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Cost Comparison Analysis of Hospitalizations for Vadadustat Versus Darbepoetin Alfa Based on the INNO$_2$VATE Trials

Wenli Luo,[1] Steven Burke,[1] Bryce Foote,[1] Todd Minga,[1] Wolfgang C. Winkelmayer,[2] Mark J. Sarnak,[3] Sakshi Kushwaha,[4] Frank Cinfio,[4] Agota Szende[5]

[1]Akebia Therapeutics Inc., Cambridge, MA, United States; [2]Baylor College of Medicine, Houston, TX, United States; [3]Tufts University School of Medicine, Boston, MA, United States; [4]Genesis Research Group, Hoboken, NJ, United States; [5]Genesis Research Group, London, United Kingdom

BACKGROUND

- Vadadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) approved for the treatment of anemia associated with chronic kidney disease (CKD) in adults on dialysis for at least 3 months[1]
- Vadadustat was studied in two phase 3 randomized, open-label clinical trials as part of the INNO$_2$VATE program: one in incident dialysis-dependent (DD)-CKD and one in prevalent DD-CKD[2]
- In the INNO$_2$VATE program, vadadustat treatment resulted in fewer serious treatment-emergent adverse events (TEAEs) that required or prolonged hospitalizations compared with darbepoetin alfa (DA; **Table 1**)[3]

Table 1. Serious TEAEs That Required or Prolonged Hospitalizations in the INNO$_2$VATE Trials[3,a]

	VADA N=1947 PY=3222.0		DA N=1955 PY=3245.8	
	n (%)[b]	Number of events (E*100/PY)	n (%)[a]	Number of events (E*100/PY)
Serious TEAEs that required or prolonged hospitalization	**986 (50.6)**	**3279 (101.8)**	**1053 (53.9)**	**3580 (110.3)**
Infections and infestations	511 (26.2)	865 (26.8)	526 (26.9)	942 (29.0)
Cardiac disorders	253 (13.0)	420 (13.0)	317 (16.2)	510 (15.7)
Injury, poisoning, and procedural complications	222 (11.4)	297 (9.2)	230 (11.8)	328 (10.1)
Metabolism and nutrition disorders	203 (10.4)	295 (9.2)	209 (10.7)	287 (8.8)
Gastrointestinal disorders	190 (9.8)	284 (8.8)	196 (10.0)	299 (9.2)
Respiratory, thoracic, and mediastinal disorders	174 (8.9)	252 (7.8)	185 (9.5)	264 (8.1)
Vascular disorders	179 (9.2)	239 (7.4)	180 (9.2)	242 (7.5)
Nervous system disorders	142 (7.3)	191 (5.9)	151 (7.7)	205 (6.3)

[a]TEAEs were coded using MedDRA v23.0. [b]TEAEs occurring in >5% of patients.
DA, darbepoetin alfa; E, events; E*100/PY; event rate per 100 patient-years; MedDRA v23.0, Medical Dictionary for Regulatory Activities version 23.0; PY, patient-years; TEAE, treatment-emergent adverse event; VADA, vadadustat.

- This study used a cost comparison analysis to estimate potential cost offsets associated with differences in hospitalization rates in vadadustat-treated patients with DD-CKD–related anemia in the United States (US)

OBJECTIVES

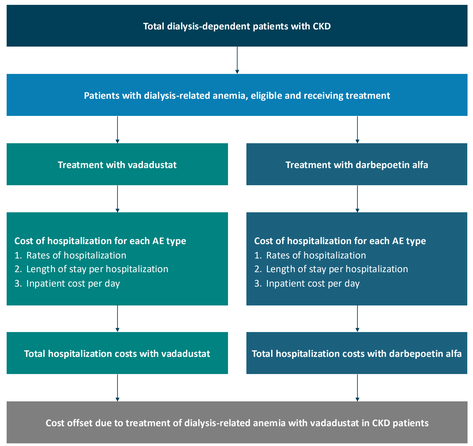
- To quantify the modeled annual difference in all-cause hospitalizations among US patients with DD-CKD–related anemia treated with vadadustat versus DA, based on hospitalization data from the INNO$_2$VATE program
- To estimate the annual hospitalization-related cost offsets associated with treatment with vadadustat at the US population level

METHODS

Cost Comparison Model Structure

- Hospitalizations and associated costs were stratified by reason for hospitalization
- Cost inputs were based on condition-specific average inpatient costs per day obtained from Medicare data, including the Healthcare Cost and Utilization Project (HCUP), and average per-patient hospitalization costs per day from the United States Renal Data System (USRDS)[4,5]
- All costs were reported in 2025 US dollars
- A subgroup analysis was conducted for patients receiving peritoneal dialysis (PD)
- The population-based cost comparison model was developed in Microsoft Excel® using a cost-accumulation framework (**Figure 1**)
  - The model evaluated an adult US population with DD-CKD–related anemia treated with vadadustat or DA
  - Vadadustat was evaluated as the key intervention, with DA as the comparator
  - Analyses were conducted from a Medicare costing perspective over a 1-year time horizon, representing the treatment-eligible US population
- Key assumptions of the cost comparison model can be found in **Table 2**

Figure 1. Cost Comparison Model



AE, adverse event; CKD, chronic kidney disease.

