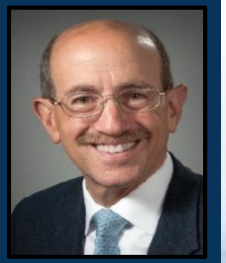
HIF-PH Inhibitors for Anemia in Chronic Kidney Disease

What Are Their Implications in Health-System Pharmacy?

Steven Fishbane, MD
Chief, Division of Nephrology
Northwell Health
Great Neck, New York



Wendy L. St. Peter, Pharm.D, FCCP, FNKF, FASN
Professor, College of Pharmacy
University of Minnesota
Minneapolis, Minnesota

Welcome and Introduction

Steven Fishbane, MD
Chief, Division of Nephrology
Northwell Health
Great Neck, New York

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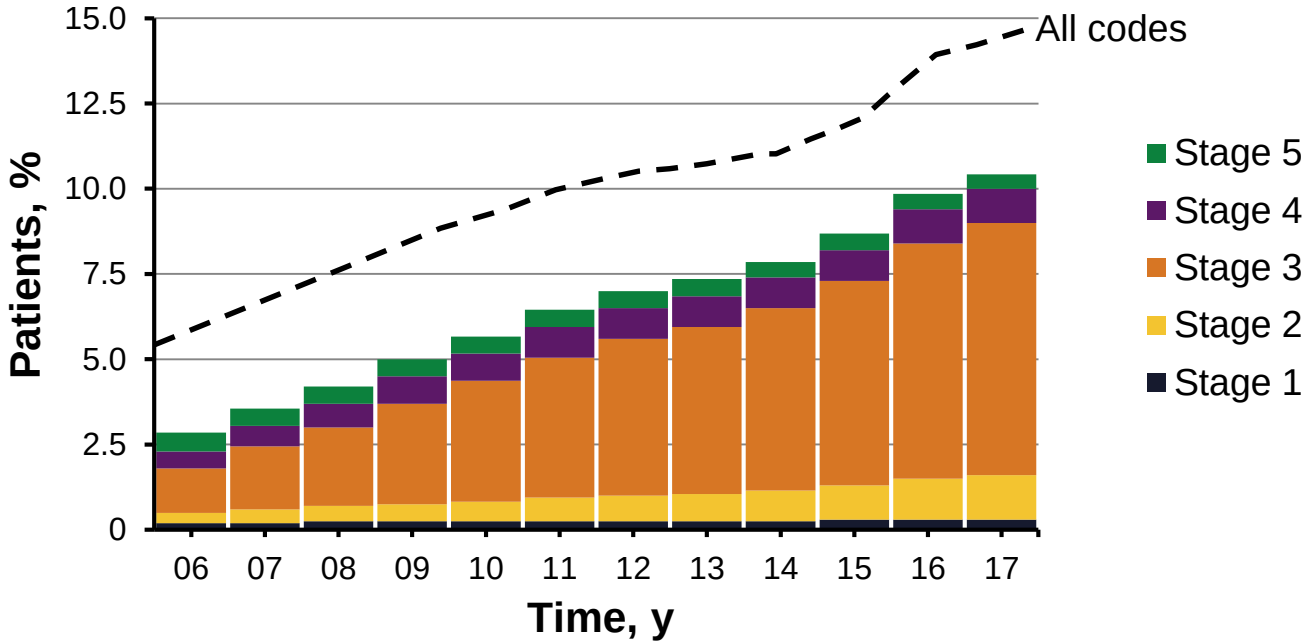
Trends in Diagnosed Chronic Kidney Disease (CKD): US Medicare, 2006-2017[1,a]



US, United States.

[a] Adults aged ≥65 years.

1. US Renal Data System. *Am J Kidney Dis*. 2019:S0272-6386(19)31008-X.

CKD Is Common Among US Adults: Fast Stats[1]

~15% of US adults—37 million people—are estimated to have CKD

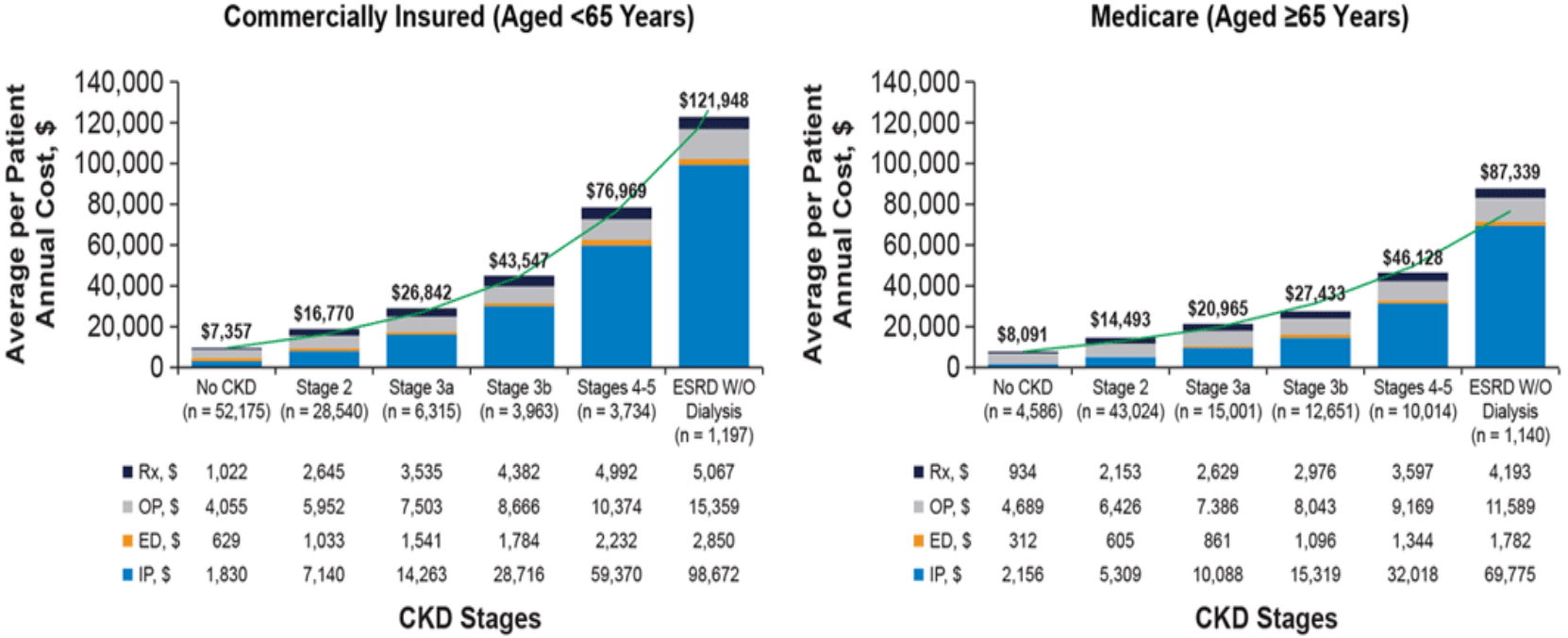
Most (9 in 10) adults with CKD do not know they have it

1 in 2 people with very low kidney function who are not on dialysis do not know they have CKD

CKD, chronic kidney disease; US, United States.

1. https://www.cdc.gov/kidneydisease/publications-resources/2019-national-facts.html.

Healthcare Costs Rise Exponentially by CKD Stage, Even When Dialysis Costs Are Excluded[1,a]

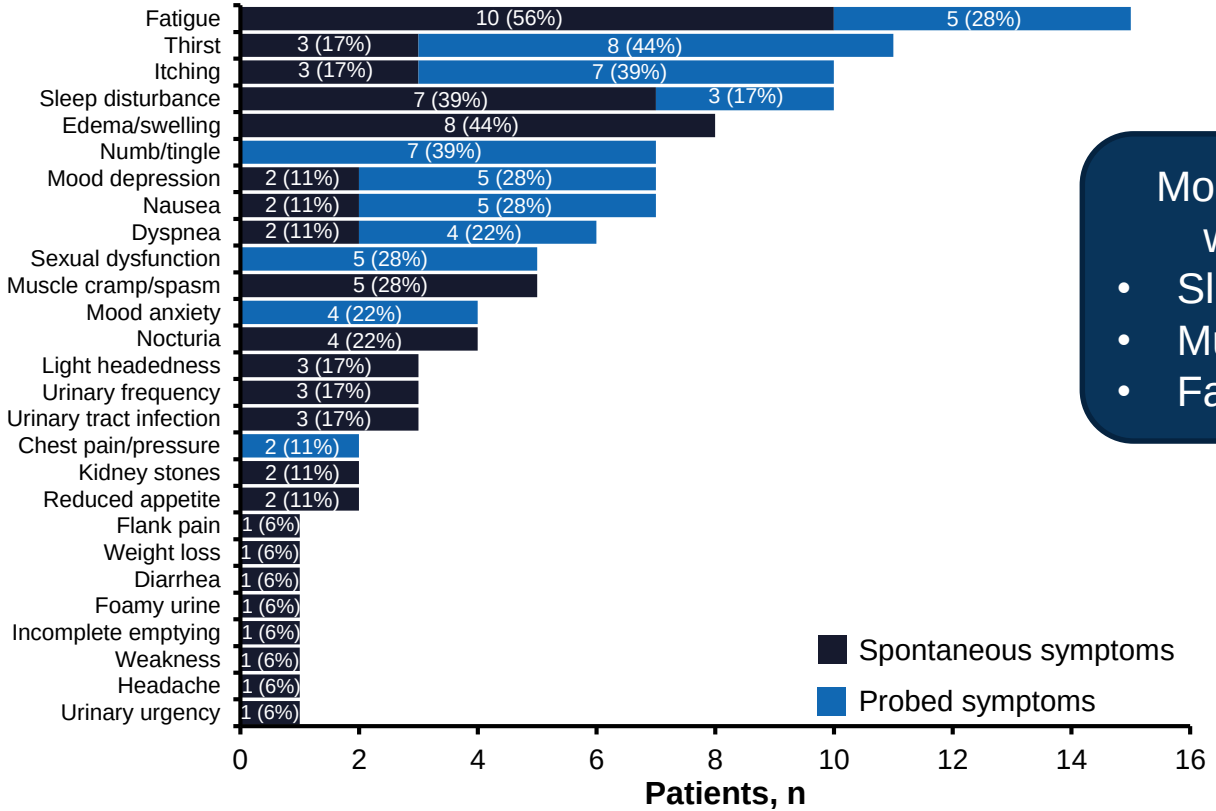


CKD, chronic kidney disease; ED, emergency department; ESRD, end-stage renal disease; IP, inpatient; OP, outpatient.

[a] Dialysis costs were excluded from the Medicare data because of analytical limitations of the commercially insured database. Adding dialysis costs would increase annual costs an estimated $120,000 per commercially insured patient and $29,000 per Medicare patient.

