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# Comprehensive Safety Profile of Vadadustat From Global Phase 3 Clinical Trials

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## BACKGROUND

- Chronic kidney disease (CKD) is estimated to affect nearly 10% of the global population, and is frequently associated with anemia.[1,2]
- Vadadustat (VADA) is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), a class of drugs that stabilizes HIF and stimulates endogenous erythropoietin and red blood cell production[3,4]
- VADA has demonstrated non-inferior hematologic efficacy versus darbepoetin alfa (DA) in patients with dialysis-dependent (DD) and non–dialysis-dependent (NDD) CKD[3,4]
  - VADA and DA demonstrated similar adverse event (AE) profiles, however, potential risks of HIF-PHI therapy have been suggested based on the mechanism of action, including cardiovascular AEs, hyperkalemia, and neoplasms[5]
  - Likewise, erythropoiesis-stimulating agent (ESA) therapy is associated with hypertension and thromboembolic events, and in rare cases, seizures[6]
- VADA has demonstrated non-inferiority to DA for major adverse cardiovascular event ([MACE], a composite of death from any cause, a nonfatal myocardial infarction (MI), or a nonfatal stroke) in patients with DD-CKD (INNO$_2$VATE trials), but not with NDD-CKD (PRO$_2$TECT trials)[3,4]
- This poster summarizes the overall AE profiles of VADA and DA from global phase 3 clinical studies in patients with anemia due to CKD

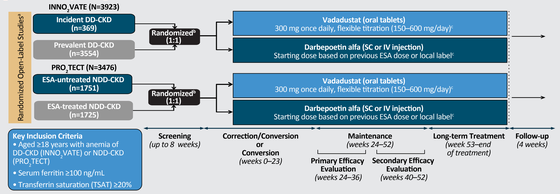
## OBJECTIVE

- To investigate the risk of AEs in 7373 patients with DD- and NDD-CKD treated with VADA compared with DA in 4 global phase 3 trials

## METHODS

- We pooled data from 4 global phase 3, randomized, open-label studies (**Figure 1**)

### Figure 1. Study Design




[a]Population: Incident (NCT02865850); Prevalent (NCT02892149); ESA-untreated (NCT02648347); ESA-treated (NCT02680574).
[b]Stratified by: Geographic region; NYHA CHF class; Hb level at study entry.
[c]Study drug is titrated to achieve target Hb levels (US: 10–11 g/dL; non-US: 10–12 g/dL).
CKD, chronic kidney disease; DD, dialysis-dependent; ESA, erythropoiesis-stimulating agents; Hb, hemoglobin; IV, intravenous; NDD, non–dialysis dependent; NYHA CHF, New York Heart Association Congestive Heart Failure; SC, subcutaneous.

### Pooled Safety Analysis

- Treatment-emergent adverse events (TEAEs) were defined as AEs that started (or a preexisting AE that worsened) on or after the first dose of study drug
- AEs of special interest (AESIs) were identified over the course of the clinical development program, from nonclinical findings, potential class effects of other HIF-PHIs, and ongoing safety surveillance
- All analyses were performed using the safety population, which included all enrolled patients who received ≥1 dose of study drug
- Duration of exposure was defined as the number of days between the date the patient received the first dose of study drug and the date the patient received the last dose of study drug

## RESULTS

- Overall, demographics and other baseline characteristics in the pooled DD-CKD, NDD-CKD, and total populations for the 4 global phase 3 studies were well balanced across the VADA and DA treatment groups (**Table 1**)
- Patients in the NDD-CKD population were older, more likely to be women, have diabetes mellitus, and use statins compared with the DD-CKD population (**Table 1**)
- In the NDD-CKD population, mean (standard deviation; [SD]) estimated glomerular filtration rate was 21.9 (11.84) mL/min/1.73 m$^2$ in the VADA treatment group and 22.3 (12.34) mL/min/1.73 m$^2$ in the DA treatment group