Table 2. Key Assumptions for the Cost Comparison Model

Assumption	Details
Population	The DD-CKD population was derived from the total US prevalence of end-stage kidney disease (Stage 5 CKD), from which DD patients were identified for inclusion in the model Due to data limitations, the proportion of patients with anemia receiving hemodialysis is assumed to adequately represent the proportion of patients with anemia across the pooled DD-CKD population
Treatment arms	All patients diagnosed with dialysis-related anemia who are eligible for treatment are assumed to receive either vadadustat or DA for a full year
Treatment discontinuation	Each patient is assumed to remain in the analysis for a full year, contributing one person-year, with no mortality or treatment discontinuation considered
Discounting	Because the analysis covers a single year, costs are reported without discounting
Costs	All cost inputs are adjusted for inflation using the Medical Care component of the US Consumer Price Index (CPI) to standardize values to the 2025 base year

CKD, chronic kidney disease; DA, darbepoetin alfa; DD-CKD, dialysis-dependent CKD.

Statistical Analysis

- Annual all-cause hospitalization rates, number of hospitalizations, and mean length of stay (LOS) were derived from the INNO$_2$VATE program. Differences in the proportion of patients with ≥1 hospitalization were summarized using odds ratios (ORs) with 95% CIs

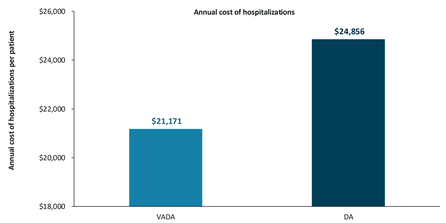
RESULTS

- In the pooled INNO$_2$VATE trial population, 50.6% and 53.9% of patients treated with vadadustat and DA, respectively, experienced at least one hospitalization (OR, 0.88; 95% CI, 0.775-0.997; *P*=0.04)

Annual Results per Patient

- Based on Medicare cost data, compared with DA, treatment with vadadustat was associated with a 7.7% reduction in the annual number of hospitalizations per patient and a 16.0% reduction in hospitalization days per patient (**Figure 2; Table 3**)
- Annual hospitalization costs per patient were 14.8% lower ($3,686 offset) for patients treated with vadadustat compared with DA (**Figure 2; Table 3**)

Figure 2. Annual Cost of Hospitalizations per Patient



DA, darbepoetin alfa; VADA, vadadustat.

Table 3. Summary of Annual Number of Hospitalizations, Hospitalization Days, and Cost of Hospitalizations per Patient

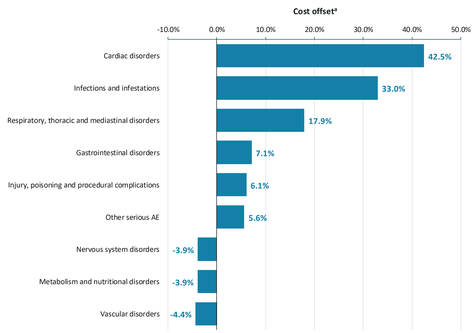
	VADA	DA	Offset	Offset (%)
Number of events	1.02	1.10	0.09	7.7%
Number of hospitalization days	8.9	10.6	1.7	16.0%
Hospitalization costs, USD	$21,171	$24,856	$3,686	14.8%

DA, darbepoetin alfa; USD, US dollar; VADA, vadadustat.

Reasons for Hospitalization

- The primary drivers of per-patient offsets were fewer hospitalizations due to cardiac disorders and infections/infestations (**Figure 3**)

Figure 3. Per-Patient Hospitalization Cost Offsets by Reason for Hospitalization

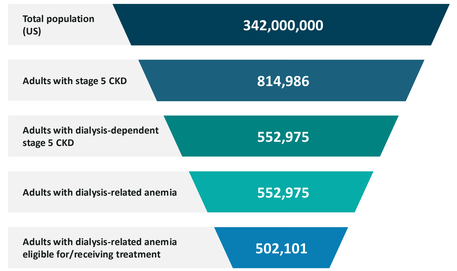


[a]Costs for vadadustat compared with DA. Negative cost offset indicates increase in cost compared with DA.
AE, adverse event; DA, darbepoetin alfa.

Base Case Results

- The base case analysis modeled an estimated 502,101 adults in the United States with DD-CKD–related anemia on dialysis (**Figure 4**)

Figure 4. Patient Selection Flow for DD-CKD Patients in the United States

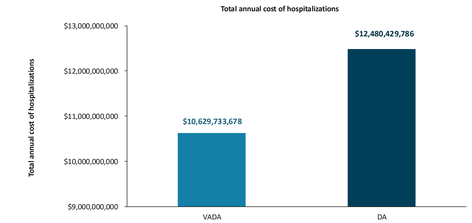


CKD, chronic kidney disease; DD-CKD, dialysis-dependent CKD.