1. Golestaneh L et al. *Am J Manag Care*. 2017;23(10 Suppl):S163-S172.

CKD Reduces Quality of Life (QOL): Survey of Patient-Reported Symptoms[1,2]



More than half of patients with HD-CKD report:

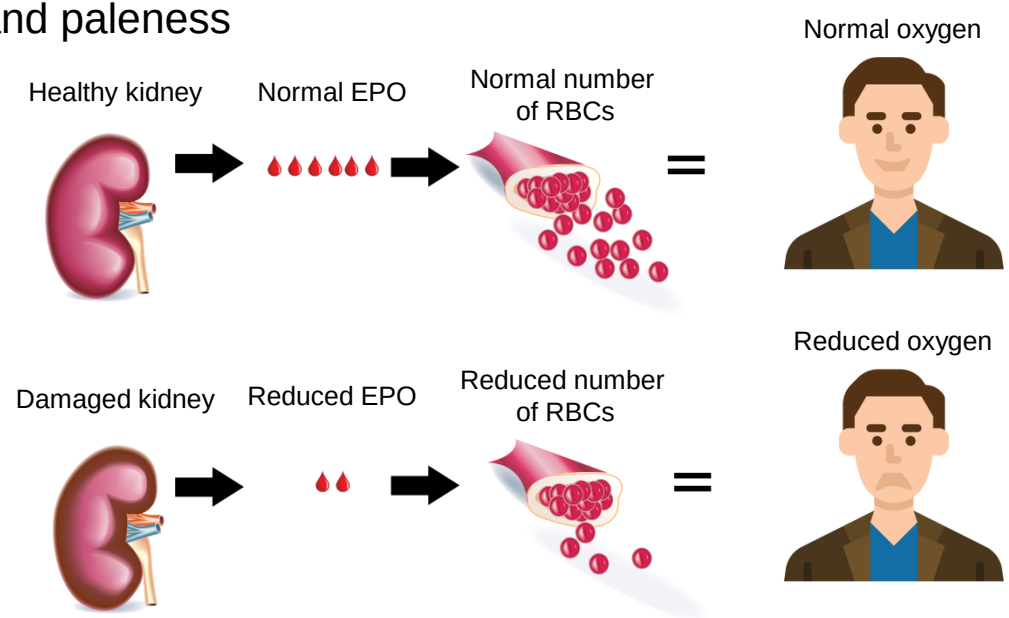
- Sleep disturbance
- Muscle cramps
- Fatigue

CKD, chronic kidney disease; HD-CKD, hemodialysis-dependent chronic kidney disease; QOL, quality of life.

1. James G et al. *J Med Internet Res*. 2020;22:e18548. 2. Flythe JE et al. *Clin J Am Soc Nephrol*. 2019;14:150-160.

Anemia in CKD[1]

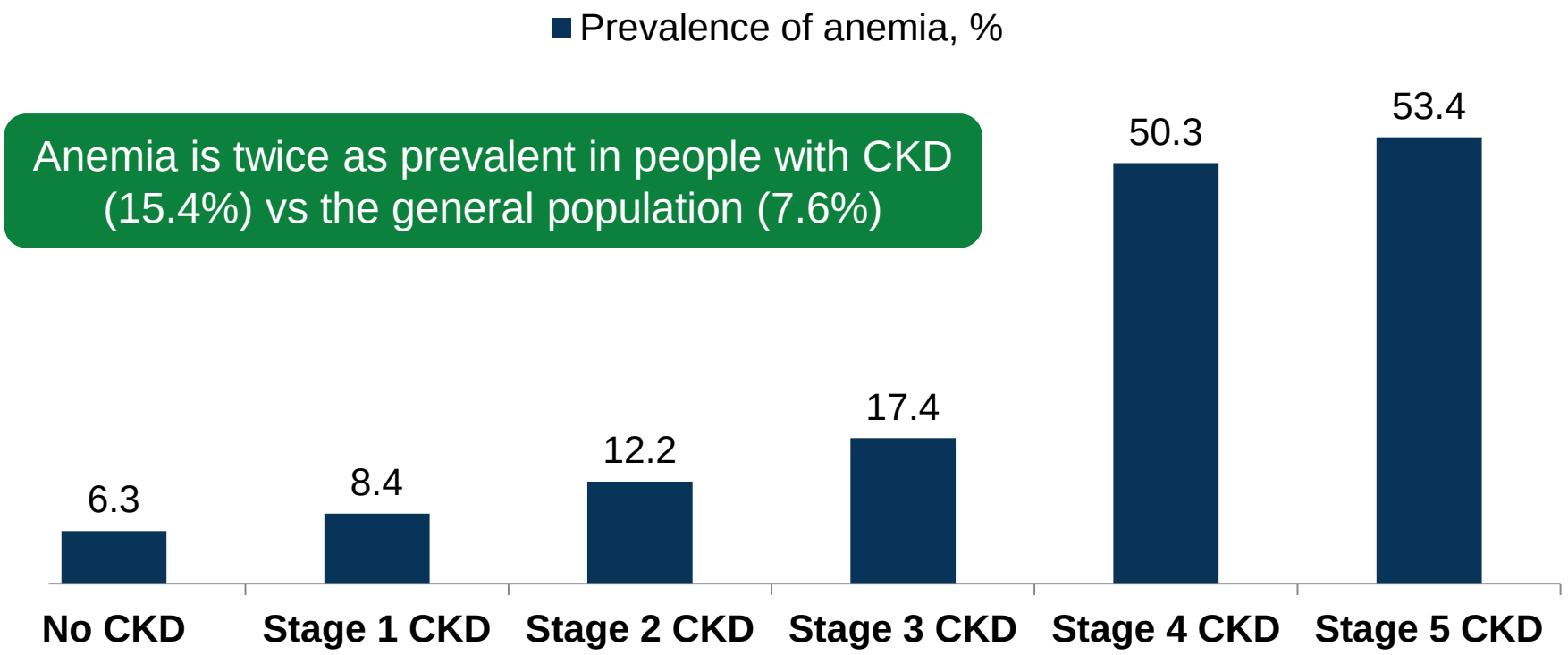
- Anemia is a condition that often develops in the early stages of CKD and typically worsens as kidney function declines
  - Common symptoms that manifest in patients with CKD and anemia include fatigue, weakness, and paleness



CKD, chronic kidney disease; EPO, erythropoietin; RBCs, red blood cells.

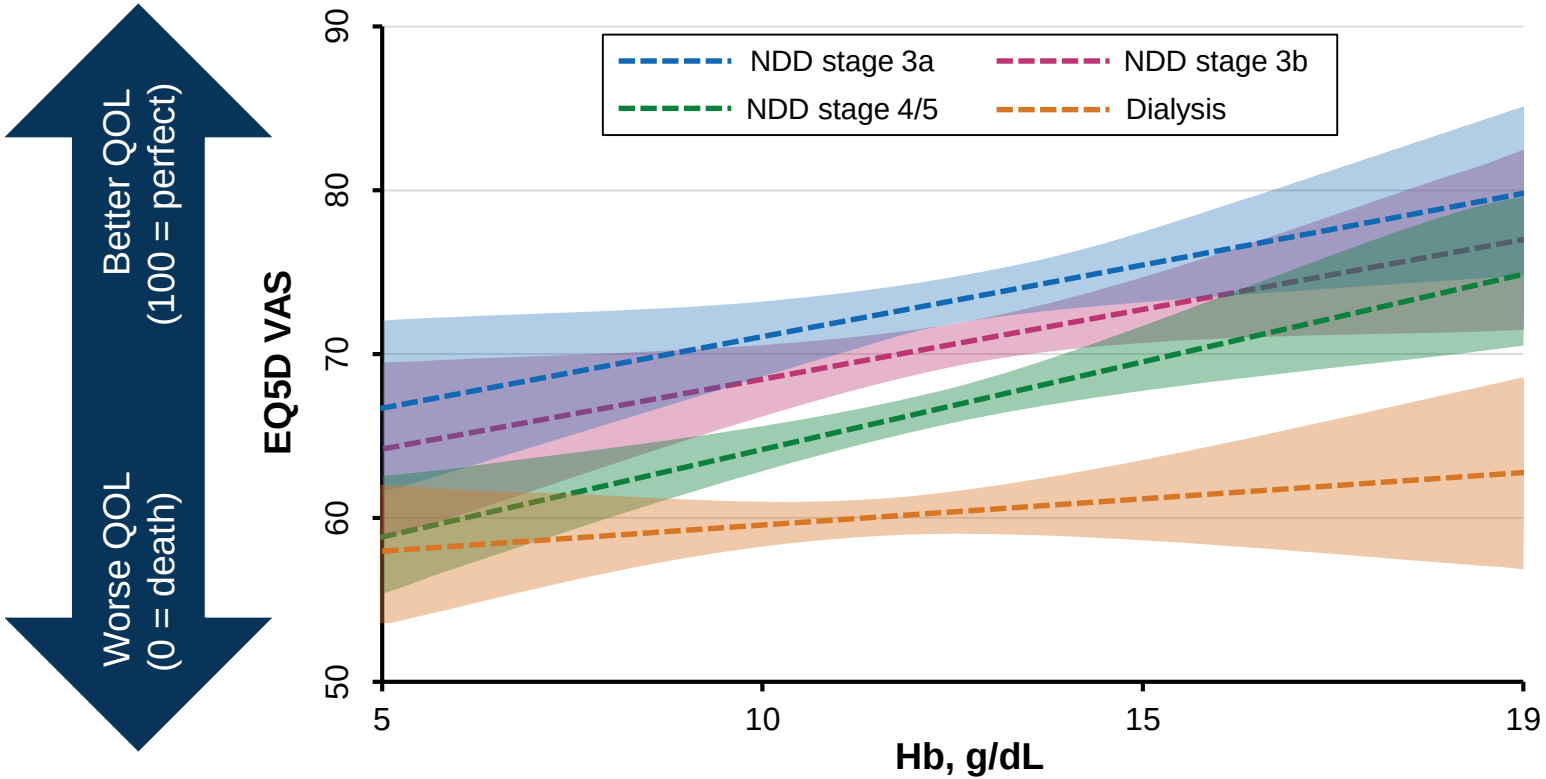
1. https://www.niddk.nih.gov/health-information/kidney-disease/anemia.

Anemia Is Increasingly Prevalent With Worsening CKD[1,a]



CKD, chronic kidney disease.
[a] NHANES 2007-2010.
1. Stauffer ME, Fan T. *PLoS ONE*. 2014;9:e84943.

Anemia Reduces QOL, Regardless of Dialysis Status[1,a]



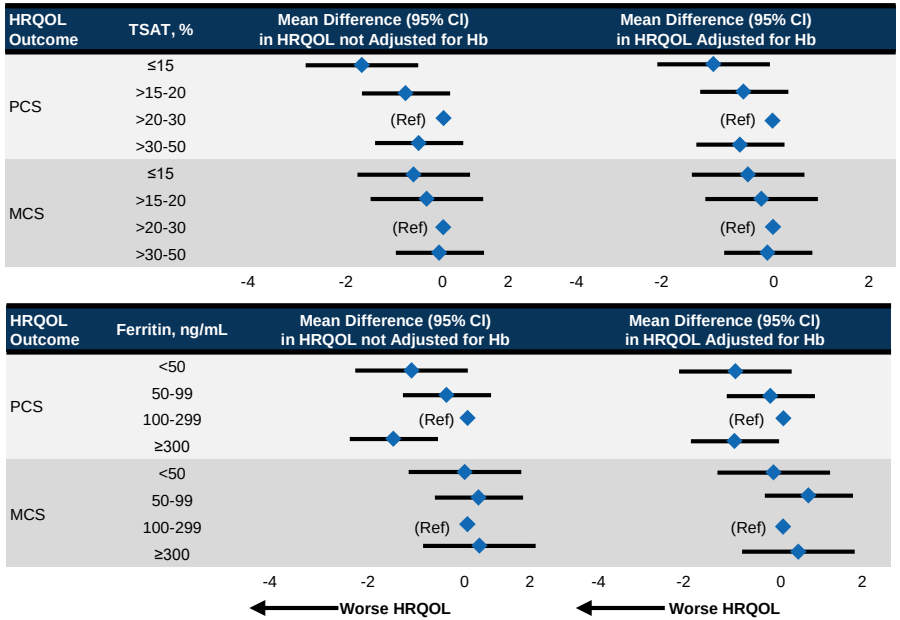
EQ5D, EuroQol-5 Dimensions; Hb, hemoglobin; NDD, nondialysis-dependent; QOL, quality of life; VAS, visual analog scale.

[a] Real-world study of 5,276 patients from Europe, United States of America, and China.

