
| PANTOPRAZOLE | 20 mg | QD | Y-M: 20[redacted] / 330 | Y-M: 20[redacted] / 489 |
| ALIZAPRIDE | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 490 | Y-M: 20[redacted] / 490 |
| CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 1000 mL | OTHER: ONCE | Y-M: 20[redacted] / 490 | Y-M: 20[redacted] / 491 |
| HYOSCINE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 490 | Y-M: 20[redacted] / 490 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 490 | Y-M: 20[redacted] / 491 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 490 | Y-M: 20[redacted] / 491 |
| ENOXAPARIN | 40 mg | OTHER: ONCE | Y-M: 20[redacted] / 491 | Y-M: 20[redacted] / 491 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 491 | Y-M: 20[redacted] / 924 |
| BISMUTH;METRONIDAZOLE;TETRACYCLINE | 3 OTHER: TABLETS | QID | Y-M: 20[redacted] / 496 | Y-M: 20[redacted] / 505 |
| DYDROGESTERONE;ESTRADIOL | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 712 | Y-M: 20[redacted] / 1016 |
| HERBAL POLLEN NOS;TOCOPHEROL | 1 DF | BID | Y-M: 20[redacted] / 712 | Not reported |
| ACICLOVIR | 800 mg | OTHER: 5/DAY | Y-M: 20[redacted] / 830 | Y-M: 20[redacted] / 837 |
| FURAZOLIDONE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 830 | Y-M: 20[redacted] / 837 |
| AMOXICILLIN;CLAVULANIC ACID | 1 OTHER: TABLET | TID | Y-M: 20[redacted] / 833 | Y-M: 20[redacted] / 836 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 833 | Y-M: 20[redacted] / 840 |
| ETHINYLESTRADIOL;LEVONORGESTREL | 1 OTHER: TABLET | QD | Y: 20[redacted] | Y-M: 20[redacted] / 681 |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | GASTRITIS WITH POSITIVE HELICOBACTER PYLORI |
| **Preferred term** | ヘリコバクター性胃炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 581 / 489 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 597 / 505 |
| **Duration of AE** | 17 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NONE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 922 / 830 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 954 / 862 |
| **Duration of AE** | 33 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，ヘリコバクター・ピロリ陽性の胃炎の事象を発現した。関連する病歴は，瘻孔の切除，元喫煙者（1 日 1 箱を 25 年間），肛門内ポリープの切除（血栓性外痔核），痔瘻切除術，潰瘍性大腸炎（左側），硬便，不安障害及び現飲酒者（1 日 2 杯未満）であった。

この被験者は，先行の M14-234 試験では，被験者番号 [redacted] であり，20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで盲検化された治験薬を投与された。

**Event 1 の臨床経過：**

投与581日後＊，被験者はヘリコバクター・ピロリ陽性の胃炎を発現した。投与597日後＊ ，ヘリコバクター・ピロリ陽性の胃炎は消失した。

投与581日後＊ の夕方，被験者は咽頭まで至る心窩部仙痛，食道の焼けるような痛み，悪心を経験したが，嘔吐はなかった。投与582日後＊ ，被験者は入院した。生化学検査では詳細は不明であり，胃内視鏡検査では，前庭部のびらん性胃炎及びグレード A の逆流性食道炎が指摘された。ヘリコバクター・ピロリの生検が行われた。超音波検査での差異は，目視では確認できなかった。不特定の鎮痛薬及び pantomed の投与が開始された。投与583日後＊ ，被験者は退院を許可された。投与587日後＊ ，免疫組織化学染色でヘリコバクター・ピロリの複数のコロニーが確認された。不特定の薬物治療が開始された。

投与された薬剤は，pantomed，tryplera，alizapride，paracetamol 及びブスコパンであった。

**The patient's past medications include:**

COLITOFALK SUPPO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CIPROXINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted]r 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted]r 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMSIMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1) Helicobacter pylori gastritis (10051790) (Helicobacter gastritis (10054272) ) [v.22.1] [10051790]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of GASTRITIS WITH POSITIVE HELICOBACTER PYLORI

**- Investigator:** None

**- AbbVie:** Event more likely related to Helicobacter pylori which is prevalent in the general population.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** normal

**Unknown date BLOOD URINE:** not reported

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** No inflammation seen (normal mucosa)

[redacted] **20[redacted] GASTROSCOPY:** Erosive antrum gastritis and reflux oesophagitis grade A.

[redacted] **20[redacted] IMMUNOHISTOCHEMICAL STAINING:** multiple colonies of Helicobacter pylori

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Herpes zoster: One dermatome.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| アラニンアミノトランスフェラーゼ増加 | | | | X |
| アスパラギン酸アミノトランスフェラーゼ増加 | | | | X |
| 肺炎 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| EYE DISEASE/DISORDER: KERATOCONJUNCTIVITIS SICCA | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| OTHER: ALLERGIC RHINITIS (HAY FEVER) | 20[redacted] |
| OTHER: BACK PAIN | 20[redacted] |
| OTHER: ERYTHEMA NODOSUM | 20[redacted] |
| OTHER: HEAD ACHE | 20[redacted] |
| OTHER: HYPERVENTILATION | 20[redacted] |
| OTHER: INSOMNIA | 20[redacted] |
| OTHER: PSORIASIS | 20[redacted] |
| OTHER: PSYCHOLOGICAL SUPPORT NEEDED | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 7.5 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 60 | 60 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 74 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1 g | TID | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: ONCE | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| BECLOMETASONE | 2.5 mg | OTHER: EOD | Y-M: 20[redacted] |
| HYDROCORTISONE | 1 OTHER: DOSE UNIT | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1 g | OTHER: EOD | Y-M: 20[redacted] |
| MESALAZINE | 500 mg | QD | Y-M: 20[redacted] |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 10 mg/kg | OTHER: Q4W | Y-M: 20[redacted] |
| HYDROCORTISONE | 1 DF | QD | Y-M: 20[redacted] |
| MESALAZINE | 1 DF | QD | Y-M: 20[redacted] |
| BECLOMETASONE | 1 DF | NOT REPORTED | Y-M: 20[redacted] |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted] |
| BECLOMETASONE | 3 mg | NOT REPORTED | Y-M: 20[redacted] |
| BECLOMETASONE | 5 mg | NOT REPORTED | Y-M: 20[redacted] |
| BECLOMETASONE | 5 mg | BID | Y-M: 20[redacted] |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| MESALAZINE | 500 mg | OTHER: 4 TIMES 2 PER DAY | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] |
| METHOTREXATE | 12 mg | 1 time per week | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 3 g | QD | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| MESALAZINE | 500 mg | OTHER: 3 TIMES 2 PER DAY | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: Q4W | Y-M: 20[redacted] |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted] / -357 |
| MESALAZINE | 3 g | QD | Y-M: 20[redacted] / -357 |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] / -357 |
| METHYLPREDNISOLONE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] / -357 |
| BUDESONIDE | 3 mg | QD | Y-M: 20[redacted] / -262 |
| ZOLPIDEM | 5 mg | PRN | Y-M: 20[redacted] / -214 |
| ADALIMUMAB | 40 mg | OTHER: Q2W | Y-M: 20[redacted] / -175 |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] / -129 |
| ETHINYLESTRADIOL;LEVONORGESTREL | 1 OTHER: TABLET | QD | Y: 20[redacted] |
| MESALAZINE | 1 DF | QD | Y: 20[redacted] |
| FLUCONAZOLE | 200 mg | OTHER: 1/MONTH | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / Stop Year-Month / RX Day | |
|---|---|---|---|---|
| MESALAZINE | 3 g | QD | Y-M: 20[redacted] / -357 | ONGOING |
| ZOLPIDEM | 5 mg | PRN | Y-M: 20[redacted] / -214 | Y-M: 20[redacted] / 707 |
| LEVOCETIRIZINE | 5 mg | QD | Y-M: 20[redacted] / 1 | Y-M: 20[redacted] / 8 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 63 | ONGOING |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 614 | Y-M: 20[redacted] / 617 |
| AMOXICILLIN | 1 g | TID | Y-M: 20[redacted] / 616 | Y-M: 20[redacted] / 617 |
| AMOXICILLIN;CLAVULANIC ACID | 1 g | OTHER: 4 X PER DAY | Y-M: 20[redacted] / 617 | Y-M: 20[redacted] / 621 |
| AZITHROMYCIN | 250 mg | BID | Y-M: 20[redacted] / 617 | Y-M: 20[redacted] / 621 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 618 | Y-M: 20[redacted] / 620 |
| AMOXICILLIN;CLAVULANIC ACID | 875/125 mg | TID | Y-M: 20[redacted] / 621 | Y-M: 20[redacted] / 625 |
| AZITHROMYCIN | 250 mg | QD | Y-M: 20[redacted] / 621 | Y-M: 20[redacted] / 621 |
| ETHINYLESTRADIOL;LEVONORGESTREL | 1 OTHER: TABLET | QD | Y: 20[redacted] | ONGOING |
| FLUCONAZOLE | 200 mg | OTHER: 1/MONTH | Y: 20[redacted] | Y-M: 20[redacted] / 169 |

**Event #1: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | ALT INCREASED |
| **Preferred term** | アラニンアミノトランスフェラーゼ増加 |

| | |
|---|---|
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 29 / -45 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 102 / 29 |
| **Duration of AE** | 74 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | AST INCREASED |
| **Preferred term** | アスパラギン酸アミノトランスフェラーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 29 / -45 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 102 / 29 |
| **Duration of AE** | 74 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

E**vent #3: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | PNEUMONIA |
| **Preferred term** | 肺炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 690 / 617 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | [redacted]20[redacted] (RX DAY 617): NPTST108-CRP: 198 [NOT REPORTED - 5] mg/L;<br>[redacted]20[redacted] (RX DAY 620): NPTST108-CRP: 140.1 [NOT REPORTED - 5] mg/L |
| **Microbiology** | NOT REPORTED |
| **AE Stopped Initial Rx Day / Rx Day** | 694 / 621 |
| **Duration of AE** | 5 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated:[redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，肺炎の事象を発現した。関連する病歴は，過換気，アレルギー性鼻炎，花粉症，乾癬，潰瘍性大腸炎（左側），非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 3 の臨床経過：**

投与690日後＊，被験者は肺炎を発現した。投与694日後＊，肺炎は消失した。

投与690日後＊　，被験者は発熱，咳嗽及び嗄声があり，救急治療室を受診し，入院した。胸部 X 線検査を行い，肺炎と診断された。抗生物質の静脈内投与による治療を開始した。被験者



＊新薬承認情報提供時に置き換え

は具合が良くなり，投与694日後＊に退院した。

投与された薬剤は，paracetamol fresensius，オーグメンチン，azithromycine，clamoxyl，duovent 及び dafalgan であった。

**The patient's past medications include:**

PENTASA for ULCERATIVE COLITIS ([redacted])

CLAVERSAL ENEMA for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted])

COLOFOAM for ULCERATIVE COLITIS ([redacted])

BECLOMETHASONE DIPROPIONATE SUPPOSITORY for ULCERATIVE COLITIS ([redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted])

COLITOFALK GRANULATE for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

SOLU-MEDROL for ULCERATIVE COLITIS ([redacted])

BUDENOFALK for ULCERATIVE COLITIS ([redacted])

HUMIRA VIAL for ULCERATIVE COLITIS ([redacted])

ALPHARIX TETRA for FLU VACCINE ([redacted])

Causality for UPADACITINIB (Open Label)

---

1) Pneumonia (10035664) (Pneumonia (10035664) ) [v.22.1] [10035664]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of PNEUMONIA

**- Investigator:** Not applicable

**- AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] CRP:** 198 MG/L (normal <5)

[redacted] **20[redacted] CRP:** 140.1 MG/L (normal <5)

[redacted] **20[redacted] WEIGHT:** 7[redacted] KG

[redacted] **20[redacted] XRAY:** pneumonia

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Aspartate aminotransferase increased: Asymptomatic.
Alanine aminotransferase increased: Asymptomatic.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| DEPRESSION: DEPRESSIVE FEELINGS | 20[redacted] |
| HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA | NOT REPORTED |
| HYPOTHYROIDISM | 20[redacted] |
| LEFT SIDED UC | 19[redacted] |
| OTHER: ANXIETY DISORDER | NOT REPORTED |
| OTHER: BACK PAIN(INTERMITTENT) | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 15 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted]20[redacted] / 57 | [redacted]20[redacted] / 84 | 28 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 91 | [redacted]20[redacted] / 100 | 10 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| BECLOMETASONE | 5 mg | OTHER: QW | Y-M: 19[redacted] |
| INFLIXIMAB | 10 mg/kg | OTHER: 1/4WEEKS | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: QW | Y-M: 20[redacted] |
| MESALAZINE | 1.5 g | BID | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: 1/8WEEKS | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: 1/4WEEKS | Y-M: 20[redacted] |
| LEVOTHYROXINE | 25 ug | QD | Y-M: 20[redacted] |
| CLORAZEPIC ACID | 10 mg | BID | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: 1/8WEEKS | Y-M: 20[redacted] / -327 |
| BECLOMETASONE | 5 mg | BID | Y-M: 20[redacted] / -279 |
| MESALAZINE | 1 g | QD | Y-M: 20[redacted] / -279 |
| VEDOLIZUMAB | 300 mg | OTHER: 1/4WEEKS | Y-M: 20[redacted] / -241 |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted] / -5 |
| LOPERAMIDE | 2 mg | PRN | Y: 19[redacted] |
| MESALAZINE | 4 g | QD | Y: 19[redacted] |
| AZATHIOPRINE | 200 mg | QD | Y: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y: 20[redacted] |
| FENOFIBRATE | 267 mg | QD | Y: 20[redacted] |
| PANTOPRAZOLE | 20 mg | QD | Y: 20[redacted] |
| PAROXETINE | 30 mg | BID | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| OLANZAPINE | 12.5 mg | QD | Not reported | ONGOING |
| MESALAZINE | 1.5 g | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 39 |
| LEVOTHYROXINE | 25 ug | QD | Y-M: 20[redacted] | ONGOING |
| CLORAZEPIC ACID | 10 mg | BID | Y-M: 20[redacted] | ONGOING |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted] / -5 | Y-M: 20[redacted] / 11 |
| BECLOMETASONE | 5 mg | BID | Y-M: 20[redacted] / 12 | Y-M: 20[redacted] / 25 |
| ASCORBIC ACID;CALCIUM CARBONATE;COLECALCIFEROL; ERGOCALCIFEROL | 1 OTHER: SACHET | QD | Y-M: 20[redacted] / 25 | Y-M: 20[redacted] / 38 |

| | | | | |
|---|---|---|---|---|
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] / 25 | Y-M: 20[redacted] / 38 |
| METHYLPREDNISOLONE | 28 mg | QD | Y-M: 20[redacted] / 39 | Y-M: 20[redacted] / 40 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 40 | ONGOING |
| HYDROCORTISONE | 50 mg | QD | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 40 |
| LEVOBUPIVACAINE | 250 mg | PRN | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 40 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 43 |
| PIPERACILLIN;TAZOBACTAM | 4 g | QID | Y-M: 20[redacted] / 40 | ONGOING |
| SUFENTANIL | 200 mL | PRN | Y-M: 20[redacted] / 40 | Y-M: 20[redacted] / 40 |
| HYDROCORTISONE | 50 mg | BID | Y-M: 20[redacted] / 41 | Y-M: 20[redacted] / 41 |
| MORPHINE | 7 mg | PRN | Y-M: 20[redacted] / 41 | Y-M: 20[redacted] / 42 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 41 | Y-M: 20[redacted] / 42 |
| HYDROCORTISONE | 25 mg | QD | Y-M: 20[redacted] / 42 | Y-M: 20[redacted] / 42 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 42 | Y-M: 20[redacted] / 42 |
| LORAZEPAM | 1 mg | QD | Y-M: 20[redacted] / 43 | Y-M: 20[redacted] / 43 |
| METHYLPREDNISOLONE | 28 mg | QD | Y-M: 20[redacted] / 43 | ONGOING |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 43 | ONGOING |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 43 | ONGOING |
| TRAMADOL | 100 mg | BID | Y-M: 20[redacted] / 43 | ONGOING |
| TRAMADOL | 50 mg | PRN | Y-M: 20[redacted] / 43 | ONGOING |
| LOPERAMIDE | 2 mg | PRN | Y: 19[redacted] | Y-M: 20[redacted] / 39 |
| FENOFIBRATE | 267 mg | QD | Y: 20[redacted] | ONGOING |
| PANTOPRAZOLE | 20 mg | QD | Y: 20[redacted] | Y-M: 20[redacted] / 40 |
| PAROXETINE | 30 mg | BID | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING UC |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 128 / 38 (28 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 38): Hemoglobin: 141 [140 - 180] G/L; NPTST064-C REACTIVE PROTEIN: 6.0 [NOT REPORTED - 5] mg/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | UNDERLYING DISEASE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code:[redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，及び潰瘍性大腸炎での入院であった。

**Event 1 の臨床経過：**

投与128日後＊，被験者は潰瘍性大腸炎の悪化を発現した。

投与100日後＊，有効性が認められないため，治験薬の投与は中止された。投与128日後＊，被験者は血性下痢があり，入院した。入院中，血性下痢が続いた。投与130日後＊，被験者は回腸瘻造設を伴う結腸全摘術を受けた。投与140日後＊，被験者は退院した。

治験責任医師によると，被験者の本事象に関連する危険因子には，潰瘍性大腸炎の病歴が含まれた。被験者は 投与の約11年7ヵ月前＊に潰瘍性大腸炎の悪化があり，入院していた。

投与された薬剤は，chirocaine，オンダンセトロン，クレキサン，モルヒネ，ピペラシリン・タゾバクタム合剤，contramal，tradonal，dafalgan，paracetamol，temesta，ソル・コーテフ及び sufentanil であった。

**The patient's past medications include:**

BECLOMETHASONE DIPROPIONATE for ULCERATIVE COLITIS ([redacted] 19[redacted]- [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900) ) [v.20.1] [10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of WORSENING UC

**- Investigator:** Underlying disease.

**- AbbVie:** Event is clearly consistent with progression or worsening of the underlying disease and is considered expected for this study.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **C REACTIVE PROTEIN:** 6.0 MG/L (normal <5.0)

[redacted] **HEMOGLOBIN:** 14.1 G/DL (normal 14.0 to 18.0)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA: IRON DEFICIENCY ANEMIA | 20[redacted] |
| EYE DISEASE/DISORDER: BILATERAL SEROSA CENTRALIS | 20[redacted] |
| EYE DISEASE/DISORDER: BLEPHARITIS | 20[redacted] |
| EYE DISEASE/DISORDER: GLAUCOMA | NOT REPORTED |
| HEPATITIS: AZATHIOPRINE INDUCED HEPATITIS | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| OTHER: ARTHRALGIA KNEES | 20[redacted] |
| OTHER: FOLIC ACID DEPLETION | 20[redacted] |
| OTHER: INTERMITTENT ARTHRALGIA | 20[redacted] |
| OTHER: TIREDNESS | NOT REPORTED |
| OTHER: TRIGEMINAL NEURALGIA | 19[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.15 PACK | 24 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 Placebo (IND) | | ORAL | QD | [redacted] / 1 | [redacted] / 53 | 53 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 54 | [redacted] / 430 | 377 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| METHYLPREDNISOLONE | NOT REPORTED | NOT REPORTED | Y-M: [redacted] |
| PARACETAMOL | 1 g | PRN | Y-M: [redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: 1/8WEEKS | Y-M: [redacted] |
| BUDESONIDE | 3 mg | NOT REPORTED | Y-M: [redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: 1/4WEEKS | Y-M: [redacted] |
| GOLIMUMAB | 50 mg | OTHER: 1/4WEEKS | Y-M: [redacted] |
| MESALAZINE | 2 g | BID | Y-M: [redacted] |
| MESALAZINE | 4 g | QD | Y-M: [redacted] |
| BLINDED THERAPY | 105 mg | OTHER: 1/4WEEKS | Y-M: [redacted] |
| ETROLIZUMAB | 105 mg | OTHER: 1/4WEEKS | Y-M: [redacted] |
| BECLOMETASONE | 5 mg | OTHER: QOD | Y-M: [redacted] |
| BLINDED THERAPY | NOT REPORTED | NOT REPORTED | Y-M: [redacted] / -335 |
| INVESTIGATIONAL DRUG | NOT REPORTED | NOT REPORTED | Y-M: [redacted] / -245 |
| INVESTIGATIONAL DRUG | NOT REPORTED | NOT REPORTED | Y-M: [redacted] / -155 |
| PANTOPRAZOLE | 20 mg | QD | Y-M: [redacted] / -129 |
| ISONIAZID | 300 mg | QD | Y-M: [redacted] / -67 |
| PYRIDOXINE | 250 mg | EVERY WEEK | Y-M: [redacted] / -67 |
| TRAMADOL | 50 mg | PRN | Y-M: [redacted] / -12 |
| SODIUM CHLORIDE;WATER | 100 mL | PRN | Y-M: [redacted] / -13 |
| ACETYLSALICYLIC ACID | 80 mg | QD | Y-M: [redacted] / -7 |
| LEVOFLOXACIN | 500 mg | QD | Y-M: [redacted] / -8 |
| AZATHIOPRINE | 150 mg | QD | Y: [redacted] |
| MESALAZINE | NOT REPORTED | QD | Y: [redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PARACETAMOL | 1 g | PRN | Y-M: [redacted] | ONGOING |

| | | | | |
|---|---|---|---|---|
| MESALAZINE | 2 g | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 401 |
| PANTOPRAZOLE | 20 mg | QD | Y-M: 20[redacted] / -129 | Y-M: 20[redacted] / 402 |
| SODIUM CHLORIDE;WATER | 100 mL | PRN | Y-M: 20[redacted] / -13 | ONGOING |
| ACETYLSALICYLIC ACID | 80 mg | QD | Y-M: 20[redacted] / -7 | ONGOING |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 107 | ONGOING |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted] / 382 | Y-M: 20[redacted] / 401 |
| IRON | 1 g | QD | Y-M: 20[redacted] / 382 | Y-M: 20[redacted] / 382 |
| TRAMADOL | 50 mg | PRN | Y-M: 20[redacted] / 399 | ONGOING |
| ALPRAZOLAM | 0.5 mg | QD | Y-M: 20[redacted] / 400 | Y-M: 20[redacted] / 402 |
| ACETYLSALICYLIC ACID | 500 mg | QD | Y-M: 20[redacted] / 401 | Y-M: 20[redacted] / 401 |
| PIPERACILLIN;TAZOBACTAM | 4 g | BID | Y-M: 20[redacted] / 401 | ONGOING |
| SODIUM PHOSPHATE | 133 mL | QD | Y-M: 20[redacted] / 401 | Y-M: 20[redacted] / 401 |
| LEVOBUPIVACAINE | 250 mg | QD | Y-M: 20[redacted] / 402 | Y-M: 20[redacted] / 403 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 402 | Y-M: 20[redacted] / 406 |
| SUFENTANIL | 10 ug | PRN | Y-M: 20[redacted] / 402 | Y-M: 20[redacted] / 403 |
| HYDROCORTISONE | 50 mg | BID | Y-M: 20[redacted] / 403 | Y-M: 20[redacted] / 403 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 403 | Y-M: 20[redacted] / 408 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 403 | Y-M: 20[redacted] / 404 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 404 | ONGOING |
| MORPHINE | 5 mg | PRN | Y-M: 20[redacted] / 404 | Y-M: 20[redacted] / 405 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 405 | Y-M: 20[redacted] / 405 |
| TRAMADOL | 50 mg | QD | Y-M: 20[redacted] / 405 | Y-M: 20[redacted] / 405 |
| AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;GLYCINE MAX;OLEA EUROPAEA | 2 ug/m2 | PRN | Y-M: 20[redacted] / 406 | ONGOING |
| LOPERAMIDE | 2 mg | TID | Y-M: 20[redacted] / 406 | Y-M: 20[redacted] / 406 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 406 | Y-M: 20[redacted] / 406 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 407 | ONGOING |
| TRAMADOL | 100 mg | BID | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 407 |
| DOMPERIDONE | 10 mg | TID | Y-M: 20[redacted] / 409 | Y-M: 20[redacted] / 409 |

**Event #1: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | WORSENING ULCERATIVE COLITIS |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 429 / 376 |
| **Age at AE Onset** | 5[redacted] |

| | |
|---|---|
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 452 / 399 (22 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 24 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING UC |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 452 / 399 (22 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | UNDERLYING DISEASE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: 3[redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.15 箱を 24 年間）及び禁酒であった。

**Event 2 の臨床経過：**

投与452日後＊，被験者は潰瘍性大腸炎の悪化を発現した。

投与429日後＊から 投与452日後＊　に，被験者は潰瘍性大腸炎の悪化（非重篤）を経験した。

投与452日後＊　，被験者は潰瘍性大腸炎の症状の悪化により予定された手術のため，入院した。被験者は血性下痢，腹部仙痛及び断続的な発熱を経験した。投与455日後＊，被験者は回 腸瘻造設を伴う腹腔鏡下での結腸全摘術を受け，合併症は認められなかった。

投与された薬剤は，pantomed，sufentanil，オンダンセトロン，ソル・コーテフ，paracetamol，tpn periolimel，imodium 及び motilium であった。

**The patient's past medications include:**

5-ASA for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

IMURAN for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BUDENOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

SIMPONI for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COLITOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted],[redacted] 20[redacted] - [redacted] 20[redacted])

ANTI IL-23 for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900) ) [v.21.1] [10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

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Event of WORSENING UC

**- Investigator:** UNDERLYING DISEASE

**- AbbVie:** EVENT IS MORE LIKELY RELATED TO RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 4[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| AMENORRHEA | 20[redacted] |
| ANAL HEMORROIDS | 20[redacted] |
| ANAL PAIN INTERMITTENT | 20[redacted] |
| ARTHRALGIA INTERMITTENT | 20[redacted] |
| CHONDROSIS L4-L5 | 20[redacted] |
| DEPRESSIVE FEELINGS INTERMITTENT | 20[redacted] |
| DISCUS BULGING L4-L5 | 20[redacted] |
| DISCUSHERNIA L5S1 | 20[redacted] |
| EPIGASTRIC PAIN INTERMITTENT | 20[redacted] |
| FATIGUE INTERMITTENT | 20[redacted] |
| HEADACHE INTERMITTENT | 20[redacted] |
| IRON DEFICIENCY INTERMITTENT | 20[redacted] |
| LEFT SIDED UC | 19[redacted] |
| LUMBO-ISCHIALGIA LEFT | 20[redacted] |
| MYALGIA | 20[redacted] |
| POLYCYSTIC OVARY SYNDROME | 20[redacted] |
| PSORIASIFORM RASH DUE TO REMICADE | 20[redacted] |
| SEBORREIC ECZEMA | 20[redacted] |
| STRESS | 20[redacted] |
| URINARY TRACT INFECTION INTERMITTENT | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: SURGERY FOR DISCUSHERNIA | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.5 PACK | 12 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 53 | 53 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / 54 | [redacted]20[redacted] / 194 | 141 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 195 | [redacted]20[redacted] / 224 | 30 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| BECLOMETASONE | 3 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| ADALIMUMAB | 160 mg | OTHER: ONCE | Y-M: 20[redacted] |
| ADALIMUMAB | 80 mg | OTHER: ONCE | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: WK 0, WK 2 AND WEK 6 | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 10 mg/kg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| MESALAZINE | 500 mg | QD | Y-M: 20[redacted] |
| BECLOMETASONE | 5 mg | OTHER: EOD | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| BECLOMETASONE | 3 mg | QD | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] |
| BECLOMETASONE | 3 mg | OTHER: EOD | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 6 WEEKS AND AFTERWARDS EVERY 4 WEEKS | Y-M: 20[redacted] / -324 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / -280 |
| BECLOMETASONE | 10 mg | QD | Y-M: 20[redacted] / -299 |
| CODEINE;PARACETAMOL | 530 mg | PRN | Y-M: 20[redacted] / -244 |
| BECLOMETASONE | 3 mg | QD | Y-M: 20[redacted] / -251 |
| BALLOTA NIGRA;CRATAEGUS LAEVIGATA;PASSIFLORA INCARNATA | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / -172 |
| ORIGANUM VULGARE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -172 |
| LOPERAMIDE | 4 mg | QD | Y-M: 20[redacted] / -19 |
| BUDESONIDE | 3 mg | QD | Y: 19[redacted] |
| SULFASALAZINE | 1 g | BID | Y: 19[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / Stop Year-Month / RX Day | |
|---|---|---|---|---|
| CODEINE;PARACETAMOL | 530 mg | PRN | Y-M: 20[redacted] / -244 | ONGOING |
| BALLOTA NIGRA;CRATAEGUS LAEVIGATA;PASSIFLORA INCARNATA | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / -172 | ONGOING |
| ORIGANUM VULGARE | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -172 | Y-M: 20[redacted] / 4 |
| LOPERAMIDE | 4 mg | QD | Y-M: 20[redacted] / -19 | ONGOING |
| PNEUMOCOCCAL VACCINE | 0.5 mL | OTHER: ONC | Y-M: 20[redacted] / 1 | Y-M: 20[redacted] / 1 |
| ESTRADIOL;NOMEGESTROL | UNKNOWN mg | QD | Y-M: 20[redacted] / 17 | ONGOING |
| DILTIAZEM | UNKNOWN OTHER: UNKNOWN | BID | Y-M: 20[redacted] / 24 | Y-M: 20[redacted] / 66 |
| ALIZAPRIDE | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 31 | Y-M: 20[redacted] / 31 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 31 | Y-M: 20[redacted] / 34 |
| METHYLPREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] / 31 | Y-M: 20[redacted] / 34 |
| PARACETAMOL | 1 g | QD | Y-M: 20[redacted] / 31 | Y-M: 20[redacted] / 34 |

| | | | | |
|---|---|---|---|---|
| TRAMADOL | 50 mg | TID | Y-M: 20[redacted] / 31 | Y-M: 20[redacted] / 34 |
| CALCIUM CARBONATE;COLECALCIFEROL | 1000 mg | QD | Y-M: 20[redacted] / 32 | Y-M: 20[redacted] / 66 |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] / 34 | Y-M: 20[redacted] / 48 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 34 | Y-M: 20[redacted] / 66 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 34 | Y-M: 20[redacted] / 66 |
| TRAMADOL | 40 mg | PRN | Y-M: 20[redacted] / 34 | Y-M: 20[redacted] / 66 |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted] / 6 | Y-M: 20[redacted] / 28 |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | WORSENING ULCERATIVE COLITIS |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 225 / 31 (1 DAY AFTER LAST TREATMENT) |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 228 / 34 (4 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 4 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | LACK OF RESPONSE TO STUDY DRUG |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病

歴は，潰瘍性大腸炎，多嚢胞性卵巣症候群，断続的な心窩部痛，断続的な鉄欠乏，ストレス，元喫煙者（1 日 0.5 箱を 12 年間），断続的な肛門痛，肛門の痔核及び禁酒であった。

**Event 1 の臨床経過：**

投与225日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与228日後＊　　，潰瘍性大腸炎の悪化は消失した。

投与225日後＊，全身状態の悪化を伴う潰瘍性大腸炎の悪化があり，入院した。症状には，触診時の左側腹部窩及び恥骨上の部位の痛みが含まれた。投与228日後＊　，被験者は退院した。

投与された薬剤は，litican 及びソル・メドロールであった。

**The patient's past medications include:**

ENTOCORT for ULCERATIVE COLITIS (19[redacted] - 20[redacted], 19[redacted] - 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BECLOMETHASONE DIPROPRIONATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

A.D.P. BIOTICS (ORAGANO EXTRACT) for SUPPLEMENT ([redacted] 20[redacted] -[redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900) )　[v.22.1]　[10009901]

C**ausality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of WORSENING ULCERATIVE COLITIS

**- Investigator:** LACK OF RESPONSE TO STUDY DRUG

**- AbbVie:** Event is more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] SIGMOIDOSCOPY:** MAYO 3 COLITIS

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 尿路結石 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ACNE | 20[redacted] |
| HEMORRHOIDS | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| ULCERATIVE COLITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0 PACK | 13 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted]20[redacted] / 57 | [redacted]20[redacted] / 113 | 57 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / 114 | [redacted]20[redacted] / 143 | 30 |

| | | | | |
|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 144 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ADALIMUMAB | 40 mg | OTHER: EVERY WEEK | Y-M: 20[redacted]-[redacted] |
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted]-[redacted] |
| CALCIUM CARBONATE;COLECALCIFEROL | UNKNOWN OTHER: UNKNOWN | QD | Y-M: 20[redacted]-[redacted] |
| INFLIXIMAB | 10 mg/kg | OTHER: EVERY 4 WEEKS | Y-M: 20[redacted]-[redacted] |
| METHOTREXATE | 5 mg/kg | 1 time per week | Y-M: 20[redacted]-[redacted] |
| BECLOMETASONE | NOT REPORTED | OTHER: UNKNOWN | Y-M: 20[redacted]-[redacted] / -326 |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted]-[redacted] / -326 |
| BECLOMETASONE | 5 mg | QD | Y-M: 20[redacted]-[redacted] / -332 |
| BUDESONIDE | NOT REPORTED | OTHER: UKNOWN | Y: 20[redacted] |
| BUDESONIDE | NOT REPORTED | OTHER: UNKNOWN | Y: 20[redacted] |
| MESALAZINE | 2 g | BID | Y: 20[redacted] |
| MESALAZINE | NOT REPORTED | OTHER: UNKNOWN | Y: 20[redacted] |
| MESALAZINE | 4 g | QD | Y: 20[redacted] / -2 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| BECLOMETASONE | NOT REPORTED | OTHER: UNKNOWN | Y-M: 20[redacted]-[redacted] / -326 | Not reported |
| PARACETAMOL | UNK mg | PRN | Y-M: 20[redacted]-[redacted] / 224 | Y-M: 20[redacted]-[redacted] / 232 |
| TRAMADOL | 50 mg | PRN | Y-M: 20[redacted]-[redacted] / 224 | Y-M: 20[redacted]-[redacted] / 232 |
| TRAMADOL | 50 mg | BID | Y-M: 20[redacted]-[redacted] / 230 | Y-M: 20[redacted]-[redacted] / 232 |
| BUDESONIDE | NOT REPORTED | OTHER: UKNOWN | Y: 20[redacted] | Not reported |
| BUDESONIDE | NOT REPORTED | OTHER: UNKNOWN | Y: 20[redacted] | Not reported |
| MESALAZINE | 2 g | BID | Y: 20[redacted] | Y: 20[redacted] / 364 |
| MESALAZINE | NOT REPORTED | OTHER: | Y: 20[redacted] | Not reported |

| | | | | |
|---|---|---|---|---|
| | | UNKNOWN | | |
| MESALAZINE | 4 g | QD | Y: 20[redacted] / -2 | Not reported |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | UROLITHIASIS |
| **Preferred term** | 尿路結石 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 367 / 224 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted] (RX DAY 229): Erythrocytes: POSITIVE [0 - 6] /?L | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 374 / 231 |
| **Duration of AE** | 8 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | INSUFFICIENT FLUID INTAKE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はベルギーの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，尿路結石症の事象を発現した。関連する病歴は，元喫煙者（13 年間）及び潰瘍性大腸炎であった。

**Event 1 の臨床経過：**

投与367日後＊　，被験者は尿路結石症を発現した。投与374日後＊　　，尿路結石症は消失した。



＊新薬承認情報提供時に置き換え

本事象発現前の 投与304日後＊，被験者は顕微鏡的血尿（非重篤）を経験した。

投与372日後＊　，被験者は入院した。被験者は同日，既知の尿路結石症に対して，体外衝撃波結石破砕術（ESWL）を受けた。数時間後に右側腹部に仙痛が生じ，救急科を受診した。被験者は全血球計算，CRP，肝機能検査，腎機能検査，生化学検査及びアルブミン検査を受けた（検査結果は提供されなかった）。投与374日後＊，被験者は退院した。

投与された薬剤は，contramal retard，tradonal 及び paracetamol であった。

**The patient's past medications include:**

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LEDERTREXAAT for ULCERATIVE COLITIS [redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TRAMADOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1)　Urolithiasis (10046707)　(Calculus urinary (10007027) )　[v.23.0]　[10046707]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of UROLITHIASIS

**- Investigator:** Insufficient fluid intake

**- AbbVie:** Renal stone is a relatively common problem with an estimated 16 percent of men will be diagnosed with a kidney stone by age of 70 years. Additional risk factor is "insufficient fluid intake" as noted by PI.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CT ABDOMEN LOW DOSE:** Regression of urolithiasis, mild hydronefrosis, some lithiasis fragments in bladder

[redacted] **20[redacted] ECHO ABDOMEN:** Suspicion of some urolithiasis fragments at the vesicoureteral junction

[redacted] **20[redacted] URINE RED BLOOD CELLS:** positive (0-6)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| COVID-19 肺炎 | X | | | X |
| 橈骨骨折 | X | | | |
| 失神 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| HERNIA | 20[redacted] |
| LEFT FOOT TRAUMA | 20[redacted] |
| LEFT HAND TRAUMA | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| LOWER LIMB PAIN | 20[redacted] |
| PTERYGIUM | 20[redacted] |
| TUBERCULOSIS | 20[redacted] |
| ULCERATIVE COLITIS | NOT REPORTED |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: LEFT FOOT ORTHOPEDIC SURGERY | 20[redacted] |
| PRIOR PROCEDURES: LEFT HAND ORTHOPEDIC SURGERY | 20[redacted] |
| PRIOR PROCEDURES: LEFT INGUINAL HERNIORRHAPHY | 20[redacted] |
| PRIOR PROCEDURES: PTERYGIUM EXERESIS | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | More than 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 81 | 81 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 82 | [redacted] / 278 | 197 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 282 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| SULFASALAZINE | 2 g | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 400 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| PROPOFOL | 100 mg | QD | Y-M: 20[redacted] / -39 |
| METRONIDAZOLE | 400 mg | TID | Y-M: 20[redacted] / -57 |
| PREDNISONE | 20 mg | BID | Y-M: 20[redacted] / -57 |
| MESALAZINE | 1 g | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| LOSARTAN | 50 mg | QD | Y-M: 20[redacted] / 35 | ONGOING |
| METAMIZOLE | 1 g | BID | Y-M: 20[redacted] / 110 | Y-M: 20[redacted] / 111 |
| AZITHROMYCIN | 500 mg | QD | Y-M: 20[redacted] / 111 | Y-M: 20[redacted] / 114 |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 111 | Y-M: 20[redacted] / 115 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 111 | Y-M: 20[redacted] / 122 |
| CODEINE;PARACETAMOL | 250 mg | TID | Y-M: 20[redacted] / 112 | Y-M: 20[redacted] / 119 |
| METAMIZOLE | 1 g | QD | Y-M: 20[redacted] / 112 | Y-M: 20[redacted] / 112 |

| | | | | |
|---|---|---|---|---|
| METAMIZOLE | 1 g | QD | Y-M: 20[redacted] / 114 | Y-M: 20[redacted] / 114 |
| PIPERACILLIN;TAZOBACTAM | 4 g | QID | Y-M: 20[redacted] / 116 | Y-M: 20[redacted] / 123 |
| DEXAMETHASONE | 6 mg | QD | Y-M: 20[redacted] / 117 | Y-M: 20[redacted] / 122 |
| COLCHICINE | 0,5 mg | TID | Y-M: 20[redacted] / 118 | Y-M: 20[redacted] / 122 |
| RIVAROXABAN | 10 mg | QD | Y-M: 20[redacted] / 123 | Y-M: 20[redacted] / 153 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 408 |
| KETOPROFEN | 100 mg | BID | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 408 |
| METAMIZOLE | 1 g | OTHER: QID (AS NEEDED) | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 409 |
| OMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 409 |
| TRAMADOL | 100 mg | TID | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 408 |
| CONTRAST MEDIA | 45 g | QD | Y-M: 20[redacted] / 409 | Y-M: 20[redacted] / 409 |
| CEFAZOLIN | 2 g | OTHER: INDUCTION OF ANESTHESIA | Y-M: 20[redacted] / 410 | Y-M: 20[redacted] / 410 |
| ONDANSETRON | 8 mg | TID | Y-M: 20[redacted] / 410 | Y-M: 20[redacted] / 410 |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | COVID-19 PNEUMONIA INFECTION |
| **Preferred term** | COVID-19 肺炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 385 / 104 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 111): Leukocytes: 13.5 [3.79 - 10.33] 10^9/L; NPTST069-C-REACTIVE PROTEIN: 42.10 [0 - 1] MG/DL; [redacted]20[redacted] (RX DAY 116): Leukocytes: 9.7 [3.79 - 10.33] 10^9/L; NPTST066-C- REACTIVE PROTEIN: 26.00 [0 - 1] MG/DL; [redacted]20[redacted] (RX DAY 119): Leukocytes: 9.1 [3.79 - 10.33] 10^9/L; NPTST066-C- REACTIVE PROTEIN: 7.50 [0 - 1] MG/DL; [redacted]20[redacted] (RX DAY 123): Leukocytes: 11.3 [3.79 - 10.33] 10^9/L; NPTST066-C-REACTIVE PROTEIN: 1.00 [0 - 1] MG/DL

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 421 / 140 |
| **Duration of AE** | 37 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | LEFT RADIUS FRACTURE |
| **Preferred term** | 橈骨骨折 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 688 / 407 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 408): Creatinine: 118.460368 [61.882282 - 114.924238] UMOL/L; Creatinine: 118.460368 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 4.82 [4.3 - 5.7] 10^12/L; Erythrocytes: 4.82 [4.3 - 5.7] 10^12/L; Hematocrit: 0.44 [0.39 - 0.5] FRACTION OF 1; Hematocrit: 0.44 [0.39 - 0.5] FRACTION OF 1; Hemoglobin: 141 [135 - 175] G/L; Hemoglobin: 141 [135 - 175] G/L; Leukocytes: 5.7 [3.5 - 10.5] 10^9/L; Leukocytes: 5.7 [3.5 - 10.5] 10^9/L; NPTST113-D DIMER: 1.19 [0 - 0.5] 099,UG/ML; NPTST113-D DIMER: 1.19 [0 - 0.5] 099,UG/ML; NPTST334-UREA: 44 [15 - 39] MG/DL; NPTST334-UREA: 44 [15 - 39] MG/DL; Potassium: 4.3 [3.5 - 5] MMOL/L; Potassium: 4.3 [3.5 - 5] MMOL/L; Sodium: 141 [135 - 145] MMOL/L; Sodium: 141 [135 - 145] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | SYNCOPE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #3: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | SYNCOPE |
| **Preferred term** | 失神 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 688 / 407 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |

[redacted]20[redacted] (RX DAY 408): Creatinine: 118.460368 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 4.82 [4.3 - 5.7] 10^12/L; Hematocrit: 0.44 [0.39 - 0.5] FRACTION OF 1; Hemoglobin: 141 [135 - 175] G/L; Leukocytes: 5.7 [3.5 - 10.5] 10^9/L; NPTST113-D DIMER: 1.19 [0 - 0.5] 099,UG/ML; NPTST334-UREA: 44 [15 - 39] MG/DL; Potassium: 4.3 [3.5 - 5] MMOL/L; Sodium: 141 [135 - 145] MMOL/L

| | |
|---|---|
| **Microbiology** | |

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 688 / 407 |
| **Duration of AE** | 1 DAY |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はブラジルの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，COVID-19 肺炎の感染症の事象を発現した。関連する病歴は，潰瘍性大腸炎，結核，非喫煙者及び元飲酒者（1 日 4 杯以上）であった。

**Event 1 の臨床経過：**

投与385日後＊ ，被験者はCOVID-19肺炎の感染症を発現した。投与421日後＊ ，COVID-19肺炎の感染症は消失した。

本事象発現前の投与288日後＊　から 投与315日後＊　，被験者は COVID-19 感染症（非重篤）を経験していた。

投与392日後＊　　，被験者は全身状態の悪化，分泌物を含む咳嗽，呼吸困難，悪寒，及び聞き取れる程度の喘鳴があり，入院した。被験者の血球数及び C-反応性タンパク質の検査値が細菌感染を示唆する数値であったため，当初は細菌性肺炎の治療を受けた。アジスロマイシン及びセフトリアキソンによる治療が開始された。投与393日後＊　，ウイルス学的に COVID-19 が確認されたが，同日に行った別の COVID-19 の検査の結果は陰性であった。被験者が COVID-19 に再感染したかは，確認できなかった。胸部 CT スキャン検査では，COVID-19 感染及び細菌性肺炎が確認された。抗生物質による治療は，病院の COVID-19 治療の実施要項にあるデキサメタゾン及びコルヒチンに加えて，タゾシンに変更され実施された。投与404日後＊　　，被験者は退院した。最終的な診断は，COVID-19 肺炎の感染症及び原因不明の同時感染であった。

投与された薬剤は，エノキサパリン，dipirone，アジスロマイシン，セフトリアキソン，タゾシン，paco，デキサメタゾン，colchicina 及びリバーロキサバンであった。

**The patient's past medications include:**

SULFASALAZINE for ULCERATIVE COLITIS ([redacted])

MESALAZINE for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

METRONIDAZOLE for WORSENING OF ULCERATIVE COLITIS ([redacted])

PREDNISONE for WORSENING OF ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　COVID-19 pneumonia (10084380)　(COVID-19 pneumonia (10084380) )　[v.24.0]　[10084380]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, outcome unknown

Alternative Etiology for UPADACITINIB (Open Label)

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Event of COVID-19 PNEUMONIA INFECTION

**- Investigator:** Not applicable.

**- AbbVie:** Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BMI:** 31.4 kg/m2

[redacted] **20[redacted] CHEST X-RAY (WEEK 0):** Normal

[redacted] **20[redacted] CHEST X-RAY:** Normal

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Positive

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Positive

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Negative

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Positive

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Negative

[redacted] **20[redacted] CT SCAN:** Compatible opacities with the hypothesis of moderate viral pneumonia of Covid-19 and right inferior bacterial or fungal pneumonia associated. Cardiomegalia and inflammatory mediastinal lymphadenopathy.

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はブラジルの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，失神及び左橈骨骨折の事象を発現した。関連する病歴は，潰瘍性大腸炎，左足整形外科手術，左足外傷，左手整形外科手術，左手外傷，非喫煙者及び元飲酒者（1 日 4 杯以上）であった。

**Event 2 及び 3 の臨床経過：**

投与688日後＊　，被験者は失神及び左橈骨骨折を発現した。投与688日後＊　，失神は消失した。

投与688日後＊　，被験者は，高さ約3メートルのはしごの上部にいるときに気を失い（失神した），地面に落ちた。被験者の息子は，被験者が目覚めたとき奇妙な動きをしたと証言した。被験者は少し混乱していたが，すぐに意識レベルは改善した。被験者は助けられ，救急治療室に搬送され，橈骨骨折と診断された。被験者は，気絶し落下する瞬間に方向感覚を失い光線過敏を感じていたことを思い出した。被験者は，すべての視覚の変化，頭痛，体震動，括約筋リリース，チアノーゼ又は舌/チーク刺激が悪化していた。被験者はこれまで失神を経験したことがなく，神経学的な疾患の既往もなかった。被験者は更なる検査を行った。同日被験者は意識喪失及び左腕痛のため入院した。

被験者は，失神の原因が特定されていないため，神経学及び一般内科によって診断された。神経内科医は，被験者は神経学的病因を示唆しない臨床状態であり，リスクの高い職業活動（常に高い階段を上っていた）に就いていたと述べた。被験者は胸部 X 線で左尖部に PTE（肺血栓塞栓症）を示唆するかもしれない低吸収域があった。D-ダイマーテストの結果は，被験者が失神のリスクが低いことを示したので，これ以上の検査は必要ではなかった。

被験者は四肢の X 線撮影と断層撮影を受け，左橈骨の遠位端の骨折及び関節が粉砕していることが明らかになった。不安定さと複雑さの基準により，これは絶対的に外科的治療の適応であった。投与691日後＊　　，掌側アプローチ及び二重柱ロックプレートを用いた左橈骨遠位端の骨折の骨接合を使用して外科的処置が行われた。同日，被験者は退院した。被験者は外来での整形外科のフォローアップを勧められた。

投与された薬剤は，トラマドール，エノキサパリン，オンダンセトロン，dipyrone，ケトプロフェン，オメプラゾール及びセファゾリンであった。

**The patient's past medications include:**

SULFASALAZINE for ULCERATIVE COLITIS ([redacted])

MESALAZINE for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ASTRAZENECA COVID-19 VACCINE for VACCINE ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Syncope (10042772) (Syncope (10042772) ) [v.24.0] [10042772]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge**: Not Applicable

2) Radius fracture (10037802) (Radius fracture (10037802) ) [v.24.0] [10037802]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of SYNCOPE

- **Investigator**: Not applicable

**- AbbVie:** Event is a common clinical issue seen in the general population and has multiple etiologies. Around 15-39 % of the total population experience syncope during their lifetime. Additional risk factor includes concomitant use of antihypertensive medication." da Silva RM. Syncope: epidemiology, etiology, and prognosis. Front Physiol. 2014;5:471. Published 2014 Dec 8.

Event of LEFT RADIUS FRACTURE

- **Investigator:** Syncope.

**- AbbVie:** Event most likely due to fall from ladder during syncopal episode.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ARM RADIOGRAPH**Y: Radius fracture

[redacted] 20[redacted] **BRAIN CT:** Absence of traumatic brain injury

[redacted] 20[redacted] **CHEST CT:** Absence of pulmonary thromboembolism

[redacted] 20[redacted] **CHEST RADIOGRAPHY:** HYPOATENUATION AT LEFT APEX

[redacted] 20[redacted] **CREATININE:** 1.34 mg/dL (normal 0.7 to 1.3)

[redacted] 20[redacted] **D DIMER:** 1.19 ug/ml (normal 0.0 to 0.5)

[redacted] 20[redacted] **EKG:** NOT CLINICALLY SIGNIFICANT

[redacted] 20[redacted] **FIST CT:** Commuted fracture of the left radius

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 急性腎不全 | X | | | X |
| COVID-19 | X | X | X | X |
| 深部静脈血栓症 | | X | | |
| 抗ナトリウム血症 | | X | | |
| 肺塞栓症 | X | X | X | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 5[redacted] | MALE | MULTIPLE |

| Medical History | Onset Year |
|---|---|
| ARTERIAL HYPERTENSION | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| LATENT TUBERCULOSIS | 20[redacted] |
| PERIPHERAL ARTHROPATHY | 20[redacted] |
| ULCERATIVE COLITE | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | | | 19[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 57 | 57 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 58 | [redacted]20[redacted] / 435 | 378 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted]20[redacted] / 436 | [redacted]20[redacted] / 600 | 165 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| CIPROFLOXACIN;METRONIDAZOLE | 500 mg | BID | Y-M: 20[redacted] |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 200 mg | QD | Y-M: 20[redacted] |
| ISONIAZID | 900 mg | QD | Y-M: 20[redacted] |
| CLONIDINE | 0.150 mg | QD | Y-M: 20[redacted] / -140 |
| LOSARTAN | 50 mg | QD | Y-M: 20[redacted] / -140 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| LOSARTAN | 50 mg | QD | Y-M: 20[redacted] / -140 | Y-M: 20[redacted] / 173 |
| AMLODIPINE | 5 mg | BID | Y-M: 20[redacted] / 56 | Y-M: 20[redacted] / 173 |
| HYDROCHLOROTHIAZIDE | 25 mg | QD | Y-M: 20[redacted] / 56 | Y-M: 20[redacted] / 170 |
| LEVOFLOXACIN | 500 mg | QD | Y-M: 20[redacted] / 165 | Y-M: 20[redacted] / 167 |
| DEXAMETHASONE | 6 mg | QD | Y-M: 20[redacted] / 168 | Y-M: 20[redacted] / 168 |
| INSULIN HUMAN | 10 IU | PRN | Y-M: 20[redacted] / 168 | Y-M: 20[redacted] / 184 |
| METAMIZOLE | 1 g | OTHER: QID OR PRN (IF PAIN) | Y-M: 20[redacted] / 168 | Y-M: 20[redacted] / 184 |
| OMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted] / 168 | Y-M: 20[redacted] / 172 |
| CEFTRIAXONE | 1 g | BID | Y-M: 20[redacted] / 169 | Y-M: 20[redacted] / 176 |
| CODEINE;PARACETAMOL | 500 + 30 mg | QD | Y-M: 20[redacted] / 169 | Y-M: 20[redacted] / 171 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted] / 169 | Y-M: 20[redacted] / 173 |
| METHYLPREDNISOLONE | 40 mg | BID | Y-M: 20[redacted] / 169 | Y-M: 20[redacted] / 172 |

| | | | | |
|---|---|---|---|---|
| FUROSEMIDE | 20 mg | OTHER: FOUR TIMES A DAY IF NEEDED | Y-M: 20[redacted] / 171 | Y-M: 20[redacted] / 180 |
| SODIUM LACTATE | 500 mL | QD | Y-M: 20[redacted] / 172 | Y-M: 20[redacted] / 172 |
| ARKETAMINE | 160 mg | QD | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 173 |
| FENTANYL | 6 mg | OTHER: 4 ML/H | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 176 |
| LACTULOSE | 20 g | TID | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 173 |
| LIDOCAINE | 160 mg | QD | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 173 |
| METHYLPREDNISOLONE | 90 mg | QD | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 173 |
| MIDAZOLAM | 600 mg | OTHER: 4 ML/H | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 176 |
| NOREPINEPHRINE | 32 mg | OTHER: 4 ML PER HOUR | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 180 |
| OMEPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 184 |
| ROCURONIUM | 1200 mg | OTHER: 6 ML PER HOUR | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 179 |
| ENOXAPARIN | 60 mg | QD | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 174 |
| HEPARIN | 5000 IU | TID | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 184 |
| HYPROMELLOSE | 0.5 gtt | OTHER: EVERY 4 HOURS | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 184 |
| LACTULOSE | 13 g | TID | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 178 |
| METHYLPREDNISOLONE | 125 mg | QD | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 181 |
| SODIUM LACTATE | 500 mL | QD | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 174 |
| INSULIN | 10 IU | TID | Y-M: 20[redacted] / 176 | Y-M: 20[redacted] / 184 |
| FENTANYL | 6 mg | OTHER: 2.5 ML/H | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 180 |
| MIDAZOLAM | 600 mg | OTHER: 3.5 ML/H | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 180 |
| AMLODIPINE | 5 mg | BID | Y-M: 20[redacted] / 178 | Y-M: 20[redacted] / 184 |
| DEXMEDETOMIDINE | 800 ug | QD | Y-M: 20[redacted] / 178 | Y-M: 20[redacted] / 180 |
| HYDROCHLOROTHIAZIDE | 25 mg | BID | Y-M: 20[redacted] / 178 | Y-M: 20[redacted] / 179 |
| LIDOCAINE | 2400 mg | QD | Y-M: 20[redacted] / 178 | Y-M: 20[redacted] / 180 |
| METHADONE | 5 mg | TID | Y-M: 20[redacted] / 178 | Y-M: 20[redacted] / 180 |
| NITROPRUSSIDE | 100 mg | QD | Y-M: 20[redacted] / 178 | Y-M: 20[redacted] / 179 |
| RISPERIDONE | 2 mg | BID | Y-M: 20[redacted] / 178 | Y-M: 20[redacted] / 184 |
| CALCIUM CARBONATE | 5 g | BID | Y-M: 20[redacted] / 179 | Y-M: 20[redacted] / 179 |
| LACTULOSE | 10 g | TID | Y-M: 20[redacted] / 179 | Y-M: 20[redacted] / 183 |
| CALCIUM GLUCONATE | 10 % | QD | Y-M: 20[redacted] / 180 | Y-M: 20[redacted] / 180 |

| | | | | |
|---|---|---|---|---|
| NITROPRUSSIDE | 50 mg | QD | Y-M: 20[redacted] / 180 | Y-M: 20[redacted] / 184 |
| TERBUTALINE | 0.5 mg | TID | Y-M: 20[redacted] / 180 | Y-M: 20[redacted] / 184 |
| CLONIDINE | 150 ug | TID | Y-M: 20[redacted] / 181 | Y-M: 20[redacted] / 184 |
| HYDROCHLOROTHIAZIDE | 25 mg | BID | Y-M: 20[redacted] / 181 | Y-M: 20[redacted] / 182 |
| QUETIAPINE | 25 mg | BID | Y-M: 20[redacted] / 181 | Y-M: 20[redacted] / 181 |
| SALBUTAMOL | 100 ug | OTHER: EVERY 4 HOURS | Y-M: 20[redacted] / 181 | Y-M: 20[redacted] / 184 |
| METHYLPREDNISOLONE | 100 mg | QD | Y-M: 20[redacted] / 182 | Y-M: 20[redacted] / 182 |
| METHYLPREDNISOLONE | 80 mg | QD | Y-M: 20[redacted] / 183 | Y-M: 20[redacted] / 184 |

**Event #1: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | COVID-19 INFECTION |
| **Preferred term** | COVID-19 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 601 / 166 (1 DAY AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 619 / 184 (19 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 19 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event, Death, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | WORSENING OF COVID-19 INFECTION |
| **Preferred term** | COVID-19 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 603 / 168 (3 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 168): Creatinine: 149.401509 [61.882282 - 114.924238] UMOL/L; NPTST334-UREA: 53.65 [19 - 49] MG/DL; [redacted]20[redacted] (RX DAY 171): Aspartate Aminotransferase: 62.6 [0 - 38] U/L; Creatinine: 75.142771 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 5.29 [4.57 - 5.98] 10^12/L; Leukocytes: 9 [3.79 - 10.33] 10^9/L; NPTST069-C-REACTIVE PROTEIN: 19.66 [0 - 1] MG/DL; NPTST069-C-REACTIVE PROTEIN: 20.16 [0 - 1] MG/DL; NPTST197-LACTATE: 1.61 [0.36 - 1.39] MMOL/L; NPTST334-UREA: 39.76 [19 - 49] MG/DL; Platelets: 273 [166 - 389] 10^9/L; [redacted]20[redacted] (RX DAY 173): NPTST243-PCO2: 38.2 [32 - 48] MMHG; NPTST254-PO2: 59.5 [83 - 108] MMOL/L; NPTST334-UREA: 75.46 [19 - 49] MG/DL; [redacted]20[redacted] (RX DAY 174): Creatinine: 206.863628 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 5.13 [4.57 - 5.98] 10^12/L; Glucose: 9.99126 [3.88549 - 5.5507] MMOL/L; Leukocytes: 10.4 [3.79 - 10.33] 10^9/L; NPTST197-LACTATE: 2.98 [0.36 - 1.39] MMOL/L; NPTST209-MAGNESIUM: 3.13 [1.6 - 2.6] MG/DL; NPTST243-PCO2: 40.8 [32 - 48] MMHG; NPTST254-PO2: 81.9 [83 - 108] MMOL/L; NPTST334-UREA: 152.80 [19 - 49] MG/DL; Platelets: 431 [166 - 389] 10^9/L; Potassium: 4.25 [3.5 - 5.1] MMOL/L; Sodium: 144 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 175): Albumin: 34.2 [32 - 48] G/L; Aspartate Aminotransferase: 34.22 [0 - 38] U/L; Bicarbonate: 23.7 [21 - 28] MMOL/L; Bilirubin: 5.473245 [5.131167 - 20.524668] UMOL/L; Calcium: 2.11335 [2.070933 - 2.644806] MMOL/L; Creatinine: 241.3409 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 5.01 [4.57 - 5.98] 10^12/L; Glucose: 17.040649 [3.88549 - 5.5507] MMOL/L; Leukocytes: 11.4 [3.79 - 10.33] 10^9/L; NPTST069-C-REACTIVE PROTEIN: 4.43 [0 - 1] MG/DL; NPTST197-LACTATE: 2.02 [0.36 - 1.39] MMOL/L; NPTST243-PCO2: 35.5 [32 - 48] MMHG; NPTST250-PHOSPHORUS: 4.67 [2.4 - 5.1] MG/DL; NPTST254-PO2: 72.71 [83 - 108] MMHG; NPTST334-UREA: 180.92 [19 - 49] MG/DL; Platelets: 318 [166 - 389] 10^9/L; Potassium: 4.04 [3.4 - 4.5] MMOL/L; Sodium: 146.5 [136 - 145] MMOL/L; pH: 7.44 [7.32 - 7.45] N/A; [redacted]20[redacted] (RX DAY 176): Creatinine: 265.20978 [61.882282 - 114.924238] UMOL/L; NPTST069-C-REACTIVE PROTEIN: 2.67 [0 - 1] MG/DL; NPTST243-PCO2: 40.6 [32 - 48] MMHG; NPTST254-PO2: 76.1 [83 - 108] MMOL/L; NPTST334-UREA: 205.74 [19 - 49] MG/DL; Sodium: 151.7 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 177): Creatinine: 181.226683 [61.882282 - 114.924238] UMOL/L; NPTST069-C-REACTIVE PROTEIN: 1.90 [0 - 1] MG/DL; NPTST334-UREA: 138.84 [19 - 49] MG/DL; Potassium: 7.06 [3.4 - 4.5] MMOL/L; [redacted]20[redacted] (RX DAY 178): Creatinine: 129.06876 [61.882282 - 114.924238] UMOL/L; NPTST243-PCO2: 37.4 [32 - 48] MMHG; NPTST254-PO2: 79.5 [83 - 108] MMOL/L; NPTST334-UREA: 99.23 [19 - 49] MG/DL; [redacted]20[redacted] (RX DAY 179): Creatinine: 266.977845 [61.882282 - 114.924238] UMOL/L; Leukocytes: 14.1 [3.79 - 10.33] 10^9/L; NPTST243-PCO2: 42.5 [32 - 48] MMHG; NPTST254-PO2: 79.8 [83 - 108] MMHG; NPTST334-UREA: 167.07 [19 - 49] MG/DL; [redacted]20[redacted] (RX DAY 180): Creatinine: 185.646846 [61.882282 - 114.924238] UMOL/L; Leukocytes: 14.5 [3.79 - 10.33] 10^9/L; NPTST069-C-REACTIVE PROTEIN: 2.49 [0 - 1] MG/DL; NPTST243-PCO2: 42.3 [32 - 48] MMHG; NPTST254-PO2: 69.4 [83 - 108] MMOL/L; NPTST334-UREA: 169.47 [19 - 49] MG/DL; Sodium: 148.2 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 181): Creatinine: 146.749412 [61.882282 - 114.924238] UMOL/L; Leukocytes: 17.2 [3.79 - 10.33] 10^9/L; NPTST334-UREA: 107.11 [19 - 49] MG/DL; Sodium: 146.4 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 182): Creatinine: 121.112466 [61.882282 - 114.924238] UMOL/L; Leukocytes: 20 [3.79 - 10.33] 10^9/L; NPTST069-C-REACTIVE PROTEIN: 7.0 [0 - 1] MG/DL; NPTST334-UREA: 98.85 [19 - 49] MG/DL; Sodium: 154 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 183): Creatinine: 121.996499 [61.882282 - 114.924238] UMOL/L; Leukocytes: 17.4 [3.79 - 10.33] 10^9/L; NPTST334-UREA: 105.18 [19 - 49] MG/DL; Sodium: 153.1 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 184): Leukocytes: 15.3 [3.79 - 10.33] 10^9/L; NPTST069-C-REACTIVE PROTEIN: 3.18 [0 - 1] MG/DL; NPTST334-UREA: 103.58 [19 - 49] MG/DL; Sodium: 153.4 [136 - 145] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 619 / 184 (19 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 17 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | COVID-19 |

| | |
|---|---|
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, DEATH OF SUBJECT |

**Event #3: Serious Adverse Event, Event of Interest - Renal Dysfunction**

| | |
|---|---|
| **Event Description** | ACUTE RENAL FAILURE |
| **Preferred term** | 急性腎不全 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 609 / 174 (9 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 615 / 180 (15 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 7 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | COVID-19 |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #4: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | HYPERNATREMIA |
| **Preferred term** | 高ナトリウム血症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 617 / 182 (17 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 619 / 184 (19 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 3 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |

| | |
|---|---|
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

**Event #5: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | SUSPECTED DEEP VEIN THROMBOSIS |
| **Preferred term** | 深部静脈血栓症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 619 / 184 (19 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 619 / 184 (19 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 1 DAY |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

