HOSPITAL MEDICINE™ SUMMIT

Taking the Kidneys to Heart:

Managing CKD-Related Anemia With Emerging HIF-PHIs

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Learning Objectives

- Clarify the disease burden imposed by untreated or undertreated anemia in patients with chronic kidney disease (CKD), including in racially diverse populations
- Correlate the pathophysiology of anemia in CKD with viable therapeutic targets
- Identify appropriate candidates for emerging CKD-related anemia treatments among patients on or not on dialysis based on efficacy and safety data from recent clinical trials

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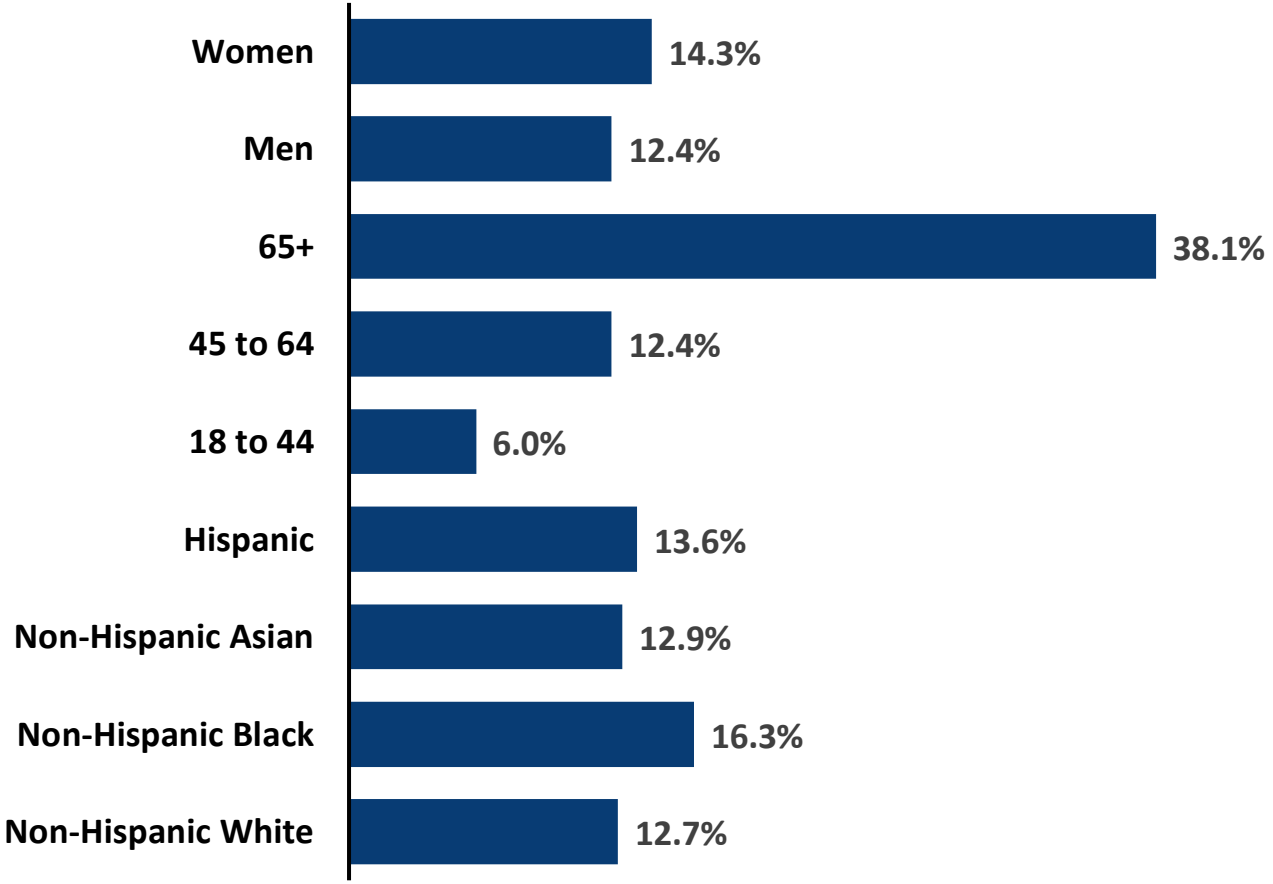
Overview of Anemia in CKD

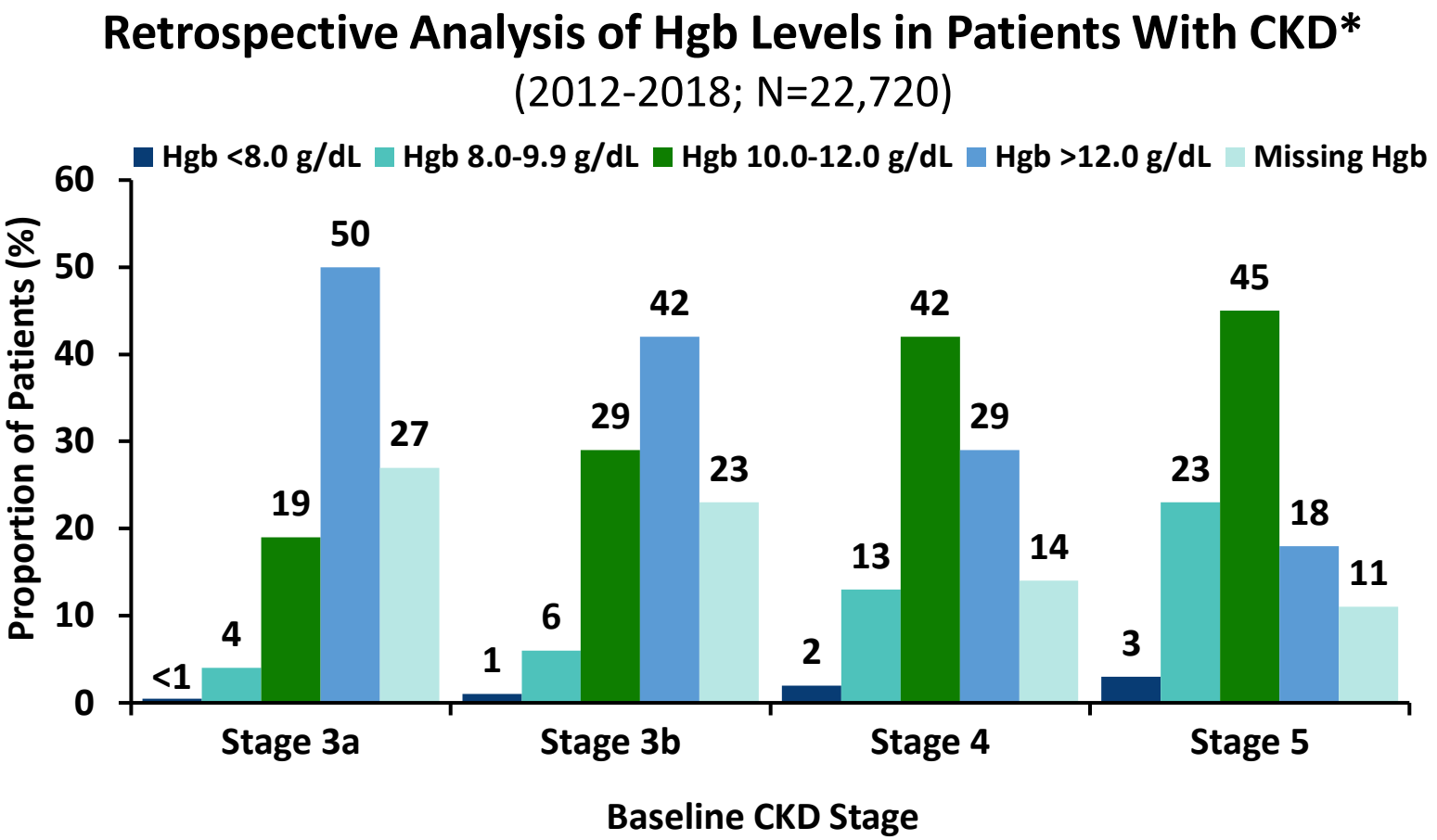
Prevalence of CKD in the US



- Over **15%** of US adults are estimated to have CKD
- Up to **90%** are undiagnosed
- **~40%** of those with severe CKD are undiagnosed

CDC. Chronic kidney disease in the United States, 2021. Available at: https://www.cdc.gov/kidneydisease/pdf/Chronic-Kidney-Disease-in-the-US-2021-h.pdf; USRDS. 2021 annual data report. Available at: https://adr.usrds.org/2021