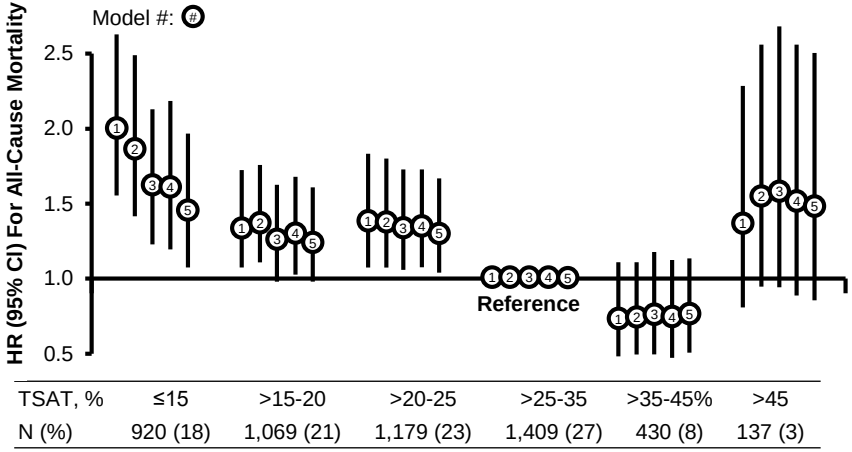
1. Van Haalen H et al. *BMC Nephrol.* 2020;21:88.

Low TSAT and/or Ferritin Is Associated With Poorer QOL and Higher Mortality in Patients With ND-CKD

QOL[1,a]



Mortality[2]



TSAT, %	≤15	>15-20	>20-25	>25-35	>35-45%	>45
N (%)	920 (18)	1,069 (21)	1,179 (23)	1,409 (27)	430 (8)	137 (3)

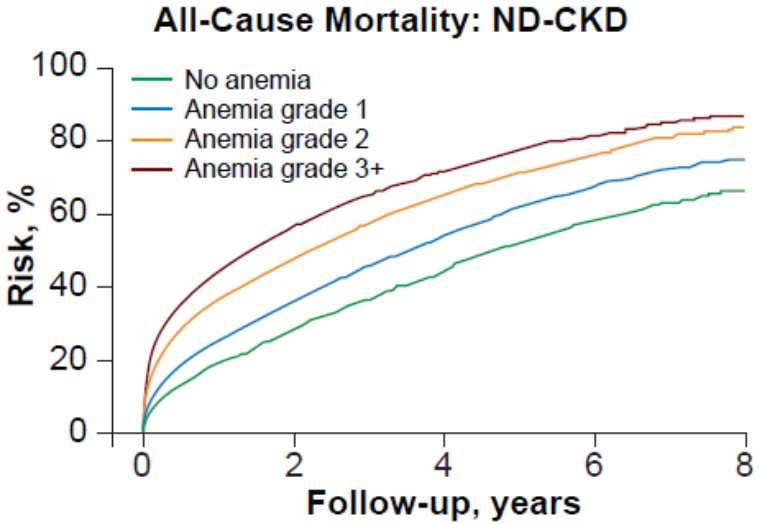
Progressive adjustments:
- Model 1: Unadjusted
- Model 2: Country, age, sex, black race, BMI, eGFR, and albuminuria
- Model 3: + ESA use and 11 summary comorbidities
- Model 4: + Serum albumin, WBC, and ferritin
- Model 5: + Hb

BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HRQOL, health-related quality of life; MCS, mental component summary; ND-CKD, nondialysis-dependent CKD; PCS, physical component summary; TSAT, transferrin saturation; WBC, white blood cell.

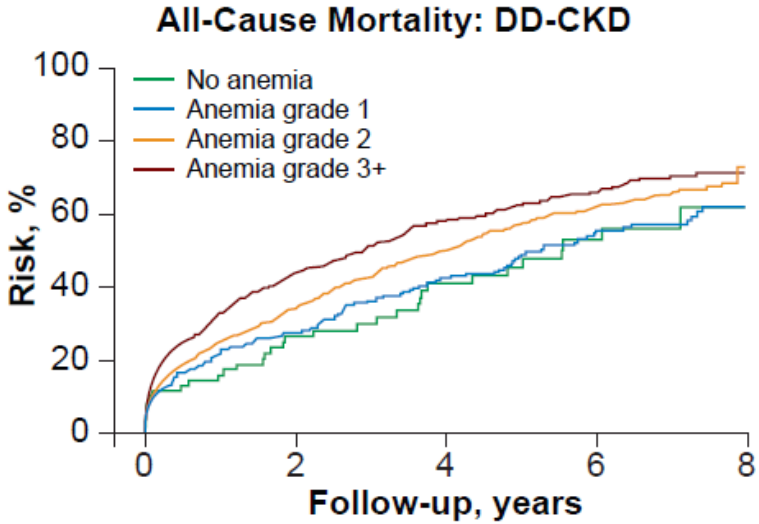
[a] Adjusted for country, age, sex, race, BMI, smoking status, eGFR, albuminuria, albumin, WBC count, ferritin (for TSAT exposure), TSAT (for ferritin exposure), diabetes, hypertension, atherosclerotic disease, congestive heart failure, other cardiovascular comorbidities, cancer, and history of ulcers/gangrene and Hb. Results for TSAT >50% are not shown because of small sample size.

1. Guedes MH et al. The Kidney Week 2020 Reimagined (Kidney Week 2020). Abstract PO0281. 2. Guedes MH et al. Kidney Week 2020. Abstract PO0280.

Anemia Is Associated With Increased Risk of Mortality in CKD, Regardless of Dialysis Status[1,a]



No anemia	2,821	1,555	815	320
Anemia grade 1	7,510	3,670	1,772	651
Anemia grade 2	7,469	2,944	1,358	499
Anemia grade 3+	3,255	1,001	422	128



No anemia	79	47	30	16
Anemia grade 1	267	157	107	62
Anemia grade 2	961	534	326	177
Anemia grade 3+	1,194	490	246	103

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

[a] Anemia grading, Hb in g/dL: no anemia: ≥12/≥13 in women/men; grade 1: 10 to <12/10 to <13 in women/men; grade 2: 8 to <10; grade 3+: <8.

1. Toft G et al. *J Nephrology.* 2020;33:147-156.

Case Studies in CKD-Related Anemia: Current Challenges

- **Tonya**
  - 54-year-old woman with longstanding HTN and T2DM
  - Stage 4 ND-CKD
  - eGFR: 18 mL/min/1.73 m^2
  - Hb: 8.5 g/dL
  - TSAT: 22%; ferritin: 150 mcg/L
  - Oral iron supplement

- **Richard**
  - 67-year-old man with longstanding HTN and glomerulonephritis
  - HD-CKD
  - Began hemodialysis 3 years ago
  - Hb: 9.5 g/dL
  - TSAT: 19%; ferritin: 900 mcg/L
  - IV iron sucrose, 50 mg/mo
  - Nonresponsive to increased doses of darbepoetin alfa

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HD-CKD, hemodialysis-dependent chronic kidney disease; HTN, hypertension; ND-CKD, nondialysis-dependent chronic kidney disease; T2DM, type 2 diabetes mellitus; TSAT, transferrin saturation.

Epidemiological and Pathological Factors Contributing to the Diagnosis and Management of CKD-Associated Anemia

Wendy L. St. Peter, Pharm.D, FCCP, FNKF, FASN
Professor, College of Pharmacy
University of Minnesota
Minneapolis, Minnesota

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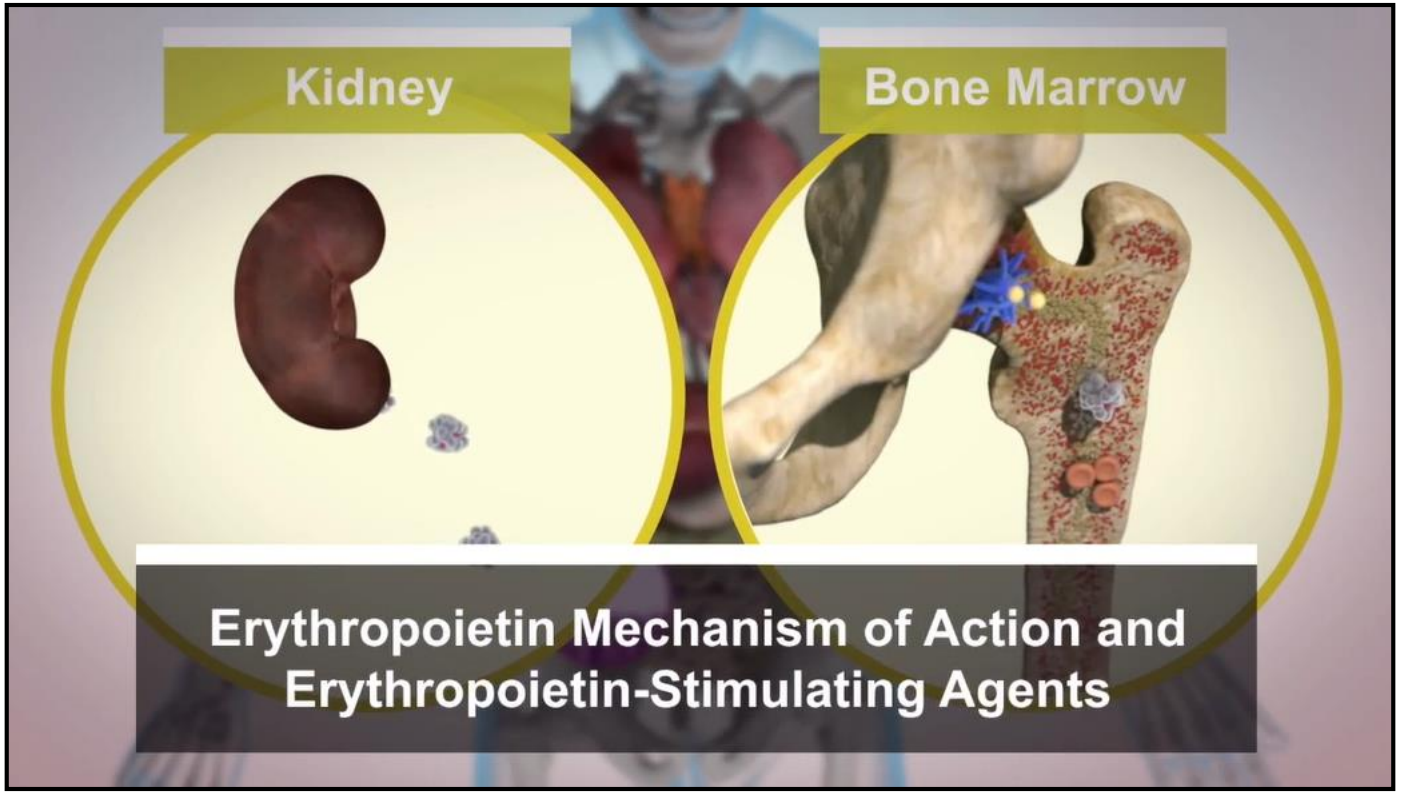
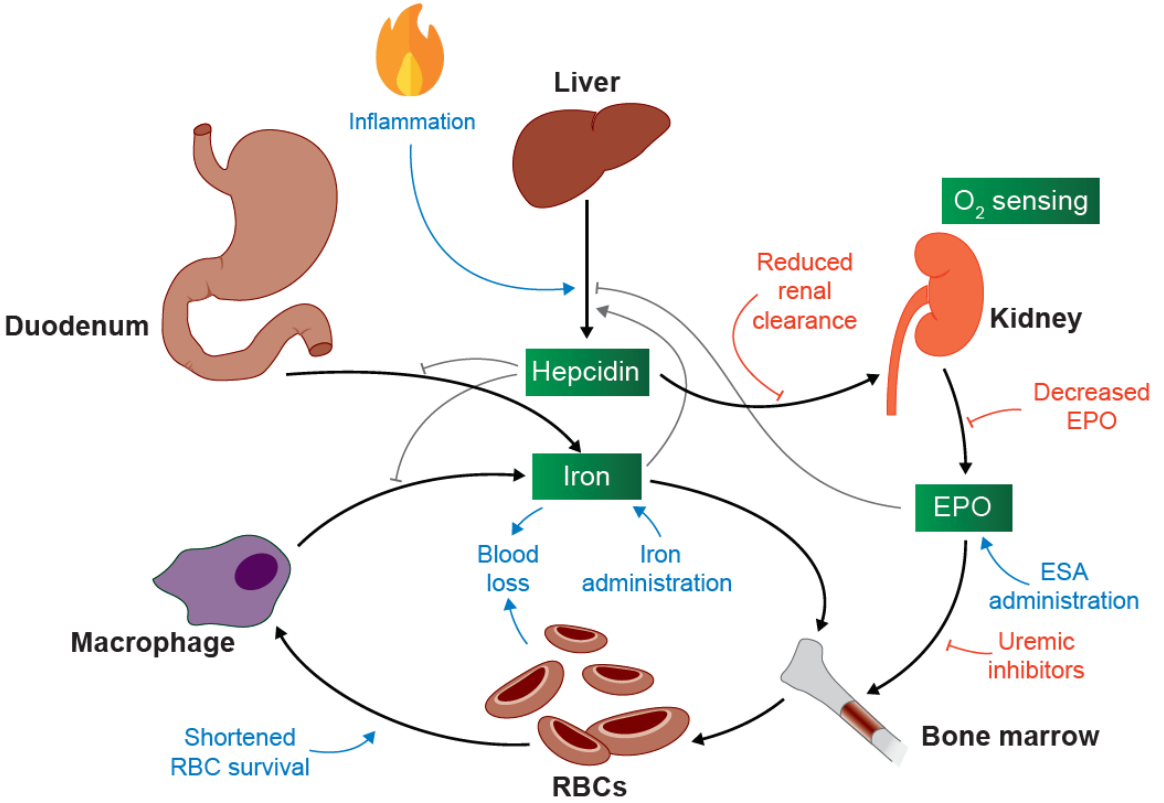


Pathophysiology of CKD-Related Anemia[1]



CKD, chronic kidney disease; EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; RBC, red blood cell.