### Table 1. Demographics and Other Baseline Characteristics

| Characteristic | DD-CKD population VADA (N=1947) | DD-CKD population DA (N=1955) | NDD-CKD population VADA (N=1739) | NDD-CKD population DA (N=1732) | Total population VADA (N=3686) | Total population DA (N=3687) |
|---|---|---|---|---|---|---|
| Age, years, mean, (SD) | 57.8 (14.0) | 58.1 (13.9) | 66.2 (13.8) | 65.7 (13.6) | 61.8 (14.5) | 61.7 (14.3) |
| >65 years, n (%) | 667 (34.3) | 663 (33.9) | 1030 (59.2) | 1022 (59.0) | 1697 (46.0) | 1685 (45.7) |
| Sex, male n (%) | 1089 (55.9) | 1110 (56.8) | 797 (45.8) | 738 (42.6) | 1886 (51.2) | 1848 (50.1) |
| Race, n (%) | | | | | | |
| White | 1255 (64.5) | 1231 (63.0) | 1177 (67.7) | 1172 (67.7) | 2432 (66.0) | 2403 (65.2) |
| Black | 470 (24.1) | 478 (24.5) | 280 (16.1) | 302 (17.4) | 750 (20.3) | 780 (21.2) |
| Asian | 88 (4.5) | 106 (5.4) | 110 (6.3) | 92 (5.3) | 198 (5.4) | 198 (5.4) |
| American Indian or Alaska Native | 20 (1.0) | 30 (1.5) | 54 (3.1) | 49 (2.8) | 74 (2.0) | 79 (2.1) |
| Other[a] | 114 (5.9) | 110 (5.6) | 118 (6.8) | 117 (6.8) | 232 (6.3) | 227 (6.2) |
| Region, n (%)[b] | | | | | | |
| US | 1180 (60.6) | 1181 (60.4) | 861 (49.5) | 862 (49.8) | 2041 (55.4) | 2043 (55.4) |
| Europe | 277 (14.2) | 295 (15.1) | 295 (17.0) | 288 (16.6) | 572 (15.5) | 583 (15.8) |
| Non-US/Europe | 490 (25.2) | 479 (24.5) | 583 (33.5) | 582 (33.6) | 1073 (29.1) | 1061 (28.8) |
| BMI, kg/m$^2$, mean (SD) | 28.5 (7.1) | 28.4 (7.1) | 29.4 (7.1) | 29.7 (7.3) | 28.9 (7.2) | 29.1 (7.2) |
| Diabetes mellitus, n (%) | 1070 (55.0) | 1088 (55.7) | 1098 (63.1) | 1115 (64.4) | 2168 (58.8) | 2203 (59.8) |
| Statin use, n (%) | 943 (48.4) | 969 (49.6) | 1055 (60.7) | 1042 (60.2) | 1998 (54.2) | 2011 (54.5) |

[a]Includes Native Hawaiian or other Pacific Islander, multiple or not reported. [b]Europe (DD-CKD population) included Bulgaria, France, Germany, Italy, Poland, Portugal, Serbia, Ukraine, United Kingdom; Europe (NDD-CKD population) included Austria, Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Poland, Romania, Serbia, Slovakia, Spain, Turkey, United Kingdom; Non-US/Europe (DD-CKD population) included Argentina, Australia, Brazil, Canada, Israel, Mexico, Russia, South Korea; Non-US/Europe (NDD-CKD population) included Argentina, Australia, Brazil, Canada, Chile, Colombia, Israel, Malaysia, Mexico, New Zealand, Russia, South Africa, South Korea, Ukraine.
BMI, body mass index; CKD, chronic kidney disease; DA, darbepoetin alfa; DD, dialysis-dependent; NDD, non–dialysis-dependent; SD, standard deviation; VADA, vadadustat.

### Treatment-Emergent Adverse Events

- Across all studies, rates of TEAEs for VADA and DA were similar (any TEAE: VADA, 88.9%; DA, 89.3%) with the exception of any drug-related TEAE (VADA 10.1%; DA, 4.7%) likely attributed to the open-label nature of the study (**Table 2**)