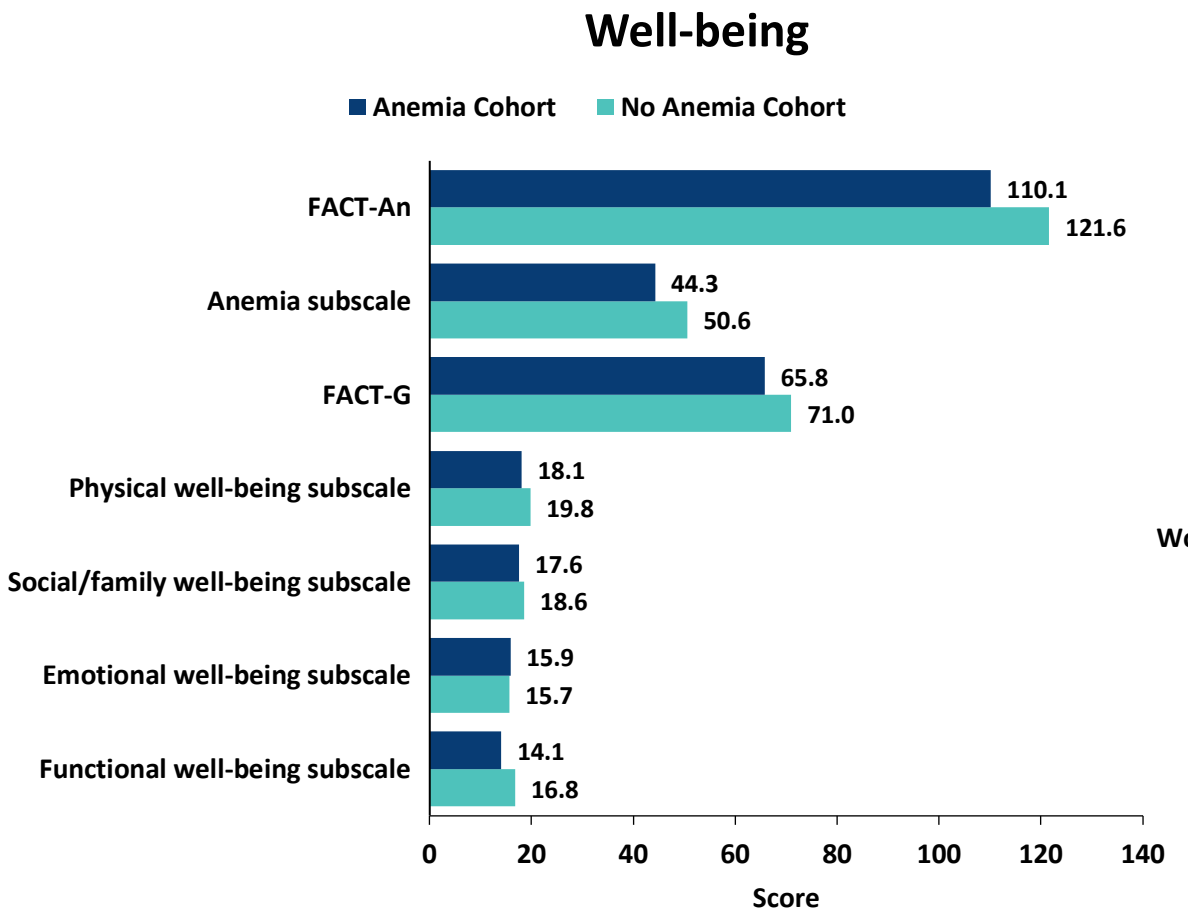
Prevalence of Anemia in CKD

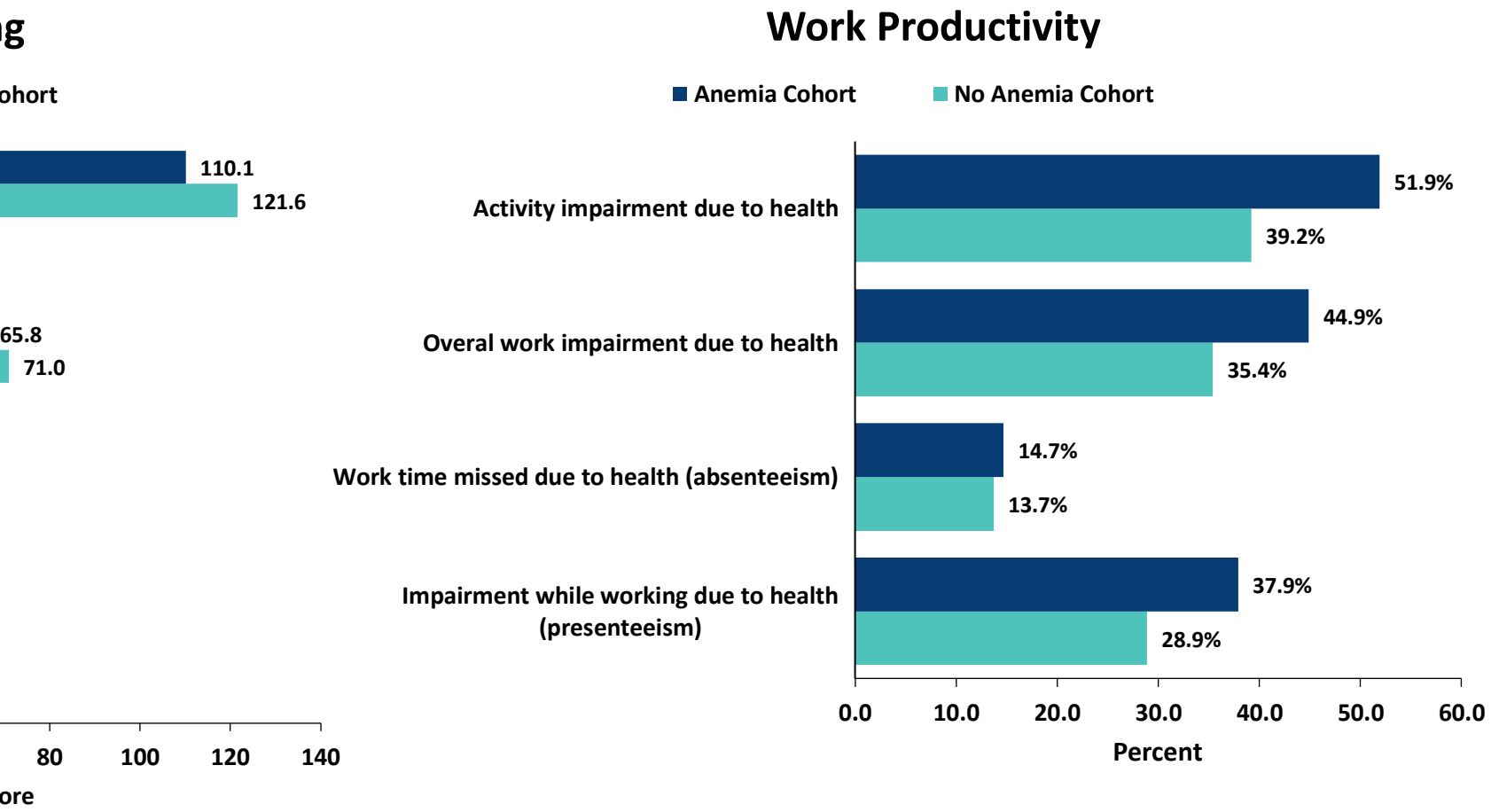


- Anemia is **2.5 times** more likely to occur in patients with CKD vs those without CKD
- **23.3%** of patients with NDD-CKD stage 3a-5 had anemia (Hgb <10 g/dL)
- Anemia prevalence increased with CKD stage from **18.2%** (stage 3a) to **72.8%** (stage 5)

*CKD definition: ≥2 eGFR measurements of <60 mL/min/1.73 m^2 ≥90d apart.
eGFR, estimated glomerular filtration rate; Hgb, hemoglobin; NDD, non-dialysis dependent.
Stauffer ME, Fan T. *PloS one*. 2014;9:e84943; Wittbrodt ET, et al. *Clin Kidney J*. 2022;15:244-252.

Burden of Anemia in CKD





FACT-An, Functional Assessment of Cancer Therapy – Anemia; FACT-G, Functional Assessment of Cancer Therapy – General.

Michalopoulos SN, et al. *Kidney Med*. 2022;4:100439.

Impact of Anemia on the Risk for Hospitalization Among Patients With CKD

- Lower Hgb is associated with higher risk of hospitalization[1]:

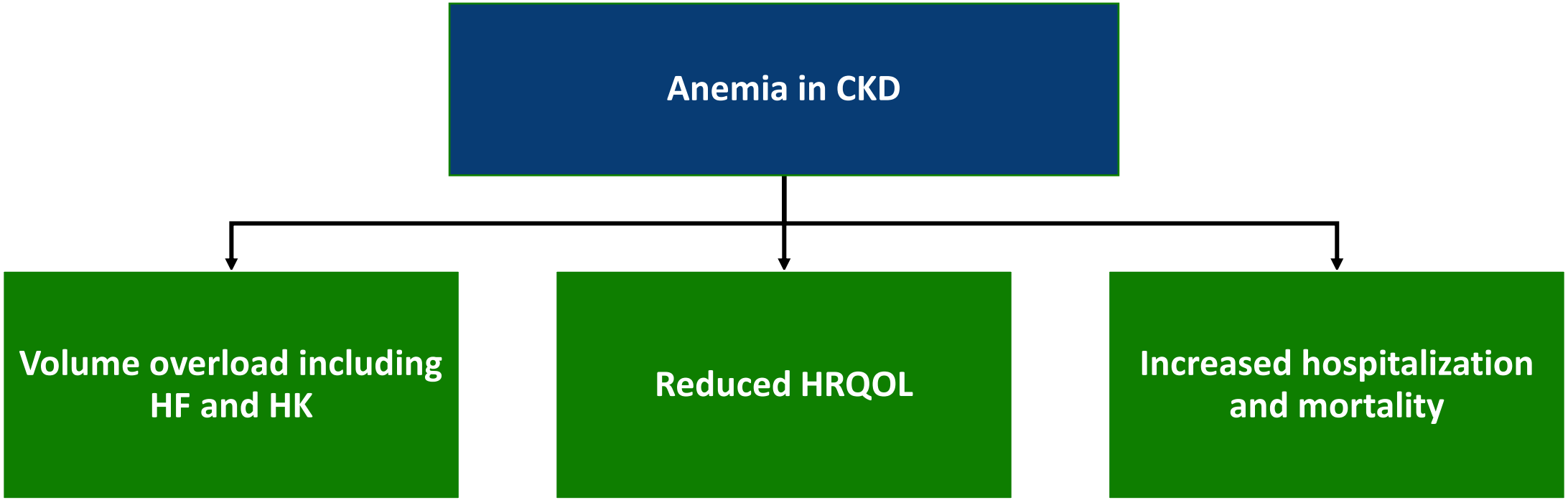
Patient Population	Hgb Level	Risk for Hospitalization HR (95% CI)
NDD-CKD	Hgb < 10 g/dL	1.46 (1.02–2.09)
DD-CKD	Hgb 10–12 g/dL Hgb >12 g/dL	1.09 (1.07–1.11) 0.91 (0.87–0.96),

- In patients on dialysis, overall risk for hospitalization decreases with increasing Hgb (HR per 1 g/dL increase in Hgb, 0.92; 95% CI, 0.87–0.98)[1]
- Severe anemia is associated with increased hospital LOS [mean 6.4 (SD 6.0) days vs mean 4.5 (SD 4.0) days; *P* <.001][2]

CI, confidence interval; HR, hazard ratio; LOS, length of stay; SD, standard deviation.