1. Babitt JL, Lin HY. *J Am Soc Nephrol*. 2012;23:1631-1634.

There Is a Difference Between Absolute and Functional Iron Deficiency[1,2]

Absolute Iron Deficiency

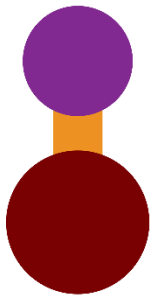
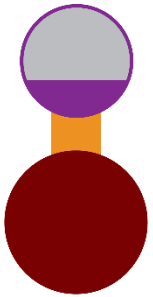
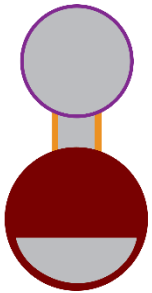
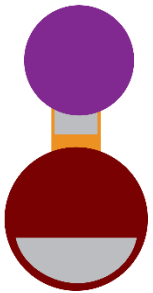
- No stainable iron in storage tissues (eg, bone marrow, liver, or spleen)

Functional Iron Deficiency

- Normal or increased total body iron; unavailable for incorporation into erythroid precursors, mainly because of increased hepcidin that inhibits iron mobilization from intracellular stores

1. Gafter-Gvili A et al. *Acta Haematol*. 2019;142:44-50. 2. Phiri KS et al. *J Clin Pathol.* 2009;62:685-689.

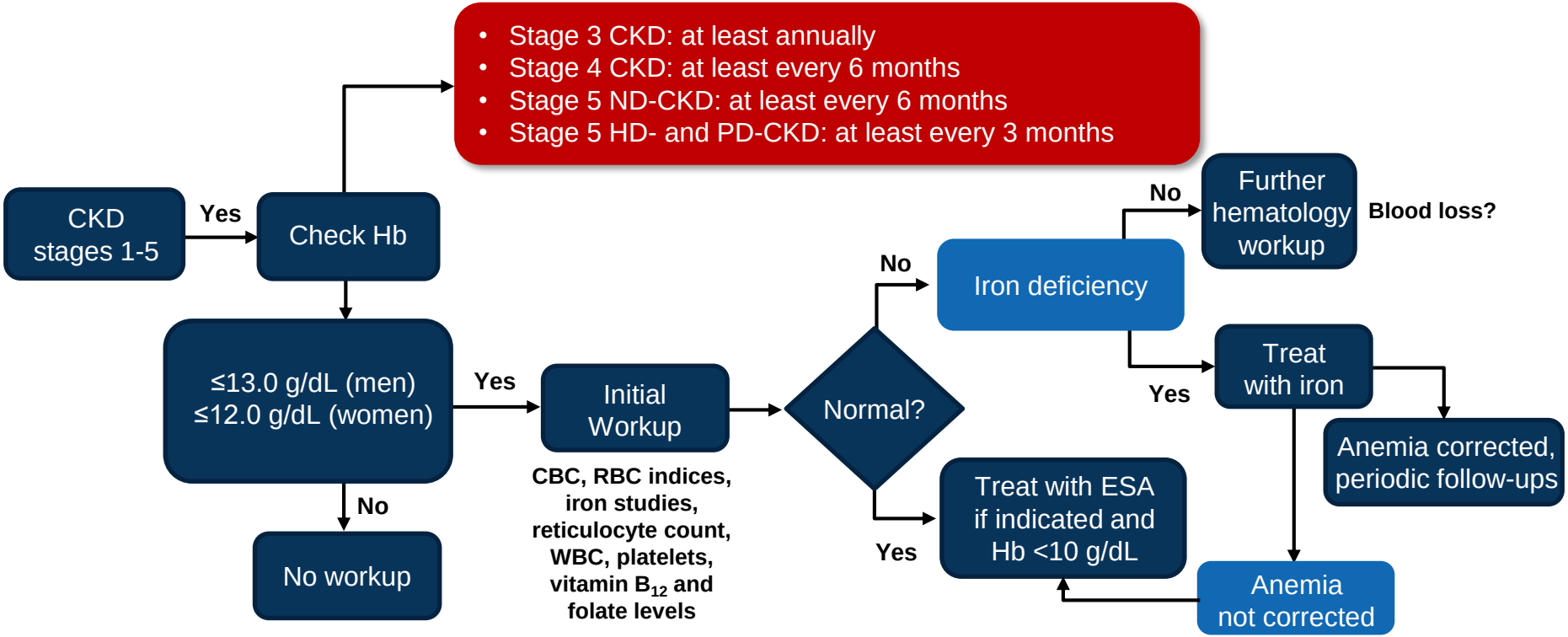
Iron Status With and Without Inflammation[1]

		Normal	Iron Depletion	Absolute Iron Deficiency	Inflammation: Functional Iron Deficiency
Ferritin →	**Storage iron**				
TSAT →	**Transport iron**				
Hb →	**Erythron iron**				
Ferritin, mcg/L		100 ± 60	<25	<10	>100
Transferrin saturation, %		35 ± 15	<30	<10	<20
Hb, g/dL		Normal	Normal	Low	Low

Hb, hemoglobin; TSAT, transferrin saturation.

1. Crichton RR et al. *Iron Therapy With a Special Emphasis on Intravenous Administration*. 4th ed. UNI-MED Verlag AG: Bremen, Germany; 2008.

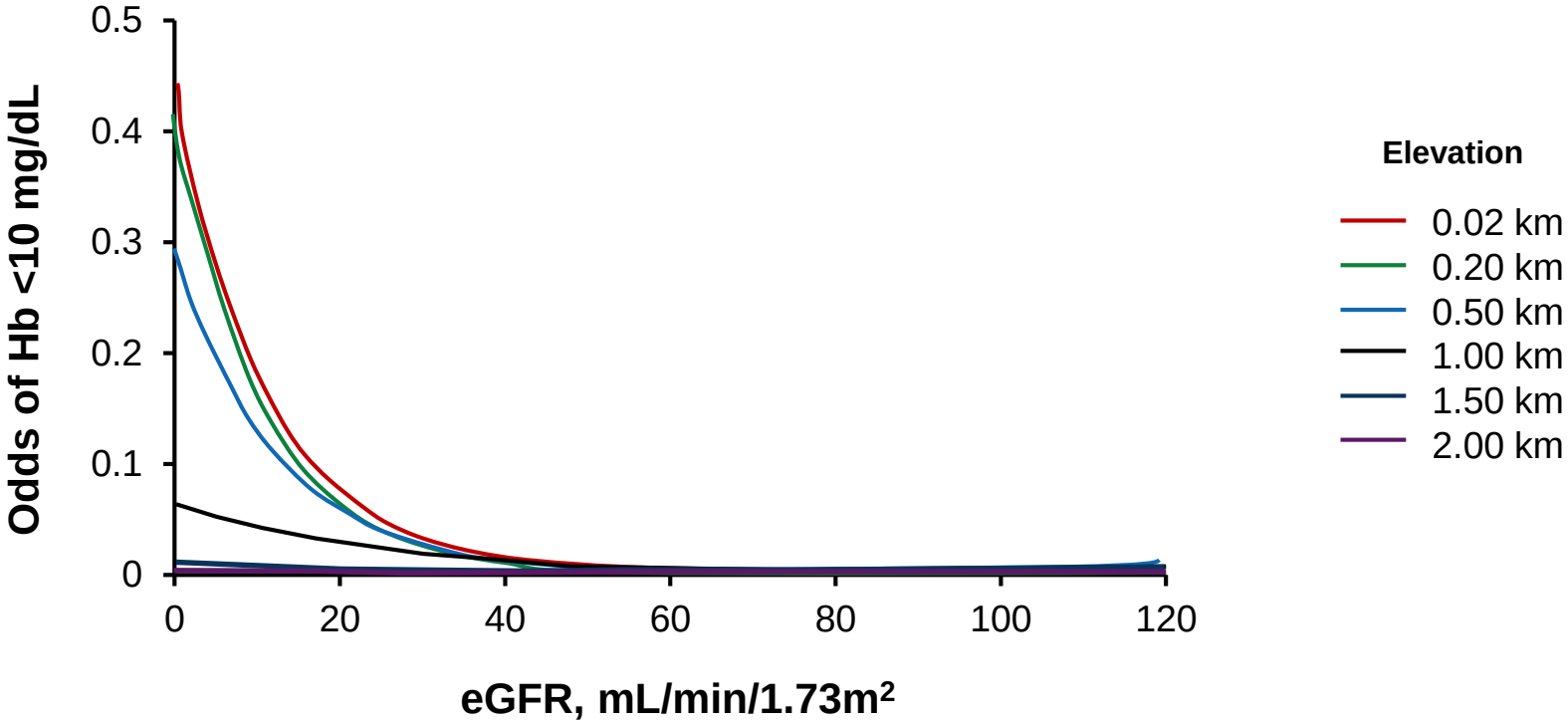
Evaluation of Anemia and Basic Management of CKD[1]



CBC, complete blood count; CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; RBC, red blood cell; WBC, white blood cell.

1. Kidney Disease International Global Outcomes Guidelines. *Kidney Int*. 2012 (suppl 2):1-335.

Prevalence of Anemia Is Lower in Patients With CKD Who Live at Higher Altitudes[1]

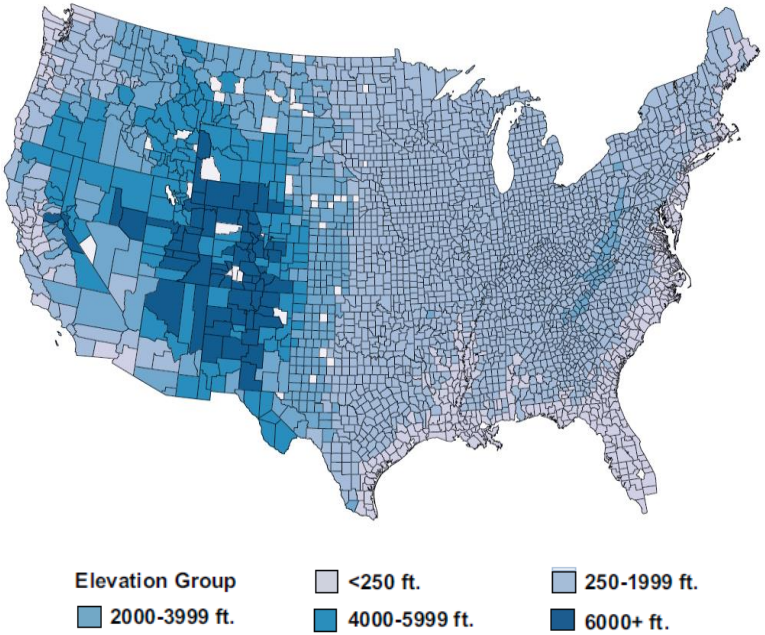


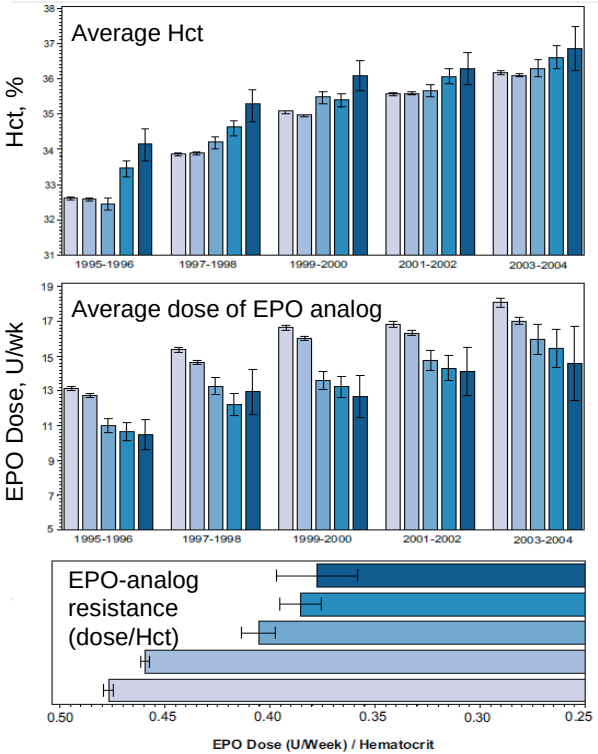
CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Hb, hemoglobin.

