**Supplementary Materials**

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**Supplemental Materials**

**Supplementl Table 1.** Definitions of safety-related terminology

|  |  |
| --- | --- |
| **Safety-Related Term** | **Definition** |
| Adverse event (AE) | An AE is any untoward medical occurrence (including an abnormal laboratory finding) that occurs in the protocol-specified AE reporting period; the event does not necessarily have a causal relationship with that treatment or usage.AEs includes medical conditions, signs, and symptoms not previously observed in the patient that emerge during the protocol-specified AE reporting period, including signs or symptoms associated with pre-existing underlying conditions that were not present prior to the AE reporting period. |
| Treatment-emergent adverse event (TEAE) | A TEAE was defined as an AE that started (or a pre-existing AE that worsened) on or after the first dose of the study drug. TEAEs are summarized by MedDRA System Organ Class and preferred term (PT) overall, by severity (mild, moderate, or severe), by seriousness, by relationship to study drug (related or not related as assessed by the investigator), over time, by actual vadadustat dose prior to TEAE onset, and whether the TEAE led to death. |
| Serious adverse event (SAE) | An AE that met 1 or more of the following criteria/outcomes was classified as serious:* Death
* Life-threatening adverse drug experience
* Inpatient hospitalization or prolongation of existing hospitalization
* Persistent or significant disability/incapacity
* Congenital anomaly/birth defect
* Was considered a medically important event not meeting the above criteria, but which may jeopardize a patient, or may require medical or surgical intervention to prevent 1 of the criteria listed in this definition

In addition to the above criteria for classifying AEs as serious, the following situations were also classified as serious for purposes of this study:* Dialysis or transplantation – Events requiring transition to chronic, ongoing dialysis or requiring an acute transient course of dialysis, or requiring an immediate kidney transplantation (ie, not preplanned) were classified as an SAE
* Malignancies – Newly diagnosed malignancies or a recurrence of a malignancy were reported as an SAE with the seriousness criterion “medically important” if no other seriousness criteria was met. If a patient developed basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or cervical carcinoma in situ during the study, or had worsening of these events from baseline, the investigator would determine if the event was to be reported as an AE or SAE
* Designated medical events (DMEs) – The sponsor maintained a list of DMEs. If an event on the DME list was reported as an AE, additional information on the event (eg, investigator confirmation of seriousness, causality) might be requested from the investigator and, based on internal review by the sponsor, the AE may have been upgraded to SAE

SAEs also included any other event that the investigator or sponsor judged to be serious. If there was any doubt whether the information constituted an AE or SAE, the information was treated as an SAE. |
| Adverse event of special interest (AESI) | AESIs were identified from nonclinical findings, potential class effect of other hypoxia-inducible factor stabilizers, and ongoing safety surveillance in the clinical development program, and included drug-drug interactions with specific statins, ferrous sulphate, furosemide, sulfasalazine, and probenecid; hepatotoxicity, thromboembolic events, malignancies, hypersensitivity, worsening of hypertension, adrenal disorders, cardiac valve disorders, hyperkalemia, congestive heart failure, pulmonary hypertension, and retinal-related TEAEs.To ensure all relevant, related TEAE terms were captured for evaluation, AESIs were retrieved by applying Standardized MedDRA Queries (SMQs) or as groups of medically relevant terms (if no SMQ was available). For the AESI analyses, these groupings of preferred terms are referred to as AESI “medical topics.” |
| **Preferred Term (PT)** | PT is a distinct descriptor (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic. |
| **System Organ Class**  | System Organ Classes are groupings by etiology (eg, infections and infestations), manifestation site (eg, gastrointestinal disorders) or purpose (eg, surgical and medical procedures). |

**Supplemental Table 2.** Mean duration of exposure in NDD-CKD, DD-CKD, and total populations with vadadustat vs darbepoetin alfa treatment

|  |  |  |  |
| --- | --- | --- | --- |
|  | **DD-CKD Population** | **NDD-CKD Population** | **Total Safety Population** |
| **VADA (N=1947)** | **DA (N=1955)** | **VADA (N=1739)** | **DA(N=1732)** | **VADA (N=3686)** | **DA(N=3687)** |
| Mean duration of exposure, weeks (SD) | 59.5 (37.6)  | 71.3 (36.7) | 69.2 (47.7)  | 75.5 (48.5) | 64.1 (42.9)  | 73.2 (42.7) |

CKD, chronic kidney disease; DA, darbepoetin alfa; DD, dialysis-dependent; NDD, non-dialysis-dependent; VADA, vadadustat.