1. Palaka E, et al. *Int J Nephrol*. 2020:7692376. 2. Garlo K, et al. *Medicine*. 2015;94:e964.

Impact of CKD-related Anemia on Long-term Health Outcomes



HF, heart failure; HK, hyperkalemia; HRQOL, health-related quality of life.

Babitt JL, et al. *Kidney Int*. 2021;99:1280-1295; Garlo K, et al. Medicine (Baltimore). 2015;94:e964; Stauffer ME, Fan T. *PloS one*. 2014;9:e84943; Wittbrodt ET, et al. *Clin Kidney J*. 2021;15:244-252.

Symptoms and Impact of CKD-related Anemia*

Symptoms of Anemia in CKD

- Very tired
- Low energy
- Weak
- Chest pain
- Shortness of breath during activity
- Shortness of breath during rest
- Bruised skin
- Difficulty remembering things

Impact of Anemia in CKD

- Difficulty standing for long periods
- Difficulty sleeping
- Lack of motivation
- Need for frequent breaks
- Need for frequent naps
- Feeling distressed
- Feeling burdensome

*Conceptual framework used in the CKD-AQ questionnaire, a PRO measure for evaluation of CKD-related anemia.
CKD-AQ, Chronic Kidney Disease and Anemia Questionnaire; PRO, patient reported outcome.
Mathias SD, et al. *J Patient Rep Outcomes*. 2020;4:64.

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Associations Between Risks for CKD and CKD-Related Anemia and Race/Ethnicity

CKD-related risk among Black, Hispanic, and American Indian individuals vs members of other race/ethnicity groups:

Kidney Disease

- Greater risk (likely due to high rates of diabetes and HTN)

Kidney Failure

- Greater risk
  - Black vs White: 4X greater
  - Hispanic vs non-Hispanic: 1.3X greater
  - American Indian vs White: 1.2X greater

ESKD Treatment

- Black patients less likely to receive transplant and home dialysis
- Treatment disparities most pronounced in 22–44YOs

CKD-related Anemia

- 2.4–3.7X more likely in non-Hispanic Black individuals vs members of other race groups

ESKD, end-stage kidney disease; HTN, hypertension; YO, year old.

St. Peter WL, et al. *BMC Nephrology*. 2018;19:67; Unruh ML, et al. *BMC Nephrology.* 2020;21:291; USRDS 2021. Available at: https://adr.usrds.org/2021; USRDS 2016. Available at: https://www.niddk.nih.gov/health-information/kidney-disease/race-ethnicity; Wilk AS, et al. *Am J Kidney Dis*. 2022;80:9-19.

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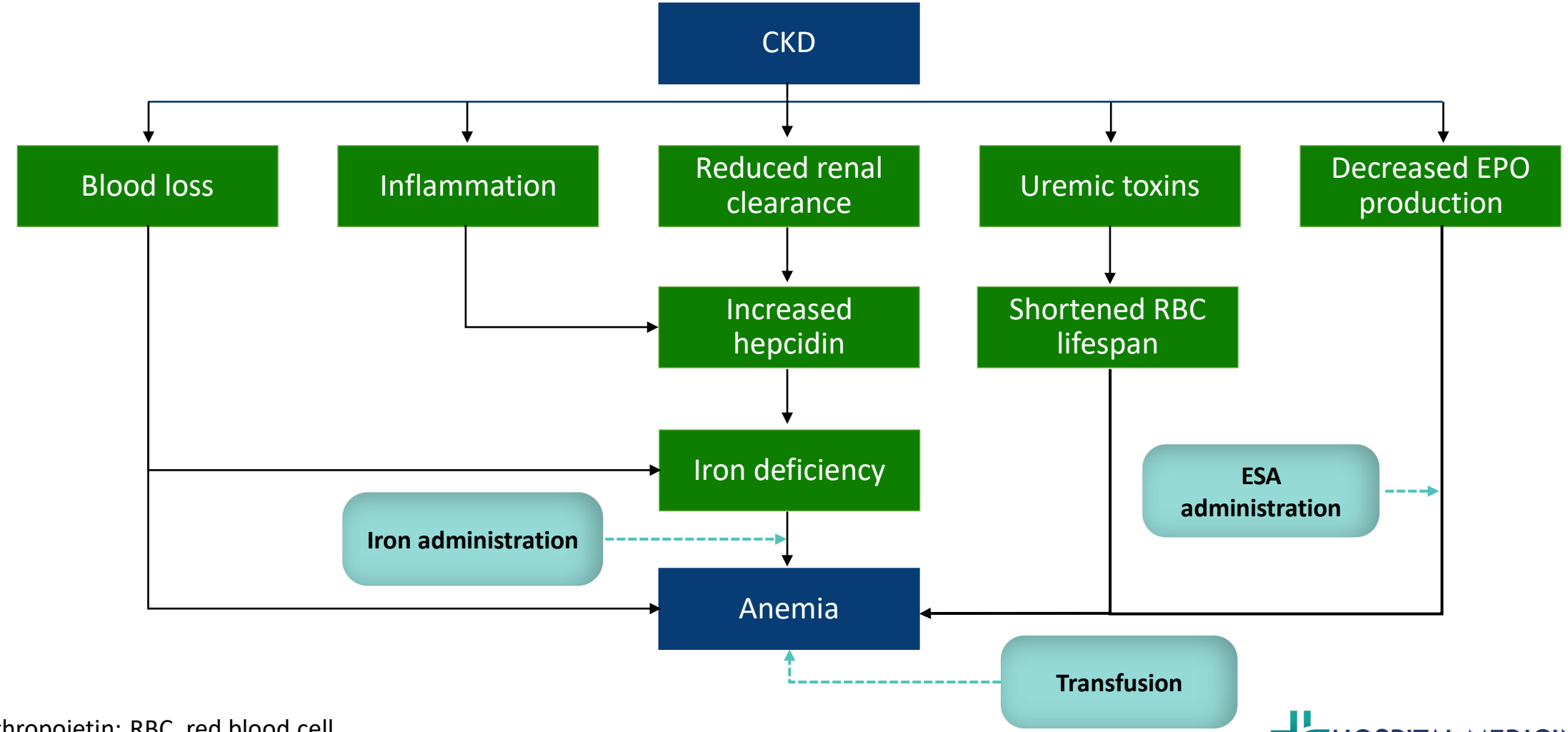
Management of Anemia in Patients With CKD

Pathophysiology of CKD-Related Anemia and Current Treatment Options



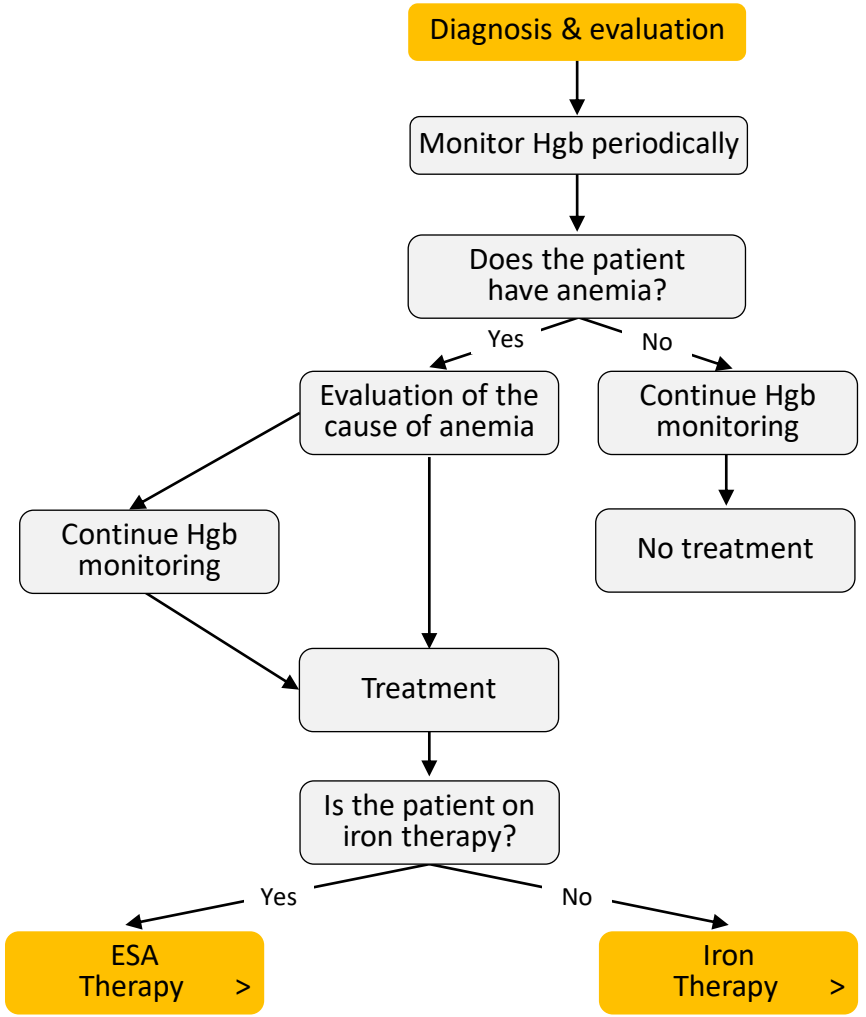
EPO, erythropoietin; RBC, red blood cell.

Adapted from: Borawski B, et al. *J Clin Med*. 2021;10(18):4149.