1. Ng YH et al. *Am J Kidney Dis*. 2019;74:715-718.

Altitude and EPO-Analog Response[1]

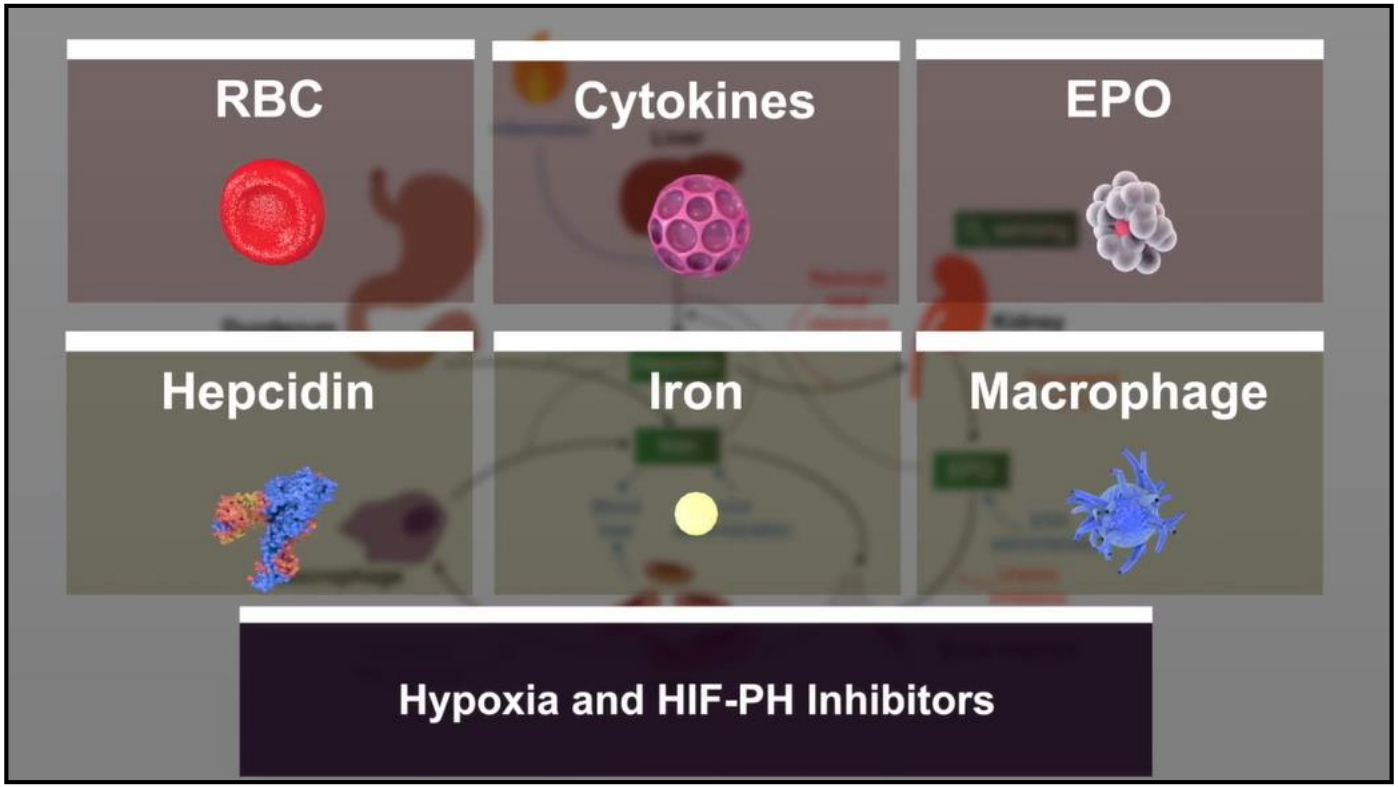
- US Renal Data System (N = 341,737 incident HD patients) combined with elevation data from the US Geological Survey





EPO, epoetin alfa; Hct, hematocrit; HD, hemodialysis; US, United States.

1. Brookhart MA et al. *J Am Soc Nephrol*. 2008;19:1389-1395.



EPO, erythropoeitin; HIF-PH, hypoxia-inducible factor prolyl hydroxylase; RBC, red blood cell.

2019 Nobel Prize in Medicine Was Awarded for HIF Research[1,2]

William G. Kaelin Jr. | Sir Peter J. Ratcliffe | Gregg L. Semenza

HIF, hypoxia-inducible factor.

1. https://www.nobelprize.org/prizes/medicine. 2. https://www.statnews.com/2019/10/07/nobel-prize-medicine-cells-oxygen-levels/.

Clinical Implications of HIF-PH Inhibitors in the Management of Anemia Associated With CKD

Steven Fishbane, MD
Chief, Division of Nephrology
Northwell Health
Great Neck, New York

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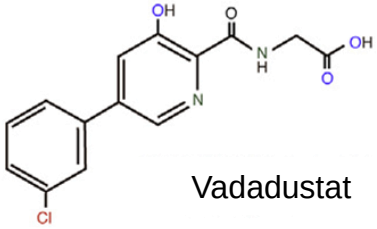
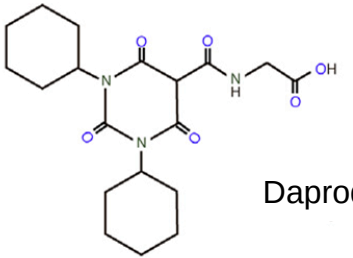
HIF-PH Inhibitors Currently in Phase 3 Clinical Trials[1]

All HIF-PH inhibitors are administered orally



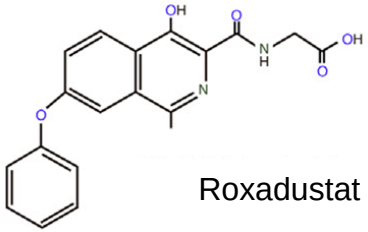
Vadadustat

- Approved in Japan



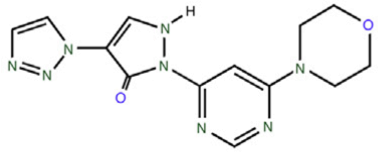
Daprodustat

- Approved in Japan



Roxadustat

- Approved in Japan and China
- Under regulatory review in the United States and European Union



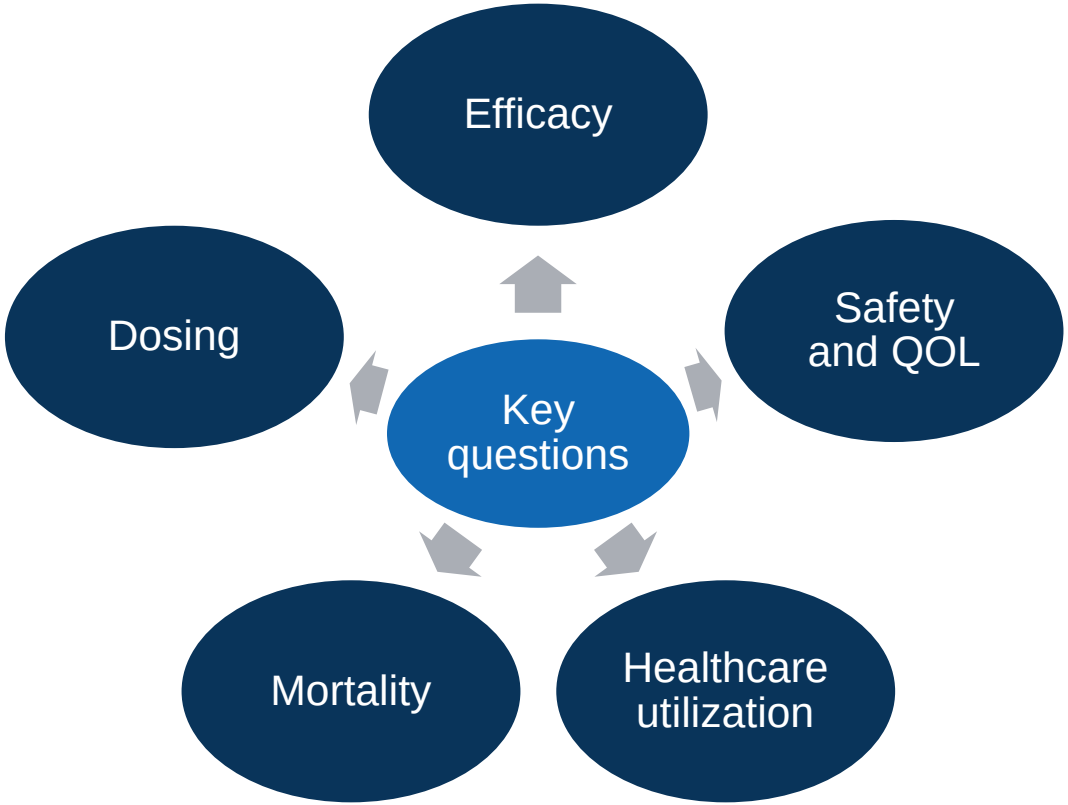
Molidustat

- Phase 3 trials completed in Japan for patients with ND-CKD

HIF-PH, hypoxia-inducible factor prolyl hydroxylase; ND-CKD, nondialysis-dependent chronic kidney disease.

1. Sanghani NS, Haase VH. *Adv Chronic Kidney Dis*. 2019;26:253-266.

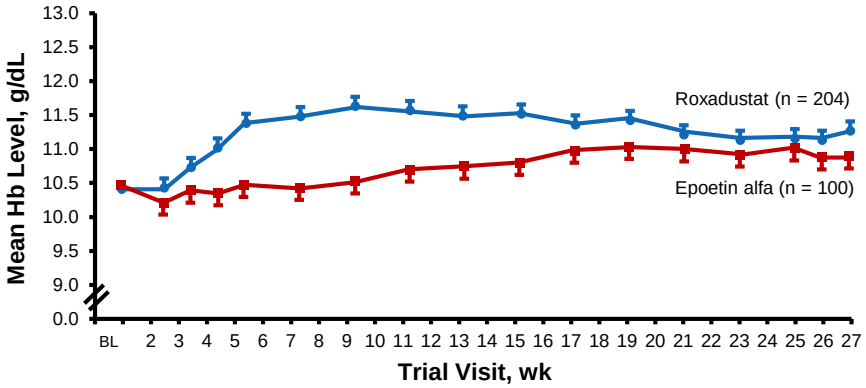
How Do HIF-PH Inhibitors Compare With ESAs and/or Iron Therapy?