**Supplemental Table 3.** Study Drug Exposure – Pooled CKD Population for Global Phase 3 Studies

(Safety Population)

|  |  |  |
| --- | --- | --- |
| **Parameter****Statistic** | **Vadadustat****N=3686** | **Darbepoetin Alfa****N=3687** |
| Total duration of exposure (weeks)a |  |  |
| Mean (SD)  | 64.06 (42.943) | 73.23 (42.720) |
| Median  | 56.71 | 70.00 |
| Q1, Q3  | 31.86, 91.71 | 39.86, 102.14 |
| Min – Max  | 0.1 – 204.1 | 0.1 – 208.1 |
| Total duration category, n (%) |  |  |
| <4 weeks  | 129 (3.5)  | 68 (1.8) |
| ≥4 and <13 weeks 317  | (8.6)  | 193 (5.2) |
| ≥13 and <26 weeks  | 317 (8.6)  | 217 (5.9) |
| ≥26 and <39 weeks  | 434 (11.8)  | 410 (11.1) |
| ≥39 and <52 weeks  | 478 (13.0)  | 431 (11.7) |
| ≥52 and <78 weeks  | 776 (21.1)  | 834 (22.6) |
| ≥78 and <104 weeks  | 540 (14.7)  | 647 (17.5) |
| ≥104 weeks  | 695 (18.9)  | 887 (24.1) |

CKD, chronic kidney disease; Max, maximum; Min, minimum; Q1, first quartile; Q3, third quartile; SD, standard deviation

aDuration (weeks) = (last treatment date – first treatment date + 1)/7

**Supplemental Table 4.** Overall Summary of Treatment-Emergent Adverse Events Over Time – Pooled CKD Population for Global

Phase 3 Studies (Safety Population)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Category** | **Day 1 to Week 13**  | **>13 to 26 Weeks** | **>26 to 39 Weeks**  | **>39 to 52 Weeks** |
| **Vada****N = 3686****n (%)** | **DA** **N = 3687****n (%)** | **Vada****N = 3347****n (%)** | **DA****N = 3483****n (%)** | **Vada****N = 3053****n (%)** | **DA****N = 3300****n (%)** | **Vada****N = 2648****n (%)** | **DA****N = 2908****n (%)** |
| Any TEAE | 2031 (55.1) | 1891 (51.3) | 1523 (45.5) | 1568 (45.0) | 1373 (45.0) | 1508 (45.7) | 1113 (42.0) | 1203 (41.4) |
| Any drug-related TEAE | 251 (6.8) | 71 (1.9) | 56 (1.7) | 29 (0.8) | 38 (1.2) | 19 (0.6) | 18 (0.7) | 20 (0.7) |
| Any severe TEAE | 383 (10.4) | 390 (10.6) | 352 (10.5) | 326 (9.4) | 297 (9.7) | 328 (9.9) | 262 (9.9) | 261 (9.0) |
| Any TE-SAE | 599 (16.3) | 602 (16.3) | 562 (16.8) | 531 (15.2) | 482 (15.8) | 526 (15.9) | 414 (15.6) | 440 (15.1) |
| Any drug-related TE-SAE | 28 (0.8) | 13 (0.4) | 10 (0.3) | 9 (0.3) | 8 (0.3) | 3 (0.1) | 3 (0.1) | 9 (0.3) |
| Any TEAE leading to discontinuation | 113 (3.1) | 27 (0.7) | 29 (0.9) | 16 (0.5) | 23 (0.8) | 18 (0.5) | 13 (0.5) | 10 (0.3) |
| Any drug-related TEAE leading to discontinuation | 52 (1.4) | 6 (0.2) | 6 (0.2) | 1 (0.0) | 4 (0.1) | 0 | 2 (0.1) | 1 (0.0) |
| Any TEAE leading to death | 53 (1.4) | 61 (1.7) | 50 (1.5) | 42 (1.2) | 52 (1.7) | 47 (1.4) | 42 (1.6) | 41 (1.4) |
| All deathsa | 30 (0.8) | 43 (1.2) | 39 (1.2) | 33 (0.9) | 50 (1.6) | 41 (1.2) | 36 (1.4) | 34 (1.2) |

CKD, chronic kidney disease; DA, darbepoetin alfa; TEAE, treatment-emergent adverse event; TE-SAE, treatment-emergent serious adverse event; VADA, vadadustat.

aAll deaths were collected during the study and presented in this table irrespective of whether a preceding TEAE was recorded.