KDIGO Guidelines for Diagnosis and Evaluation of Anemia in Patients With CKD

Recommended investigations:
- Complete blood count (CBC)
- Absolute reticulocyte count
- Ferritin
- Transferrin saturation (TSAT)
- Vitamin B12 (some cases)
- Folic acid (some cases)

Address correctable causes of anemia (eg, iron deficiency and inflammatory states) prior to initiation of ESA therapy



Diagnosis of anemia in CKD

>15YO:
- Hgb <13 g/dL (Males)
- Hgb <12 g/dL (Females)

<15YO:
- Hgb <11 g/dL (0.5-5YO)
- Hgb <11.5 g/dL (5-12YO)
- Hgb <12 g/dL (12-15YO)

Administer intravenous iron if oral iron is not tolerated or is ineffective

KDIGO. Anemia in CKD: visual guidelines. Available at: http://www.treatalgo.com/kdigo-anemia/index.html

Standard of Care Therapy Challenges and Considerations

	ESAs	Iron Supplementation
Efficacy	• Stimulate RBC production & raise Hgb • ~10% rate of hyporesponsiveness/resistance	• Raise Hgb
Dosing & administration challenges	• Parenteral administration • Lowest dose needed to reduce RBC transfusion requirements vs a specific target Hgb	• Oral administration: Poor absorption, adherence challenges, GI AEs • IV administration: Better tolerability with larger doses
Safety concerns	• CV risk at higher doses	• Potential for iron overload and risk for organ dysfunction, infection, worse CKD-associated inflammation • Risk for anaphylactic reactions (rare)
Other	• Cold storage, expense, neutralizing anti-EPO antibodies	• Need for IV access & transfusion clinic

AE, adverse event; CV, cardiovascular; GI, gastrointestinal; IV, intravenous.

Hanna RM, et al. *Advances Ther*. 2021;38:52-75.

Safety Concerns Associated With ESA Administration

Study	Normal Hematocrit Study (NHS) (N=1265)	CHOIR (N=1432)	TREAT (N=4038)
Time period	1993 to 1996	2003 to 2006	2004 to 2009
Patient population	• DD-CKD • CHF or CAD • Hematocrit 30±3% on epoetin alfa	• NDD-CKD • Hgb <11 g/dL • Not previously on epoetin	• NDD-CKD • T2DM • Hgb ≤11 g/dL
Hgb target: higher vs lower (g/dL)	14.0 vs 10.0	13.5 vs 11.3	13.0 vs ≥9.0
Median (Q1, Q3) achieved Hgb (g/dL)	12.6 (11.6, 13.3) vs 10.3 (10.0, 10.7)	13.0 (12.2, 13.4) vs 11.4 (11.1, 11.6)	12.5 (12.0, 12.8) vs 10.6 (9.9, 11.3)
Primary endpoint	All-cause mortality or nonfatal MI	All-cause mortality, MI, hospitalization for CHF, stroke	All-cause mortality, MI, myocardial ischemia, HF, stroke
HR or RR (95% CI)	1.28 (1.06 – 1.56)	1.34 (1.03 – 1.74)	1.05 (0.94 – 1.17)
Adverse outcome for higher target group	All-cause mortality	All-cause mortality	Stroke
HR or RR (95% CI)	1.27 (1.04 – 1.54)	1.48 (0.97 – 2.27)	1.92 (1.38 – 2.68)

CAD, coronary artery disease; CHF, congestive heart failure; MI, myocardial infarction; RR, relative risk; T2DM, type 2 diabetes mellitus.

FDA. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-modified-dosing-recommendations-improve-safe-use-erythropoiesis#table

Shortcomings in Current Treatment Practices

Wong et al. 2020

- Prospective cross-sectional analysis of data from nephrology clinics in 4 countries, including the US
- 6,766 patients with Stage 3–5 CKD

Study findings:

- Hgb measured less often than recommended by guidelines
- Anemia rarely treated to guideline-recommended target (10–12 g/dL)

Wittbrodt et al. 2021

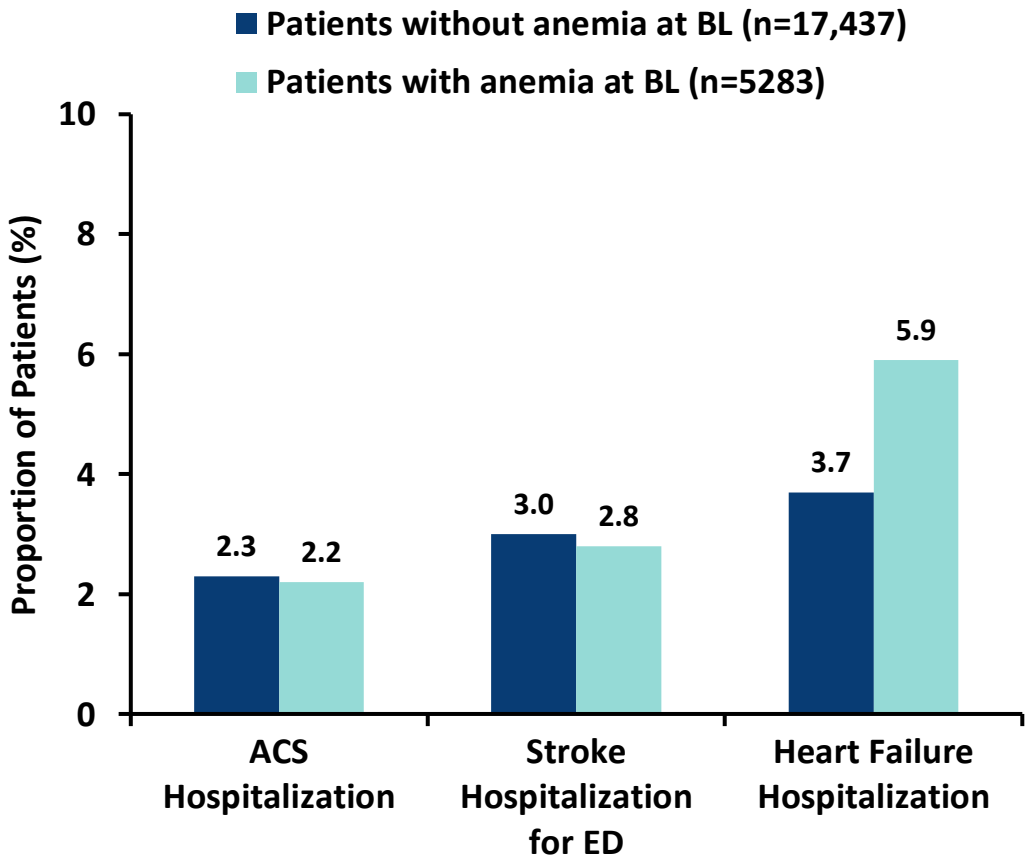
- US retrospective claims analysis
- 22,720 patients with CKD stage 3a-5 and related anemia

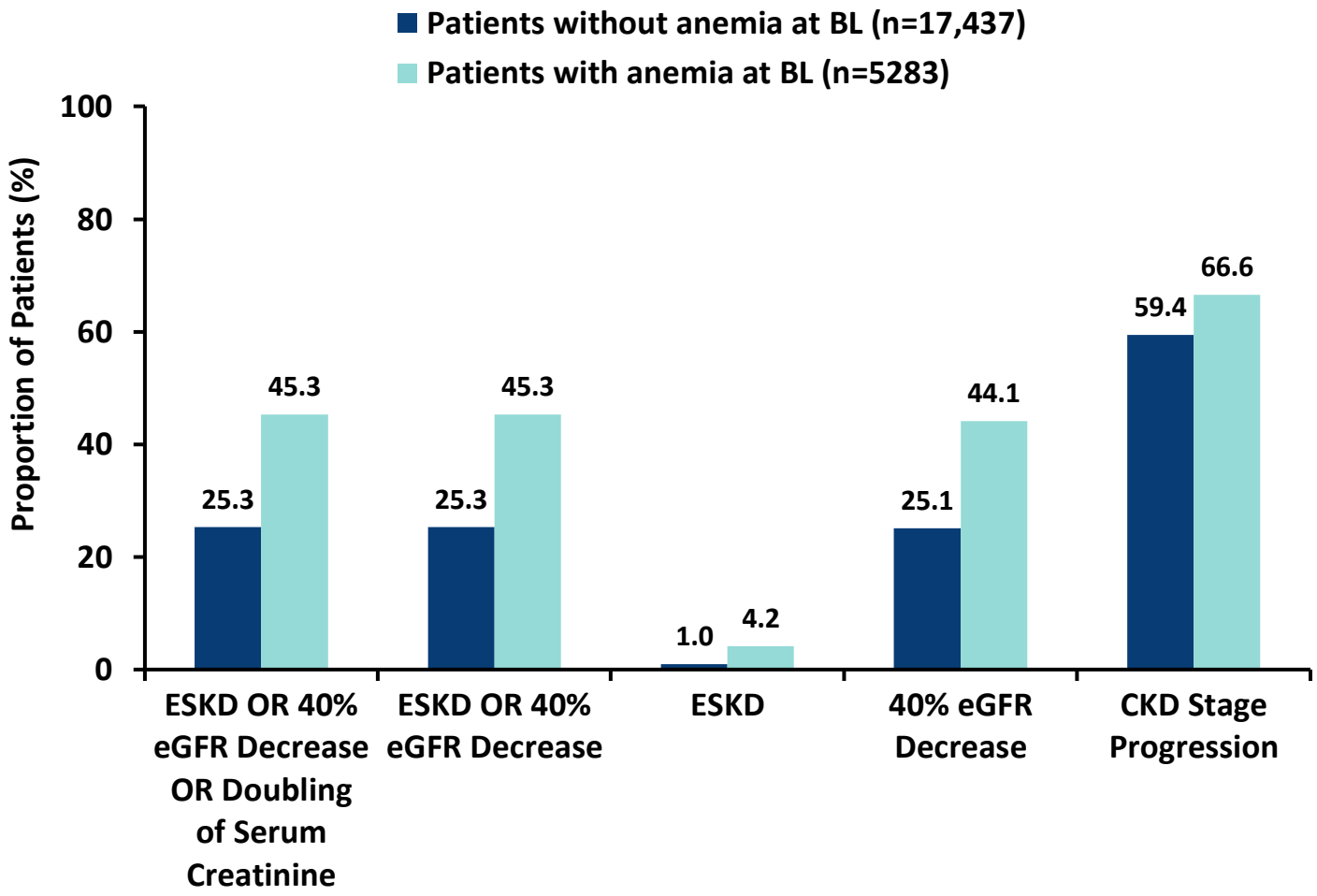
Study findings:

- **<0.1%** of patients with CKD-related anemia received IV iron supplementation
- Only **1.9%** treated with ESAs

Wong MMY, et al. *Clin Kidney J*. 2020;13:613-624; Wittbrodt ET, et al. *Clin Kidney J*. 2021;15:244-252.