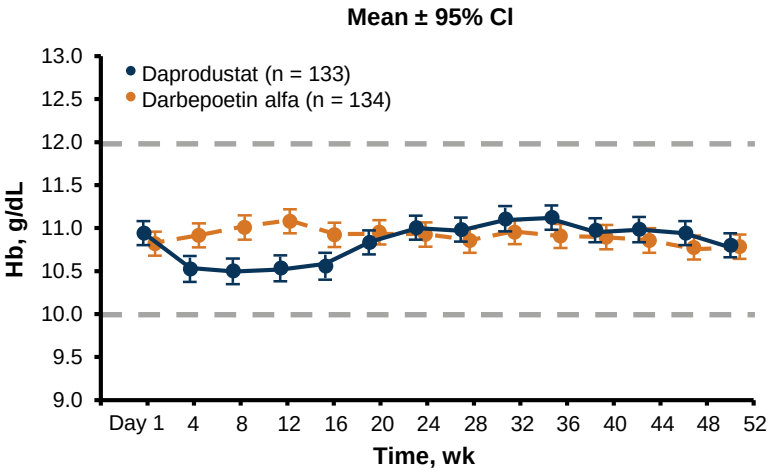
ESA, erythropoiesis-stimulating agent; HIF-PH, hypoxia-inducible factor prolyl hydroxylase; QOL, quality of life.

Effects of HIF-PH Inhibitors on Hemoglobin in Patients With HD-CKD

Roxadustat[1]



Daprodustat[2]



No. of Participants at Visits

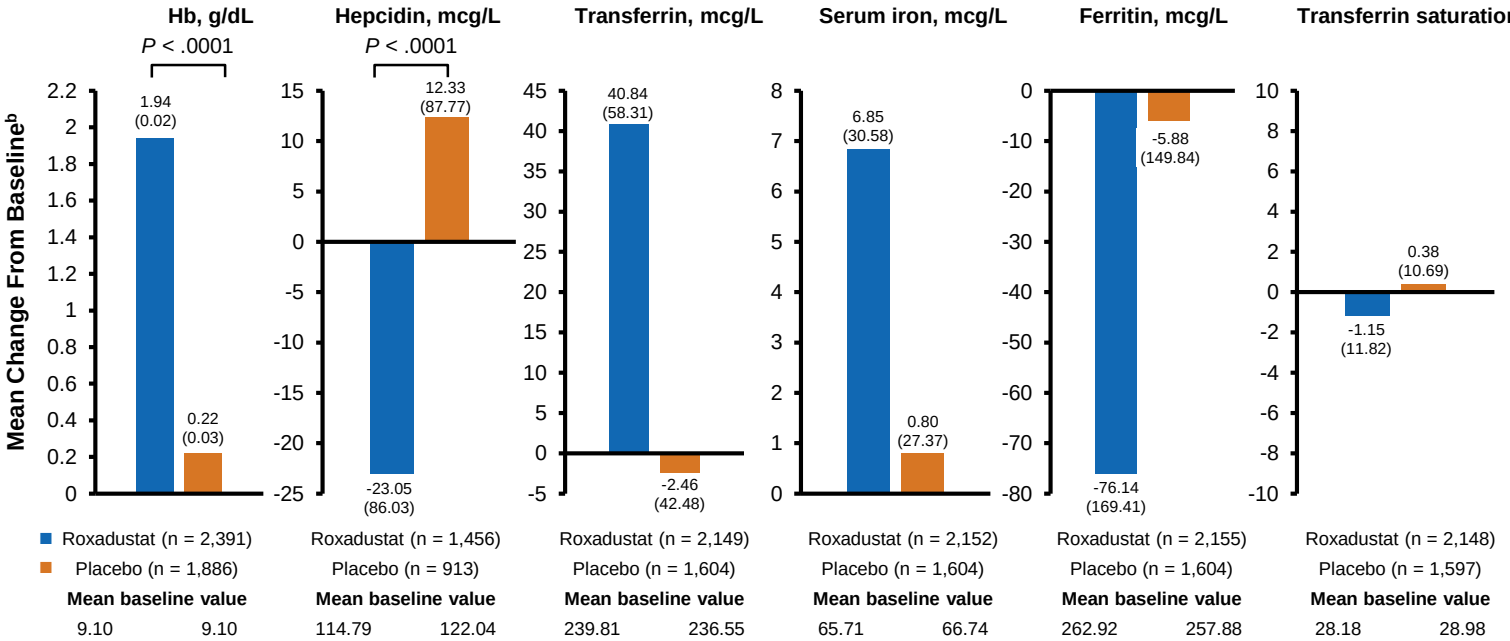
Daprodustat	133	133	127	125	124	123	123	123	122	121	120	117	117	115
Darbepoetin alfa	134	134	132	129	129	129	129	129	127	127	125	125	124	120

Hb, hemoglobin; HD-CKD, hemodialysis-dependent chronic kidney disease; HIF-PH, hypoxia-inducible factor prolyl hydroxylase.

1. Chen N et al. *N Engl J Med*. 2019;381:1011-1022. 2. Akizawa T et al. *Clin J Am Soc Nephrol*. 2020;15:1155-1165.

Effects of HIF-PH Inhibitors on Iron Indices and Inflammation in Patients With ND-CKD: Roxadustat[1]

Mean Change in Hb From Baseline to the Average Over Weeks 28 to 52 and Mean Change in Iron Markers to Week 20 to 24[a]



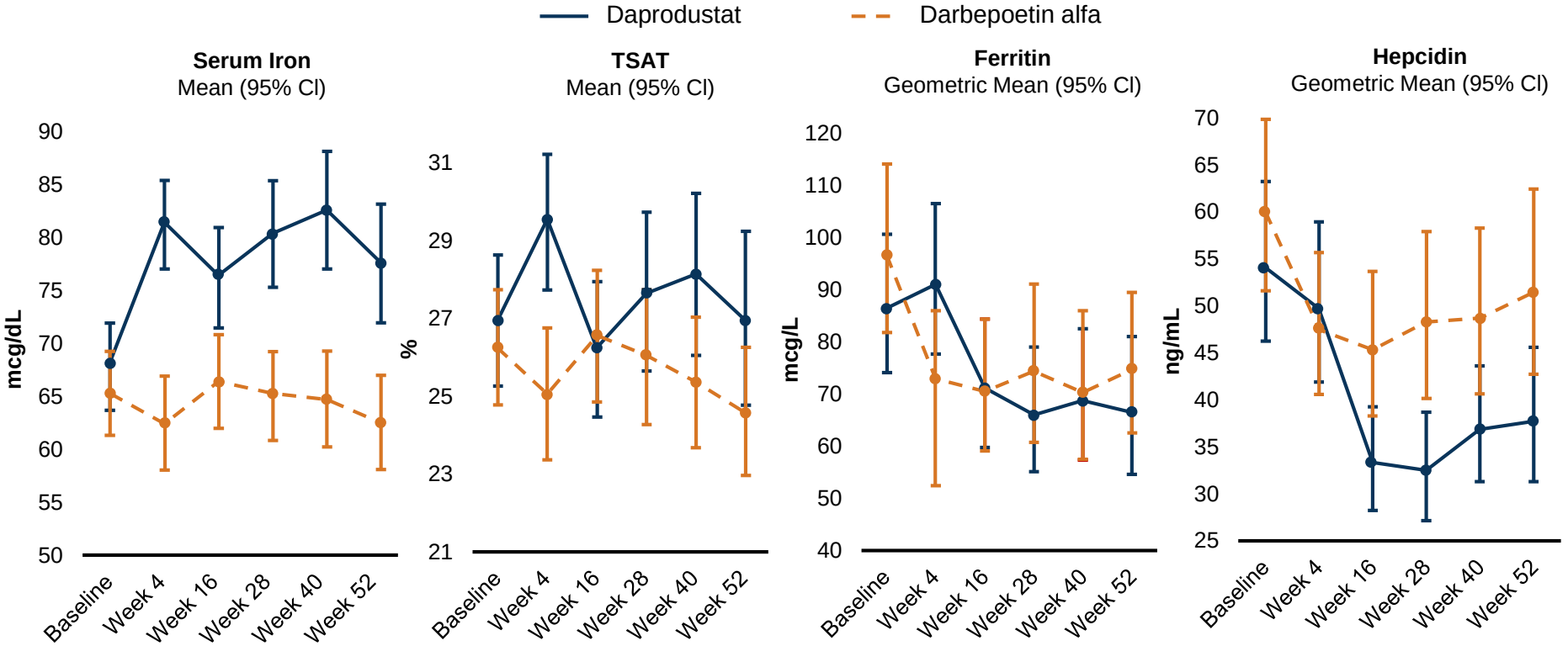
Hb, hemoglobin; HIF-PH, hypoxia-inducible factor prolyl hydroxylase; ND-CKD, nondialysis-dependent chronic kidney disease.

[a] Mean change for ferritin, serum iron, transferrin, and transferrin saturation at week 20 is changed from baseline to the average over weeks 12 to 28, and mean change in serum hepcidin is from baseline to week 24.

[b] Mean change for Hb is least squares mean (SEM) and all others are mean (SD).

1. Fishbane S et al. Kidney Week 2020. Abstract PO0257.

Effects of HIF-PH Inhibitors on Iron Indices and Inflammation in Patients With HD-CKD: Daprodustat[1,a]

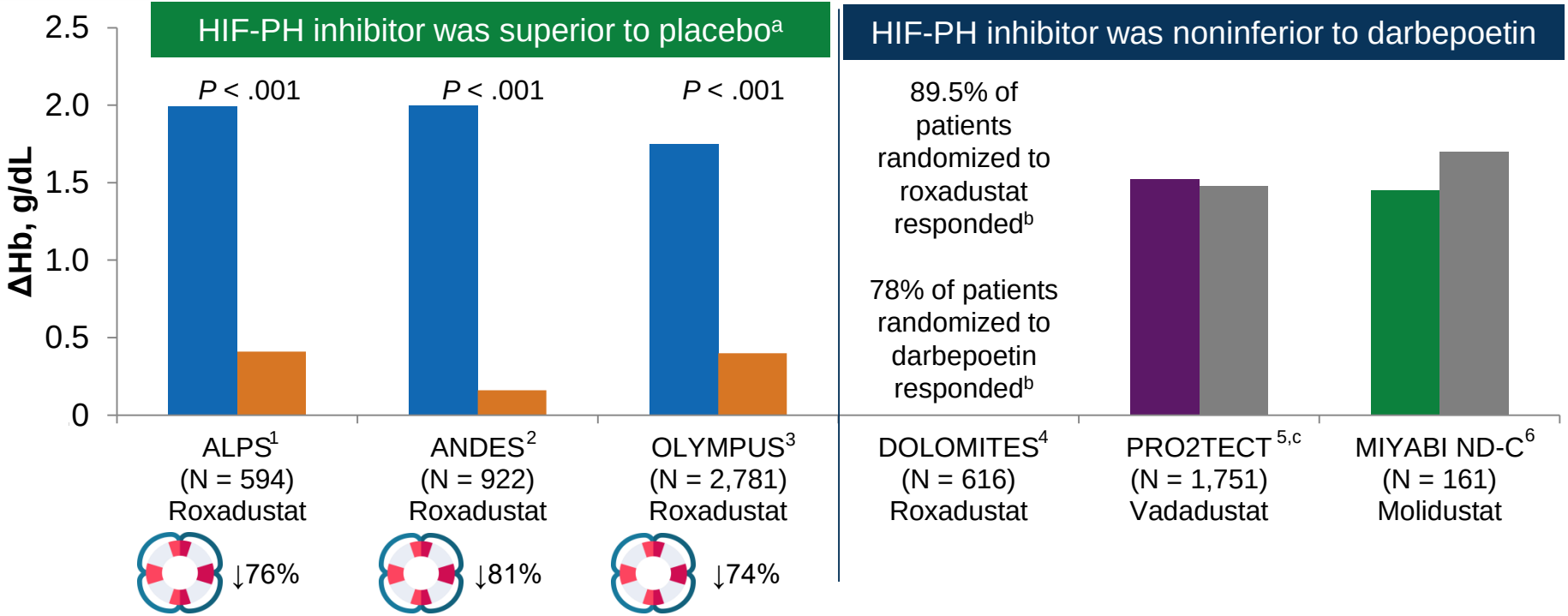


HD-CKD, hemodialysis-dependent chronic kidney disease; HIF-PH, hypoxia-inducible factor prolyl hydroxylase; TSAT, transferrin saturation.