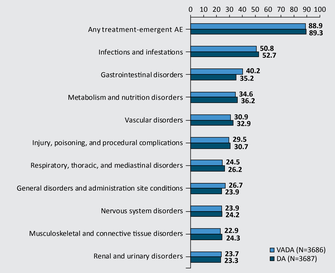
### Table 2. Summary of TEAEs—Pooled Total Population

| MedDRA Preferred Term | VADA (N=3686; Exposure=6335.3 PY) n (%) | VADA Events (per 100 PY) | DA (N=3687; Exposure=6420.1 PY) n (%) | DA Events (per 100 PY) |
|---|---|---|---|---|
| Any TEAE | 3277 (88.9) | 27417 (432.8) | 3292 (89.3) | 28340 (441.4) |
| Severity | | | | |
| Mild | 589 (16.0) | 12477 (196.9) | 601 (16.3) | 12781 (199.1) |
| Moderate | 1106 (30.0) | 10361 (163.5) | 1095 (29.7) | 10926 (170.2) |
| Severe | 1582 (42.9) | 4579 (72.3) | 1596 (43.3) | 4633 (72.2) |
| Any drug-related TEAE | 371 (10.1) | 576 (9.1) | 174 (4.7) | 218 (3.4) |
| Any severe TEAE | 1582 (42.9) | 4579 (72.3) | 1596 (43.3) | 4633 (72.2) |
| Any treatment-emergent SAE | 2139 (58.0) | 6981 (110.2) | 2186 (59.3) | 7159 (111.5) |
| Any drug-related treatment-emergent SAE | 66 (1.8) | 75 (1.2) | 55 (1.5) | 64 (1.0) |
| Any TEAE leading to discontinuation from study drug | 259 (7.0) | 321 (5.1) | 126 (3.4) | 159 (2.5) |
| Any drug-related TEAE leading to discontinuation from study drug | 73 (2.0) | 85 (1.3) | 11 (0.3) | 12 (0.2) |

DA, darbepoetin alfa; MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-years; SAE, serious adverse event; TEAE, treatment-emergent adverse event; VADA, vadadustat.

- The most common TEAEs in the VADA and DA groups by system organ class (SOC) were infections and infestations (50.8% and 52.7%), gastrointestinal disorders (40.2% and 35.2%), metabolism and nutrition disorders (34.6% and 36.2%), and injury, poisoning, and procedural complications (29.5% and 30.7%). Event rates of any TEAE in the VADA group and DA group were 432.8 and 441.4 events per 100 patient-years, respectively (**Figure 2**)
  - The most common TEAEs by MedDRA preferred term (PT) reported in >10% of patients were kidney failure, hypertension, diarrhea, and pneumonia with VADA exposure leading to fewer events of hypertension (**Table 3**)
- The most common drug-related TEAEs (≥1% of patients) in the VADA group were diarrhea (2.2%) and nausea (1.2%)
  - Diarrhea and nausea were the most common drug-related TEAEs which led to study drug discontinuation in 0.4% and 0.2% of patients, respectively

### Figure 2. TEAEs by SOC Reported in ≥5% of Patients in Any Treatment Group—Pooled Total Population




| Events per 100 PY | VADA (Exposure=6335.3 PY) | DA (Exposure=6420.1 PY) |
|---|---|---|
| Infections and infestations | 68.6 | 71.6 |
| Gastrointestinal disorders | 52.4 | 46.7 |
| Metabolism and nutrition disorders | 42.3 | 42.1 |
| Vascular disorders | 30.6 | 32.8 |
| Injury, poisoning, and procedural complications | 36.8 | 39.7 |
| Respiratory, thoracic, and mediastinal disorders | 26.9 | 28.9 |
| General disorders and administration site conditions | 24.1 | 21.9 |
| Nervous system disorders | 23.7 | 22.4 |
| Musculoskeletal and connective tissue disorders | 22.7 | 24.3 |
| Renal and urinary disorders | 19.1 | 18.8 |

DA, darbepoetin alfa; PY, patient-years; SOC, system organ class; TEAE, treatment-emergent adverse event; VADA, vadadustat.

### Table 3. TEAEs by MedDRA PT Reported in ≥5% of Patients in Any Treatment Group—Pooled Total Population

| MedDRA System Organ Class Preferred Term | VADA (N=3686; Exposure=6335.3 PY) n (%) | VADA Events (per 100 PY) | DA (N=3687; Exposure=6420.1 PY) n (%) | DA 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) |
| Urinary tract infection | 339 (9.2) | 445 (7.0) | 362 (9.8) | 541 (8.4) |
| Upper respiratory tract infection | 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) |
| Gastrointestinal disorders | 1483 (40.2) | 3320 (52.4) | 1297 (35.2) | 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) |
| Kidney failure | 558 (15.1) | 582 (9.2) | 563 (15.3) | 602 (9.4) |

DA, darbepoetin alfa; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; PY, patient-years; TEAE, treatment-emergent adverse event; VADA, vadadustat.