Impact of Inadequately Treated Anemia on Health Outcomes in Patients With CKD





ACS, acute coronary syndrome; BL, baseline; ED, emergency department.

Wittbrodt ET, et al. *Clin Kidney J*. 2022;15:244-252.

Current Barriers to Adequate Treatment of CKD-Related Anemia

- The vast majority of patients with CKD-related anemia are not treated with IV iron and ESAs despite high prevalence, incidence, and persistence
- Previously identified barriers include the following:

CV safety concerns over ESA use (especially in the presence of CV morbidities)

Difficulties in administering parenteral therapies

Potential lack of access to therapies

Necessity of follow-up visits

Under-reporting

Wittbrodt ET, et al. *Clin Kidney J*. 2021;15:244-252.

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Treatment of Anemia in CKD
Emerging Therapies: HIF-PHIs

Regulation of Oxygen Homeostasis and the Effects of HIF-PHIs

Hypoxia-inducible factors (**HIFs**):

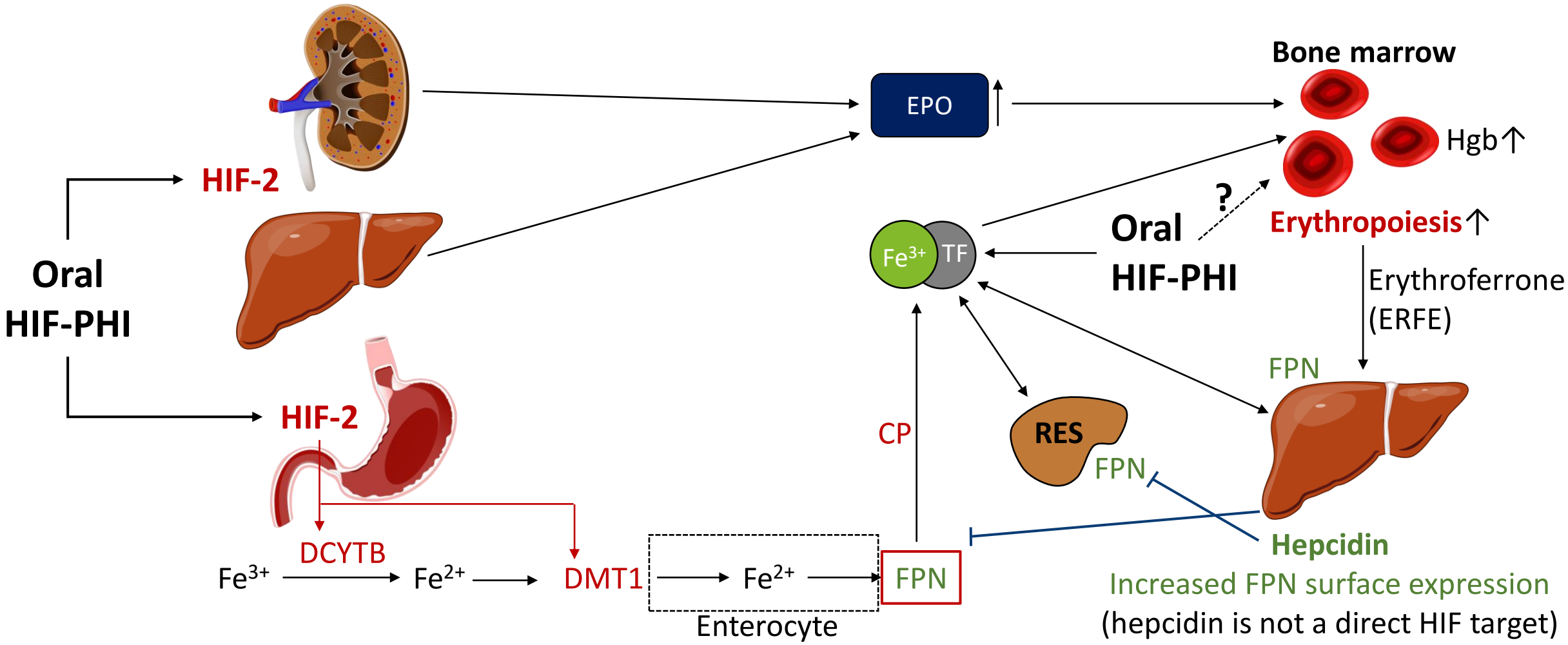
- Function as master regulators of oxygen homeostasis via transcription of genes involved in regulating tissue oxygen balance
- Increase EPO production in the kidney and liver, enhance iron uptake and utilization, and adjust the bone marrow microenvironment to facilitate erythroid progenitor maturation and proliferation

HIF prolyl hydroxylase (**HIF-PH**) is an enzyme that catalyzes hydroxylation of HIF leading to its proteasomal degradation

HIF-PH inhibitors (**HIF-PHIs**) stabilize HIFs, allowing them to act on downstream target genes to restore oxygen homeostasis

Souza E, et al. *Exp Op Invest Drugs*. 2020;29:831-844.

Mechanism of Action of HIF-PHIs for Anemia in CKD



CP, ceruloplasmin; DCYTB, duodenal cytochrome B; FPN, ferroportin; RES, reticulocyte endothelial system.
Haase VH. *Kidney Int Suppl*. 2021;11:8-25.

Current Status of Emerging HIF-PHIs

	FDA Status	Phase 3 Clinical Trials	
Daprodustat	Decision pending (NDA submitted Apr 2022; decision expected Feb 2023)	ASCEND-D ASCEND-ND ASCEND-ID	ASCEND-TD ASCEND-NHQ
Vadadustat	Rejected Mar 2022	INNO$_2$VATE INNO$_2$VATE-CONVERSION	PRO$_2$TECT PRO$_2$TECT-CORRECTION
Roxadustat	Rejected Aug 2021	OLYMPUS ANDES ALPS	HIMALAYAS SIERRAS ROCKIES

Akebia. Available at: https://ir.akebia.com/news-releases/news-release-details/ akebia-therapeutics-receives-complete-response-letter-fda; Fibrogen. Available at: https://investor.fibrogen.com/news-releases/news-release-details/fibrogen-receives-complete-response-letter-fda-roxadustat-anemia; GSK. Available at: https://www.fibrogen.com/ roxadustat-trials; https://www.gsk.com/en-gb/media/press-releases/gsk-announces-update-on-us-fda-regulatory-review-of-daprodustat-in-anaemia-of-chronic-kidney-disease/

Efficacy and Safety of HIF-PHIs in RCTs: Overview

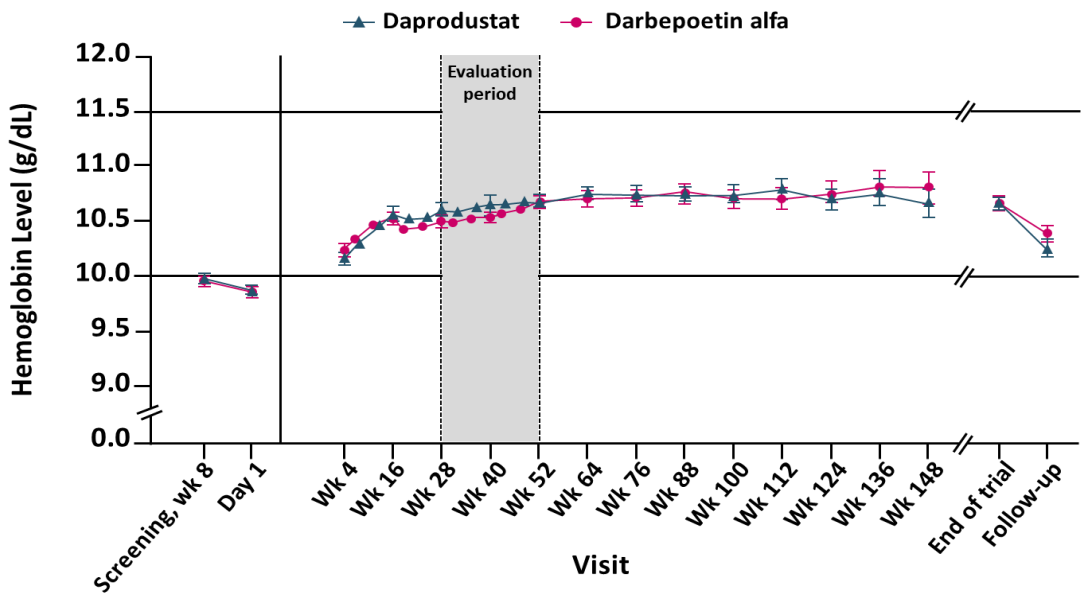
Agent	In DD-CKD & NDD-CKD				CV Safety Noninferior to ESAs	
	Increase Hgb	Noninferior to ESAs	Reduce Need for RBC Transfusion	AEs Comparable to PBO/ESA	DD-CKD	NDD-CKD
Daprodustat	✓	✓	✓	✓	✓	✓
Vadadustat	✓	✓	✓	✓	✓	–
Roxadustat	✓	✓	✓	✓	–	–

PBO, placebo.

Chertow GM, et al. *N Engl J Med*. 2021;384:1589-1600; Eckardt KU, et al. *N Engl J Med*. 2021;384:1601-1612; Fishbane S, et al. *J Am Soc Nephrol*. 2021;32:737-755; Fishbane S, et al. *J Am Soc Nephrol*. 2022;33:850-866; Singh AK, et al. *N Engl J Med*. 2021;385:2313-2324; Singh AK, et al. *N Engl J Med*. 2021;385:2325-2335.