[a] Randomized, double-blind, phase 3 trial in a Japanese population of patients on hemodialysis (N = 271).

1. Akizawa T et al. *Clin J Am Soc Nephrol*. 2020;15:1155-1165.

Phase 3 Trials of HIF-PH Inhibitors in Patients With ND-CKD



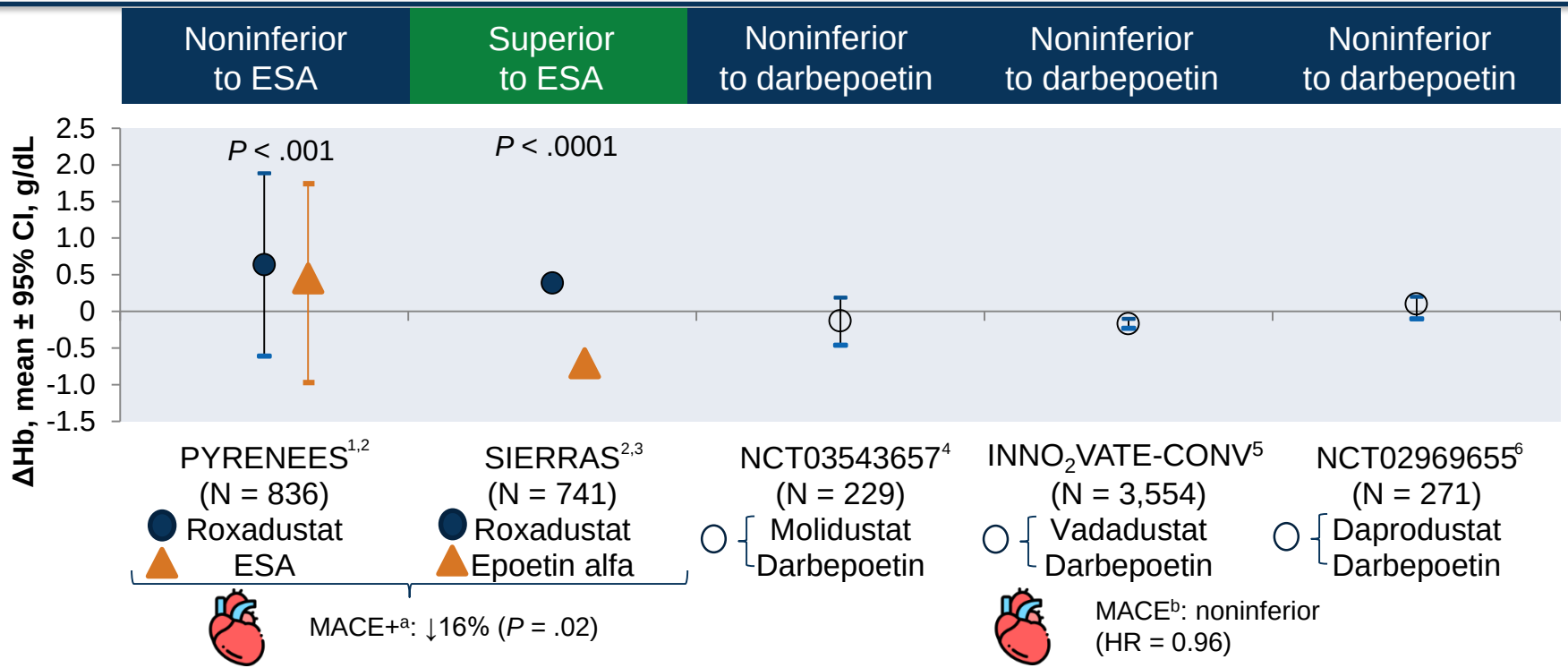
Hb, hemoglobin; HIF-PH, hypoxia-inducible factor prolyl hydroxylase, ND-CKD, nondialyisis-dependent chronic kidney disease.

[a] Rescue medications included iron, ESAs, and/or blood transfusions. [b] Hb ≥11 g/dL and ΔHb ≥1 g/dL if BL Hb > 8 g/dL or ΔHb ≥ 2 g/dL if BL Hb ≤8 g/dL.

[c] ESA-naïve cohort.

1. Esposito C et al. Kidney Week 2019. Abstract SA-PO225. 2. Coyne DW et al. Kidney Week 2019. Abstract SA-PO228.
3. Fishbane S et al. Kidney Week 2019. Abstract TH-OR023. 4. Barratt J et al. ERA-EDTA 2020;MO001.
5. Chertow GM et al. Kidney Week 2020. Abstract FR-OR54. 6. Yamamoto H et al. 57th ERA-EDTA Congress (ERA-EDTA 2020) Abstract P1866.

Phase 3 Trials of HIF-PH Inhibitors in Patients With DD-CKD



DD-CKD, dialysis-dependent chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; HIF-PH, hypoxia-inducible factor prolyl hydroxylase; MACE, major adverse cardiovascular event.

[a] MACE outcomes pooled across all phase 3 studies (N = 3,917). [b] MACE outcomes pooled across both INNO2VATE studies (N = 3,902).

1. Esposito C et al. Kidney Week 2019. Abstract SA-PO225. 2. Provenzano R et al. Kidney Week 2019. Abstract FR-OR131.
3. Charytan C et al. Kidney Week 2019. Abstract SA-PO227. 4. Akizawa T et al. Kidney Week 2020. Abstract PO2623.
5. Eckardt KU et al. Kidney Week 2020. Abstract TH-OR01. 6. Akizawa T et al. Clin J Am Soc Nephrol. 2020;15:1155-1165.

HIF-PH Inhibitors Reduce the Need for Rescue Therapies

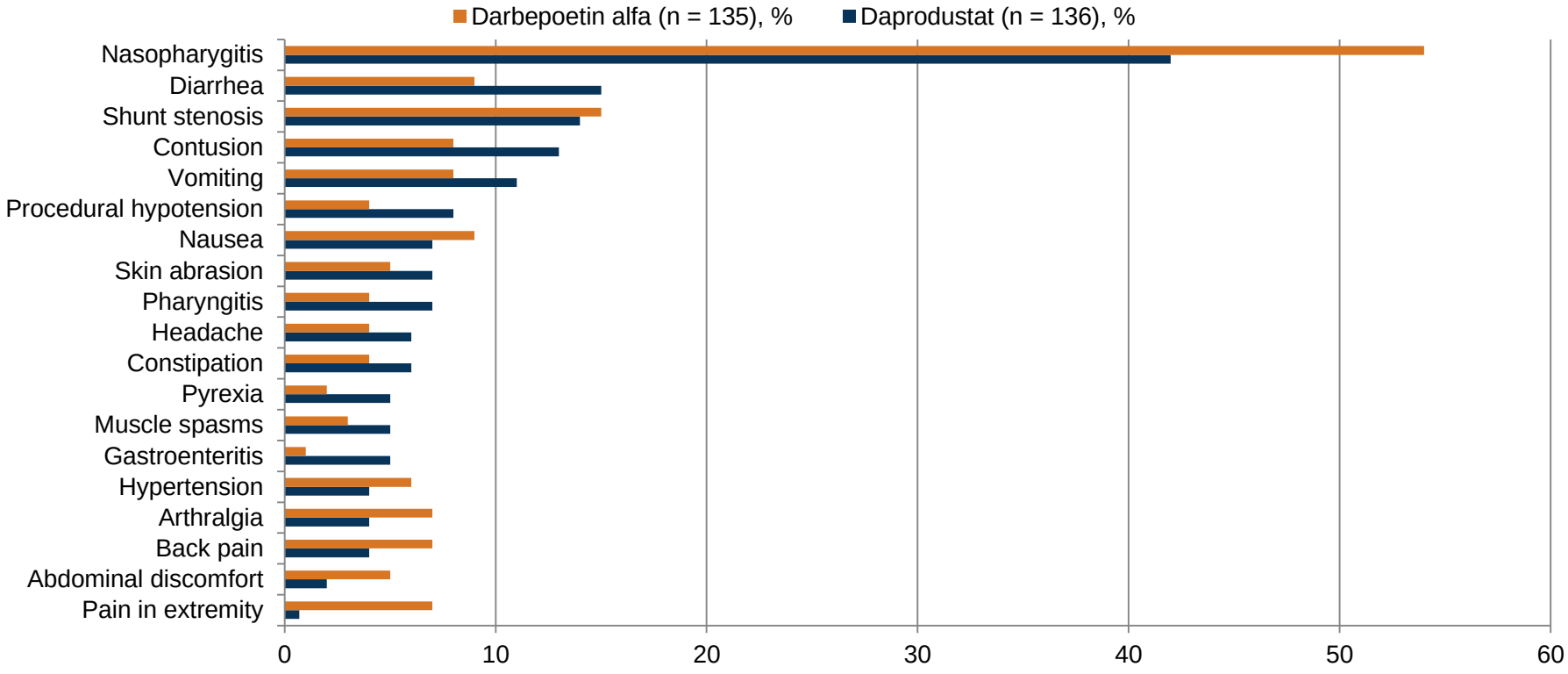
Roxadustat reduced the need for RBC transfusion by 18% versus epoetin alfa in a pooled analysis of phase 3 studies of patients with DD-CKD[1]

Daprodustat reduced the need for IV iron supplementation in patients with HD-CKD (32% daprodustat and 43% darbepoetin alfa throughout the treatment period)[2]

DD-CKD, dialysis-dependent chronic kidney disease; HD-CKD, hemodialysis-dependent chronic kidney disease; HIF-PH, hypoxia-inducible factor prolyl hydroxylase; RBC, red blood cell.

1. Provenzano R et al. Kidney Week 2020. Abstract PO0268. 2. Akizawa T et al. *Clin J Am Soc Nephrol*. 2020;15:1155-1165.

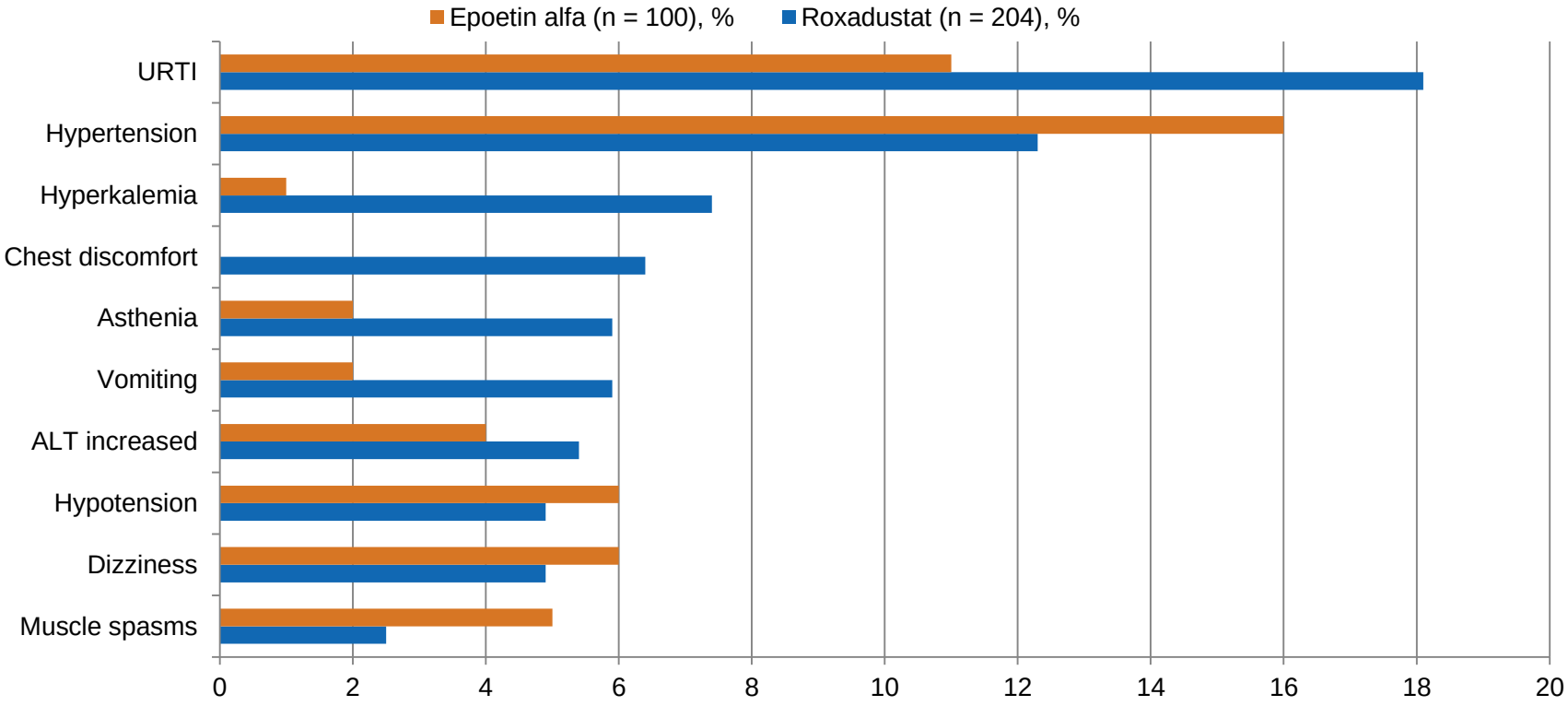
AEs in a Conversion/Maintenance Study in Patients With HD-CKD: Daprodustat[1]



AEs, adverse events; HD-CKD, hemodialysis-dependent chronic kidney disease.