### Treatment-Emergent Serious Adverse Events

- The most common treatment-emergent serious adverse events (SAE) by MedDRA PT was kidney failure, followed by pneumonia, fluid overload, and acute MI (**Table 4**)
  - Most frequent treatment-emergent SAEs for VADA and DA groups, in the NDD-CKD population was kidney failure (30.1% and 30.6%), and in the DD-CKD population was pneumonia (7.6% and 6.4%; data not shown)

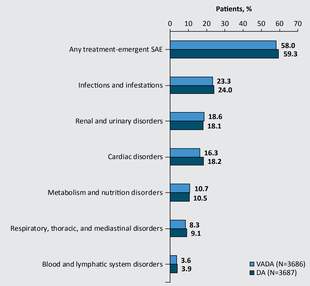
### Table 4. Treatment-Emergent SAEs by MedDRA PT Reported in ≥2% of Patients in Any Treatment Group—Pooled Total Population

| MedDRA System Organ Class Preferred Term | VADA (N=3686; Exposure=6335.3 PY) n (%) | VADA Events (per 100 PY) | DA (N=3687; Exposure=6420.1 PY) n (%) | DA 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) |
| Kidney failure | 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 myocardial infarction | 150 (4.1) | 171 (2.7) | 133 (3.6) | 149 (2.3) |
| Cardiac failure congestive | 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) |

DA, darbepoetin alfa; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; PY, patient-years; SAE, serious adverse event; VADA, vadadustat.

- The most frequent treatment-emergent SAEs in the VADA and DA groups occurred in the SOCs for infections and infestations (23.3% and 24.0%) and renal and urinary disorders (18.6% and 18.1%; **Figure 3**)

### Figure 3. Treatment-Emergent SAEs by SOC Reported in ≥2% of Patients in Any Treatment Group—Pooled Total Population




| Events per 100 PY | VADA (Exposure=6335.3 PY) | DA (Exposure=6420.1 PY) |
|---|---|---|
| Any treatment-emergent SAE | 110.2 | 111.5 |
| Infections and infestations | 23.6 | 23.4 |
| Renal and urinary disorders | 12.5 | 11.9 |
| Cardiac disorders | 16.1 | 17.2 |
| Metabolism and nutrition disorders | 9 | 8.4 |
| Respiratory, thoracic, and mediastinal disorders | 7.1 | 7.5 |
| Blood and lymphatic system disorders | 2.5 | 2.7 |

DA, darbepoetin alfa; PY, patient-years; SOC, system organ class; SAE, serious adverse event; VADA, vadadustat.

### TEAEs Leading to Death

- TEAEs leading to death were reported by 16.1% and 16.2% of patients administered VADA and DA, respectively (**Table 5**)
- TEAEs leading to death in the VADA and DA groups for >1% of patients occurred in the SOCs for cardiac disorders (5.5% and 5.6%), infections and infestations (2.4% and 2.5%), general disorders and administration site conditions (2.4% and 2.0%), renal and urinary disorders (1.8% in both groups) and respiratory, thoracic, and mediastinal disorders (0.8% and 1.1%; **Table 5**)
  - The most common PTs for TEAEs leading to death by MedDRA PT in the VADA and DA groups were cardiac arrest (1.7% in each group), kidney failure disease (1.1% and 1.3%), and cardio-respiratory arrest (0.9% and 1.0%; **Table 5**)
- Deaths considered related to study drug included 1 death (cardiac arrest) reported in patients administered VADA versus 4 deaths (aspiration pneumonia, cardiac arrest, MI, and acute MI) in patients administered DA

### Table 5. TEAEs That Led to Death in >1% of Patients in Any Treatment Group—Pooled Total Population

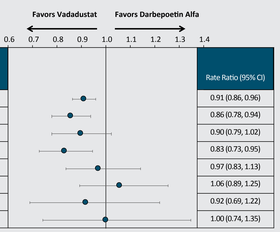
| MedDRA System Organ Class Preferred Term | VADA (N=3686; Exposure=6335.3 PY) n (%) | VADA Events (per 100 PY) | DA (N=3687; Exposure=6420.1 PY) n (%) | DA Events (per 100 PY) |
|---|---|---|---|---|
| Any TEAE leading to death[a] | 593 (16.1) | 593 (9.4) | 596 (16.2) | 597 (9.3) |
| Cardiac disorders | 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) |
| Cardio-respiratory 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) |
| Kidney failure | 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) |

[a]Deaths not due to TEAEs are not listed in this table.
DA, darbepoetin alfa; MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-years; TEAE, treatment-emergent adverse event; VADA, vadadustat.