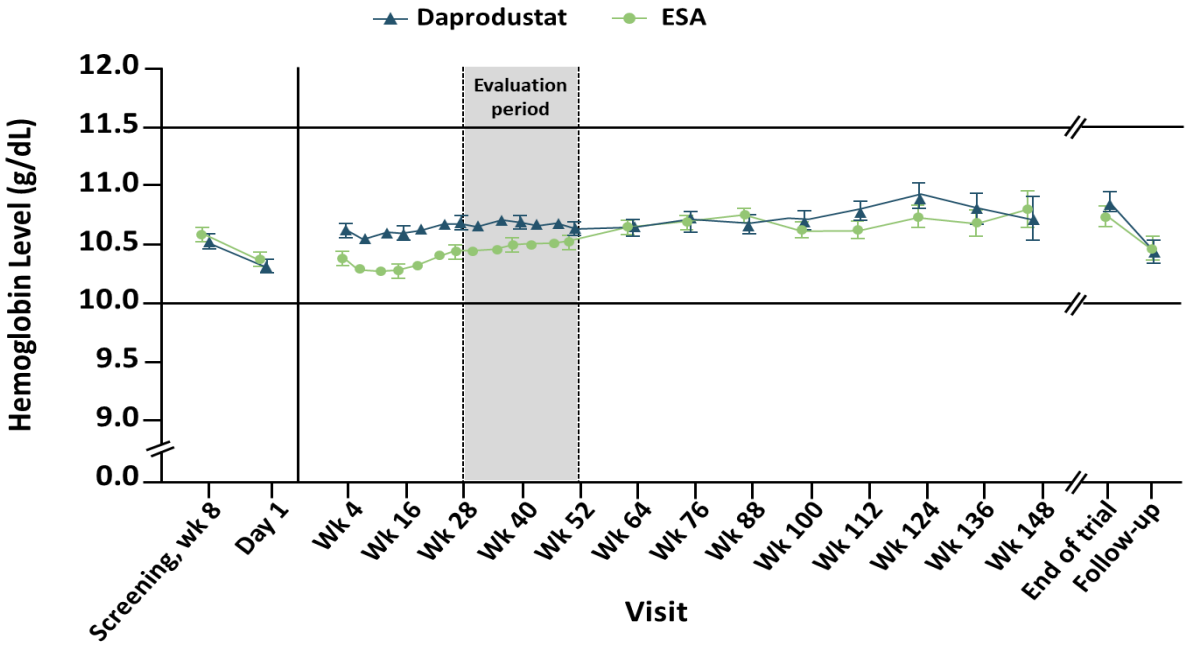
Daprodustat for the Treatment of CKD-Related Anemia

ASCEND-ND



Hgb change from baseline to Wks 28–52 was 0.74±0.02 g/dL with daprodustat vs 0.66±0.02 g/dL with darbepoetin alfa (difference, 0.08 g/dL; 95% CI, 0.03 to 0.13), meeting the prespecified noninferiority margin

ASCEND-D

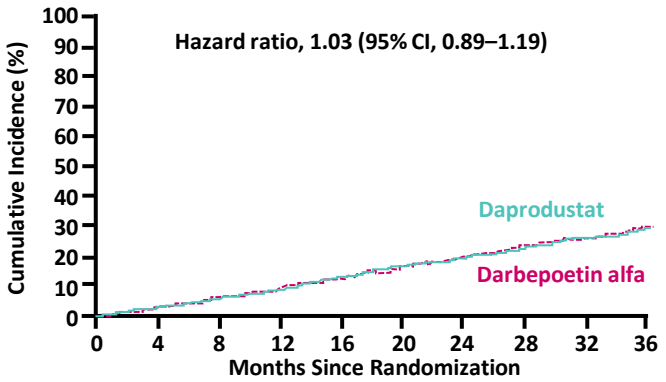


Hgb change from baseline to Wks 28–52 was 0.28±0.02 g/dL with daprodustat and 0.10±0.02 g/dL with ESA (difference, 0.18 g/dL; 95% CI, 0.12 to 0.24), meeting the prespecified noninferiority margin

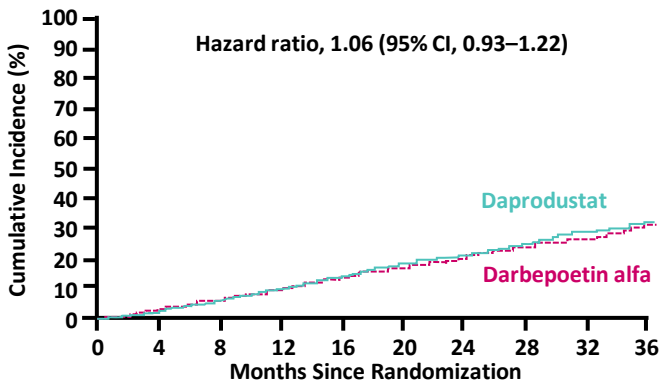
Singh AK, et al. *N Engl J Med*. 2021;385:2313-2324; Singh AK, et al. *N Engl J Med*. 2021;385:2325-2335.

ASCEND-ND: MACE and CKD Progression

MACE

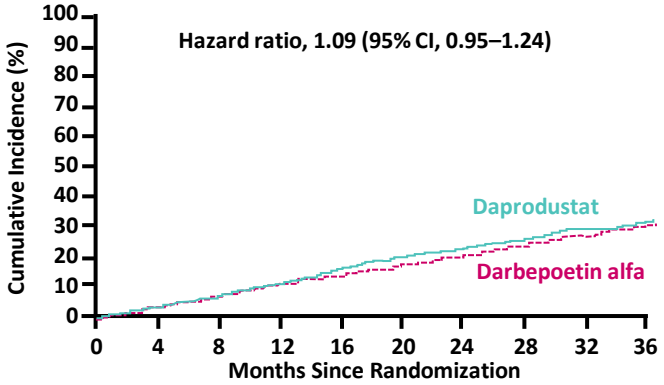


MACE or Thromboembolic Events

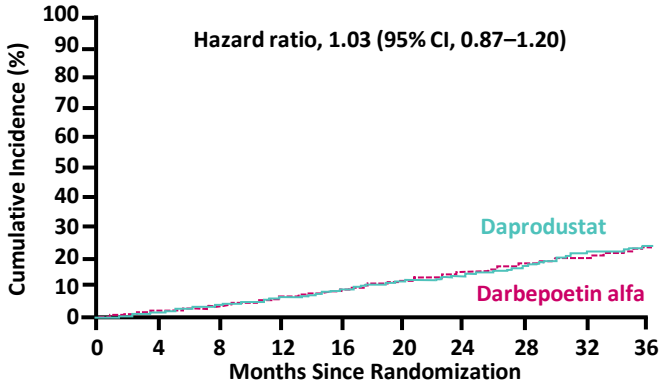


During a median follow-up of 1.9 years, a first MACE occurred in 19.5% of daprodustat-treated patients vs 19.2% in darbepoetin alfa-treated patients (HR, 1.03; 95% CI, 0.89 to 1.19), meeting the prespecified noninferiority margin.

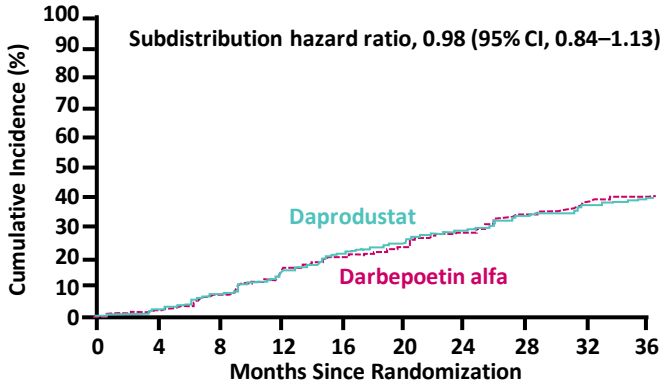
MACE or Hospitalization for HF



Death from Any Cause



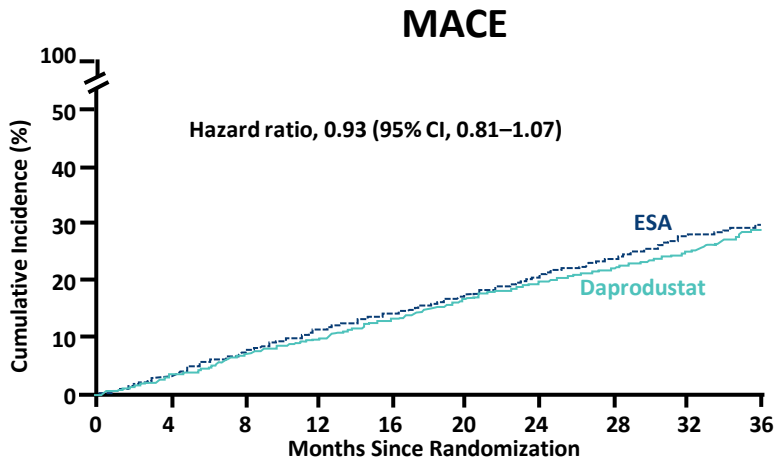
CKD Progression

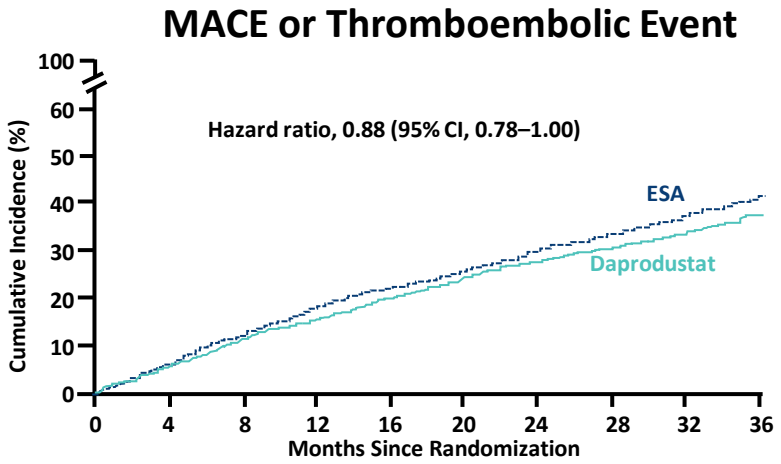


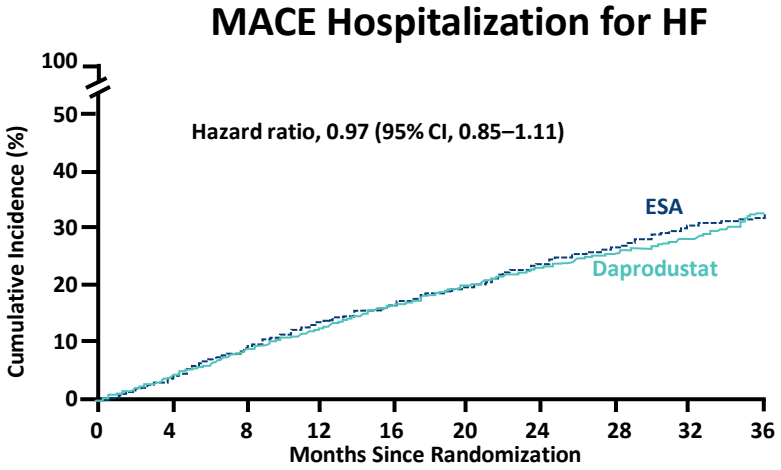
MACE, major adverse cardiovascular event.