**Supplemental Table 5.** Treatment-emergent adverse events by MedDRA preferred term reported in ≥5% of patients in any treatment group—pooled total population

|  |  |  |
| --- | --- | --- |
| **MedDRA System Organ Class****Preferred Term** | **Vadadustat** **(N=3686; exposure=6335.3 PY)** | **Darbepoetin Alfa(N=3687; exposure=6420.1 PY)** |
| **n (%)** | **Events** **(Events per 100 PY)** | **n (%)** | **Events****(Events per 100 PY)** |
| Infections and infestations | 1873 (50.8) | 4347 (68.6) | 1942 (52.7) | 4596 (71.6) |
| Pneumonia | 380 (10.3) | 487 (7.7) | 346 (9.4) | 416 (6.5) |
| UTI | 339 (9.2) | 445 (7.0) | 362 (9.8) | 541 (8.4) |
| URTI | 211 (5.7) | 253 (4.0) | 237 (6.4) | 281 (4.4) |
| Nasopharyngitis | 205 (5.6) | 267 (4.2) | 201 (5.5) | 255 (4.0) |
| Bronchitis | 150 (4.1) | 171 (2.7) | 185 (5.0) | 208 (3.2) |
| GI disorders | 1483 (40.2) | 3320 (52.4) | 1297 (35.5) | 2998 (46.7) |
| Diarrhea | 489 (13.3) | 596 (9.4) | 359 (9.7) | 455 (7.1) |
| Nausea | 324 (8.8) | 393 (6.2) | 276 (7.5) | 340 (5.3) |
| Vomiting | 233 (6.3) | 279 (4.4) | 228 (6.2) | 282 (4.4) |
| Constipation | 206 (5.6) | 229 (3.6) | 207 (5.6) | 231 (3.6) |
| Metabolism and nutrition disorders | 1274 (34.6) | 2679 (42.3) | 1336 (36.2) | 2704 (42.1) |
| Hyperkalemia | 357 (9.7) | 458 (7.2) | 422 (11.4) | 527 (8.2) |
| Fluid overload | 276 (7.5) | 377 (6.0) | 275 (7.5) | 372 (5.8) |
| Hypoglycemia | 203 (5.5) | 296 (4.7) | 191 (5.2) | 264 (4.1) |
| Vascular disorders | 1140 (30.9) | 1939 (30.6) | 1213 (32.9) | 2105 (32.8) |
| Hypertension | 495 (13.4) | 646 (10.2) | 586 (15.9) | 774 (12.1) |
| Hypotension | 253 (6.9) | 349 (5.5) | 246 (6.7) | 327 (5.1) |
| Injury, poisoning, and procedural complications | 1088 (29.5) | 2329 (36.8) | 1132 (30.7) | 2549 (39.7) |
| Fall | 314 (8.5) | 406 (6.4) | 320 (8.7) | 437 (6.8) |
| Respiratory, thoracic, and mediastinal disorders | 902 (24.5) | 1703 (26.9) | 966 (26.2) | 1854 (28.9) |
| Cough | 198 (5.4) | 233 (3.7) | 222 (6.0) | 253 (3.9) |
| Dyspnea | 181 (4.9) | 231 (3.6) | 218 (5.9) | 267 (4.2) |
| General disorders and administration site conditions | 984 (26.7) | 1526 (24.1) | 883 (23.9) | 1408 (21.9) |
| Peripheral edema | 255 (6.9) | 311 (4.9) | 252 (6.8) | 305 (4.8) |
| Nervous system disorders | 880 (23.9) | 1499 (23.7) | 892 (24.2) | 1440 (22.4) |
| Headache | 237 (6.4) | 419 (6.6) | 234 (6.3) | 317 (4.9) |
| Musculoskeletal and connective tissue disorders | 843 (22.9) | 1436 (22.7) | 895 (24.3) | 1558 (24.3) |
| Back pain | 178 (4.8) | 207 (3.3) | 185 (5.0) | 211 (3.3) |
| Pain in extremity | 164 (4.4) | 202 (3.2) | 194 (5.3) | 230 (3.6) |
| Renal and urinary disorders | 872 (23.7) | 1209 (19.1) | 860 (23.3) | 1210 (18.8) |
| End-stage renal disease | 558 (15.1) | 582 (9.2) | 563 (15.3) | 602 (9.4) |

GI, gastrointestinal; MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-year; URTI, upper respiratory tract infection; UTI, urinary tract infection.