**Event #6: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Death**

| | |
|---|---|
| **Event Description** | PULMONARY THROMBOEMBOLISM |
| **Preferred term** | 肺塞栓症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 619 / 184 (19 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 619 / 184 (19 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 1 DAY |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |

| | |
|---|---|
| **Investigator Alternative Etiology** | COVID-19 |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | DEATH OF SUBJECT |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はブラジルの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 感染症の悪化，致命的な肺血栓塞栓症及び急性腎不全の事象を発現した。関連する病歴は，元喫煙者，動脈性高血圧，汎大腸炎，潰瘍性大腸炎，潜伏結核，末梢関節症および現飲酒者（1 日 2 杯未満）であった。

**Event 2，3 及び 6 の臨床経過：**

投与603日後＊　，被験者は COVID-19 感染症が悪化した。投与610日後＊　　，被験者は急性腎不全を発現した。投与615日後＊　，急性腎不全は消失した。投与619日後＊　，被験者は肺血栓塞栓症を発現し，同日死亡した。死因は，COVID-19 感染症の悪化と肺血栓塞栓症として報告された。剖検は行われなかった。

日付は不明であるが，被験者は鼻漏，鼻閉塞，持続性の乾いた咳，胸痛，背部痛，発熱，悪寒，軽度の頭痛，呼吸困難，食欲不振及び無力症の症状が発現し始めた。

投与600日後＊　，これらの症状のために鼻咽頭ぬぐい液による検査が行われ，COVID-19 感染が示唆された。翌日，陽性が判明し，さらに多くの検査が行われた。

投与603日後＊　，被験者は症状が悪化の方向に進んだため入院となった。理学療法士の診断では，呼吸数は毎分 30 で，酸素飽和度は 89%–96%であった。被験者は鼻カニューレあたり 3L /分の酸素で治療された。被験者は監視下の状態のままであった。投与606日後＊　，臨床的にも検査結果からも明らかな悪化がみられた。呼吸困難及び酸素飽和度悪化後，集中治療室での入院となり，高流量の鼻カニューレにより治療された。投与607日後＊　，被験者は 60 L/分のカテーテルを使用しても，低酸素飽和度の悪化は進行し，呼吸数酸素化（ROX）指数の悪化を示した。投与608日後＊　，チューブ番号 9 の気管挿管が挿入された。同日，中心静脈カテーテルを留置し，侵襲的血圧モニタリングのために橈骨動脈カテーテル法を施行した。どちらの手順も問題なく実行された。投与610日後，被験者は腎機能が悪化し，クレアチンホスホキナーゼが増加した。被験者は透析療法を開始したが，腎機能の改善により投与615日後＊ に中止された。

同日遅い時間に，換気パラメータの改善により抜管され，12 L/分の酸素の鼻カニューレで換気サポートを維持した。抗生物質とコルチコステロイド療法が完了した。被験者には集中治療が続けられた。投与619日後＊ ，被験者は，高度の動脈性低血圧及び心停止を伴う広範囲に及ぶ肺血栓塞栓症の可能性と考えられる不飽和化を示したとき，臨床症状は安定していた。その後，被験者は CPR 操作を開始した医療チームに診察された。しかし，被験者はすべての侵襲的な生命維持手段に反応せず，16 分間の蘇生の試み後に死亡に至った。死亡は投与619日後＊ 午前 8 時 45 分，医療チームによって宣言された。

治験責任医師によると，肥満は当該事象の危険因子であった。

投与された薬剤は，metilprednisone，paracetamol，codeine，enoxaparin，lacted ringer，フロセミド，ミダゾラム，fentanil，ラクツロース，リドカイン，dextroketamine，hipromelose，heparin，precedex，nipride，metadone，リスペリドン，amlodipine，hydrochlorothlazine，炭酸カルシウム，terbutaline，calcium gluconate，clonidine，quetiapine，salbutamol，levofloxacin，ceftriaxone，メチルプレドニゾロン，ミダゾラム，フェンタニル，norepinephrine，dipirone，rocuronium，デキサメタゾン及びオメプラゾールであった。

**The patient's past medications include:**

CIPROFLOXACIN + METRONIDAZOLE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ISONIAZID for TB PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COVID-19 VACCINE ASTRAZENECA for COVID-19 PREVENTION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) COVID-19 aggravated (10084657) (COVID-19 (10084268) ) [v.24.0] [10084657]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

2) Pulmonary thromboembolism (10037436) (Pulmonary embolism (10037377) ) [v.24.0][10037436]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

3) Acute renal failure (10001041) (Acute kidney injury (10069339) ) [v.24.0] [10001041]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of WORSENING OF COVID-19 INFECTION

**- Investigator:** COVID-19

**- AbbVie:** Event is more likely related to the COVID-19 pandemic outbreak.

Event of PULMONARY THROMBOEMBOLISM

**- Investigator:** COVID-19

**- AbbVie:** Event is more likely related to concurrent COVID-19 infection and concurrent prolonged hospitalization.

Event of ACUTE RENAL FAILURE

**- Investigator:** COVID-19

**- AbbVie:** Event is more likely related to concurrent COVID-19 infection.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 62.60 U/L (normal 0.0 to 38.0)

[redacted] 20[redacted] **ASPARTATE AMINOTRANSFERASE:** 34.22 U/L (normal 0.0 to 38)

[redacted] 20[redacted] **BICARBONATE:** 23.7 MMOL/L (normal 21 to 28)

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 19.66 mg/dL (normal 0.0 to 1.0)

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 20.16 mg/dL (normal 0.0 to 1.0)

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 4.43 mg/dL (normal 0.0 to 1.0)

[redacted] 20[redacted] **CHEST X RAY:** Increased cardiac area, atelectasis with potential pneumonia in left lung base

[redacted] 20[redacted] **COVID-19 NASOPHARYNGEAL SWAB:** Positive

[redacted] 20[redacted] **CREATININE:** 0.85 mg/dL (normal 0.70 to 1.30)

[redacted] 20[redacted] **CREATININE:** 2.34 mg/dL (normal 0.70 to 1.30)

[redacted] 20[redacted] **CREATININE:** 2.73 mg/dL (normal 0.70 to 1.30)

[redacted] 20[redacted] **GLUCOSE:** 180 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **GLUCOSE:** 307 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **LACTATE:** 2.98 MMOL/L (normal 0.36 to 1.39)

[redacted] 20[redacted] **LACTATE:** 2.02 MMOL/L (normal 0.36 to 1.39)

[redacted] 20[redacted] **OXYGEN SATURATION:** 89-96% on 3 liters of o2 per minute, per nasal cannula

[redacted] 20[redacted] **PCO2:** 35.5 mmHg (normal 32 to 48)

[redacted] 20[redacted] **PLATELET COUNT:** 273 X10**3/MCL (normal 166 to 389)

[redacted] 20[redacted] **PLATELET COUNT:** 431 X10**3/MCL (normal 166 to 389)

[redacted] 20[redacted] **PLATELET COUNT:** 318 X10**3/MCL (normal 166 to 389)

[redacted] 20[redacted] **PO2:** 72.71 mmHg (normal 83 to 108)

[redacted] 20[redacted] **RADIAL ARTERY CATHETERIZATION FOR INVASIVE BLOOD PRESSURE MONITORING:** No problems

[redacted] 20[redacted] **RED BLOOD CELLS:** 5.29 X10**6/MCL (normal 4.57 to 5.98)

[redacted] 20[redacted] **RED BLOOD CELLS:** 5.13 X10**6/MCL (normal 4.57 to 5.98)

[redacted] 20[redacted] **RED BLOOD CELLS:** 5.01 X10**6/MCL (normal 4.57 to 5.98)

[redacted] 20[redacted] **RESPIRATORY RATE:** 30 /min

[redacted] 20[redacted] **RT-PCR FOR CORONAVIRUS:** Positive

[redacted] 20[redacted] **UREA:** 39.76 mg/dL (normal 19 to 49)

[redacted] 20[redacted] **UREA:** 152.80 mg/dL (normal 19 to 49)

[redacted] 20[redacted] **UREA:** 180.92 mg/dL (normal 19 to 49)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 9.0 X10**3/MCL (normal 3.79 to 10.33)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 10.4 X10**3/MCL (normal 3.79 to 10.33)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 11.4 X10**3/MCL (normal 3.79 to 10.33)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 貧血 | | | | X |
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| 好中球減少症 | | | | X |
| 非感染性気管支炎 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| CYSTICERCOSIS | 20[redacted] |
| DIABETES | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 19[redacted] |
| HYPERECPLEXY | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| INSOMNIA | 20[redacted] |
| MIGRANEA | 20[redacted] |
| OBSTRUCTIVE SLEEP APNEA SYNDROME | 20[redacted] |
| TREMOR OF INTENTION | 20[redacted] |
| TREMOR OF REST | 20[redacted] |
| ULCERATIVE COLITIS | 19[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: TOOTH EXTRACTION | 20[redacted] |
| PRIOR PROCEDURES: VASECTOMY | 20[redacted] |
| SAE SUPPLEMENTAL PROCEDURE: CHEST XRAY | 20[redacted] |
| SAE SUPPLEMENTAL PROCEDURE: CT SCAN | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 15 | 19[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | More than 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 55 | 55 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 56 | [redacted]20[redacted] / 422 | 367 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted]20[redacted] / 423 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| AZATHIOPRINE | 150 mg | QD | Y-M: 19[redacted]-[redacted] |
| SULFASALAZINE | 4 g | QD | Y-M: 20[redacted]-[redacted] |
| HYDROCHLOROTHIAZIDE | 25 mg | QD | Y-M: 20[redacted]-[redacted] |
| LAMOTRIGINE | 100 mg | QID | Y-M: 20[redacted]-[redacted] |
| PRAMIPEXOLE | 1 g | QD | Y-M: 20[redacted]-[redacted] |
| PREDNISONE | 40 mg | QD | Y-M: 20[redacted]-[redacted] |
| CARVEDILOL | 12.5 mg | BID | Y-M: 20[redacted]-[redacted] |
| CLONIDINE | 150 ug | BID | Y-M: 20[redacted]-[redacted] |
| DOXAZOSIN | 2 mg | QD | Y-M: 20[redacted]-[redacted] |
| HYDRALAZINE | 50 mg | BID | Y-M: 20[redacted]-[redacted] |
| CALCITRIOL | 0.25 ug | OTHER: EVERY WEEK | Y-M: 20[redacted]-[redacted] / -352 |
| GLICLAZIDE | 30 mg | BID | Y-M: 20[redacted]-[redacted] / -352 |
| LINAGLIPTIN | 5 mg | QD | Y-M: 20[redacted]-[redacted] / -352 |
| FORMOTEROL | 12 ug | BID | Y-M: 20[redacted]-[redacted] / -91 |
| OTHER VIRAL VACCINES | NOT REPORTED | ONCE | Y-M: 20[redacted]-[redacted] / -91 |

| | | | |
|---|---|---|---|
| OTHER VIRAL VACCINES | NOT REPORTED | ONCE | Y-M: 20[redacted] / -1 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| HYDROCHLOROTHIAZIDE | 25 mg | QD | Y-M: 20[redacted] | Not reported |
| LAMOTRIGINE | 100 mg | QID | Y-M: 20[redacted] | Not reported |
| PRAMIPEXOLE | 1 g | QD | Y-M: 20[redacted] | Not reported |
| CARVEDILOL | 12.5 mg | BID | Y-M: 20[redacted] | Not reported |
| CLONIDINE | 150 ug | BID | Y-M: 20[redacted] | Not reported |
| DOXAZOSIN | 2 mg | QD | Y-M: 20[redacted] | Not reported |
| HYDRALAZINE | 50 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 75 |
| CALCITRIOL | 0.25 ug | OTHER: EVERY WEEK | Y-M: 20[redacted] / -352 | Y-M: 20[redacted] / 75 |
| GLICLAZIDE | 30 mg | BID | Y-M: 20[redacted] / -352 | Not reported |
| LINAGLIPTIN | 5 mg | QD | Y-M: 20[redacted] / -352 | Not reported |
| FORMOTEROL | 12 ug | BID | Y-M: 20[redacted] / -91 | Not reported |
| FUROSEMIDE | 40 mg | QD | Y-M: 20[redacted] / 11 | Not reported |
| TADALAFIL | 20 mg | OTHER: ONE TABLET 1 HOUR BEFORE THE SEXUAL INTERCOURSE | Y-M: 20[redacted] / 72 | Not reported |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] / 75 | ONGOING |
| IRON | 200 mg | BID | Y-M: 20[redacted] / 75 | Not reported |
| VITAMIN D NOS | 7000 IU | OTHER: ONCE A WEEK | Y-M: 20[redacted] / 75 | Not reported |
| CALCITRIOL | 0.50 ug | OTHER: EVERY WEEK | Y-M: 20[redacted] / 76 | Not reported |
| AZITHROMYCIN | 500 mg | QD | Y-M: 20[redacted] / 79 | Y-M: 20[redacted] / 83 |

**Event #1: Event of Interest - Neutropenia**

| | |
|---|---|
| **Event Description** | NEUTROPENIA |
| **Preferred term** | 好中球減少症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 127 / -296 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

NOT APPLICABLE

| | |
|---|---|
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 137 / -286 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #3: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | INFLAMMATORY BRONCHOPATHY |
| **Preferred term** | 非感染性気管支炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 291 / -132 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY -130): Hematocrit: 0.301 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 108 [140 - 180] G/L; [redacted]20[redacted] (RX DAY -126): NPTST069-C-REACTIVE PROTEIN: 14.2 [0 - 8] MG/L; NPTST118-DENGUE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #4: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | INCREASE OF CREATINE PHOSPHOKINASE |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 423 / 1 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-234

治験責任医師からの報告。本被験者はブラジルの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，非感染性気管支炎を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 15 年間），潰瘍性大腸炎，高血圧，糖尿病，閉塞性睡眠時無呼吸症候群及び元飲酒者であった。

**Event 3 の臨床経過：**

投与291日後＊　　，被験者が炎症性気管支疾患を発現した。

投与297日後＊　，被験者は呼吸困難と発熱を訴えて入院した。発熱は薬の使用によって回復することはなく，被験者はこの発熱の検査のために入院した。被験者は，抗生物質とコルチコ療法で治療された。投与298日後＊　，被験者は退院し，自宅で治療を継続した。

投与された薬剤は，azithromycin，decadron，dipirone，オメプラゾール，heparin，paracetamol 及び rosefin であった。

**The patient's past medications include:**

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 19[redacted] - [redacted] 20[redacted])

SULFASALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　Noninfective bronchitis (10062644)　(Noninfective bronchitis (10062644) )　[v.24.0]　[10062644]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr.　(Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

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Event of INFLAMMATORY BRONCHOPATHY

**- Investigator:** Not Applicable

**- AbbVie:** Event triggers include airway bronchospasm, inhalation of air pollutants and chemical exposures.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BODY TEMPERATURE:** 38.5 Degrees C

[redacted] **20[redacted] CRP:** 14.7 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] CT SCAN:** Inflammatory Bronchopathy

[redacted] **20[redacted] RESPIRATORY RATE:** 18 breaths/min

[redacted] **20[redacted] SCREENING CHEST X-RAY:** Normal

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Neutropenia: Intermittent. Study drug interrupted.
Anaemia: Intermittent. Study drug interrupted.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 静脈血栓症 | X | X | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA | 20[redacted] |
| CHICKENPOX | NOT REPORTED |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| POST MENOPAUSAL | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted]20[redacted] / 57 | [redacted]20[redacted] / 117 | 61 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / 118 | [redacted]20[redacted] / 201 | 84 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 209 | [redacted]20[redacted] / 236 | 28 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1000 mg | BID | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | BID | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EACH 8 WEEKS | Y-M: 20[redacted] |
| ETROLIZUMAB | 105 mg | OTHER: EACH 4 WEEKS | Y-M: 20[redacted] |
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] / -18 |
| PREGABALIN | 75 mg | QD | Y-M: 20[redacted] / -22 |
| ASCORBIC ACID | 500 mg | QD | Y: 20[redacted] |
| CRATAEGUS SPP. | 1 OTHER: CAPSULE | QD | Y: 20[redacted] |
| CYANOCOBALAMIN;PYRIDOXINE;THIAMINE | 5000 ug | OTHER: EACH 3 MONTHS | Y: 20[redacted] |
| FOLIC ACID | 5 mg | QD | Y: 20[redacted] |
| VITAMIN D NOS | 1000 IU | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] / -18 | Y-M: 20[redacted] / 254 |
| PREGABALIN | 75 mg | QD | Y-M: 20[redacted] / -22 | Not reported |
| ENOXAPARIN | 60 mg | BID | Y-M: 20[redacted] / 18 | Y-M: 20[redacted] / 21 |
| RIVAROXABAN | 15 mg | BID | Y-M: 20[redacted] / 21 | Y-M: 20[redacted] / 34 |
| ASCORBIC ACID | 500 mg | QD | Y: 20[redacted] | Not reported |
| CRATAEGUS SPP. | 1 OTHER: CAPSULE | QD | Y: 20[redacted] | Not reported |
| CYANOCOBALAMIN;PYRIDOXINE;THIAMINE | 5000 ug | OTHER: EACH 3 MONTHS | Y: 20[redacted] | Not reported |
| FOLIC ACID | 5 mg | QD | Y: 20[redacted] | Not reported |
| VITAMIN D NOS | 1000 IU | QD | Y: 20[redacted] | Not reported |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event**

| | |
|---|---|
| **Event Description** | ACUTE VENOUS THROMBOSIS |
| **Preferred term** | 静脈血栓症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 226 / 18 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted] (RX DAY 20): NPTST260-PROTHROMBIN ACTIVITY TIME: 12.6 [11 - 15] SEC; Platelets: 238 [140 - 440] 10^9/L | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 229 / 21 |
| **Duration of AE** | 4 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はブラジルの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，急性静脈血栓症の事象を発現した。関連する病歴は，閉経後，広範囲な潰瘍性大腸炎（全大腸炎型），貧血，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与226日後＊　　，被験者は急性静脈血栓症を発現した。投与229日後＊　　，急性静脈血栓症は消失した。

本事象発現前の投与の約5ヵ月後＊に，被験者は潰瘍性大腸炎の悪化（非重篤）と診断され，発現時に継続していた。

投与226日後＊　　，被験者は左下腿の疼痛及び重度の浮腫があり，救急治療室を受診した。超音波検査で，左総大腿静脈及び左大腿深静脈の急性血栓症と診断された。投与226日後＊　，被験者は入院した。被験者は，血栓症に対して，圧迫包帯，体位の調節，内服薬及び皮下注射薬で治療された。投与229日後＊　，被験者はイグザレルトを投与され，退院した。

治験責任医師によると，本事象に関連する危険因子は，被験者の年齢が 40 歳以上であること，及び炎症性腸疾患であった。

本事象により，被験者の治験は中止された。

投与された薬剤は，エノキサパリン，イグザレルト及びプレガバリンであった。

**The patient's past medications include:**

MESALAZINE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　Venous thrombosis (10047249)　(Venous thrombosis (10047249) )　[v.23.1]　[10047249]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of ACUTE VENOUS THROMBOSIS

**- Investigator:** Not applicable

**- AbbVie:** Risk factors include concurrent worsening of ulcerative colitis (Chronic inflammatory diseases have been associated with activation of coagulation and an increased risk of venous thromboembolic events (VTEs), in particular during active disease. This has been shown for inflammatory bowel disease) and advanced age (Per the AHA -American Heart Associaton - patients older than 40 years are at higher risk, and that risk doubles with each subsequent decade.)

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] DOPPLER ULTRASOUND LEFT LOWER EXTREMITY:** Acute thrombosis of the left femoral common, femoral and deep femoral veins

[redacted] **20[redacted] PLATELET COUNT:** 238 X10**3/MM**3 (normal 140 to 440)

[redacted] **20[redacted] PT:** 12.6 SEC (normal 11 to 15)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 腹部膿瘍 | X | X | | X |
| 腎機能障害 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| CARENTIAL ANEMIA | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| PRIMARY SCLEROSING CHOLANGITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 54 | 54 |
| M14-675 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted]20[redacted] / 55 | [redacted]20[redacted] / 110 | 56 |

| | | | | | |
|---|---|---|---|---|---|
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / [redacted]20[redacted] / 271 111 | 161 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 272 [redacted]20[redacted] / 438 | 167 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| INFLIXIMAB | 5 mg/kg | OTHER: EACH 8 WEEKS | Y-M: 20[redacted]-[redacted] |
| ADALIMUMAB | 40 mg | OTHER: EACH 2 WEEKS | Y-M: 20[redacted]-[redacted] |
| URSODEOXYCHOLIC ACID | 900 mg | OTHER: 2 TABLETS 300 MG MORNING AND 1 TABLET 300MG NIGHT | Y-M: 20[redacted]-[redacted] |
| ETROLIZUMAB | 105 mg | OTHER: EACH 4 WEKS | Y-M: 20[redacted]-[redacted] |
| IRON | 2 OTHER: AMPULES | OTHER: EACH 2 WEEKS | Y-M: 20[redacted]-[redacted] / -62 |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted]-[redacted] / -48 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| URSODEOXYCHOLIC ACID | 900 mg | OTHER: 2 TABLETS 300 MG MORNING AND 1 TABLET 300MG NIGHT | Y-M: 20[redacted]-[redacted] | ONGOING |
| IRON | 2 OTHER: AMPULES | OTHER: EACH 2 WEEKS | Y-M: 20[redacted]-[redacted] / -62 | ONGOING |
| PREDNISONE | 35 mg | QD | Y-M: 20[redacted]-[redacted] / 118 | Y-M: 20[redacted]-[redacted] / 148 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted]-[redacted] / 134 | Y-M: 20[redacted]-[redacted] / 154 |
| PREDNISONE | 30 mg | QD | Y-M: 20[redacted]-[redacted] / 149 | Y-M: 20[redacted]-[redacted] / 166 |
| CIPROFLOXACIN | 200 mg | BID | Y-M: 20[redacted]-[redacted] / 167 | Y-M: 20[redacted]-[redacted] / 168 |
| ENOXAPARIN | 40 mg | QD | Y-M: 20[redacted]-[redacted] / 167 | Y-M: 20[redacted]-[redacted] / 177 |
| HYDROCORTISONE | 300 mg | QD | Y-M: 20[redacted]-[redacted] / 167 | Y-M: 20[redacted]-[redacted] / 167 |
| METAMIZOLE | 500 mg | QID | Y-M: 20[redacted]-[redacted] / 167 | ONGOING |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted]-[redacted] / 167 | Y-M: 20[redacted]-[redacted] / 170 |
| PREDNISONE | 40 mg | QD | Y-M: 20[redacted]-[redacted] / 167 | Y-M: 20[redacted]-[redacted] / 167 |
| TRAMADOL | 100 mg | TID | Y-M: 20[redacted]-[redacted] / 167 | ONGOING |

| | | | | |
|---|---|---|---|---|
| CIPROFLOXACIN | 400 mg | BID | Y-M: 20[redacted] / 168 | Y-M: 20[redacted] / 183 |
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] / 168 | Y-M: 20[redacted] / 196 |
| PIPERACILLIN;TAZOBACTAM | 4000 mg | QID | Y-M: 20[redacted] / 170 | Y-M: 20[redacted] / 174 |
| PIPERACILLIN;TAZOBACTAM | 4500 mg | QID | Y-M: 20[redacted] / 170 | Y-M: 20[redacted] / 170 |
| VANCOMYCIN | 1100 mg | BID | Y-M: 20[redacted] / 170 | Y-M: 20[redacted] / 172 |
| VANCOMYCIN | 2000 mg | BID | Y-M: 20[redacted] / 170 | Y-M: 20[redacted] / 170 |
| VANCOMYCIN | 1350 mg | BID | Y-M: 20[redacted] / 172 | Y-M: 20[redacted] / 173 |
| VANCOMYCIN | 1200 mg | BID | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 175 |
| PIPERACILLIN;TAZOBACTAM | 4500 mg | QID | Y-M: 20[redacted] / 174 | Y-M: 20[redacted] / 176 |
| PIPERACILLIN;TAZOBACTAM | 4000 mg | QID | Y-M: 20[redacted] / 176 | Y-M: 20[redacted] / 177 |
| VANCOMYCIN | 1000 mg | BID | Y-M: 20[redacted] / 176 | Y-M: 20[redacted] / 177 |
| PREDNISONE | 30 mg | QD | Y-M: 20[redacted] / 197 | ONGOING |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections, Event of Interest - Adjudicated Gastrointestinal Perforations**

| | |
|---|---|
| **Event Description** | INTRAABDOMINAL ABSCESS |
| **Preferred term** | 腹部膿瘍 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 438 / 167 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 167): Leukocytes: 11.7 [4 - 11] 10^9/L; [redacted]20[redacted] (RX DAY 173): Creatinine: 123.764564 [58.346152 - 110.504075] UMOL/L; [redacted]20[redacted] (RX DAY 177): Creatinine: 185.646846 [58.346152 - 110.504075] UMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 167): BLOOD NPTST052-BLOOD CULTURE: Positive-POSITIVE BLOOD CULTURE FOR GRAM POSITIVE COCCI.

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 471 / 200 (33 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 34 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Event of Interest - Renal Dysfunction**

| | |
|---|---|
| **Event Description** | WORSENING OF KIDNEY FUNCTION |
| **Preferred term** | 腎機能障害 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 444 / 173 (6 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はブラジルの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腹腔内膿瘍の事象を発現した。関連する病歴は，原発性硬化性胆管炎，潰瘍性大腸炎及び貧血であった。

**Event 1 の臨床経過：**

投与438日後＊　，被験者は腹腔内膿瘍を発現し，投与471日後＊　，消失した。

投与353日後＊　，被験者は非重篤で現在も継続している「大腸炎の悪化」を発現した。

日付は不明であるが，被験者は下腹部痛及び筋痙攣を発現し排便の緊急性を感じたが，少量の排便があった。投与438日後＊　，患者は腹腔内膿瘍の治療のために入院した。

被験者は当該事象のため，治験を中止した。

投与された薬剤は，シプロフロキサシン，メトロニダゾール，dipyrone，enoxaparin，トラマドール，ヒドロコルチゾン，vancomycin，tazocin 及び prednisone であった。

**The patient's past medications include:**

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS and WORSENING OF COLITIS ([redacted])

ASTRAZENECA COVID 19 VACCINE for PROPHYLAXIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Intra-abdominal abscess (10059621) (Abdominal abscess (10060921) ) [v.24.1] [10059621]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as perMfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of INTRA-ABDOMINAL ABSCESS

**- Investigator:** Not applicable

**- AbbVie:** Event more likely related to pre-existing ulcerative colitis in the setting of ongoing worsening of colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BLOOD CULTURE:** POSITIVE BLOOD CULTURE FOR GRAM POSITIVE COCCI

[redacted] **20[redacted] CREATININE:** 1.40 mg/dL (normal 0.66 to 1.25)

[redacted] **20[redacted] CREATININE:** 2.10 mg/dL (normal 0.66 to 1.25)

[redacted] **20[redacted] TOTAL ABDOMEN TOMOGRAPHY:** IMPORTANT REDUCTION IN THE LEFT PERIRECTAL COLLECTION. SIGNS OF ULCERATIVE COLITIS ACTIVITY. BLADDER.

[redacted] **20[redacted] WHITE BLOOD CELLS COUNT:** 11.7 10^3/mm3 (normal 4 to 11)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 腎仙痛 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 4[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| IRON DEFICIENT ANEMIA | 20[redacted] |
| LATENT TB INFECTION | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| STEROID ASSOCIATED ACNE | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 55 | 55 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted]20[redacted] / 56 | [redacted]20[redacted] / 147 | 92 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 148 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| VEDOLIZUMAB | 300 mg | OTHER: Q 8 WEEKS | Y-M: 20[redacted] |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] / -350 |
| ISONIAZID | 300 mg | QD | Y-M: 20[redacted] / -167 |
| AZELAIC ACID | 1 OTHER: APPLICATION | BID | Y-M: 20[redacted] / -133 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| VALACICLOVIR | 1000 mg | BID | Y-M: 20[redacted] / 451 | Y-M: 20[redacted] / 457 |
| FOSFOMYCIN | 3 g | OTHER: ONCE | Y-M: 20[redacted] / 481 | Y-M: 20[redacted] / 481 |
| NAPROXEN | 500 mg | BID | Y-M: 20[redacted] / 481 | Y-M: 20[redacted] / 482 |
| PARACETAMOL | 1000 mg | OTHER: ONCE | Y-M: 20[redacted] / 482 | Y-M: 20[redacted] / 482 |
| SODIUM CHLORIDE | 30 mL | OTHER: HOURLY | Y-M: 20[redacted] / 482 | Y-M: 20[redacted] / 483 |
| SODIUM CHLORIDE | 5 mL | QD | Y-M: 20[redacted] / 482 | Y-M: 20[redacted] / 483 |
| CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE | 125 mL | OTHER: HOURLY | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| CEFAZOLIN | 2 g | OTHER: ONCE | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| CEFTRIAXONE | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| HYDROMORPHONE | 2 mg | PRN | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| ONDANSETRON | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| SODIUM CHLORIDE | 1000 mL | OTHER: ONCE | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| SODIUM CHLORIDE | 200 mL | OTHER: HOURLY | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| TAMSULOSIN | 0.4 mg | OTHER: AS DIRECTED | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] / 484 | Y-M: 20[redacted] / 486 |
| KETOROLAC | 10 mg | TID | Y-M: 20[redacted] / 484 | Y-M: 20[redacted] / 490 |
| TAMSULOSIN | 0.4 mg | QD | Y-M: 20[redacted] / 484 | Y-M: 20[redacted] / 490 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | RENAL COLIC RIGHT KIDNEY |
| **Preferred term** | 腎仙痛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 629 / 482 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 631 / 484 |
| **Duration of AE** | 3 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，右腎の腎仙痛の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与629日後＊　，被験者は右腎の腎疝痛を発現した。投与631日後＊　，右腎の腎疝痛は消失した。

本事象発現前の 投与の約4ヵ月後＊，被験者は腎結石症（非重篤）を発現した。

投与629日後＊　，被験者は右側腹部痛，頻尿，尿意切迫，血尿及び排尿困難で救急治療室を受診した。投与629日後＊　　，被験者は入院した。投与630日後＊，CT 検査で尿管結石が認め

られ，同日，尿管ステント留置を伴う尿管鏡検査が実施された。投与630日後＊　，被験者は退院した。

治験責任医師によると，被験者は以前，投与の約2ヵ月後＊に同事象を発現していた。

投与された薬剤は，ヒドロモルフォン，アセトアミノフェン，セフトリアキソン，オンダンセトロン，塩化ナトリウム，セファゾリン，ホスホマイシン，シプロフロキサシン，ketorolac，ナプロキセン，タムスロシン及びラクトリンゲルであった。

**The patient's past medications include:**

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PFIZER BIONTECH COVID-19 VACCINE for COVID-19 VACCINATION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1)　Renal colic (10038419)　(Renal colic (10038419) )　[v.24.1]　[10038419]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of RENAL COLIC RIGHT KIDNEY

**- Investigator:** Not applicable

**- AbbVie:** Event more likely related to concurrent nephrolithiasis. Renal stone is a relatively common problem with an estimated 16 percent of men will be diagnosed with a kidney stone by age of 70 years.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BMI:** 26.28 kg/m2

[redacted] **20[redacted] BODY WEIGHT: 7[redacted] KG**

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** evidence of right ureteric stone

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| ヘモグロビン減少 | | | | X |
| 肺塞栓症 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | FEMALE | BLACK OR AFRICAN AMERICAN |

| Medical History | Onset Year |
|---|---|
| ALLERGY TO IMMURAN | 20[redacted] |
| HEAVY MENSES | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| NAUSEA | 20[redacted] |
| PULMONARY EMBOLI | 20[redacted] |
| SICKLE CELL ANEMIA | 19[redacted] |
| VOMITTING | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: APPENDECTOMY | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 59 | 59 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted]20[redacted] / 60 | [redacted]20[redacted] / 101 | 42 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 102 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 4.8 g | QD | Y-M: 20[redacted]-[redacted] / -219 |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted]-[redacted] / -14 |
| INFLIXIMAB | 5 mg | OTHER: MONTHLY | Y: 20[redacted] |
| ADALIMUMAB | 40 mg | QD | Y: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: Q 8 WEEKS | Y: 20[redacted] |
| PREDNISONE | 5 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted]-[redacted] / -14 | Y-M: 20[redacted]-[redacted] / 169 |
| CALCIUM | 500 mg | BID | Y-M: 20[redacted]-[redacted] / 7 | ONGOING |
| IRON | 200 mg | OTHER: ONCE | Y-M: 20[redacted]-[redacted] / 7 | Y-M: 20[redacted]-[redacted] / 7 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted]-[redacted] / 7 | ONGOING |
| RIVAROXABAN | 15 mg | BID | Y-M: 20[redacted]-[redacted] / 7 | ONGOING |
| VITAMIN D NOS | 1000 IU | QD | Y-M: 20[redacted]-[redacted] / 7 | ONGOING |
| PREDNISONE | 7.5 mg | QD | Y-M: 20[redacted]-[redacted] / 170 | Y-M: 20[redacted]-[redacted] / 201 |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted]-[redacted] / 202 | Y-M: 20[redacted]-[redacted] / 230 |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted]-[redacted] / 231 | Y-M: 20[redacted]-[redacted] / 306 |
| SODIUM PHOSPHATE | 1 OTHER: BOTTLE | OTHER: X 1 | Y-M: 20[redacted]-[redacted] / 666 | Y-M: 20[redacted]-[redacted] / 666 |
| IRON | 300 mg | OTHER: X 1 | Y-M: 20[redacted]-[redacted] / 796 | Y-M: 20[redacted]-[redacted] / 796 |

**Event #1: Serious Adverse Event, Event of Interest - Adjudicated Venous Thromboembolic Event**

| | |
|---|---|
| **Event Description** | PULMONARY EMBOLUS |
| **Preferred term** | 肺塞栓症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 102 / 1 |

| | |
|---|---|
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted] (RX DAY 2): NPTST054-BLOOD GASES: PH 7.46 PCO2 35 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 108 / 7 |
| **Duration of AE** | 7 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | WORSENING OF ULCERATIVE COLITIS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #2: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | LOW HEMAGLOBIN |
| **Preferred term** | ヘモグロビン減少 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 188 / 87 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-234

治験責任医師からの報告。本被験者はカナダの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びウパダシチニブが投与され，肺塞栓症の事象を発現した。関連する病歴は，鎌状赤血球貧血，潰瘍性大腸炎，肺塞栓症，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与102日後＊　，被験者は肺塞栓症を発現した。投与108日後＊　，肺塞栓症は消失した。

投与102日後＊　，被験者は胸痛と頻呼吸があり，入院した。被験者は抗凝固剤による治療を受け肺塞栓症は改善した。投与108日後＊ ，被験者は退院した。

診療録によると，被験者は 投与102日後＊　に救急治療室を受診し，受診前夜に突然胸痛を発症したと訴えた。めまいも発現していた。被験者は，潰瘍性大腸炎の病歴により，2 週間ほとんど 1 日中ベッドにいたが，圧迫ストッキングをつけ，歩こうとしていたと話した。救急治療室で，被験者は発熱及び頻脈を伴うコーヒー残渣様吐血を発現し，心拍数は 200 近くとなった。被験者は集中治療室（ICU）に入院した。ICU での治療中，酸素の供給は中止となり，それ以上の吐血はなかった。被験者のヘモグロビンは安定しており，胃腸出血の兆候もなかった。被験者は入院中，幾度か嚥下障害を訴えた。投与108日後＊ ，被験者は退院した。

治験責任医師によると，被験者は肺塞栓症の既往の危険因子があった。

投与された薬剤は，セフトリアキソン，pantoloc，フラグミン，タイレノール，normal saline，ジルチアゼム，crystalloid，ヒドロモルフォン，モルヒネ及びイグザレルトであった。

**The patient's past medications include:**

REMICADE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

HUMIRA for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

---

1) Pulmonary embolus (10037380) (Pulmonary embolism (10037377) ) [v.23.1] [10037380]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Causality for UPADACITINIB (Open Label)

---

1) Pulmonary embolus (10037380) (Pulmonary embolism (10037377) ) [v.23.1] [10037380]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of PULMONARY EMBOLUS

**- Investigator:** Worsening of ulcerative colitis - chest pain deemed by PI as likely due to decreased HGB due to active UC.

**- AbbVie:** Risk factors include pre-existing history of pulmonary emboli, sickle cell anemia, and recent ulcerative colitis flare resulting in subject spending prolong time in bed for 2 weeks.

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of PULMONARY EMBOLUS

**- Investigator:** Worsening of ulcerative colitis - chest pain deemed by PI as likely due to decreased HGB due to active UC.

**- AbbVie:** Risk factors include pre-existing history of pulmonary emboli, sickle cell anemia, and recent ulcerative colitis flare resulting in subject spending prolong time in bed for 2 weeks.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] 20[redacted] **AEROBIC BLOOD CULTURES:** According to medical records, no growth after 5 days.

[redacted] 20[redacted] **ANAEROBIC BLOOD CULTURES:** According to medical records, no growth after 5 days.

[redacted] 20[redacted] **CHEST X-RAY:** RLL Opacity

[redacted] 20[redacted] **CLOSTRIDIUM DIFFICILE TEST:** stool sample negative

[redacted] 20[redacted] **CT CHEST:** Right pulmonary infarct suspected

[redacted] 20[redacted] **CT SCAN CHEST:** Right pulmonary infarct suspected. From medical records: Extensive thromboembolic disease with evidence of early right cardiac strain and irregular opacity of left lower lobe, likely inflammatory. There was also a suspicion of right basilar pulmonary infarct versus hemorrhage.

[redacted] 20[redacted] **D DIMER:** 1761 No units

[redacted] 20[redacted] **ECHOCARDIOGRAM:** Left ventricular systolic function normal, EF calculated by Simpson's bi-plane is 68, normal diastolic function, no significant valvular abnormalities.

[redacted] 20[redacted] **HEART RATE:** Approaching 200

[redacted] 20[redacted] **HGB:** 79 No units

[redacted] 20[redacted] **INR:** 2.4 No units

[redacted] 20[redacted] **LACTATE:** 2.1 No units

[redacted] 20[redacted] **PCO2:** 35 No units

[redacted] 20[redacted] **PLATELETS:** 311 No units

[redacted] 20[redacted] **WBC:** 17.4 No units

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 頚髄圧迫 | X | X | | |
| 髄膜腫 | | X | | |
| 脊髄症 | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 6[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| HEARTBURN | 20[redacted] |
| HYPERCHOLESTRLEMIA | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| LATENT TB | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| LOW IRON | 20[redacted] |
| TYPE 2 DIABETES | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 53 | 53 |
| M14-675 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted] / 54 | [redacted] / 144 | 91 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted] / 145 | [redacted] / 508 | 364 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted] / 509 | [redacted] / 676 | 168 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| INFLIXIMAB | 300 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| IRON | 300 mg | BID | Y-M: 20[redacted] |
| ISONIAZID | 300 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 800 mg | TID | Y: 20[redacted] |
| METFORMIN | 1000 mg | BID | Y: 20[redacted] |
| PANTOPRAZOLE | 40 mg | QD | Y: 20[redacted] |
| RAMIPRIL | 1.25 mg | QD | Y: 20[redacted] |
| ROSUVASTATIN | 40 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| IRON | 300 mg | BID | Y-M: 20[redacted] | ONGOING |
| CANDESARTAN | 16 mg | QD | Y-M: 20[redacted] / 41 | ONGOING |
| MESALAZINE | 800 mg | TID | Y: 20[redacted] | ONGOING |
| METFORMIN | 1000 mg | BID | Y: 20[redacted] | ONGOING |
| PANTOPRAZOLE | 40 mg | QD | Y: 20[redacted] | ONGOING |
| RAMIPRIL | 1.25 mg | QD | Y: 20[redacted] | ONGOING |
| ROSUVASTATIN | 40 mg | QD | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | CERVICAL SPINE CORD COMPRESSION |
| **Preferred term** | 頚髄圧迫 |

| | |
|---|---|
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 676 / 168 |
| **Age at AE Onset** | 7[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 748 / 240 (72 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 73 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | MYELOPATHY |
| **Preferred term** | 脊髄症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 676 / 168 |
| **Age at AE Onset** | 7[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 748 / 240 (72 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 73 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #3: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | MENINGIOMA |

| | |
|---|---|
| **Preferred term** | 髄膜腫 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 679 / 171 (3 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 7[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，脊髄症に伴う頚髄圧迫の事象を発現した。関連する病歴は，高血圧，2 型糖尿病，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 1 及び 2 の臨床経過：**

投与676日後＊　，被験者は脊髄症に伴う頚髄圧迫を発現した。投与748日後＊　，脊髄症に伴う頚髄圧迫は消失した。

投与678日後＊　，左側のしびれ感に関連する全身の脱力，並びに左側の肩，手指及び腰の痛みにより入院した。CT 検査，MRI 検査及び X 線検査が実施された。被験者は，脊髄症に伴う頚髄圧迫と診断された。投与690日後＊　，被験者は両側の C2 から T1 まで椎弓切除術を受け，C3 から C7 まで頸椎後方固定術を受けた。入院期間中，被験者は同施設内のリハビリテーション科

に転科した。投与748日後＊　，被験者はリハビリテーション科から退院した。

本事象により治験薬の投与は完全に中止された。

**The patient's past medications include:**

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ISONIAZID for TB PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PFIZER BIONTECH COVID-19 VACCINE for PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Cervical cord compression (10008252) (Cervical cord compression (10008252) ) [v.24.1] [10008252]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

2) Cervical myelopathy (10008289) (Myelopathy (10028570) ) [v.24.1] [10008289]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of CERVICAL SPINE CORD COMPRESSION WITH MYELOPATHY

**- Investigator:** Not Applicable

**- AbbVie:** Event of cervical cord compression is most likely due to c3/c4 disc herniation and cervical spine degenerative disease. Risk factors include advanced age and obesity. Event of cervical myelopathy is most likely secondary to cervical cord compression.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BMI:** 31.4 kg/m2

[redacted] **20[redacted] BODY WEIGHT:** 9[redacted] KG

[redacted] **20[redacted] CT CHEST, ABDOMEN, PELVIS ENHANCED:** There is no finding to indicate a primary malignant process. No adenopathy. Thickened appearance to the urinary bladder.

[redacted] **20[redacted] CT HEAD UNENHANCED:** There are two left frontal lobe mass lesions, with mass effect noted with the left anterior parafalcine mass lesion. These may reflect a meningiomas. Further assessment and MRI are advised. The posterior fossa is unremarkable.

[redacted] **20[redacted] MR CERVICAL SPINE LUMBAR SPINE UNENHANCED:** Multilevel degenerative changes in the cervical and lumbar spine. Degenerative disease and facet arthropathy at C3/C4 with a posterior disc protrusion causing significant central canal and bilateral from stenosis. Small focus of increased T2 signal in the cord at this level compatible with myelopathy. Large disc extrusion at L2/L3 causing significant compression of thedescending left L3 nerve root.

[redacted] **20[redacted] MR HEAD ENHANCED:** Findings most consistent with three left hemispheric meningiomas, one with mass effect and edema.

[redacted] **20[redacted] X-RAY CERVICAL SPINE:** Multilevel degenerative changes are present.

[redacted] **20[redacted] X-RAY LEFT SHOULDER (LIMITED):** No acute bony injury.

[redacted] **20[redacted] X-RAY PELVIS, LEFT HIP:** No acute bony injury seen. There is minimal irregularity to the left superior pubic ramus at the anterior column, no obvious fracture seen.

[redacted] **20[redacted] X-RAY THORACIC SPINE:** There are 12 ribbed vertebral bodies and five lumbar type vertebral bodies. There is a mild scoliotic curve of the low thoracic spine, convex left. Vertebral body heights look preserved in the thoracic and lumbar spine. There is mild disc space narrowing at L2/L3, with annular osteophytes at L2/L3 and L3/L4. The sacroiliac joints look unremarkable.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 自然流産 | X | X | | |
| 貧血 | | | | X |
| 帯状疱疹 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | FEMALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| CHICKEN POX VIRUS | 19[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| IRON DEFICIENT ANEMIA | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |
| M14-675 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted]20[redacted] / 57 | [redacted]20[redacted] / 118 | 62 |

| | | | | | |
|---|---|---|---|---|---|
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / 119 | [redacted]20[redacted] / 167 | 49 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 168 | [redacted]20[redacted] / 581 | 414 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1.2 g | BID | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: Q2WEEKS | Y-M: 20[redacted] |
| AZATHIOPRINE | 200 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 500 mg | QD | Y-M: 20[redacted] |
| IRON | 300 mg | QD | Y-M: 20[redacted] / -239 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| IRON | 300 mg | QD | Y-M: 20[redacted] / -239 | ONGOING |
| VALACICLOVIR | 1 g | TID | Y-M: 20[redacted] / 287 | Y-M: 20[redacted] / 294 |
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] / 338 | Y-M: 20[redacted] / 414 |
| OTHER VIRAL VACCINES | 0.3 mL | OTHER: X 1 | Y-M: 20[redacted] / 387 | Y-M: 20[redacted] / 387 |
| IRON | 300 mg | OTHER: X 1 | Y-M: 20[redacted] / 415 | Y-M: 20[redacted] / 415 |
| PREDNISONE | 40 mg | QD | Y-M: 20[redacted] / 415 | ONGOING |

**Event #1: Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | SHINGLES |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 453 / 286 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 461 / 294 |
| **Duration of AE** | 9 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |

| | |
|---|---|
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | SPONTANEOUS ABORTION |
| **Preferred term** | 自然流産 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 579 / 412 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 415): Hematocrit: 0.24 [0.35 - 0.49] FRACTION OF 1; Hemoglobin: 73 [115 - 155] G/L; Leukocytes: 8.1 [4 - 11] 10'9/L; NPTST164-HCG QUANT: 197.98 [25 - 25] IU/L; NPTST213-MCV: 63.0 [82 - 97] FL; NPTST272-RDW: 18.1 [11.5 - 14.5] CV

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | UNKNOWN AT THIS TIME, NOT BELIEVED TO BE STUDY RELATED. |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #3: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 589 / 422 (8 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |

| | |
|---|---|
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，非重篤な妊娠中の母体の曝露の事象を発現した。関連する病歴は，潰瘍性大腸炎，鉄欠乏性貧血，非喫煙者及び前飲酒者（1 日 2 杯未満）であった。

**Event 2 の臨床経過：**

被験者は，妊娠中の母体の曝露を発現した（日付不明）。投与579日後＊ ，被験者は自然流産を発現した。

被験者は，投与の約17ヵ月後＊に子宮内避妊用具を除去し，経口避妊薬に切り替えるはずであったが，切り替えなかった。

投与579日後＊ ，被験者は血塊を伴う腟出血があった。投与582日後＊ ，被験者は救急治療室を受診し，血液検査が実施され，妊娠が確定した。投与583日後＊ ，被験者は経腟超音波検査を受け，自然流産が確定した。

投与582日後＊ ，尿妊娠検査により妊娠が確定した。胎児は，受胎前及び第 1 期中，子宮内で母体のウパダシチニブ投与に曝露した。最終月経は投与の約17ヵ月後＊であった。出産予定日は投与787日後＊であった。母体のウパダシチニブ投与は中止された。報告時点の推定在胎期間は 10 週であった。

**The patient's past medications include:**

MESAVANT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IMMURAN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1) Spontaneous abortion (10041687) (Abortion spontaneous (10000234) ) [v.24.0] [10041687]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

2) Maternal exposure during pregnancy (10071408) (Maternal exposure during pregnancy (10071408) ) [v.24.0] [10071408]

**Causality as per reporter (Drug/Vaccine):** Not Reported

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of SPONTANEOUS ABORTION

**- Investigator:** UNKNOWN AT THIS TIME, NOT BELIEVED TO BE STUDY RELATED.

**- AbbVie:** Spontaneous abortions in the 1st trimester are common and are more likely associated to structural or chromosomal abnormalities of the embryo.

Event of MATERNAL EXPOSURE DURING PREGNANCY

**- Investigator:** Not Reproted

**- AbbVie:** Special situation of maternal use of active pharmaceutical ingredient.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] HCG QUANTITATIVE:** 197.98 IU/L (normal 25 to 25)

[redacted] **20[redacted] HEMATOCRIT:** 0.24 L/L (normal 0.35 to 0.49)

[redacted] **20[redacted] HEMOGLOBIN:** 73 G/L (normal 115 to 155)

[redacted] **20[redacted] MCV:** 63.0 FL (normal 82 to 97)

[redacted] **20[redacted] RDW:** 18.1 CV (normal 11.5 to 14.5)

[redacted] **20[redacted] TRANSVAGINAL ULTRASOUND:** NO INTRAUTERINE GESTATION IS DEMONSTRATED. FINDINGS MAY RELATE TO NEAR COMPLETE EARLY PREGNANCY FAILURE (WHICH IS FAVORED), PREGNANCY OF UNCERTAIN LOCATION, OR INACCURATE DATES.

[redacted] **20[redacted] URINE PREGNANCY:** Negative

[redacted] **20[redacted] URINE PREGNANCY:** Positive

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.1 X10**9/L (normal 4.0 to 11.0)

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Herpes zoster: One dermatome.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| ラクナ梗塞 | X | X | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 4[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| LEFT SIDED UC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: SHOULDER SURGERY | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |
| M14-675 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted]20[redacted] / 57 | [redacted]20[redacted] / 119 | 63 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 120 | [redacted]20[redacted] / 168 | 49 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 169 | [redacted]20[redacted] / 225 | 57 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] / 30 | ONGOING |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] / 30 | Y-M: 20[redacted] / 49 |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated MACE ***

| | |
|---|---|
| **Event Description** | ACUTE LACUNAR INFARCT RIGHT THALAMUS |
| **Preferred term** | ラクナ梗塞 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 197 / 29 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 199 / 31 |
| **Duration of AE** | 3 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | INVESTIGATIONS ONGOING |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

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Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，右視床部の急性期ラクナ梗塞の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与197日後＊　，被験者は右視床部の急性期ラクナ梗塞を発現した。投与199日後＊　，右視床部の急性期ラクナ梗塞は消失した。

投与197日後＊　，被験者は全身の脱力感，左側（顔及び腕）の動作及び/又は感覚の喪失，失語症，並びに浮動性及び回転性めまいがあり，入院した。被験者は，これらの症状はあるものの，重大な障害は認められず，通常の業務及び活動が全て可能であった。投与197日後＊　，被験者は退院した。

投与された薬剤は，プラビックス及びアセチルサリチル酸腸溶錠であった。

**The patient's past medications include:**

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1)　Lacunar infarction (10051078)　(Lacunar infarction (10051078) )　[v.23.1]　[10051078]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of ACUTE LACUNAR INFARCT RIGHT THALAMUS

**- Investigator:** Investigations ongoing

**- AbbVie:** The prevalence of ischemic stroke is double in Ulcerative colitis patients 20-60 years of age. (Horta,E., et.al., Prevalence of Ischemic Stroke in Cohort of Ulcerative Colitis Patients, Neurology, April

18,2017; 88). Additional risk factor includes obesity (BMI is 30 at time of event and 29.8 at screening in M14-675).

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BMI:** 29.9 kg/m2

[redacted] **20[redacted] CAROTID DOPPLER:** Normal

[redacted] **20[redacted] HEAD MRI:** Acute lacunar infarct right thalamus

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 急性心筋梗塞 | X | X | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| BILATERAL GLAUCOMA | 20[redacted] |
| HERNIA | 20[redacted] |
| LATENT TUBERCULOSIS | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 60 | 60 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 61 | [redacted]20[redacted] / 631 | 571 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| AZATHIOPRINE | 175 mg | QD | Y-M: 20[redacted] |
| LATANOPROST | 0.005 % | QD | Y-M: 20[redacted] / -219 |
| PARACETAMOL | 325 mg | PRN | Y-M: 20[redacted] / -13 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| LATANOPROST | 0.005 % | QD | Y-M: 20[redacted] / -219 | ONGOING |
| HEPARIN | 5000 OTHER: UNITS | OTHER: Q12 HOUR | Y-M: 20[redacted] / 563 | Y-M: 20[redacted] / 568 |
| HEPARIN | 8000 OTHER: UNITS | OTHER: ONCE | Y-M: 20[redacted] / 563 | Y-M: 20[redacted] / 563 |
| FENTANYL | 25 OTHER: MCG | PRN | Y-M: 20[redacted] / 566 | Y-M: 20[redacted] / 567 |
| HEPARIN | 7000 OTHER: UNITS | OTHER: ONCE | Y-M: 20[redacted] / 566 | Y-M: 20[redacted] / 566 |
| LIDOCAINE | 2 mL | OTHER: ONCE | Y-M: 20[redacted] / 566 | Y-M: 20[redacted] / 566 |
| MIDAZOLAM | 1 mg | OTHER: ONCE | Y-M: 20[redacted] / 566 | Y-M: 20[redacted] / 566 |
| GLYCERYL TRINITRATE | 0.4 mg | PRN | Y-M: 20[redacted] / 568 | ONGOING |
| PERINDOPRIL | 2 mg | OTHER: QHS | Y-M: 20[redacted] / 568 | ONGOING |
| TICAGRELOR | 90 mg | BID | Y-M: 20[redacted] / 568 | ONGOING |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated MACE ***

| | |
|---|---|
| **Event Description** | POSTEROLATERAL ST ELEVATION MYOCARDIAL INFARCTION |
| **Preferred term** | 急性心筋梗塞 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 623 / 563 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 563): Cholesterol: 6.7 [3.5 - 5.2] MMOL/L; Creatine Kinase: 4369 [52 - 256] U/L; NPTST322-TROP T: 6979 [0 - 14] NG/ML; NPTST322-TROP T: 15,944 [0 - 14] ng/mL; [redacted]20[redacted] (RX DAY 567): Creatine Kinase: 468 [52 - 256] U/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 628 / 568 |
| **Duration of AE** | 6 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |

| | |
|---|---|
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，後側壁 ST 上昇型心筋梗塞の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

**Event 1 の臨床経過：**

投与623日後＊　，被験者は後側壁 ST 上昇型心筋梗塞を発現した。投与628日後＊　，後側壁 ST 上昇型心筋梗塞は消失した。

投与623日後＊　　，被験者は急性の胸痛で入院した。同日，血管造影及び左心カテーテル検査を受けた。投与626日後＊　　，被験者は経皮的冠動脈インターベンションを受け，ステントを留置された。入院中，状態は安定し，症状の再発はなかった。投与628日後＊　　，被験者は退院した。

治験責任医師によると，被験者の母親は 6[redacted] 歳で心筋梗塞を経験し，その後心血管イベントにより死亡した。

投与された薬剤は，ビソプロロール，パントプラゾール，ロスバスタチン，ニトログリセリン，ペリンドプリルエルブミン，チカグレロル及びアスピリンであった。

**The patient's past medications include:**

IMURAN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1) ST segment elevation myocardial infarction (10064345) (Acute myocardial infarction (10000891) ) [v.24.1] [10064345]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of POSTEROLATERAL ST ELEVATION MYOCARDIAL INFARCTION

**- Investigator:** Not applicable

**- AbbVie:** Risk factors include age, male sex, maternal family history of myocardial infarction and pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] ANGIOGRAM:** Diffuse multivessel coronary artery disease with occlusion of the left circumflex artery

[redacted] **20[redacted] CHOLESTEROL:** 6.7 MMOL/L (normal 3.5 to 5.2)

[redacted] **20[redacted] CK:** 179 NG/ML (normal 52 to 256)

[redacted] **20[redacted] ECG:** STEMI positive criteria (posterior lead)

[redacted] **20[redacted] ECG:** Abnormal, occasional premature ventricular complexes, T-wave abnormality, consider ischemia

[redacted] **20[redacted] ECG:** No premature ventricular complexes from earlier; normal sinus rhythm; T-wave abnormality; consider ischemia

[redacted] **20[redacted] ECG:** Non-specific ST-T wave abnormality; sinus bradycardia

[redacted] **20[redacted] ECG:** Abnormal: sinus bradycardia, increased R/S ration in V1, non specific T wave changes in inferior leads

[redacted] 20[redacted] **TRANSTHORACIC ECHO:** Sinus rhythm with frequent PVCs. Concentric L remodeling; Low-Normal EF, posterolateral wall motion abnormality; Normal RV size and function, no valvular abnormality

[redacted] **20[redacted] TROPONIN T:** 6979 NG/ML (normal 0 to 14)

[redacted] **20[redacted] TROPONIN T:** 15944 NG/ML (normal 0 to 14)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| INTRA ABDOMINAL THROMBOEMBOLISM | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 55 | 55 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 56 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1.2 g | QD | Y-M: 20[redacted] |
| MESALAZINE | 3 OTHER: TABLETTES | QD | Y-M: 20[redacted] |
| RIVAROXABAN | 10 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 600 mg | OTHER: MONTHLY | Y-M: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| RIVAROXABAN | 10 mg | QD | Y-M: 20[redacted] | Not reported |
| MESALAZINE | 4.8 g | QD | Y-M: 20[redacted] / 419 | Not reported |
| CINCHOCAINE;ESCULOSIDE;FRAMYCETIN;HYDROCORTISONE | 1 OTHER: APPLICATION | QD | Y-M: 20[redacted] / 451 | Y-M: 20[redacted] / 463 |
| SODIUM CHLORIDE | 30 mL | OTHER: HOURLY | Y-M: 20[redacted] / 468 | Y-M: 20[redacted] / 469 |
| DIMENHYDRINATE | 50 mg | OTHER: Q4H | Y-M: 20[redacted] / 469 | Y-M: 20[redacted] / 473 |
| ONDANSETRON | 4 mg | TID | Y-M: 20[redacted] / 469 | Y-M: 20[redacted] / 473 |
| PARACETAMOL | 650 mg | OTHER: Q4H | Y-M: 20[redacted] / 469 | Y-M: 20[redacted] / 473 |
| CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE | 75 mL | OTHER: HOURLY | Y-M: 20[redacted] / 470 | Y-M: 20[redacted] / 471 |
| ENEMAS | 1 OTHER: APPLICATION | OTHER: X2 | Y-M: 20[redacted] / 471 | Y-M: 20[redacted] / 471 |
| FENTANYL | 75 ug | OTHER: ONCE | Y-M: 20[redacted] / 471 | Y-M: 20[redacted] / 471 |
| HYDROCORTISONE | 100 mg | QD | Y-M: 20[redacted] / 471 | Not reported |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] / 471 | Not reported |
| MIDAZOLAM | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 471 | Y-M: 20[redacted] / 471 |
| MESALAZINE | 1000 mg | QD | Y-M: 20[redacted] / 472 | Not reported |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 472 | Y-M: 20[redacted] / 473 |
| PREDNISONE | 40 mg | QD | Y-M: 20[redacted] / 473 | Y-M: 20[redacted] / 486 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | UC FLARE |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 524 / 469 |

| | |
|---|---|
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted] (RX DAY 468): Platelets: 547 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 469): Platelets: 512 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 470): Platelets: 536 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 471): Platelets: 542 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 472): Platelets: 542 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 473): Platelets: 567 [150 - 400] 10^9/L | |
| **Microbiology** | |
| [redacted]20[redacted] (RX DAY 471): STOOL NPTST045-BACTERIAL ENTERIC PANEL: Negative; STOOL NPTST068-C-DIFFICILE: Negative | |
| **AE Stopped Initial Rx Day / Rx Day** | 528 / 473 |
| **Duration of AE** | 5 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の再燃の事象を発現した。関連する病歴は，潰瘍性大腸炎，腹部内血栓塞栓症，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与524日後＊ ，被験者は潰瘍性大腸炎の再燃を発現した。投与528日後＊ ，潰瘍性大腸炎の再燃は消失した。

本事象発現前の投与の約6ヵ月後＊，投与の約8ヵ月後＊及び投与の11ヵ月後＊，被験者は潰瘍性大腸炎の再燃（非重篤）を発現した。

投与524日後＊ ，被験者は過去 7 日間持続したしぶり及び時折の切迫，過去 5 日間の便通の増加（平常時 1～2 回/日が 3～4 回/日に増加，直近は 15 回/日），並びに夜通しの便通（一晩で最

大 5 回）で入院した。被験者は，ブリストルスケール 1 の便で，下痢を経験した前回の再燃とは異なる便通時の緊迫感があると説明した。また，最初，便通時に出血はなかったが，入院前の最後の 3～4 回の便通では便に血液と粘液が混ざっていることを認識したと説明した。さらに，便通時に下腹部のけいれん性の痛み及び緊迫感による肩の痛みがあったと説明した。被験者は，食欲が減退していたが，経口補液は摂取可能であった。被験者は直近 5 日間で 10 ポンド体重が減少し，非常に疲労していた。悪心，嘔吐，発熱，悪寒及び寝汗は否定した。被験者はステロイド治療によく反応した。投与528日後＊ ，被験者は退院した。

投与された薬剤は，ヒドロコルチゾン，salofalk 及び prednisone であった。

**The patient's past medications include:**

5-ASA for ULCERATIVE COLITIS ([redacted])

MEZEVANT for ULCERATIVE COLITIS ([redacted])

INFLECTRA for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

PROCTOL for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS

METHOTREXATE for ULCERATIVE COLITIS

Causality for UPADACITINIB (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900) ) [v.24.0] [10009901]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of ULCERATIVE COLITIS FLARE

**- Investigator:** Not applicable

**- AbbVie:** The event is more likely related to the pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] COLONOSCOPY:** Mayo 1 in distal 25cm, Mayo 0 in rectum, transverse, and descending colon. Mild area that was mildly narrowed, not yet strictured - biopsy showed mildly active inflammation, no dysplasia.