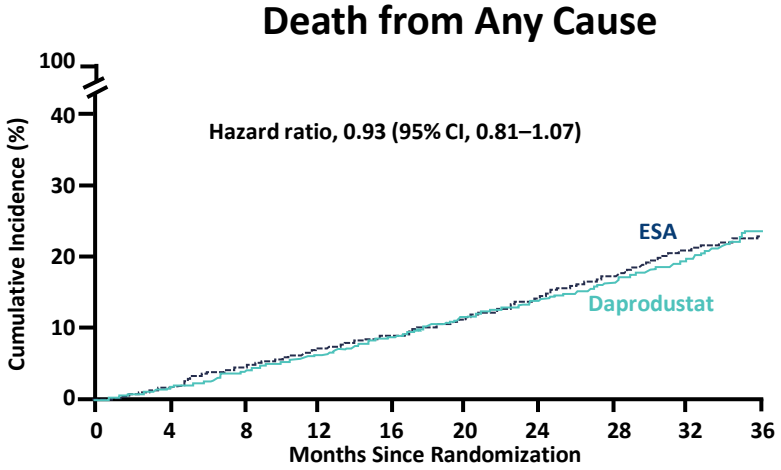
Singh AK, et al. *N Engl J Med.* 2021;385:2313-2324.

ASCEND-D: MACE







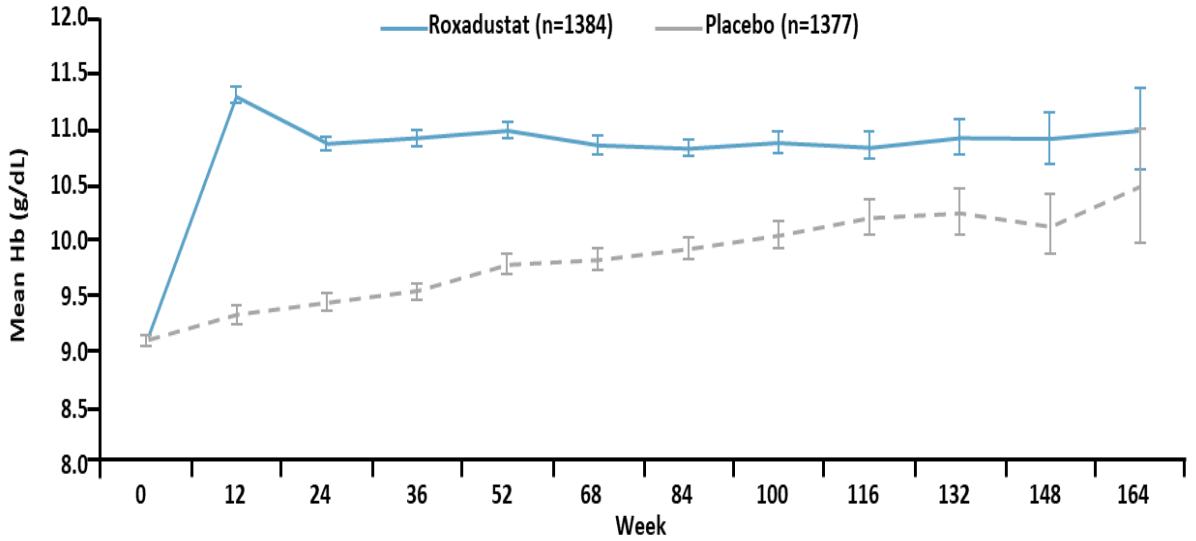


During a median follow-up of 2.5 years, a MACE occurred in 25.2% of daprodustat-treated patients vs 26.7% in ESA-treated patients (HR, 0.93; 95% CI, 0.81 to 1.07), meeting the prespecified noninferiority margin.

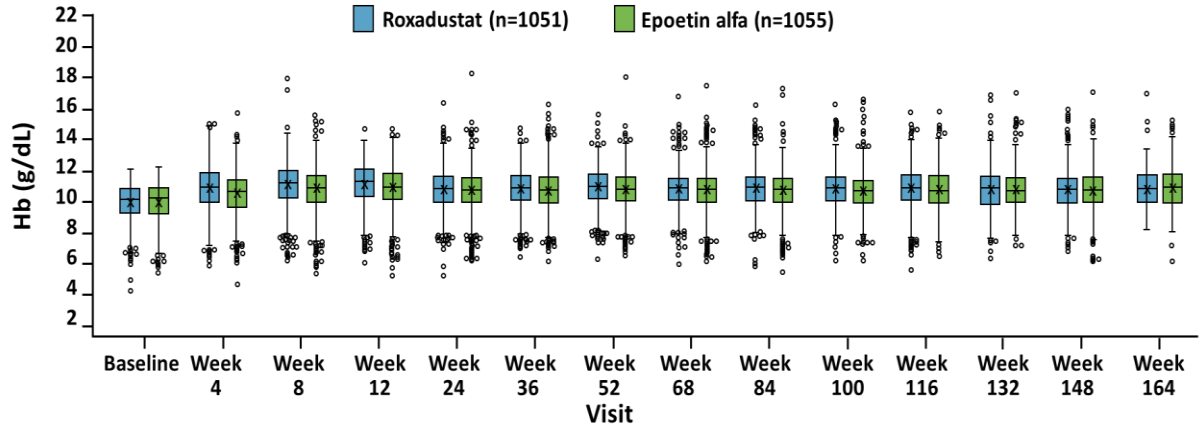
Singh AK, et al. *N Engl J Med*. 2021;385:2325-2335.

Roxadustat for the Treatment of CKD-Related Anemia

NDD-CKD



DD-CKD (ROCKIES)



Roxadustat vs PBO in NDD-CKD:

- Increased Hgb from baseline (+11.35 g/dl WK 28 to WK 52)†
- Reduced risk for transfusion by 63%‡
- Similar AE profile

Roxadustat vs epoetin alfa in DD-CKD:

- Noninferior correction & maintenance of Hgb
- Noninferior CV safety
- Similar AE profile

*P <.001 for both; †P <.001; ‡HR, 0.37; 95% CI, 0.30 to 0.44.

Fishbane S, et al. *J Am Soc Nephrol*. 2021;32:737-755; Fishbane S, et al. *J Am Soc Nephrol*. 2022;33:850-866.

Roxadustat Safety

NDD-CKD

AE Summary (ITT Analysis Set)

AE Category	Roxadustat (n=1348) %	PBO (n=1377) %
Any AE:	89.8	88.3
With an outcome of death	18.9	15.5
In the cardiac disorders SOC	22.8	21.3
Any SAE (including events with an outcome of death)	57.4	54.4
In the cardiac disorders SOC	12.6	11.4
All-cause mortality	20.5	17.8

DD-CKD (ROCKIES)

AE Summary

AE Category	Roxadustat (n=1048) %	Epoetin Alfa (n=1053) %
Any AE:	85.0	84.5
Leading to discontinuation	5.4	2.5
Leading to interruption	9.3	4.2
Leading to an outcome of death	15.9	17.8
In the cardiac disorders SOC	23.4	26.3
Any SAE (including event with an outcome of death)	57.6	57.5
In the cardiac disorders SOC	14.6	16.0

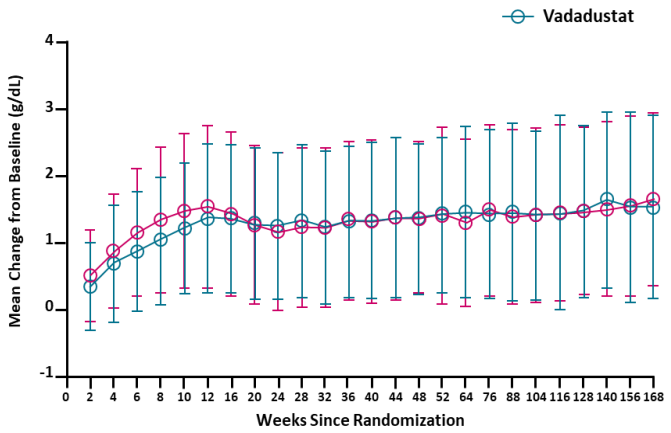
ITT, intent to treat; SAE, severe adverse event, SOC, system organ class.

Fishbane S, et al. *J Am Soc Nephrol*. 2021;32:737-755; Fishbane S, et al. *J Am Soc Nephrol*. 2022;33:850-866.