**Supplemental Table 6.** Treatment-emergent serious adverse events by MedDRA preferred term reported in ≥2% of patients in any treatment group—pooled total population

|  |  |  |
| --- | --- | --- |
| **MedDRA System Organ Class****Preferred Term** | **Vadadustat** **(N=3686; exposure=6335.3 PY)** | **Darbepoetin Alfa** **(N=3687; exposure=6420.1 PY)** |
| **n (%)** | **Events** **(Events per 100 PY)** | **n (%)** | **Events****(Events per 100 PY)** |
| Infections and infestations | 858 (23.3) | 1494 (23.6) | 884 (24.0) | 1504 (23.4) |
| Pneumonia | 264 (7.2) | 331 (5.2) | 224 (6.1) | 260 (4.0) |
| Sepsis | 124 (3.4) | 137 (2.2) | 129 (3.5) | 138 (2.1) |
| Renal and urinary disorders | 684 (18.6) | 790 (12.5) | 667 (18.1) | 763 (11.9) |
| End-stage renal disease | 539 (14.6) | 555 (8.8) | 541 (14.7) | 557 (8.7) |
| Acute kidney injury | 80 (2.2) | 96 (1.5) | 75 (2.0) | 81 (1.3) |
| Cardiac disorders | 600 (16.3) | 1017 (16.1) | 670 (18.2) | 1106 (17.2) |
| Acute MI | 150 (4.1) | 171 (2.7) | 133 (3.6) | 149 (2.3) |
| CHF | 124 (3.4) | 156 (2.5) | 137 (3.7) | 173 (2.7) |
| Cardiac arrest | 83 (2.3) | 86 (1.4) | 95 (2.6) | 96 (1.5) |
| Atrial fibrillation | 74 (2.0) | 86 (1.4) | 62 (1.7) | 72 (1.1) |
| Metabolism and nutrition disorders | 394 (10.7) | 569 (9.0) | 387 (10.5) | 537 (8.4) |
| Fluid overload | 159 (4.3) | 214 (3.4) | 134 (3.6) | 186 (2.9) |
| Hyperkalemia | 93 (2.5) | 109 (1.7) | 115 (3.1) | 132 (2.1) |
| Respiratory, thoracic, and mediastinal disorders | 307 (8.3) | 449 (7.1) | 336 (9.1) | 480 (7.5) |
| Acute respiratory failure | 78 (2.1) | 95 (1.5) | 81 (2.2) | 90 (1.4) |
| Blood and lymphatic system disorders | 131 (3.6) | 159 (2.5) | 142 (3.9) | 172 (2.7) |
| Anemia | 71 (1.9) | 81 (1.3) | 81 (2.2) | 91 (1.4) |

CHF, congestive heart failure; MedDRA, Medical Dictionary for Regulatory Activities; MI, myocardial infarction; PY, patient-year.

**Supplemental Table 7.** Treatment-emergent adverse events that led to death in >1% of patients in any treatment group—pooled total population

|  |  |  |
| --- | --- | --- |
| **MedDRA System Organ Class****Preferred Term** | **Vadadustat****(N=3686; exposure=6335.3 PY)** | **Darbepoetin Alfa** **(N=3687; exposure=6420.1 PY)** |
| **n (%)** | **Events** **(Events per 100 PY)** | **n (%)** | **Events****(Events per 100 PY)** |
| Cardiac disorders | 203 (5.5) | 203 (3.2) | 205 (5.6) | 205 (3.2) |
| Cardiac arrest | 64 (1.7) | 64 (1.0) | 63 (1.7) | 63 (1.0) |
| Cardiorespiratory arrest | 33 (0.9) | 33 (0.5) | 37 (1.0) | 37 (0.6) |
| Infections and infestations | 87 (2.4) | 87 (1.4) | 94 (2.5) | 94 (1.5) |
| General disorders and administration site conditions | 89 (2.4) | 89 (1.4) | 72 (2.0) | 72 (1.1) |
| Renal and urinary disorders | 68 (1.8) | 68 (1.1) | 67 (1.8) | 67 (1.0) |
| End-stage renal disease | 41 (1.1) | 41 (0.6) | 48 (1.3) | 48 (0.7) |
| Respiratory, thoracic, and mediastinal disorders | 28 (0.8) | 28 (0.4) | 41 (1.1) | 41 (0.6) |

MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-year.