[redacted] **20[redacted] CT ABDOMEN PELVIS:** no evidence of bowel obstruction, active inflammation of the distal sigmoid colon and rectum, most likely related to the patient's ulcerative colitis

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** The cecum, right colon, and transverse colon were all normal with stool coating, the descending colon was normal; there was loss of vascular pattern in the sigmoid colon consistent with mayo 1 colitis. Beginning at 20 cm and extending to the anal verge there was erythema and areas of superficial ulceration consistent with mayo 3 colitis

[redacted] **20[redacted] PLATELET COUNT:** 547 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT:** 536 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] PLATELET COUNT:** 567 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] STOOL BACTERIAL ENTERIC PANEL:** Negative

[redacted] **20[redacted] STOOL C DIFFICILE:** Negative

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 深部静脈血栓症 | | | | X |
| 処置による腸管穿孔 | X | X | | |
| 子宮穿孔 | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA: IRON DEFICIENT ANEMIA | 20[redacted] |
| CLOTTING/BLEEDING PROBLEMS: DVT | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| OTHER: BILATERAL HIP PAIN | 20[redacted] |
| OTHER: MENOPAUSE | 20[redacted] |
| OTHER: OSTEOPENIA | 20[redacted] |
| OTHER: RT SHOULDER PAIN | 20[redacted] |
| OTHER: SALMONELLA | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: ROTATOR CUFF REPAIR | 20[redacted] |
| SURGERY: TUBALIGATION | 19[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | 2 - 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 57 | [redacted]20[redacted] / 478 | 422 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1000 mg | QD | Y-M: 20[redacted] |
| HYDROCORTISONE | 1 OTHER: DOSE | QD | Y-M: 20[redacted] |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] |
| MESALAZINE | 4000 mg | QD | Y-M: 20[redacted] |
| METRONIDAZOLE | 500 mg | BID | Y-M: 20[redacted] |
| ADALIMUMAB | 80 mg | OTHER: Q 2 WEEKS | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | BID | Y-M: 20[redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: Q 8 WEEKS | Y-M: 20[redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] |
| METRONIDAZOLE | 500 mg | BID | Y-M: 20[redacted] |
| INFLIXIMAB | 400 mg | OTHER: Q 4 WEEKS | Y-M: 20[redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted] |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] |
| BUDESONIDE | 9 mg | QD | Y-M: 20[redacted] / -258 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / -166 |
| PREDNISONE | 10 mg | QD | Y-M: 20[redacted] / -166 |
| CALCIUM | 500 mg | QD | Y: 20[redacted] |
| VITAMIN D NOS | 2000 IU | QD | Y: 20[redacted] |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y: 20[redacted] |
| RISEDRONIC ACID | 35 mg | OTHER: WEEKLY | Y: 20[redacted] |
| ASCORBIC ACID | 1000 mg | QD | Y: 20[redacted] |
| IRON | 11 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / -166 | ONGOING |
| PARACETAMOL | 1 OTHER: TABLET | PRN | Y-M: 20[redacted] / 158 | ONGOING |
| CODEINE;PARACETAMOL | 1 OTHER: TABLET | PRN | Y-M: 20[redacted] / 178 | ONGOING |
| DIMENHYDRINATE | 50 mg | PRN | Y-M: 20[redacted] / 424 | Y-M: 20[redacted] / 425 |
| MORPHINE | 10 mg | PRN | Y-M: 20[redacted] / 424 | Y-M: 20[redacted] / 425 |
| PIPERACILLIN;TAZOBACTAM | 3.75 g | QID | Y-M: 20[redacted] / 424 | Y-M: 20[redacted] / 434 |
| TRANEXAMIC ACID | 1000 mg | QD | Y-M: 20[redacted] / 424 | Y-M: 20[redacted] / 425 |
| FLUCONAZOLE | 400 mg | QD | Y-M: 20[redacted] / 425 | Y-M: 20[redacted] / 433 |
| HEPARIN | 5000 ug | QD | Y-M: 20[redacted] / 425 | Y-M: 20[redacted] / 432 |
| METOCLOPRAMIDE | 10 mg | QD | Y-M: 20[redacted] / 425 | Y-M: 20[redacted] / 432 |
| ONDANSETRON | 8 mg | PRN | Y-M: 20[redacted] / 425 | Y-M: 20[redacted] / 435 |
| FUROSEMIDE | 20 mg | QD | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 432 |
| HYDROMORPHONE | 0.25 mg | PRN | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 435 |
| MAGNESIUM SULFATE | 4 g | QD | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 432 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 431 |
| POTASSIUM | 40 mEq | BID | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 436 |
| TINZAPARIN | 4500 ug | QD | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 436 |
| DICLOFENAC | 2.32 % | BID | Y-M: 20[redacted] / 427 | Y-M: 20[redacted] / 436 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 432 | Y-M: 20[redacted] / 436 |

| | | | | |
|---|---|---|---|---|
| AMOXICILLIN;CLAVULANIC ACID | AMOXICILLIN: 875 POTASSIUM: 125 mg | BID | Y-M: 20[redacted]-[redacted] / 434 | Y-M: 20[redacted]-[redacted] / 436 |
| MACROGOL | 17 g | QD | Y-M: 20[redacted]-[redacted] / 434 | Y-M: 20[redacted]-[redacted] / 435 |
| CALCIUM | 500 mg | QD | Y: 20[redacted] | ONGOING |
| VITAMIN D NOS | 2000 IU | QD | Y: 20[redacted] | ONGOING |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y: 20[redacted] | ONGOING |
| RISEDRONIC ACID | 35 mg | OTHER: WEEKLY | Y: 20[redacted] | ONGOING |
| ASCORBIC ACID | 1000 mg | QD | Y: 20[redacted] | ONGOING |
| IRON | 11 mg | QD | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | PROCEDURAL SMALL BOWEL PERFORATION |
| **Preferred term** | 処置による腸管穿孔 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 479 / 423 (1 DAY AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 424): Creatinine: 108 [40 - 100] UMOL/L; NPTST197-LACTATE: 3.6 [0.5 - 2.2] MMOL/L; NPTST334-UREA: 9.3 [2.5 - 8] MMOL/L; [redacted]20[redacted] (RX DAY 425): Albumin: 22 [35 - 50] G/L; Aspartate Aminotransferase: 69 [0 - 40] U/L; NPTST189-INR: 1.6 [0.8 - 1.2] RATIO; NPTST209-MAGNESIUM: 0.59 [0.7 - 1] MMOL/L; NPTST255-PO4: 0.56 [0.8 - 1.45] MMOL/L; NPTST317-TOTAL CO2: 20 [23 - 31] MMOL/L; [redacted]20[redacted] (RX DAY 426): Chloride: 109 [96 - 107] MMOL/L; NPTST257-POTASSIUM - WBK (WHOLE BODY): 2.9 [3.3 - 4.8] MMOL/L; [redacted]20[redacted] (RX DAY 427): Hemoglobin: 95 [120 - 160] G/L; [redacted]20[redacted] (RX DAY 429): Calcium: 1.99 [2.1 - 2.6] MMOL/L; [redacted]20[redacted] (RX DAY 432): Leukocytes: 14 [4 - 11] 10^9/L; [redacted]20[redacted] (RX DAY 436): Platelets: 591 [140 - 450] 10^9/L

**Microbiology**

[redacted]20[redacted] (RX DAY 423): OTHER UTERUS/ENDOMETRIAL POLYP BIOPSY NPTST030-ANATOMICAL PATHOLOGY: Negative-COMPATIBLE WITH ATROPHIC ENDOMETRIUM, NO DEFINITE POLYP OR MALIGNANCY IS IDENTIFIED; [redacted]20[redacted] (RX DAY 425): OTHER SMALL BOWEL EXCISION NPTST312-SURGICAL PATHOLOGY REPORT: Positive-PORTION OF SMALL BOWEL WITH TRANSMURAL ACUTE INFLAMMATORY CHANGES, COMPATIBLE WITH SITE OF SMALL BOWEL PERFORATION INJURY; [redacted]20[redacted] (RX DAY 432): OTHER PELVIC FLUID NPTST144-FLUID CULTURE: Negative-NO GROWTH AEROBICALLY OR ANAEROBICALLY AFTER 72HRS.; [redacted]20[redacted] (RX DAY 433): OTHER ABSCESS PELVIC FLUID NPTST144-FLUID CULTURE: Negative

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 481 / 425 (3 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 3 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |

| | |
|---|---|
| **Investigator Alternative Etiology** | PT HAD A SCHEDULED DILATION AND CURETTAGE PROCEDURE TO REMOVE AN ENDOMETRIAL POLYP ON [redacted] TH WHICH RESULTED IN A BOWEL PERFORATION |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING |

**Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | PROCEDURAL UTERINE PERFORATION |
| **Preferred term** | 子宮穿孔 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 479 / 423 (1 DAY AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 424): Creatinine: 108 [40 - 100] UMOL/L; Creatinine: 108 [40 - 100] UMOL/L; NPTST197-LACTATE: 3.6 [0.5 - 2.2] MMOL/L; NPTST197-LACTATE: 3.6 [0.5 - 2.2] MMOL/L; NPTST334-UREA: 9.3 [2.5 - 8] MMOL/L; NPTST334-UREA: 9.3 [2.5 - 8] MMOL/L; [redacted]20[redacted] (RX DAY 425): Albumin: 22 [35 - 50] G/L; Albumin: 22 [35 - 50] G/L; Aspartate Aminotransferase: 69 [0 - 40] U/L; Aspartate Aminotransferase: 69 [0 - 40] U/L; NPTST189-INR: 1.6 [0.8 - 1.2] RATIO; NPTST189-INR: 1.6 [0.8 - 1.2] RATIO; NPTST209-MAGNESIUM: 0.59 [0.7 - 1] MMOL/L; NPTST209-MAGNESIUM: 0.59 [0.7 - 1] MMOL/L; NPTST255-PO4: 0.56 [0.8 - 1.45] MMOL/L; NPTST255-PO4: 0.56 [0.8 - 1.45] MMOL/L; NPTST317-TOTAL CO2: 20 [23 - 31] MMOL/L; NPTST317-TOTAL CO2: 20 [23 - 31] MMOL/L; [redacted]20[redacted] (RX DAY 426): Chloride: 109 [96 - 107] MMOL/L; Chloride: 109 [96 - 107] MMOL/L; NPTST257-POTASSIUM - WBK (WHOLE BODY): 2.9 [3.3 - 4.8] MMOL/L; NPTST257-POTASSIUM - WBK (WHOLE BODY): 2.9 [3.3 - 4.8] MMOL/L; [redacted]20[redacted] (RX DAY 427): Hemoglobin: 95 [120 - 160] G/L; Hemoglobin: 95 [120 - 160] G/L; [redacted]20[redacted] (RX DAY 429): Calcium: 1.99 [2.1 - 2.6] MMOL/L; Calcium: 1.99 [2.1 - 2.6] MMOL/L; [redacted]20[redacted] (RX DAY 432): Leukocytes: 14 [4 - 11] 10^9/L; Leukocytes: 14 [4 - 11] 10^9/L; [redacted]20[redacted] (RX DAY 436): Platelets: 591 [140 - 450] 10^9/L; Platelets: 591 [140 - 450] 10^9/L

**Microbiology**

[redacted]20[redacted] (RX DAY 423): OTHER UTERUS/ENDOMETRIAL POLYP BIOPSY NPTST030-ANATOMICAL PATHOLOGY: Negative-COMPATIBLE WITH ATROPHIC ENDOMETRIUM, NO DEFINITE POLYP OR MALIGNANCY IS IDENTIFIED; [redacted]20[redacted] (RX DAY 425): OTHER SMALL BOWEL EXCISION NPTST312-SURGICAL PATHOLOGY REPORT: Positive-PORTION OF SMALL BOWEL WITH TRANSMURAL ACUTE INFLAMMATORY CHANGES, COMPATIBLE WITH SITE OF SMALL BOWEL PERFORATION INJURY; [redacted]20[redacted] (RX DAY 432): OTHER PELVIC FLUID NPTST144-FLUID CULTURE: Negative-NO GROWTH AEROBICALLY OR ANAEROBICALLY AFTER 72HRS.; [redacted]20[redacted] (RX DAY 433): OTHER ABSCESS PELVIC FLUID NPTST144-FLUID CULTURE: Negative

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 481 / 425 (3 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 3 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | PT HAD A SCHEDULED DILATION AND CURETTAGE PROCEDURE TO REMOVE AN ENDOMETRIAL POLYP ON [redacted] TH WHICH |

| | |
|---|---|
| | RESULTED IN AN UTERINE PERFORATION. |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING |

**Event #3: Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event**

| | |
|---|---|
| **Event Description** | RIGHT ARM DEEP VEIN THROMBOSIS AT PICC LINE INSERTION SITE |
| **Preferred term** | 深部静脈血栓症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 495 / 439 (17 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，処置による子宮穿孔，及び処置による小腸穿孔の事象を発現した。関連する病歴は，卵管結紮，閉経，潰瘍性大腸炎（左側），非喫煙者及び中程度の

現飲酒者であった。

**Event 1 及び 2 の臨床経過：**

投与479日後＊ ，被験者は処置による子宮穿孔，及び処置による小腸穿孔を発現した。投与481日後＊ ，処置による子宮穿孔，及び処置による小腸穿孔は消失した。

投与381日後＊ ，被験者は子宮内膜ポリープ（非重篤）と診断され，投与479日後＊ に頸管拡張及び掻爬術により，ポリープが切除された。ポリープ切除後の 投与480日後＊ ，被験者は腹痛の増強，悪寒，悪心及び嘔吐があり，救急治療室を受診した。受診当初は無熱であったが，その後発熱した。投与480日後＊ ，被験者は入院した。CT スキャン検査で，腹腔内の遊離ガス及び液体が確認された（子宮穿孔の可能性あり）。投与481日後＊ ，被験者は開腹手術を受け，洗浄，創傷郭清及び小腸の修復が行われ，成功した投与488日後＊ の再 CT スキャン検査では，術後の膿瘍と考えうる液体が骨盤の深部に貯留していた。投与489日後＊ ，被験者は CT ガイド下での膿瘍ドレナージ及び経皮的ドレーン挿入を受けた。投与492日後＊ ，ドレーンが抜去され，同日，被験者は退院した。

治験薬の投与は完全に中止され，最終投与日は 投与478日後＊ であった。

投与された薬剤は，ラシックス，maxeran，pantoloc 及びピペラシリンであった。

**The patient's past medications include:**

SALOFALK SUPPOSITORY for ULCERATIVE COLITIS ([redacted])

CORTIFOAM for ULCERATIVE COLITIS ([redacted])

SALOFALK ENEMA for ULCERATIVE COLITIS ([redacted])

CIPROFLOXACIN for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Uterine perforation (10046810) (Uterine perforation (10046810) ) [v.21.1] [10046810]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

2) Procedural intestinal perforation (10074065) (Procedural intestinal perforation (10074065) ) [v.21.1] [10074065]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of PROCEDURAL UTERINE PERFORATION

**- Investigator:** Patient had a scheduled dilation and curettage procedure to remove an endometrial polyp on [redacted] 20[redacted] which resulted in a uterine perforation.

**- AbbVie:** Event is more likely a complication of dilation and curettage procedure, as reported by the investigator.

Event of PROCEDURAL SMALL BOWEL PERFORATION

**- Investigator:** Patient had a scheduled dilation and curettage procedure to remove an endometrial polyp on [redacted] which resulted in a bowel perforation.

**- AbbVie:** Event is more likely a complication of dilation and curettage procedure, as reported by the investigator.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **ABDOMEN 2 OR MORE PROJECTIONS:** PNUEMOPERITONEUM IS IDENTIFIED, MAY RELATE TO POSSIBLE UTERINE PERFORMATION

[redacted] **ABSCESS PELVIC FLUID CULTURE:** negative

[redacted] **ALBUMIN:** 22 G/L (normal 35 to 50)

[redacted] **ASPARTATE AMINO TRANSFERASE:** 69 U/L (normal 0 to 40)

[redacted] **CALCIUM:** 1.99 MMOL/L (normal 2.10 to 2.60)

[redacted] **CHLORIDE:** 109 MMOL/L (normal 96 to 107)

[redacted] **CREATININE:** 108 MCMOL/L (normal 40 to 100)

[redacted] **CT ABDOMEN AND PELVIS ENHANCED:** SMALL VOLUMES OF INRAPERITONEAL FREE AIR AND FREE FLUIDWITH A HYPOATTENUATING TRACK THROUGH THE ANTERIOR WALL OF THE UTERUS LIKELY REPRESENTS A UTERINE WALL PERFORATION IN THE CONTEXT OF THE RECENT D &C. ADJACENT BOWEL INJURY IS NOT DEFINITELY IDENTIFIED, BUT CANNOT BE RULED OUT

[redacted] **CT ABDOMEN AND PELVIS ENHANCED:** LARGE VOLUME OF FREE INTRAPERITONEAL FLUID WITH MILD PNUEMOPERITONEUM IN KEEPING WITH KNOWN UTERINE PERFORATION. WORSENING LARGE COMPLEX FLUID COLLECTIONS IN THE PELVIS SUSPICIOUS FOR BOWEL PERFORATION (TOO EARLY FOR ABSCESS). INTERVAL DEVELOPMENT OF SMALL RIGHT AND TRACE LEFT PLEURAL EFFUSIONS WITH MODERATE BIBASILAR ATELECTASIS. MILDLY DILATED SMALL BOWEL LOOPS WITH NO TRANSITION POINT FAVOURED TO REPRESENT ILEUS.

[redacted] **CT ABDOMEN AND PELVIS ENHANCED:** SMALL PERIPHERALLY ENHANCING FLUID COLLECTION WITH THE LEFT LOWER QUADRANT. THERE IS MURAL THICKENING OF THE RECTOSIGMOID COLON AS WELL AS THE DESCENDING COLON EXTENDING TO THE SPLENIC FLEXURE POSSIBLY SECONDARY TO PT'S KNOWN ULCERATIVE COLITIS. MILD RECTAL WALL MURAL THICKENING IS NOTED LIKELY SECONDARY TO THE ADJACENT ABSCESS WITHIN THE PELVIS. EVIDENCE OF A SUSPECTED LOW-GRADE/PARTIAL SMALL BOWEL OBSTRUCTION WITH A TRANSITION POINT WITHIN THE PROXIMAL ILEUM WITHIN

THE RIGHT LOWER QUADRANT. SMALL R SIDED PLEURAL EFFUSION.

[redacted] 20[redacted] **CT ABSCESS ASPIRATION OR DRAINAGE:** SUCCESSFUL PLACEMENT OF A LOCKING LOOP PIGTAIL DRAIN WITHIN A PELVIC ABSCESS

[redacted] 20[redacted] **HGB:** 95 G/L (normal 120 to 160)

[redacted] 20[redacted] **INR:** 1.6 NO UNIT (normal 0.8 to 1.2)

[redacted] 20[redacted] **LACTATE:** 3.6 MMOL/L (normal 0.5 to 2.2)

[redacted] 20[redacted] **MAGNESIUM:** 0.59 MMOL/L (normal 0.70 to 1.00)

[redacted] 20[redacted] **PELVIC FLUID CULTURE:** NO GROWTH AEROBICALLY OR ANAEROBICALLY AFTER 72HRS.

[redacted] 20[redacted] **PLATELET COUNT:** 591 X10**9/L (normal 140 to 450)

[redacted] 20[redacted] **PO4:** 0.56 MMOL/L (normal 0.80 to 1.45)

[redacted] 20[redacted] **POTASSIUM - WBK (WHOLE BODY)):** 2.9 MMOL/L (normal 3.3 to 4.8)

[redacted] 20[redacted] **SMALL BOWEL EXCISION SURGICAL PATHOLOGY REPORT:** Positive, portion of small bowel with transmural acute inflammatory changes, compatible with site of small bowel perforation injury.

[redacted] 20[redacted] **PATHOLOGY:** SMALL BOWEL: PORTION OF SMALL BOWEL WITH TRANSMURAL ACUTE INFLAMMATORY CHANGES, COMPATIBLE WITH SITE OF SMALL BOWEL PERFORATION INJURY

[redacted] 20[redacted] **TEMPERATURE:** 39.2 Degrees C

[redacted] 20[redacted] **TOTAL CO2:** 20 MMOL/L (normal 23 to 31)

[redacted] 20[redacted] **UREA:** 9.3 MMOL/L (normal 2.5 to 8.0)

[redacted] 20[redacted] **US ABSCESS ASPIRATION/DRAINAGE:** U/S GUIDED ASPIRATION OF COMPLEX FLUID COLLECTION WITHIN THE ANTERIOR PELVIS YEILDING 15 CC OF CLOUDY YELLOW FLUID. POST PROCEDURE IMAGES SHOW THAT NEARLY ALL OF THE LIQUIFIED FLUID HAS RESOLVED. U/S GUIDED DIAGNOSTIC AND THERAPEUTIC ASPIRATION OF A SMALL FLUID COLLECTION WITHIN THE RIGHT UPPER QUADRANT.

[redacted] 20[redacted] **UTERINE ENDOMETRIAL POLYP BIOPSY:** Negative, compatible with atrophic endometrium, no definite polyp or malignancy is identified.

[redacted] 20[redacted] **WBC:** 14.0 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] **X-RAY CHEST ERECT AP:** SIGNIFICANT DECREASE IN LUNG VOLUME (COMPARED TO PREVIOUS EXAM ON [redacted] 20[redacted]). LED TO EXTENSIVE BIBASAL

ATELECTASIS. TRACE PLEURAL EFFUSIONS ARE FELT LIKELY TO BE PRESENT. {NEUMOPERITONEUM IDENTIFIED ON THE PREVIOUS DAY'S STUDY IS NO LONGER VISIBLE. A NUMBER OF GAS-FILLED LOOPS OF BOWEL ARE NOTED WHICH MAY INDICATE THE PRESENCE OF ADYNAMIC ILEUS.

[redacted] **20[redacted] X-RAY CHEST ERECT AP:** ENDOTRACHEAL TUBE HAS BEEN REMOVED WITH CONCOMITANT INCREASING BIBASAL ATELECTASIS. ESOPHAGOENTERIC TUBE REMAINS IN SITU. NO ADDITIONAL INTERVAL CHANGE SINCE THE EXAMINATION OF PREVIOUS DAY, ALLOWING FOR DIFFERENCES IN TECHNIQUE.

[redacted] [redacted] **20[redacted] X-RAY CHEST ERECT PA:** PNEUMOPERITONEUM UNDER RIGHT HEMIDIAPHRAGM IS IDENTIFIED, SOME MINOR LEFT BASAL ATELACTASIS IS SEEN

[redacted] **20[redacted] X-RAY CHEST ERECT PA:** ONGOING SMALL BILATERAL PLEURAL EFFUSIONS, RIGHT GREATER THAN LEFT. MULTIPLE GASEOUS DISTENDED SMALL BOWEL LOOPS WHICH MEASURE AT THE UPPER LIMITS OF NORMAL IN CALIBER WITH MULTIPLE AIR-FLUID LEVELS, AND FINDINGS RAISE CONCERN FOR A DEVELOPING/PARTIAL SMALL BOWEL OBSTRUCTION. THE COLON APPEARS RELATIVELY OLLAPSED, AND THEREFORE, ILEUS IS THOUGHT LESS LIKELY DESPITE THE PATIENT'S STATUS POST OP.

[redacted] **20[redacted] X-RAY CHEST SUPINE AP:** SOME IMPROVEMENT IN THE BIBASAL ATELACTASIS BUT PATCHY ATELECTASIS PERSISTS. SMALL BILATERAL EFFUSIONS. ENDOTRACHEAL TUBE JUST INTO THE RIGHT MAINSTEM BRONCHUS. THIS SHOULD BE PULLED BACK APPROX. 2.5 - 3 CM.

[redacted] **20[redacted] X-RAY CHEST SUPINE AP:** INTERVAL REPOSITIONING OF THE ENDOTRACHEAL TUBE WITH THE TIP NOW LOCATED APPORX. 2 CM ABOVE THE CARINA. OTHERWISE NO SIGNIFICANT INTERVAL CHANGE. PERSISTENT BIBASILAR ATELECTASIS

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Deep vein thrombosis: Upper Limb. Risk factors: prolonged immobilization, recent surgical procedure or hospitalization.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 子宮平滑筋腫 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA: ANEMIA | 20[redacted] |
| ASTHMA: EXERCISE INDUCED ASTHMA | 20[redacted] |
| DEPRESSION: DEPRESSION | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: 10MM CYST ON KIDNEY | 20[redacted] |
| OTHER: ALLERGY DUST MITES | 20[redacted] |
| OTHER: ALLERGY LINALOOL OIL | 20[redacted] |
| OTHER: BLOOD TRANSFUSION | 20[redacted] |
| OTHER: C-DIFF POSITIVE | 20[redacted] |
| OTHER: ENVIROMENTAL ALLERGY | 19[redacted] |
| OTHER: HEMORRHOIDS | 20[redacted] |
| OTHER: LYCHEN SIMPLEX | 20[redacted] |
| OTHER: OCCASIONAL HEADACHES | 20[redacted] |
| OTHER: OCCASIONAL MIGRAINE HEADACHES | 20[redacted] |
| OTHER: ROSACEA | 20[redacted] |
| OTHER: STYE | 20[redacted] |
| OTHER: UTERINE FIBROIDS | 20[redacted] |
| OTHER: VITAMIN A DEFICENCY | 20[redacted] |
| OTHER: VITAMIN E DEFICIENCY | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: BARTHOLIN CYST REMOVAL | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.25 PACK | 20 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 30 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 54 | 54 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / 55 | [redacted]20[redacted] / 427 | 373 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 428 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ASCORBIC ACID;CALCIUM PHOSPHATE;COLECALCIFEROL;COPPER; CYANOCOBALAMIN;DL-ALPHA TOCOPHEROL;FOLIC ACID;IODINE;IRON;MANGANESE;NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RETINOL;RIBOFLAVIN;THIAMINE;ZINC | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| HYDROCORTISONE | 100 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: 20[redacted] |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| FISH OIL | 500 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 4.8 g | QD | Y-M: 20[redacted] |
| MESALAZINE | 4.8 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 800 mg | QD | Y-M: 20[redacted] |
| HYDROCORTISONE | 100 mg | QD | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| PARACETAMOL | 1 OTHER: TAB | PRN | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / Stop Year-Month / RX Day | |
|---|---|---|---|---|
| ASCORBIC ACID;CALCIUM PHOSPHATE;COLECALCIFEROL;COPPER;CYANOCOBALAMIN;DL-ALPHA TOCOPHEROL;FOLIC ACID;IODINE;IRON;MANGANESE;NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RETINOL;RIBOFLAVIN;THIAMINE;ZINC | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | Not reported |
| VITAMINS NOS | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | ONGOING |
| FISH OIL | 500 mg | QD | Y-M: 20[redacted] | ONGOING |
| ULIPRISTAL | 5 mg | QD | Y-M: 20[redacted] / 120 | Y-M: 20[redacted] / 210 |
| BISACODYL | 3 OTHER: TABLETS | OTHER: ONCE | Y-M: 20[redacted] / 334 | Y-M: 20[redacted] / 334 |
| CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE | 2 OTHER: SATCHETS | OTHER: ONCE | Y-M: 20[redacted] / 334 | Y-M: 20[redacted] / 334 |
| FENTANYL | 75 ug | OTHER: ONCE | Y-M: 20[redacted] / 335 | Y-M: 20[redacted] / 335 |
| MESALAZINE | 2.4 g | QD | Y-M: 20[redacted] / 335 | Not reported |
| MIDAZOLAM | 3 mg | OTHER: ONCE | Y-M: 20[redacted] / 335 | Y-M: 20[redacted] / 335 |
| PREDNISONE | 40 mg | QD | Y-M: 20[redacted] / 335 | Y-M: 20[redacted] / 342 |
| ESCITALOPRAM | 10 mg | QD | Y-M: 20[redacted] / 342 | Not reported |
| BUDESONIDE | 9 mg | QD | Y-M: 20[redacted] / 343 | Y-M: 20[redacted] / 391 |
| HYDROCORTISONE | 1 OTHER: APPLICATION | PRN | Y-M: 20[redacted] / 413 | Y-M: 20[redacted] / 420 |
| MINOCYCLINE | 100 mg | QD | Y-M: 20[redacted] / 485 | Y-M: 20[redacted] / 577 |
| ANESTHETICS, GENERAL | UNKNOWN OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 674 | Y-M: 20[redacted] / 674 |
| CEFAZOLIN | 2 g | OTHER: ONCE | Y-M: 20[redacted] / 674 | Y-M: 20[redacted] / 674 |
| HYDROMORPHONE | 0.4 mg | PRN | Y-M: 20[redacted] / 674 | Y-M: 20[redacted] / 674 |
| METOCLOPRAMIDE | 10 mg | PRN | Y-M: 20[redacted] / 674 | Y-M: 20[redacted] / 674 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 674 | Y-M: 20[redacted] / 674 |
| TINZAPARIN | 8,000 IU | OTHER: QHS | Y-M: 20[redacted] / 674 | Y-M: 20[redacted] / 675 |
| PARACETAMOL | 1 OTHER: TAB | PRN | Y: 20[redacted] | Not reported |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF UTERINE FIBROIDS |

| | |
|---|---|
| **Preferred term** | 子宮平滑筋腫 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 547 / 120 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 1101 / 674 |
| **Duration of AE** | 555 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | UTERINE FIBROIDS ARE PART OF MEDICAL HISTORY FOR THIS SUBJECT |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，子宮類線維症の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，子宮類線維症，元喫煙者（1 日 0.25 箱を 20 年間）及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与547日後＊ ，被験者は子宮類線維症の悪化を発現した。投与1101日後＊ ，子宮類線維症の悪化は消失した。

投与1101日後＊，子宮類線維症（投与3年前＊-）による異常出血があり，子宮全摘術及び両側卵管摘除術を受けるために入院した。被験者は fiberstal を試したが，効果は認められなかった。被験者の最新の超音波検査では，左側面の子宮筋腫が最大で 8 × 7.4 × 6 cm，後側の子宮筋腫が 3 × 2 × 3 cm であった。被験者には，本事象に関連する危険因子及び家族歴はなかった。 投与

1103日後＊，被験者は，合併症もなく退院した。

投与された薬剤は，tramacet，tinzaparin，セファゾリン，maxeran，zofran 及びヒドロモルフォンであった。

**The patient's past medications include:**

CORTENEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK ENEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FIBRISTAL for UTERINE FIBROIDS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Uterine fibroids aggravated (10048417) (Uterine leiomyoma (10046798) ) [v.23.1] [10048417]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of WORSENING OF UTERINE FIBROIDS

**- Investigator:** Uterine fibroids are part of medical history for this subject

**- AbbVie:** More likely related to pre-existing uterine fibroids.

Relevant Laboratory & Other Diagnostic Tests

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**Unknown date ULTRASOUND:** LEFT LATERAL FIBROID MEASURED UP TO 8 X 7.4 X 6 CM. POSTERIOR FIBROID OF 3 X 2 X 3 CM

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| COVID-19 肺炎 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| COLD SORES | 19[redacted] |
| DRY COUGH | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| LOWER BACK PAIN | 19[redacted] |
| NON INSULIN DEPENDANT DIABETES | 20[redacted] |
| SLEEP APNEA | 20[redacted] |
| SLEEP DISTURBANCE | 20[redacted] |
| STEROID INDUCED FOLLICULITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.5 PACK | 20 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 55 | 55 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted] / 56 | [redacted] / 417 | 362 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted] / 419 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1000 mg | QD | Y-M: [redacted] |
| MESALAZINE | 2400 mg | QD | Y-M: [redacted] |
| METFORMIN | 800 mg | BID | Y-M: [redacted] |
| BUDESONIDE | 3 mg | QD | Y-M: [redacted] |
| BUDESONIDE | 6 mg | QD | Y-M: [redacted] |
| ZOPICLONE | 7.5 mg | PRN | Y-M: [redacted] / -84 |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y: [redacted] |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y: [redacted] |
| VITAMIN D NOS | 1000 IU | QD | Y: [redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| METFORMIN | 800 mg | BID | Y-M: [redacted] | NY-M: [redacted] / 412 |
| ZOPICLONE | 7.5 mg | PRN | Y-M: [redacted] / -84 | Not reported |
| MELOXICAM | 7.5 mg | PRN | Y-M: [redacted] / 238 | Not reported |
| CODEINE;PARACETAMOL | 1 OTHER: TAB | PRN | Y-M: [redacted] / 243 | Y-M: [redacted] / 454 |
| GABAPENTIN | 300 mg | BID | Y-M: [redacted] / 318 | Not reported |
| BUDESONIDE;FORMOTEROL | 200 OTHER: MCG | BID | Y-M: [redacted] / 394 | Not reported |
| SALBUTAMOL | 2 OTHER: PUFFS | PRN | Y-M: [redacted] / 394 | Not reported |
| AZITHROMYCIN | 500 mg | QD | Y-M: [redacted] / 412 | Y-M: [redacted] / 414 |
| CEFTRIAXONE | 2 g | QD | Y-M: [redacted] / 412 | Y-M: [redacted] / 412 |
| DEXAMETHASONE | 6 mg | QD | Y-M: [redacted] / 412 | Y-M: [redacted] / 417 |
| CEFTRIAXONE | 1 g | QD | Y-M: [redacted] / 413 | Y-M: [redacted] / 413 |
| FISH OIL | 1 OTHER: TABLET | QD | Y-M: [redacted] / 413 | Not reported |

| | | | | |
|---|---|---|---|---|
| METFORMIN | 500 mg | TID | Y-M: 20[redacted] / 413 | Not reported |
| PARACETAMOL | 325 mg | TID | Y-M: 20[redacted] / 413 | Y-M: 20[redacted] / 417 |
| TINZAPARIN | 4500 OTHER: UNITS | QD | Y-M: 20[redacted] / 413 | Y-M: 20[redacted] / 413 |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 414 | Y-M: 20[redacted] / 416 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 414 | Y-M: 20[redacted] / 416 |
| TINZAPARIN | 8000 OTHER: UNITS | QD | Y-M: 20[redacted] / 414 | Y-M: 20[redacted] / 416 |
| DOXYCYCLINE | 100 mg | QD | Y-M: 20[redacted] / 428 | Y-M: 20[redacted] / 489 |
| SULFADIAZINE | 1 OTHER: APP | QD | Y-M: 20[redacted] / 431 | Y-M: 20[redacted] / 441 |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y: 20[redacted] | Not reported |
| VITAMINS NOS | 1 OTHER: TAB | QD | Y: 20[redacted] | Not reported |
| VITAMIN D NOS | 1000 IU | QD | Y: 20[redacted] | Not reported |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | COVID -19 RELATED PNEUMONIA |
| **Preferred term** | COVID-19 肺炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 824 / 406 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 412): NPTST110-CULTURES: NO GROWTH IN 5 DAYS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 413): Hematocrit: 0.4 [0.41 - 0.52] FRACTION OF 1; Lymphocytes: 0.4 [1 - 4.5] 10^9/L

**Microbiology**

[redacted]20[redacted] (RX DAY 412): BLOOD NPTST053-BLOOD CULTURES: Negative-NO GROWTH IN 5 DAYS FROM TIME OF RECEIPT IN LABORATORY

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 855 / 437 |
| **Duration of AE** | 32 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 関連の肺炎の事象を発現した。関連する病歴は，元喫煙者（1 日 0.5 箱を 20 年間），乾性咳嗽，高血圧，非インスリン依存性糖尿病，潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与824日後＊　，被験者は COVID-19 関連の肺炎を発現した。投与855日後＊　，COVID-19 関連の肺炎は消失した。

投与824日後＊　　，被験者は高熱，疲労，体の痛み，持続性の咳嗽，及び胸部うっ血を発現した。肺の聴診では，右中肺野に轟音が認められた。その後，COVID-19 感染症の検査で陽性が確認された。投与830日後＊　　，被験者は入院した。胸部 X 線検査では，COVID-19 関連の肺炎が認められた。入院 4 日目及び 5 日目に劇的な改善を示した。被験者の酸素飽和度は室内気で 90%以上を維持していた。投与835日後＊　，被験者は退院した。

投与された薬剤は，アセトアミノフェン，セフトリアキソン，アジスロマイシン，デキサメタゾン，zithromax 及び tinzaparin であった。

**The patient's past medications include:**

SALOFALK SUPPOSITORIES for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1)　COVID-19 pneumonia (10084380)　(COVID-19 pneumonia (10084380) )　[v.24.0]　[10084380]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

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Event of COVID-19 RELATED PNEUMONIA

**- Investigator:** Not applicable

**- AbbVie:** Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] BLOOD CULTURES:** Negative - No growth for 5 days.

[redacted] **20[redacted] BMI:** 32 kg/m2

[redacted] **20[redacted] BODY TEMPERATURE:** 41 Degrees C

[redacted] **20[redacted] BODY WEIGHT:** 10[redacted] KG

[redacted] **20[redacted] CHEST X-RAY:** Cardiac outline was normal. There was aortic unfolding. Hyperinflation suspected. Development of confluent area of opacification in the lateral segment of right middle lobe, left lung remains clear. Right middle lobe pneumonia has developed since [redacted] 20[redacted], COPD suspected.

[redacted] **20[redacted] CHEST X-RAY:** Findings indicate right middle lobe pneumonia again demonstrated, there was slight decreased opacification since the previous exam. There were a few patchy areas of pneumonia also seen in the left lower lobe, which in retrospect can be seen on previous exam. Hyperinflation again seen.

[redacted] **20[redacted] COVID-19 VIRUS TEST:** Positive

[redacted] **20[redacted] ECG:** Normal

[redacted] **20[redacted] HCT:** 0.40 L/L (normal 0.41 to 0.52)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.4 X10**9/L (normal 1.0 to 4.5)

[redacted] **20[redacted] OXYGEN SATURATION:** > 90% on room air

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 直腸膿瘍 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| CLOSTRIDIUM DIFFICILE POSITIVE | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| INTERNAL HEMORRHOIDS | 20[redacted] |
| IRON DEFICIENT ANEMIA | 20[redacted] |
| KNEE PAIN BILATERAL | 20[redacted] |
| LOWER BACK PAIN | 20[redacted] |
| MOUTH ULCERS | 20[redacted] |
| OCCASIONAL HEADACHES | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 7 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 57 | 57 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted] / 58 | [redacted] / 86 | 29 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 87 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISONE | 2.5 mg | QD | Y-M: [redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: [redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: [redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: [redacted] |
| INFLIXIMAB | 400 mg | OTHER: Q 8 WEEKS | Y-M: [redacted] |
| PREDNISONE | 2.5 mg | QD | Y-M: [redacted] |
| BETAMETHASONE | 1 OTHER: APPLICATION | OTHER: Q 3 DAY | Y-M: [redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: Q 4 WEEKS | Y-M: [redacted] |
| PREDNISONE | 20 mg | QD | Y-M: [redacted] / -134 |
| VANCOMYCIN | 125 mg | QD | Y-M: [redacted] / -101 |
| IRON | 300 mg | QD | Y: [redacted] |
| MESALAZINE | 4.8 g | QD | Y: [redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| CEFTRIAXONE | 2 g | QD | Y-M: [redacted] / 871 | Y-M: [redacted] / 887 |
| DEXAMETHASONE | 6 mg | OTHER: ONCE | Y-M: [redacted] / 871 | Y-M: [redacted] / 871 |
| DIMENHYDRINATE | 25 mg | OTHER: ONCE | Y-M: [redacted] / 871 | Y-M: [redacted] / 871 |
| HEPARIN | 5000 OTHER: UNITS | OTHER: ONCE | Y-M: [redacted] / 871 | Y-M: [redacted] / 871 |
| HYDROMORPHONE | 0.6 mg | PRN | Y-M: [redacted] / 871 | Y-M: [redacted] / 871 |
| HYDROMORPHONE | 1.0 mg | PRN | Y-M: [redacted] / 871 | Y-M: [redacted] / 874 |
| IOHEXOL | 80 mL | OTHER: ONCE | Y-M: [redacted] / 871 | Y-M: [redacted] / 871 |

| | | | | |
|---|---|---|---|---|
| KETAMINE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 871 | Y-M: 20[redacted] / 871 |
| LIDOCAINE | 2.5 mL | OTHER: ONCE | Y-M: 20[redacted] / 871 | Y-M: 20[redacted] / 871 |
| METRONIDAZOLE | 500 mg | BID | Y-M: 20[redacted] / 871 | Y-M: 20[redacted] / 888 |
| PROPOFOL | 150 mg | OTHER: ONCE | Y-M: 20[redacted] / 871 | Y-M: 20[redacted] / 871 |
| REMIFENTANIL | 80 OTHER: MCG | OTHER: ONCE | Y-M: 20[redacted] / 871 | Y-M: 20[redacted] / 871 |
| ROCURONIUM | 0.25 mg | OTHER: ONCE | Y-M: 20[redacted] / 871 | Y-M: 20[redacted] / 871 |
| BUPIVACAINE | 20 mL | OTHER: ONCE | Y-M: 20[redacted] / 872 | Y-M: 20[redacted] / 872 |
| HYDROMORPHONE | 1.5 mg | PRN | Y-M: 20[redacted] / 872 | Y-M: 20[redacted] / 872 |
| HYDROMORPHONE | 2 mg | PRN | Y-M: 20[redacted] / 872 | Y-M: 20[redacted] / 887 |
| PARACETAMOL | 650 mg | PRN | Y-M: 20[redacted] / 872 | Y-M: 20[redacted] / 890 |
| PARACETAMOL;TRAMADOL | 2 OTHER: TAB | PRN | Y-M: 20[redacted] / 873 | Y-M: 20[redacted] / 873 |
| BUPIVACAINE | 10 mL | OTHER: ONCE | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 877 |
| FENTANYL | 100 OTHER: MCG | OTHER: ONCE | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 877 |
| FENTANYL | 25 OTHER: MCG | PRN | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 877 |
| HYDROMORPHONE | 0.2 mg | PRN | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 879 |
| HYDROMORPHONE | 0.4 mg | PRN | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 877 |
| LIDOCAINE | 80 mg | OTHER: ONCE | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 877 |
| PROPOFOL | 200 OTHER: MCG | OTHER: ONCE | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 877 |
| REMIFENTANIL | 80 OTHER: MCG | OTHER: ONCE | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 877 |
| TINZAPARIN | 4500 OTHER: UNITS | QD | Y-M: 20[redacted] / 877 | Y-M: 20[redacted] / 889 |
| BUPIVACAINE | 10 mL | OTHER: ONCE | Y-M: 20[redacted] / 879 | Y-M: 20[redacted] / 879 |
| FENTANYL | 25 OTHER: MCG | PRN | Y-M: 20[redacted] / 879 | Y-M: 20[redacted] / 879 |
| KETAMINE | 10 mg | OTHER: ONCE | Y-M: 20[redacted] / 879 | Y-M: 20[redacted] / 879 |
| MIDAZOLAM | 2 mg | OTHER: ONCE | Y-M: 20[redacted] / 879 | Y-M: 20[redacted] / 879 |
| PROPOFOL | 163.2 OTHER: MCG | OTHER: ONCE | Y-M: 20[redacted] / 879 | Y-M: 20[redacted] / 879 |
| ASCORBIC ACID;CALCIUM PHOSPHATE;COLECALCIFEROL;COPPER;CYANOCOBALAMIN;DL-ALPHA TOCOPHEROL;FOLIC ACID;IODINE;IRON;MANGANESE;NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RETINOL;RIBOFLAVIN;THIAMINE;ZINC | 15 mL | QD | Y-M: 20[redacted] / 881 | Y-M: 20[redacted] / 890 |
| HYDROMORPHONE | 4 mg | PRN | Y-M: 20[redacted] / 883 | Y-M: 20[redacted] / 887 |

| | | | | |
|---|---|---|---|---|
| IOHEXOL | 75 mL | OTHER: ONCE | Y-M: 20[redacted] / 883 | Y-M: 20[redacted] / 883 |
| HYDROMORPHONE | 2 mg | PRN | Y-M: 20[redacted] / 886 | Y-M: 20[redacted] / 886 |
| CODEINE | 60 mg | PRN | Y-M: 20[redacted] / 887 | Y-M: 20[redacted] / 887 |
| HYDROMORPHONE | 1 mg | PRN | Y-M: 20[redacted] / 887 | Y-M: 20[redacted] / 887 |
| LORAZEPAM | 1 mg | PRN | Y-M: 20[redacted] / 887 | Y-M: 20[redacted] / 887 |
| PARACETAMOL | 975 mg | PRN | Y-M: 20[redacted] / 887 | Y-M: 20[redacted] / 887 |
| MORPHINE | 10 mg | PRN | Y-M: 20[redacted] / 888 | Y-M: 20[redacted] / 890 |
| MORPHINE | 7.5 mg | PRN | Y-M: 20[redacted] / 888 | Y-M: 20[redacted] / 888 |
| IRON | 300 mg | QD | Y: 20[redacted] | Not reported |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | ISCHIORECTAL ABSCESS |
| **Preferred term** | 直腸膿瘍 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 957 / 871 |
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 871): Erythrocytes: 4.14 [4.3 - 6] 10^12/L; Hematocrit: 0.38 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 126 [135 - 175] G/L; Leukocytes: 19.7 [4 - 11] 10^9/L; NPTST108-CRP: 202.9 [0 - 8] MG/L; Neutrophils: 17.9 [1.8 - 7.5] 10^9/L; Platelets: 628 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 872): Erythrocytes: 3.4 [4.3 - 6] 10^12/L; Hematocrit: 0.33 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 103 [135 - 175] G/L; Leukocytes: 16.1 [4 - 11] 10^9/L; NPTST108-CRP: 271.0 [0 - 8] MG/L; Platelets: 447 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 873): Erythrocytes: 3.12 [4.3 - 6] 10^12/L; Hematocrit: 0.3 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 94 [135 - 175] G/L; Leukocytes: 13.5 [4 - 11] 10^9/L; NPTST108-CRP: 307.3 [0 - 8] MG/L; Platelets: 417 [140 - 400] 10^9/L; Sodium: 134 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 874): Erythrocytes: 3.34 [4.3 - 6] 10^12/L; Hematocrit: 0.32 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 100 [135 - 175] G/L; Leukocytes: 12.4 [4 - 11] 10^9/L; NPTST108-CRP: 276.3 [0 - 8] MG/L; NPTST334-UREA: 2.4 [3 - 8] MMOL/L; Platelets: 451 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 875): Erythrocytes: 3.73 [4.3 - 6] 10^12/L; Hematocrit: 0.36 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 111 [135 - 175] G/L; Leukocytes: 8.8 [4 - 11] 10^9/L; NPTST031-ANION GAP: 11 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST108-CRP: 238.9 [0 - 8] MG/L; NPTST212-MCHC: 308 [310 - 360] G/L; NPTST334-UREA: 2.8 [3 - 8] MMOL/L; Platelets: 589 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 876): Erythrocytes: 3.39 [4.3 - 6] 10^12/L; Hematocrit: 0.32 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 101 [135 - 175] G/L; Leukocytes: 6.5 [4 - 11] 10^9/L; NPTST108-CRP: 127.4 [0 - 8] MG/L; NPTST334-UREA: 2.9 [3 - 8] MMOL/L; Platelets: 488 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 877): Erythrocytes: 3.64 [4.3 - 6] 10^12/L; Hematocrit: 0.35 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 107 [135 - 175] G/L; Leukocytes: 7.8 [4 - 11] 10^9/L; NPTST108-CRP: 66.4 [0 - 8] MG/L; NPTST212-MCHC: 308 [310 - 360] G/L; Platelets: 514 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 878): Erythrocytes: 3.72 [4.3 - 6] 10^12/L; Hematocrit: 0.36 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 109 [135 - 175] G/L; Leukocytes: 7.6 [4 - 11] 10^9/L; NPTST108-CRP: 54.8 [0 - 8] MG/L; NPTST212-MCHC: 302 [310 - 360] G/L; NPTST334-UREA: 2.8 [3 - 8] MMOL/L; Platelets: 592 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 879): Erythrocytes: 3.62 [4.3 - 6] 10^12/L; Hematocrit: 0.35 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 107 [135 - 175] G/L; Leukocytes: 6.7 [4 - 11] 10^9/L; NPTST108-CRP: 49.1 [0 - 8] MG/L; NPTST212-MCHC: 307 [310 - 360] G/L; Platelets: 555 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 880): Erythrocytes: 3.43 [4.3 - 6] 10^12/L; Hematocrit: 0.33 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 103 [135 - 175] G/L; Leukocytes: 5.3 [4 - 11] 10^9/L; NPTST108-CRP: 30.2 [0 - 8] MG/L; Platelets: 525 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 881): Erythrocytes: 3.64 [4.3 - 6] 10^12/L; Hematocrit: 0.35 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 110 [135 - 175] G/L; Leukocytes: 5.1

[4 - 11] 10^9/L; Platelets: 556 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 882): Erythrocytes: 3.86 [4.3 - 6] 10^12/L; Hematocrit: 0.37 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 115 [135 - 175] G/L; Leukocytes: 6.2 [4 - 11] 10^9/L; NPTST108-CRP: 12.2 [0 - 8] MG/L; NPTST212-MCHC: 309 [310 - 360] G/L; Platelets: 571 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 884): Erythrocytes: 3.7 [4.3 - 6] 10^12/L; Hematocrit: 0.36 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 112 [135 - 175] G/L; Leukocytes: 5.9 [4 - 11] 10^9/L; Platelets: 477 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 887): Erythrocytes: 3.79 [4.3 - 6] 10^12/L; Hematocrit: 0.37 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 116 [135 - 175] G/L; Leukocytes: 5.7 [4 - 11] 10^9/L; Platelets: 409 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 889): Erythrocytes: 3.98 [4.3 - 6] 10^12/L; Hematocrit: 0.38 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 122 [135 - 175] G/L; Leukocytes: 4.1 [4 - 11] 10^9/L; NPTST272-RDW: 16.1 [0 - 16] %; [redacted]20[redacted] (RX DAY 890): Erythrocytes: 3.77 [4.3 - 6] 10^12/L; Hematocrit: 0.36 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 113 [135 - 175] G/L; Leukocytes: 2.8 [4 - 11] 10^9/L; NPTST272-RDW: 16.2 [0 - 16] %; Neutrophils: 0.9 [1.8 - 7.5] 10^9/L

**Microbiology**

[redacted]20[redacted] (RX DAY 872): WOUND NPTST117-DEEP WOUND CULTURE (SWAB/RECTAL: Positive-4+ STREPTOCOCCUS ANGINOSUS, 2+ MIXED ANAEROBIC ORGANISMS (MULTIPLE) INCLUDING GRAM-NEGATIVE BACILLI X2, AND GRAM-POSITIVE BACILLI X2; [redacted]20[redacted] (RX DAY 877): WOUND NPTST116-DEEP WOUND CULTURE (SWAB/PERINE: Positive-+1 STREPTOCOCCUS ANGINOSUS, 1+ ANAEROBIC GRAM-NEGATIVE BACILLI, 1+ ANAEROBIC NON-SPORE FORMING GRAM-POSITIVE BACILLI; [redacted]20[redacted] (RX DAY 879): WOUND NPTST117-DEEP WOUND CULTURE (SWAB/RECTAL: Positive-1+ ENTEROCOCCUS FAECALIS

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，坐骨直腸膿瘍の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 7 年間），内痔核，鉄欠乏性貧血，潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与957日後＊　，被験者は坐骨直腸膿瘍を発現した。

投与954日後＊　以降，被験者は腸の症状が増加していた。粘液及び血液を伴わない複数回の水性下痢があった。また，左臀部痛及びしぶりもあった。投与957日後＊　，被験者は便通時に突然の引き裂くような痛みがあり，病院を受診した。入院に際し，被験者は意識清明で見当識が保たれており，体液貯留で血圧は安定していたにも関わらず頻脈であった。発熱はなく，左下腹部及び骨盤下に軽度の圧痛があった。身体検査では，左臀部に腫脹，紅斑，圧痛及び浮腫が顕著であり，肛門縁まで広がっていた。炎症が最も顕著な部位では捻髪音があった。被験者は坐骨直腸膿瘍と診断され，抗生物質による治療を受け，切開排膿がなされた。入院期間中，被験者はさらに2回洗浄され，排膿及び創傷部を除去された。投与976日後＊　，被験者は退院し，自宅で創傷部を管理した。

投与された薬剤は，レミフェンタニル，トラマドール・アセトアミノフェン，ジフェンヒドラミン，ヘパリン，オムニパーク，デキサメタゾン，ケタミン，マルチビタミン&ミネラル，フラジール，リドカイン，ミダゾラム，プロポフォール，tinzaparin，フェンタニル，タイレノール，モルヒネ，コデイン，ロラゼパム，ヒドロモルフォン，ブピバカイン，セフトリアキソン及びロクロニウムであった。

**The patient's past medications include:**

PREDNISONE for ULCERATIVE COLITIS ([redacted])

MEZAVANT for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

BETNESOL [BETAMETHASONE SODIUM PHOSPHATE] for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

VANCOMYCIN for ULCERATIVE COLITIS ([redacted])

CORTIMENT [BUDESONIDE] for ULCERATIVE COLITIS [redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted])

FOLIC ACID for ULCERATIVE COLITIS ([redacted])

MODERNA COVID-19 VACCINE for PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PFIZER BIONTECH COVID-19 VACCINE for PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Ischiorectal abscess (10023046) (Rectal abscess (10048947) ) [v.24.1] [10023046]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Open Label)

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Event of ISCHIORECTAL ABSCESS

**- Investigator:** Not Applicable

**- AbbVie:** Event is more likely related to the pre-existing ulcerative colitis

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CRP:** 203.9 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] CRP:** 307.3 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] CRP:** 66.4 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] CRP:** 12.2 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] CT ABDOMEN PELVIS ENHANCED:** Complex collection along the medial aspect of the left buttocks extending into the ischiorectal/intrapelvic space. External to pelvis, the collection is primarily composed of soft tissue. Gas in the perirectal/intrapelvic region, it is composed of phlegmonous material, small volumes of fluid and gas.

[redacted] 20[redacted] **CT ABDOMEN PELVIS ENHANCED:** Significant improvement. Large perirectal and associated interstitial rectal abscess has decreased post drainage. Perirectal component shows just residual stranding and minimal soft tissue thickening but no significant fluid collection or air. Ischiorectal component contains a small amount of air, but does track to skin surface.

[redacted] 20[redacted] **DEEP WOUND CULTURE:** Rectal swab: 4+ Streptococcus Anginosus, 2+ mixed Anaerobic organisms (multiple) including gram-negative Bacilli x2, and gram-positive Bacilli x2.

[redacted] 20[redacted] **DEEP WOUND CULTURE:** Perineum swab: +1 Streptococcus Anginosus, 1+ Anaerobic gram-negative Bacilli, 1+ Anaerobic non-spore forming gram-positive Bacilli.

[redacted] 20[redacted] **DEEP WOUND CULTURE:** Rectal swab: 1+ Enterococcus Faecalis.

[redacted] 20[redacted] **HEMATOCRIT:** 38 % (normal 40 to 52)

[redacted] 20[redacted] **HEMATOCRIT:** 30 % (normal 40 to 52)

[redacted] 20[redacted] **HEMOGLOBIN:** 126 G/DL (normal 135 to 175)

[redacted] 20[redacted] **HEMOGLOBIN:** 113 G/DL (normal 135 to 175)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 17.9 X10**9/L (normal 1.8 to 7.5)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 0.9 X10**9/L (normal 1.8 to 7.5)

[redacted] 20[redacted] **PLATELET COUNT:** 628 X10**9/L (normal 140 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 417 X10**9/L (normal 140 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 409 X10**9/L (normal 140 to 400)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.14 X10**12/L (normal 4.3 to 6.0)

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.12 X10**12/L (normal 4.3 to 6.0)

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.77 X10**12/L (normal 4.3 to 6.0)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 19.7 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 13.5 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 2.8 X10**9/L (normal 4.0 to 11.0)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 双極 1 型障害 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ADHD- ATTENTION DEFICIT HYPERACTIVITY DISORDER | 19[redacted] |
| ANXIETY | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| FATIGUE | 20[redacted] |
| GENERALIZED ARTHRALGIA | 20[redacted] |
| IDIOPATHIC ELEVATED LIVER FUNCTION TESTS | 20[redacted] |
| INTOLERANT TO PREDNISONE | 20[redacted] |
| OCCASIONAL MIGRAINE HEADACHES | 20[redacted] |
| PAIN IN KNEES - BILATERALLY | 20[redacted] |
| PRIOR EXPOSURE TO THE EPSTEIN?BARR VIRUS - TEST POSITIVE | NOT REPORTED |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 Placebo (IND) | | ORAL | QD | [redacted] / 1 | [redacted] / 58 | 58 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted] / 59 | [redacted] / 114 | 56 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted] / 115 | [redacted] / 149 | 35 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 150 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISONE | 15 mg | QD | Y-M: [redacted] |
| INFLIXIMAB | 400 mg | OTHER: EVERY 4 WEEKS | Y-M: [redacted] |
| PREDNISONE | 20 mg | QD | Y-M: [redacted] / -304 |
| BUDESONIDE | 9 mg | QD | Y-M: [redacted] / -273 |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 4 WEEKS | Y-M: [redacted] / -273 |
| CALCIUM | 1600 mg | QD | Y-M: [redacted] / -243 |
| PREDNISONE | 25 mg | QD | Y-M: [redacted] / -243 |
| VITAMIN D NOS | 1000 OTHER: IU | QD | Y-M: [redacted] / -243 |
| LOPERAMIDE | 1 OTHER: TAB | PRN | Y-M: [redacted] / -212 |
| METHYLPHENIDATE | 20 mg | QD | Y-M: [redacted] / -122 |
| PREDNISONE | 20 mg | QD | Y-M: [redacted] / -20 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| CALCIUM | 1600 mg | QD | Y-M: [redacted] / -243 | Not reported |
| VITAMIN D NOS | 1000 OTHER: IU | QD | Y-M: [redacted] / -243 | Not reported |
| LOPERAMIDE | 1 OTHER: TAB | PRN | Y-M: [redacted] / -212 | Not reported |
| METHYLPHENIDATE | 20 mg | QD | Y-M: [redacted] / -122 | Not reported |
| BUSPIRONE | 5 mg | TID | Y-M: [redacted] / 544 | Not reported |
| AMLODIPINE | 10 mg | QD | Y-M: [redacted] / 660 | Not reported |
| LITHIUM | 750 mg | QD | Y-M: [redacted] / 759 | Not reported |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | BIPOLAR DISORDER MANIC EPISODE |
| **Preferred term** | 双極 1 型障害 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 993 / 844 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |

[redacted]20[redacted] (RX DAY 844): Leukocytes: 11 [4 - 11] 10^9/L; Neutrophils: 8.6 [1.8 - 7.5] 10^9/L; [redacted]20[redacted] (RX DAY 845): NPTST107-CREATININE TOXICOLOGY URINE: 5.940 [NOT REPORTED - NOT REPORTED] mmol/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | BIPOLAR DISORDER |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，双極性障害の躁病エピソードの事象を発現した。関連する病歴は，注意欠如・多動性障害，不安，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与993日後＊　，被験者は双極性障害の躁病エピソードを発現した。

本事象発現前の投与638日後＊　以降，被験者は非重篤な双極性障害を発現した。

投与993日後＊　　，被験者は入院した。被験者は少なくとも 4 日間，眠れないことを報告した。気分の高揚，精神運動性激越，狂気，論理的コミュニケーションのトラブルが出現した。被験者は，処方されたとおりに薬物治療を継続し，症状を安定させるための追加の薬物を投与された。一連の入院を経て，被験者の行動は，平常時と思われる程度まで落ち着いた。　投与1009日後＊，被験者は退院した。

治験責任医師によると，本事象に関連する危険因子は，以前の双極性障害の診断であった。

**The patient's past medications include:**

PREDNISONE for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

QUEITIAPINE for BIPOLAR DISORDER ([redacted])

LATUDA for BIPOLAR DISORDER ([redacted])

COVID-19 VACCINE for PROPHYLAXIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Bipolar affective disorder, manic (10004919) (Bipolar I disorder (10004939) ) [v.24.1] [10004919]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of BIPOLAR DISORDER MANIC EPISODE

**- Investigator:** Bipolar disorder

**- AbbVie:** Risk factors include pre-existing Attention deficit hyperactivity disorder, anxiety and concurrent ongoing bipolar disorder.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CREATININE TOXICOLOGY URINE:** 5.940 MMOL/L

[redacted] **20[redacted] NEUTROPHILS ABS:** 8.6 X10**9/L (normal 1.8 to 7.5)