### Adverse Events of Special Interest

- The most common AESIs (>10%) in the VADA and DA groups were hypertension (18.0% and 21.0%), congestive heart failure (10.3% and 11.5%), and hyperkalemia (9.9% and 11.9%), all of which were more frequent with DA (**Figure 4**)
- In general, all AESIs were less frequent in the VADA group compared to the DA group

### Figure 4. AESIs Reported in ≥1% of Patients in Any Treatment Group—Pooled Total Population




| | VADA (N=3686) 6335.3 PY n (%) | VADA Events (per 100 PY) | DA (N=3687) 6420.1 PY n (%) | DA Events (per 100 PY) | Rate Ratio (95% CI) |
|---|---|---|---|---|---|
| Any AESI | 1514 (41.1) | 3139 (49.5) | 1667 (45.2) | 3524 (54.9) | 0.91 (0.86, 0.96) |
| Hypertension | 663 (18.0) | 974 (15.4) | 776 (21.0) | 1142 (17.8) | 0.86 (0.78, 0.94) |
| Congestive heart failure | 381 (10.3) | 582 (9.2) | 425 (11.5) | 633 (9.9) | 0.90 (0.79, 1.02) |
| Hyperkalemia | 364 (9.9) | 467 (7.4) | 439 (11.9) | 549 (8.6) | 0.83 (0.73, 0.95) |
| Hypersensitivity | 282 (7.7) | 351 (5.5) | 291 (7.9) | 360 (5.6) | 0.97 (0.83, 1.13) |
| Hepatotoxicity | 252 (6.8) | 341 (5.4) | 239 (6.5) | 368 (5.7) | 1.06 (0.89, 1.25) |
| Pulmonary hypertension | 87 (2.4) | 108 (1.7) | 95 (2.6) | 118 (1.8) | 0.92 (0.69, 1.22) |
| Cardiac valve disorders | 84 (2.3) | 138 (2.2) | 84 (2.3) | 121 (1.9) | 1.00 (0.74, 1.35) |

AESI, adverse event of special interest; CI, confidence interval; DA, darbepoetin alfa; PY, patient-years; VADA, vadadustat.

- TEAEs of seizures were low, and generally similar between the VADA and DA groups across the 4 trials (**Table 6**).

### Table 6. TEAEs of Seizure By Individual Global Phase 3 Studies

| Seizure | VADA, n/N (%) | DA, n/N (%) |
|---|---|---|
| ESA-untreated NDD-CKD Study | 5/878 (0.6) | 6/870 (0.7) |
| ESA-treated NDD-CKD Study | 3/861 (0.3) | 3/862 (0.3) |
| Incident dialysis DD-CKD Study | 2/179 (1.1) | 2/186 (1.1) |
| Prevalent dialysis DD-CKD Study | 21/1768 (1.2) | 19/1769 (1.1) |

DA, darbepoetin alfa; DD-CKD, dialysis dependent chronic kidney disease; ESA, erythropoiesis-stimulating agent; NDD-CKD, non–dialysis dependent chronic kidney disease; TEAE, treatment-emergent adverse event; VADA, vadadustat.

## CONCLUSIONS

- In a pooled analysis of the safety populations from 4 phase 3 trials evaluating the treatment of anemia in patients with DD-CKD or NDD-CKD, the AE profile of VADA was generally comparable with DA.
- No clinically relevant differences in the prevalence and incidence of TEAEs, treatment-emergent SAEs, or deaths were observed.
- Furthermore, the occurrence of AESIs potentially thought to be implicated with use of HIF-PHIs, such as hypertension, congestive heart failure, and hyperkalemia, were generally favorable with VADA.
- No difference in the prevalence of AEs that could potentially be linked to the mechanism of action of HIF-PHIs was observed versus DA.

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## DISCLOSURES

RA and GC currently serve as study consultants for Akebia Therapeutics, Inc. DV, WL, and CS are employees of Akebia Therapeutics, Inc. The results presented here have not been published previously in whole or part, except in abstract format

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