**Supplemental Table 8.** Hepatic safety-related treatment-emergent adverse events in any treatment group—pooled total population

|  |  |  |
| --- | --- | --- |
| **MedDRA System Organ Class****Preferred Term** | **Vadadustat(N=3686; exposure=6335.3 PY)** | **Darbepoetin Alfa(N=3687; exposure=6420.1 PY)** |
| **n (%)** | **Events** **(Events per 100 PY)** | **n (%)** | **Events** **(Events per 100 PY)** |
| Alanine aminotransferase increased | 36 (1.0) | 40 (0.6) | 39 (1.1) | 42 (0.7) |
| Aspartate aminotransferase increased | 27 (0.7) | 27 (0.4) | 44 (1.2) | 46 (0.7) |
| Transaminases increased | 47 (1.3) | 54 (0.9) | 43 (1.2) | 48 (0.7) |
| Hepatic enzyme increased | 15 (0.4) | 15 (0.2) | 19 (0.5) | 20 (0.3) |
| Liver function test abnormal | 2 (0.1) | 2 (0.0) | 1 (0.0) | 1 (0.0) |
| Total | 127 (3.4) | 138 (2.2) | 146 (4.0) | 157 (2.4) |

PY, patient years.

**Supplemental Table 9.** Number of patients with abnormal liver enzyme results in the DD- and NDD-CKD populations (safety population)