[redacted] **20[redacted] URINE GENERAL TOXICOLOGY PANEL-TOXICOLOGY TESTING:** No drugs detected in specimen.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.0 X10**9/L (normal 4.0 to 11.0)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血管肉腫 | X | X | X | X |
| 心嚢液貯留 | X | | | |
| 心膜炎 | X | | | |
| 胸水 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ADHD | 20[redacted] |
| ALOPECIA | 20[redacted] |
| ANEMIA | 20[redacted] |
| C DIFF POSITIVE | 20[redacted] |
| DENGUE FEVER | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| GASTRO ESOPHAGEAL REFLUX DISEASE | 20[redacted] |
| MILD LEVOCONVEX THORACIC SCOLIOSIS | 20[redacted] |
| OCCASIONAL HEADACHES | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 Placebo (IND) | | ORAL | QD | [redacted] / 1 | [redacted] / 56 | 56 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted] / 58 | [redacted] / 113 | 56 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 114 | [redacted] / 141 | 28 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 142 | [redacted] / 790 | 649 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| AZATHIOPRINE | 100 mg | QD | Y-M: [redacted] |
| INFLIXIMAB | 500 mg | OTHER: Q4W | Y-M: [redacted] |
| METRONIDAZOLE | 500 mg | TID | Y-M: [redacted] |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| METRONIDAZOLE | 500 mg | TID | Y-M: [redacted] |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| VANCOMYCIN | 125 mg | QID | Y-M: [redacted] |
| METRONIDAZOLE | 250 mg | BID | Y-M: [redacted] |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| CALCIUM CARBONATE | 2 OTHER: TABS | PRN | Y-M: [redacted] |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| TRAMADOL | 1 OTHER: TAB | PRN | Y-M: [redacted] |
| VANCOMYCIN | 125 mg | QID | Y-M: [redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: Q4W | Y-M: [redacted] |
| VANCOMYCIN | 125 mg | QD | Y-M: [redacted] / -318 |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] / -272 |
| PREDNISONE | 15 mg | QD | Y-M: [redacted] / -218 |
| PREDNISONE | 25 mg | QD | Y-M: [redacted] / -10 |
| VANCOMYCIN | 125 mg | QID | Y-M: [redacted] / -10 |
| PARACETAMOL | 1 OTHER: TAB | PRN | Y: [redacted] |
| CURCUMA LONGA | 1 OTHER: TEA BAG | QD | Y: [redacted] / -338 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| CALCIUM CARBONATE | 2 OTHER: TABS | PRN | Y-M: 20[redacted] | ONGOING |
| TRAMADOL | 1 OTHER: TAB | PRN | Y-M: 20[redacted] | ONGOING |
| ONDANSETRON | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 545 | Y-M: 20[redacted] / 545 |
| COLCHICINE | 0.6 mg | BID | Y-M: 20[redacted] / 546 | Y-M: 20[redacted] / 557 |
| FENTANYL | 50 OTHER: MCG | PRN | Y-M: 20[redacted] / 546 | Y-M: 20[redacted] / 548 |
| NAPROXEN | 500 mg | BID | Y-M: 20[redacted] / 546 | Y-M: 20[redacted] / 556 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 546 | Y-M: 20[redacted] / 556 |
| PARACETAMOL | 325 mg | PRN | Y-M: 20[redacted] / 547 | Y-M: 20[redacted] / 548 |
| ASCORBIC ACID | 500 mg | QD | Y-M: 20[redacted] / 548 | Y-M: 20[redacted] / 557 |
| PARACETAMOL | 650 mg | PRN | Y-M: 20[redacted] / 548 | Y-M: 20[redacted] / 556 |
| VITAMIN D NOS | 1000 IU | QD | Y-M: 20[redacted] / 548 | Y-M: 20[redacted] / 557 |
| HYDROMORPHONE | 1 mg | PRN | Y-M: 20[redacted] / 549 | Y-M: 20[redacted] / 549 |
| IRON POLYSACCHARIDE COMPLEX | 150 mg | QD | Y-M: 20[redacted] / 549 | Y-M: 20[redacted] / 556 |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 550 | Y-M: 20[redacted] / 553 |
| METRONIDAZOLE | 500 mg | BID | Y-M: 20[redacted] / 550 | Y-M: 20[redacted] / 556 |
| VANCOMYCIN | 1.5 g | OTHER: Q8H | Y-M: 20[redacted] / 550 | Y-M: 20[redacted] / 554 |
| VANCOMYCIN | 2 g | OTHER: ONCE | Y-M: 20[redacted] / 550 | Y-M: 20[redacted] / 550 |
| FUROSEMIDE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 551 | Y-M: 20[redacted] / 551 |
| POTASSIUM | 40 mEq | BID | Y-M: 20[redacted] / 551 | Y-M: 20[redacted] / 552 |
| POTASSIUM | 40 mEq | TID | Y-M: 20[redacted] / 552 | Y-M: 20[redacted] / 554 |
| FUROSEMIDE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 554 | Y-M: 20[redacted] / 554 |
| LIDOCAINE | UNKNOWN mg | OTHER: ONCE | Y-M: 20[redacted] / 554 | Y-M: 20[redacted] / 554 |
| POTASSIUM | 20 mEq | BID | Y-M: 20[redacted] / 555 | Y-M: 20[redacted] / 556 |
| VANCOMYCIN | 1 g | OTHER: Q8H | Y-M: 20[redacted] / 555 | Y-M: 20[redacted] / 556 |
| ANESTHETICS, GENERAL | UNK mg | OTHER: ONCE | Y-M: 20[redacted] / 558 | Y-M: 20[redacted] / 558 |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 558 | Y-M: 20[redacted] / 579 |
| CHLORHEXIDINE | 10 mL | BID | Y-M: 20[redacted] / 558 | Y-M: 20[redacted] / 558 |

| | | | | |
|---|---|---|---|---|
| GLUCONATE SODIUM;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE | 100 mL | OTHER: ONCE | Y-M: 20[redacted] / 558 | Y-M: 20[redacted] / 558 |
| GLUCONATE SODIUM;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE | 500 mL | OTHER: ONCE | Y-M: 20[redacted] / 558 | Y-M: 20[redacted] / 558 |
| HYDROMORPHONE | 0.4 mg | PRN | Y-M: 20[redacted] / 558 | Y-M: 20[redacted] / 558 |
| ACETYLSALICYLIC ACID | 81 mg | QD | Y-M: 20[redacted] / 559 | Y-M: 20[redacted] / 559 |
| GABAPENTIN | 200 mg | PRN | Y-M: 20[redacted] / 559 | Y-M: 20[redacted] / 559 |
| GLUCONATE SODIUM;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE | 500 mL | OTHER: ONCE | Y-M: 20[redacted] / 559 | Y-M: 20[redacted] / 559 |
| HYDROMORPHONE | 0.6 mg | PRN | Y-M: 20[redacted] / 559 | Y-M: 20[redacted] / 559 |
| HYDROMORPHONE | 0.8 mg | PRN | Y-M: 20[redacted] / 559 | Y-M: 20[redacted] / 559 |
| HYDROMORPHONE | 2 mg | PRN | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 560 |
| MAGNESIUM SULFATE | 2 g | OTHER: ONCE | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 560 |
| PARACETAMOL | 975 mg | PRN | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 561 |
| GABAPENTIN | 300 mg | BID | Y-M: 20[redacted] / 561 | Y-M: 20[redacted] / 561 |
| CODEINE;PARACETAMOL | 1 OTHER: TAB | PRN | Y-M: 20[redacted] / 562 | Y-M: 20[redacted] / 665 |
| COLCHICINE | 0.6 mg | BID | Y-M: 20[redacted] / 562 | Y-M: 20[redacted] / 665 |
| METOPROLOL | 12.5 mg | BID | Y-M: 20[redacted] / 562 | Y-M: 20[redacted] / 623 |
| METOPROLOL | 12.5 mg | BID | Y-M: 20[redacted] / 624 | Y-M: 20[redacted] / 651 |
| PARACETAMOL | 650 mg | QID | Y-M: 20[redacted] / 624 | Y-M: 20[redacted] / 665 |
| CONTRAST MEDIA | UNKNOWN OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 625 | Y-M: 20[redacted] / 625 |
| IRON | 300 mg | QD | Y-M: 20[redacted] / 626 | Y-M: 20[redacted] / 628 |
| POTASSIUM | 20 mmol | OTHER: TWICE | Y-M: 20[redacted] / 627 | Y-M: 20[redacted] / 627 |
| ALTEPLASE | 10 mg | QD | Y-M: 20[redacted] / 628 | Y-M: 20[redacted] / 629 |

| | | | | |
|---|---|---|---|---|
| DORNASE ALFA | 5 mg | QD | Y-M: 20[redacted] / 628 | Y-M: 20[redacted] / 629 |
| IRON | 300 mg | QD | Y-M: 20[redacted] / 630 | Y-M: 20[redacted] / 632 |
| IVERMECTIN | 15 mg | QD | Y-M: 20[redacted] / 630 | Y-M: 20[redacted] / 632 |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 633 |
| VANCOMYCIN | 1250 mg | BID | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 634 |
| HYDROMORPHONE | 0.5-1.0 mg | PRN | Y-M: 20[redacted] / 632 | Y-M: 20[redacted] / 635 |
| LIDOCAINE | UNKNOWN mL | OTHER: ONCE | Y-M: 20[redacted] / 632 | Y-M: 20[redacted] / 632 |
| PARACETAMOL | 650 mg | PRN | Y-M: 20[redacted] / 632 | Y-M: 20[redacted] / 632 |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] / 633 | Y-M: 20[redacted] / 634 |
| IRON | 150 mg | QD | Y-M: 20[redacted] / 633 | Y-M: 20[redacted] / 633 |
| METRONIDAZOLE | 500 mg | BID | Y-M: 20[redacted] / 633 | Y-M: 20[redacted] / 634 |
| ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE | 30 mL | OTHER: ONCE | Y-M: 20[redacted] / 635 | Y-M: 20[redacted] / 635 |
| LIDOCAINE | UNKNOWN mL | OTHER: ONCE | Y-M: 20[redacted] / 635 | Y-M: 20[redacted] / 635 |
| ONDANSETRON | 8 mg | PRN | Y-M: 20[redacted] / 637 | Y-M: 20[redacted] / 637 |
| OTHER MAGNETIC RESONANCE IMAGING CONTRAST MEDIA | UNK OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 637 | Y-M: 20[redacted] / 637 |
| ONDANSETRON | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 638 | Y-M: 20[redacted] / 638 |
| RANITIDINE | 150 mg | BID | Y-M: 20[redacted] / 638 | Y-M: 20[redacted] / 647 |
| TINZAPARIN | 4500 IU | QD | Y-M: 20[redacted] / 638 | Y-M: 20[redacted] / 650 |
| ANESTHETICS, GENERAL | UNK mg | OTHER: ONCE | Y-M: 20[redacted] / 640 | Y-M: 20[redacted] / 640 |
| HYDROMORPHONE | 2 mg | PRN | Y-M: 20[redacted] / 641 | Y-M: 20[redacted] / 648 |
| MACROGOL | 17 g | QD | Y-M: 20[redacted] / 641 | Y-M: 20[redacted] / 651 |
| CONTRAST MEDIA | UNK OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 644 | Y-M: 20[redacted] / 644 |
| ONDANSETRON | 8 mg | PRN | Y-M: 20[redacted] / 646 | Y-M: 20[redacted] / 651 |
| PARACETAMOL;TRAMADOL | 2 OTHER: TABS | PRN | Y-M: 20[redacted] / 646 | Y-M: 20[redacted] / 650 |
| METOCLOPRAMIDE | 10 mg | PRN | Y-M: 20[redacted] / 647 | Y-M: 20[redacted] / 648 |
| PANTOPRAZOLE | 40 mg | OTHER: ONCE | Y-M: 20[redacted] / 647 | Y-M: 20[redacted] / 647 |
| ANESTHETICS, GENERAL | UNK mg | OTHER: ONCE | Y-M: 20[redacted] / 648 | Y-M: 20[redacted] / 648 |
| HALOPERIDOL | 1 mg | OTHER: ONCE | Y-M: 20[redacted] / 648 | Y-M: 20[redacted] / 648 |
| RANITIDINE | 150 mg | PRN | Y-M: 20[redacted] / 648 | Y-M: 20[redacted] / 651 |
| CONTRAST MEDIA | UNK OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 651 | Y-M: 20[redacted] / 651 |

| | | | | |
|---|---|---|---|---|
| AZITHROMYCIN | 500 mg | OTHER: ONCE | Y-M: 20[redacted] / 656 | Y-M: 20[redacted] / 656 |
| CEFTRIAXONE | 2 g | OTHER: ONCE | Y-M: 20[redacted] / 656 | Y-M: 20[redacted] / 656 |
| DIMENHYDRINATE | 50 mg | OTHER: ONCE | Y-M: 20[redacted] / 656 | Y-M: 20[redacted] / 656 |
| AZITHROMYCIN | 500 mg | QD | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 659 |
| CEFTRIAXONE | 1 g | QD | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 661 |
| DIMENHYDRINATE | 50 mg | PRN | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 660 |
| HYDROMORPHONE | 1 mg | PRN | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 665 |
| HYDROMORPHONE | 2 mg | PRN | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 665 |
| PANTOPRAZOLE | 40 mg | BID | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 665 |
| PARACETAMOL | 975 mg | PRN | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 665 |
| ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE | 30 mL | PRN | Y-M: 20[redacted] / 659 | Y-M: 20[redacted] / 659 |
| PREDNISONE | 20 mg | OTHER: Q12H | Y-M: 20[redacted] / 659 | Y-M: 20[redacted] / 664 |
| RANITIDINE | 150 mg | BID | Y-M: 20[redacted] / 659 | Y-M: 20[redacted] / 665 |
| TINZAPARIN | 4500 OTHER: UNITS | QD | Y-M: 20[redacted] / 659 | Y-M: 20[redacted] / 665 |
| PROPOFOL | UNK mg | OTHER: ONCE | Y-M: 20[redacted] / 660 | Y-M: 20[redacted] / 660 |
| QUETIAPINE | 12.5 mg | PRN | Y-M: 20[redacted] / 660 | Y-M: 20[redacted] / 665 |
| ZOPICLONE | 7.5 mg | PRN | Y-M: 20[redacted] / 662 | Y-M: 20[redacted] / 665 |
| LORAZEPAM | 2 mg | PRN | Y-M: 20[redacted] / 664 | Y-M: 20[redacted] / 665 |
| ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE | 15 mL | PRN | Y-M: 20[redacted] / 665 | Y-M: 20[redacted] / 665 |
| CONTRAST MEDIA | UNK OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 665 | Y-M: 20[redacted] / 665 |
| LIDOCAINE | 15 mL | QD | Y-M: 20[redacted] / 665 | Y-M: 20[redacted] / 665 |
| PIPERACILLIN;TAZOBACTAM | 4.5 g | OTHER: ONCE | Y-M: 20[redacted] / 665 | Y-M: 20[redacted] / 665 |
| PARACETAMOL | 1 OTHER: TAB | PRN | Y: 20[redacted] | ONGOING |
| CURCUMA LONGA | 1 OTHER: TEA BAG | QD | Y: 20[redacted] / -338 | Y-M: 20[redacted] / 623 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | PERICARDITIS, PERICARDIAL EFFUSION |
| **Preferred term** | 心嚢液貯留，心膜炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 687 / 546 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 546): Erythrocytes: 4.01 [4.3 - 6] 10^12/L; Erythrocytes: 4.16 [4.3 - 6] 10^12/L; Hematocrit: 0.32 [0.41 - 0.52] FRACTION OF 1; Hematocrit: 0.33 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 105 [135 - 175] G/L; Hemoglobin: 104 [135 - 175] G/L; Hemoglobin: 101 [135 - 175] G/L; Leukocytes: 11.5 [4 - 11] 10^9/L; Leukocytes: 13.2 [4 - 11] 10^9/L; Lymphocytes: 0.7 [1 - 4.5] 10^9/L; Monocytes: 1.2 [0 - 1.1] 10^9/L; NPTST064-C REACTIVE PROTEIN: 18.5 [0 - 8] MG/L; NPTST096-CO2: 21 [23 - 31] MMOL/L; NPTST096-CO2: 22.0 [23 - 31] MMOL/L; NPTST174-HIGH SENSITIVITY TROPONIN: 13 [0 - 19] NG/L; NPTST189-INR: 1.3 [0.8 - 1.5] N/A; NPTST191-IONIZED CALCIUM: 1.06 [1.09 - 1.25] MMOL/L; NPTST193-IRON: 3 [8 - 35] UMOL/L; NPTST194-IRON SAT: 0.05 [0.12 - 0.6] NO UNIT; NPTST197-LACTATE: 2.4 [0.5 - 2.2] MMOL/L; NPTST270-PTT: 31 [24 - 39] SEC; NPTST271-QUANTITATIVE D-DIMER ASSAY: 4.19 [0 - 0.5] MG/L; NPTST272-RDW: 16.2 [0 - 15.6] %; NPTST272-RDW: 16.2 [0 - 15.6] %; Neutrophils: 9.1 [1.8 - 7.5] 10^9/L; Neutrophils: 11.4 [1.8 - 7.5] 10^9/L; Protein: 60 [64 - 84] G/L; [redacted]20[redacted] (RX DAY 547): Erythrocytes: 3.18 [4.3 - 6] 10^12/L; Hematocrit: 0.25 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 82 [135 - 175] G/L; Leukocytes: 10.2 [4 - 11] 10^9/L; NPTST064-C REACTIVE PROTEIN: 66.3 [0 - 8] MG/L; NPTST213-MCV: 79 [80 - 100] FL; NPTST272-RDW: 16.3 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 548): Erythrocytes: 3.54 [4.3 - 6] 10^12/L; Hematocrit: 0.28 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 89 [135 - 175] G/L; Leukocytes: 11 [4 - 11] 10^9/L; NPTST064-C REACTIVE PROTEIN: 130.1 [0 - 8] MG/L; NPTST213-MCV: 79 [80 - 100] FL; NPTST272-RDW: 15.8 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 549): Erythrocytes: 3.63 [4.3 - 6] 10^12/L; Hematocrit: 0.28 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 91 [135 - 175] G/L; Leukocytes: 12.1 [4 - 11] 10^9/L; NPTST064-C REACTIVE PROTEIN: 153.4 [0 - 8] MG/L; NPTST213-MCV: 77 [80 - 100] FL; NPTST272-RDW: 16.3 [0 - 15.6] %; NPTST340-URINE MACROSCOPIC (KETONES): TRACE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST341-URINE MACROSCOPIC (PROTEIN): 1+ [NOT REPORTED - 0] NOT APPLICABLE; NPTST343-URINE MICROSCOPY (EPITHELIAL CE: 1-5 [NOT REPORTED - NOT REPORTED] HPF; NPTST344-URINE MICROSCOPY (LEUKOCYTES): 6-10 [NOT REPORTED - NOT REPORTED] HPF; Occult Blood: FEW [NOT REPORTED - NOT REPORTED] N/A; [redacted]20[redacted] (RX DAY 550): Erythrocytes: 3.73 [4.3 - 6] 10^12/L; Hematocrit: 0.29 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 91 [135 - 175] G/L; Leukocytes: 12.3 [4 - 11] 10^9/L; NPTST064-C REACTIVE PROTEIN: 183.3 [0 - 8] MG/L; NPTST213-MCV: 77 [80 - 100] FL; NPTST272-RDW: 16.4 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 551): Erythrocytes: 3.35 [4.3 - 6] 10^12/L; Hematocrit: 0.26 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 83 [135 - 175] G/L; Leukocytes: 11 [4 - 11] 10^9/L; Lymphocytes: 0.9 [1 - 4.5] 10^9/L; Monocytes: 1.7 [0 - 1.1] 10^9/L; NPTST064-C REACTIVE PROTEIN: 148.4 [0 - 8] MG/L; NPTST213-MCV: 77 [80 - 100] FL; NPTST272-RDW: 16.4 [0 - 15.6] %; Neutrophils: 8.1 [1.8 - 7.5] 10^9/L; Potassium: 3.4 [3.4 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 552): Erythrocytes: 3.36 [4.3 - 6] 10^12/L; Hematocrit: 0.26 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 83 [135 - 175] G/L; Leukocytes: 10.3 [4 - 11] 10^9/L; Lymphocytes: 0.7 [1 - 4.5] 10^9/L; Monocytes: 1.5 [0 - 1.1] 10^9/L; NPTST064-C REACTIVE PROTEIN: 124.6 [0 - 8] MG/L; NPTST096-CO2: 22 [23 - 31] MMOL/L; NPTST213-MCV: 76 [80 - 100] FL; NPTST272-RDW: 16.7 [0 - 15.6] %; Neutrophils: 7.8 [1.8 - 7.5] 10^9/L; Potassium: 3.4 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 553): Erythrocytes: 3.44 [4.3 - 6] 10^12/L; Hematocrit: 0.26 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 85 [135 - 175] G/L; Leukocytes: 9.9 [4 - 11] 10^9/L; Lymphocytes: 0.8 [1 - 4.5] 10^9/L; Monocytes: 1.4 [0 - 1.1] 10^9/L; NPTST063-C REACTIVE PROTEIN: 95.2 [0 - 8] MG/L; NPTST096-CO2: 22 [23 - 31] MMOL/L; NPTST213-MCV: 76 [80 - 100] FL; NPTST272-RDW: 17.2 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 554): Erythrocytes: 3.72 [4.3 - 6] 10^12/L; Hematocrit: 0.28 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 91 [135 - 175] G/L; Leukocytes: 10.2 [4 - 11] 10^9/L; Monocytes: 1.6 [0 - 1.1] 10^9/L; NPTST064-C REACTIVE PROTEIN: 95.2 [0 - 8] MG/L; NPTST213-MCV: 76 [800 - 100] FL; NPTST272-RDW: 17.2 [0 - 15.6] %; Platelets: 463 [140 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 555): NPTST065-C REATIVE PROTEIN: 51.0 [0 - 8] MG/L; [redacted]20[redacted] (RX DAY 556): Erythrocytes: 3.36 [4.3 - 6] 10^12/L; Hematocrit: 0.25 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 81 [135 - 175] G/L; Leukocytes: 10 [4 - 11] 10^9/L; Monocytes: 1.4 [0 - 1.1] 10^9/L; NPTST065-C REATIVE PROTEIN: 28.8 [0 - 8] MG/L; NPTST213-MCV: 75 [80 - 100] FL; NPTST272-RDW: 17.5 [0 - 15.6] %; Platelets: 493 [140 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 557): Erythrocytes: 3.38 [4.3 - 6] 10^12/L; Hematocrit: 0.25 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 81 [135 - 175] G/L; Leukocytes: 9.9 [4 - 11] 10^9/L; Monocytes: 1.2 [0 - 1.1] 10^9/L; NPTST064-C REACTIVE PROTEIN: 16.4 [0 - 8] MG/L; NPTST213-MCV: 75 [80 - 100] FL; NPTST272-RDW: 17.4 [0 - 15.6] %; Platelets: 524 [140 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 558): NPTST189-INR: 1.4 [0.8 - 1.2] N/A;

[redacted]20[redacted] (RX DAY 559): Sodium: 131 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 562): NPTST031-ANION GAP: 11 [5 - 10] MMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 546): BLOOD NPTST052-BLOOD CULTURE: Negative; OTHER PERICARDIAL FLUID NPTST144-FLUID CULTURE: Positive-CUTIBACTERIUM ACNES (GRAM-POSITIVE BACILLI); [redacted]20[redacted] (RX DAY 547): OTHER PERICARDIAL DRAIN (FLUID) NPTST224-MYCOBACTERIA (AFB) SMEAR AND ST: Negative; [redacted]20[redacted] (RX DAY 549): BLOOD NPTST052-BLOOD CULTURE: Negative; URINE NPTST339-URINE CULTURE, ROUTINE: Positive-GROWTH (1X10E5 CFU/L) NO ORGANISM SPECIFIED. NOT CLINICALLY SIGNIFICANT

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | MOST LIKELY A VIRAL INFECTION. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | BILATERAL PLURAL EFFUSIONS |
| **Preferred term** | 胸水 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 764 / 623 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 623): Hematocrit: 0.39 [0.41 - 0.52] FRACTION OF 1; Hematocrit: 0.4 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 112 [135 - 175] G/L; Hemoglobin: 116 [135 - 175] G/L; Leukocytes: 6.6 [4 - 11] 10^9/L; Leukocytes: 5.7 [4 - 11] 10^9/L; NPTST142-FERRITIN: 10 [30 - 500] UG/L; NPTST212-MCHC: 289 [310 - 360] G/L; NPTST212-MCHC: 288 [310 - 360] G/L; NPTST213-MCV: 70 [80 - 100] FL; NPTST213-MCV: 70 [80 - 100] FL; NPTST271-QUANTITATIVE D-DIMER ASSAY: 0.97 [0 - 0.5] MG/L; NPTST272-RDW: 21.0 [0 - 15.6] %; NPTST272-RDW: 20.9 [0 - 15.6] %; Potassium: 3.5 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 625): NPTST142-FERRITIN: 9 [30 - 500] UG/L; [redacted]20[redacted] (RX DAY 627): Erythrocytes: 6.05 [4.3 - 6] 10^12/L; Hemoglobin: 123 [135 - 175] G/L; Leukocytes: 9.6 [4 - 11] 10^9/L; Lymphocytes: 0.4 [1 - 4.5] 10^9/L; NPTST212-MCHC: 285 [310 - 360] G/L; NPTST213-MCV: 71 [80 - 100] FL; NPTST272-RDW: 21.7 [0 - 15.6] %; Neutrophils: 7.9 [1.8 - 7.5] 10^9/L; Potassium: 3.3 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 628): Erythrocytes: 6.07 [4.3 - 6] 10^12/L; Hemoglobin: 124 [135 - 175] G/L; Leukocytes: 8.9 [4 - 11] 10^9/L; NPTST212-MCHC: 290 [310 - 360] G/L; NPTST213-MCV: 71 [80 - 100] FL; NPTST272-RDW: 21.7 [0 - 15.6] %; Potassium: 3.4 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 629): Hematocrit: 0.39 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 118 [135 - 175] G/L; Leukocytes: 9.1 [4 - 11] 10^9/L; NPTST212-MCHC: 299 [310 - 360] G/L; NPTST213-MCV: 69 [80 - 100] FL; NPTST272-RDW: 22.2 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 631): Hemoglobin: 120 [135 - 175] G/L; NPTST212-MCHC: 294 [310 - 360] G/L; NPTST213-MCV: 71 [80 - 100] FL; NPTST272-RDW: 23.7 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 632): Hemoglobin: 119 [135 - 175] G/L; NPTST212-MCHC: 292 [310 - 360] G/L; NPTST213-MCV: 72 [80 - 100] FL; NPTST272-RDW: 24.2 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 633): Hemoglobin: 123 [135 - 175] G/L; NPTST096-CO2: 21 [23 - 31] MMOL/L; NPTST212-MCHC: 294 [310 - 360] G/L; NPTST213-MCV: 74 [80 - 100] FL; NPTST272-RDW: 25.4 [0 - 15.6] %; Potassium: 3.3 [3.5 - 5] MMOL/L; Protein: 49 [64 - 84] G/L; [redacted]20[redacted] (RX

DAY 634): Erythrocytes: 6.13 [4.3 - 6] 10^12/L; Hemoglobin: 131 [135 - 175] G/L; NPTST096-CO2: 22 [23 - 31] MMOL/L; NPTST212-MCHC: 296 [310 - 360] G/L; NPTST213-MCV: 72 [80 - 100] FL; NPTST272-RDW: 26.5 [0 - 15.6] %; Potassium: 3.2 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 635): Hemoglobin: 135 [135 - 175] G/L; Leukocytes: 9.5 [4 - 11] 10^9/L; Lymphocytes: 0.6 [1 - 4.5] 10^9/L; NPTST096-CO2: 19 [23 - 31] MMOL/L; NPTST212-MCHC: 297 [310 - 360] G/L; NPTST213-MCV: 74 [80 - 100] FL; NPTST272-RDW: 27.0 [0 - 15.6] %; Potassium: 3.2 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 637): Erythrocytes: 6.26 [4.3 - 6] 10^12/L; NPTST096-CO2: 22 [23 - 31] MMOL/L; NPTST212-MCHC: 302 [310 - 360] G/L; NPTST213-MCV: 72 [80 - 100] FL; NPTST272-RDW: 27.9 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 638): Erythrocytes: 6.44 [4.3 - 6] 10^12/L; NPTST096-CO2: 22 [23 - 31] MMOL/L; NPTST212-MCHC: 293 [310 - 360] G/L; NPTST213-MCV: 75 [80 - 100] %; NPTST272-RDW: 28.6 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 639): Erythrocytes: 6.32 [4.3 - 6] 10^12/L; NPTST212-MCHC: 306 [310 - 360] G/L; NPTST213-MCV: 74 [80 - 100] FL; NPTST272-RDW: 28.4 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 644): Erythrocytes: 6.28 [4.3 - 6] 10^12/L; Leukocytes: 12.5 [4 - 11] 10^9/L; NPTST064-C REACTIVE PROTEIN: 12.6 [0 - 8] MG/L; NPTST213-MCV: 74 [80 - 100] FL; NPTST272-RDW: 29.3 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 645): Erythrocytes: 6.04 [4.3 - 6] 10^12/L; NPTST212-MCHC: 309 [310 - 360] G/L; NPTST213-MCV: 75 [80 - 100] FL; NPTST272-RDW: 29.3 [0 - 15.6] %; [redacted]20[redacted] (RX DAY 647): Albumin: 23 [30 - 45] G/L; Erythrocytes: 6.86 [4.3 - 6] 10^12/L; Hematocrit: 0.53 [0.41 - 0.52] FRACTION OF 1; Leukocytes: 16.9 [4 - 11] 10^9/L; NPTST096-CO2: 22 [23 - 31] MMOL/L; NPTST213-MCV: 77 [80 - 100] FL; NPTST272-RDW: 29.1 [0 - 15.6] %; Sodium: 130 [133 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 649): Hemoglobin: 133 [135 - 175] G/L; Leukocytes: 14.2 [4 - 11] 10^9/L; NPTST213-MCV: 75 [80 - 100] FL; NPTST272-RDW: 28.2 [0 - 15.6] %; Sodium: 130 [133 - 146] MMOL/L

**Microbiology**

[redacted]20[redacted] (RX DAY 630): OTHER PLEURAL FLUID/PLEURA NPTST145-FLUID CULTURE, ROUTINE: Positive-ACINETOBACTER RADIORESISTENS, STAPHYLOCOCCUS HAEMOLYTICUS, ENTEROCOCCUS FAECIUM, BACILLUS CEREUS GROUP, STAPHYLOCOCCUS EPIDERMIDIS; [redacted]20[redacted] (RX DAY 631): OTHER PLEURAL FLUID/PLEURAL CAVITY, LEFT NPTST145-FLUID CULTURE, ROUTINE: Positive-ENTEROCOCCUS FAECIUM, BACILLUS CEREUS GROUP, STAPHYLOCOCCUS EPIDERMIDIS

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING |

**Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Death, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC**

| | |
|---|---|
| **Event Description** | EPITHELIOID ANGIOSARCOMA |
| **Preferred term** | 血管肉腫 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 766 / 625 |
| **Age at AE Onset** | 2[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 294): Calcium: 2.01 [2.1 - 2.6] MMOL/L; [redacted]20[redacted] (RX DAY 657): Calcium: 1.79 [2.1 - 2.6] MMOL/L; Chloride: 95 [98 - 112] MMOL/L; Hemoglobin: 129 [135 - 175] G/L; Leukocytes: 10 [4 - 11] 10^9/L; Lymphocytes: 0.5 [1 - 4.5] 10^9/L; Monocytes: 1.3 [0 - 1.1] 10^9/L; NPTST096-CO2: 19 [23 - 31] MMOL/L; NPTST213-MCV: 79 [80 - 100] FL; NPTST226-MYELOCYTES: 0.2 [0 - 0.1] 10^9/L; NPTST227-MYELOID CELLS %: 2 [0 - 1] %; NPTST272-RDW: 28.2 [0 - 15.6] %; NPTST324-TROPONIN I: 46 [0 - 19] NG/L; Occult Blood: 54 [0 - 19] NG/L; Sodium: 126 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 659): Chloride: 95 [98 - 112] MMOL/L; Leukocytes: 13.2 [4 - 11] 10^9/L; Lymphocytes: 0.5 [1 - 4.5] 10^9/L; NPTST096-CO2: 20 [23 - 31] MMOL/L; NPTST212-MCHC: 308 [310 - 360] G/L; NPTST226-MYELOCYTES: 0.3 [0 - 0.1] 10^9/L; NPTST227-MYELOID CELLS %: 2 [0 - 1] %; NPTST249-PHOSPHATE: 1.69 [0.8 - 1.45] MMOL/L; Neutrophils: 11 [1.8 - 7.5] 10^9/L; Sodium: <10 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Sodium: 126 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 660): Hematocrit: 0.38 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 120 [135 - 175] G/L; Leukocytes: 9.4 [4 - 11] 10^9/L; Lymphocytes: 0.3 [1 - 4.5] 10^9/L; NPTST096-CO2: 20 [23 - 31] MMOL/L; NPTST213-MCV: 78 [80 - 100] FL; NPTST226-MYELOCYTES: 0.2 [0 - 0.1] 10^9/L; NPTST227-MYELOID CELLS %: 2 [0 - 1] %; Neutrophils: 8.7 [1.8 - 7.5] 10^9/L; Sodium: 126 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 661): Creatinine: 130 [50 - 120] UMOL/L; Erythrocytes: 4.05 [4.3 - 6] 10^12/L; Hematocrit: 0.32 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 102 [135 - 175] G/L; Leukocytes: 14.9 [4 - 11] 10^9/L; Lymphocytes: 0.4 [1 - 4.5] 10^9/L; NPTST096-CO2: 18 [23 - 31] MMOL/L; NPTST213-MCV: 78 [80 - 100] FL; NPTST226-MYELOCYTES: 0.3 [0 - 0.1] 10^9/L; NPTST227-MYELOID CELLS %: 2 [0 - 1] %; Neutrophils: 13.3 [1.8 - 7.5] 10^9/L; Potassium: 5.3 [3.5 - 5] MMOL/L; Sodium: 125 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 662): Hematocrit: 0.36 [0.41 - 0.52] FRACTION OF 1; Hemoglobin: 114 [135 - 175] G/L; Leukocytes: 21.3 [4 - 11] 10^9/L; Lymphocytes: 0.3 [1 - 4.5] 10^9/L; NPTST226-MYELOCYTES: 0.7 [0 - 0.1] 10^9/L; NPTST227-MYELOID CELLS %: 3 [0 - 1] %; Neutrophils: 19 [1.8 - 7.5] 10^9/L; [redacted]20[redacted] (RX DAY 665): Chloride: 92 [98 - 112] MMOL/L; NPTST031-ANION GAP: 17 [5 - 10] MMOL/L; NPTST096-CO2: 11 [23 - 31] MMOL/L; NPTST197-LACTATE: 10 [0.5 - 2.2] MMOL/L; Potassium: 5.6 [3.5 - 5] MMOL/L; Sodium: 120 [135 - 145] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 806 / 665 (16 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 41 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, DEATH OF SUBJECT |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はカナダの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，致死性の類上皮血管肉腫，両側の胸水，並びに心膜炎及び心嚢液貯留の事象を発現した。関連する病歴は，デング熱，潰瘍性大腸炎，胃食道逆流性疾患，貧血，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 1，2 及び 3 の臨床経過：**

投与687日後＊ ，被験者は心膜炎及び心嚢液貯留を発現した。投与764日後＊ ，被験者は両側の胸水を発現した。投与766日後＊ ，被験者は類上皮血管肉腫を発現した。 投与806日後＊，被験者は死亡した。死因は，類上皮血管肉腫であると報告された。剖検が実施された。

投与687日後＊ ，被験者は自転車に乗車中及び乗車後に浮動性めまい，息切れ，呼吸困難及び失神で救急治療室に運ばれた。さらに，被験者は胸部の重苦しさ及び締め付けを伴う悪心及び 2 回の嘔吐があった。身体検査では，心音の減弱及び四肢の温かさが認められ，浮腫はなかった。同日，被験者は精査及びモニタリングのため，入院した。心エコーベッドサイド検査では，心タンポナーデを伴う大量の心嚢液貯留が認められた。心臓穿刺術が成功した。液体培養ではキューティバクテリウム・アクネスが検出された。免疫が抑制されており，感染性の心嚢液であったため，感染症チームに助言を求めた。被験者は，バンコマイシンの静脈内投与及びフラジールを静脈内投与された。末梢挿入型中心静脈カテーテルが挿入された。心嚢液貯留が持続し，フィブリンを含んでいたため，循環器科の医師は被験者のモニタリングを継続した。洗浄を伴う外科的介入が必要であると判断された。被験者は外科手術のために他院に転院した。投与699日後＊ ，心膜切開が行われ，両側の心室機能は術前及び術後のいずれも正常であった。抗生物質が継続され，化膿性心膜炎のモニタリングが行われた。投与703日後＊ ，被験者は退院した。

投与764日後＊ ，被験者は突然の息切れで入院した。息切れは労作時に始まったが，その後仰向けになった際に増加した。被験者はドキドキする感覚を伴う動悸及び軽度の咳嗽を伴う速い心拍数を訴えた。被験者は胸痛，発熱，鼻汁，咽頭痛，寝汗，食欲減退，鈍い痛み，鋭い痛み，及び身体の瘤若しくはしこりを否定した。被験者は歩行，特に階段を上がる時，疲労をより感じると報告した。被験者は診断検査を受け，重大な両側の胸水が認められ，左側の方がより悪化していた。

投与された薬剤は，コルヒチン，ナプロキセン，pantoloc，フェンタニル，アセトアミノフェン，ビタミン D，ビタミン C，feramax，セフトリアキソン，バンコマイシン，フラジール，K-DUR，ラシックス，ヒドロモルフォン，グルコン酸クロルヘキシジン，plasma-lyte A，ガバペンチン，アセチルサリチル酸，硫酸マグネシウム，tylenol #3，メトプロロール，オンダンセトロン，シプロフロキサシン，iron sucrose，イベルメクチン，almagel，tissue plasminogen，ハロペリドール，maxeran，pantoprazole magnesium，polyethylene glycol，tinzaparin，tramacet，kelixer，ゾピク

ロン，ativan，piptazo，リドカイン，gravol，prednisone，ザンタック，クエチアピン及びアジスロマイシンであった。

**The patient's past medications include:**

PREDNISONE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLECTRA for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PFIZER BIONTECH COVID-19 VACCINE for PROPHYLAXIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Epithelioid hemangioendothelioma (10079873) (Angiosarcoma (10002476) ) [v.24.1] [10079873]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

2) Bilateral pleural effusion (10078037) (Pleural effusion (10035598) ) [v.24.1] [10078037]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

3) Pericarditis (10034484) (Pericarditis (10034484) ) [v.24.1] [10034484]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

4) Pericardial effusion (10034474) (Pericardial effusion (10034474) ) [v.24.1] [10034474]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Open Label)

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Event of EPITHELIOID ANGIOSARCOMA

**- Investigator:** Not applicable

**- AbbVie:** Epithelioid angiosarcoma is a rare malignancy with male predilection that arises in a variety of age groups. Furthermore, analysis of study drug safety data to date has not confirmed that upadacitinib therapy increases the risk of malignancies.

Event of BILATERAL PLEURAL EFFUSIONS

**- Investigator:** Not applicable

**- AbbVie:** Event is more likely related to concurrent metastatic epithelioid angiosarcoma

Event of PERICARDITIS, PERICARDIAL EFFUSION

**- Investigator:** Not applicable

**- AbbVie:** Event is more likely related to concurrent metastatic epithelioid angiosarcoma.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] AFP:** Normal

[redacted] **20[redacted] ALBUMIN:** 37 G/L (normal 30 to 45)

[redacted] **20[redacted] ALBUMIN:** 23 G/L (normal 30 to 45)

[redacted] **20[redacted] ALKPHOS:** 53 No unit

[redacted] **20[redacted] ALT:** 26 No unit

[redacted] **20[redacted] ANION GAP:** 11 MMOL/L (normal 5 to 10)

[redacted] **20[redacted] BILIRUBIN:** 7 No unit

[redacted] **20[redacted] BIOPSY:** (right pleural cavity) - Pleural biopsy shows high grade, mostly epithelial-appearing, but with spindled areas as well. The tumor forms sheets with few papillary structures. It is pankeratin, S100, p40, CD20, chromogranin, synaptophysin, OCT3/4, CD45, CD3, CK7, CK20, BerEP4, and calretinin negative. Tumor cells are diffusely and moderately-strong. WT-1 positive and focally strong CD30 and CD117 positive. The malignant lesion has a wide differential including mesothelioma, a germ cell tumor and NUT carcinoma. However, angiosarcoma can be CD117, CD30, and WT-1 positive. The ERG stain is very strongly and diffusely positive, confirming diagnosis. Epitheloid angiosarcoma

[redacted] **20[redacted] BLOOD CULTURE:** Negative

[redacted] **20[redacted] BLOOD CULTURE:** Negative

[redacted] **20[redacted] BLOOD LACTATE:** 10 MMOL/L (normal 0.5 to 2.2)

[redacted] **20[redacted] BLOOD PRESSURE:** 118/71 mmHg

[redacted] **20[redacted] BODY WEIGHT:** 7[redacted] KG

[redacted] **20[redacted] C REACTIVE PROTEIN:** 153.4 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 18.5 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 66.3 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 130.1 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 183.3 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 124.6 MG/L (normal 0.0 to 0.8)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 95.2 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 51.0 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 16.4 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 12.6 MG/L (normal 0 to 8)

[redacted] **20[redacted] CARDIOVASCULAR EXAMINATION:** S1, S2, PALPABLE PULSUS PARADOXUS ON RADIAL PALPATION, DISTENDED NECK VEINS, MUFFLED HEART SOUNDS, WARM EXTREMITIES, NO EDEMA.

[redacted] **20[redacted] CHEST CT:** INCREASE IN LOCULATED BILATERAL PLEURAL EFFUSIONS. POSTSURGICAL INFLAMMATORY MEDIASTINAL SOFT TISSUES/RESIDUAL HETEROGENOUS PERICARDIAL FLUID SURROUNDING THE GREAT VESSELS WITH COMPRESSION OF THE SVC. ECHOCARDIOGRAPHIC CORRELATION ADVISED.

[redacted] **20[redacted] CHESTERECT AP:** Improving bilateral pleural effusions

[redacted] **20[redacted] CHEST ERECT PA + LATERAL:** SUSPECTED PERICARDIAL EFFUSION

[redacted] **20[redacted] CHEST ERECT PA + LATERAL:** (PRE-OP) RIGHT PICC LINE INSERTED. MILD CARDIOMEGALY. MILD TO MODERATE LEFT BASAL PLEURAL EFFUSION AND TRACE RIGHT BASAL PLEURAL EFFUSION. LEFT BASAL ATELECTASIS. NO CONSOLIDATION OR PULMONARY EDEMA. NO ACUTE OSSEOUS ABNORMALITY

[redacted] **20[redacted] CHEST ERECT PA + LATERAL:** Bilateral pleural effusions, cardiomegaly

[redacted] **20[redacted] CHEST ERECT PA AND LATERAL**: Bilateral pleural effusion. Left unchanged. Right enlarging.

[redacted] **20[redacted] CHEST ULTRASOUND:** BILATERAL PLEURAL EFFUSIONS

[redacted] **20[redacted] CHEST XRAY:** SMALL TO MODERATE BILATERAL PLEURAL EFFUSIONS

[redacted] **20[redacted] CHEST XRAY:** (POST-OP) INTERVAL IMPROVEMENT OF THE RIGHT THORAX POST RIGHT CHEST TUBE REPLACEMENT. TINY APICAL PNEUMOTHORAX

[redacted] **20[redacted] CHEST XRAY:** LEFT BASAL EFFUSION, SMALL RIGHT BASAL EFFUSION

[redacted] **20[redacted] CHEST XRAY:** NO SIGNIFICANT CHANGE FROM PREVIOUS

[redacted] **20[redacted] CHEST XRAY:** INTERVAL REMOVAL OF THE RIGHT-SIDED CHEST TUBE. BILATERAL PLEURAL EFFUSIONS. THERE IS BIBASILAR COLLAPSE/CONSOLIDATION

[redacted] 20[redacted] **CHEST XRAY:** (PRE-OP) SMALL LEFT APICAL PNEUMOTHORAX NOTED.

[redacted] 20[redacted] **CHEST XRAY:** (POST-OP) PIGTAIL CATHETERS REMOVED WITH PLACEMENT OF LOWER CHEST DRAINS ON BOTH SIDES. DECREASE OF THE LEFT PLEURAL EFFUSION

[redacted] 20[redacted] **CHEST XRAY:** RIGHT APICAL PNEUMOTHORAX RESOLVED. TRACE LEFT APICAL PNEUMOTHORAX. LEFT PLEURAL EFFUSION NOW MODERATE. MILD INCREASE IN LOCULATED SMALL RIGHT PLEURAL EFFUSION. MILD BIBASILAR COMPRESSIVE ATELECTASIS.

[redacted] 20[redacted] **COVID-19 NASOPHARYNGEAL SWAB:** Negative

[redacted] 20[redacted] **CT CHEST:** No evidence of malignancy in the chest, abdomen or pelvis. Small bilateral pleural effusions with pigtail chest tubes, no pleural thickening or enhancement. Small right and trace left pneumothorax and small volume pneumomediastinum.

[redacted] 20[redacted] **CT CHEST, ABDOMEN AND PELVIS ENHANCED:** Small bilateral pleural effusion. Small right and trace left pneumonthorax. Small volume pneumomediastinum.

[redacted] 20[redacted] **CT HEAD:** NO ACUTE INTRACRANIAL ABNORMALITY IS IDENTIFIED

[redacted] 20[redacted] **CT HEAD:** No acute intra-cranial process

[redacted] 20[redacted] **CYTOLOGY:** left pleural cavity fluid: atypical cells

[redacted] 20[redacted] **CYTOLOGY:** (right pleural cavity) - malignant neoplastic lesion.

[redacted] 20[redacted] **CYTOLOGY:** chest tube fluid: atypical

[redacted] 20[redacted] **CYTOLOGY:** chest tube fluid: atypical cells

[redacted] 20[redacted] **CYTOLOGY:** right pleural cavity fluid: atypical cells

[redacted] 20[redacted] **CYTOLOGY:** right pleural cavity fluid: suspicious for malignancy

[redacted] 20[redacted] **D DIMER:** 4.9 MG/L (normal 0 to 0.50)

[redacted] 20[redacted] **DI-CHEST ERECT PA AND LATERAL:** STABLE ENLARGEMENT OF THE CADIAC SILHOUETTE CONSISTENT WITH PREICARDIAL EFFUSION. GROSSLY STABLE BILATERAL PLEURAL EFFUSIONS WITH BIBASILAR ATELECTASIS.

[redacted] 20[redacted] **DI-CHEST ERECT PA AND LATERAL:** INTERVAL DEVELOPMENT OF BILATERAL SMALL PNEUMOTHORACES, LEFT GREATER THAN RIGHT.THE RIGHT PLEURAL EFFUSION AND ASSOCIATED PASSIVE ATELECTASIS HAVE SLIGHTLY IMPROVED. GROSSLY UNCHANGED LEFT PLEURAL EFFUSION.

[redacted] 20[redacted] **DI-CHEST PA AND LATERAL:** BILATERAL PLEURX CATHETERS IN PLACE. PLEURAL EFFUSIONS HAVE ENLARGED. INCREASED DENSITY IN ADJACENT LUNG BASES

IS DEMONSTRATED. MAY RELFECT ATELECTASIS PR PNEUMONIA

[redacted] **20[redacted] DI-CT CHEST:** LARGE BILATERAL PLEURAL EFFUSIONS. ASSOCIATED COMPLETE COMPRESSIVE ATELECTASIS OF THE LOWER LOBES. BILATERAL CHEST TUBES IN POSITION. SMALL MODERATE PERICARDIAL EFFUSION. PROBABLE INCREASING MEDIASTINAL SOFT TISSUE DENSITY, COMPATIBLE LYMPHADENOPATHY. THIS IS NON SPECIFIC AND COULD BE RELATED TO METASTASES OR MEDIASTINITIS.

[redacted] **20[redacted] DI-CT CHEST:** PERSISTING LARGE LOBULATED PLEURAL EFFUSIONS. INCREASING RIND OF FLUID AROUND THE HEART, SUGGESTIVE OF PERICARDIAL EFFUSION, POSSIBLY HELD IN THE PERICARDIAL SPACE BY ADHESIONS. MODERATELY INCREASING CONFLUENT SOFT TISSUE DENSITY WITHIN MEDIASTINUM, WHICH MAY BE RELATED TO METASTATIC DISEASE. MEDIASTINITIS CANNOT BE EXCLUDED.

[redacted] **20[redacted] DI-US THORACENTESIS:** PIGTAIL CATHETER PLACED (LEFT PLEURAL SPACE).

[redacted] **20[redacted] DI-US THORACENTESIS:** PIGTAIL CATHETER PLACED (RIGHT PLEURAL SPACE).

[redacted] **20[redacted] ECG:** Sinus rhythm. Short PR interval.

[redacted] **20[redacted] ECG:** Sinus rhythm, borderline T abnormalities, borderline ECG

[redacted] **20[redacted] ECG:** Borderline T abnormalities, prolonged QT interval

[redacted] **20[redacted] ECG:** Non specific T abnormalities, possible ischemia

[redacted] **20[redacted] ECHOCARDIOGRAPHY:** FOUND TO HAVE PERICARDIAL EFFUSION, AND CARDIAC TAMPONADE

[redacted] **20[redacted] FERRITIN:** 10 ug/L (normal 30 to 500)

[redacted] **20[redacted] GASTROSCOPY:** SUSPECTED EXTRINSIC COMPRESSION OF THE DUODENUM (WITH NO OBSTRUCTIVE APPEARANCE).

[redacted] **20[redacted] GR CHEST 2 PROJECTIONS:** Bilateral pleural effusions with lower lobe atelectasis

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.4 X10**9/L (normal 1.0 to 4.5)

[redacted] **20[redacted] MR CARDIAC:** with and without enhancements: Ongoing inflammatory pericardial process. Moderate bilateral pleural effusion with extensive dependant compressive atelectasis.

[redacted] **20[redacted] MYCOBACTERIA (AFB) SMEAR AND STAIN:** Negative

[redacted] **20[redacted] NEUTROPHILS ABS:** 11.0 X10**9/L (normal 1.8 to 7.5)

[redacted] **20[redacted] NON-GYNECOLOGICAL CYTOLOGY (PERICARDIUM, PERICARDIAL FLUID):** BENIGN. REACTIVE CHANGES, INFLAMMATORY CELLS.

[redacted] 20[redacted] **PATHOLOGY:** pericardium/pericardial fluid: patchy areas of inflammation-acute and chronic. Negative for malignancy.

[redacted] 20[redacted] **PATHOLOGY:** gastric body, mucosal biopsies: No diagnostic abnormality

[redacted] 20[redacted] **PERICARDIAL FLUID CULTURE:** Positive for CUTIBACTERIUM ACNES (GRAM-POSITIVE BACILLI)

[redacted] 20[redacted] **PLEURAL FLUID CULTURE:** Positive: Acinetobacter radioresistens, staphylococcus haemolyticus, enterococcus faecium, bacillus cereus group, staphylococcus epidermidis

[redacted] 20[redacted] **PLT:** 304 No unit

[redacted] 20[redacted] **RADIOLOGY (DI)-GR CHEST 1 PROJECTION:** RIGHT IJ LINE, NASOGASTRIC TUBE, MEDIASTINAL DRAINAGE CATHETERS, AND ENDOTRACHEAL TUBE APPEAR APPROPRIATELY POSITIONED. RIGHT PICC WITH TIP IN THE CAVOATRIAL JUNCTION, UNCHANGED. HEART IS NORMAL IN SIZE. NO EFFUSION OR PNEUMOTHORAX. NO FOCAL CONSOLIDATION. LUNGS AND PLEURAL SPACES CLEAR. NO ACUTE OSSEOUS ABNORMAILITY

[redacted] 20[redacted] **RADIOLOGY (DI)-GR CHEST 1 PROJECTION:** 1. INCREASED DENSITY IN THE PERIHILAR AND BASILAR REGIONS HAS OCCURRED FOLLOWING EXTUBATION, CONSISTENT WITH POST-OP ATELECTASIS AND EDEMA. 2. A DIMINUTIVE LEFT PNEUMOTHORAX IS DEMONSTRATED ALONG WITH A SMALL LEFT PLEURAL EFFUSION.

[redacted] 20[redacted] **URINE CULTURE:** GROWTH

[redacted] 20[redacted] **URINE MACROSCOPIC PROTEIN:** 1+ no units (Normal: >=0)

[redacted] 20[redacted] **URINE MACROSOPIC KETONES:** Trace

[redacted] 20[redacted] **URINE MICROSCOPY EPITHELIAL CELLS:** 1-5 HPF

[redacted] 20[redacted] **URINE MICROSCOPY LEUKOCYTES:** 6-10 HPF

[redacted] 20[redacted] **URINE OCCULT BLOOD:** Few

[redacted] 20[redacted] **US ABDOMEN COMPLETE, 2 OR MORE ORGANS:** No significant intra-abdominal abnormalities identified

[redacted] 20[redacted] **US CARDIAC COMPLETE:** MILD TO MODERATE CIRCUMFERENTIAL PERICARDIAL EFFUSION WITH FIBRINOUS MATERIAL NOTED IN IT. IT MEASURES 2 CM NEAR THE RIGHT ATRIUM, 1 CM LATERALLY AND 0.5 CM POSTERIORLY

[redacted] 20[redacted] **US CARDIAC COMPLETE:** Large bilateral pleural effusions

[redacted] 20[redacted] **US CARDIAC, LIMITED:** 1. INTERVAL IMPROVEMENT IN PERICARDIAL EFFUSION. 2. TRACE TO SMALL RESIDUAL CIRCUMFERENTIAL PERICARDIAL EFFUSION.

[redacted] 20[redacted] **US SCROTAL STUDY:** Normal study

[redacted] 20[redacted] **WBC:** 13.2 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] **WHOLE BODY PET/CT:** EXTENSIVE, DIFFUSE HYPERMETABOLISM THROUGHOUT MEDIASTINUM. DECREASED BILATERAL PLEURAL EFFUSIONS AFTER NEW PLEURAL DRAIN INSERTIONS. ENLARGING HYPERMETABOLIC UPPER ABDOMINAL RETROPERITONEAL LYMPHADENOPATHY CONCERNING FOR METASTATIC DISEASE. BILATERAL HILAR LYMPHADENOPATHY AND LOWER MEDIASTINAL LYMPHADENOPATHY. SOLITARY HYPERMETABOLIC CT OCCULT LESION IN T8 SPINOUS PROCESS CONSISTENT WITH OSSEOUS METASTASIS. HYPERMETABOLIC DERMAL THICKENING ALONG LEFT MEDIAL BUTTOCK NONSPECIFIC.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 消化管感染 | X | | | X |
| イレウス | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ACNE | 20[redacted] |
| ANEMIA | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| GINGIVITIS | 20[redacted] |
| ORAL APHTHOUS ULCERS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: CHEST X-RAY | 20[redacted] |
| PRIOR PROCEDURES: COLONOSCOPY | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 Placebo (IND) | | ORAL | QD | [redacted] / 1 | [redacted] / 56 | 56 |
| M14-675 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted] / 57 | [redacted] / 112 | 56 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted] / 113 | [redacted] / 177 | 65 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 178 | [redacted] / 415 | 238 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1 g | OTHER: 3 TIMES A DAY | Y-M: 20[redacted] |
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 100 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 600 mg | OTHER: EVERY 6 WEEKS | Y-M: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 1 g | OTHER: 3 TIMES A DAY | Y-M: 20[redacted] | ONGOING |
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] | ONGOING |
| CIPROFLOXACIN | 200 mg | QD | Y-M: 20[redacted] / 226 | Y-M: 20[redacted] / 233 |
| METRONIDAZOLE | 500 mg | QD | Y-M: 20[redacted] / 226 | Y-M: 20[redacted] / 233 |
| CIPROFLOXACIN | 500 mg | QD | Y-M: 20[redacted] / 234 | Y-M: 20[redacted] / 247 |
| METRONIDAZOLE | 500 mg | QD | Y-M: 20[redacted] / 234 | Y-M: 20[redacted] / 247 |
| MACROGOL 3350 | 20 g | QD | Y-M: 20[redacted] / 241 | ONGOING |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | INTESTINAL INFECTION |
| **Preferred term** | 消化管感染 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 403 / 226 |
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 226): Basophils: 0.08 [0 - 1] 10^9/L; Basophils/Leukocytes: 0.7 [0 - 1] %; Eosinophils: 0.1 [0 - 1] 10^9/L; Eosinophils/Leukocytes: 0.1 [0 - 1] %; Erythrocytes: 4.78 [4.5 - 6.3] 10^12/L; Hematocrit: 0.407 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 124 [130 - 175] G/L; Leukocytes: 11.3 [4 - 10] 10^9/L; Lymphocytes: 1.59 [1 - 4] 10^9/L; Lymphocytes/Leukocytes: 14.1 [25 - 40] %; Monocytes: 0.69 [0 - 1] 10^9/L; Monocytes/Leukocytes: 6.1 [2 - 8] %; NPTST108-CRP: 4.4 [0.1 - 0.5] MG/DL; Neutrophils: 8.83 [2 - 8] 10^9/L; Neutrophils/Leukocytes: 78.1 [40 - 75] %; Platelets: 459 [140 - 450] 10^9/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 424 / 247 (9 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 22 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | FREE FLUID IN EDEMATOUS INTESTINAL WALL, WITHOUT EVIDENCE OF PERFORATION OR SIGNS OF INTESTINAL OBSTRUCTION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | ILEUS |
| **Preferred term** | イレウス |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 415 / 238 |
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 442 / 265 (27 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 28 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

**Event #3: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | ILEUS |

| | |
|---|---|
| **Preferred term** | イレウス |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 430 / 253 (15 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 442 / 265 (27 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 13 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | INTESTINAL INFECTION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はチリの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腸管感染症の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与403日後＊　，被験者は腸管感染症を発現した。

投与403日後＊　，被験者は，下痢，血便及び嘔吐を伴わない腹痛のために入院した。被験者は緊急の診察を受け，検体検査及び診断が行われた。投与410日後＊　，被験者は退院した。投与424日後＊　，腸管感染症は消失した。

投与された薬剤は，メトロニダゾール及び ciprofloxacino であった。

**The patient's past medications include:**

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Gastrointestinal infection (10017964) (Gastrointestinal infection (10017964) ) [v.24.0] [10017964]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of INTESTINAL INFECTION

**- Investigator:** Free fluid in edematous intestinal wall, without evidence of perforation or signs of intestinal obstruction.

**- AbbVie:** Gastrointestinal tract infections are common in both developing and developed countries and are produced by a wide variety of enteropathogens, including bacteria, viruses and parasites.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] 20[redacted] **ABSOLUTE BASOPHIL COUNT:** 0.08 X10**3/MCL (normal 0 to 1)

[redacted] 20[redacted] **ABSOLUTE EOSINOPHIL COUNT:** 0.1 X10**3/MCL (normal 0 to 1)

[redacted] 20[redacted] **ABSOLUTE LYMPHOCYTE COUNT:** 1.59 X10**3/MCL (normal 1 to 4)

[redacted] 20[redacted] **ABSOLUTE MONOCYTE COUNT:** 0.69 X10**3/MCL (normal 0 to 1)

[redacted] 20[redacted] **ABSOLUTE NEUTROPHIL COUNT:** 8.83 X10**3/MCL (normal 2 to 8)

[redacted] 20[redacted] **BASOPHIL COUNT:** 0.7 % (normal 0 to 1)

[redacted] 20[redacted] **CRP:** 4.4 mg/dL (normal 0.1 to 0.5)

[redacted] 20[redacted] **ABDOMINAL CT SCAN:** Intestinal infection

[redacted] 20[redacted] **EOSINOPHIL COUNT:** 0.1 % (normal 0 to 1)

[redacted] 20[redacted] **HEMATOCRIT:** 40.7 % (normal 40 to 52)

[redacted] 20[redacted] **HEMOGLOBIN:** 12.4 G/DL (normal 13 to 17.5)

[redacted] 20[redacted] **LYMPHOCYTE COUNT:** 14.1 % (normal 25 to 40)

[redacted] 20[redacted] **MONOCYTES:** 6.1 % (normal 2 to 8)

[redacted] 20[redacted] **NEUTROPHIL COUNT:** 78.1 % (normal 40 to 75)

[redacted] 20[redacted] **PLATELET COUNT:** 459 X10**3/MCL (normal 140 to 450)

[redacted] 20[redacted] **RBC:** 4.78 X10**6/MCL (normal 4.5 to 6.3)

[redacted] 20[redacted] **WBC:** 11.3 X10**3/MCL (normal 4 to 10)

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はチリの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，イレウスの事象を発現した。関連する病歴は潰瘍性大腸炎であった。

**Event 2 及び 3 の臨床経過：**

投与430日後＊ ，被験者はイレウスを発現した。投与442日後＊ ，イレウスは消失した。

投与415日後＊ ，被験者は非重篤なイレウスを発現した。

投与430日後＊ ，被験者は過去 3 週間に，腹痛，及び下痢を伴わないイレウスがあり，入院した。投与442日後＊ ，被験者は退院した。

本事象により，治験薬の投与は完全に中止された。

**The patient's past medications include:**

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATIOPRINE for ULCERATIVE COLITIS

Causality for UPADACITINIB (Open Label)

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1) Ileus (10021328) (Ileus (10021328) ) [v.24.1] [10021328]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of ILEUS

**- Investigator:** INTESTINAL INFECTION

**- AbbVie:** Risk factor includes pre-existing Ulcerative Colitis

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 帯状疱疹 | X | X | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| ANEMIA | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| HYPELURICEMIA | 20[redacted] |
| INTERNAL HEMORRHOIDS | 20[redacted] |
| TRACHEITIS | 20[redacted] |
| URINE PROTEIN POSITIVE | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 55 | 55 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / 56 | [redacted]20[redacted] / 208 | 153 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 209 | [redacted]20[redacted] / 457 | 249 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM | 500 mg | TID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] |
| PREDNISONE | 20 mg | QD | Y-M: 20[redacted] |
| CEFOPERAZONE;SULBACTAM | 3 g | TID | Y-M: 20[redacted] |
| HYDROCORTISONE | 80 mg | QD | Y-M: 20[redacted] |
| METRONIDAZOLE | 0.5 g | BID | Y-M: 20[redacted] |
| SODIUM CHLORIDE | 100 mL | TID | Y-M: 20[redacted] |
| BLINDED THERAPY | 40 mL | OTHER: BIWEEKLY | Y-M: 20[redacted] |
| PIPERACILLIN;TAZOBACTAM | 4.5 g | TID | Y-M: 20[redacted] |
| SODIUM CHLORIDE | 100 mL | TID | Y-M: 20[redacted] |
| MESALAZINE | 2 g | QD | Y-M: 20[redacted] / -252 |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] / -68 |
| MESALAZINE | 1 g | QD | Y: 20[redacted] |
| MESALAZINE | 1 g | QID | Y: 20[redacted] |
| RIFAXIMIN | 200 mg | QID | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM | 500 mg | TID | Y-M: 20[redacted] | ONGOING |
| ANGELICA DAHURICA;ARISAEMA SPP.;BOMBYX MORI;GASTRODIA ELATA;NOTOPTERYGIUM SPP.;PANAX NOTOGINSENG;SAPOSHNIKOVIA DIVARICATA;TYPHONIUM GIGANTEUM | 0.56 g | TID | Y-M: 20[redacted] / 250 | Y-M: 20[redacted] / 252 |

| | | | | |
|---|---|---|---|---|
| FAMCICLOVIR | 0.25 g | TID | Y-M: 20[redacted] / 250 | Y-M: 20[redacted] / 252 |
| OTHER DERMATOLOGICAL PREPARATIONS | NA OTHER: NA | BID | Y-M: 20[redacted] / 250 | Y-M: 20[redacted] / 252 |
| PREGABALIN | 75 mg | BID | Y-M: 20[redacted] / 250 | Y-M: 20[redacted] / 252 |
| RABBIT VACCINIA EXTRACT | 2 OTHER: TROCHE | BID | Y-M: 20[redacted] / 250 | Y-M: 20[redacted] / 252 |
| DIHYDROCODEINE;PARACETAMOL | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 251 | Y-M: 20[redacted] / 252 |
| BRIVUDINE | 125 mg | QD | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 258 |
| CIPROFLOXACIN | 10 g | OTHER: NA | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 264 |
| COBAMAMIDE | 1.5 mg | QD | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 263 |
| GANODERMA LUCIDUM | 4 mL | QD | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 263 |
| INTERFERON ALFA-2B | 10 g | OTHER: NA | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 264 |
| PREGABALIN | 75 mg | BID | Y-M: 20[redacted] / 252 | ONGOING |
| THIAMINE | 10 mg | TID | Y-M: 20[redacted] / 252 | ONGOING |
| UNSPECIFIED HERBAL | NA OTHER: NA | BID | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 260 |
| UNSPECIFIED HERBAL | NA OTHER: TOPICAL TREATMENT | OTHER: TOPICAL TREATMENT | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 264 |
| MESALAZINE | 0.5 g | QD | Y-M: 20[redacted] / 253 | ONGOING |
| CLINDAMYCIN;METRONIDAZOLE | 10 g | OTHER: NA | Y-M: 20[redacted] / 255 | ONGOING |
| SODIUM CHLORIDE | 20 mL | OTHER: NA | Y-M: 20[redacted] / 255 | Y-M: 20[redacted] / 262 |
| BOVINE BASIC FIBROBLAST GROWTH FACTOR | NA OTHER: NA | OTHER: NA | Y-M: 20[redacted] / 264 | ONGOING |
| GANCICLOVIR | NA OTHER: NA | OTHER: NA | Y-M: 20[redacted] / 264 | ONGOING |
| MECOBALAMIN | 0.5 mg | TID | Y-M: 20[redacted] / 264 | ONGOING |
| PRANOPROFEN | NA OTHER: NA | OTHER: NA | Y-M: 20[redacted] / 264 | ONGOING |
| UROGASTRONE | NA OTHER: NA | OTHER: NA | Y-M: 20[redacted] / 264 | ONGOING |
| MESALAZINE | 1 g | QID | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 456 / 248 |
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 253): NPTST001-(PUS BULB) STOOL: 8-10 [NOT REPORTED - NOT REPORTED] /HP; NPTST069-C-REACTIVE PROTEIN: 22.12 [0 - 10] MG/L; NPTST134-ERYTHROCYTE SEDIMENTATION RATE: 23

[0 - 15] MM/H; NPTST282-RED BLOOD CELLS (STOOL): 1-2 [NOT REPORTED - NOT REPORTED] /HP; NPTST300-SERUM AMYLOID A: 267.76 [0 - 10] MG/L

**Microbiology**

[redacted]20[redacted] (RX DAY 252): OTHER SECRETA NPTST217-MICROORGANISM: Positive-STAPHYLOCOCCUS AUREUS

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は中国の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，帯状疱疹の事象を発現した。関連する病歴は，潰瘍性大腸炎，貧血，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与456日後＊ ，被験者は帯状疱疹を発現した。

投与456日後＊ ，被験者は腫脹を伴う右目の疼痛，及び頭痛を経験し始めた。病変の範囲は，1 つの皮膚分節までであった。投与458日後＊ ，皮膚科医により眼帯状疱疹と診断された。被験者には右目の腫脹及び頭痛も認められた。身体的診察では，右側の頭皮及び右目の周囲に散在した紅斑及び集簇性の水疱が確認された。発疹は正中線を越えていなかった。

投与460日後＊ ，被験者は治療のために入院した。被験者は刺鍼法，ヘリウムネオンレーザー治療及びカッピング治療を受けた。投与472日後＊ ，被験者は発疹が消失し，すべての水疱が乾燥して痂皮化し，頭痛も寛解した。同日，被験者は退院した。

被験者には，水痘及び帯状疱疹の病歴並びに帯状疱疹ワクチン接種歴はなかった。

治験責任医師により，本事象のために治験薬の投与は完全に中止された。

投与された薬剤は，zhoongtongan capsule（漢方薬），リリカ，recombinant bovine basic fibroblast growth factor eye-gel，ノイロトロピン，クロラムフェニコール，シプロフロキサシン，クリンダマイシン塩酸塩及びメトロニダゾール，pranopulin，メコバラミン，paracetamol 及びジヒドロコデイン，ビタミン B1，bozhi glycopeptide，コバマミド，ブリブジン，recombinant human interferon α2b gel，recombinant human epidermal growth factor derivative eye drops，ガンシクロビル並びにファムシクロビルであった。

**The patient's past medictions include:**

RIFAXIMIN for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

SUBTILIS ENTERIC SOLUTION CAPSULE WITH TWO LIVE BACTERIA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CEFOPERAZONE SODIUM; SULBACTAM SODIUM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOLE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SODIUM CHLORIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HYDROCORTISONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INTERLEUKIN 6 for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PIPERACILLIN SODIUM TAZOBACTAM SODIUM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Herpes zoster (10019974) (Herpes zoster (10019974) ) [v.23.1] [10019974]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr.(Drug/Vaccine):** Reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of HERPES ZOSTER

**- Investigator:** Not applicable

**- AbbVie:** Not applicable.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ABDOMINAL US:** THE GALLBLADDER WALL IS NOT SMOOTH- CHOLECYSTITIS

[redacted] **20[redacted] CRP:** 22.12 MG/L (normal 0 to 10)

[redacted] **20[redacted] ESR:** 23 MM/HR (normal 0 to 15)

[redacted] **20[redacted] MICROORGANISM SECRETA:** POSITIVE - STAPHYLOCOCCUS AUREUS

[redacted] **20[redacted] PCR:** positive for herpes zoster

[redacted] **20[redacted] SERUM AMYLOID A:** 267.76 MG/L (normal 0 to 10)

[redacted] **20[redacted] STOOL ANALYSIS - PUS BULB:** 8 to 10 INDIVIDUAL/HP

[redacted] **20[redacted] STOOL ANALYSIS - RBC:** 1 TO 2 INDIVIDUAL/HP

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| イレウス | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA: SUBJECT HADD AN ANEMIA IN 20[redacted] RELATED TO ULCERATIVE COLITIS. NOWDAYS IS HEMOGLOBIN LEVEL IS NORMAL | 20[redacted] |
| DEPRESSION: DEPRESION | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: AMOCLEN ALERGY | 19[redacted] |
| OTHER: MUTATED HETEROZYGOTE - THIOPURINE METHYLTRANSFERASE - NOT ABLE TO BE TREATED WITH AZATHIOPRINE | 20[redacted] |
| OTHER: PSORIASIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 30 mg | ORAL | QD | [redacted] / 1 | [redacted] / 56 | 56 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 57 | [redacted] / 365 | 309 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 367 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISONE | 0 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | TID | Y-M: 20[redacted] |
| PREDNISONE | 7.5 mg | QD | Y-M: 20[redacted] |
| METRONIDAZOLE | 250 mg | BID | Y: 20[redacted] |
| BROMAZEPAM | 1,5 mg | PRN | Y: 20[redacted] |
| ESCITALOPRAM | 20 mg | QD | Y: 20[redacted] |
| MESALAZINE | 2 g | BID | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| DIAZEPAM | 5 mg | QD | Y-M: 20[redacted] / 157 | Y-M: 20[redacted] / 432 |
| SERTRALINE | 200 mg | QD | Y-M: 20[redacted] / 157 | Not reported |
| COLECALCIFEROL | 10- 3 0 OTHER: DROPS | OTHER: ONCE A WEEK OR ONCE IN TWO WEEKS | Y-M: 20[redacted] / 230 | Y-M: 20[redacted] / 432 |
| METOPROLOL | 25 mg | BID | Y-M: 20[redacted] / 230 | Not reported |
| THIAMAZOLE | 10 mg | BID | Y-M: 20[redacted] / 230 | Not reported |
| SODIUM CHLORIDE | NOT SPECIFIED mL | QD | Y-M: 20[redacted] / 326 | Y-M: 20[redacted] / 327 |
| BROMAZEPAM | 1,5 mg | PRN | Y: 20[redacted] | Not reported |
| MESALAZINE | 2 g | BID | Y: 20[redacted] | Not reported |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | ILEUS OF SMALL INTESTINE |
| **Preferred term** | イレウス |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 691 / 325 |

| | |
|---|---|
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 326): Alanine Aminotransferase: 0.95 [NOT REPORTED - NOT REPORTED] ukat/L; Glucose: 5.9 [4.1 - 5.9] MMOL/L; Leukocytes: 13.6 [4.5 - 11] 10^9/L; NPTST108-CRP: 6.2 [NOT REPORTED - NOT REPORTED] mg/L; NPTST157-GGT: 1.27 [NOT REPORTED - NOT REPORTED] ukat/L; [redacted]20[redacted] (RX DAY 327): NPTST108-CRP: 92.3 [NOT REPORTED - NOT REPORTED] mg/L; [redacted]20[redacted] (RX DAY 329): Hematocrit: 0.395 [0.39 - 0.49] FRACTION OF 1; Hemoglobin: 132 [132 - 173] G/L; Leukocytes: 5.8 [4.5 - 11] 10^9/L; NPTST108-CRP: 11.7 [NOT REPORTED - NOT REPORTED] mg/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 695 / 329 |
| **Duration of AE** | 5 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | CAUSE IS UNKNOWN AT THE MOMENT |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はチェコ共和国の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，小腸イレウスの事象を発現した。関連する病歴は，潰瘍性大腸炎，乾癬，うつ病，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与691日後＊　，被験者は小腸イレウスを発現した。投与695日後＊　，小腸イレウスは消失した。

投与692日後＊　　，被験者は発熱，悪心，嘔吐，並びに上腹部及び右中腹部の腹痛があり，入院した。診察の結果，被験者は腹部の触診時に広範囲にわたり過敏であり，軽い痛みを感じた。検体検査及び腹部 X 線検査が行われた。保存的治療として，経鼻胃管を用いた胃腸管の減圧及び静脈内投与での水分補給を開始した。本事象は自然に消失した。投与695日後＊　　，被験者は

退院した。

**The patient's past medications include:**

ENTIZOL for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AMOCLAN for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1) Ileus of intestine (10021332) (Ileus (10021328) ) [v.24.0] [10021332]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of ILEUS OF SMALL INTESTINE

**- Investigator:** CAUSE IS UNKNOWN AT THE MOMENT

**- AbbVie:** Reported event more likely related to pre-existing Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ABDOMEN X-RAY:** small intestine ileus, no sign of pneumoperitoneum

[redacted] **20[redacted] ABDOMEN X-RAY:** No signs of small intestine ileus, no signs of penumoperitoneum

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 0.95 ukal/L

[redacted] **20[redacted] CRP:** 6.2 MG/L

[redacted] **20[redacted] CRP:** 92.3 MG/L

[redacted] **20[redacted] CRP:** 11.7 MG/L

[redacted] **20[redacted] GGT:** 1.27 ukal/.L

[redacted] **20[redacted] HEMATOCRIT:** 0.395 L/L

[redacted] **20[redacted] HEMOGLOBIN:** 132 G/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 13.6 X10**9/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.8 X10**9/L

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 貧血 | | | | X |
| 子宮頚部障害 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| LEFT SIDED UC | 20[redacted] |
| OTHER: ALERGIC RHINITIS | 19[redacted] |
| OTHER: AXIAL ARTHROPATHY | 20[redacted] |
| OTHER: CUSHING-LIKE CHANGES | 20[redacted] |
| OTHER: PERIPHERAL ARTHROPATHY | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: UMBILICAL HERNIA | 19[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 15 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 57 | 57 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted]20[redacted] / 58 | [redacted]20[redacted] / 365 | 308 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 366 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 500 mg | BID | Y-M: 20[redacted] |
| MESALAZINE | 1600 mg | BID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | BID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] |
| PREDNISONE | 5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 100 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 300 mg | OTHER: E6W | Y-M: 20[redacted] |
| ETROLIZUMAB | 105 mg | OTHER: E4W | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1600 mg | BID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] |
| FAMOTIDINE | 40 mg | QD | Y-M: 20[redacted] |
| CALCIUM CARBONATE | 1 OTHER: TBL | QD | Y-M: 20[redacted] / -320 |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / -17 |
| DESOGESTREL;ETHINYLESTRADIOL | 1 OTHER: TBL | QD | Y: 20[redacted] |
| METHYLPREDNISOLONE | 2 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 1600 mg | BID | Y-M: 20[redacted] | ONGOING |
| FAMOTIDINE | 40 mg | QD | Y-M: 20[redacted] | ONGOING |
| CALCIUM CARBONATE | 1 OTHER: TBL | QD | Y-M: 20[redacted] / -320 | ONGOING |
| FOLIC ACID;IRON | 1 OTHER: TBL | QD | Y-M: 20[redacted] / 591 | Y-M: 20[redacted] / 622 |
| CLINDAMYCIN | 0.5 g | QD | Y-M: 20[redacted] / 625 | Y-M: 20[redacted] / 629 |
| NIFURATEL | 1 OTHER: TABLET | TID | Y-M: 20[redacted] / 625 | Y-M: 20[redacted] / 632 |
| DESOGESTREL;ETHINYLESTRADIOL | 1 OTHER: TBL | QD | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | CERVIX CONISATION AFTER PREBIOPSIAN SUSPECT |
| **Preferred term** | 子宮頚部障害 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 590 / 225 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 592 / 227 |
| **Duration of AE** | 3 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | DUE TO SCREENING PROCEDURE, NO SYMPTOMS, PAITIENT INDICATED TO CONISATION OF CERVIX OF UTERUS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 954 / 589 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 1002 / 637 |
| **Duration of AE** | 49 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はチェコ共和国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，生検のための子宮頚部の円錐切除の事象を発現した。関連する病歴は，臍ヘルニア，潰瘍性大腸炎（左側），非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与590日後＊　，被験者は生検のための子宮頚部の円錐切除を発現した。投与592日後＊，生検のための子宮頚部の円錐切除は消失した。

投与590日後＊　，年 1 回の婦人科受診時に「生検の必要性」を指摘され，子宮頚部の円錐切除術を受けるために入院した。投与591日後＊ に手術を受けた。手術は成功し，　投与592日後＊に被験者は退院した。

**The patient's past medications include:**

ASACOL SUPPOSITORY for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS and AE DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted], 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CIPLOX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1) Cervix lesion (10008353) (Cervix disorder (10008351) ) [v.23.0] [10008353]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not ApplicableAlternative Etiology for UPADACITINIB (Open Label)

---

Event of CERVIX CONISATION AFTER PREBIOPSIAN SUSPECT

**- Investigator:** due to screening procedure, no symptoms, patient indicated to conisation of cervix of uterus.

**- AbbVie:** Event more likely related to suspected cervical neoplasia. Human papillomavirus (HPV) is central to the development of cervical neoplasia and can be detected in 99.7 percent of cervical cancers.