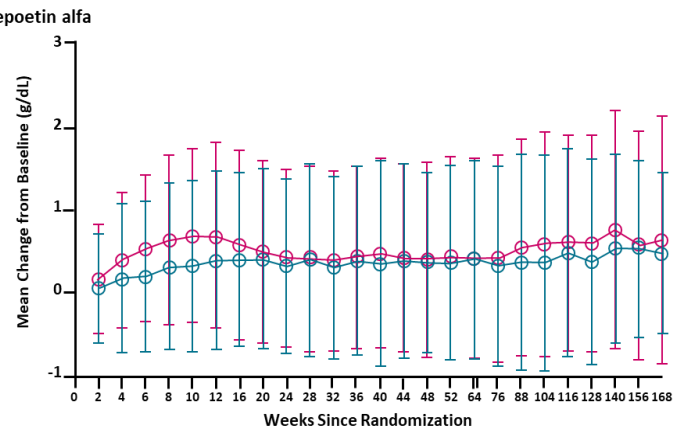
Vadadustat for the Treatment of CKD-Related Anemia

PRO$_2$TECT

Hemoglobin Concentration in ESA-Untreated Patients



Hemoglobin Concentration in ESA-Treated Patients

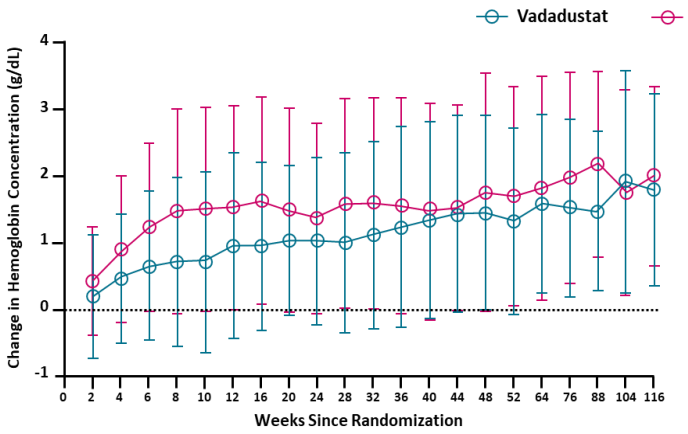


Vadadustat vs DA in NDD-CKD

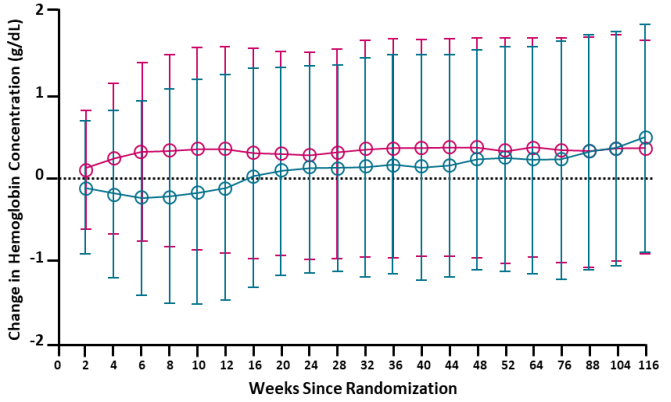
- Noninferior for hematologic efficacy
- Did *not* meet noninferiority for MACE

INNO$_2$VATE

Incident DD-CKD Trial



Prevalent DD-CKD Trial



Vadadustat vs DA in DD-CKD

- Noninferior for hematologic efficacy
- MACE: HR=0.96 (95% CI, 0.83 – 1.11)
- Expanded MACE: HR=0.96 (95% CI, 0.84 – 1.10)

Chertow GM, et al. *N Engl J Med*. 2021;384:1589-1600; Eckardt KU, et al. *N Engl J Med*. 2021;384:1601-1612.

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Shared Decision-making

- Shared decision-making (SDM) enables patient to actively participate in their own care
- Specific strategies can facilitate more effective SDM:

Promote effective communication

- Encourage patients to engage in open clinician-patient dialogue
- Provide information specific to anemia to facilitate the dialogue

Describe treatment options

- Explain rationale for treatment selection
- Outline advantages and disadvantages
- Explain potential effects on lifestyle and how they might align/conflict with personal values
- Assess patient preferences

Make decisions collaboratively

- Ensure both you and the patient are comfortable with the choice of treatment

American Kidney Fund. Talk to your patient guide. Available at: https://www.kidneyfund.org/assets/pdf/anemia/anemia-ask-your-patient.pdf

Discharge Planning

Patient & caregiver education

- Nutritional guidance (regarding salt, potassium, protein, phosphorus, and fluid intake)
- Managing fatigue
- Obtaining adequate sleep
- Monitoring weight
- Managing HTN, diabetes

Medications

- Medication reconciliation
- Confirm access to prescribed medications

Medical care

- Schedule early nephrology care follow-up
- Review when to seek prompt medical care

reference

Case Study Assessments

Case 1: Patient Description

A 68-year-old Black woman with history of Stage 4 CKD, HTN, and overweight presents to the ED for weakness and shortness of breath over the past 5 days. She reports that she has felt increasingly fatigued over the past six months and had increasing dyspnea on exertion. Her current medications include an ACEi and thiazide diuretic.

ACEi, angiotensin-converting enzyme inhibitor.

Case 1: Physical Exam

Physical Exam Findings	
BP	140/70
Pulse	82
Respiratory rate	20
Fever	No
Body weight	150 lbs
BMI	27 kg/m^2
Edema	No

BMI, body mass index; BP, blood pressure.

Case Patient 1: Laboratory Findings

Chemistry	Result	Reference Range
Hgb	9.5 gm/dL	14-17 gm/dL
Sodium	WNL	136-146 mmol/L
Potassium	5.4 mmol/L	3.5-5.3 mmol/L
Phosphorus	6.5 mg/dL	2.6-6.4 mg/dL
Chloride	WNL	98-108 mmol/L
Total CO_2	20 mmol/L	23-27 mmol/L
BUN	63 mg/dL	7-22 mg/dL
Creatinine	3.7 mg/dL	0.7-1.5 mg/dL
eGFR	Low	>60 mL/min/1.73m^2
Glucose	105 mg/dL	70-110 mg/dL
HbA1c	5.7%	<5.7%
Hematocrit	27%	40-54 %
Mean cell volume	WNL	85-95 FL
Transferrin saturation	24%	20-50%
Serum ferritin	120 ng/mL	12-263 ng/mL

Urinalysis
pH: 6 **Specific gravity**: 1010 **Protein**: 1+ **Glucose**: Neg **Acetone**: Neg **Occult blood**: Neg **Bile**: Neg **uACR**: 0.8g/g creatinine

BUN, blood urea nitrogen; uACR, urine albumin to creatinine ratio; WNL, within normal limits.

Case Discussion Question

How would you characterize this patient's level of risk for adverse outcomes?

A. High
B. Low
C. Moderate

Case Discussion Question

What type of treatment would you prescribe for this patient?

A. Iron supplementation
B. ESA therapy
C. HIF stabilizer therapy
D. Transfusion

Case 2: Patient Description

A 61-year-old Hispanic man with history of Stage 5 CKD, HTN, hyperlipidemia, and T2DM is brought to the ED by his family for fatigue, shortness of breath, and generalized weakness over the past 3 days. His current treatment regimen includes an ACEi, statin, DPP4i, epoetin alfa, iron sucrose, and maintenance hemodialysis.

DPP4I, dipeptidyl peptidase IV inhibitor.

Case 2: Physical Exam

Physical Exam Findings	
BP (predialysis)	145/90
Pulse	75
Respiratory rate	18
Fever	No
Body weight	170 lbs
BMI	29 kg/m^2
Edema	1+ lower extremity

Case Patient 2: Laboratory Findings

Chemistry	Result	Reference Range
Hgb	9.2 gm/dL	14-17 gm/dL
Sodium	WNL	136-146 mmol/L
Potassium	5.0	3.5-5.3 mmol/L
Phosphorus	5.4	2.6-6.4 mg/dL
Chloride	WNL	98-108 mmol/L
Total CO_2	24	23-27 mmol/L
BUN	74	7-22 mg/dL
Creatinine	9.65	0.7-1.5 mg/dL
Glucose	95 mg/dL	70-110 mg/dL
HbA1c	7.0%	<5.7%
Hematocrit	WNL	40-54 %
Mean cell volume	60	85-95 FL
Transferrin saturation	25%	20-50%
Serum ferritin	840 ng/mL	12-263 ng/mL

Case Discussion Question

What is the most likely cause of the patient's persistent anemia despite ESA therapy?

A. Hyporesponsiveness to EPO
B. Inflammatory process
C. Iron deficiency

Case Discussion Question

What changes would you make to the patient's current treatment regimen?

A. Increase iron supplementation
B. Increase ESA dose
C. Switch to an HIF stabilizer therapy
D. Transfusion

Key Points

- Anemia is a common complication of CKD that exerts a significant negative impact on patient well-being, work productivity, and HRQOL
- Patients with CKD-related anemia are at greater risk for poor health outcomes such as volume overload, and increased hospitalization and mortality
- CKD-related risk is increased among Black, Hispanic, and American Indian individuals, and Black patients are more likely to have CKD-related anemia
- Better understanding of the pathophysiology of CKD-related anemia has led to the development of HIF-PHIs, which exert their therapeutic effects via stimulation of endogenous EPO production
- In clinical trials, HIF-PHIs have consistently been shown to be noninferior to conventional ESAs for Hgb efficacy in both DD-CKD and NDD-CKD
- In terms of safety, disparate outcomes (including risk for MACE) have been reported for roxadustat, vadadustat, and daprodustat; studies to better characterize the safety of each are currently ongoing

Clinical Pearls

- Maintain a high index of suspicion and apply recommended diagnostic criteria to identify anemia in all patients with CKD

Adults & children >15YO	**<13 g/dL in males** **<12 g/dl in females**
Children <15YO	**<11 g/dl (0.5-5YO)** **<11.5 g/dl (5-12YO)** **<12 g/dl (12-15YO)**

- Evaluate anemia using appropriate assessments (eg, CBC, absolute, reticulocyte count, ferritin, TSAT) and treat promptly if needed
- Address all correctable causes of anemia (including iron deficiency and inflammatory states) prior to initiation of ESA therapy
- Administer intravenous iron if oral iron is not tolerated or is ineffective
- Individualize selection of treatment for anemia taking into account patient characteristics including cardiovascular risk

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Thank you!

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