|  |  |  |
| --- | --- | --- |
| **Study Period/Visit****Parameter****Criterion** | **Vadadustat****N=3686****n (%)** | **Darbepoetin Alfa****N=3678****n (%)** |
| Weeks 2–8 |  |  |
| Alanine aminotransferase |  |  |
| N1 | 3591 | 3610 |
| >2 × and ≤3 × ULN | 22 (0.6) | 18 (0.5) |
| >3 × and ≤5 × ULN | 13 (0.4) | 14 (0.4) |
| >5 × and ≤10 × ULN | 4 (0.1) | 5 (0.1) |
| >10 × ULN | 3 (0.1) | 0 |
| Aspartate aminotransferase |  |  |
| N1  | 3591 | 3609 |
| >2 × and ≤3 × ULN  | 19 (0.5) | 29 (0.8) |
| >3 × and ≤5 × ULN  | 11 (0.3) | 10 (0.3) |
| >5 × and ≤10 × ULN  | 4 (0.1) | 5 (0.1) |
| >10 × ULN  | 2 (0.1) | 2 (0.1) |
| Bilirubin |  |  |
| N1  | 3589 | 3609 |
| >2 × and ≤3 × ULN  | 3 (0.1) | 1 (0.0) |
| >3 × ULN  | 0 | 2 (0.1) |
| Weeks 10–20 |  |  |
| Alanine aminotransferase |  |  |
| N1  | 3465 | 3523 |
| >2 × and ≤3 × ULN  | 24 (0.7) | 29 (0.8) |
| >3 × and ≤5 × ULN  | 11 (0.3) | 19 (0.5) |
| >5 × and ≤10 × ULN  | 6 (0.2) | 5 (0.1) |
| >10 × ULN  | 4 (0.1) | 3 (0.1) |
| Aspartate aminotransferase |  |  |
| N1  | 3465 | 3523 |
| >2 × and ≤3 × ULN  | 30 (0.9) | 32 (0.9) |
| >3 × and ≤5 × ULN  | 8 (0.2) | 15 (0.4) |
| >5 × and ≤10 × ULN  | 4 (0.1) | 5 (0.1) |
| >10 × ULN  | 4 (0.1) | 5 (0.1) |
| Bilirubin |  |  |
| N1  | 3466 | 3523 |
| >2 × and ≤3 × ULN  | 1 (0.0) | 2 (0.1) |
| >3 × ULN  | 0 | 2 (0.1) |
| Weeks 24–36 |  |  |
| Alanine aminotransferase |  |  |
| N1  | 3262  | 3356 |
| >2 × and ≤3 × ULN  | 24 (0.7)  | 30 (0.9) |
| >3 × and ≤5 × ULN  | 7 (0.2)  | 16 (0.5) |
| >5 × and ≤10 × ULN  | 8 (0.2)  | 6 (0.2) |
| >10 × ULN  | 2 (0.1)  | 4 (0.1) |
| Aspartate aminotransferase |  |  |
| N1  | 3262  | 3356 |
| >2 × and ≤3 × ULN  | 30 (0.9)  | 43 (1.3) |
| >3 × and ≤5 × ULN  | 11 (0.3)  | 21 (0.6) |
| >5 × and ≤10 × ULN  | 5 (0.2)  | 5 (0.1) |
| >10 × ULN  | 0  | 3 (0.1) |
| Bilirubin |  |  |
| N1  | 3261  | 3355 |
| >2 × and ≤3 × ULN  | 3 (0.1)  | 3 (0.1) |
| >3 × ULN  | 1 (0.0)  | 2 (0.1) |
| Weeks 40–52 |  |  |
| Alanine aminotransferase |  |  |
| N1  | 2812  | 2909 |
| >2 × and ≤3 × ULN  | 9 (0.3)  | 15 (0.5) |
| >3 × and ≤5 × ULN  | 6 (0.2)  | 10 (0.3) |
| >5 × and ≤10 × ULN  | 5 (0.2)  | 3 (0.1) |
| >10 × ULN  | 1 (0.0)  | 2 (0.1) |
| Aspartate aminotransferase |  |  |
| N1  | 2811  | 2909 |
| >2 × and ≤3 × ULN  | 13 (0.5)  | 27 (0.9) |
| >3 × and ≤5 × ULN  | 4 (0.1)  | 9 (0.3) |
| >5 × and ≤10 × ULN  | 5 (0.2)  | 1 (0.0) |
| >10 × ULN  | 2 (0.1)  | 1 (0.0) |
| Bilirubin |  |  |
| N1  | 2812  | 2909 |
| >2 × and ≤3 × ULN  | 1 (0.0)  | 2 (0.1) |
| >3 × ULN  | 2 (0.1)  | 2 (0.1) |

If there were assessments falling into different categories of criteria for a patient, then the patient was counted in the worst category only.

CKD, chronic kidney disease; DD, dialysis-dependent; N, number of patients; n, number of patients with events; N1, number of patients with any non-missing post-baseline assessments; NDD, non-dialysis-dependent; ULN, upper limit of normal.

**Supplemental Table 10.** Neoplasm-related treatment-emergent adverse events and serious adverse events in any treatment group—pooled total population

|  |  |  |
| --- | --- | --- |
|  | **Vadadustat** **(N=3686; exposure=6335.3 PY)** | **Darbepoetin Alfa(N=3687; exposure=6420.1 PY)** |
| **n (%)** | **Events** **(Events per 100 PY)** | **n (%)** | **Events****(Events per 100 PY)** |
| TEAEs of neoplasm | 174 (4.7) | 199 (3.1) | 223 (6.0) | 264 (4.1) |
| Drug-related AEs of neoplasm | 5 (0.1) | 5 (0.1) | 1 (0) | 1 (0) |
| TE-SAEs of neoplasm | 99 (2.7) | 104 (1.6) | 131 (3.6) | 143 (2.2) |
| Drug-related SAEs of neoplasm | 2 (0.1) | 2 (0) | 1 (0.0) | 1 (0) |
| TEAEs of neoplasm leading to study drug withdrawal | 13 (0.4) | 13 (0.2) | 12 (0.3) | 13 (0.2) |
| TEAEs of neoplasm resulting in death | 16 (0.4) | 16 (0.3) | 31 (0.8) | 31 (0.5) |

Neoplasms include benign, malignant, and unspecified growths including cysts and polyps per MedDRA.

AEs, adverse events; MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-years; SAEs, serious adverse events; TEAEs, treatment-emergent adverse events; TE-SAEs, treatment-emergent serious adverse events.