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Anaemia: Intermittent.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANXIETY DISORDER | 20[redacted] |
| HYPOCHROMIC ANEMIA | 20[redacted] |
| HYPOVITAMINOSIS VITAMIN D3 | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| SWELLING OF THE WRIST | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SAE SUPPLEMENTAL PROCEDURE: ECG | 20[redacted] |
| SAE SUPPLEMENTAL PROCEDURE: SIGMOIDEOSCOPY | 20[redacted] |
| SAE SUPPLEMENTAL PROCEDURE: ULTRASOUND OF ABDOMEN | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.7 PACK | 16 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | 2 - 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 66 | 66 |
| M14-675 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted] / 69 | [redacted] / 112 | 44 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted] / 113 | [redacted] / 211 | 99 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 220 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1200 mg | BID | Y-M: 20[redacted] |
| PREDNISONE | 20 mg | BID | Y-M: 20[redacted] |
| ANTIBIOTICS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| CORTICOSTEROIDS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| INFLIXIMAB | 7.5 mg/kg | OTHER: EVERY 6 WEEKS | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: EVERY 14 DAYS | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: 4 WEEKS | Y-M: 20[redacted] |
| CIPROFLOXACIN | 200 mg | BID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] |
| TOFACITINIB | 10 mg | BID | Y-M: 20[redacted] |
| CIPROFLOXACIN | 200 mg | BID | Y-M: 20[redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 60 mg | QD | Y-M: 20[redacted] |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 16 mg | BID | Y-M: 20[redacted] / -303 |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] / -305 |
| METRONIDAZOLE | 500 mg | BID | Y-M: 20[redacted] / -305 |
| CIPROFLOXACIN | 200 mg | BID | Y-M: 20[redacted] / -311 |
| METHYLPREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] / -311 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / -311 |

| | | | |
|---|---|---|---|
| CIPROFLOXACIN | 200 mg | BID | Y-M: 20[redacted] / -255 |
| METHYLPREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] / -255 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / -255 |
| SERTRALINE | 100 mg | QD | Y-M: 20[redacted] / -27 |
| TRAZODONE | 75 mg | QD | Y-M: 20[redacted] / -27 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / -15 |
| COLECALCIFEROL | 20 gtt | OTHER: WEEKLY | Y-M: 20[redacted] / -16 |
| IRON | 100 mg | QD | Y-M: 20[redacted] / -16 |
| AZATHIOPRINE | 50 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| SERTRALINE | 100 mg | QD | Y-M: 20[redacted] / -27 | Not reported |
| TRAZODONE | 75 mg | QD | Y-M: 20[redacted] / -27 | Not reported |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / -15 | Y-M: 20[redacted] / 60 |
| COLECALCIFEROL | 20 gtt | OTHER: WEEKLY | Y-M: 20[redacted] / -16 | Y-M: 20[redacted] / 107 |
| IRON | 100 mg | QD | Y-M: 20[redacted] / -16 | Y-M: 20[redacted] / 10 |
| OTHER VIRAL VACCINES | 0.5 mL | OTHER: ONCE | Y-M: 20[redacted] / 60 | Y-M: 20[redacted] / 60 |
| METHYLPREDNISOLONE | 12 mg | QD | Y-M: 20[redacted] / 61 | Y-M: 20[redacted] / 68 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 69 | Y-M: 20[redacted] / 76 |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / 77 | Y-M: 20[redacted] / 107 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | RELAPS OF ULCERATIVE COLITIS |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 193 / -27 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY -27): Albumin: 44 [35 - 55] G/L; Erythrocytes: 4.55 [4 - 5.8] 10^12/L; Glucose: 8.32 [3.9 - 5.6] MMOL/L; Hematocrit: 0.362 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 120 [135 - 175] G/L; Leukocytes: 5.4 [4 - 10] 10^9/L; NPTST108-CRP: 34.9 [0 - 10] MG/L; NPTST256-POTASSIUM: 4.56 [3.8 - 5.2] MMOL/L; Platelets: 396 [150 - 400] 10^9/L; Protein: 69.3 [64 - 80] G/L

**Microbiology**

[redacted]20[redacted] (RX DAY -27): STOOL NPTST091-CLOSTRIDIUM DIFFICILE: Negative; OTHER NOSE NPTST244-PCR COVID-19 VIRAL TEST: Negative; [redacted]20[redacted] (RX DAY -22): OTHER NOSE NPTST244-PCR COVID-19 VIRAL TEST: Positive-CORONAVIRUS

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 304 / 85 |
| **Duration of AE** | 112 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | RELAPS OF ULCERATIVE COLITIS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-234

治験責任医師からの報告。本被験者はチェコ共和国の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び元飲酒者（1 日 2–4 杯）であった。

**Event 1 の臨床経過：**

投与193日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。

投与193日後＊　，被験者は入院した。被験者は，COVID-19 陽性者と接触した後，検査で陽性となった（非重篤）。COVID-19 は無症状であった。

本報告時点では，その他の情報はなかった。

**The patient's past medications include:**

AZATHIOPRIN for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CORTICOSTEROIDS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NOLPAZA for PROPHYLAXIS OF HYPERSECRETION OF HYDROCHLORIC ACID ([redacted] 20[redacted] - [redacted] 20[redacted])

REMSIMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SOLUMEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CIPROFLOXACIN for ULCERATIVE COLITIS [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TOFACITINIB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CIPLOX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ENTIZOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900) ) [v.23.1] [10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of WORSENING OF ULCERATIVE COLITIS

**- Investigator:** RELAPS OF ULCERATIVE COLITIS

**- AbbVie:** Event is more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BODY WEIGHT:** 6[redacted].[redacted] KG

[redacted] **20[redacted] NASOPHARYNGEAL SWAB:** COVID-19: Tested positive"

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 子宮頚部の炎症 | X | | | |
| 潰瘍性大腸炎 | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANAEMIA | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.3 PACK | 2 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-675 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 55 | 55 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted] / 56 | [redacted]20[redacted] / 88 | 33 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 89 | [redacted]20[redacted] / 280 | 192 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 4 g | BID | Y-M: 20[redacted] |
| MESALAZINE | 3.2 g | BID | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | OTHER: 1/4 TABL. PER DAY | Y-M: 20[redacted] |
| AZATHIOPRINE | 100 mg | TID | Y-M: 20[redacted] |
| BUDESONIDE | 2 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| BUDESONIDE | 3 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 75 mg | QD | Y-M: 20[redacted] |
| BUDESONIDE | 3 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 75 mg | QD | Y-M: 20[redacted] |
| BUDESONIDE | 6 mg | BID | Y-M: 20[redacted] |
| IRON | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| RED BLOOD CELLS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| IRON | NOR REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| CIPROFLOXACIN | 400 mg | BID | Y-M: 20[redacted] / -286 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / -286 |
| AZATHIOPRINE | 150 mg | OTHER: 1 TABL.X 3 TIMES PER DAY | Y-M: 20[redacted] / -299 |
| INTRAUTERINE CONTRACEPTIVE DEVICE | N/A OTHER: NON APLICABLE | OTHER: N/A | Y-M: 20[redacted] / -252 |
| IRON | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -104 |
| BUDESONIDE | 9 mg | TID | Y-M: 20[redacted] / -33 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| INTRAUTERINE CONTRACEPTIVE DEVICE | N/A OTHER: NON APLICABLE | OTHER: N/A | Y-M: 20[redacted] / -252 | Y-M: 20[redacted] / 143 |
| BUDESONIDE | 9 mg | TID | Y-M: 20[redacted] / -33 | Y-M: 20[redacted] / 118 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 54 | Y-M: 20[redacted] / 68 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 89 | Y-M: 20[redacted] / 113 |
| BUDESONIDE | 9 mg | QD | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 144 |
| CEFUROXIME | 500 mg | BID | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 138 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 138 |
| AMOXICILLIN | 1000 mg | TID | Y-M: 20[redacted] / 142 | Y-M: 20[redacted] / 144 |

| | | | | |
|---|---|---|---|---|
| CLAVULANIC ACID | 200 mg | TID | Y-M: 20[redacted] / 142 | Y-M: 20[redacted] / 144 |
| DOXYCYCLINE | 100 mg | BID | Y-M: 20[redacted] / 145 | Y-M: 20[redacted] / 154 |
| ERTAPENEM | 1 g | QD | Y-M: 20[redacted] / 145 | Y-M: 20[redacted] / 151 |
| PREDNISOLONE | 75 mg | QD | Y-M: 20[redacted] / 145 | Y-M: 20[redacted] / 151 |
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted] / 152 | Y-M: 20[redacted] / 158 |
| METHYLPREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / 159 | Y-M: 20[redacted] / 165 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 166 | Y-M: 20[redacted] / 172 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 173 | Y-M: 20[redacted] / 179 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 180 | Y-M: 20[redacted] / 186 |
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted] / 187 | Y-M: 20[redacted] / 193 |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] / 194 | Y-M: 20[redacted] / 260 |
| ADALIMUMAB | 160 mg | QD | Y-M: 20[redacted] / 246 | Y-M: 20[redacted] / 246 |
| ADALIMUMAB | 80 mg | OTHER: Q2WK | Y-M: 20[redacted] / 260 | Y-M: 20[redacted] / 260 |
| METHYLPREDNISOLONE | 28 mg | QD | Y-M: 20[redacted] / 261 | Y-M: 20[redacted] / 267 |
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted] / 268 | Y-M: 20[redacted] / 274 |
| ADALIMUMAB | 40 mg | OTHER: Q2W | Y-M: 20[redacted] / 274 | Y-M: 20[redacted] / 274 |
| METHYLPREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / 275 | Y-M: 20[redacted] / 281 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 282 | Y-M: 20[redacted] / 288 |
| ADALIMUMAB | 40 mg | OTHER: Q2WK | Y-M: 20[redacted] / 288 | Y-M: 20[redacted] / 288 |
| METHYLPREDNISOLONE | 12 mg | QD | Y-M: 20[redacted] / 289 | Y-M: 20[redacted] / 298 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 299 | Y-M: 20[redacted] / 315 |
| ADALIMUMAB | 40 mg | OTHER: Q2WK | Y-M: 20[redacted] / 302 | Y-M: 20[redacted] / 302 |
| ADALIMUMAB | 40 mg | OTHER: QW | Y-M: 20[redacted] / 309 | Y-M: 20[redacted] / 309 |
| ADALIMUMAB | 40 mg | OTHER: QW | Y-M: 20[redacted] / 316 | Y-M: 20[redacted] / 316 |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] / 316 | Y-M: 20[redacted] / 350 |
| ADALIMUMAB | 40 mg | OTHER: QW | Y-M: 20[redacted] / 323 | Y-M: 20[redacted] / 323 |
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 326 | Y-M: 20[redacted] / 326 |

| | | | | |
|---|---|---|---|---|
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 340 | Y-M: 20[redacted] / 340 |
| METHYLPREDNISOLONE | 28 mg | QD | Y-M: 20[redacted] / 351 | Y-M: 20[redacted] / 360 |
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted] / 361 | Y-M: 20[redacted] / 370 |
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 368 | Y-M: 20[redacted] / 368 |
| METHYLPREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / 371 | Y-M: 20[redacted] / 380 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 381 | Y-M: 20[redacted] / 390 |
| METHYLPREDNISOLONE | 12 mg | QD | Y-M: 20[redacted] / 391 | Y-M: 20[redacted] / 400 |
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 396 | Y-M: 20[redacted] / 396 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 401 | Y-M: 20[redacted] / 411 |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] / 412 | Y-M: 20[redacted] / 427 |
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 421 | Y-M: 20[redacted] / 421 |
| METHYLPREDNISOLONE | 28 mg | QD | Y-M: 20[redacted] / 428 | Y-M: 20[redacted] / 437 |
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted] / 438 | Y-M: 20[redacted] / 447 |
| METHYLPREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / 448 | Y-M: 20[redacted] / 457 |
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 450 | Y-M: 20[redacted] / 450 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 458 | Y-M: 20[redacted] / 467 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 468 | Y-M: 20[redacted] / 478 |
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 478 | Y-M: 20[redacted] / 478 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 479 | Y-M: 20[redacted] / 500 |
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted] / 501 | Y-M: 20[redacted] / 511 |
| METHYLPREDNISOLONE | 32 mg | QD | Y-M: 20[redacted] / 512 | Y-M: 20[redacted] / 532 |
| VEDOLIZUMAB | 300 mg | QD | Y-M: 20[redacted] / 513 | Y-M: 20[redacted] / 513 |
| USTEKINUMAB | 390 mg | QD | Y-M: 20[redacted] / 526 | Y-M: 20[redacted] / 526 |
| METHYLPREDNISOLONE | 28 mg | QD | Y-M: 20[redacted] / 533 | Y-M: 20[redacted] / 542 |

| | | | | |
|---|---|---|---|---|
| METHYLPREDNISOLONE | 24 mg | QD | Y-M: 20[redacted] / 543 | Y-M: 20[redacted] / 552 |
| METHYLPREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / 553 | Y-M: 20[redacted] / 562 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 563 | Y-M: 20[redacted] / 573 |
| METHYLPREDNISOLONE | 12 mg | QD | Y-M: 20[redacted] / 574 | Y-M: 20[redacted] / 583 |
| USTEKINUMAB | 90 mg | QD | Y-M: 20[redacted] / 582 | Y-M: 20[redacted] / 582 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 584 | Y-M: 20[redacted] / 593 |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / 594 | Y-M: 20[redacted] / 603 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | ULCERATIVE COLITIS WORSENING |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 78 / -11 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 257 / 169 |
| **Duration of AE** | 180 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | WORSENING OF ULCERATIVE COLITIS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | INFLAMMATION OF THE CERVIX DUE TO AN IUD |
| **Preferred term** | 子宮頚部の炎症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 212 / 124 |
| **Age at AE Onset** | 2[redacted] |

| | |
|---|---|
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 239 / 151 |
| **Duration of AE** | 28 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | INFLAMMATION OF INTRAUTERINE DEVICE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #3: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | WORSENING OF ULCERATIVE COLITIS |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 273 / 185 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-234

治験責任医師からの報告。本被験者はエストニアの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，汎大腸炎，貧血，元喫煙者（1 日 0.3 箱を 2 年間）及び非飲酒者であった。

**Event 1 の臨床経過：**

投与78日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与257日後＊　，潰瘍性大腸炎の悪化は消失した。

当該事象の発現前，投与70日後＊　，被験者は潰瘍性大腸炎の悪化の兆候を感じたが，重篤ではなかった。

投与78日後＊　，被験者は，1 日 10 回超の頻度の排便及び血便があり，入院した。入院中改善したが寛解ではなかった。投与86日後＊　，被験者は退院した。

投与された薬剤は，メトロニダゾール，シプロフロキサシン，メチルプレドニゾロン及びプレドニゾロンであった。

**The patient's past medications include:**

MESALAMINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ERYTHROCYTE MASS for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

MONOFER for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CIPROFLOXACINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOLE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900) ) [v.23.0] [10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of ULCERATIVE COLITIS WORSENING

**- Investigator:** Worsening of ulcerative colitis.

**- AbbVie:** Event more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] CALPROTECTINE:** >3000 (<49-49)

[redacted] **20[redacted] CAMPYLOBACTER:** Negative

[redacted] **20[redacted] CLOSTRIDIUM DEFICILE**: Negative

[redacted] **20[redacted] CRP:** 83.4 mg/L (normal <5.0)

[redacted] **20[redacted] FE:** 2.0 umol/L (normal 9.0 to 30.0)

[redacted] **20[redacted] HEMOGLOBIN:** 111 G/L (normal 110 to 150)

[redacted] **20[redacted] PLATELET COUNT:** 827 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.00 X10**12/L (normal 3.8 to 5.50)

[redacted] **20[redacted] SALMONELLA TEST:** Negative

[redacted] **20[redacted] SHIGELLA:** Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.1 X10**9/L (normal 3.8 to 10.0)

[redacted] **20[redacted] YERSINIA:** Negative

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はエストニアの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，子宮内避妊器具による子宮頚部の炎症の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.3 箱を 2 年間）及び非飲酒者であった。

**Event 2 の臨床経過：**

投与212日後＊　，被験者は子宮内避妊器具による子宮頚部の炎症を発現した。　投与239日後＊，子宮内避妊器具による子宮頚部の炎症は消失した。

本事象発現前の 投与の163日前＊　，被験者は避妊のために子宮内避妊器具装着の処置を受けた。

投与230日後＊　，被験者は下腹部痛及び高熱があり，入院した。被験者は抗生物質での治療を受けた。投与239日後＊　，炎症は消失し，被験者は退院した。

投与された薬剤は，セフロキシム，アモキシシリン，クラブラン酸，ertapenem 及びドキシサイクリンであった。

**The patient's past medications include:**

MESALASINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CIPROFLOXACINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METRONIDAZOLE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Cervix inflammation (10068402) (Cervix inflammation (10068402) ) [v.23.1] [10068402]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of INFLAMMATION OF THE CERVIX DUE TO AN IUD

**- Investigator:** inflammation of intrauterine device.

**- AbbVie:** Event is not consistent with study drug's mechanism of action. Additionally, inflammation can occur anytime following IUD insertion.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] TEMPERATURE:** High.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| 気管支炎 | X | | | X |
| 構語障害 | X | | | |
| 帯状疱疹 | | | | X |
| 腸閉塞 | X | | | |
| 口腔咽頭痛 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| DRUG ALLERGIES/REACTIONS: ALLERGIC REACTION TO REMICADE | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| HYPERTENSION: HIGH BLOOD PRESSURE MEASUREMENTS IN 20[redacted] AND 20[redacted]. MEASUREMENTS NORMALIZED 20[redacted] AND NO MEDICATIONS FOR HYPERTENSION ARE IN USE. | 20[redacted] |
| OTHER: ARTHROSIS OF THE KNEES | 20[redacted] |
| OTHER: CHICKEN POX | NOT REPORTED |
| OTHER: LEFT GLENOHUMERAL JOINT LUXATION | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 25 | 19[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | 2 - 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 53 | 53 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 54 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PARACETAMOL | 665 mg | PRN | Y-M: 20[redacted] |
| MESALAZINE | 2400 mg | TID | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | QD | Y-M: 20[redacted] |
| SULFASALAZINE | 1000 mg | BID | Y-M: 20[redacted] |
| MESALAZINE | 4000 mg | TID | Y-M: 20[redacted] |
| MERCAPTOPURINE | 50 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 400 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| PREDNISOLONE | 15 mg | QD | Y-M: 20[redacted] / -292 |
| VITAMIN D NOS | 15 ug | QD | Y-M: 20[redacted] / -117 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PARACETAMOL | 665 mg | PRN | Y-M: 20[redacted] | ONGOING |
| MESALAZINE | 4000 mg | TID | Y-M: 20[redacted] | ONGOING |
| VITAMIN D NOS | 15 ug | QD | Y-M: 20[redacted] / -117 | ONGOING |
| CLOPIDOGREL | 75 mg | QD | Y-M: 20[redacted] / 447 | Y-M: 20[redacted] / 449 |
| SIMVASTATIN | 10 mg | QD | Y-M: 20[redacted] / 447 | Y-M: 20[redacted] / 449 |
| LOSARTAN | 50MG mg | QD | Y-M: 20[redacted] / 647 | Y-M: 20[redacted] / 1290 |
| ACICLOVIR | 800 mg | OTHER: 5 TIMES PER DAY | Y-M: 20[redacted] / 1197 | Y-M: 20[redacted] / 1204 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | BRONCHITIS, SORE THROAT |
| **Preferred term** | 気管支炎，口腔咽頭痛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 317 / 264 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 268): Hemoglobin: 142 [134 - 167] G/L; Leukocytes: 9 [3.4 - 8.2] 10^9/L; NPTST108-CRP: 133 [0 - 10] MG/L; [redacted]20[redacted] (RX DAY 269): Hemoglobin: 137 [134 - 167] G/L; Leukocytes: 9.7 [3.4 - 8.2] 10^9/L; NPTST108-CRP: 87 [0 - 10] MG/L; [redacted]20[redacted] (RX DAY 273): Hemoglobin: 141 [134 - 167] G/L; Leukocytes: 7.5 [3.4 - 8.2] 10^9/L; NPTST108-CRP: 44 [0 - 10] MG/L; [redacted]20[redacted] (RX DAY 275): Hemoglobin: 143 [134 - 167] G/L; NPTST108-CRP: 22 [0 - 10] MG/L

**Microbiology**

[redacted]20[redacted] (RX DAY 268): BLOOD NPTST052-BLOOD CULTURE: Negative; URINE NPTST338-URINE CULTURE: Negative; [redacted]20[redacted] (RX DAY 269): OTHER PHARYNX NPTST248-PHARYNGEAL STREPTOCOCCAL CULTUR: Negative

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 330 / 277 |
| **Duration of AE** | 14 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | DYSARTRIA |
| **Preferred term** | 構語障害 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 492 / 439 |
| **Age at AE Onset** | 6[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 447): Cholesterol: 5 [0 - 5] MMOL/L; Creatinine: 97 [60 - 100] UMOL/L; HDL Cholesterol: 2.1 [0.8 - 2.1] MMOL/L; Hemoglobin: 132 [134 - 167] G/L; LDL Cholesterol: 2.7 [0 - 3] MMOL/L; NPTST108-CRP: <1 [0 - 10] MG/L; NPTST330-TROPONINE T: 12 [0 - 15] NG/L; Potassium: 3.9 [3.3 - 4.9] MMOL/L; Sodium: 136 [137 - 145] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 502 / 449 |
| **Duration of AE** | 11 DAYS |
| **Severity** | MILD |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | CK ELEVATION |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 565 / 512 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 651 / 598 |
| **Duration of AE** | 87 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #4: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | OCCLUSIO INTESTINI |
| **Preferred term** | 腸閉塞 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 724 / 671 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |

[redacted]20[redacted] (RX DAY 671): Creatinine: 63 [60 - 100] UMOL/L; Hemoglobin: 144 [134 - 167] G/L; Leukocytes: 10.4 [3.4 - 8.2] 10^9/L; NPTST108-CRP: <1 [0 - 10] MG/L; Platelets: 346 [150 - 360] 10^9/L; Potassium: 3.9 [3.3 - 4.9] MMOL/L; Sodium: 134 [137 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 672): Creatinine: 65 [60 - 100] UMOL/L; Hemoglobin: 139 [134 - 167] G/L; Leukocytes: 7.4 [3.4 - 8.2] 10^9/L; NPTST108-CRP: 3 [0 - 10] MG/L; Platelets: 327 [150 - 360] 10^9/L; Potassium: 3.5 [3.3 - 4.9] MMOL/L; Sodium: 135 [137 - 145] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 725 / 672 |
| **Duration of AE** | 2 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #5: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | CK ELEVATION |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 825 / 772 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 901 / 848 |
| **Duration of AE** | 77 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #6: Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1243 / 1190 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 1257 / 1204 |

| | |
|---|---|
| **Duration of AE** | 15 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はフィンランドの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，気管支炎及び咽頭痛の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 25 年間），潰瘍性大腸炎，高血圧及び現飲酒者（1 日 2–4 杯）であった。

**Event 1 の臨床経過：**

投与317日後＊　，被験者は気管支炎及び咽頭痛を発現した。投与330日後＊　，気管支炎及び咽頭痛は消失した。

投与317日後＊　，被験者は咽頭痛及びインフルエンザ様症状を訴えた。被験者は摂氏 39°C の発熱があった。投与321日後＊　，被験者は入院した。インフルエンザの検査は陰性で，CRP 検査の結果は 133 mg/dL であった。身体検査では異常は認められなかった。投与322日後＊　，被験者の熱は下がり，感染症のパラメータは低下していた。被験者は問題なく回復し，投与322日後＊　，被験者は退院した。

**The patient's past medications include:**

AZAMUN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALAZOPYRIN EN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MERKAPTOPURIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

---

1) Sore throat (10041367) (Oropharyngeal pain (10068319) ) [v.21.1] [10041367]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

2) Bronchitis (10006451) (Bronchitis (10006451) ) [v.21.1] [10006451]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Open Label)

---

Event of BRONCHITIS, SORE THROAT

**- Investigator:** Not applicable

**- AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BLOOD CULTURES:** negative

[redacted] **20[redacted] BODY TEMPERATURE:** 39 Degrees C

[redacted] **20[redacted] CHEST X-RAY (SCREENING):** Normal

[redacted] **20[redacted] CRP:** 133 mg/dL (normal 0 to 10)

[redacted] **20[redacted] CRP:** 22 mg/dL

[redacted] **20[redacted] HEMOGLOBIN:** 142 G/L (normal 134 to 167)

[redacted] **20[redacted] INFLUENZA TEST:** Negative

[redacted] **20[redacted] PHARYNGEAL STREPTOCOCCAL CULTURE:** negative

[redacted] **20[redacted] URINE CULTURE:** negative

[redacted] **20[redacted] WBC:** 9.0 X10**9/L (normal 3.4 to 8.2)

[redacted] **20[redacted] WBC:** 9.7 X10**9/L

[redacted] **20[redacted] WBC:** 7.5 X10**9/L (normal 3.4 to 8.2)

[redacted] **20[redacted] X-RAY THORAX:** No signs of infection
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はフィンランドの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，構語障害の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 25 年間），潰瘍性大腸炎，高血圧，現飲酒者（1 日 2–4 杯），並びに心疾患及び高血圧の家族歴であり，父親が 5[redacted] 歳の時に心筋梗塞を発現していた。

**Event 2 の臨床経過：**

投与492日後＊　，被験者は構語障害を発現した。投与502日後＊　，構語障害は消失した。

投与500日後＊　，被験者は 1–2 週間続く構語障害があり，入院した。他の神経学的症状は認められなかった。入院時には，舌の側面にいくつかのアフタ性潰瘍が認められた。脳血管発作が疑われたため，画像診断及び検体検査が行われた。プラビックス及びシンバスタチンの投与も開始された。被験者の症状は，入院中に消失した。投与502日後＊　，被験者は障害もなく，退院した。

投与された薬剤は，シンバスタチン及びプラビックスであった。

**The patient's past medications include:**

AZAMUN for ULCERATIVE COLITIS ([redacted])

SALAZOPYRIN EN for ULCERATIVE COLITIS ([redacted])

MERKAPTOPURIN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for COLITIS ULCEROSA ([redacted])

Causality for ABT-494 (Open Label)

---

1) Dysarthria (10013887) (Dysarthria (10013887) ) [v.22.0] [10013887]

**Causality as per repoer (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Open Label)

---

Event of DYSARTHRIA

**- Investigator:** Not applicable.

**- AbbVie:** More likely related to history of hypertension, smoking, alcohol use, family history of cardiovascular disease, and obesity.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] 20[redacted] **CAROTID ARTERY COMPUTED TOMOGRAPHY-ANGIO:** NO STENOSIS IN ICA, NO THROMBOTIC CHANGES.

[redacted] 20[redacted] **CHOLESTEROL:** 5.0 MMOL/L (normal 0 to 5)

[redacted] 20[redacted] **CREATININE:** 97 MMOL/L (normal 60 to 100)

[redacted] 20[redacted] **CRP:** <1 mg/L

[redacted] 20[redacted] **HDL:** 2.1 MMOL/L (normal 0.8 to 2.1)

[redacted] 20[redacted] **HEAD COMPUTED TOMOGRAPHY:** NO SIGNS OF INFARCTION OR HEMORRHAGIA. NORMAL.

[redacted] 20[redacted] **HEAD MRI:** NO INFARCTION. NO SIGNS OF ISCHEMIA.

[redacted] 20[redacted] **HEMOGLOBIN:** 132 G/L (normal 134 to 167)

[redacted] 20[redacted] **LDL:** 2.7 MMOL/L (normal 0 to 3)

[redacted] 20[redacted] **POTASSIUM:** 3.9 MMOL/L (normal 3.3 to 4.9)

[redacted] 20[redacted] **SODIUM:** 136 MMOL/L (normal 137 to 145)

[redacted] 20[redacted] **THORAX RTG:** Normal

[redacted] 20[redacted] **TROPONINE T:** 12 NG/L (normal 0 to 15)
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はフィンランドの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腸閉塞の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 25 年間），広範囲な潰瘍性大腸炎（全大腸炎型）及び現飲酒者（1 日 2–4 杯）であった。

**Event 4 の臨床経過：**

投与724日後＊　，被験者は腸閉塞を発現した。投与725日後＊　，腸閉塞は消失した。

投与724日後＊　　，被験者は結腸内視鏡検査の準備のために入院した。被験者は準備の一環として，3 L の colonsteril を飲んだ。colonsteril を飲んだ後，被験者の胃が膨張し，痛み出した。被験者は colonsteril を飲んだ後，腸からの排出がなかった。経鼻胃管を留置し，2 L の液体を採取

したところ，被験者の症状が緩和され，腸が正常化した。投与725日後＊　，被験者は退院した。

**The patient's past medications include:**

ASACOL for ULCERATIVE COLITIS ([redacted])

AZAMUN for ULCERATIVE COLITIS ([redacted])

SALAZOPYRIN EN for ULCERATIVE COLITIS ([redacted])

MERKAPTOPURIN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for COLITIS ULCEROSA ([redacted])

REMICADE for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

---

1)　Intestinal obstruction (10022687)　(Intestinal obstruction (10022687) )　[v.22.1]　[10022687]

**Causality　per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of OCCLUSIO INTESTINI

**- Investigator:** Not applicable

**- AbbVie:** Event more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ABDOMINAL COMPUTED TOMOGRAPHY:** No signs of occlusion was found.

[redacted] **20[redacted] CREATININE:** 63 umol/L (normal 60 to 100)

[redacted] **20[redacted] CREATININE:** 65 umol/L (normal 60 to 100)

[redacted] **20[redacted] CRP:** <1 MG/L (normal 0 to 10)

[redacted] **20[redacted] CRP:** 3 MG/L (normal 0 to 10)

[redacted] **20[redacted] HEMOGLOBIN:** 144 G/L (normal 134 to 167)

[redacted] **20[redacted] HEMOGLOBIN:** 139 G/L (normal 134 to 167)

[redacted] **20[redacted] PLATELET COUNT:** 346 X10**9/L (normal 150 to 360)

[redacted] **20[redacted] PLATELET COUNT:** 327 X10**9/L (normal 150 to 360)

[redacted] **20[redacted] POTASSIUM:** 3.9 MMOL/L (normal 3.3 to 4.9)

[redacted] **20[redacted] POTASSIUM:** 3.5 MMOL/L (normal 3.3 to 4.9)

[redacted] **20[redacted] SODIUM:** 134 MMOL/L (normal 137 to 145)

[redacted] **20[redacted] SODIUM:** 135 MMOL/L (normal 137 to 145)

[redacted] **20[redacted] WEIGHT:** 9[redacted] KG

[redacted] **20[redacted] WHITE BLOOD CELLS:** 10.4 X10**9/L (normal 3.4 to 8.2)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.4 X10**9/L (normal 3.4 to 8.2)

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Herpes zoster: One dermatome.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 貧血 | | | | X |
| 低リン酸血症 | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: ANEMIA | 20[redacted] |
| OTHER: DERMATITIS IGA LINEAR | 20[redacted] |
| OTHER: GILBERT SYNDROM | 20[redacted] |
| OTHER: HEMMORHOIDS | 20[redacted] |
| OTHER: SLEEP DISORDER | 20[redacted] |
| OTHER: SPONDYLITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 57 | 57 |

| | | | | | |
|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 57 [redacted]20[redacted] / 111 | 55 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ADALIMUMAB | 160 mg | NOT REPORTED | Y-M: 20[redacted] |
| MERCAPTOPURINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| METHOTREXATE | NOT REPORTED | 1 time per week | Y-M: 20[redacted] |
| MESALAZINE | 4 g | QD | Y-M: 20[redacted] |
| CERTOLIZUMAB | 400 mg | OTHER: OTHER EVERY WEEKS | Y-M: 20[redacted] |
| PREDNISONE | NOT REPORTED | QD | Y-M: 20[redacted] |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 6 WEEKS | Y-M: 20[redacted] |
| PREDNISOLONE | NOT REPORTED | QD | Y-M: 20[redacted] |
| GOLIMUMAB | 100 mg | OTHER: EVERY WEEK | Y-M: 20[redacted] |
| AMINOSALICYLIC ACID | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -210 |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -233 |
| PREDNISOLONE | 25 mg | QD | Y-M: 20[redacted] / -90 |
| AZATHIOPRINE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | NOT REPORTED | Y: 20[redacted] |
| AMINOSALICYLIC ACID | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |
| METHOTREXATE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |
| PREDNISONE | NOT REPORTED | QD | Y: 20[redacted] |
| ESOMEPRAZOLE | 20 mg | QD | Y: 20[redacted] |
| POTASSIUM | 600 mg | QD | Y: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] / -141 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| AMINOSALICYLIC ACID | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] / -210 | Y: 20[redacted] / 224 |
| PREDNISOLONE | 25 mg | QD | Y-M: 20[redacted] / -90 | Y-M: 20[redacted] / 52 |
| FOLIC ACID | 5 mg | BID | Y-M: 20[redacted] / 18 | ONGOING |
| IRON | 1000 mg | QD | Y-M: 20[redacted] / 29 | Y-M: 20[redacted] / 29 |

| | | | | |
|---|---|---|---|---|
| GLUCOSE 1-PHOSPHATE DISODIUM | ND mg | NOT REPORTED | Y-M: 20[redacted] / 45 | Y-M: 20[redacted] / 47 |
| CALCIUM PHOSPHATE;MAGNESIUM;PHOSPHORIC ACID;SODIUM PHOSPHATE | 65 OTHER: DROPS | TID | Y-M: 20[redacted] / 47 | Y-M: 20[redacted] / 50 |
| GLUCOSE 1-PHOSPHATE DISODIUM | ND mg | NOT REPORTED | Y-M: 20[redacted] / 51 | Y-M: 20[redacted] / 51 |
| CALCIUM PHOSPHATE;MAGNESIUM;PHOSPHORIC ACID;SODIUM PHOSPHATE | 150 OTHER: DROPS | TID | Y-M: 20[redacted] / 52 | ONGOING |
| COLECALCIFEROL | 100 000 IU | OTHER: EVERY OTHER WEEKS | Y-M: 20[redacted] / 53 | ONGOING |
| PREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] / 53 | ONGOING |
| ESOMEPRAZOLE | 20 mg | QD | Y: 20[redacted] | ONGOING |
| POTASSIUM | 600 mg | QD | Y: 20[redacted] | ONGOING |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] / -141 | Y: 20[redacted] / 224 |

**Event #1: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 57 / 1 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | HYPOPHOSPHOREMIA |
| **Preferred term** | 低リン酸血症 |

| | |
|---|---|
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 99 / 43 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted](RX DAY 45): NPTST250-PHOSPHORUS: 8 [25 - 45] MG/L;<br>[redacted]20[redacted] (RX DAY 47): NPTST250-PHOSPHORUS: 13 [25 - 45] MG/L;<br>[redacted]20[redacted] (RX DAY 53): NPTST250-PHOSPHORUS: 21 [25 - 45] MG/L | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 106 / 50 |
| **Duration of AE** | 8 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | RECIDIVISM HYPOPHOSPHOREMIA |
| **Preferred term** | 低リン酸血症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 107 / 51 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted] (RX DAY 52): Glucose: 4.496067 [3.607955 - 5.5507] MMOL/L; NPTST250-PHOSPHORUS: 27 [25 - 45] MG/L | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はフランスの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，低リン酸血症及び習慣性の低リン酸血症の事象を発現した。関連する病歴は，潰瘍性大腸炎及び貧血であった。

**Event 2 及び 3 の臨床経過：**

投与99日後＊　，被験者は低リン酸血症を発現した。投与103日後＊　，低リン酸血症は消失した。投与107日後＊　　，被験者は習慣性の低リン酸血症を発現した。

投与101日後＊　，被験者は低リン値及び尿検査で糖尿があり，入院した。投与103日後＊　，被験者は退院した。投与107日後＊　，被験者は低リン酸血症の再発により再入院した。投与109日後＊　　，被験者は退院した。

投与された薬剤は，静注用リン，phocytan 及び phosphoneuros であった。

**The patient's past medications include:**

FERINJECT for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

---

1)　Hypophosphataemia (10021058)　(Hypophosphataemia (10021058) )　[v.21.0]　[10021058]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, outcome unknown

2) Hypophosphataemia (10021058) (Hypophosphataemia (10021058) ) [v.21.0] [10021058]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of HYPOPHOSPHOREMIA

**- Investigator:** NOT APPLICABLE

**- AbbVie:** RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT.

Event of RECIDIVISM HYPOPHOSPHOREMIA

**- Investigator:** NOT APPLICABLE

**- AbbVie:** RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] PHOSPHORUS:** 8 MG/L (normal 25 to 45)

[redacted] **20[redacted] PHOSPHORUS:** 13 MG/L (normal 25 to 45)

[redacted] **20[redacted] PHOSPHORUS:** 21 MG/L (normal 25 to 45)

[redacted] **20[redacted] URINE TEST:** glycosuria

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| 肝酵素上昇 | | | | X |
| 精巣癌 | X | X | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 4[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| LEFT SIDED UC | 20[redacted] |
| LIVER DISEASE (EXCLUDING HEPATITIS): STEATOSIS HEPATIS | 20[redacted] |
| OTHER: ABDOMINAL PAIN | NOT REPORTED |
| OTHER: ARTHRITIS RIGHT HAND | NOT REPORTED |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: HIPS, MULTIPLE CORRECTIONS OF LEFT AND RIGHT HIP | 19[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 56 | 56 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 57 | [redacted]20[redacted] / 375 | 319 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 376 | [redacted]20[redacted] / 1035 | 660 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| INFLIXIMAB | 5 mg/kg | OTHER: 8 WEEKS | Y-M: 20[redacted] |
| AZATHIOPRINE | 150 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 2 g | BID | Y-M: 20[redacted] |
| AZATHIOPRINE | 250 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 60 mg | QD | Y-M: 20[redacted] |
| TACROLIMUS | 5 mg | BID | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | OTHER: UNK | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| LIDOCAINE | 2 % | QD | Y-M: 20[redacted] / 368 | Y-M: 20[redacted] / 368 |
| PROPOFOL | 150 mg | QD | Y-M: 20[redacted] / 368 | Y-M: 20[redacted] / 368 |
| SODIUM PHOSPHATE | 120 mL | QD | Y-M: 20[redacted] / 368 | Y-M: 20[redacted] / 368 |
| PROBIOTICS NOS | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / 528 | Y-M: 20[redacted] / 532 |

**Event #1: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | ELEVATED CK LEVEL |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 456 / 81 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 1058 / 683 (23 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 603 DAYS |
| **Severity** | MILD |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | ELEVATED LIVER ENZYMES |
| **Preferred term** | 肝酵素上昇 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 792 / 417 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 1058 / 683 (23 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 267 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC**

| | |
|---|---|
| **Event Description** | MALIGNANT TESTICULAR TUMOR (LEFT SIDED) |
| **Preferred term** | 精巣癌 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1033 / 658 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |

[redacted]20[redacted] (RX DAY 658): NPTST003-?HCG: 112.1 [0.1 - 7] 099,MLU/ML; NPTST019-AFP: 2443 [0 - 16] NG/ML; NPTST201-LDH: 399 [NOT REPORTED - 250] U/L; [redacted]20[redacted] (RX DAY 667): Creatinine: 106.083912 [61.882282 - 106.083912] UMOL/L; Erythrocytes: 4.51 [4.57 - 5.98] 10^12/L; Hematocrit: 0.424 [0.396 - 0.518] FRACTION OF 1; Hemoglobin: 138 [139 - 177] G/L; Leukocytes: 7.12 [3.79 - 10.33] 10^9/L; NPTST003-?HCG: 91.1 [0.1 - 7] 099,MLU/ML; NPTST019-AFP: 2125 [0 - 16] NG/ML; NPTST152-GFR CKD-EPI: 73 [60 - NOT REPORTED] ML/MIN; NPTST153-GFR MDRD: >60 [60 - NOT REPORTED] ML/MIN; NPTST201-LDH: 217 [NOT REPORTED - 250] U/L; Platelets: 286 [166 - 389] 10^9/L; Potassium: 4.6 [3.4 - 5.4] MMOL/L; Sodium: 143 [130 - 152] MMOL/L; [redacted]20[redacted] (RX DAY 680): NPTST003-?HCG: 51 [0.1 - 7] 099,MLU/ML; NPTST025-ALPHA-FETOPROTEIN: 3251 [0 - 16] NG/ML; NPTST201-

LDH: 238 [NOT REPORTED - 250] U/L; [redacted]20[redacted] (RX DAY 685): NPTST003-?HCG: 53.7 [0.1 - 7] 099,MLU/ML; NPTST025-ALPHA-FETOPROTEIN: 2805 [0 - 16] NG/ML; NPTST201-LDH: 195 [NOT REPORTED - 250] U/L; [redacted]20[redacted] (RX DAY 706): NPTST003-?HCG: 0.1 [0.1 - 7] 099,MLU/ML; NPTST025-ALPHA-FETOPROTEIN: 107.6 [0 - 16] NG/ML; NPTST201-LDH: 694 [NOT REPORTED - 250] U/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | UNKNOWN |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はドイツの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，悪性の精巣腫瘍（左側）の事象を発現した。関連する病歴は，潰瘍性大腸炎，腹痛，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 3 の臨床経過：**

投与1033日後＊ ，被験者は悪性の精巣腫瘍（左側）を発現した。

投与1034日後＊ ，被験者は左精巣及び腹部の超音波検査を受け，精巣腫瘍が確認され，悪性腫瘍が疑われた。

投与1037日後＊ ，被験者は左精巣の切除のために入院した。徴候及び症状には，陰嚢の左半分の肥大，食欲不振及び体重減少が含まれた。停留精巣，クラインフェルター症候群，精巣癌及びヒト免疫不全ウイルス感染の病歴はなかった。職業上の危険性や発がん性物質への暴露は確認されなかった。臨床経過では，非セミノーマの精巣腫瘍，後腹膜リンパ節腫脹，及び両側の肺腫瘤が認められ，脳転移の徴候は認められなかった。病期分類では，pT2 V1 R0 cN2 cM1a

S2CS であり，中程度の予後を示していた。投与1042日後＊　，被験者は退院した。

被験者は PEB 療法及びブレオマイシンの化学療法を受けた。

本事象により，治験薬の投与は完全に中止された。

投与された薬剤は，ブレオマイシンであった。

**The patient's past medications include:**

5-ASA for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PENTASA XTEND for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1)　Testis neoplasm malignant (10043362)　(Testis cancer (10057644) )　[v.23.1]　[10043362]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of MALIGNANT TESTICULAR TUMOR (LEFT SIDED)

**- Investigator:** UNKNOWN

**- AbbVie:** Currently published literature in both clinical trial and post-marketing setting indicates that Janus kinase inhibitors are unlikely to increase the risk of testicular neoplasm. Additionally, the exact cause of testicular cancer is not fully understood, and researchers speculate that multiple factors are involved in its development.

Relevant Laboratory& Other Diagnostic Tests

---

[redacted] **20[redacted] AFP:** 2443 NG/ML (normal 0 to 16)

[redacted] **20[redacted] AFP:** 2125 NG/ML (normal 0 to 16)

[redacted] **20[redacted] BETA HCG:** 112.1 MIU/ML (normal 0.1 to 7.0)

[redacted] **20[redacted] BETA HCG:** 91.1 MIU/ML (normal 0.1 to 7.0)

[redacted] **20[redacted] CREATININE:** 1.2 mg/dL (normal 0.7 to 1.2)

[redacted] **20[redacted] HGB:** 13.8 G/DL (normal 13.9 to 17.7)

[redacted] **20[redacted] HISTOLOGY:** 70% embryonic carcinoma, 20% seminoma, 10% yolk sac tumor. PT2 L0 V1 R0

[redacted] **20[redacted] MRI NEOCRANIUM:** No presence of cerebral metastases

[redacted] **20[redacted] PLT:** 286 X10**3/MCL (normal 166 to 389)

[redacted] **20[redacted] POTASSIUM:** 4.6 MMOL/L (normal 3.4 to 5.4)

[redacted] **20[redacted] SODIUM:** 143 MMOL/L (normal 130 to 152)

[redacted] **20[redacted] SONOGRAPHY ABDOMINAL:** Testicular tumor malignancy suspected. Kidneys and bladder are normal.

[redacted] **20[redacted] SONOGRAPHY TESTIS:** Testicular tumor malignancy suspected. Right testicular microlithiasis. Doppler signs normal.

[redacted] **20[redacted] WBC:** 7.12 X10**3/MCL (normal 3.79 to 10.33)

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Hepatic enzyme increased: Asymptomatic. No alternative etiology.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 結腸異形成 | | X | | |
| 精巣炎 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: ORCHITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 30 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 57 | 57 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 58 | [redacted]20[redacted] / 182 | 125 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| AZATHIOPRINE | 150 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 400 mg | OTHER: EVERY 2 MONTH | Y-M: 20[redacted] / -350 |
| SULFASALAZINE | 4 g | QD | Y: 20[redacted] |
| ADALIMUMAB | NOT REPORTED | OTHER: EVERY 2 WEEKS | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| METHYLPREDNISOLONE | 12 mg | QD | Y-M: 20[redacted] / 2 | Y-M: 20[redacted] / 8 |
| METHYLPREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 9 | Y-M: 20[redacted] / 15 |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] / 16 | Y-M: 20[redacted] / 22 |
| CEFUROXIME | 500 mg | BID | Y-M: 20[redacted] / 84 | Y-M: 20[redacted] / 88 |
| METHYLPREDNISOLONE | 16 mg | QD | Y-M: 20[redacted] / 88 | ONGOING |
| CIPROFLOXACIN | 500 mg | BID | Y-M: 20[redacted] / 89 | Y-M: 20[redacted] / 90 |
| GENTAMICIN | 16 mg | QD | Y-M: 20[redacted] / 89 | ONGOING |
| UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE | 1 OTHER: CAPSULE | QD | Y-M: 20[redacted] / 98 | ONGOING |
| SULFASALAZINE | 4 g | QD | Y: 20[redacted] | ONGOING |

**Event #1: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | LOW GRADE COLONIC DYSPLAISA |
| **Preferred term** | 結腸異形成 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 58 / 1 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |

| | |
|---|---|
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | ORCHITIS |
| **Preferred term** | 精巣炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 140 / 83 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| [redacted]20[redacted] (RX DAY 91): URINE NPTST342-URINE MICROBIOLOGY TEST: Positive-E. COLI 10'5 | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | BACTERIAL INFECTION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はハンガリーの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，精巣炎の事象を発現した。関連する病歴は，精巣炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 2 の臨床経過：**

投与140日後＊ ，被験者は精巣炎を発現した。

投与145日後＊　，被験者は左精巣上体の過敏及び発熱があり，入院した。入院中の 投与148日後＊　，尿培養検査で大腸菌が陽性であることも判明した。投与150日後＊　，被験者は退院した。

投与された薬剤は，ゲンタマイシン，シプロフロキサシン，xylamin plusz 及び zinnat であった。

Causality for ABT-494 (Open Label)

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1)　Orchitis (10031064)　(Orchitis (10031064) )　[v.21.0]　[10031064]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** No

Alternative Etiology for ABT-494 (Open Label)

---

Event of ORCHITIS

**- Investigator:** Bacterial infection

**- AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] URINE MICROBIOLOGY TEST:** Positive for E. coli 10'5

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| COVID-19 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 4[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| ULCERATIV COLITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 57 | 57 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 58 | [redacted]20[redacted] / 425 | 368 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted]20[redacted] / 426 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| AZATHIOPRINE | 150 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 3000 mg | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: ONCE A WEEK | Y-M: 20[redacted] |
| METHYLPREDNISOLONE | 4 mg | QD | Y-M: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 3000 mg | QD | Y-M: 20[redacted] | Not reported |
| CEFTRIAXONE | 2 g | QD | Y-M: 20[redacted] / 228 | Y-M: 20[redacted] / 236 |
| DEXAMETHASONE | 6 mg | QD | Y-M: 20[redacted] / 228 | Y-M: 20[redacted] / 239 |
| ENOXAPARIN | 0,4 mL | QD | Y-M: 20[redacted] / 228 | Y-M: 20[redacted] / 249 |
| DIHYDROCODEINE | 10 mg | TID | Y-M: 20[redacted] / 229 | Y-M: 20[redacted] / 238 |
| ACETYLSALICYLIC ACID | 100 mg | QD | Y-M: 20[redacted] / 231 | Y-M: 20[redacted] / 239 |
| FAVIPIRAVIR | 1600 mg | BID | Y-M: 20[redacted] / 231 | Y-M: 20[redacted] / 231 |
| FAVIPIRAVIR | 600 mg | BID | Y-M: 20[redacted] / 232 | Y-M: 20[redacted] / 235 |
| PANTOPRAZOLE | 40 mg | QD | Y-M: 20[redacted] / 236 | Y-M: 20[redacted] / 239 |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | WORSENING OF COVID 2019 INFECTION |
| **Preferred term** | COVID-19 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 653 / 228 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 664 / 239 |
| **Duration of AE** | 12 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | COVID 19 INFECTION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はハンガリーの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 の感染の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与の約21ヵ月後＊，被験者は COVID-19 の感染（非重篤）を発現し始めた。

投与653日後＊　　，被験者は COVID-19 の感染の悪化を発現した。投与664日後＊　　，COVID-19 の感染の悪化は消失した。

投与653日後＊　　，被験者は COVID-19 の症状悪化があり，入院した。症状には，発熱，脱力，咳嗽，及び酸素投与を必要とする息切れが含まれた。投与664日後＊　，被験者は退院した。

本事象の危険因子は，被験者が看護師であることと考えられた。

**The patient's past medications include:**

IMURAN [AZATHIOPRINE] for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　COVID-19 (10084268)　(COVID-19 (10084268) )　[v.24.0]　[10084268]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

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Event of WORSENING OF COVID 2019 INFECTION

**- Investigator:** Covid-19 infection.

**- AbbVie:** Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CHEST X-RAY:** double sided pneumonia

[redacted] **20[redacted] CHEST X-RAY:** full radiological regression

[redacted] **20[redacted] COVID NASOPHARYNGEAL SWAB:** POSITIVE

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 無水晶体眼 | X | | | |
| 角膜浮腫 | X | | | |
| 回転性めまい | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 7[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ASTHMA | 19[redacted] |
| BIPEDAL PITTING OEDEMA | 20[redacted] |
| CATARACTS | 20[redacted] |
| CHRONIC COUGH | 20[redacted] |
| DECREASED EJECTION FRACTION | 20[redacted] |
| DECREASED ENERGY LEVELS (COLITIS SYMPTOM) | 20[redacted] |
| FRACTURED CLAVICLE | 19[redacted] |
| INCREASED BOWEL MOTIONS | 20[redacted] |
| INTERMITTENT CHEST PAIN | 20[redacted] |
| IRON DEFICIENCY ANAEMIA | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| MACULAR EYE DEGENERATION | 20[redacted] |
| MITRIAL REGURURATION | NOT REPORTED |
| PERMANENT ATRIAL FIBRILATION | 20[redacted] |
| POSTERIOR CIRCULATION STROKE | 20[redacted] |
| PURE HYPERCHOLESTERAEMIA | 20[redacted] |
| RESTLESS LEG SYNDROME | 20[redacted] |
| RIGHT FOOT DROP | 20[redacted] |
| SINUSITUS | 20[redacted] |
| VARICOSE VEINS | 19[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| PRIOR PROCEDURES: ANGIOGRAM | 20[redacted] |
| PRIOR PROCEDURES: BRONCOSCOPY | 20[redacted] |
| PRIOR PROCEDURES: BRONSCHOSCOPY | 20[redacted] |
| PRIOR PROCEDURES: CARDIOVERSION | 20[redacted] |
| PRIOR PROCEDURES: COLONOSCOPY | 20[redacted] |
| PRIOR PROCEDURES: LIGATION OF VARICOSE VEINS | 19[redacted] |
| PRIOR PROCEDURES: NASAL ENDOSCOPY | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 56 | 56 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted] / 57 | [redacted] / 113 | 57 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted] / 114 | [redacted] / 477 | 364 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted] / 478 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 4.8 g | QID | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 150 mg | QD | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| INFLIXIMAB | 750 mg | OTHER: MONTHLY | Y-M: 20[redacted] |
| IRON | 100 mg/kg | PRN | Y-M: 20[redacted] |
| MESALAZINE | 1 g | NOT REPORTED | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: MONTHLY | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| DIFLUCORTOLONE;ISOCONAZOLE | TOPICAL APPICATION TO AFFECTED AREA OTHER: TOPICAL APPLICATION TO AFFECTED AREA | BID | Y-M: 20[redacted] |
| APIXABAN | 5 mg | BID | Y-M: 20[redacted] / -301 |
| PROCHLORPERAZINE | 5 mg | QD | Y-M: 20[redacted] / -306 |
| ATORVASTATIN | 40 mg | QD | Y-M: 20[redacted] / -309 |
| PARACETAMOL | 1 g | QID | Y-M: 20[redacted] / -310 |
| BUMETANIDE | 1 mg | QD | Y-M: 20[redacted] / -179 |
| MIDODRINE | 2.5 mg | BID | Y-M: 20[redacted] / -24 |
| ESOMEPRAZOLE | 20 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| IRON | 100 mg/kg | PRN | Y-M: 20[redacted] | Not reported |
| DIFLUCORTOLONE;ISOCONAZOLE | TOPICAL APPICATION TO AFFECTED AREA OTHER: TOPICAL APPLICATION TO AFFECTED AREA | BID | Y-M: 20[redacted] | Not reported |
| APIXABAN | 5 mg | BID | Y-M: 20[redacted] / -301 | Y-M: 20[redacted] / 438 |
| PROCHLORPERAZINE | 5 mg | QD | Y-M: 20[redacted] / -306 | Not reported |
| ATORVASTATIN | 40 mg | QD | Y-M: 20[redacted] / -309 | Not reported |
| PARACETAMOL | 1 g | QID | Y-M: 20[redacted] / -310 | Not reported |
| BUMETANIDE | 1 mg | QD | Y-M: 20[redacted] / -179 | Not reported |
| ACETAZOLAMIDE | 250 mg | BID | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 132 |
| CHLORAMPHENICOL | 0.5% OTHER: PER DROP | QID | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 134 |

| | | | | |
|---|---|---|---|---|
| CICLOSPORIN | 1% OTHER: PER EYE DROP | OTHER: STAT | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 127 |
| DICLOFENAC | 0.1% OTHER: PER DROP | OTHER: STAT | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 127 |
| PHENYLEPHRINE | 2.5% OTHER: PER EYE DROPS | OTHER: STAT | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 127 |
| PREDNISOLONE | 1% OTHER: PER DROP | OTHER: 8 DROPS / DAY | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 157 |
| TETRACAINE | 0.9% OTHER: PER DROP | OTHER: STAT | Y-M: 20[redacted] / 127 | Y-M: 20[redacted] / 127 |
| HYALURONIC ACID;TREHALOSE | 1 OTHER: EYE DROP | QID | Y-M: 20[redacted] / 155 | Y-M: 20[redacted] / 161 |
| PARACETAMOL | 1 g | PRN | Y-M: 20[redacted] / 314 | Y-M: 20[redacted] / 316 |
| BETAHISTINE | 8 mg | PRN | Y-M: 20[redacted] / 315 | Y-M: 20[redacted] / 316 |
| ONDANSETRON | 4 mg | PRN | Y-M: 20[redacted] / 315 | Y-M: 20[redacted] / 316 |
| PROCHLORPERAZINE | 5 mg | TID | Y-M: 20[redacted] / 315 | ONGOING |
| MIDAZOLAM | 2 mg | QD | Y-M: 20[redacted] / 333 | Y-M: 20[redacted] / 333 |
| FENTANYL | UNKNOWN OTHER: UNKNOWN | OTHER: ONCE | Y-M: 20[redacted] / 440 | Y-M: 20[redacted] / 440 |
| MORPHINE | 2 -10 mg | OTHER: ONCE | Y-M: 20[redacted] / 440 | Y-M: 20[redacted] / 440 |
| ONDANSETRON | 4 mg | OTHER: ONCE | Y-M: 20[redacted] / 440 | Y-M: 20[redacted] / 440 |
| OXYCODONE | 5 mg | OTHER: ONCE | Y-M: 20[redacted] / 440 | Y-M: 20[redacted] / 440 |
| APIXABAN | 5 mg | BID | Y-M: 20[redacted] / 441 | ONGOING |
| OFLOXACIN | ONE DROP OTHER: EYE DROPS | OTHER: ODS | Y-M: 20[redacted] / 441 | Y-M: 20[redacted] / 455 |
| PREDNISOLONE | ONE DROP OTHER: EYE DROP | OTHER: EVERY 2 HOURS | Y-M: 20[redacted] / 441 | Y-M: 20[redacted] / 455 |
| ESOMEPRAZOLE | 20 mg | QD | Y: 20[redacted] | Not reported |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | RIGHT EYE CORNEAL OEDEMA, APHAKIA - RIGHT EYE |
| **Preferred term** | 無水晶体眼，角膜浮腫 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 605 / 128 |
| **Age at AE Onset** | 7[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 920 / 443 |
| **Duration of AE** | 316 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | APHAKIC FOLLOWING PREVIOUS CATARACT SURGERY |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | VERTIGO |
| **Preferred term** | 回転性めまい |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 791 / 314 |
| **Age at AE Onset** | 7[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 793 / 316 |
| **Duration of AE** | 3 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | SYMPTOMS LIKELY RESIDUAL FROM PREVIOUS STROKE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はアイルランドの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，回転性めまいの事象を発現した。関連する病歴は，静脈瘤，喘息，静脈瘤結紮，永続性心房細動，純型高コレステロール血症，慢性咳嗽，

潰瘍性大腸炎，心臓除細動，鉄欠乏性貧血，両足圧痕性浮腫，駆出率減少，活力レベル低下（大腸炎の症状），黄斑変性，断続的な胸痛，僧帽弁逆流，非喫煙者及び非飲酒者であった。本被験者は，先行の M14-234 試験では，被験者番号 [redacted] であり，20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted]年 [redacted] 月 [redacted] 日まで盲検化された治験薬を投与された。

**Event 2 の臨床経過：**

投与791日後＊　，被験者は回転性めまいを発現した。投与793日後＊　　，回転性めまいは消失した。本事象発現前，被験者は投与の14ヵ月後＊に非重篤な体位性低血圧，投与の19ヵ月後＊に失神のエピソード，投与の23ヵ月後＊に原因不明の失神寸前状態のエピソードの事象を発現した。

投与791日後＊　，被験者は左下肢脱力，浮動性めまい，悪心，嘔吐及び失神の急性発症のため入院した。エピソード中，視覚障害，耳鳴及び括約筋障害はなかった。静脈内に輸液が行われた。投与792日後＊　，被験者は後頭部痛を訴え，体位性の血圧低下が認められた。被験者は意識清明及び見当識ありで，かなり改善したと感じた。投与793日後＊　，被験者は横になっている時又は起立時に継続的な浮動性めまいがあった。同日，被験者は退院した。

本事象に関連する危険因子として，以前の脳卒中から症状が残存している可能性があった。

投与された薬剤は，stemetil，zofran，serc であった。

**The patient's past medications include:**

ASOCOLON for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted] [redacted] 20[redacted]- [redacted] 20[redacted] 20[redacted]- [redacted] 20[redacted] 20[redacted]- [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted]

SALFALK for ULCERATIVE COLITIS

Causality for UPADACITINIB (Blinded)

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1)　Vertigo (10047340)　(Vertigo (10047340) )　[v.24.0]　[10047340]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of VERTIGO

**- Investigator:** SYMPTOMS LIKELY RESIDUAL FROM PREVIOUS STROKE

**- AbbVie:** Risk factors include previous stroke as reported by Pi, advanced age, pre-existing atrial fibrillation and mitrial regurgitation

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CT BRAIN:** NIL HAEMORRHAGE

[redacted] **20[redacted] MRI BRAIN:** NIL ACUTE. OLD CHANGES CORRESPONDING WITH PREVIOUS POSTERIOR CURCULATION STROKE

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はアイルランドの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右眼の角膜浮腫及び右眼の無水晶体眼の事象を発現した。関連する病歴は，永続性心房細動，高コレステロール血症，レストレスレッグス症候群，心臓除細動，両足圧痕性浮腫，駆出率減少，黄斑変性，白内障，後方循環脳卒中，潰瘍性大腸炎，僧帽弁逆流，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与605日後＊　　，被験者は右眼の角膜浮腫及び右眼の無水晶体眼を発現した。投与920日後＊，右眼の角膜浮腫及び右眼の無水晶体眼は消失した。

投与の約1年後＊，被験者は右眼の白内障の外科手術を受け，外科手術中，植え込まれた強膜縫合術のレンズにより角膜浮腫及び無水晶体眼に至った。

投与917日後＊　，被験者は無水晶体症であり，この問題を解決するために角膜移植を受け，成功した。投与920日後＊，被験者は退院した。

投与された薬剤は，フェンタニル，oxynorm，モルヒネ，G. オフロキサシン，G. pred forte であった。

**The patient's past medications include:**

ASOCOLON for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

AZOTHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLIXAMAB for ULCERATIVE COLITIS ([redacted])

SALFALK for ULCERATIVE COLITIS ([redacted])

VEDOLIZAMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Corneal edema (10011007)　(Corneal oedema (10011033) )　[v.24.1]　[10011007]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

2)　Aphakia (10002945)　(Aphakia (10002945) )　[v.24.1]　[10002945]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

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Event of RIGHT EYE CORNEAL OEDEMA

**- Investigator:** Aphakic following previous cataract surgery.

**- AbbVie:** The event is more likely related to a complication of previous cataract surgery (for pre-existing cataracts), as reported by PI.