Annual Results for Pooled Population

- At the population level, total annual hospitalization cost was 14.8% lower ($1,850,696,107 offset) for patients treated with vadadustat compared with DA (**Figure 5; Table 4**)
  - Model estimates indicated that differences in hospitalizations due to cardiac disorders and infections/infestations contributed most to the observed cost differences

Figure 5. Total Annual Cost of Hospitalization for US DD-CKD Population With Anemia (n=502,101)



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

Table 4. Summary of Total Annual Hospitalizations, Hospitalization Days, and Cost of Hospitalization for Pooled Population

	VADA	DA	Offset	Offset (%)
Number of events	510,984	553,799	42,816	7.7%
Number of hospitalization days	4,461,608	5,308,938	847,331	16.0%
Hospitalization costs, USD	$10,629,733,678	$12,480,429,786	$1,850,696,107	14.8%

DA, darbepoetin alfa; USD, US dollar; VADA, vadadustat.

- The scenario analyses using an alternative costing approach based on average inpatient cost per day from the USRDS produced results consistent with the base case

Peritoneal Dialysis Subgroup

- In patients with PD, annual number of hospitalizations per patient and the number of hospitalization days were 22.6% and 18.0% lower, respectively, in the modeled vadadustat scenario compared with DA (**Table 5**)
  - Annual hospitalization costs per patient were $27,751 for vadadustat compared with $30,718 for DA, corresponding to a 9.7% modeled cost offset among patients receiving PD
- The US PD subgroup analysis included 51,203 adults with DD-CKD–related anemia
- Population-level annual results for the PD subgroup were consistent with the per-patient analysis

Table 5. Per-Patient and Population-Level Results for the PD Subgroup

	VADA	DA	Offset	Offset (%)
Annual results per patient				
Number of events	0.97	1.25	0.28	22.6%
Number of hospitalization days	10.4	12.7	2.3	18.0%
Annual total hospitalization costs, USD	$27,751	$30,718	$2,967	9.7%
Annual results for the PD population (n=51,203)				
Number of events	49,722	64,248	14,526	22.6%
Number of hospitalization days	533,741	650,800	117,060	18.0%
Annual total hospitalization costs, USD	$1,420,954,660	$1,572,870,822	$151,916,162	9.7%

DA, darbepoetin alfa; PD, peritoneal dialysis; USD, US dollar; VADA, vadadustat.

LIMITATIONS

- Hospitalization rates and average LOS per hospitalization were derived from clinical trial data and may not fully reflect real-world outcomes. Additional analyses using other definitions of hospitalization rates are required to confirm consistency of data
- The use of average hospital costs per day assumes uniform cost across all days of hospitalization
- The results rely on simplified assumptions, including no treatment switching or discontinuation
- Medicare inpatient costs for each adverse event were based on the overall population rather than specifically on patients with DD-CKD, which may lead to underestimation of total hospitalization costs
- The INNO$_2$VATE program comprised two randomized, open-label clinical trials stratified by multiple factors, but not by dialysis type (i.e., hemodialysis versus PD); therefore, PD subgroup analyses are descriptive only, as treatment groups were not randomized by dialysis type
- The cost comparison analysis does not fully capture the patient-level cost or health outcomes and does not account for differences in drug administration costs; as a result, the analysis does not capture the full economic impact of treatment

CONCLUSIONS

- In the modeled US treatment-eligible DD-CKD population and PD subgroup, treatment with vadadustat was associated with lower hospitalization and hospitalization-related costs compared with DA
- When applied at the national level, modeled hospitalization-related cost offsets were observed with vadadustat compared with DA

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DISCLOSURES

WL, SB, BF, and **TM** are employees of Akebia Therapeutics, Inc.
WCM holds the Gordon A. Cain Chair in Nephrology at Baylor College of Medicine and has served as a consultant and received honoraria from Anthos, Akebia Therapeutics, Inc., Ardelyx, AstraZeneca, Bayer, Boehringer Ingelheim, GlaxoSmithKline, Merck Sharp & Dohme/Merck, Natera, Novartis, Pharmacosmos, Unicycive, Vera, and Zydus.
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SK, FC, and **AS** were employees of Genesis Research Group at the time this work was conducted. Genesis Research Group received consulting fees from Akebia Therapeutics for this project.

REFERENCES

1. Vafseo® (vadadustat) [package insert]. Cambridge, MA: Akebia Therapeutics, Inc.; 2024.
2. Eckardt KU, et al. *N Engl J Med.* 2021;384(17):1601-1612.
3. Chertow G, et al. Poster Presented at: American Society of Nephrology (ASN) Kidney Week 2025; November 5-9, 2025; Houston, TX.
4. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUPnet). Rockville, MD: U.S. Department of Health & Human Services. https://datatools.ahrq.gov/hcupnet/. Accessed February 18, 2026.
5. United States Renal Data System. 2024 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2024. https://usrds-adr.niddk.nih.gov/2024. Accessed February 18, 2026.

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