Event of APHAKIC-RIGHT EYE

**- Investigator:** Aphakic following previous cataract surgery.

**- AbbVie:** The event is more likely related to a complication of previous cataract surgery (for pre-existing cataracts), as reported by PI.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 耳帯状疱疹 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANKYLOSING SPONDYLITIS | 20[redacted] |
| CHICKENPOX | 19[redacted] |
| LEFT SIDED UC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted]/ 1 | [redacted]20[redacted]/ 53 | 53 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted]20[redacted]/ 54 | [redacted]20[redacted]/ 112 | 59 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted]20[redacted]/ 113 | [redacted]20[redacted]/ 476 | 364 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted]/ 477 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 480 mg | QD | Y: 20[redacted] |
| FOLIC ACID | 10MG OTHER: PILL | OTHER: WEEKLY | Y: 20[redacted] |
| METHOTREXATE | 25 mg | OTHER: ONCE / WEEK | Y: 20[redacted] |
| VEDOLIZUMAB | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PREDNISOLONE | 60 mg | QD | Y-M: 20[redacted] / 24 | Y-M: 20[redacted] / 31 |
| ACICLOVIR | 900 mg | TID | Y-M: 20[redacted] / 29 | Y-M: 20[redacted] / 36 |
| CALCIUM CHLORIDE;CARMELLOSE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 1 OTHER: DROP | OTHER: N/A | Y-M: 20[redacted] / 30 | Y-M: 20[redacted] / 87 |
| RETINOL | 1 OTHER: DROP | OTHER: NIGHTLY | Y-M: 20[redacted] / 30 | Y-M: 20[redacted] / 87 |
| ACICLOVIR | 1.00 g | TID | Y-M: 20[redacted] / 32 | Y-M: 20[redacted] / 36 |
| HYDROCORTISONE | NOT REPORTED | PRN | Y-M: 20[redacted] / 269 | Y-M: 20[redacted] / 330 |
| SODIUM PHOSPHATE | NOT AVAILABLE g | PRN | Y-M: 20[redacted] / 335 | Y-M: 20[redacted] / 335 |
| FENTANYL | 50 OTHER: MCG | PRN | Y-M: 20[redacted] / 336 | Y-M: 20[redacted] / 336 |
| MIDAZOLAM | 4 mg | PRN | Y-M: 20[redacted] / 336 | Y-M: 20[redacted] / 336 |
| MESALAZINE | 240 mg | QD | Y-M: 20[redacted] / 404 | Not reported |
| MESALAZINE | 480 mg | QD | Y: 20[redacted] | Y-M: 20[redacted] / 403 |
| FOLIC ACID | 10MG OTHER: PILL | OTHER: WEEKLY | Y: 20[redacted] | Y-M: 20[redacted] / 24 |
| METHOTREXATE | 25 mg | OTHER: ONCE / WEEK | Y: 20[redacted] | Y-M: 20[redacted] / 38 |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | RAMSAY HUNT SYNDROME |
| **Preferred term** | 耳帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 500 / 24 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 29): Albumin: 48 [39 - 51] G/L; Alkaline Phosphatase: 66 [40 - 129] U/L; Aspartate Aminotransferase: 43 [0 - 40] U/L; Basophils: 0.04 [0 - 0.1] 10^9/L; Bilirubin: 12 [1 - 21] UMOL/L; Calcium: 2.39 [2.15 -

2.55] MMOL/L; Chloride: 98 [98 - 106] MMOL/L; Creatinine: 91 [64 - 104] UMOL/L; Eosinophils: 0.05 [0 - 0.5] 10^9/L; Erythrocytes: 3.9 [4.5 - 5.5] 10^12/L; Hematocrit: 0.356 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 128 [130 - 170] G/L; Leukocytes: 15.1 [4 - 10] 10^9/L; Lymphocytes: 1.8 [1 - 3] 10^9/L; Neutrophils: 12.32 [2 - 7] 10^9/L; Phosphate: 0.97 [0.87 - 1.45] MMOL/L; Platelets: 491 [150 - 400] 10^9/L; Potassium: 4.7 [3.3 - 5.1] MMOL/L; Protein: 72 [64 - 83] G/L; Sodium: 135 [136 - 145] MMOL/L; [redacted]20[redacted](RX DAY 31): Eosinophils: 0 [0.2 - 0.5] 10^9/L; Erythrocytes: 3.87 [4.5 - 5.5] 10^12/L; Hematocrit: 0.34 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 120 [130 - 170] G/L; Leukocytes: 17.4 [4 - 10] 10^9/L; Lymphocytes: 3.7 [1 - 3] 10^9/L; Neutrophils: 11.5 [2 - 7] 10^9/L; Platelets: 460 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 32): Albumin: 42 [39 - 51] G/L; Alkaline Phosphatase: 60 [40 - 129] U/L; Aspartate Aminotransferase: 46 [0 - 40] U/L; Bilirubin: 12 [1 - 21] UMOL/L; Calcium: 2.32 [2.15 - 2.55] MMOL/L; Chloride: 101 [98 - 106] MMOL/L; Creatinine: 85 [64 - 104] UMOL/L; Potassium: 4.1 [3.3 - 5.1] MMOL/L; Sodium: 137 [136 - 145] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]16:51

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はアイルランドの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，ラムゼーハント症候群の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），強直性脊椎炎，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

**Event 1 の臨床経過：**

投与500日後＊，被験者はラムゼーハント症候群を発現した。

被験者は顔面麻痺を経験した。投与502日後＊　　，被験者は医学的評価を受け，当初はベル麻痺と診断され，ステロイドの経口投与を受けた。投与505日後＊　，被験者は左耳の炎症及び腫脹があり，顔面左側の下垂が解消されないため，入院した。その他の症状及び徴候には，左

耳の紅斑及び顔面神経麻痺が含まれた。前頭部での残存は認められなかった。感染症の可能性が検討された。その他の神経経路は無傷であり，顔面の感覚も問題なかった。口腔や耳の小嚢は認められなかった。最終的な診断は，ラムゼーハント症候群であった。抗ウイルス薬の静脈内投与及び高用量のプレドニゾロンの投与が継続された。投与507日後＊　，プレドニゾロンは8 日間の投与後に中止され，聴力検査では両耳とも正常であった。投与508日後＊　，被験者は抗ウイルス薬を経口投与に切り替えられ，退院した。

投与された薬剤は，celluvisc drops，viva pos eye drops，アシクロビル及びプレドニゾロンであった。

**The patient's past medications include:**

VEDOLIZUMAB for ULCERATIVE COLITIS (20[redacted]- [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　Ramsay-Hunt syndrome (10037834)　(Herpes zoster oticus (10063491) )　[v.24.0]　[10037834]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Blinded)

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Event of RAMSAY HUNT SYNDROME

**- Investigator:** Not applicable

**- AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

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**[redacted] 20[redacted]COVID-19 NASOPHARYNGEAL SWAB:** Negative for COVID-19

[redacted] **20[redacted] HEMATOCRIT:** 0.356 L/L (normal 0.4 to 0.5)

[redacted] **20[redacted] HEMOGLOBIN:** 12.8 G/DL (normal 13.0 to 17.0)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 1.8 X10**9/L (normal 1 to 3)

[redacted] **20[redacted] NEUTROPHILS ABS:** 12.32 X10**9/L (normal 2 to 7)

[redacted] **20[redacted] PLATELET COUNT:** 491 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 15.1 X10**9/L (normal 4 to 10)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 5[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA: ANEMIA SECONDARY TO IBD | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: PANCYTOPENIA DEVELOPED AS A RESULT OF USE OF HUMIRA AND IMURAN | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 11 | 19[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted]/ 1 | [redacted]20[redacted]/ 57 | 57 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted]/ 58 | [redacted] 0[redacted]/ 198 | 141 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted]/ 199 | [redacted]20[redacted]/ 229 | 31 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISOLONE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: 4 WEEKLY | Y-M: 20[redacted] |
| AZATHIOPRINE | 150 mg | QD | Y-M: 20[redacted] |
| HYDROCORTISONE | 2013 OTHER: 1 RECTAL SUPPOSITORY | PRN | Y-M: 20[redacted] |
| SULFASALAZINE | 3 g | PRN | Y-M: 20[redacted] |
| AZATHIOPRINE | 25 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1 g | PRN | Y-M: 20[redacted] |
| SULFASALAZINE | 2 g | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: WEEKLY | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | QD | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: 8 WEEKLY | Y-M: 20[redacted] |
| INFLIXIMAB | 400 mg | OTHER: 8 WEEKLY | Y-M: 20[redacted] |
| CALCIUM | II OTHER: CAPSULES | QD | Y-M: 20[redacted] / -220 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -15 |
| SULFASALAZINE | 1.5 g | PRN | Y: 20[redacted] |
| FISH OIL | I OTHER: CAPSULE | QD | Y: 20[redacted] |
| HERPES ZOSTER IMMUNIZATION | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| SULFASALAZINE | 2 g | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 58 |
| CALCIUM | II OTHER: CAPSULES | QD | Y-M: 20[redacted] / -220 | ONGOING |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -15 | ONGOING |
| FISH OIL | I OTHER: CAPSULE | QD | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | MODERATE ULCERATIVE COLITIS FLARE |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 150 / -49 DAYS BEFORE TREATMENT |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 256 / 58 (27 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 107 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | DISEASE WORSENING. ULCERATIVE COLITIS FLARE. PANPROCTOCOLECTOMY COMPLETED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-234

治験責任医師からの報告。本被験者はアイルランドの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，中等症の潰瘍性大腸炎の再燃の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 11 年間），潰瘍性大腸炎（広範囲の潰瘍性大腸炎/全大腸炎），ヒュミラ及びイムランの使用による汎血球減少症，並びに飲酒者（1 日 2 杯未満）であった。本被験者は，20[redacted]年[redacted]月[redacted]日，継続投与試験である M14-533 試験に移行し，被験者番号は [redacted] であった。

**Event 1 の臨床経過：**

投与150日後＊　，被験者は中等症の潰瘍性大腸炎の再燃を発現した。投与256日後＊　，中等症の潰瘍性大腸炎の再燃は消失した。

投与156日後＊以降，被験者は疾患の悪化の兆候を示していた。投与164日後＊　　，被験者は潰瘍性大腸炎の悪化のため入院した。診断法が実施された。

投与254日後＊　　，被験者は回腸嚢肛門吻合術を伴う全直腸結腸切除術を受けた。投与266日後＊，被験者は退院した。投与259日後＊，治験薬の投与は早期に中止された。

投与された薬剤は，クレキサン及びプレドニゾロンであった。

**The patient's past medications include:**

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

COLIFOAM ENEMAS for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900) )　[v.23.0]　[10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

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Event of MODERATE ULCERATIVE COLITIS FLARE

**- Investigator:** DISEASE WORSENING. ULCERATIVE COLITIS FLARE. PANPROCTOCOLECTOMY COMPLETED.

**- AbbVie:** EVENT MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted]ABDOMINAL XRAY:** FECAL LOADING IN THE ASCENDING AND TRANSVERSE COLON WITHOUT APPRECIABLE MURAL THICKENING OR EVIDENCE OF FREE INTRAPERITONEAL GAS. NO EVIDENCE OF LARGE OR SMALL BOWEL LUMINAL DILATATION

[redacted] **20[redacted]CHEST X-RAY:** Normal

[redacted] **20[redacted]CT ABDOMEN AND PELVIS:** THICKENING OF THE RECTUM AND SIGMOID COLON WITH FATTY INFILTRATION OF THE WALL INDICATING LONG-STANDING CHANGE. HOWEVER, THERE IS PROBABLE SUPERIMPOSED ACUTE SIGMOID COLITIS. NO COLLECTION.

[redacted] **20[redacted]SIGMOIDOSCOPY:** MAYO 2

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 3[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA: LOW HEMOGLOBIN | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 15 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 59 | 59 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 59 | [redacted]20[redacted] / 96 | 38 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| ADALIMUMAB | 40 mg | OTHER: MONTHLY | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| INFLIXIMAB | 300 mg | OTHER: MONTHLY | Y-M: 20[redacted] |
| PREDNISONE | 40 mg | OTHER: DAILY | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: 8 WEEKS | Y-M: 20[redacted] |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] |
| PREDNISONE | 2.5 mg | OTHER: DAILY | Y-M: 20[redacted] |
| PREDNISONE | 30 mg | OTHER: DAILY | Y-M: 20[redacted] |
| MERCAPTOPURINE | 50 mg | OTHER: DAILY | Y-M: 20[redacted] / -188 |
| IRON | UNK | NOT REPORTED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| HYDROCORTISONE | 100 mg | TID | Y-M: 20[redacted] / 30 | Y-M: 20[redacted] / 34 |
| OMEPRAZOLE | 20 mg | OTHER: DAILY | Y-M: 20[redacted] / 31 | ONGOING |
| CALCIUM | 1 OTHER: TABLET | OTHER: DAILY | Y-M: 20[redacted] / 35 | ONGOING |
| PREDNISONE | 40 mg | OTHER: DAILY | Y-M: 20[redacted] / 35 | Y-M: 20[redacted] / 37 |
| VITAMIN D NOS | 2000 OTHER: UNITS | OTHER: DAILY | Y-M: 20[redacted] / 35 | ONGOING |
| CICLOSPORIN | 110 mg | OTHER: DAILY | Y-M: 20[redacted] / 38 | Y-M: 20[redacted] / 63 |
| HYDROCORTISONE | 300 mg | TID | Y-M: 20[redacted] / 38 | ONGOING |
| PREDNISONE | 60 mg | OTHER: DAILY | Y-M: 20[redacted] / 38 | ONGOING |
| IRON | UNK | NOT REPORTED | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | UC EXACBERATION |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 88 / 30 |
| **Age at AE Onset** | 3[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

[redacted]20[redacted](RX DAY 30): STOOL NPTST242-PARASITES: Negative

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 92 / 34 |
| **Duration of AE** | 5 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NO |
| **Discontinued Study Drug Due to the** | NO |

| | |
|---|---|
| **Event** | |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | UC EXACBERATION |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 96 / 38 |
| **Age at AE Onset** | 3[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 121 / 63 (25 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 26 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | UC EXACBERATION |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はイスラエルの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，貧血，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与88日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与92日後＊　，潰瘍性大腸炎の悪化は消失した。

投与88日後＊　，被験者は血便があり入院し，潰瘍性大腸炎の悪化と診断された。投与92日後＊，被験者は退院した。

投与された薬剤は，フラジール及びヒドロコルチゾンであった。

**The patient's past medications include:**

HUMIRA for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

PURINETHOL for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

---

1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900) )　[v.21.1]　[10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction recurred

Alternative Etiology for ABT-494 (Open Label)

---

Event of UC EXACERBATION

**- Investigator:** Not reported.

**- AbbVie:** Event is more likely related to recurring flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted]COLONOSCOPY:** Left sided ulcerative colitis

[redacted] **20[redacted]COLONOSCOPY:** demonstrated chronic disease

[redacted] **20[redacted]PARASITE STOOL TEST:** negative
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はイスラエルの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，貧血，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 2 の臨床経過：**
投与96日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与121日後＊　，潰瘍性大腸炎の悪化は消失した。

投与96日後＊　，被験者は血性下痢及び腹痛の悪化のため入院し，潰瘍性大腸炎の悪化と診断された。投与121日後＊　，被験者は退院した。入院中の本事象の臨床経過に関する詳細な情報は入手しなかった。

被験者の治験薬投与は早期に，及び完全に中止された。

投与された薬剤は，シクロスポリン，prednisone 及びヒドロコルチゾンであった。

**The patient's past medications include:**

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted]

ENTIVYO for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted], [redacted] 20[redacted]- [redacted] 20[redacted], [redacted] 20[redacted]- [redacted] 20[redacted])

PURINITHOL for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900) ) [v.22.0] [10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Open Label)

---

Event of UC EXACERBATION

**- Investigator:** UC EXACBERATION.

**- AbbVie:** RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 肛門膿瘍 | X | | | X |
| 基底細胞癌 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 4[redacted] | MALE | WHITE |

| Medical History | Onset Year |
|---|---|
| BASOCELLULAR CARCINOMA | 20[redacted] |
| CHICKEN POX | 19[redacted] |
| EXTENSIVE UC/PANCOLITIS | 19[redacted] |
| HYPERTENSION | 20[redacted] |
| LOCALIZED HERPES ZOSTER | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted]/ 1 | [redacted]20[redacted]/ 55 | 55 |

| | | | | | |
|---|---|---|---|---|---|
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted] / 56 [redacted] / 419 | 364 |
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted] / 420 | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| NEBIVOLOL | 5 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 8 WEEKS | Y-M: 20[redacted] |
| PREDNISONE | 35 mg | QD | Y-M: 20[redacted] |
| RAMIPRIL | 10 mg | QD | Y-M: 20[redacted] / -199 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / -91 |
| MESALAZINE | 4.8 g | QD | Y: 19[redacted] |
| AZATHIOPRINE | 200 mg | QD | Y: 19[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| NEBIVOLOL | 5 mg | QD | Y-M: 20[redacted] | Not reported |
| RAMIPRIL | 10 mg | QD | Y-M: 20[redacted] / -199 | Not reported |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / -91 | Not reported |
| PARACETAMOL | 1000 mg | TID | Y-M: 20[redacted] / 319 | Y-M: 20[redacted] / 325 |
| TINIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 324 | Y-M: 20[redacted] / 326 |
| AMOXICILLIN;CLAVULANIC ACID | 1 g | TID | Y-M: 20[redacted] / 327 | Y-M: 20[redacted] / 335 |
| ENOXAPARIN | 4000 IU | QD | Y-M: 20[redacted] / 327 | Y-M: 20[redacted] / 335 |
| METRONIDAZOLE | 500 mg | TID | Y-M: 20[redacted] / 327 | Y-M: 20[redacted] / 335 |
| TINIDAZOLE | 500 mg | BID | Y-M: 20[redacted] / 434 | Y-M: 20[redacted] / 442 |
| ACETYLSALICYLIC ACID | 100 OTHER: MG | QD | Y-M: 20[redacted] / 436 | Not reported |
| ATORVASTATIN | 20 mg | QD | Y-M: 20[redacted] / 436 | Not reported |
| AMOXICILLIN;CLAVULANIC ACID | 1 g | BID | Y-M: 20[redacted] / 524 | Not reported |
| PARACETAMOL | 1000 mg | PRN | Y-M: 20[redacted] / 524 | Not reported |
| MESALAZINE | 4.8 g | QD | Y: 19[redacted] | Not reported |

**Event #1: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | PERIANAL ABSCESS |
| **Preferred term** | 肛門膿瘍 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 743 / 324 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 326): Alanine Aminotransferase: 103 [9 - 59] U/L; Creatinine: 145.865379 [59.230184 - 103.431814] UMOL/L; Erythrocytes: 4.03 [4.5 - 6] 10^12/L; Hematocrit: 0.356 [0.42 - 0.54] FRACTION OF 1; Hemoglobin: 123 [130 - 175] G/L; Leukocytes: 15.62 [4.3 - 11] 10^9/L; NPTST201-LDH: 233 [125 - 220] U/L; NPTST277-REACTIVE C PROTEIN: 143.1 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 328): Alanine Aminotransferase: 72 [9 - 59] U/L; Creatinine: 104.315847 [59.230184 - 103.431814] UMOL/L; Erythrocytes: 3.71 [4.5 - 6] 10^12/L; Hematocrit: 0.33 [0.42 - 0.54] FRACTION OF 1; Hemoglobin: 113 [130 - 175] G/L; Leukocytes: 15.4 [4.3 - 11] 10^9/L; NPTST277-REACTIVE C PROTEIN: 98.8 [0 - 5] MG/L

**Microbiology**

[redacted]20[redacted] (RX DAY 327): OTHER ABSCESS DRAINAGE NPTST044-BACTERIAL CULTURE AND ANTIBIOGR: Positive-MULTISENSITIVE ESCHERICHIA COLI

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | GASTROENTERITIS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Event of Interest - Possible Malignancies, Event of Interest - Malignancy, Event of Interest - Non-melanoma Skin Cancer (NMSC)**

| | |
|---|---|
| **Event Description** | BASALIOMA (NON MELANOMA SKIN CANCER) ON LEFT NASAL ALA |
| **Preferred term** | 基底細胞癌 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 816 / 397 |
| **Age at AE Onset** | 5[redacted] |

**Laboratory Testing**

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |

| | |
|---|---|
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はイタリアの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肛門周囲膿瘍の事象を発現した。関連する病歴は，潰瘍性大腸炎，高血圧，軟性 S 状結腸鏡検査，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与743日後＊，被験者は肛門周囲膿瘍を発現した。

被験者は 38.5°C の発熱があった（COVID-19 検査は陰性であった）ため，paracetamol を服用したが，熱は高いままで，胃腸炎（非重篤），下痢，悪心及び関節痛を伴っていた。被験者は trimonase（チニダゾール）を服用したが，明らかな改善がみられなかったため，被験者は救急治療室を受診した。投与746日後＊　，被験者は入院し，肛門周囲膿瘍の外科的排膿を受けた。膿瘍排液の培養結果は，多剤感受性の大腸菌陽性であった。投与749日後＊　，被験者は，発熱を伴わず良好な臨床状態で退院した。排膿部位は清浄で，感染の徴候はなかった。

投与762日後＊　，被験者は，排膿部位の検診を受けるためにフォローアップ受診し，感染の徴候は認められなかった。排膿部位は清浄であったことが記録された。

投与された薬剤は，メトロニダゾール，エノキサパリン，アモキシリン/クラブラン酸及び trimonase であった。

**The patient's past medications include:**

AZATIOPRINA for ULCERATIVE COLITIS (19[redacted]- 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

DELTACORTENE for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Perianal abscess (10034447) (Anal abscess (10048946) ) [v.24.0] [10034447]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of PERIANAL ABSCESS

**- Investigator:** Gastroenteritis

**- AbbVie:** Risk factor includes pre-existing ulcerative colitis

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BACTERIAL CULTURE AND ANTIBIOGRAM:** Abscess drainage- Positive for Multisensitive Escherichia Coli

[redacted] **20[redacted] BODY TEMPERATURE:** 38.5 Degrees C

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 98.8 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] COVID-19 SWAB:** Negative

[redacted] **20[redacted] CREATININE:** 1.65 mg/dL (normal 0.67 to 1.17)

[redacted] **20[redacted] CREATININE:** 1.18 mg/dL (normal 0.67 to 1.17)

[redacted] **20[redacted]CRP:** 143.1 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted]FLEXIBLE SIGMOIDOSCOPY:** No inflammation seen(normal mucosa)

[redacted] **20[redacted]LOWER ABDOMEN CT SCAN:** 27 mm x 27 mm abscess in left perianal region. Soft tissue swelling. Absence of abdominal and pelvic abscess.

[redacted] **20[redacted]SARS-COV-2 TEST**: Nasopharyngeal swab-Negative

[redacted] **20[redacted]WBC:** 15.62 X10**9/L (normal 4.30 to 11)

[redacted] **20[redacted]WBC:** 15.4 X10**9/L (normal 4.30 to 11)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| 腎結石症 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 5[redacted] | FEMALE | WHITE |

| Medical History | Onset Year |
|---|---|
| ANEMIA | 20[redacted] |
| DEFICIT OF VITAMINE D | 20[redacted] |
| EARLY MENOPAUSE | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| HEARING LOSS | NOT REPORTED |
| HYPERTENSION | 20[redacted] |
| RENAL COLIC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | NEVER | |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted]/ 1 | [redacted]20[redacted]/ 54 | 54 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 55 | [redacted] / 98 | 44 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 99 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| INFLIXIMAB | 5 mg/kg | OTHER: EVERY 4 WEEKS | Y-M: [redacted] |
| MESALAZINE | 2 g | QD | Y-M: [redacted] |
| VEDOLIZUMAB | 300 mg | OTHER: EVERY 4 WEEKS | Y-M: [redacted] |
| PREDNISONE | 5 mg | QD | Y-M: [redacted] |
| OZANIMOD | NOT REPORTED | NOT REPORTED | Y-M: [redacted] |
| PREDNISONE | 10 mg | QD | Y-M: [redacted] / -160 |
| BISOPROLOL;HYDROCHLOROTHIAZIDE | 2.50 mg | QD | Y-M: [redacted] / -148 |
| CICLOSPORIN | NOT REPORTED | NOT REPORTED | Y: [redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| BISOPROLOL;HYDROCHLOROTHIAZIDE | 2.50 mg | QD | Y-M: [redacted] / -148 | Not reported |
| MESALAZINE | 800 mg | TID | Y-M: [redacted] / 1 | Not reported |
| ASCORBIC ACID;IRON | 1 OTHER: TABLET | QD | Y-M: [redacted] / 66 | Y-M: [redacted] / 157 |
| AMOXICILLIN;CLAVULANIC ACID | 875/125 mg | TID | Y-M: [redacted] / 143 | Y-M: [redacted] / 149 |
| CEFIXIME | 400 mg | QD | Y-M: [redacted] / 489 | Y-M: [redacted] / 493 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | KIDNEY STONES |
| **Preferred term** | 腎結石症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 237 / 139 |
| **Age at AE Onset** | [redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 246 / 148 |

| | |
|---|---|
| **Duration of AE** | 10 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | SAE DUE TO KIDNEY STONES SURGERY |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | KIDNEY STONE |
| **Preferred term** | 腎結石症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 310 / 212 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| [redacted]20[redacted](RX DAY 202): URINE NPTST338-URINE CULTURE: Positive-E.COLI 1.000.000 UFC/ML | |
| **AE Stopped Initial Rx Day / Rx Day** | 313 / 215 |
| **Duration of AE** | 4 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | KIDNEY STONES (COMORBIDITY) |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #3: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | CPK INCREASED |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 603 / 505 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |

| | |
|---|---|
| **Duration of AE** | NOT REPORTED |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

Generated: [redacted]
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はイタリアの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腎結石の事象を発現した。関連する病歴は，早発閉経，高血圧，ビタミン D の欠乏，腎仙痛，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 1 の臨床経過：**

投与237日後＊，被験者は，腎結石を発現した。投与246日後＊，腎結石は消失した。

本事象発現前の投与51日後＊，被験者は腎結石（非重篤）を経験した。

投与237日後＊　，被験者は血尿及び腎疝痛の徴候及び症状があり，左側の腎結石砕石術のために入院した。経皮的に左側の尿管鏡検査を行い，両側にダブル J ステントを留置した。 投与240日後＊，被験者は左側の腎瘻造設を行い，退院した。投与245日後＊，腎瘻を抜去した。

投与された薬剤は，アモキシシリン・クラブラン酸合剤であった。

**The patient's past medications include:**

DELTACORTENE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

PENTACOL for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

OZANIMOD for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

---

1) Kidney stones (10023437) (Nephrolithiasis (10029148) ) [v.24.0] [10023437]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of KIDNEY STONES

**- Investigator:** SAE due to kidney stones surgery.

**- AbbVie:** The event is more likely related to pre-existing history of renal colic. Nephrolithiasis is relatively common problem with increased prevalence in Italy over the years with a rate of 9%.

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者はイタリアの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腎結石の手術の事象を発現した。関連する病歴は，早発閉経，ビタミンDの欠乏，腎仙痛，貧血，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

**Event 2 の臨床経過：**

投与310日後＊ ，被験者は腎結石の手術を発現した。投与313日後＊ ，腎結石の手術は消失した。

投与310日後＊　，被験者は右側の尿管鏡検査及び右側のダブル J ステントの抜去のために入院した。被験者は血尿の徴候及び症状があった。被験者は腎結石及び腎仙痛の病歴があった。投与313日後＊，被験者はダブル J ステントを留置し，右側の腎瘻造設を行い，退院した。

被験者の危険因子には，尿路結石，尿路閉塞，尿路感染の再発及び高血圧の病歴が含まれた。

投与された薬剤は，cefiximina であった。

**The patient's past medications include:**

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

PENTACOL ([redacted])

DELTACORTENE for ULCERATIVE COLITIS ([redacted])

OZANIMOD for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

---

1)　Kidney stone (10023436)　(Nephrolithiasis (10029148) )　[v.24.0]　[10023436]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of KIDNEY STONE SURGERY

**- Investigator:** KIDNEY STONES (COMORBIDITY)

**- AbbVie:** The event is more likely related to pre-existing history of renal colic. Nephrolithiasis is relatively common problem with increased prevalence in Italy over the years with a rate of 9%.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted]CHEST X-RAY:** normal

[redacted] **20[redacted]SARS COV 2 SWAB:** negative

[redacted] **20[redacted]URINE CULTURE:** Positive - E.coli 1.000.000 UFC/ml

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | X | | |
| 好中球数減少 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 1[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| ALLERGIC RHINITIS | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| HEADACHE | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted]/ 1 | [redacted]20[redacted]/ 55 | 55 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted]/ 57 | [redacted]20[redacted]/ 427 | 371 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted]20[redacted]/ 428 | [redacted]20[redacted]/ 836 | 409 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] |
| BETAMETHASONE | 3 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| CLOSTRIDIUM BUTYRICUM | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS | 3 OTHER: TAB | BID | Y-M: 20[redacted] |
| BUDESONIDE | 2 mg | BID | Y-M: 20[redacted] |
| PARACETAMOL | 300 mg | PRN | Y-M: 20[redacted] |
| FEXOFENADINE | 60 mg | PRN | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted]/ 400 |
| BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS | 3 OTHER: TAB | BID | Y-M: 20[redacted] | Y-M: 20[redacted]/ 400 |
| PARACETAMOL | 300 mg | PRN | Y-M: 20[redacted] | ONGOING |
| CARBAZOCHROME | 100 mg | QD | Y-M: 20[redacted]/ 401 | Y-M: 20[redacted]/ 401 |
| GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE | 500 mL | BID | Y-M: 20[redacted]/ 401 | Y-M: 20[redacted]/ 404 |
| PREDNISOLONE | 60 mg | QD | Y-M: 20[redacted]/ 401 | Y-M: 20[redacted]/ 404 |
| TRANEXAMIC ACID | 500 mg | QD | Y-M: 20[redacted]/ 401 | Y-M: 20[redacted]/ 401 |
| ESOMEPRAZOLE | 20 mg | QD | Y-M: 20[redacted]/ 402 | ONGOING |

| | | | | |
|---|---|---|---|---|
| GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE | 500 mL | QD | Y-M: 20[redacted] / 405 | Y-M: 20[redacted] / 405 |
| PREDNISOLONE | 50 mg | QD | Y-M: 20[redacted] / 405 | Y-M: 20[redacted] / 407 |
| MAGNESIUM CITRATE | 100 g | PRN | Y-M: 20[redacted] / 406 | Y-M: 20[redacted] / 406 |
| GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE | 500 mL | QD | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 407 |
| HYDROXYZINE | 50 mg | PRN | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 407 |
| LIDOCAINE | 1 mL | PRN | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 407 |
| MIDAZOLAM | 3 mg | PRN | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 407 |
| PENTAZOCINE | 15 mg | PRN | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 407 |
| TIMEPIDIUM | 7.5 mg | PRN | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 407 |
| PREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 417 |
| FEXOFENADINE | 60 mg | PRN | Y: 20[redacted] | ONGOING |

**Event #1: Event of Interest - Neutropenia**

| | |
|---|---|
| **Event Description** | NEUTROPHIL COUNT DECREASED |
| **Preferred term** | 好中球数減少 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 456 / 29 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 477 / 50 |
| **Duration of AE** | 22 DAYS |
| **Severity** | SEVERE |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | WORSENING OF UC |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 828 / 401 |
| **Age at AE Onset** | [redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 839 / 412 (3 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 12 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | WORSENING OF UC |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の [redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

**Event 2 の臨床経過：**

投与828日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与839日後＊　　，潰瘍性大腸炎の悪化は消失した。

投与813日後＊　，被験者は発熱を経験した。投与816日後＊　　，被験者は左側腹部痛を発現した。投与820日後＊　，被験者は悪心及び嘔吐を発現した。投与827日後＊　　，被験者は受診し，腹部 CT 検査が実施された。治験責任医師は，潰瘍性大腸炎が悪化したと判断した。　投与828日後＊，被験者は，発熱，左側腹部痛，悪心及び嘔吐があり入院した。投与834日後＊，被験者は結腸内視鏡検査を受けた結果，下行結腸狭窄が顕著であった。投与839日後＊　，被験者は退院した。

治験責任医師によると，被験者の危険因子は潰瘍性大腸炎であった。被験者には関連する家族歴はなかった。本事象により，治験薬の投与は完全に中止された。

投与された薬剤はプレドニンであった。

**The patient's past medications include:**

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

STERONEMA for ULCERATIVE COLITIS ([redacted])

MIYA BM for ULCERATIVE COLITIS ([redacted])

RECTABUL for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900) )　[v.24.0]　[10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

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Event of WORSENING OF UC

**- Investigator:** Worsening of Ulcerative Colitis

**- AbbVie:** Event is more likely related to pre-existing ulcerative colitis

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ABDOMINAL CT SCAN:** Wall thickening from distal portion of the transverse colon to the rectum. It is considered to be active lesion of US

[redacted] **20[redacted] COLONOSCOPY:** Descending colon stenosis. Total colitis (mayo endoscopy subscore 2)

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Neutrophil count decreased: Study drug interrupted.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| 深部静脈血栓症 | | X | | X |
| 大腸ポリープ | X | | | |
| 腎結石症 | X | | | |
| 腎盂腎炎 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| ANEMIA: NOT APPLICABLE | 20[redacted] |
| DRUG ALLERGIES/REACTIONS: NOT APPLICABLE | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| HYPERLIPIDEMIA: NOT APPLICABLE | 20[redacted] |
| NEPHROLITHIASIS: NOT APPLICABLE | 20[redacted] |
| OTHER: CHRONIC RENAL FAILURE | 20[redacted] |
| OTHER: HYPERURICEMIA | 20[redacted] |
| OTHER: OVERACTIVE BLADDER | 20[redacted] |
| PNEUMONIA: LATENT TUBERCULOSIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 10 | 19[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | FORMER | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 30 mg | ORAL | QD | [redacted] / 1 | [redacted] / 57 | 57 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 58 | [redacted] / 161 | 104 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 162 | [redacted] / 1666 | 1505 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| DIMETICONE | 100 mg | OTHER: ONCE | Y-M: 20[redacted] |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] |
| PREDNISOLONE | 15 mg | OTHER: UNKNOWN | Y-M: 20[redacted] |
| PREDNISOLONE | 30 mg | QD | Y-M: 20[redacted] |
| ALL OTHER NON-THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] |
| AZATHIOPRINE | 25 mg | QD | Y-M: 20[redacted] |
| TACROLIMUS | NOT REPORTED | OTHER: UNK | Y-M: 20[redacted] |
| TACROLIMUS | 5 mg | BID | Y-M: 20[redacted] |
| PREDNISOLONE | 1 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 250 mg | OTHER: WEEK0,2,6 | Y-M: 20[redacted] |
| AMINO ACIDS NOS;CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;VITAMINS NOS | 80 g | PRN | Y-M: 20[redacted] |
| BETAMETHASONE | 1 g | QD | Y-M: 20[redacted] |
| OTHER THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| TACROLIMUS | 4 mg | BID | Y-M: 20[redacted] |
| FAMOTIDINE | 20 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1 g | QD | Y-M: 20[redacted] |
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] |
| TACROLIMUS | 5 mg | BID | Y-M: 20[redacted] |
| TACROLIMUS | 4 mg | BID | Y-M: 20[redacted] |
| MERCAPTOPURINE | 10 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| POLAPREZINC | 75 mg | BID | Y-M: 20[redacted] |
| ARNICA MONTANA;CONVALLARIA MAJALIS;ECHINACEA ANGUSTIFOLIA;EQUISETUM ARVENSE;MAGNESIUM PHOSPHATE;RUBIA TINCTORUM;SOLIDAGO VIRGAUREA | 2 OTHER: TABLETS | TID | Y-M: 20[redacted] / -187 |
| ISONIAZID | 300 mg | QD | Y-M: 20[redacted] / -187 |
| BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS | 2 OTHER: TABLETS | TID | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| DIMETICONE | 100 mg | OTHER: ONCE | Y-M: 20[redacted] | Y-M: 20[redacted] / 1011 |
| AMINO ACIDS NOS;CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;VITAMINS NOS | 80 g | PRN | Y-M: 20[redacted] | ONGOING |
| FAMOTIDINE | 20 mg | QD | Y-M: 20[redacted] | ONGOING |
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] | ONGOING |
| POLAPREZINC | 75 mg | BID | Y-M: 20[redacted] | ONGOING |
| ARNICA MONTANA;CONVALLARIA MAJALIS;ECHINACEA ANGUSTIFOLIA;EQUISETUM ARVENSE;MAGNESIUM PHOSPHATE;RUBIA TINCTORUM;SOLIDAGO VIRGAUREA | 2 OTHER: TABLETS | TID | Y-M: 20[redacted] / -187 | Y-M: 20[redacted] / 660 |
| SENNOSIDE A+B | 24 mg | QD | Y-M: 20[redacted] / 336 | Y-M: 20[redacted] / 336 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 336 | Y-M: 20[redacted] / 336 |
| DIMETICONE | 100 mg | QD | Y-M: 20[redacted] / 337 | Y-M: 20[redacted] / 337 |
| LACTULOSE | 90 mL | QD | Y-M: 20[redacted] / 337 | Y-M: 20[redacted] / 337 |
| LIDOCAINE | 15 mL | QD | Y-M: 20[redacted] / 337 | Y-M: 20[redacted] / 337 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 10 mL | QD | Y-M: 20[redacted] / 337 | Y-M: 20[redacted] / 337 |
| SODIUM PICOSULFATE | 75 mg | OTHER: ONCE | Y-M: 20[redacted] / 443 | Y-M: 20[redacted] / 443 |
| DIMETICONE | 100 mg | OTHER: ONCE | Y-M: 20[redacted] / 444 | Y-M: 20[redacted] / 444 |
| HYOSCINE | 20 mg | OTHER: ONCE | Y-M: 20[redacted] / 444 | Y-M: 20[redacted] / 444 |
| LACTULOSE | 58500 mg | OTHER: ONCE | Y-M: 20[redacted] / 444 | Y-M: 20[redacted] / 444 |

| | | | | |
|---|---|---|---|---|
| LIDOCAINE | 15 mL | OTHER: ONCE | Y-M: 20[redacted] / 444 | Y-M: 20[redacted] / 444 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | OTHER: ONCE | Y-M: 20[redacted] / 444 | Y-M: 20[redacted] / 444 |
| CEFTRIAXONE | 1 g | BID | Y-M: 20[redacted] / 589 | Y-M: 20[redacted] / 591 |
| LIDOCAINE | 10 mL | QD | Y-M: 20[redacted] / 589 | Y-M: 20[redacted] / 589 |
| CEFACLOR | 250 mg | TID | Y-M: 20[redacted] / 591 | Y-M: 20[redacted] / 595 |
| CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE | 500 mL | OTHER: ONCE | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 631 |
| CEFOTIAM | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 631 |
| DICLOFENAC | 25 mg | OTHER: ONCE | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 631 |
| GLYCEROL | 120 mL | OTHER: ONCE | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 631 |
| HYDROXYZINE | 25 mg | OTHER: ONCE | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 631 |
| PENTAZOCINE | 15 mg | OTHER: ONCE | Y-M: 20[redacted] / 631 | Y-M: 20[redacted] / 631 |
| CEFACLOR | 250 mg | TID | Y-M: 20[redacted] / 632 | Y-M: 20[redacted] / 632 |
| SENNOSIDE A+B | 24 mg | OTHER: ONCE | Y-M: 20[redacted] / 1197 | Y-M: 20[redacted] / 1197 |
| SODIUM PICOSULFATE | 10 mL | OTHER: ONCE | Y-M: 20[redacted] / 1198 | Y-M: 20[redacted] / 1198 |
| DIMETICONE | 100 mg | OTHER: ONCE | Y-M: 20[redacted] / 1199 | Y-M: 20[redacted] / 1199 |
| LACTULOSE | 58500 mg | OTHER: ONCE | Y-M: 20[redacted] / 1199 | Y-M: 20[redacted] / 1199 |
| LIDOCAINE | 15 mL | OTHER: ONCE | Y-M: 20[redacted] / 1199 | Y-M: 20[redacted] / 1199 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | OTHER: ONCE | Y-M: 20[redacted] / 1199 | Y-M: 20[redacted] / 1199 |
| ROSUVASTATIN | 2.5 mg | QD | Y-M: 20[redacted] / 1228 | ONGOING |
| VALSARTAN | 80 mg | QD | Y-M: 20[redacted] / 1228 | ONGOING |
| CALCIUM CHLORIDE;NEOSTIGMINE;POTASSIUM ASPARTATE;SODIUM BICARBONATE;SODIUM CHLORIDE | 2-3 OTHER: DROPS | QID | Y-M: 20[redacted] / 1318 | ONGOING |
| PIRENOXINE | 1-2 OTHER: DROPS | QID | Y-M: 20[redacted] / 1318 | ONGOING |
| SENNOSIDE A+B | 24 mg | OTHER: ONCE | Y-M: 20[redacted] / 1345 | Y-M: 20[redacted] / 1345 |
| SODIUM PICOSULFATE | 75 mg | OTHER: ONCE | Y-M: 20[redacted] / 1345 | Y-M: 20[redacted] / 1345 |

| | | | | |
|---|---|---|---|---|
| DIMETICONE | 100 mg | OTHER: ONCE | Y-M: 20[redacted] / 1346 | Y-M: 20[redacted] / 1346 |
| LACTULOSE | 58500 mg | OTHER: ONCE | Y-M: 20[redacted] / 1346 | Y-M: 20[redacted] / 1346 |
| LIDOCAINE | 15 mL | OTHER: ONCE | Y-M: 20[redacted] / 1346 | Y-M: 20[redacted] / 1346 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | OTHER: ONCE | Y-M: 20[redacted] / 1346 | Y-M: 20[redacted] / 1346 |
| SENNOSIDE A+B | 24 mg | QD | Y-M: 20[redacted] / 1448 | Y-M: 20[redacted] / 1448 |
| SODIUM PICOSULFATE | 75 mg | QD | Y-M: 20[redacted] / 1449 | Y-M: 20[redacted] / 1449 |
| DIMETICONE | 100 mg | QD | Y-M: 20[redacted] / 1450 | Y-M: 20[redacted] / 1450 |
| LACTULOSE | 90 mL | QD | Y-M: 20[redacted] / 1450 | Y-M: 20[redacted] / 1450 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | QD | Y-M: 20[redacted] / 1450 | Y-M: 20[redacted] / 1450 |
| PANCREATIN;SIMETICONE | 2.5 g | QD | Y-M: 20[redacted] / 1450 | Y-M: 20[redacted] / 1450 |
| APIXABAN | 10 mg | BID | Y-M: 20[redacted] / 1512 | Y-M: 20[redacted] / 1518 |
| APIXABAN | 5 mg | BID | Y-M: 20[redacted] / 1519 | ONGOING |
| BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS | 2 OTHER: TABLETS | TID | Y: 20[redacted] | ONGOING |

**Event #1: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | HIGH CPK |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 484 / 323 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 498 / 337 |
| **Duration of AE** | 15 DAYS |

| | |
|---|---|
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | COLONIC POLYP |
| **Preferred term** | 大腸ポリープ |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 498 / 337 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 611 / 450 |
| **Duration of AE** | 114 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | SPORADIC LESION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: Serious Adverse Event, Event of Interest - Serious Infections**

| | |
|---|---|
| **Event Description** | CALCULOUS PYELONEPHRITIS |
| **Preferred term** | 腎結石症，腎盂腎炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 750 / 589 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 757 / 596 |
| **Duration of AE** | 8 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |

| | |
|---|---|
| **Investigator Alternative Etiology** | NEPHROLITHIASIS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #4: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | WORSENING OF NEPHROLITHIASIS(RIGHT) |
| **Preferred term** | 腎結石症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 792 / 631 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 794 / 633 |
| **Duration of AE** | 3 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | TREATMENT FOR ADVERSE EVENT "WORSENING OF NEPHROLITHIASIS(RIGHT)". |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #5: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | COLON POLYP |
| **Preferred term** | 大腸ポリープ |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1360 / 1199 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 1360 / 1199 |
| **Duration of AE** | 1 DAY |
| **Severity** | MILD |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NONE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #6: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | COLON POLYP |
| **Preferred term** | 大腸ポリープ |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1507 / 1346 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 1507 / 1346 |
| **Duration of AE** | 1 DAY |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NONE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #7: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | COLON POLYP |
| **Preferred term** | 大腸ポリープ |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1611 / 1450 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 1678 / 1517 (12 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 68 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |

| | |
|---|---|
| **Investigator Alternative Etiology** | NONE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #8: AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event**

| | |
|---|---|
| **Event Description** | LEFT LEG DEEP VEIN THROMBOSIS |
| **Preferred term** | 深部静脈血栓症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 1668 / 1507 (2 DAYS AFTER LAST TREATMENT) |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

Generated: [redacted]
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，大腸ポリープの事象を発現した。

**Event 2 の臨床経過：**

投与498日後＊，被験者は大腸ポリープを発現した。投与611日後＊　，大腸ポリープは消失した。

投与604日後＊　，被験者は 投与605日後＊に実施の大腸ポリープ切除術のために入院した。投与606日後＊，被験者は退院した。

Causality for ABT-494 (Open Label)

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1)　Colonic polyp (10010003)　(Large intestine polyp (10051589) )　[v.21.0]　[10010003]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:**Not Applicable

Alternative Etiology for ABT-494 (Open Label)

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Event of COLONIC POLYP

**- Investigator:** Sporadic lesion.

**- AbbVie:** Risk factors include male gender, age and pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted]COLONOSCOPY:** clear demarcation between normal and inflamed colonic mucosa seen; distance of demarcation from the anal verge 20.

[redacted] **20[redacted] HYSTOLOGY:** Rectum(biopsy),active stage of ulcerative colitis Rectum(EMR),tubular adenoma
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，結石性腎盂腎炎の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），腎結石症，慢性腎不全，高脂血症，高尿酸血症，広範囲な潰瘍性大腸炎（全大腸炎型），過活動性膀胱及び少量の元飲酒者（1 日 2 杯未満）であった。

**Event 3 の臨床経過：**

投与750日後＊　，被験者は結石性腎盂腎炎を発現した。投与757日後＊　，結石性腎盂腎炎は消失した。

投与750日後＊　，被験者は結石性腎盂腎炎と診断された右側の腹痛のために入院した。同日，尿管ステントが留置された。投与757日後＊，被験者は退院した。

投与された薬剤は，セフトリアキソンナトリウム及びケフラールであった。

**The patient's past medications include:**

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

LEUKERIN POWDER for ULCERATIVE COLITIS ([redacted])

LCAP during hemodialysis for ULCERATIVE COLITIS ([redacted])

GCAP during hemodialysis for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1) Pyelonephritis (10037596) (Pyelonephritis (10037596) ) [v.21.1] [10037596]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

2) Renal calculus (10038386) (Nephrolithiasis (10029148) ) [v.21.1] [10038386]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Open Label)

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Event of CALCULOUS PYELONEPHRITIS

**- Investigator:** Nephrolithiasis

**- AbbVie:** Event more likely related to pre-existing history of nephrolithiasis. Additional risk factor is pre-existing hyperuricemia.
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の成人男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腎結石症の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），腎結石症，慢性腎不全，高脂血症，高尿酸血症，潰瘍性大腸炎及び元飲酒者（1 日 2 杯未満）であった。

**Event 4 の臨床経過：**

投与792日後＊　　，被験者は腎結石症の悪化を発現した。投与794日後＊　，腎結石症の悪化は消失した。

投与792日後＊に被験者は入院し，投与794日後＊に退院した。

投与された薬剤は，ソルアセトＦ輸液，セフォチアム塩酸塩，アタラックス-P 及びソセゴンであった。

**The patient's past medications include:**

CEFTRIAXONE SODIUM HYDRATE for CALCULOUS PYELONEPHRITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

LIDOCAINE HYDROCHLORIDE INJ for URETER STENT PLACEMENT ([redacted] 20[redacted]- [redacted] 20[redacted])

KEFRAL for CALCULOUS PYELONEPHRITIS ([redacted] 20[redacted]- [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1)　Nephrolithiasis (10029148)　(Nephrolithiasis (10029148) )　[v.21.1]　[10029148]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

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Event of WORSENING OF NEPHROLITHIASIS

**- Investigator:** TREATMENT FOR ADVERSE EVENT "WORSENING OF NEPHROLITHIASIS(RIGHT)".

**- AbbVie:** EVENT IS MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF NEPHROLITHIASIS.
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，大腸ポリープの事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），高脂血症，広範囲な潰瘍性大腸炎（全大腸炎型），内視鏡下での粘膜切除術及び元飲酒者（1 日 2 杯未満）であった。

**Event 5 の臨床経過：**

投与1360日後＊ ，被験者は大腸ポリープを発現した。投与1360日後＊ ，大腸ポリープは消失した。

本事象発現前に，被験者は大腸ポリープの事象を複数回経験していた。投与の39ヵ月後＊，被験者は大腸ポリープ（非重篤）を発現した。

投与1360日後＊ ，被験者は結腸内視鏡検査のために入院した。同日，被験者は結腸内視鏡検査及び内視鏡下での粘膜切除術を受けた。投与1361日後＊，被験者は退院した。

**The patient's past medications include:**

ASACOL TABLETS for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

GCAP for ULCERATIVE COLITIS ([redacted])

PENTASA TAB for ULCERATIVE COLITIS ([redacted])

PROGRAF CAPSULES for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE FOR I.V. INFUSION100 for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

LCAP for ULCERATIVE COLITIS ([redacted])

PENTASA SUPPOSITORIES for ULCERATIVE COLITIS ([redacted])

LEUKERIN POWDER 10% for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Colonic polyp (10010003) (Large intestine polyp (10051589) ) [v.23.1] [10010003]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of COLON POLYP

**- Investigator:** None

**- AbbVie:** Colon polyps are common in the general population and in men between age 65-69, there was a 34% prevalence on routine colonoscopy.
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の成人男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，大腸ポリープの事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），高脂血症，潰瘍性大腸炎及び元飲酒者（1 日 2 杯未満）であった。

**Event 6 の臨床経過：**

投与1507日後＊ ，被験者は大腸ポリープを発現した。投与1507日後＊，大腸ポリープは消失した。

投与1507日後＊ ，被験者は結腸内視鏡検査のために入院した。同日，ポリープが発見され，被験者は内視鏡下での粘膜切除術を受けた。投与1508日後＊，被験者は退院した。

**The patient's past medications include:**

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

GCAP for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

LCAP for ULCERATIVE COLITIS ([redacted])

LEUKERIN for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

---

1) Colonic polyp (10010003) (Large intestine polyp (10051589) ) [v.23.1] [10010003]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of COLON POLYP

**- Investigator:** Not reported

**- AbbVie:** Colon polyps are common in the general population and in men between age 65-69, there was a 31% prevalence on routine colonoscopy.

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は 6[redacted] 歳の日本人男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，大腸ポリープの事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），潰瘍性大腸炎及び元飲酒者（1 日 2 杯未満）であった。

この被験者は，先行の M14-234 試験では，被験者番号[redacted] であり，20[redacted] 年[redacted] 月[redacted] 日から 20[redacted]年[redacted] 月[redacted] 日まで盲検化された被験薬を投与された。

**Event 7 の臨床経過：**

投与1611日後＊　，被験者は大腸ポリープを発現した。投与1678日後＊ ，大腸ポリープは消失した。

投与1666日後＊　，被験者は入院した。投与1667日後＊　，被験者は内視鏡的粘膜下層剥離術を受けた。投与1668日後＊　，被験者は四肢静脈超音波検査を受け，左脚深部静脈血栓症の非重篤な事象を発現した。投与1678日後＊，被験者は退院した。

**The patient's past medications include:**

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

LEUKERIN POWDER 10% for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

LIALDA for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

---

1) Colonic polyp (10010003) (Large intestine polyp (10051589) ) [v.24.0] [10010003]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

---

Event of COLON POLYP

- **Investigator:** None

**- AbbVie:** Colonic polyps are highly prevalent in the general population. Additional risk factors include advanced age and male gender.

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Deep vein thrombosis: lower limb. Asymptomatic. Study drug discontinued. Ongoing AE of Hypertension.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 埋伏歯 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 2[redacted] | FEMALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| LEFT SIDED UC | 20[redacted] |
| TEMPORARILY ALLERGIC FOR SKIN URTICARIA DUE TO ADALIMUMAB | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 Placebo (IND) | | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 53 | 53 |
| M14-234 SS2 ABT-494 (OL) | 45 mg | ORAL | QD | [redacted]20[redacted] / 54 | [redacted]20[redacted] / 111 | 58 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 112 | [redacted]20[redacted] / 480 | 369 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted]20[redacted]/ 481 | [redacted]20[redacted]/ 834 | 354 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | NOT REPORTED | Y-M: 20[redacted] |
| FEXOFENADINE | 60 mg | BID | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: EVRY OTHER WEEK | Y-M: 20[redacted] |
| AZATHIOPRINE | 25 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | QD | Y-M: 20[redacted] |
| BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] | ONGOING |
| FEXOFENADINE | 60 mg | BID | Y-M: 20[redacted] | ONGOING |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] / 61 | Y-M: 20[redacted] / 362 |
| ALENDRONIC ACID | 35 mg | OTHER: ONCE A WEEK | Y-M: 20[redacted] / 169 | Y-M: 20[redacted] / 288 |
| SENNOSIDE A+B | 24 mg | QD | Y-M: 20[redacted] / 329 | Y-M: 20[redacted] / 329 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 329 | Y-M: 20[redacted] / 329 |
| DIMETICONE | 5 mL | QD | Y-M: 20[redacted] / 330 | Y-M: 20[redacted] / 330 |
| LACTULOSE | 90 mL | QD | Y-M: 20[redacted] / 330 | Y-M: 20[redacted] / 330 |
| LIDOCAINE | 5 mL | QD | Y-M: 20[redacted] / 330 | Y-M: 20[redacted] / 330 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | QD | Y-M: 20[redacted] / 330 | Y-M: 20[redacted] / 330 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | BILATERALLY-BURIED THIRD MOLARS IN THE LOWER JAW |
| **Preferred term** | 埋伏歯 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 756 / 276 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | PERSONALLY DENTAL MANIFESTATION DURING GROWTH-UP |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 2[redacted]歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，下顎両側第三大臼歯埋伏の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

## Event 1 の臨床経過：

投与756日後＊，被験者は下顎両側第三大臼歯埋伏を発現した。

投与842日後＊，被験者は疼痛及び埋伏した下顎両側第三大臼歯抜去のために入院した。

治験責任医師によると，被験者の関連する危険因子は，成長中にみられる個人的な歯科症状であった。

**The patient's past medications include:**

BIO-THREE for ULCERATIVE COLITIS (20[redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

---

1) Impacted wisdom tooth (10021514) (Tooth impacted (10044042) ) [v.24.1] [10021514]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of BILATERALLY-BURIED THIRD MOLARS IN THE LOWER JAW

**- Investigator:** Personally dental manifestation during growth-up.

**- AbbVie:** Event more likely due to overcrowding in mouth. Event not consistent with study drug's mechanism of action.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **BODY WEIGHT:** 5[redacted] KG

[redacted] **X-RAY TEETH:** bilaterally buried third molars in the lower jaw

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 完全房室ブロック | X | | | |
| 網膜静脈閉塞 | | X | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 7[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| COLONIC POLYP | 19[redacted] |
| HYPERCHOLESTEROLEMIA | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 2 PACK | 37 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | 2 - 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2<br>ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 53 | 53 |

| | | | | | |
|---|---|---|---|---|---|
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted] / 54 [redacted] / 420 | 367 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 421 [redacted] / 696 | 276 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1 g | QD | Y-M: 20[redacted] |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 3 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 800 mg | TID | Y-M: 20[redacted] |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 25 mg | QD | Y-M: 20[redacted] |
| BUDESONIDE | 2 mg | PRN | Y-M: 20[redacted] |
| BUDESONIDE | 2 mg | PRN | Y-M: 20[redacted] |
| BETAMETHASONE | 0.5 mg | QD | Y-M: 20[redacted] |
| BUDESONIDE | 2 mg | BID | Y-M: 20[redacted] |
| BETAMETHASONE | 0.5 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1 g | QD | Y: 20[redacted] |
| AMLODIPINE;VALSARTAN | 1 OTHER: TABLET | QD | Y: 20[redacted] |
| ATORVASTATIN | 5 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] | ONGOING |
| AMLODIPINE | 7.5 mg | QD | Y-M: 20[redacted] / 164 | Y-M: 20[redacted] / 196 |
| TELMISARTAN | 80 mg | QD | Y-M: 20[redacted] / 164 | Y-M: 20[redacted] / 196 |
| AMLODIPINE;TELMISARTAN | 1 OTHER: TABELT | QD | Y-M: 20[redacted] / 197 | ONGOING |
| LEVOFLOXACIN | 1 gtt | TID | Y-M: 20[redacted] / 269 | ONGOING |
| RANIBIZUMAB | 0.5 mg | OTHER: 1 TIME PER MONTH | Y-M: 20[redacted] / 269 | ONGOING |
| SENNOSIDE A+B | 24 mg | QD | Y-M: 20[redacted] / 291 | Y-M: 20[redacted] / 291 |

| | | | | |
|---|---|---|---|---|
| SODIUM PICOSULFATE | 75 mg | QD | Y-M: 20[redacted] / 291 | Y-M: 20[redacted] / 291 |
| DIMETICONE | 100 mg | QD | Y-M: 20[redacted] / 292 | Y-M: 20[redacted] / 292 |
| LACTULOSE | 90 mL | QD | Y-M: 20[redacted] / 292 | Y-M: 20[redacted] / 292 |
| LIDOCAINE | 15 mL | QD | Y-M: 20[redacted] / 292 | Y-M: 20[redacted] / 292 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | QD | Y-M: 20[redacted] / 292 | Y-M: 20[redacted] / 292 |
| AMLODIPINE;VALSARTAN | 1 OTHER: TABLET | QD | Y: 20[redacted] | Y-M: 20[redacted] / 163 |
| ATORVASTATIN | 5 mg | QD | Y: 20[redacted] | ONGOING |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | COMPLETE ATRIOVENTRICULAR BLOCK |
| **Preferred term** | 完全房室ブロック |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 583 / 163 |
| **Age at AE Onset** | 7[redacted] |

**Laboratory Testing**

[redacted]20[redacted](RX DAY 163): Potassium: 3.8 [3.6 - 4.8] MMOL/L; [redacted]20[redacted](RX DAY 164): Potassium: 3.9 [3.6 - 4.8] MMOL/L; [redacted]20[redacted](RX DAY 165): Potassium: 4 [3.6 - 4.8] MMOL/L; [redacted]20[redacted](RX DAY 166): Potassium: 3.9 [3.6 - 4.8] MMOL/L; [redacted]20[redacted](RX DAY 169): Potassium: 3.8 [3.6 - 4.8] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 592 / 172 |
| **Duration of AE** | 10 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | ARTERIOSCLERPOSIS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING |

**Event #2: AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | BRANCH RETINA VEIN OCCLUSION(LEFT) |
| **Preferred term** | 網膜静脈閉塞 |

| | |
|---|---|
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 674 / 254 |
| **Age at AE Onset** | 7[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

Generated: [redacted]20[redacted]16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，完全房室ブロックの事象を発現した。関連する病歴は，元喫煙者（1 日 2 箱を 37 年間），高コレステロール血症，高血圧，潰瘍性大腸炎及び現飲酒者（1 日 2–4 杯）であった。

**Event 1 の臨床経過：**

投与583日後＊ ，被験者は完全房室ブロックを発現した。投与592日後＊ ，完全房室ブロックは消失した。

投与583日後＊ ，被験者は徐脈のために入院した。房室ブロックと診断された。同日，体外型心臓ペースメーカが装着された。投与585日後＊ ，体外型心臓ペースメーカは永久的心臓ペースメーカに切り替えられた。投与592日後＊，被験者は退院した。

治験責任医師は，本事象の危険因子は動脈硬化症であると述べた。

**The patient's past medications include:**

PENTASA for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

RECTABUL for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

COMIRNATY for PROPHYLAXIS OF COVID-19 ([redacted])

Causality for UPADACITINIB (Blinded)

---

1) Atrioventricular block complete (10003673) (Atrioventricular block complete (10003673) ) [v.24.1] [10003673]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

---

Event of COMPLETE ATRIOVENTRICULAR BLOCK

**- Investigator:** ARTERIOSCLERPOSIS

**- AbbVie:** Risk factors include advanced age, pre-existing hypertension and hypercholesterolemia.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] **20[redacted] BMI:** 25.97 kg/m2

[redacted] **20[redacted] ECG:** abnormal - left bundle branch block

[redacted] **20[redacted] ECG:** Not provided

[redacted] **20[redacted] POTASSIUM:** 3.8 MMOL/L (normal 3.6 to 4.8)

[redacted] **20[redacted] POTASSIUM:** 3.9 MMOL/L (normal 3.6 to 4.8)

[redacted] **20[redacted] POTASSIUM:** 4.0 MMOL/L (normal 3.6 to 4.8)

[redacted] **20[redacted] POTASSIUM:** 3.9 MMOL/L (normal 3.6 to 4.8)[redacted] 20[redacted] POTASSIUM: 3.8 MMOL/L (normal 3.6 to 4.8)

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 潰瘍性大腸炎 | X | X | | |
| γ-グルタミルトランスフェラーゼ増加 | | | | X |
| 肝機能異常 | | | | X |
| 骨壊死 | X | | | |
| 尿管結石症 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 4[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| ANEMIA: ANEMIA | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: CLAVICLE FRACTURE | 19[redacted] |
| OTHER: DORSI MANUS FRACTURE | 19[redacted] |
| OTHER: HUMERUS FRACTURE | 20[redacted] |
| OTHER: LUMBER FRACTURE | 20[redacted] |
| OTHER: SILENT CALCULUS URETERIC | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 1 PACK | 20 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 15 mg | ORAL | QD | [redacted] / 1 | [redacted] / 56 | 56 |
| M14-234 SS3 ABT-494 (MAIN) | 15 mg | ORAL | QD | [redacted] / 57 | [redacted] / 99 | 43 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 100 | [redacted] / 1043 | 944 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | 1 g | PRN | Y-M: 20[redacted] |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] |
| PREDNISOLONE | 10 mg | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: 1 TIME PER 2WEEKS | Y-M: 20[redacted] |
| ALL OTHER NON-THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| CEFTRIAXONE | 1 g | BID | Y-M: 20[redacted] |
| ENTEROCOCCUS FAECALIS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| LACTOMIN | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MEROPENEM | 0.5 g | TID | Y-M: 20[redacted] |
| PREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| CLOSTRIDIUM BUTYRICUM | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| TACROLIMUS | 0.5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | QD | Y-M: 20[redacted] / -346 |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] / -353 |
| PREDNISOLONE | 10 mg | QD | Y-M: 20[redacted] / -361 |
| PREDNISOLONE | 40 mg | QD | Y-M: 20[redacted] / -322 |
| INFLIXIMAB | 300 mg | OTHER: 1 TIME PER 8WEEKS | Y-M: 20[redacted] / -328 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -333 |

| | | | |
|---|---|---|---|
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] / -284 |
| PREDNISOLONE | 2.5 mg | BID | Y-M: 20[redacted] / -300 |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] / -307 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -256 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -229 |
| MESALAZINE | 1 g | PRN | Y-M: 20[redacted] / -235 |
| PREDNISOLONE | 15 mg | QD | Y-M: 20[redacted] / -207 |
| MESALAZINE | 1 g | QD | Y-M: 20[redacted] / -183 |
| PREDNISOLONE | 15 mg | QD | Y-M: 20[redacted] / -122 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -14 |
| BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM INFANTIS | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] | Y-M: 20[redacted] / 951 |
| ALENDRONIC ACID | 35 mg | OTHER: ONCE AWEEK | Y-M: 20[redacted] / 173 | ONGOING |
| PREDNISOLONE | 25 mg | QD | Y-M: 20[redacted] / 214 | Y-M: 20[redacted] / 226 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / 227 | Y-M: 20[redacted] / 240 |
| PREDNISOLONE | 17.5 mg | QD | Y-M: 20[redacted] / 241 | Y-M: 20[redacted] / 254 |
| ZOLPIDEM | 10 mg | QD | Y-M: 20[redacted] / 246 | Y-M: 20[redacted] / 296 |
| LOXOPROFEN | 60 mg | TID | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 259 |
| REBAMIPIDE | 100 mg | TID | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 259 |
| PREDNISOLONE | 15 mg | QD | Y-M: 20[redacted] / 255 | Y-M: 20[redacted] / 268 |
| PREDNISOLONE | 12.5 mg | QD | Y-M: 20[redacted] / 269 | Y-M: 20[redacted] / 282 |
| MECOBALAMIN | 500 ug | TID | Y-M: 20[redacted] / 273 | Y-M: 20[redacted] / 296 |
| PREDNISOLONE | 10 mg | QD | Y-M: 20[redacted] / 283 | Y-M: 20[redacted] / 296 |
| HYALURONIC ACID | 25 mg | OTHER: ONCE A WEEK | Y-M: 20[redacted] / 296 | Y-M: 20[redacted] / 327 |
| LIDOCAINE | 1 mL | OTHER: ONCE A WEEK | Y-M: 20[redacted] / 296 | Y-M: 20[redacted] / 327 |
| PREDNISOLONE | 9 mg | QD | Y-M: 20[redacted] / 297 | Y-M: 20[redacted] / 317 |
| PREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 318 | Y-M: 20[redacted] / 339 |
| SODIUM PICOSULFATE | 10 mL | PRN | Y-M: 20[redacted] / 339 | Y-M: 20[redacted] / 339 |
| LIDOCAINE | 15 mL | PRN | Y-M: 20[redacted] / 340 | Y-M: 20[redacted] / 340 |

| | | | | |
|---|---|---|---|---|
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 2 L | PRN | Y-M: 20[redacted] / 340 | Y-M: 20[redacted] / 340 |
| PREDNISOLONE | 25 mg | QD | Y-M: 20[redacted] / 340 | Y-M: 20[redacted] / 363 |
| ZOLPIDEM | 10 mg | QD | Y-M: 20[redacted] / 342 | Y-M: 20[redacted] / 886 |
| PREDNISOLONE | 15 mg | QD | Y-M: 20[redacted] / 385 | Y-M: 20[redacted] / 830 |
| EFINACONAZOLE | PROPER AMOUNT<br>OTHER: PROPER AMOUNT | QD | Y-M: 20[redacted] / 418 | Y-M: 20[redacted] / 652 |
| VANCOMYCIN | 0.25 g | OTHER: EVERY OTHER DAY | Y-M: 20[redacted] / 474 | Y-M: 20[redacted] / 494 |
| BUDESONIDE | 2 mg | BID | Y-M: 20[redacted] / 508 | Y-M: 20[redacted] / 562 |
| ATROPINE | 0.5 mg | PRN | Y-M: 20[redacted] / 521 | Y-M: 20[redacted] / 521 |
| HYDROXYZINE | 25 mg | PRN | Y-M: 20[redacted] / 521 | Y-M: 20[redacted] / 521 |
| LOXOPROFEN | 60 mg | PRN | Y-M: 20[redacted] / 521 | Y-M: 20[redacted] / 521 |
| PARACETAMOL | 1000 mg | PRN | Y-M: 20[redacted] / 521 | Y-M: 20[redacted] / 522 |
| REBAMIPIDE | 100 mg | PRN | Y-M: 20[redacted] / 521 | Y-M: 20[redacted] / 521 |
| TRAMADOL | 100 mg | PRN | Y-M: 20[redacted] / 521 | Y-M: 20[redacted] / 522 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 522 | Y-M: 20[redacted] / 525 |
| CEFTERAM | 100 mg | TID | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 564 |
| CEFTRIAXONE | 1 g | QD | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 560 |
| GUALENIC ACID | PROPER AMOUNT<br>OTHER: PROPER AMOUNT | PRN | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 566 |
| MICONAZOLE | PROPER AMOUNT<br>OTHER: PROPER AMOUNT | PRN | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 564 |
| TRANEXAMIC ACID | 250 mg | TID | Y-M: 20[redacted] / 560 | Y-M: 20[redacted] / 564 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 562 | Y-M: 20[redacted] / 567 |
| PIPERACILLIN;TAZOBACTAM | 4.5 g | | QD[redacted]M: 20[redacted] / 564 | Y-M: 20[redacted] / 567 |
| CEFCAPENE | 100 mg | TID | Y-M: 20[redacted] / 567 | Y-M: 20[redacted] / 574 |
| GENTAMICIN | PROPER AMOUNT<br>OTHER: PROPER AMOUNT | PRN | Y-M: 20[redacted] / 567 | Y-M: 20[redacted] / 582 |

| | | | | |
|---|---|---|---|---|
| POVIDONE-IODINE | PROPER AMOUNT OTHER: PROPER AMOUNT | PRN | Y-M: 20[redacted] / 567 | Y-M: 20[redacted] / 595 |
| VALACICLOVIR | 1000 mg | TID | Y-M: 20[redacted] / 567 | Y-M: 20[redacted] / 574 |
| DEXTROMETHORPHAN | 30 mg | TID | Y-M: 20[redacted] / 571 | Y-M: 20[redacted] / 601 |
| HEPARINOID | PROPER AMOUNT OTHER: PROPER AMOUNT | PRN | Y-M: 20[redacted] / 581 | Y-M: 20[redacted] / 583 |
| BUDESONIDE | 2 mg | BID | Y-M: 20[redacted] / 583 | Y-M: 20[redacted] / 606 |
| BUDESONIDE | 2 mg | BID | Y-M: 20[redacted] / 645 | Y-M: 20[redacted] / 646 |
| VANCOMYCIN | 0.25 g | QID | Y-M: 20[redacted] / 647 | Y-M: 20[redacted] / 657 |
| VANCOMYCIN | 0.25 g | BID | Y-M: 20[redacted] / 658 | Y-M: 20[redacted] / 664 |
| LEVOFLOXACIN | 500 mg | QD | Y-M: 20[redacted] / 666 | Y-M: 20[redacted] / 676 |
| LOPERAMIDE | 1 mg | TID | Y-M: 20[redacted] / 672 | Y-M: 20[redacted] / 676 |
| LOXOPROFEN | 300 mg | BID | Y-M: 20[redacted] / 865 | Y-M: 20[redacted] / 917 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 866 | Y-M: 20[redacted] / 906 |
| PREDNISOLONE | 9 mg | QD | Y-M: 20[redacted] / 882 | Y-M: 20[redacted] / 951 |
| PREGABALIN | 50 mg | BID | Y-M: 20[redacted] / 886 | Y-M: 20[redacted] / 906 |
| PREGABALIN | 75 mg | BID | Y-M: 20[redacted] / 907 | Y-M: 20[redacted] / 917 |
| ZOLPIDEM | 10 mg | QD | Y-M: 20[redacted] / 919 | ONGOING |
| CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM CITRATE | 1800 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| CALCIUM GLUCONATE;GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE;SODIUM CITRATE | 900 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| CEFAZOLIN | 1 g | TID | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 939 |
| CLOSTRIDIUM BUTYRICUM | 2 OTHER: TABLETS | TID | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 951 |
| DESFLURANE | 40.89 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| DROPERIDOL | 0.5 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| FENTANYL | 100 ug | BID | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| FLURBIPROFEN | 5 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| HEPARIN | 5 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |

| | | | | |
|---|---|---|---|---|
| HYDROCORTISONE | 100 mg | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| LEVOBUPIVACAINE | 30 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| LIDOCAINE | 20 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| NICARDIPINE | 0.2 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| PARACETAMOL | 1000 mg | BID | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| PROPOFOL | 9 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| REMIFENTANIL | 1.8 mg | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| ROCURONIUM | 1 mL | TID | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| ROCURONIUM | 5 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| SUGAMMADEX | 2 mL | QD | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| TRANEXAMIC ACID | 10 mL | TID | Y-M: 20[redacted] / 938 | Y-M: 20[redacted] / 938 |
| CELECOXIB | 300 mg | BID | Y-M: 20[redacted] / 939 | Y-M: 20[redacted] / 939 |
| DEXMEDETOMIDINE | 50 mL | QD | Y-M: 20[redacted] / 939 | Y-M: 20[redacted] / 939 |
| EDOXABAN | 30 mg | QD | Y-M: 20[redacted] / 939 | Y-M: 20[redacted] / 945 |
| ELECTROLYTES NOS | 500 mL | QD | Y-M: 20[redacted] / 939 | Y-M: 20[redacted] / 939 |
| PARACETAMOL | 1000 mg | QD | Y-M: 20[redacted] / 939 | Y-M: 20[redacted] / 939 |
| CELECOXIB | 200 mg | BID | Y-M: 20[redacted] / 940 | Y-M: 20[redacted] / 945 |
| PREDNISOLONE | 9 mg | QD | Y-M: 20[redacted] / 954 | Y-M: 20[redacted] / 956 |
| PREDNISOLONE | 8 mg | QD | Y-M: 20[redacted] / 957 | Y-M: 20[redacted] / 967 |
| PREDNISOLONE | 7 mg | QD | Y-M: 20[redacted] / 968 | Y-M: 20[redacted] / 977 |

**Event #1: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | GAMMA GTP INCREASE |
| **Preferred term** | γ-グルタミルトランスフェラーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 344 / 245 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 439 / 340 |
| **Duration of AE** | 96 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |

| | |
|---|---|
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | DETERIORATION OF CALCULUS URETERIC |
| **Preferred term** | 尿管結石症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 620 / 521 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

[redacted]20[redacted] (RX DAY 368): NPTST337-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 438): NPTST337-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 445): NPTST337-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 459): NPTST337-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 494): Leukocytes: 1-4 [0 - 0] /HPF; NPTST278-RED BLOOD CELL: 1-4 [0 - 0] /HPF; NPTST337-URINARY OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 536): NPTST337-URINARY OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 635 / 536 |
| **Duration of AE** | 16 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | THE PATIENT WAS FOUND TO HAVE ASYMPTOMATIC CALCULUS BEFORE THE STUDY TREATMENT. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #3: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | HEPATIC FUNCTION ABNORMAL |
| **Preferred term** | 肝機能異常 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 663 / 564 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 771 / 672 |

| | |
|---|---|
| **Duration of AE** | 109 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #4: Serious Adverse Event , AE Leading to Discontinuation of Study Drug**

| | |
|---|---|
| **Event Description** | WORSENING OF ULCERATIVE COLITIS |
| **Preferred term** | 潰瘍性大腸炎 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1020 / 921 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

[redacted]20[redacted](RX DAY 956): NPTST017-ACTH: 47.1 [7.2 - 63.3] PG/ML; NPTST102-CORTISOL: 10.4 [4.4 - 21.1] UG/DL

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 1066 / 967 (23 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 47 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | DUE TO LONG-TERM USE OF STEROIDS |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

**Event #5: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | AVASCULAR NECROSIS FEMORAL HEAD |
| **Preferred term** | 骨壊死 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1020 / 921 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

NOT REPORTED

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 1076 / 977 (33 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 57 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | DUE TO LONG TERM USE OF STEROIDS |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，尿管結石の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 20 年間），貧血，無症候性の尿管結石，潰瘍性大腸炎及び少量の現飲酒者であった。

**Event 2 の臨床経過：**

投与620日後＊　，被験者は尿管結石の悪化を発現した。投与635日後＊　，尿管結石の悪化は消失した。

投与439日後＊及び 投与467日後＊　　，被験者は尿潜血が陽性であった。　　投与537日後＊，被験者は 2 日前から肉眼的血尿があると訴え，泌尿器科を紹介された。膀胱鏡検査が行われ，異常所見は認められなかった。CT スキャン検査の結果，8.5 mm の尿管結石が確認された。泌尿器科医は，被験者に十分な量の水分を摂取するように指示した。投与593日後＊　，再度 CT スキャン検査を行ったところ，尿管結石が同じ位置に残っており，体外衝撃波結石破砕術が予定された。投与620日後＊　，被験者は腰痛があり入院し，同日，予定されていた体外衝撃波結石破砕術が行われた。被験者は術後の痛みに対し，鎮痛薬の静脈内投与を受けた。X 線検査で結石の残存が確認され，被験者は引き続き十分な量の水分を摂取するように指示された。投与621日後＊，被験者は退院した。

投与624日後＊　，退院後も激しい痛みが続いていたが，その後痛みが消えたため，鎮痛薬の服用を中止した。投与635日後＊　，被験者は泌尿器科を再び受診し，超音波検査及び X 線検査

が行われた。腎結石は消失していることが確認された。

投与された薬剤は，カロナール，アセリオ及びトラマールであった。

**The patient's past medications include:**

PENTASA for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1) Ureteral calculus (10046383) (Ureterolithiasis (10077989) ) [v.21.1] [10046383]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

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Event of DETERIORATION OF CALCULUS URETERIC

**- Investigator:** The patient was found to have asymptomatic calculus before the study treatment.

**- AbbVie:** The investigator reports asymptomatic calculus was present before the study treatment. Pre-existing ulcerative colitis is an additional risk factor.

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，大腿骨頭の虚血性骨壊死及び潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，背側の手骨骨折，鎖骨骨折，上腕骨骨折，腰椎骨折，元喫煙者（1 日 1 箱を 20 年間），潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

**Event 4 及び 5 の臨床経過：**

投与1020日後＊，被験者は大腿骨頭の虚血性骨壊死及び潰瘍性大腸炎の悪化を発現した。投与1066日後＊　，潰瘍性大腸炎の悪化は消失した。投与1076日後＊　，大腿骨頭の虚血性骨壊死は消失した。

本事象発現前，被験者は 投与950日後＊　に MRI 検査を受け，腰椎椎間板ヘルニア（非重篤）と診断された。

入院前の 投与964日後＊　　，被験者は整形外科を受診し，仕事で重いものを持ち上げた後，投与962日後＊　より左臀部から左下肢のしびれ感及び痛みが始まったと訴えた。X 線検査が行われ，骨頭の明らかな壊死は認められなかった。投与985日後＊　，被験者は左臀部から左下肢のしびれ感及び痛みが改善しないため，再び整形外科を受診し，リリカが処方された。投与1016日後＊　，被験者は腰椎の治療のために専門医を訪れた。左股関節及び膝の X 線検査が行われ，左大腿骨頭の壊死の疑いが認められた。被験者は股関節及び膝関節の治療のため，別の専門医を紹介された。投与1020日後＊　，被験者は関節の専門医を受診し，大腿骨頭（左）の壊死と診断された。投与1030日後＊，治験薬の投与は中止された。

投与1036日後＊　，被験者は予定された手術のために入院した。投与1037日後＊　，被験者は人工骨移植を伴う左股関節の人工関節及び靭帯の置換術を受けた。術後，被験者は集中治療室に入った。投与1038日後＊　，被験者は集中治療室から一般病棟に移った。術後経過では，合併症は認められなかった。しかし，被験者の大腿骨頭の壊死を引き起こしたと考えられるため，治験薬投与と併用した副腎皮質ステロイド療法は継続できなかった。投与1046日後＊　，潰瘍性大腸炎が悪化したため，結腸切除術のために後日再入院する予定で退院した。

投与1049日後＊　，被験者は予定された結腸切除術のために入院した。投与1051日後＊　，回腸瘻造設を伴う，腹腔鏡下での直腸結腸全摘術が行われた。投与1053日後＊　，被験者は副腎皮質ステロイド療法を再開した。投与1054日後＊　，被験者は通常の食事を再開した。術後，回腸瘻からの排液量が増加した。投与1057日後＊　，排液量は減少した。投与1066日後＊　，被験者

は退院した。

潰瘍性大腸炎が悪化したため，治験薬の投与は完全に中止された。

投与された薬剤は，セファメジン，ミヤ BM 及びセレコックスであった。

**The patient's past medications include:**

LAC-B GRANULAR POWDER N for ULCERATIVE COLITIS (20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

BIOFERMIN-R for ULCERATIVE COLITIS ([redacted])

CEFTRIAXONE SODIUM HYDRATE for ULCERATIVE COLITIS ([redacted])

ADACOLUMN for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

MEROPEN for ULCERATIVE COLITIS ([redacted])

BIOFERMIN for ULCERATIVE COLITIS ([redacted])

MIYA-BM for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

PREDONEMA for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

RECTABUL for ULCERATIVE COLITIS ([redacted])

LOXONIN for LUMBAR DISC HERNIATION ([redacted])

LYRICA OD for LUMBAR DISC HERNIATION ([redacted])

Causality for UPADACITINIB (Open Label)

---

1) Avascular necrosis femoral head (10003860) (Osteonecrosis (10031264) ) [v.23.0] [10003860]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900) ) [v.23.0] [10009901]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of AVASCULAR NECROSIS FEMORAL HEAD

**- Investigator:** Due to long term use of steroids

**- AbbVie:** Risk factor includes long term and current use of corticosteroids.

Event of WORSENING OF ULCERATIVE COLITIS

**- Investigator:** Due to long-term use of steroids

**- AbbVie:** Event is more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

---

[redacted] 20[redacted] **ACTH:** 47.1 PG/ML (normal 7.2 to 63.3)

[redacted] 20[redacted] **CORTISOL: 10**.4 MCG/DL (normal 4.4 to 21.1)

[redacted] 20[redacted] **CT SCAN:** Normal after joint replacement.

[redacted] 20[redacted] **HIP X-RAY:** no apparent necrosis of the bone head

[redacted] 20[redacted] **HIP X-RAY:** diagnosis of necrosis of femoral head in the left made on [redacted] 20[redacted]

[redacted] 20[redacted] **MRI:** lumbar disc herniation

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Gamma-glutamyltransferase: Asymptomatic. Alcohol Use 20% alcohol 400 ml/Day.
Hepatic function abnormal: Asymptomatic. No alternative etiology.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 血中クレアチンホスホキナーゼ増加 | | | | X |
| 帯状疱疹 | X | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 6[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| GOUT | 20[redacted] |
| HYPERTENSION | 20[redacted] |
| OTHER: CHICKENPOX | NOT REPORTED |
| OTHER: HYPOKALEMIA | 20[redacted] |
| OTHER: LEFT RIB FRACTURE | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 30 mg | ORAL | QD | [redacted]20[redacted]/ 1 | [redacted]20[redacted]/ 57 | 57 |

| | | | | | |
|---|---|---|---|---|---|
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 58 | [redacted] / 174 117 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 175 | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| BIFIDOBACTERIUM LACTIS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| POLYCARBOPHIL | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MESALAZINE | 2000 mg | BID | Y-M: 20[redacted] |
| OTHER THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] |
| MESALAZINE | 1 g | PRN | Y-M: 20[redacted] |
| OTHER THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | OTHER: EVERY TWO DAYS | Y-M: 20[redacted] |
| AZATHIOPRINE | 75 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1 g | PRN | Y-M: 20[redacted] / -342 |
| CLOSTRIDIUM BUTYRICUM | 1 g | TID | Y-M: 20[redacted] / -315 |
| MESALAZINE | 4800 mg | QD | Y-M: 20[redacted] / -220 |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] / -146 |
| HYDROCHLOROTHIAZIDE;LOSARTAN | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -146 |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| CLOSTRIDIUM BUTYRICUM | 1 g | TID | Y-M: 20[redacted] / -315 | ONGOING |
| MESALAZINE | 4800 mg | QD | Y-M: 20[redacted] / -220 | ONGOING |
| AMLODIPINE | 5 mg | QD | Y-M: 20[redacted] / -146 | ONGOING |
| HYDROCHLOROTHIAZIDE;LOSARTAN | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / -146 | ONGOING |
| PREGABALIN | 75 mg | BID | Y-M: 20[redacted] / 117 | Y-M: 20[redacted] / 140 |
| RABBIT VACCINIA EXTRACT | 2 OTHER: TABLET | BID | Y-M: 20[redacted] / 117 | Y-M: 20[redacted] / 140 |
| REBAMIPIDE | 100 mg | BID | Y-M: 20[redacted] / 117 | Y-M: 20[redacted] / 140 |
| VALACICLOVIR | 1000 mg | TID | Y-M: 20[redacted] / 117 | Y-M: 20[redacted] / 126 |

| | | | | |
|---|---|---|---|---|
| SODIUM PICOSULFATE | 10 mg | QD | Y-M: 20[redacted] / 347 | Y-M: 20[redacted] / 347 |
| HYOSCINE | 20 mg | QD | Y-M: 20[redacted] / 348 | Y-M: 20[redacted] / 348 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 2 L | QD | Y-M: 20[redacted] / 348 | Y-M: 20[redacted] / 348 |
| SODIUM PICOSULFATE | 10 mg | QD | Y-M: 20[redacted] / 681 | Y-M: 20[redacted] / 681 |
| HYOSCINE | 20 mg | QD | Y-M: 20[redacted] / 682 | Y-M: 20[redacted] / 682 |
| MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE | 2 L | QD | Y-M: 20[redacted] / 682 | Y-M: 20[redacted] / 682 |
| BETAMETHASONE;GENTAMICIN | ADEQUATE DOSE<br>OTHER: APPLICATION | QD | Y-M: 20[redacted] / 883 | Y-M: 20[redacted] / 889 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 883 | Y-M: 20[redacted] / 889 |
| ACETAZOLAMIDE | 250 mg | BID | Y-M: 20[redacted] / 890 | Y-M: 20[redacted] / 900 |
| ACICLOVIR | ADEQUATE DOSE<br>OTHER: APPLICATION | OTHER: 5 TIMES IN A DAY | Y-M: 20[redacted] / 890 | Y-M: 20[redacted] / 920 |
| AMENAMEVIR | 400 mg | QD | Y-M: 20[redacted] / 890 | Y-M: 20[redacted] / 896 |
| FLUOROMETHOLONE | 1 gtt | QID | Y-M: 20[redacted] / 890 | Y-M: 20[redacted] / 896 |
| MOXIFLOXACIN | 1 gtt | QID | Y-M: 20[redacted] / 890 | Y-M: 20[redacted] / 920 |
| PARACETAMOL | 600 mg | TID | Y-M: 20[redacted] / 890 | Y-M: 20[redacted] / 900 |
| POTASSIUM ASPARTATE | 600 mg | BID | Y-M: 20[redacted] / 890 | Y-M: 20[redacted] / 900 |
| FLUOROMETHOLONE | 1 gtt | BID | Y-M: 20[redacted] / 897 | Y-M: 20[redacted] / 988 |
| ACETAZOLAMIDE | 125 mg | BID | Y-M: 20[redacted] / 901 | Y-M: 20[redacted] / 917 |
| LOXOPROFEN | 60 mg | TID | Y-M: 20[redacted] / 901 | Y-M: 20[redacted] / 951 |
| POTASSIUM ASPARTATE | 300 mg | BID | Y-M: 20[redacted] / 901 | Y-M: 20[redacted] / 917 |
| REBAMIPIDE | 100 mg | TID | Y-M: 20[redacted] / 901 | Y-M: 20[redacted] / 920 |
| ACETAZOLAMIDE | 250 mg | BID | Y-M: 20[redacted] / 918 | Y-M: 20[redacted] / 988 |

| | | | | |
|---|---|---|---|---|
| POTASSIUM ASPARTATE | 600 mg | BID | Y-M: 20[redacted] / 918 | Y-M: 20[redacted] / 988 |
| ACICLOVIR | ADEQUATE DOSE OTHER: APPLICATION | TID | Y-M: 20[redacted] / 921 | Y-M: 20[redacted] / 935 |
| CARTEOLOL | 1 gtt | QD | Y-M: 2 [redacted] / 921 | Y-M: 20[redacted] / 935 |
| ACICLOVIR | ADEQUATE DOSE OTHER: APPLICATION | QD | Y-M: 20[redacted] / 936 | Y-M: 20[redacted] / 941 |
| AMENAMEVIR | 400 mg | QD | Y-M: 20[redacted] / 936 | Y-M: 20[redacted] / 942 |
| CARTEOLOL | 1 gtt | BID | Y-M: 20[redacted] / 936 | Y-M: 20[redacted] / 988 |
| ACICLOVIR | ADEQUATE DOSE OTHER: APPLICATION | TID | Y-M: 20[redacted] / 942 | Y-M: 20[redacted] / 987 |
| BRIMONIDINE;BRINZOLAMIDE | 1 gtt | BID | Y-M: 20[redacted] / 954 | Y-M: 20[redacted] / 988 |
| GATIFLOXACIN | 1 gtt | OTHER: 4 TIMES IN A DAY | Y-M: 20[redacted] / 985 | Y-M: 20[redacted] / 988 |
| BETAMETHASONE | 1 gtt | OTHER: 4 TIMES 1N A DAY | Y-M: 20[redacted] / 989 | ONGOING |
| BROMFENAC | 1 gtt | BID | Y-M: 20[redacted] / 989 | Y-M: 20[redacted] / 1023 |
| LEVOFLOXACIN | 1 gtt | OTHER: 4 TIMES IN A DAY | Y-M: 20[redacted] / 989 | ONGOING |
| ACICLOVIR | ADEQUATE DOSE OTHER: APPLICATION | QD | Y-M: 20[redacted] / 996 | Y-M: 20[redacted] / 1102 |
| SODIUM PICOSULFATE | 10 mg | QD | Y-M: 20[redacted] / 996 | Y-M: 20[redacted] / 996 |
| BISACODYL | 10 mg | QD | Y-M: 20[redacted] / 997 | Y-M: 20[redacted] / 997 |
| GLYCEROL | 120 mL | QD | Y-M: 20[redacted] / 997 | Y-M: 20[redacted] / 997 |

**Event #1: Event of Interest - Creatine Phosphokinase (CPK) Elevation**

| | |
|---|---|
| **Event Description** | CPK INCREASED |
| **Preferred term** | 血中クレアチンホスホキナーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 200 / 26 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 1106 / 932 |

| | |
|---|---|
| **Duration of AE** | 907 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | ZOSTER HERPES |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 291 / 117 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 329 / 155 |
| **Duration of AE** | 39 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #3: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1045 / 871 |
| **Age at AE Onset** | 6[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | SEVERE |

| | |
|---|---|
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]20[redacted]16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，帯状疱疹の事象を発現した。関連する病歴は，高血圧，潰瘍性大腸炎，水痘，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

この被験者は，先行の M14-234 試験では，被験者番号 [redacted] であり，20[redacted]年[redacted]月[redacted]日から 20[redacted]年[redacted]月[redacted]日まで盲検化された治験薬を投与された。

**Event 3 の臨床経過：**

投与1045日後＊，被験者は帯状疱疹を発現した。

本事象発現前の 投与の約9ヵ月後＊，被験者は帯状疱疹（非重篤）を経験していた。

治験責任医師によると，本事象に関連する被験者の危険因子は，幼少期の水痘の病歴であった。

投与1045日後＊　，被験者は帯状疱疹の症状を発現した。被験者は 1 つの皮膚分節の病変及び眼の病変を有していた。被験者は，帯状疱疹ワクチンを受けていなかった。　投与1064日後＊，被験者は，左三叉神経第一枝の帯状疱疹，左目の帯状疱疹性角結膜炎/眼瞼炎，及び左眼の高眼圧と診断された。投与1162日後＊，被験者は眼圧を下げるための眼球の手術のために入院した。投与1163日後＊，被験者は退院した。

投与された薬剤は，アメナリーフ，アセトアミノフェン，ミケラン LA，アスパラカリウム，フルメトロン，ベガモックス，ゾビラックス眼軟膏及びダイアモックスであった。

**The patient's past medications include:**

PENTASA for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDONINE for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Herpes zoster (10019974) (Herpes zoster (10019974) ) [v.24.0] [10019974]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Open Label)

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Event of HERPES ZOSTER

**- Investigator:** Not Applicable

**- AbbVie:** Not Applicable

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 腹痛 | X | | | |
| 貧血 | | | | X |
| γ-グルタミルトランスフェラーゼ増加 | | X | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 2[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| ANEMIA: ANEMIA | 20[redacted] |
| EXTENSIVE UC/PANCOLITIS | 20[redacted] |
| OTHER: ASTHENOPIA | 20[redacted] |
| OTHER: CHRONIC COUGH | 20[redacted] |
| OTHER: PRIMARY SCLEROSING CHOLANGITIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 7.5 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 57 | 57 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 58 | [redacted]20[redacted] / 384 | 327 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| URSODEOXYCHOLIC ACID | 300 mg | TID | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 75 mg | QD | Y-M: 20[redacted] |
| ALL OTHER NON-THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MESALAZINE | 1 g | BID | Y-M: 20[redacted] |
| INFLIXIMAB | 300 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1 g | QD | Y-M: 20[redacted] / -233 |
| TACROLIMUS | 2 mg | BID | Y-M: 20[redacted] / -248 |
| MESALAZINE | 1000 mg | QID | Y-M: 20[redacted] / -217 |
| MESALAZINE | 4800 mg | QD | Y-M: 20[redacted] / -175 |
| MERCAPTOPURINE | 20 mg | QD | Y-M: 20[redacted] / -196 |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] / -105 |
| PRANLUKAST | 225 mg | BID | Y-M: 20[redacted] / -105 |
| RABEPRAZOLE | 10 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| URSODEOXYCHOLIC ACID | 300 mg | TID | Y-M: 20[redacted] | ONGOING |
| MESALAZINE | 4800 mg | QD | Y-M: 20[redacted] / -175 | ONGOING |
| PRANLUKAST | 225 mg | BID | Y-M: 20[redacted] / -105 | ONGOING |
| NAPHAZOLINE;POLYSORBATE 80 | APPROPRIATE AMOUNT | PRN | Y-M: 20[redacted] / 22 | ONGOING |
| BORIC ACID;EPHEDRINE;MAFENIDE;TAURINE;ZINC | APPROPRIATE AMOUNT | PRN | Y-M: 20[redacted] / 29 | ONGOING |
| DESLORATADINE | 5 mg | QD | Y-M: 20[redacted] / 57 | ONGOING |
| ASCORBIC ACID;CAFFEINE;CHLORPHENAMINE;DIHYDROCODEINE;GLYCYRRHIZIC ACID;METHYLEPHEDRINE;PARACETAMOL;PROPYPHENAZONE;RIBOFLAVIN | 2 OTHER: CAP | BID | Y-M: 20[redacted] / 67 | Y-M: 20[redacted] / 69 |

| | | | | |
|---|---|---|---|---|
| LOXOPROFEN | 60 mg | PRN | Y-M: 20[redacted] / 67 | Y-M: 20[redacted] / 70 |
| BERBERINE;GERANIUM THUNBERGII | 1 OTHER: TAB | QD | Y-M: 20[redacted] / 99 | Y-M: 20[redacted] / 112 |
| IRON | 50 mg | QD | Y-M: 20[redacted] / 113 | Y-M: 20[redacted] / 168 |
| IRON | 80 mg | QD | Y-M: 20[redacted] / 113 | Y-M: 20[redacted] / 113 |
| LOXOPROFEN | 60 mg | PRN | Y-M: 20[redacted] / 321 | Y-M: 20[redacted] / 322 |
| CEFMETAZOLE | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 322 | Y-M: 20[redacted] / 322 |
| HYOSCINE | 1 g | OTHER: ONCE | Y-M: 20[redacted] / 322 | Y-M: 20[redacted] / 322 |
| LOXOPROFEN | 60 mg | PRN | Y-M: 20[redacted] / 322 | Y-M: 20[redacted] / 324 |
| CEFMETAZOLE | 1 g | TID | Y-M: 20[redacted] / 323 | Y-M: 20[redacted] / 326 |
| CEFMETAZOLE | 1 g | QD | Y-M: 20[redacted] / 327 | Y-M: 20[redacted] / 327 |
| RABEPRAZOLE | 10 mg | QD | Y: 20[redacted] | ONGOING |

**Event #1: Event of Interest - Anemia**

| | |
|---|---|
| **Event Description** | WORSING OF ANEMIA |
| **Preferred term** | 貧血 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 156 / 99 |
| **Age at AE Onset** | [redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 226 / 169 |
| **Duration of AE** | 71 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | ABDOMINAL PAIN |
| **Preferred term** | 腹痛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 378 / 321 |
| **Age at AE Onset** | [redacted] |
| **Laboratory Testing** | |

[redacted]20[redacted] (RX DAY 177): Creatinine: 68.954543 [31.825174 - 93.707456] UMOL/L; NPTST275-RDW-CV: 15.5 [0 - 35] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 180): Alkaline Phosphatase: 441 [115 - 359] U/L; NPTST028-AMYLASE: 74 [33 - 120] U/L; NPTST119-DIRECT BILIRUBIN: 3.2 [0 - 0.4] MG/DL; [redacted]20[redacted] (RX DAY 322): Alanine Aminotransferase: 88 [8 - 42] U/L; Albumin: 39 [40 - 52] G/L; Alkaline Phosphatase: 455 [115 - 359] U/L; Aspartate Aminotransferase: 69 [13 - 33] U/L; Basophils/Leukocytes: 0.8 [0 - 1] %; Bilirubin: 2+ [NOT REPORTED - NOT REPORTED] N/A; Blood Urea Nitrogen: 6.42546 [2.85576 - 7.1394] MMOL/L; Chloride: 105 [99 - 109] MMOL/L; Creatine Kinase: 125 [62 - 287] U/L; Creatinine: 60.114217 [31.825174 - 93.707456] UMOL/L; Eosinophils/Leukocytes: 3.2 [2 - 7] %; Erythrocytes: 1~4 [NOT REPORTED - NOT REPORTED] /HIGH POWER FIELD; Erythrocytes: 4.95 [4.1 - 5.5] 10^12/L; Glucose: 0.00 [NOT REPORTED - 0.05] g/dL; Glucose: - [NOT REPORTED - NOT REPORTED] N/A; Hematocrit: 0.405 [0.39 - 0.51] FRACTION OF 1; Ketones: - [NOT REPORTED - NOT REPORTED] N/A; Leukocytes: 5-9 [NOT REPORTED - NOT REPORTED] /HPF; Leukocytes: 7.24 [4 - 9] 10^9/L; Leukocytes: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Lymphocytes/Leukocytes: 12.2 [26 - 47] %; Monocytes/Leukocytes: 5.4 [3 - 8] %; NPTST028-AMYLASE: 92 [33 - 120] U/L; NPTST042-BACTERIA: - [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST108-CRP: 0.16 [NOT REPORTED - 0.3] mg/dL; NPTST119-DIRECT BILIRUBIN: 1.4 [0 - 0.4] MG/DL; NPTST120-EGFR: 114 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST148-GAMMA GLUTAMYLTRANSFERASE: 245 [11 - 58] U/L; NPTST158-GLASS COLUMN: 0-1 [NOT REPORTED - NOT REPORTED] /LPF; NPTST167-HEMOGLOBIN: 12.6 [13 - 17] G/DL; NPTST180-IG%: 0.3 [NOT REPORTED - NOT REPORTED] %; NPTST198-LACTATE DEHYDROGENASE: 232 [119 - 229] U/L; NPTST209-MAGNESIUM: 2.0 [1.9 - 2.5] MG/DL; NPTST211-MCH: 25.5 [28 - 34] PG; NPTST212-MCHC: 31.1 [32 - 36] G/DL; NPTST213-MCV: 81.8 [83 - 100] FL; NPTST275-RDW-CV: 14.9 [0 - 15] %; NPTST279-RED BLOOD CELL SEDIMENTATION RA: 31 [1 - 10] MM; NPTST280-RED BLOOD CELL SEDIMENTATION RA: 61 [NOT REPORTED - NOT REPORTED] MM; NPTST281-RED BLOOD CELL SEDIMENTATION RA: 11 [NOT REPORTED - NOT REPORTED] MM; NPTST283-RENAL TUBULAR EPITHELIAL CELLS: 1-4 [NOT REPORTED - NOT REPORTED] /HPF; NPTST306-SQUAMOUS CELL: 0-1 [NOT REPORTED - NOT REPORTED] /HPF; NPTST316-TOTAL BILIRUBIN: 1.8 [0.2 - 1.2] MG/DL; NPTST318-TOTAL PROTEIN: 8.0 [6.6 - 8.7] G/DL; NPTST321-TRANSITIONAL CELL: 0-1 [NOT REPORTED - NOT REPORTED] /HPF; NPTST332-TURBIDITY: - [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils/Leukocytes: 78.4 [38 - 58] %; Nitrite: - [NOT REPORTED - NOT REPORTED] N/A; Occult Blood: - [NOT REPORTED - NOT REPORTED] N/A; Platelets: 290 [150 - 350] 10^9/L; Potassium: 3.7 [3.6 - 4.9] MMOL/L; Protein: 100 [NOT REPORTED - 30] mg/dL; Protein: 2+ [NOT REPORTED - NOT REPORTED] N/A; Sodium: 139 [138 - 146] MMOL/L; Specific Gravity: 1.038 [1.005 - 1.03] UNIT NOT REPORTED; Urobilinogen: 2.0 [NOT REPORTED - NOT REPORTED] mg/dL; [redacted]20[redacted] (RX DAY 323): Alanine Aminotransferase: 114 [8 - 42] U/L; Alanine Aminotransferase: 115 [8 - 42] U/L; Albumin: 35 [40 - 52] G/L; Albumin: 34 [40 - 52] G/L; Alkaline Phosphatase: 473 [115 - 359] U/L; Alkaline Phosphatase: 474 [115 - 359] U/L; Aspartate Aminotransferase: 89 [13 - 33] U/L; Aspartate Aminotransferase: 89 [13 - 33] U/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Bilirubin: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Calcium: 2.120835 [2.021031 - 2.594904] MMOL/L; Chloride: 104 [99 - 109] MMOL/L; Chloride: 103 [99 - 109] MMOL/L; Creatine Kinase: 106 [62 - 287] U/L; Creatine Kinase: 104 [62 - 287] U/L; Creatinine: 55.694054 [31.825174 - 93.707456] UMOL/L; Creatinine: 58.346152 [31.825174 - 93.707456] UMOL/L; Eosinophils/Leukocytes: 1.4 [2 - 7] %; Erythrocytes: 4.66 [4.1 - 5.5] 10^12/L; Erythrocytes: 4.66 [4.1 - 5.5] 10^12/L; Glucose: 0 [NOT REPORTED - 0.05] g/dL; Glucose: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Hematocrit: 0.379 [0.39 - 0.51] FRACTION OF 1; Hematocrit: 0.374 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 120 [130 - 170] G/L; Hemoglobin: 121 [130 - 170] G/L; Ketones: NA [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Leukocytes: 11.18 [4 - 9] 10^9/L; Leukocytes: 11.11 [4 - 9] 10^9/L; Leukocytes: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Lymphocytes/Leukocytes: 7.7 [26 - 47] %; Monocytes/Leukocytes: 5.8 [3 - 8] %; NPTST028-AMYLASE: 59 [33 - 120] U/L; NPTST028-AMYLASE: 60 [33 - 120] U/L; NPTST089-CHOLINESTERASE: 212 [168 - 470] U/L; NPTST108-CRP: 2.51 [NOT REPORTED - 0.3] mg/dL; NPTST119-DIRECT BILIRUBIN: 2.7 [0 - 0.4] MG/DL; NPTST119-DIRECT BILIRUBIN: 2.7 [0 - 0.4] MG/DL; NPTST120-EGFR: 124 [NOT REPORTED - NOT REPORTED] ML/MIN/1.73M2; NPTST120-EGFR: 117 [NOT REPORTED - NOT REPORTED] ML/MIN/1.73M2; NPTST148-GAMMA GLUTAMYLTRANSFERASE: 229 [11 - 58] U/L; NPTST148-GAMMA GLUTAMYLTRANSFERASE: 230 [11 - 58] U/L; NPTST180-IG%: 0.6 [NOT REPORTED - NOT REPORTED] %; NPTST198-LACTATE DEHYDROGENASE: 207

[119 - 229] U/L; NPTST198-LACTATE DEHYDROGENASE: 230 [119 - 229] U/L; NPTST209-MAGNESIUM: 1.9 [1.9 - 2.5] MG/DL; NPTST211-MCH: 26.0 [28 - 34] PG; NPTST211-MCH: 25.8 [28 - 34] PG; NPTST212-MCHC: 32.1 [32 - 36] G/DL; NPTST212-MCHC: 31.9 [32 - 36] G/DL; NPTST213-MCV: 80.3 [83 - 100] FL; NPTST213-MCV: 81.3 [83 - 100] FL; NPTST250-PHOSPHORUS: 3.0 [2.5 - 4.5] MG/DL; NPTST259-PROCALCITONIN: 0.23 [NOT REPORTED - 0.05] ng/mL; NPTST262-PROTHROMBIN RATIO: 1.01 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST267-PT-%: 99.0 [70 - 120] %; NPTST268-PT-INR: 1.01 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST269-PT-SEC: 11.5 [NOT REPORTED - NOT REPORTED] sec; NPTST275-RDW-CV: 15.3 [0 - 15] NOT APPLICABLE; NPTST275-RDW-CV: 15.5 [0 - 15] NOT APPLICABLE; NPTST279-RED BLOOD CELL SEDIMENTATION RA: 75 [NOT REPORTED - NOT REPORTED] MM; NPTST279-RED BLOOD CELL SEDIMENTATION RA: 41 [1 - 10] MM; NPTST281-RED BLOOD CELL SEDIMENTATION RA: 15 [NOT REPORTED - NOT REPORTED] MM; NPTST316-TOTAL BILIRUBIN: 3.3 [0.2 - 1.2] MG/DL; NPTST316-TOTAL BILIRUBIN: 3.3 [0.2 - 1.2] MG/DL; NPTST318-TOTAL PROTEIN: 7.6 [6.6 - 8.7] G/DL; NPTST318-TOTAL PROTEIN: 7.5 [6.6 - 8.7] G/DL; NPTST332-TURBIDITY: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Neutrophils/Leukocytes: 85 [38 - 58] %; Nitrite: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Occult Blood: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Platelets: 251 [150 - 350] 10^9/L; Platelets: 255 [150 - 350] 10^9/L; Potassium: 3.3 [3.6 - 4.9] MMOL/L; Potassium: 3.4 [3.6 - 4.9] MMOL/L; Protein: 0 [NOT REPORTED - 30] mg/dL; Protein: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Sodium: 138 [138 - 146] MMOL/L; Sodium: 138 [138 - 146] MMOL/L; Specific Gravity: 1.003 [1.005 - 1.03] UNIT NOT REPORTED; Urate: 249.835782 [202.248014 - 416.39297] UMOL/L; Urobilinogen: NORMAL [NOT REPORTED - NOT REPORTED] mg/dL; pH: 7.0 [5 - 7.5] UNIT NOT REPORTED; [redacted] 0[redacted](RX DAY 326): Alanine Aminotransferase: 179 [8 - 42] U/L; Albumin: 30 [40 - 52] G/L; Alkaline Phosphatase: 470 [115 - 359] U/L; Aspartate Aminotransferase: 123 [13 - 33] U/L; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Chloride: 103 [99 - 109] MMOL/L; Creatine Kinase: 102 [62 - 287] U/L; Creatinine: 63.650347 [31.825174 - 93.707456] UMOL/L; Erythrocytes: 4.5 [4.1 - 5.5] 10^12/L; Hematocrit: 0.37 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 116 [130 - 170] G/L; Leukocytes: 4.39 [4 - 9] 10^9/L; NPTST028-AMYLASE: 74 [33 - 120] U/L; NPTST089-CHOLINESTERASE: 180 [168 - 470] U/L; NPTST108-CRP: 3.18 [NOT REPORTED - 0.3] mg/dL; NPTST119-DIRECT BILIRUBIN: 2.7 [0 - 0.4] MG/DL; NPTST120-EGFR: 107 [NOT REPORTED - NOT REPORTED] ML/MIN/1.73M2; NPTST148-GAMMA GLUTAMYLTRANSFERASE: 165 [11 - 58] U/L; NPTST198-LACTATE DEHYDROGENASE: 164 [119 - 229] U/L; NPTST211-MCH: 25.8 [28 - 34] PG; NPTST212-MCHC: 31.4 [32 - 36] G/DL; NPTST213-MCV: 82.2 [83 - 100] FL; NPTST259-PROCALCITONIN: 0.05 [NOT REPORTED - 0.05] ng/mL; NPTST262-PROTHROMBIN RATIO: 1.03 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST267-PT-%: 95.9 [70 - 120] %; NPTST268-PT-INR: 1.03 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST269-PT-SEC: 11.7 [NOT REPORTED - NOT REPORTED] sec; NPTST275-RDW-CV: 15.5 [0 - 15] NOT APPLICABLE; NPTST316-TOTAL BILIRUBIN: 3.1 [0.2 - 1.2] MG/DL; NPTST318-TOTAL PROTEIN: 7.1 [6.6 - 8.7] G/DL; Platelets: 275 [150 - 350] 10^9/L; Potassium: 3.7 [3.6 - 4.9] MMOL/L; Sodium: 138 [138 - 146] MMOL/L; [redacted]20[redacted](RX DAY 328): Alanine Aminotransferase: 180 [8 - 42] U/L; Albumin: 34 [40 - 52] G/L; Alkaline Phosphatase: 513 [115 - 359] U/L; Aspartate Aminotransferase: 95 [13 - 33] U/L; Blood Urea Nitrogen: 2.85576 [2.85576 - 7.1394] MMOL/L; Chloride: 104 [99 - 109] MMOL/L; Creatine Kinase: 93 [62 - 287] U/L; Erythrocytes: 5.23 [4.1 - 5.5] 10^12/L; Hematocrit: 0.426 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 136 [130 - 170] G/L; Leukocytes: 5.39 [4 - 9] 10^9/L; NPTST028-AMYLASE: 130 [33 - 120] U/L; NPTST089-CHOLINESTERASE: 211 [168 - 470] U/L; NPTST108-CRP: 1.35 [NOT REPORTED - 0.3] mg/dL; NPTST119-DIRECT BILIRUBIN: 3.3 [0 - 0.4] MG/DL; NPTST120-EGFR: 98 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST148-GAMMA GLUTAMYLTRANSFERASE: 157 [11 - 58] U/L; NPTST198-LACTATE DEHYDROGENASE: 169 [119 - 229] U/L; NPTST211-MCH: 26.0 [28 - 34] PG; NPTST212-MCHC: 31.9 [32 - 36] G/DL; NPTST213-MCV: 81.5 [83 - 100] FL; NPTST259-PROCALCITONIN: 0.04 [NOT REPORTED - 0.05] ng/mL; NPTST262-PROTHROMBIN RATIO: 1.15 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST267-PT-%: 78.0 [70 - 120] %; NPTST268-PT-INR: 1.16 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST269-PT-SEC: 13.1 [NOT REPORTED - NOT REPORTED] fmol; NPTST316-TOTAL BILIRUBIN: 3.8 [0.2 - 1.2] MG/DL; NPTST318-TOTAL PROTEIN: 8.1 [6.6 - 8.7] G/DL; Platelets: 356 [150 - 350] 10^9/L; Potassium: 4.1 [3.6 - 4.9] MMOL/L; Sodium: 138 [138 - 146] MMOL/L; [redacted]20[redacted](RX DAY 331): Alanine Aminotransferase: 87 [8 - 42] U/L; Albumin: 31 [40 - 52] G/L; Aspartate Aminotransferase: 37 [13 - 33] U/L; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Chloride: 105 [99 - 109] MMOL/L; Creatine Kinase: 47 [62 -

287] U/L; Creatinine: 67.186478 [31.825174 - 93.707456] UMOL/L; Erythrocytes: 4.78 [4.1 - 5.5] 10^12/L; Hematocrit: 0.394 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 123 [130 - 170] G/L; Leukocytes: 6.03 [4 - 9] 10^9/L; NPTST089-CHOLINESTERASE: 175 [168 - 470] U/L; NPTST108-CRP: 0.43 [NOT REPORTED - 0.3] mg/dL; NPTST120-EGFR: 101 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST148-GAMMA GLUTAMYLTRANSFERASE: 100 [11 - 58] U/L; NPTST198-LACTATE DEHYDROGENASE: 189 [119 - 229] U/L; NPTST211-MCH: 25.7 [28 - 34] PG; NPTST212-MCHC: 31.2 [32 - 36] G/DL; NPTST213-MCV: 82.4 [83 - 100] FL; NPTST262-PROTHROMBIN RATIO: 1.14 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST267-PT-%: 78.6 [70 - 120] %; NPTST268-PT-INR: 1.15 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST269-PT-SEC: 13.1 [NOT REPORTED - NOT REPORTED] sec; NPTST275-RDW-CV: 16.2 [0 - 15] NOT APPLICABLE; NPTST316-TOTAL BILIRUBIN: 3.8 [0.2 - 1.2] MG/DL; NPTST318-TOTAL PROTEIN: 7.1 [6.6 - 8.7] G/DL; Platelets: 329 [150 - 350] 10^9/L; Potassium: 4 [3.6 - 4.9] MMOL/L; Sodium: 138 [138 - 146] MMOL/L

**Microbiology**

NOT REPORTED

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | 391 / 334 (7 DAYS AFTER LAST TREATMENT) |
| **Duration of AE** | 14 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | MEDICAL HISTORY OF PRIMARY SCLEROSING CHDANGITIS AND GALLBLADDER ENLARGEMENT WAS FOUND. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: AE Leading to Discontinuation of Study Drug, Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | ELEVATION OF GAMMA GLUTAMYLTRANSTERASE |
| **Preferred term** | γ-グルタミルトランスフェラーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 379 / 322 |
| **Age at AE Onset** | 2[redacted] |
| **Laboratory Testing** | |

NOT APPLICABLE

**Microbiology**

NOT APPLICABLE

| | |
|---|---|
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | YES |
| **SAE Criteria** | NONE |

Generated: [redacted]16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腹痛の事象を発現した。関連する病歴は，原発性硬化性胆管炎，貧血，潰瘍性大腸炎，非喫煙者及び少量の現飲酒者（1 日 2 杯未満）であった。

**Event 2 の臨床経過：**

投与378日後＊，被験者は腹痛を発現した。投与391日後＊，腹痛は消失した。

投与378日後＊　，被験者は右上腹部痛があった。投与379日後＊　，被験者は圧痛のある胆嚢肥大があり，入院した。肝酵素の軽度の上昇（肝機能異常［非重篤］）があり，口から何も摂取しないように指示された。投与383日後＊，被験者は腹痛から回復し，食事を再開した。
投与384日後＊　，被験者は腹痛がなかった。投与391日後＊　，全身状態が安定していることが確認され，被験者は退院した。

投与された薬剤は，ブチルスコポラミン臭化物，セフメタゾールナトリウム，ロキソニン及びロキソプロフェン Na であった。

**The patient's past medications include:**

PENTASA for ULCERATIVE COLITIS ([redacted])

PREDONISOLONE for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

ADACOLUM for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

LEUKERIN for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted]- [redacted] 20[redacted]

LOXONINS for ABDOMONAL PAIN and HEADACHE ([redacted] 20[redacted]- [redacted] 20[redacted] [redacted] 20[redacted]- [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Abdominal pain (10000081) (Abdominal pain (10000081) ) [v.21.1] [10000081]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Open Label)

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Event of ABDOMINAL PAIN

**- Investigator:** MEDICAL HISTORY OF PRIMARY SCLEROSING CHOLANGITIS AND GALLBLADDER ENLARGEMENT WAS FOUND.

**- AbbVie:** EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS AND PRIMARY SCLEROSING CHOLANGITIS.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] ABDOMINAL ECHO:** Suspicion of cholecytitis

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 88 U/L (normal 8 to 42)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 115 U/L (normal 8 to 42)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 179 U/L (normal 8 to 42)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 180 U/L (normal 8 to 42)

[redacted] 20[redacted] **ALANINE AMINO TRANSFERASE:** 87 U/L (normal 8 to 42)

[redacted] 20[redacted] **ALBUMIN:** 3.9 G/DL (normal 4.0 to 5.2)

[redacted] 20[redacted] **ALBUMIN:** 3.4 G/DL (normal 4.0 to 5.2)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 455 U/L (normal 115 to 359)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 473 U/L (normal 115 to 359)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 470 U/L (normal 115 to 359)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 513 U/L (normal 115 to 359)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 441 U/L (normal 115 to 359)

[redacted] 20[redacted] **AMYLASE:** 92 U/L (normal 33 to 120)

[redacted] 20[redacted] **AMYLASE:** 59 U/L (normal 33 to 120)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 69 U/L (normal 13 to 33)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 89 U/L (normal 13 to 33)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 123 U/L (normal 13 to 33)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 95 U/L (normal 13 to 33)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 37 U/L (normal 13 to 33)

[redacted] 20[redacted] **BASOPHILS:** 0.8 % (normal 0.0 to 1.0)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 18 mg/dL (normal 8 to 20)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 11 mg/dL (normal 8 to 20)

[redacted] 20[redacted] **CREATINE KINASE:** 125 U/L (normal 62 to 287)

[redacted] 20[redacted] **CREATINE KINASE:** 106 U/L (normal 62 to 287)

[redacted] 20[redacted] **CREATININE:** 0.68 mg/dL (normal 0.36 to 1.06)

[redacted] 20[redacted] **CREATININE:** 0.63 mg/dL (normal 0.36 to 106)

[redacted] 20[redacted] **CRP:** 0.16 mg/dL (normal >0.03)

[redacted] 20[redacted] **DIRECT BILIRUBIN:** 1.4 mg/dL (normal 0.0 to 0.4)

[redacted][redacted]20[redacted] **DIRECT BILIRUBIN:** 2.7 mg/dL (normal 0 to 0.4)

[redacted][redacted]20[redacted] **EGFR:** 114 ML/MIN/1.73M2

[redacted][redacted]20[redacted] **EGFR:** 117 (ML/MIN/1.73M2

[redacted][redacted]20[redacted] **EOSINOPHILS:** 3.2 % (normal 2.0 to 7.0)

[redacted][redacted]20[redacted] **GLUTAMYLTRANSFERASE:** 245 U/L (normal 11 to 58)

[redacted][redacted]20[redacted] **GLUTAMYLTRANSFERASE:** 229 U/L (normal 11 to 58)

[redacted][redacted]20[redacted] **GLUTAMYLTRANSFERASE:** 157 U/L (normal 11 to 58)

[redacted][redacted]20[redacted] **HEMATOCRIT:** 40.5 % (normal 39 to 51)

[redacted][redacted]20[redacted] **HEMATOCRIT:** 39.4 % (normal 39 to 51)

[redacted][redacted]20[redacted] **HEMOGLOBIN:** 12.6 G/DL (normal 13 to 17)

[redacted][redacted]20[redacted] **HEMOGLOBIN:** 12.3 G/DL (normal 13 to 17)

[redacted][redacted]20[redacted] **INR:** 1.15 no unit

[redacted][redacted]20[redacted] **LACTATE DEHYDROGENASE:** 232 U/L (normal 119 to 229)

[redacted][redacted]20[redacted] **LYMPHOCYTES:** 12.2 % (normal 26.0 to 47.0)

[redacted][redacted]20[redacted] **MCH:** 25.5 PG (normal 28 to 34)

[redacted][redacted]20[redacted] **MCH:** 26 PG (normal 28 to 34)

[redacted][redacted]20[redacted] **MCHC:** 31.1 G/DL (normal 32.0 to 36.0)

[redacted][redacted]20[redacted] **MCHC:** 31.9 G/DL (normal 32.0 to 36.0)

[redacted][redacted]20[redacted] **MCV:** 81.8 FL (normal 83 to 100)

[redacted][redacted]20[redacted] **MCV:** 81.5 FL (normal 83 to 100)

[redacted][redacted]20[redacted] **MONOCYTES:** 5.4 % (normal 3.0 to 8.0)

[redacted][redacted]20[redacted] **NEUTROPHILS:** 78.4 % (normal 38.0 to 58.0)

[redacted][redacted]20[redacted] **PLATELET COUNT:** 290 No unit (normal 150 to 350)

[redacted][redacted]20[redacted] **PLATELET COUNT:** 329 10^3/uL (normal 150 to 350)

[redacted] **20[redacted] PROTHROMBIN RATIO:** 1.14 no unit

[redacted] **20[redacted] PT:** 13.1 SEC

[redacted] **20[redacted] RED BLOOD CELL SEDIMENTATION RATE 1HOUR:** 31 MM (normal 1 to 10)

[redacted] **20[redacted] RED BLOOD CELL SEDIMENTATION RATE 2HOUR:** 61 MM

[redacted] **20[redacted] RED BLOOD CELL SEDIMENTATION RATE 30MIN:** 11 MM

[redacted] **20[redacted] RED BLOOD CELLS:** 4.95 No unit (normal 4.10 to 5.50)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.78 No unit (normal 4.10 to 5.50)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 1.8 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 3.3 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL PROTEIN:** 8.0 G/DL (normal 6.6 to 8.7)

[redacted] **20[redacted] URIC ACID:** 4.2 mg/dL (normal 3.4 to 7.0)

[redacted] **20[redacted] URINE BACTERIA:** NEGATIVE

[redacted] **20[redacted] URINE BLOOD:** NEGATIVE

[redacted] **20[redacted] URINE KETONES:** NEGATIVE

[redacted] **20[redacted] URINE PROTEIN:** 100 mg/dL (normal 0 to 30)

[redacted] **20[redacted] URINE RED BLOOD CELLS:** 1-4 HPF

[redacted] **20[redacted] URINE SQUAMOUS CELL:** 0-1 HPF

[redacted] **20[redacted] URINE UROBILINOGEN:** 2.0 mg/dL

[redacted] **20[redacted] URINE WHITE BLOOD CELLS:** 5-9 HPF

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.24 10^3/uL (normal 4.0 to 9.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.39 No unit (normal 4.0 to 9.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6.03 10^3/uL (normal 4.0 to 9.0)

**NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST**

Gamma-glutamyltransferase increased: Study drug discontinued.

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 帯状疱疹 | X | | | X |
| 好中球減少症 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 30 mg | 4[redacted] | FEMALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| DERMATITIS ATOPIC | 19[redacted] |
| LEFT SIDED UC | 20[redacted] |
| MIGRAINE | 20[redacted] |
| POLLINOSIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS2 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 53 | 53 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 54 | [redacted]20[redacted] / 412 | 359 |

| | | | | | | |
|---|---|---|---|---|---|---|
| M14-533 ABT-494 (LTE) | 30 mg | ORAL | QD | [redacted]20[redacted] / 413 | [redacted]20[redacted] / 746 | 334 |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| MESALAZINE | NOT REPORTED | OTHER: UNK | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| PREDNISOLONE | 20 mg | PRN | Y-M: 20[redacted] |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 25 mg | OTHER: 2 TIME PAR WEEK | Y-M: 20[redacted] |
| MESALAZINE | 1500 mg | BID | Y-M: 20[redacted] |
| USTEKINUMAB | 130 mg | OTHER: 1TIME PAR 8WEEKS | Y-M: 20[redacted] |
| RIZATRIPTAN | 10 mg | PRN | Y-M: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MESALAZINE | 1500 mg | BID | Y-M: 20[redacted] | ONGOING |
| RIZATRIPTAN | 10 mg | PRN | Y-M: 20[redacted] | ONGOING |
| MIDAZOLAM | 2.0 mg | OTHER: ONCE | Y-M: 20[redacted] / 50 | Y-M: 20[redacted] / 50 |
| PETHIDINE | 35 mg | OTHER: ONCE | Y-M: 20[redacted] / 50 | Y-M: 20[redacted] / 50 |
| ACICLOVIR | 250 mg | BID | Y-M: 20[redacted] / 155 | Y-M: 20[redacted] / 155 |
| DOMPERIDONE | 10 mg | PRN | Y-M: 20[redacted] / 155 | Y-M: 20[redacted] / 189 |
| PARACETAMOL | 400 mg | BID | Y-M: 20[redacted] / 155 | Y-M: 20[redacted] / 189 |
| PARACETAMOL;TRAMADOL | 1 OTHER: TABLET | PRN | Y-M: 20[redacted] / 155 | Y-M: 20[redacted] / 189 |
| ACICLOVIR | 250 mg | TID | Y-M: 20[redacted] / 156 | Y-M: 20[redacted] / 161 |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] | Not reported |

**Event #1: Event of Interest - Neutropenia**

| | |
|---|---|
| **Event Description** | NEUTROPENIA |
| **Preferred term** | 好中球減少症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 462 / 50 |
| **Age at AE Onset** | 4[redacted] |

**Laboratory Testing**

NOT APPLICABLE

| | |
|---|---|
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 655 / 243 |
| **Duration of AE** | 194 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted] / 566 / 154 |
| **Age at AE Onset** | [redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 614 / 202 |
| **Duration of AE** | 49 DAYS |
| **Severity** | SEVERE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

Generated: [redacted]

Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，帯状疱疹の事象を発現した。関連する病歴は，アトピー性皮膚炎，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

**Event 2 の臨床経過：**

投与566日後＊，被験者は帯状疱疹を発現した。投与614日後＊，帯状疱疹は消失した。

投与566日後＊　，被験者は頚部痛を感じ始め，発疹が現れた。激しい頚部痛のため，救急科を受診したが，原因は不明であった。投与567日後＊　，被験者は皮膚科医を受診し，帯状疱疹と診断された。同日，頚部の発疹に伴う左肩部，左胸部及び左頚部の激しい痛みのため，被験者は入院した。帯状疱疹の治療が開始された。投与574日後＊，被験者は退院した。

被験者に帯状疱疹ワクチン接種歴はなかった。

投与された薬剤は，トアラセット，アセトアミノフェン及びドンペリドンであった。

**The patient's past medications include:**

MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

PREDONEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDONINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZANIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

STELARA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　Herpes zoster (10019974)　(Herpes zoster (10019974) )　[v.23.1]　[10019974]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

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Event of HERPES ZOSTER

**- Investigator:** Not applicable

**- AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

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**[redacted] 20[redacted] BODY WEIGHT:** 4[redacted] KG

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 頭痛 | X | | | |
| 帯状疱疹 | X | | | X |
| リンパ球減少症 | | | | X |
| 好中球減少症 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 5[redacted] | FEMALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| ANEMIA: ANEMIA | 20[redacted] |
| DRUG ABUSE: AZATHIOPRINE | 20[redacted] |
| LEFT SIDED UC | 19[redacted] |
| MIGRAINE HEADACHE: SOMETIME | 19[redacted] |
| OTHER: CERVICAL DISC HERNIATION | NOT REPORTED |
| OTHER: CHICKENPOX | NOT REPORTED |
| OTHER: CRP INCREASED | 20[redacted] |
| OTHER: DEHYDRATION | 20[redacted] |
| OTHER: ILIOTIBIAL BAND FRICTION SYNDROME | NOT REPORTED |
| OTHER: LYMPHOPENIA | 20[redacted] |
| OTHER: NEUTROPHILIA | 20[redacted] |
| OTHER: POLLINOSIS | 20[redacted] |
| OTHER: THROMOBOCYTOSIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: FOR APPENDICITIS | 19[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | NEVER | | | |
| CIGARS | NEVER | | | |

PIPES NEVER

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 7.5 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 55 | 55 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 56 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: ONE TIME PER TWO WEEKS | Y-M: 20[redacted] |
| ALENDRONIC ACID | 35 mg | OTHER: ONE TIME PER A WEEK | Y-M: 20[redacted] |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] |
| RABEPRAZOLE | 10 mg | QD | Y-M: 20[redacted] |
| SULFAMETHOXAZOLE;TRIMETHOPRIM | 1 OTHER: TABLET | QD | Y-M: 20[redacted] |
| TACROLIMUS | 2 mg | BID | Y-M: 20[redacted] |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] |
| ALUMINIUM HYDROXIDE;BISMUTH;CALCIUM CARBONATE;MAGNESIUM TRISILICATE;SODIUM BICARBONATE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| BETAMETHASONE | 1 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] |
| MESALAZINE | 1200 mg | TID | Y-M: 20[redacted] |
| SULFASALAZINE | 2000 mg | BID | Y-M: 20[redacted] |
| BETAMETHASONE | 1 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 260 mg | OTHER: ONE TIME PER SIX WEEKS | Y-M: 20[redacted] |
| METHOTREXATE | 3 mg | OTHER: TWO DAYS PER A WEEK | Y-M: 20[redacted] |
| PREDNISOLONE | 7.5 mg | QD | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| CLOSTRIDIUM BUTYRICUM | 2 OTHER: TABLET | QD | Y-M: 20[redacted] |
| ALUMINIUM HYDROXIDE;BISMUTH;CALCIUM CARBONATE;MAGNESIUM TRISILICATE;SODIUM BICARBONATE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| BECLOMETASONE | 20 mg | QD | Y-M: 20[redacted] |
| BETAMETHASONE | 3 mg | QD | Y-M: 20[redacted] / -303 |
| MERCAPTOPURINE | 10 mg | QD | Y-M: 20[redacted] / -259 |
| MESALAZINE | 3600 mg | QD | Y-M: 20[redacted] / -243 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -243 |
| MESALAZINE | 4800 mg | QD | Y-M: 20[redacted] / -251 |
| PREDNISOLONE | 10 mg | QD | Y-M: 20[redacted] / -65 |
| PARACETAMOL | 200 mg | PRN | Y: 19[redacted] |
| ALL OTHER NON-THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |
| PREDNISOLONE | 5 mg | OTHER: ONE TIME PER TWO DAYS | Y: 20[redacted] |
| AZATHIOPRINE | NOT REPORTED | OTHER: UNK | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| ALENDRONIC ACID | 35 mg | OTHER: ONE TIME PER A WEEK | Y-M: 20[redacted] | Y-M: 20[redacted] / 169 |
| RABEPRAZOLE | 10 mg | QD | Y-M: 20[redacted] | ONGOING |
| SULFAMETHOXAZOLE;TRIMETHOPRIM | 1 OTHER: TABLET | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 114 |
| CLOSTRIDIUM BUTYRICUM | 2 OTHER: TABLET | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 676 |
| MESALAZINE | 3600 mg | QD | Y-M: 20[redacted] / -243 | Y-M: 20[redacted] / 326 |
| PREDNISOLONE | 10 mg | QD | Y-M: 20[redacted] / -65 | Y-M: 20[redacted] / 86 |
| PREDNISOLONE | 7.5 mg | QD | Y-M: 20[redacted] / 87 | Y-M: 20[redacted] / 128 |
| PREDNISOLONE | 5 mg | QD | Y-M: 20[redacted] / 129 | Y-M: 20[redacted] / 176 |
| AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE | 500 mL | PRN | Y-M: 20[redacted] / 167 | Y-M: 20[redacted] / 169 |
| CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE | 500 mL | QD | Y-M: 20[redacted] / 167 | Y-M: 20[redacted] / 167 |
| GLUCOSE | 20 mL | QD | Y-M: 20[redacted] / 167 | Y-M: 20[redacted] / 167 |

| | | | | |
|---|---|---|---|---|
| LOXOPROFEN | 60 mg | QD | Y-M: 20[redacted] / 167 | Y-M: 20[redacted] / 170 |
| METOCLOPRAMIDE | 10 mg | QD | Y-M: 20[redacted] / 167 | Y-M: 20[redacted] / 167 |
| METOCLOPRAMIDE | 5 mg | TID | Y-M: 20[redacted] / 167 | Y-M: 20[redacted] / 170 |
| ALENDRONIC ACID | 35 mg | OTHER: ONE TIME PER A WEEK | Y-M: 20[redacted] / 170 | Y-M: 20[redacted] / 326 |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] / 177 | Y-M: 20[redacted] / 211 |
| DEXAMETHASONE | PROPER DOSE OTHER: PROPER DOSE | BID | Y-M: 20[redacted] / 200 | Y-M: 20[redacted] / 202 |
| ASCORBIC ACID;PANTOTHENIC ACID | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 204 | ONGOING |
| TRANEXAMIC ACID | 250 mg | TID | Y-M: 20[redacted] / 246 | Y-M: 20[redacted] / 253 |
| CARBOCISTEINE | 500 mg | TID | Y-M: 20[redacted] / 248 | Y-M: 20[redacted] / 252 |
| CEFDITOREN | 100 mg | TID | Y-M: 20[redacted] / 248 | Y-M: 20[redacted] / 252 |
| CHLORPHENAMINE;DIHYDROCODEINE;METHYLEPHEDRINE | 2 OTHER: TABLETS | TID | Y-M: 20[redacted] / 248 | Y-M: 20[redacted] / 252 |
| PARACETAMOL | 400 mg | PRN | Y-M: 20[redacted] / 248 | Y-M: 20[redacted] / 252 |
| TULOBUTEROL | 2 mg | QD | Y-M: 20[redacted] / 248 | Y-M: 20[redacted] / 252 |
| AMBROXOL | 15 mg | TID | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 256 |
| GARENOXACIN | 400 mg | BID | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 256 |
| TRANEXAMIC ACID | 500 mg | TID | Y-M: 20[redacted] / 252 | Y-M: 20[redacted] / 256 |
| CARBOCISTEINE | 500 mg | TID | Y-M: 20[redacted] / 256 | Y-M: 20[redacted] / 281 |
| GARENOXACIN | 200 mg | BID | Y-M: 20[redacted] / 256 | Y-M: 20[redacted] / 260 |
| PARACETAMOL | 300 mg | PRN | Y-M: 20[redacted] / 256 | Y-M: 20[redacted] / 260 |
| CLARITHROMYCIN | 200 mg | QD | Y-M: 20[redacted] / 260 | Y-M: 20[redacted] / 281 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 2 L | PRN | Y-M: 20[redacted] / 326 | Y-M: 20[redacted] / 326 |
| HYOSCINE | 20 mg | QD | Y-M: 20[redacted] / 326 | Y-M: 20[redacted] / 326 |
| RISEDRONIC ACID | 75 mg | OTHER: ONCE A MONTH | Y-M: 20[redacted] / 326 | ONGOING |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 326 | Y-M: 20[redacted] / 326 |
| PARACETAMOL | 400 mg | PRN | Y-M: 20[redacted] / 331 | Y-M: 20[redacted] / 331 |
| BEPOTASTINE | 10 mg | BID | Y-M: 20[redacted] / 332 | Y-M: 20[redacted] / 336 |
| CARBOCISTEINE | 500 mg | TID | Y-M: 20[redacted] / 332 | Y-M: 20[redacted] / 338 |
| CEFDITOREN | 100 mg | BID | Y-M: 20[redacted] / 332 | Y-M: 20[redacted] / 336 |
| CLOPERASTINE | 20 mg | TID | Y-M: 20[redacted] / 332 | Y-M: 20[redacted] / 336 |
| DEXTROMETHORPHAN | 15 mg | TID | Y-M: 20[redacted] / 332 | Y-M: 20[redacted] / 336 |

| | | | | |
|---|---|---|---|---|
| AMOXICILLIN;CLAVULANIC ACID | 375 mg | TID | Y-M: 20[redacted] / 336 | Y-M: 20[redacted] / 338 |
| AMBROXOL | 15 mg | TID | Y-M: 20[redacted] / 338 | Y-M: 20[redacted] / 345 |
| MESALAZINE | 1200 mg | BID | Y-M: 20[redacted] / 339 | ONGOING |
| DEXAMETHASONE | PROPER DOSE OTHER: PROPER DOSE | PRN | Y-M: 20[redacted] / 424 | ONGOING |
| ROSUVASTATIN | 2.5 mg | QD | Y-M: 20[redacted] / 430 | Y-M: 20[redacted] / 676 |
| BEPOTASTINE | 100 mg | BID | Y-M: 20[redacted] / 462 | Y-M: 20[redacted] / 469 |
| CARBOCISTEINE | 500 mg | TID | Y-M: 20[redacted] / 462 | Y-M: 20[redacted] / 469 |
| CEFDITOREN | 100 mg | TID | Y-M: 20[redacted] / 462 | Y-M: 20[redacted] / 469 |
| CLOPERASTINE | 100 mg | TID | Y-M: 20[redacted] / 462 | Y-M: 20[redacted] / 469 |
| CARBOCISTEINE | 500 mg | TID | Y-M: 20[redacted] / 529 | Y-M: 20[redacted] / 535 |
| CEFCAPENE | 100 mg | TID | Y-M: 20[redacted] / 529 | Y-M: 20[redacted] / 535 |
| GUALENIC ACID | PROPERDOSE OTHER: PROPERDOSE | PRN | Y-M: 20[redacted] / 529 | Y-M: 20[redacted] / 680 |
| DIAZEPAM | 10 mg | QD | Y-M: 20[redacted] / 585 | Y-M: 20[redacted] / 585 |
| HYOSCINE | 20 mg | QD | Y-M: 20[redacted] / 585 | Y-M: 20[redacted] / 585 |
| LIDOCAINE | PROPER DOSE OTHER: PROPER DOSE | PRN | Y-M: 20[redacted] / 585 | Y-M: 20[redacted] / 615 |
| MIDAZOLAM | 3 mg | QD | Y-M: 20[redacted] / 585 | Y-M: 20[redacted] / 585 |
| PARACETAMOL | 200 mg | PRN | Y-M: 20[redacted] / 585 | ONGOING |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 675 | Y-M: 20[redacted] / 675 |
| HYOSCINE | 20 mg | QD | Y-M: 20[redacted] / 676 | Y-M: 20[redacted] / 676 |
| ROSUVASTATIN | 2.5 mg | QD | Y-M: 20[redacted] / 677 | ONGOING |
| MECOBALAMIN | 500 ug | TID | Y-M: 20[redacted] / 840 | Y-M: 20[redacted] / 851 |
| VALACICLOVIR | 1000 ug | TID | Y-M: 20[redacted] / 841 | Y-M: 20[redacted] / 846 |
| CALCIUM CHLORIDE;GLUCOSE;POTASSIUM;SODIUM ACETATE | 500 mL | PRN | Y-M: 20[redacted] / 842 | Y-M: 20[redacted] / 843 |
| CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE | 500 mL | PRN | Y-M: 20[redacted] / 842 | Y-M: 20[redacted] / 842 |
| METOCLOPRAMIDE | 10 mg | PRN | Y-M: 20[redacted] / 842 | Y-M: 20[redacted] / 844 |
| CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 500 mL | PRN | Y-M: 20[redacted] / 843 | Y-M: 20[redacted] / 847 |
| PREGABALIN | 25 mg | QD | Y-M: 20[redacted] / 848 | Y-M: 20[redacted] / 848 |

| | | | | |
|---|---|---|---|---|
| PREGABALIN | 25 mg | BID | Y-M: 20[redacted] / 953 | Y-M: 20[redacted] / 955 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 2 L | PRN | Y-M: 20[redacted] / 1005 | Y-M: 20[redacted] / 1005 |
| HYOSCINE | 20 mg | PRN | Y-M: 20[redacted] / 1005 | Y-M: 20[redacted] / 1005 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 1005 | Y-M: 20[redacted] / 1005 |
| ALLIUM SATIVUM;BIOTIN;LIVER EXTRACT;THIAMINE | 1 mL | OTHER: ONCE A WEEK | Y-M: 20[redacted] / 1131 | ONGOING |
| HYOSCINE | 10 mg | QD | Y-M: 20[redacted] / 1248 | Y-M: 20[redacted] / 1248 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 2 L | PRN | Y-M: 20[redacted] / 1334 | Y-M: 20[redacted] / 1334 |
| HYOSCINE | 20 mg | PRN | Y-M: 20[redacted] / 1334 | Y-M: 20[redacted] / 1334 |
| MIDAZOLAM | 5 mg | QD | Y-M: 20[redacted] / 1334 | Y-M: 20[redacted] / 1334 |
| SODIUM PICOSULFATE | 10 mg | QD | Y-M: 20[redacted] / 1334 | Y-M: 20[redacted] / 1334 |
| PARACETAMOL | 200 mg | PRN | Y: 19[redacted] | ONGOING |

**Event #1: Event of Interest - Lymphopenia**

| | |
|---|---|
| **Event Description** | LYMPHOCYTOPENIA |
| **Preferred term** | リンパ球減少症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 124 / 69 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | HEADACHE |
| **Preferred term** | 頭痛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 222 / 167 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 224 / 169 |
| **Duration of AE** | 3 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | 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. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: Event of Interest - Neutropenia**

| | |
|---|---|
| **Event Description** | NEUTROPENIA |
| **Preferred term** | 好中球減少症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 489 / 434 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | ONGOING |
| **Duration of AE** | ONGOING |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #4: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster**

| | |
|---|---|
| **Event Description** | HERPES ZOSTER |
| **Preferred term** | 帯状疱疹 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 893 / 838 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | 906 / 851 |
| **Duration of AE** | 14 DAYS |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT REPORTED |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，頭痛の事象を発現した。関連する病歴は，花粉症，貧血，脱水，非喫煙者，現飲酒者（1 日 2 杯未満）及び片頭痛であった。

**Event 2 の臨床経過：**

投与222日後＊，被験者は頭痛を発現した。投与224日後＊，頭痛は消失した。

投与221日後＊，被験者は，悪寒及び嘔吐を伴う頭痛を発現し始めた。投与222日後＊　　，症状が改善しなかったため，被験者は救急治療室を受診した。頭部 CT 検査では，異常所見は認められなかった。対症療法及び点滴注入で治療を行い，投与222日後＊，被験者は経過観察の

ために入院した。入院後，補液及び制吐薬を投与したところ，頭痛が改善し始めた。被験者は夕方には食事を摂ることができた。投与224日後＊，症状が安定し，被験者は退院した。

投与された薬剤は，プリンペランであった。

**The patient's past medications include:**

PREDONINE for ULCERATIVE COLITIS ([redacted] - [redacted])

Causality for ABT-494 (Open Label)

---

1) Headache (10019211) (Headache (10019211) ) [v.21.0] [10019211]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for ABT-494 (Open Label)

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Event of HEADACHE

**- Investigator:** She has a history of severe headache with vomiting. In addition, time has passed since the start of the investigational agent, so I think the symptoms are not due to investigational agent but functional headaches.

**- AbbVie:** Event more likely related to pre-existing history of migraine headache.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **HEAD CT:** no abnormal findings
**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，帯状疱疹の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者，現飲酒者（1 日 2 杯未満）及び水痘であった。

**Event 4 の臨床経過：**

投与893日後＊，被験者は帯状疱疹を発現した。投与906日後＊ ，帯状疱疹は消失した。

投与893日後＊ ，被験者は右後頚部及び右後頭部の皮膚の痛みを発現した。投与896日後＊ ，症状が改善しないため，外来を受診した。発疹は認められなかったが，帯状疱疹が疑われ，バラシクロビルが処方された。被験者は摂氏 38°C の発熱と，右後頭部及び後頚部を含む 2 つの皮膚分節に限局した発疹を発現した。投与897日後＊ ，被験者は入院した。投与906日後＊ ，被験者は退院した。

投与された薬剤は，リリカ，プリンペラン注射液，ソリューゲン F，ソリューゲン G，バラシクロビル粒状錠，メチコバール及びソルデム 3A であった。

**The patient's past medications include:**

PREDONINE for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

RHEUMATREX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BECLOMETASONE DIPROPIONATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

STERONEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LEUKERIN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

---

1) Herpes zoster (10019974) (Herpes zoster (10019974) ) [v.23.1] [10019974]

**Causality as per reporter (Drug/Vaccine):** Reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** Reasonable possibility

**Dechallenge:** Yes

**Rechallenge:** rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

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Event of HERPES ZOSTER

**- Investigator:** Not applicable

**- AbbVie:** Not applicable

Relevant Laboratory & Other Diagnostic Tests

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**20[redacted] BODY TEMPERATURE:** 38 Degrees C

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| 背部痛 | X | | | |
| 椎間板突出 | X | | | |
| 腰部脊柱管狭窄症 | X | | | |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 5[redacted] | FEMALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| ASTHMA | NOT REPORTED |
| HYPERTENSION | NOT REPORTED |
| LEFT SIDED UC | 19[redacted] |
| OSTEOPOROSIS | NOT REPORTED |
| OTHER: HEADACHE | 20[redacted] |
| OTHER: INSOMNIA | NOT REPORTED |
| OTHER: LATENT TUBERCULOSIS INFECTION | 20[redacted] |
| OTHER: LUMBAR DISC HERNIATION | 20[redacted] |
| OTHER: SHOULDER STIFFNESS | NOT REPORTED |

| Prior Procedures | Procedure Year |
|---|---|
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 0.2 PACK | 0.3 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | 2 - 4 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted] / 1 | [redacted] / 55 | 55 |
| M14-234 SS3 Placebo (MAIN) | | ORAL | QD | [redacted] / 56 | [redacted] / 329 | 274 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted] / 330 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| SULFASALAZINE | NOT REPORTED | NOT REPORTED | Y-M: 19[redacted] |
| INFLIXIMAB | 5 mg/kg | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 80 mg | OTHER: EVERY TWO WEEKS | Y-M: 20[redacted] |
| TACROLIMUS | 8 mg | QD | Y-M: 20[redacted] |
| MINODRONIC ACID | 50 mg | OTHER: ONCE PER 4WEEKS | Y-M: 20[redacted] |
| ISONIAZID | 250 mg | QD | Y-M: 20[redacted] / -350 |
| OLMESARTAN | 20 mg | QD | Y-M: 20[redacted] / -301 |
| RABEPRAZOLE | 10 mg | QD | Y-M: 20[redacted] / -301 |
| LOXOPROFEN | 1 OTHER: SHEET | QD | Y-M: 20[redacted] / -314 |
| FELBINAC | PROPER AMOUNT g | PRN | Y-M: 20[redacted] / -226 |
| PREGABALIN | 25 mg | BID | Y-M: 20[redacted] / -214 |
| ETIZOLAM | 0.5 mg | PRN | Y-M: 20[redacted] / -185 |
| GLYCYRRHIZIC ACID | 2 OTHER: TABLET | TID | Y-M: 20[redacted] / -190 |
| URSODEOXYCHOLIC ACID | 200 mg | TID | Y-M: 20[redacted] / -190 |
| PARACETAMOL | 300 mg | PRN | Y-M: 20[redacted] / -132 |
| CAMPHOR;CAPSICUM SPP.;SALICYLIC ACID | 1 OTHER: SHEET | PRN | Y-M: 20[redacted] / -24 |
| PREDNISOLONE | 20 mg | QD | Y-M: 20[redacted] / -9 |
| AZATHIOPRINE | 50 mg | QD | Y: 19[redacted] |
| MESALAZINE | 3000 mg | QD | Y: 19[redacted] |
| BETAMETHASONE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |
| PREDNISOLONE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |
| MESALAZINE | 1 g | BID | Y: 20[redacted] |

| | | | |
|---|---|---|---|
| MESALAZINE | 3000 mg | QD | Y: 20[redacted] |
| PREDNISOLONE | 15 mg | QD | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| MINODRONIC ACID | 50 mg | OTHER: ONCE PER 4WEEKS | Y-M: 20[redacted] | ONGOING |
| RABEPRAZOLE | 10 mg | QD | Y-M: 20[redacted] / -301 | ONGOING |
| LOXOPROFEN | 1 OTHER: SHEET | QD | Y-M: 20[redacted] / -314 | ONGOING |
| FELBINAC | PROPER AMOUNT g | PRN | Y-M: 20[redacted] / -226 | ONGOING |
| ETIZOLAM | 0.5 mg | PRN | Y-M: 20[redacted] / -185 | ONGOING |
| GLYCYRRHIZIC ACID | 2 OTHER: TABLET | TID | Y-M: 20[redacted] / -190 | Y-M: 20[redacted] / 490 |
| URSODEOXYCHOLIC ACID | 200 mg | TID | Y-M: 20[redacted] / -190 | Not reported |
| PARACETAMOL | 300 mg | PRN | Y-M: 20[redacted] / -132 | ONGOING |
| CAMPHOR;CAPSICUM SPP.;SALICYLIC ACID | 1 OTHER: SHEET | PRN | Y-M: 20[redacted] / -24 | Not reported |
| HYALURONIC ACID | 1 OTHER: GTT. | OTHER: 6 TIMES PER DAY | Y-M: 20[redacted] / 155 | Y-M: 20[redacted] / 1205 |
| OLMESARTAN | 40 mg | QD | Y-M: 20[redacted] / 240 | ONGOING |
| TRICHLORMETHIAZIDE | 1 mg | QD | Y-M: 20[redacted] / 310 | Y-M: 20[redacted] / 474 |
| BUDESONIDE;FORMOTEROL | 2 OTHER: PUFF | BID | Y-M: 20[redacted] / 386 | Y-M: 20[redacted] / 553 |
| LOXOPROFEN | 1 OTHER: SHEET | QD | Y-M: 20[redacted] / 400 | Y-M: 20[redacted] / 531 |
| PREGABALIN | 75 mg | BID | Y-M: 20[redacted] / 407 | Y-M: 20[redacted] / 563 |
| METOCLOPRAMIDE | 5 mg | TID | Y-M: 20[redacted] / 456 | Y-M: 20[redacted] / 462 |
| TRAMADOL | 25 mg | BID | Y-M: 20[redacted] / 456 | Y-M: 20[redacted] / 531 |
| PARACETAMOL | 1000 mg | QD | Y-M: 20[redacted] / 483 | Y-M: 20[redacted] / 483 |
| LOXOPROFEN | 1 OTHER: SHEET | QD | Y-M: 20[redacted] / 532 | ONGOING |
| METOCLOPRAMIDE | 5 mg | TID | Y-M: 20[redacted] / 532 | Y-M: 20[redacted] / 545 |
| PARACETAMOL;TRAMADOL | 1 OTHER: TABLET | TID | Y-M: 20[redacted] / 532 | Y-M: 20[redacted] / 569 |
| DULOXETINE | 20 mg | QD | Y-M: 20[redacted] / 553 | Y-M: 20[redacted] / 594 |
| METOCLOPRAMIDE | 5 mg | TID | Y-M: 20[redacted] / 553 | Y-M: 20[redacted] / 566 |
| BUDESONIDE;FORMOTEROL | 1 OTHER: PUFF | BID | Y-M: 20[redacted] / 554 | Y-M: 20[redacted] / 822 |

| | | | | |
|---|---|---|---|---|
| PREGABALIN | 150 mg | BID | Y-M: 20[redacted] / 564 | Y-M: 20[redacted] / 786 |
| PARACETAMOL;TRAMADOL | 1 OTHER: TABLET | BID | Y-M: 20[redacted] / 570 | Y-M: 20[redacted] / 570 |
| PARACETAMOL;TRAMADOL | 1 OTHER: TABLET | QD | Y-M: 20[redacted] / 571 | Y-M: 20[redacted] / 602 |
| IOHEXOL | 10 mL | QD | Y-M: 20[redacted] / 573 | Y-M: 20[redacted] / 573 |
| LIDOCAINE | 3 mL | QD | Y-M: 20[redacted] / 573 | Y-M: 20[redacted] / 573 |
| DULOXETINE | 40 mg | QD | Y-M: 20[redacted] / 595 | Y-M: 20[redacted] / 602 |
| DULOXETINE | 60 mg | QD | Y-M: 20[redacted] / 603 | Y-M: 20[redacted] / 786 |
| LIDOCAINE | 3 mL | QD | Y-M: 20[redacted] / 608 | Y-M: 20[redacted] / 608 |
| GUALENIC ACID | 1 OTHER: PUSH | PRN | Y-M: 20[redacted] / 617 | ONGOING |
| MAGNESIUM OXIDE | 330 mg | PRN | Y-M: 20[redacted] / 642 | ONGOING |
| PARACETAMOL;TRAMADOL | 1(TRAMADOL YDROCHLORIDE 37.5MG,ACETAMINOPHEN 325MG OTHER: TABLETS | TID | Y-M: 20[redacted] / 642 | Y-M: 20[redacted] / 822 |
| ASCORBIC ACID | 500 mg | QD | Y-M: 20[redacted] / 663 | Y-M: 20[redacted] / 663 |
| CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 500 mL | QID | Y-M: 20[redacted] / 663 | Y-M: 20[redacted] / 663 |
| RIBOFLAVIN | 20 mg | QD | Y-M: 20[redacted] / 663 | Y-M: 20[redacted] / 663 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 663 | Y-M: 20[redacted] / 663 |
| THIAMINE | 10 mg | QD | Y-M: 20[redacted] / 663 | Y-M: 20[redacted] / 663 |
| DIMETICONE | 10 mL | QD | Y-M: 20[redacted] / 664 | Y-M: 20[redacted] / 664 |
| GLUCAGON | 1 mg | QD | Y-M: 20[redacted] / 664 | Y-M: 20[redacted] / 664 |
| LIDOCAINE | 5 mL | QD | Y-M: 20[redacted] / 664 | Y-M: 20[redacted] / 664 |
| POTASSIUM;SODIUM BICARBONATE;SODIUM SULFATE | 1 OTHER: BOTTLE | QD | Y-M: 20[redacted] / 664 | Y-M: 20[redacted] / 664 |
| CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE | 500 mL | BID | Y-M: 20[redacted] / 671 | Y-M: 20[redacted] / 671 |
| IOHEXOL | 10 mL | QD | Y-M: 20[redacted] / 671 | Y-M: 20[redacted] / 671 |
| LIDOCAINE | 3 mL | QD | Y-M: 20[redacted] / 671 | Y-M: 20[redacted] / 671 |

| | | | | |
|---|---|---|---|---|
| IOHEXOL | 10 mL | QD | Y-M: 20[redacted] / 722 | Y-M: 20[redacted] / 722 |
| LIDOCAINE | 3 mL | QD | Y-M: 20[redacted] / 722 | Y-M: 20[redacted] / 722 |
| PROCATEROL | 10 ug | PRN | Y-M: 20[redacted] / 734 | ONGOING |
| DIPHENHYDRAMINE | PROPER AMOUNT g | PRN | Y-M: 20[redacted] / 787 | Y-M: 20[redacted] / 790 |
| FEXOFENADINE | 60 mg | BID | Y-M: 20[redacted] / 787 | Y-M: 20[redacted] / 790 |
| AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE | 500 mL | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 789 |
| CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE | 500 mL | BID | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| CALCIUM GLUCONATE;GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE;SODIUM CITRATE | 500 mL | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| CARBAZOCHROME | 100 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 500 mL | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| CEFAZOLIN | 1 g | TID | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 789 |
| EPHEDRINE | 40 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| EPINEPHRINE | UNK mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| FENTANYL | 0.6 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| GLYCEROL | 120 mL | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| HYDROCORTISONE | 300 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| KETAMINE | 40 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| MAGNESIUM CHLORIDE;MALTOSE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE;SODIUM CHLORIDE | 500 mL | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |

| | | | | |
|---|---|---|---|---|
| PARACETAMOL | 1000 mg | PRN | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| PROPOFOL | 50 mL | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| REMIFENTANIL | 2 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| TRANEXAMIC ACID | 500 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| VECURONIUM | 5 mg | QD | Y-M: 20[redacted] / 788 | Y-M: 20[redacted] / 788 |
| HYDROCORTISONE | 100 mg | QD | Y-M: 20[redacted] / 789 | Y-M: 20[redacted] / 789 |
| GLYCEROL | 120 mL | QD | Y-M: 20[redacted] / 790 | Y-M: 20[redacted] / 790 |
| PARACETAMOL;TRAMADOL | 1 OTHER: TAB | TID | Y-M: 20[redacted] / 792 | Y-M: 20[redacted] / 801 |
| PARACETAMOL;TRAMADOL | 1 OTHER: TAB | BID | Y-M: 20[redacted] / 802 | Y-M: 20[redacted] / 822 |
| SUMATRIPTAN | 50 mg | PRN | Y-M: 20[redacted] / 803 | ONGOING |
| BUDESONIDE;FORMOTEROL | 2 OTHER: PUFF | BID | Y-M: 20[redacted] / 823 | Y-M: 20[redacted] / 878 |
| CHLORPHENAMINE; DIHYDROCODEINE; METHYLEPHEDRINE | 2 OTHER: TABLETS | TID | Y-M: 20[redacted] / 823 | Y-M: 20[redacted] / 852 |
| BUDESONIDE;FORMOTEROL | 3 OTHER: PUFF | BID | Y-M: 20[redacted] / 879 | Y-M: 20[redacted] / 983 |
| CHLORPHENAMINE; DIHYDROCODEINE; METHYLEPHEDRINE | 2 OTHER: TABLETS | PRN | Y-M: 20[redacted] / 879 | ONGOING |
| BUDESONIDE;FORMOTEROL | 4 OTHER: PUFF | BID | Y-M: 20[redacted] / 984 | Not reported |
| CARBOCISTEINE | 500 mg | TID | Y-M: 20[redacted] / 984 | Not reported |
| GARENOXACIN | 400 mg | QD | Y-M: 20[redacted] / 984 | Y-M: 20[redacted] / 989 |
| PREDNISOLONE | 30 mg | QD | Y-M: 20[redacted] / 1000 | Y-M: 20[redacted] / 1003 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 1008 | Y-M: 20[redacted] / 1008 |
| DIMETICONE | 10 mL | QD | Y-M: 20[redacted] / 1009 | Y-M: 20[redacted] / 1009 |
| GLUCAGON | 1 mg | QD | Y-M: 20[redacted] / 1009 | Y-M: 20[redacted] / 1009 |
| LIDOCAINE | 5 mL | QD | Y-M: 20[redacted] / 1009 | Y-M: 20[redacted] / 1009 |
| POTASSIUM;SODIUM BICARBONATE;SODIUM SULFATE | 1 OTHER: BOTTLE | QD | Y-M: 20[redacted] / 1009 | Y-M: 20[redacted] / 1009 |
| POTASSIUM;SODIUM BICARBONATE;SODIUM SULFATE | PROPER AMOUNT OTHER: PROPER AMOUNT | QD | Y-M: 20[redacted] / 1009 | Y-M: 20[redacted] / 1009 |
| INFLUENZA VACCINE | 0.5 mL | QD | Y-M: 20[redacted] / 1012 | Y-M: 20[redacted] / 1012 |
| TRIAMCINOLONE | PROPER AMOUNT g | PRN | Y-M: 20[redacted] / 1027 | Y-M: 20[redacted] / 1047 |

| | | | | |
|---|---|---|---|---|
| TIOTROPIUM | 2 OTHER: PUFF | QD | Y-M: 20[redacted] / 1103 | Not reported |
| DEQUALINIUM | 0.25 mg | PRN | Y-M: 20[redacted] / 1205 | Y-M: 20[redacted] / 1210 |
| DIQUAFOSOL | 1 OTHER: GTT. | OTHER: 6TIMES PER DAY | Y-M: 20[redacted] / 1205 | Not reported |
| DIMETICONE | 5 mL | QD | Y-M: 20[redacted] / 1258 | Y-M: 20[redacted] / 1258 |
| LIDOCAINE | 4 mL | QD | Y-M: 20[redacted] / 1258 | Y-M: 20[redacted] / 1258 |
| LIDOCAINE | 5 mL | QD | Y-M: 20[redacted] / 1258 | Y-M: 20[redacted] / 1258 |
| NAPHAZOLINE | 2 mL | QD | Y-M: 20[redacted] / 1258 | Y-M: 20[redacted] / 1258 |
| PRONASE | 0.5 g | QD | Y-M: 20[redacted] / 1258 | Y-M: 20[redacted] / 1258 |
| SODIUM BICARBONATE | 1 g | QD | Y-M: 20[redacted] / 1258 | Y-M: 20[redacted] / 1258 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 1341 | Y-M: 20[redacted] / 1341 |
| DIMETICONE | 5 mL | QD | Y-M: 20[redacted] / 1342 | Y-M: 20[redacted] / 1342 |
| GLUCAGON | 1 mg | QD | Y-M: 20[redacted] / 1342 | Y-M: 20[redacted] / 1342 |
| LIDOCAINE | 5 mL | QD | Y-M: 20[redacted] / 1342 | Y-M: 20[redacted] / 1342 |
| POTASSIUM;SODIUM BICARBONATE;SODIUM SULFATE | 1 OTHER: BOTTLE | QD | Y-M: 20[redacted] / 1342 | Y-M: 20[redacted] / 1342 |

**Event #1: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | LUMBAGO |
| **Preferred term** | 背部痛 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 812 / 483 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY |

**Event #2: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | LUMBAR SPINAL CANAL STENOSIS |
| **Preferred term** | 腰部脊柱管狭窄症 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1000 / 671 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #3: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | EXACERBATION OF LUMBAR DISC HERNIATION |
| **Preferred term** | 椎間板突出 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 1117 / 788 |
| **Age at AE Onset** | 5[redacted] |
| **Laboratory Testing** | |
| NOT REPORTED | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MODERATE |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION |

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腰痛症の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.2 箱を 0.3 年間），骨粗鬆症及び中程度の現飲酒者（1 日 2–4 杯）であった。

**Event 1 の臨床経過：**

投与812日後＊，被験者は腰痛症を発現した。

本事象発現前の 投与の10ヵ月後＊，被験者は軽度の腰痛症（非重篤）を経験していた。

投与812日後＊　，被験者は整形外科を受診した。身体所見から，仙腸骨炎及び脊椎炎の徴候は認められなかった。歩行障害及び下背部痛があり，同日，重症度が中等度の腰痛症のために入院した。被験者は鎮痛薬を投与され，安静を指示された。被験者は歩行訓練及び運動を行い，日ごとに改善した。投与822日後＊，被験者は退院した。

投与された薬剤は，トラマール OD であった。

**The patient's past medications include:**

ASACOL for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

IMURAN for ULCERATIVE COLITIS (Started 19[redacted], Stopped [redacted] [redacted] 20[redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted] [redacted] 19[redacted] - 19[redacted])

PENTASA for ULCERATIVE COLITIS (20[redacted] - 20[redacted], 20[redacted] - [redacted] [redacted] 20[redacted], 20[redacted] - [redacted] [redacted] 20[redacted])

RINDERON for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ISONIAZID for TB PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Lumbago (10024988) (Back pain (10003988) ) [v.23.1] [10024988]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

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Event of LUMBAGO

**- Investigator:** More likely sporadic and common mechanical causation.

**- AbbVie:** Risk factors include history of lumbar disc herniation and pre-existing osteoporosis.

**Investigator No.:** [redacted]

**Subject Number:** [redacted]

**Protocol Number:** M14-533

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腰部脊柱管狭窄症及び腰椎椎間板ヘルニアの悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，腰椎椎間板ヘルニア，元喫煙者（1 日 0.2 箱を 0.3 年間），高血圧，骨粗鬆症，喘息及び現飲酒者（1 日 2–4 杯）であった。

**Event 2 及び 3 の臨床経過：**

投与1000日後＊ ，被験者は腰部脊柱管狭窄症を発現した。投与1117日後＊ ，被験者は腰椎椎間板ヘルニアの悪化を発現した。

入院前，被験者は 投与の3年前＊ に腰椎椎間板ヘルニアと診断されていた（病歴）。被験者は，腰痛症を経験していた。

投与1088日後＊ ，被験者は腰痛，下肢痛及びしびれ感のために入院した。入院中，合併症として腰椎椎間板ヘルニアが確認された。

投与1114日後＊ ，被験者は手術のために入院した。被験者は，歩行に支障をきたすほどの下背部痛のため，手術を選択した。整形外科医が腰部脊柱管狭窄症の手術中に，必要に応じて椎間板切除を行う予定であった。投与1117日後＊ ，腰部脊柱管狭窄症及び腰椎椎間板ヘルニアの悪化の診断により，椎間板切除を伴う手術を行った。整形外科医は，手術中に腰椎椎間板ヘルニアの悪化を確認した。

腰椎椎間板ヘルニアが腰部脊柱管狭窄症に影響していたため，腰椎椎間板ヘルニアに対して椎間板切除術を行った。摘出したヘルニアの量は 0.6 g であった。被験者は，傷口の痛みに対して鎮痛薬を服用した。

投与1124日後＊ ，整形外科医は傷口が感染していないことを確認した。治験責任医師は，血液検査データがほぼ正常であること，問題がないことを確認した。治験薬投与が再開された。投与1127日後＊ ，被験者は独力で安定して歩けた。投与1133日後＊ ，被験者は改善し，退院した。

投与された薬剤は，ketalar 及びプロポフォールであった。

**The patient's past medications include:**

ASACOL for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

IMURAN for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted] 19[redacted] - 19[redacted])

PENTASA for ULCERATIVE COLITIS (20[redacted] - 20[redacted], 20[redacted] - [redacted] 20[redacted], 20[redacted] - [redacted] 20[redacted])

PREDONINE for ULCERATIVE COLITIS (20[redacted] - 20[redacted], 20[redacted] - [redacted] 20[redacted], Started [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

ISONIAZID for TB PROPHYLAXIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Lumbar spinal stenosis (10025005) (Lumbar spinal stenosis (10025005) ) [v.24.1] [10025005]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

2) Lumbar disc herniation (10066256) (Intervertebral disc protrusion (10050296) ) [v.24.1] [10066256]

**Causality as per reporter (Drug/Vaccine):** No reasonable possibility

**Causality as per Mfr. (Drug/Vaccine):** No reasonable possibility

**Dechallenge:** No

Alternative Etiology for UPADACITINIB (Open Label)

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Event of LUMBAR SPINAL CANAL STENOSIS

**- Investigator:** More likely sporadic and common mechanical causation

**- AbbVie:** Event is more likely related to pre-existing history of lumbar disc herniation.

Event of EXACERBATION OF LUMBAR DISC HERNIATION

**- Investigator:** More likely sporadic and common mechanical causation

**- AbbVie:** Event is more likely related to pre-existing history of lumbar disc herniation.

Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CT MYELOGRAPHY:** L4/5 STENOSIS(LUMBAR SPINAL CANAL STENOSIS.

[redacted] **20[redacted] MRI:** L4/5 stenosis (lumbar spinal canal stenosis) Left L4/5 level hernia Exclusion in L5 nerve root

被験者番号 [redacted] (Investigator [redacted])

**Reason for Narrative**

| Adverse Event Preferred Term(s) | Serious Adverse Event | Adverse Event Leading to Discontinuation of Study Drug | Death | Event of Interest |
|---|---|---|---|---|
| アラニンアミノトランスフェラーゼ増加 | | | | X |
| アスパラギン酸アミノトランスフェラーゼ増加 | | | | X |
| COVID-19 | X | | | X |
| γ-グルタミルトランスフェラーゼ増加 | | | | X |
| 胃食道逆流性疾患 | X | | | |
| 好中球数減少 | | | | X |

| Treatment Group | Age at Induction Study Start | Sex | Race |
|---|---|---|---|
| ABT-494 15 mg | 4[redacted] | MALE | ASIAN |

| Medical History | Onset Year |
|---|---|
| HEARING DISORDER: HIGH FREQUENCY BILATERAL DEAFNESS | 20[redacted] |
| LEFT SIDED UC | 20[redacted] |
| OSTEOARTHRITIS: RIGHT ANKLE ARTHRALGIA | 20[redacted] |
| OTHER: APPENDICITIS | 19[redacted] |
| OTHER: DRUGINESS PANCREATITIS | 20[redacted] |
| OTHER: EPIGASTRIC PAIN | 20[redacted] |
| OTHER: FOLLICULITIS | 20[redacted] |
| OTHER: HEADACHE | NOT REPORTED |
| OTHER: NUMBNESS OF THE RIGHT HAND | NOT REPORTED |
| OTHER: PALPITATION | 20[redacted] |
| OTHER: PHARYNGITIS | NOT REPORTED |
| OTHER: POLLINOSIS | NOT REPORTED |
| TUBERCULOSIS: PLEURAL TUBERCULOSIS | 20[redacted] |

| Prior Procedures | Procedure Year |
|---|---|
| SURGERY: APPENDECTOMY | 19[redacted] |
| SURGERY: BACK NEVUS EXTRACTION | 20[redacted] |
| ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY | 20[redacted] |

| Tobacco Use | Status | Number/Day | Number of Years | Year Stopped |
|---|---|---|---|---|
| CHEWING TOBACCO | NEVER | | | |
| CIGARETTES | FORMER | 2 PACK | 15 | 20[redacted] |
| CIGARS | NEVER | | | |
| PIPES | NEVER | | | |

| Alcohol Use | Status | Number/Day |
|---|---|---|
| ALCOHOL | CURRENT | Less than 2 DRINKS |

**Study Drug Administration**

| Study Drug | Dose/Units | Route of Administration | Frequency | First Dose Date/Day | Last Dose Date/Day | Duration (Days) |
|---|---|---|---|---|---|---|
| M14-234 SS1 ABT-494 (IND) | 45 mg | ORAL | QD | [redacted]20[redacted] / 1 | [redacted]20[redacted] / 54 | 54 |
| M14-234 SS3 ABT-494 (MAIN) | 30 mg | ORAL | QD | [redacted]20[redacted] / 55 | [redacted]20[redacted] / 364 | 310 |
| M14-533 ABT-494 (LTE) | 15 mg | ORAL | QD | [redacted]20[redacted] / 365 | | |

**Previous Therapy - Prior to baseline/enrollment**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day |
|---|---|---|---|
| OTHER THERAPEUTIC PRODUCTS | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| AZATHIOPRINE | 50 mg | QD | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: 1 TIME PER WEEK | Y-M: 20[redacted] |
| PYRIDOXAL | 30 mg | BID | Y-M: 20[redacted] |
| PREDNISOLONE | 2.5 mg | QD | Y-M: 20[redacted] |
| TACROLIMUS | 7 mg | BID | Y-M: 20[redacted] |
| THIAMINE | 50 mg | BID | Y-M: 20[redacted] |
| ADALIMUMAB | 40 mg | OTHER: 1 TIME PER 2 WEEKS | Y-M: 20[redacted] |
| INFLIXIMAB | 300 mg | QD | Y-M: 20[redacted] |
| INFLIXIMAB | 300 mg | QD | Y-M: 20[redacted] |
| ASCORBIC ACID;PANTOTHENIC ACID | 2 OTHER: TABLET | BID | Y-M: 20[redacted] |
| FLAVINE ADENINE DINUCLEOTIDE | 20 mg | BID | Y-M: 20[redacted] |

| | | | |
|---|---|---|---|
| INFLIXIMAB | 300 mg | QD | Y-M: 20[redacted] |
| TRANEXAMIC ACID | 500 mg | BID | Y-M: 20[redacted] |
| ALUMINIUM HYDROXIDE;BISMUTH;CALCIUM CARBONATE;MAGNESIUM TRISILICATE;SODIUM BICARBONATE | NOT REPORTED | NOT REPORTED | Y-M: 20[redacted] |
| INFLIXIMAB | 300 mg | QD | Y-M: 20[redacted] |
| MECOBALAMIN | 500 ug | TID | Y-M: 20[redacted] |
| VONOPRAZAN | 20 mg | QD | Y-M: 20[redacted] |
| CAMPHOR;CAPSAICIN;SALICYLIC ACID | 20 g | PRN | Y-M: 20[redacted] |
| BACTERIA NOS;HYDROCORTISONE | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] |
| GENTAMICIN | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] |
| CEFCAPENE | 100 mg | TID | Y-M: 20[redacted] / -364 |
| LOXOPROFEN | 60 mg | PRN | Y-M: 20[redacted] / -364 |
| HEPARINOID | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / -14 |
| SULFASALAZINE | NOT REPORTED | NOT REPORTED | Y: 19[redacted] |
| MESALAZINE | NOT REPORTED | NOT REPORTED | Y: 20[redacted] |

**Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study**

| Medication Name (WHO Drug) | Dose/Units | Frequency | Start Year-Month / RX Day | Stop Year-Month / RX Day |
|---|---|---|---|---|
| PYRIDOXAL | 30 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 924 |
| THIAMINE | 50 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 924 |
| ASCORBIC ACID;PANTOTHENIC ACID | 2 OTHER: TABLET | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 924 |
| FLAVINE ADENINE DINUCLEOTIDE | 20 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 924 |
| TRANEXAMIC ACID | 500 mg | BID | Y-M: 20[redacted] | Y-M: 20[redacted] / 924 |
| MECOBALAMIN | 500 ug | TID | Y-M: 20[redacted] | Y-M: 20[redacted] / 924 |
| VONOPRAZAN | 20 mg | QD | Y-M: 20[redacted] | Y-M: 20[redacted] / 414 |
| CAMPHOR;CAPSAICIN;SALICYLIC ACID | 20 g | PRN | Y-M: 20[redacted] | ONGOING |
| BACTERIA NOS;HYDROCORTISONE | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] | ONGOING |
| LOXOPROFEN | 60 mg | PRN | Y-M: 20[redacted] / -364 | Y-M: 20[redacted] / 249 |
| HEPARINOID | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / -14 | ONGOING |
| LORATADINE | 10 mg | QD | Y-M: 20[redacted] / 27 | Y-M: 20[redacted] / 82 |
| MOMETASONE | 100 ug | BID | Y-M: 20[redacted] / 27 | Y-M: 20[redacted] / 82 |
| OLOPATADINE | PROPER QUANTITY OTHER: PROPER QUANTITY | BID | Y-M: 20[redacted] / 27 | Y-M: 20[redacted] / 82 |
| MINOCYCLINE | 100 mg | BID | Y-M: 20[redacted] / 55 | Y-M: 20[redacted] / 61 |
| MINOCYCLINE | 100 mg | BID | Y-M: 20[redacted] / 68 | Y-M: 20[redacted] / 71 |
| LOXOPROFEN | 60 mg | PRN | Y-M: 20[redacted] / 140 | Y-M: 20[redacted] / 145 |
| CHLORPHENAMINE | 0.01 % | PRN | Y-M: 20[redacted] / 141 | Y-M: 20[redacted] / 147 |
| CHONDROITIN | 0.3 % | PRN | Y-M: 20[redacted] / 141 | Y-M: 20[redacted] / 147 |

| | | | | |
|---|---|---|---|---|
| GUALENIC ACID | 0.02 % | PRN | Y-M: 20[redacted] / 141 | Y-M: 20[redacted] / 147 |
| SULFAMETHOXAZOLE | 4.0 % | | PRN M: 20[redacted] / 141 | Y-M: 20[redacted] / 147 |
| AMOXICILLIN;CLAVULANIC ACID | 1 OTHER: TAB | TID | Y-M: 20[redacted] / 143 | Y-M: 20[redacted] / 147 |
| CARBOCISTEINE | 500 mg | TID | Y-M: 20[redacted] / 145 | Y-M: 20[redacted] / 147 |
| DEXTROMETHORPHAN | 15 mg | TID | Y-M: 20[redacted] / 145 | Y-M: 20[redacted] / 147 |
| AZULENE | PRN mL | PRN | Y-M: 20[redacted] / 266 | Not reported |
| ELETRIPTAN | 20 mg | PRN | Y-M: 20[redacted] / 268 | Not reported |
| PARACETAMOL | 400 mg | PRN | Y-M: 20[redacted] / 271 | Y-M: 20[redacted] / 417 |
| LOXOPROFEN | 100 mg | PRN | Y-M: 20[redacted] / 274 | Y-M: 20[redacted] / 417 |
| CARBOCISTEINE | 500 mg | PRN | Y-M: 20[redacted] / 286 | Y-M: 20[redacted] / 937 |
| DEXTROMETHORPHAN | 15 mg | PRN | Y-M: 20[redacted] / 286 | Y-M: 20[redacted] / 937 |
| LOXOPROFEN | 100 mg | PRN | Y-M: 20[redacted] / 307 | Y-M: 20[redacted] / 314 |
| LOPERAMIDE | 1 mg | PRN | Y-M: 20[redacted] / 314 | Y-M: 20[redacted] / 314 |
| RAMOSETRON | 5 ug | PRN | Y-M: 20[redacted] / 314 | Y-M: 20[redacted] / 636 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 326 | Y-M: 20[redacted] / 326 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 2000 mL | PRN | Y-M: 20[redacted] / 327 | Y-M: 20[redacted] / 327 |
| AZITHROMYCIN | 500 mg | QD | Y-M: 20[redacted] / 329 | Y-M: 20[redacted] / 331 |
| PARACETAMOL | 400 mg | PRN | Y-M: 20[redacted] / 338 | Y-M: 20[redacted] / 344 |
| OSELTAMIVIR | 75 mg | BID | Y-M: 20[redacted] / 342 | Y-M: 20[redacted] / 346 |
| FLUOROMETHOLONE | 1 OTHER: DROP | QID | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 421 |
| LEVOFLOXACIN | 1 OTHER: DROP | QID | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 421 |

| | | | | |
|---|---|---|---|---|
| METHYLPREDNISOLONE; NEOMYCIN | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 408 | Y-M: 20[redacted] / 412 |
| VONOPRAZAN | 20 mg | QD | Y-M: 20[redacted] / 415 | Not reported |
| LORATADINE | 10 mg | PRN | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 447 |
| OLOPATADINE | 1 OTHER: DROP | PRN | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 447 |
| TEPRENONE | 150 mg | TID | Y-M: 20[redacted] / 426 | Y-M: 20[redacted] / 636 |
| SULPIRIDE | 50 mg | TID | Y-M: 20[redacted] / 432 | Y-M: 20[redacted] / 636 |
| CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 2000 mL | QD | Y-M: 20[redacted] / 449 | Y-M: 20[redacted] / 453 |
| CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE | 1000 mL | QD | Y-M: 20[redacted] / 454 | Y-M: 20[redacted] / 454 |
| LOXOPROFEN | 100 mg | PRN | Y-M: 20[redacted] / 468 | Y-M: 20[redacted] / 501 |
| FLUOROMETHOLONE | 1 OTHER: DROP | PRN | Y-M: 20[redacted] / 486 | Y-M: 20[redacted] / 501 |
| LEVOFLOXACIN | 1 OTHER: DROP | PRN | Y-M: 20[redacted] / 486 | Y-M: 20[redacted] / 501 |
| FLUOROMETHOLONE | 1 OTHER: DROP | PRN | Y-M: 20[redacted] / 533 | Y-M: 20[redacted] / 571 |
| OFLOXACIN | 1 OTHER: DROP | PRN | Y-M: 20[redacted] / 533 | Y-M: 20[redacted] / 537 |
| AZITHROMYCIN | 250 mg | BID | Y-M: 20[redacted] / 557 | Y-M: 20[redacted] / 559 |
| LOXOPROFEN | PROPER QUANTITY mg | PRN | Y-M: 20[redacted] / 634 | Y-M: 20[redacted] / 695 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 665 | Y-M: 20[redacted] / 665 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 2000 mL | PRN | Y-M: 20[redacted] / 666 | Y-M: 20[redacted] / 666 |

| | | | | |
|---|---|---|---|---|
| DIMETICONE | 10 mL | QD | Y-M: 20[redacted] / 666 | Y-M: 20[redacted] / 666 |
| POVIDONE-IODINE | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 673 | Not reported |
| LORATADINE | 10 mg | QD | Y-M: 20[redacted] / 755 | Y-M: 20[redacted] / 837 |
| MOMETASONE | 100 ug | BID | Y-M: 20[redacted] / 755 | Y-M: 20[redacted] / 837 |
| OLOPATADINE | PROPER QUANTITY OTHER: PROPER QUANTITY | BID | Y-M: 20[redacted] / 755 | Y-M: 20[redacted] / 837 |
| TERBINAFINE | PROPER QUANTITY OTHER: PROPER QUANTITY | QD | Y-M: 20[redacted] / 755 | Y-M: 20[redacted] / 847 |
| TERBINAFINE | PROPER QUANTITY OTHER: PROPER QUANTITY | QD | Y-M: 20[redacted] / 755 | Y-M: 20[redacted] / 1112 |
| AZITHROMYCIN | 1000 mg | BID | Y-M: 20[redacted] / 838 | Y-M: 20[redacted] / 840 |
| ASCORBIC ACID;PANTOTHENIC ACID | 2 OTHER: TABLET | PRN | Y-M: 20[redacted] / 938 | Not reported |
| FLAVINE ADENINE DINUCLEOTIDE | 20 mg | PRN | Y-M: 20[redacted] / 938 | Not reported |
| MECOBALAMIN | 500 ug | PRN | Y-M: 20[redacted] / 938 | Not reported |
| PYRIDOXAL | 30 mg | PRN | Y-M: 20[redacted] / 938 | Not reported |
| THIAMINE | 50 mg | PRN | Y-M: 20[redacted] / 938 | Not reported |
| TRANEXAMIC ACID | 500 mg | PRN | Y-M: 20[redacted] / 938 | Not reported |
| VONOPRAZAN | 20 mg | PRN | Y-M: 20[redacted] / 938 | Not reported |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 1000 | Y-M: 20[redacted] / 1000 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | QD | Y-M: 20[redacted] / 1001 | Y-M: 20[redacted] / 1001 |
| DIMETICONE | 10 mL | QD | Y-M: 20[redacted] / 1001 | Y-M: 20[redacted] / 1001 |

| | | | | |
|---|---|---|---|---|
| FLUMAZENIL | 0.5 mg | QD | Y-M: 20[redacted] / 1001 | Y-M: 20[redacted] / 1001 |
| MIDAZOLAM | 10 mg | QD | Y-M: 20[redacted] / 1001 | Y-M: 20[redacted] / 1001 |
| HYALURONIC ACID | PROPER QUANTITY<br>OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1015 | Not reported |
| LOXOPROFEN | PROPER QUANTITY<br>OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1015 | Not reported |
| LOXOPROFEN | PROPER QUANTITY<br>OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1017 | Y-M: 20[redacted] / 1064 |
| AZITHROMYCIN | 500 mg | QD | Y-M: 20[redacted] / 1055 | Y-M: 20[redacted] / 1057 |
| LOXOPROFEN | PROPER QUANTITY<br>OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1101 | Y-M: 20[redacted] / 1127 |
| LOXOPROFEN | PROPER QUANTITY<br>OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1104 | Y-M: 20[redacted] / 1127 |
| POVIDONE-IODINE | PROPER QUANTITY<br>OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1107 | ONGOING |
| CEFCAPENE | 100 mg | TID | Y-M: 20[redacted] / 1125 | Y-M: 20[redacted] / 1133 |
| PARACETAMOL | 400 mg | PRN | Y-M: 20[redacted] / 1184 | Y-M: 20[redacted] / 1190 |
| CEFTRIAXONE | 2 g | BID | Y-M: 20[redacted] / 1190 | Y-M: 20[redacted] / 1195 |
| REMDESIVIR | 200 mg | QD | Y-M: 20[redacted] / 1191 | Y-M: 20[redacted] / 1191 |
| FLUOROMETHOLONE | PROPER QUANTITY<br>OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1192 | Y-M: 20[redacted] / 1200 |

| | | | | |
|---|---|---|---|---|
| LEVOFLOXACIN | PROPER QUANTITY OTHER: PROPER QUANTITY | PRN | Y-M: 20[redacted] / 1192 | Y-M: 20[redacted] / 1200 |
| REMDESIVIR | 100 mg | QD | Y-M: 20[redacted] / 1192 | Y-M: 20[redacted] / 1195 |
| CARBOCISTEINE | 500 mg | PRN | Y-M: 20[redacted] / 1246 | Y-M: 20[redacted] / 1268 |
| DEXTROMETHORPHAN | 15 mg | PRN | Y-M: 20[redacted] / 1246 | Y-M: 20[redacted] / 1268 |
| DIMEMORFAN | 30 mg | TID | Y-M: 20[redacted] / 1275 | Y-M: 20[redacted] / 1305 |
| PARACETAMOL | 500 mg | PRN | Y-M: 20[redacted] / 1275 | Not reported |
| AZITHROMYCIN | 500 mg | BID | Y-M: 20[redacted] / 1322 | Y-M: 20[redacted] / 1324 |
| UNSPECIFIED HERBAL | 20 OTHER: TABLETS | QD | Y-M: 20[redacted] / 1334 | Y-M: 20[redacted] / 1334 |
| SODIUM PICOSULFATE | 10 mL | QD | Y-M: 20[redacted] / 1350 | Y-M: 20[redacted] / 1350 |
| ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE | 1 OTHER: PACK | QD | Y-M: 20[redacted] / 1351 | Y-M: 20[redacted] / 1351 |
| DIMETICONE | 10 mL | QD | Y-M: 20[redacted] / 1351 | Y-M: 20[redacted] / 1351 |
| FLUMAZENIL | 0.5 mg | QD | Y-M: 20[redacted] / 1351 | Y-M: 20[redacted] / 1351 |
| MIDAZOLAM | 10 mg | QD | Y-M: 20[redacted] / 1351 | Y-M: 20[redacted] / 1351 |

**Event #1: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | ALT INCREASED |
| **Preferred term** | アラニンアミノトランスフェラーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 440 / 76 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 461 / 97 |
| **Duration of AE** | 22 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #2: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | AST INCREASED |
| **Preferred term** | アスパラギン酸アミノトランスフェラーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 440 / 76 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 461 / 97 |
| **Duration of AE** | 22 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #3: Event of Interest - Hepatic Disorder**

| | |
|---|---|
| **Event Description** | GGT INCREASED |
| **Preferred term** | γ-グルタミルトランスフェラーゼ増加 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 440 / 76 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 509 / 145 |
| **Duration of AE** | 70 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #4: Event of Interest - Neutropenia**

| | |
|---|---|
| **Event Description** | NEUTROPHIL COUNT DECREASED |

| | |
|---|---|
| **Preferred term** | 好中球数減少 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 706 / 342 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| NOT APPLICABLE | |
| **Microbiology** | |
| NOT APPLICABLE | |
| **AE Stopped Initial Rx Day / Rx Day** | 713 / 349 |
| **Duration of AE** | 8 DAYS |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | NOT APPLICABLE |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | NONE |

**Event #5: Serious Adverse Event**

| | |
|---|---|
| **Event Description** | REFLUX ESOPHAGITIS |
| **Preferred term** | 胃食道逆流性疾患 |
| **AE Onset Date / Initial Rx Day / Rx Day** | [redacted]20[redacted] / 779 / 415 |
| **Age at AE Onset** | 4[redacted] |
| **Laboratory Testing** | |
| [redacted]20[redacted] (RX DAY 432): Hemoglobin: 147 [137 - 168] G/L; NPTST028-AMYLASE: 76 [44 - 132] U/L; NPTST207-LIPASE: 47 [13 - 49] IU/L; [redacted]20[redacted] (RX DAY 448): Blood Urea Nitrogen: 3.676791 [2.85576 - 7.1394] MMOL/L; Hemoglobin: 149 [137 - 168] G/L; NPTST028-AMYLASE: 86 [44 - 132] U/L; NPTST207-LIPASE: 37 [13 - 49] IU/L | |
| **Microbiology** | |
| NOT REPORTED | |
| **AE Stopped Initial Rx Day / Rx Day** | NOT REPORTED |
| **Duration of AE** | NOT REPORTED |
| **Severity** | MILD |
| **Relation to Study Drug by Investigator** | NO REASONABLE POSSIBILITY |
| **Investigator Alternative Etiology** | REFLUX ESOPHAGITIS　WAS OCCUERED BY DIETARY DISORDER AND ESOPHAGEAL HERNIA.THUS,IT WAS CONSIDERED TO HAVE NO RELATIONSHIP WITH THE INVESTIGATIONAL AGENT. |
| **Discontinued Study Drug Due to the Event** | NO |
| **SAE Criteria** | HOSPITALIZATION OR PROLONGED HOSPITALIZATION |

**Event #6: Event of Interest - Neutropenia**

| | |
|---|---|
| **Event Description** | NEUTROPHIL COUNT DECREASED |