1. Akizawa T et al. *Clin J Am Soc Nephrol*. 2020;15:1155-1165.

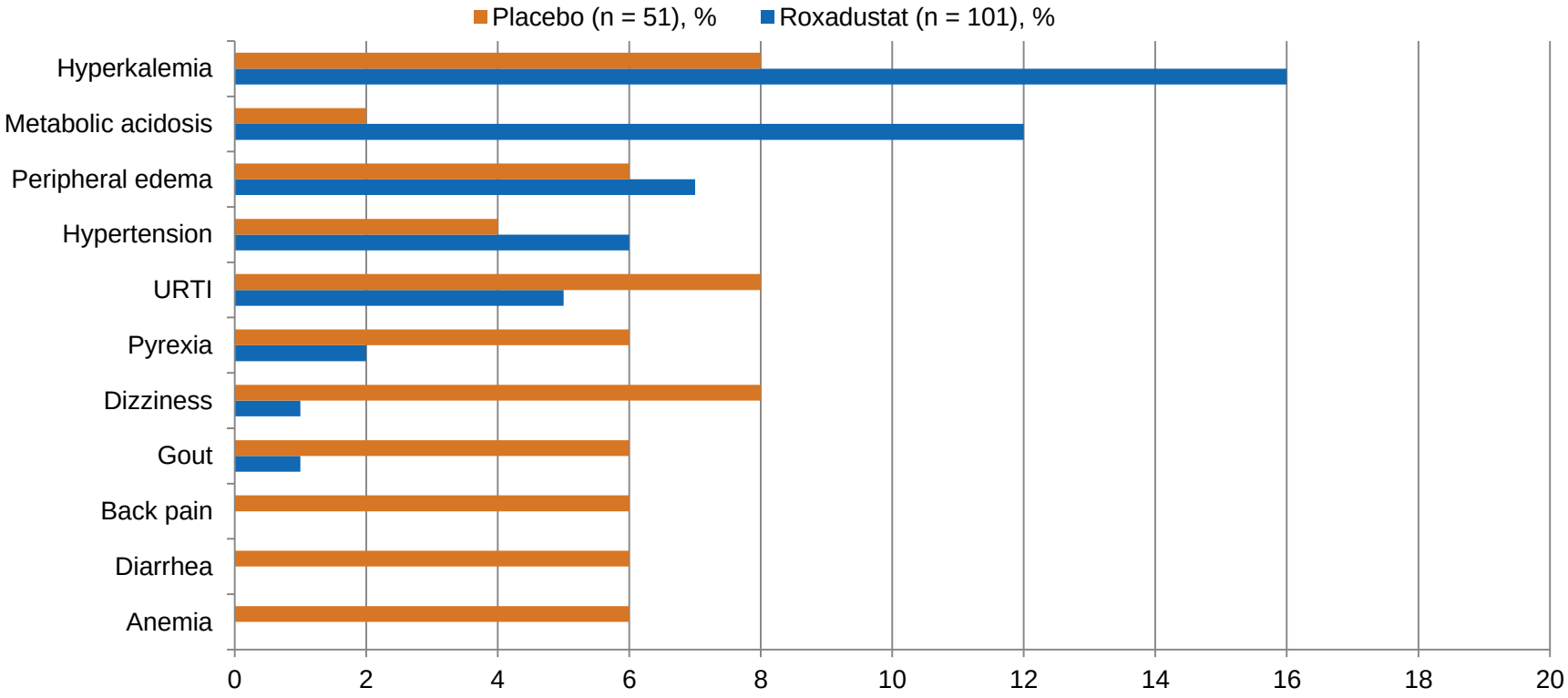
AEs in a Conversion/Maintenance Study in Patients With HD-CKD: Roxadustat[1]



AEs, adverse events; ALT, alanine aminotransferase; HD-CKD, hemodialysis-dependent chronic kidney disease; URTI, upper respiratory tract infection.

1. Chen N et al. *N Engl J Med*. 2019;381:1011-1022.

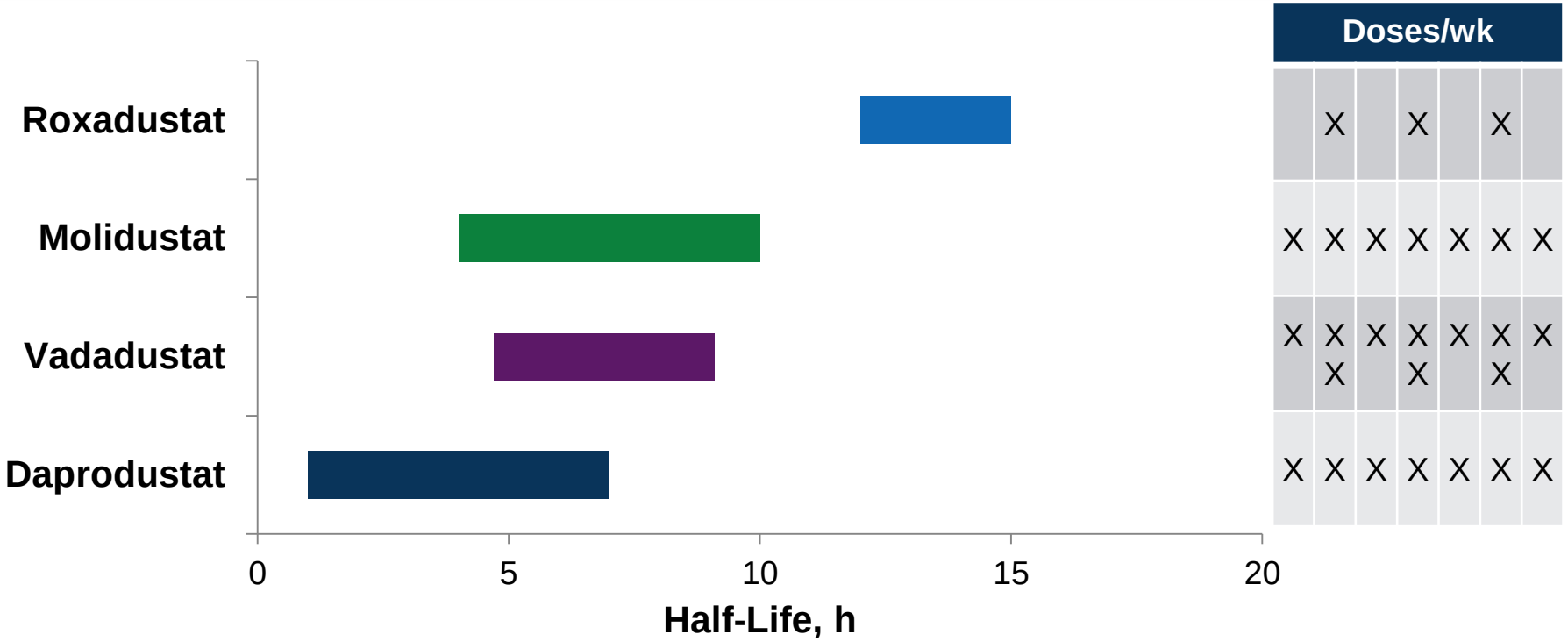
AEs in Patients With ND-CKD: Roxadustat[1]



AEs, adverse events; ND-CKD, nondialysis-dependent chronic kidney disease; URTI, upper respiratory tract infection.

1. Chen N et al. *N Engl J Med*. 2019;381:1001-1010.

Pharmacokinetics of HIF-PH Inhibitors in Phase 3 Trials[1]



HIF-PH, hypoxia-inducible factor prolyl hydroxylase.

1. Sanghani NS, Haase VH. *Adv Chronic Kidney Dis*. 2019;26:253-266.

Roxadustat Is Dosed According to Hemoglobin Level[1]

Dose Increase/Decrease Table

Change in Hb From 4 Weeks Before to the Current Week, g/dL	Current Week Hb, g/dL			
	<10.5	>10.5 to ≤11.5	>11.5 to ≤12.5	>12.5
<-1.0	Increase by 1 step	Increase by 1 step	No change	Suspend treatment until Hb decreases below 11.0; resume treatment at the dose 1 step lower than the presuspension dose
≥-1.0 to ≤1.0	Increase by 1 step	No change	Decrease by 1 step	
>1.0 to ≤2.0	No change	Decrease by 1 step	Decrease by 1 step	
>2.0	Decrease by 1 step			

Dose Adjustment Table

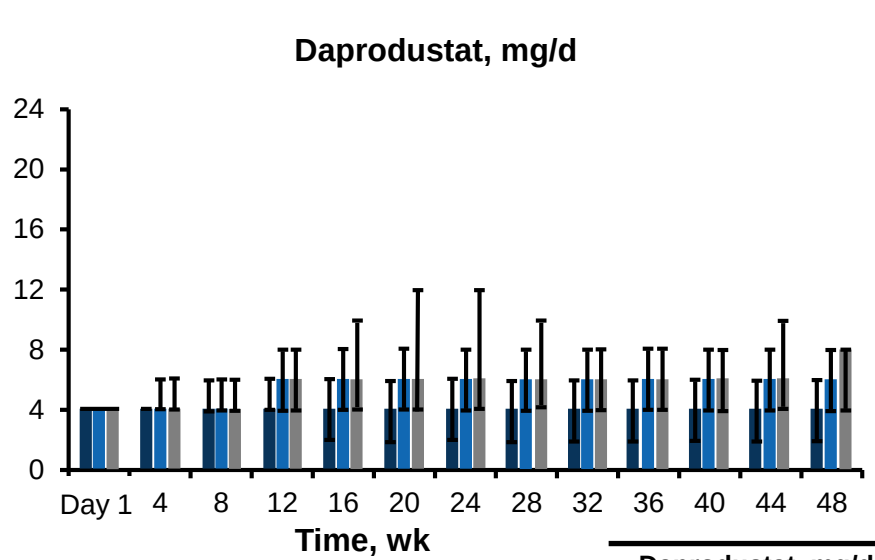
Step	1	2	3	4	5	6	7	8
Roxadustat dose	20 mg	40 mg	50 mg	70 mg	100 mg	120 mg	150 mg	200 mg

- In Japan, tablets are available in 3 doses: 20 mg, 50 mg, 100 mg
- Recommended starting dose: 50 mg TIW in ESA-naïve patients and 70 mg or 100 mg TIW in ESA-treated patients
- Maintenance dose: 20-150 mg TIW
- Maximum dose: 300 mg or 3.0 mg/kg/dose

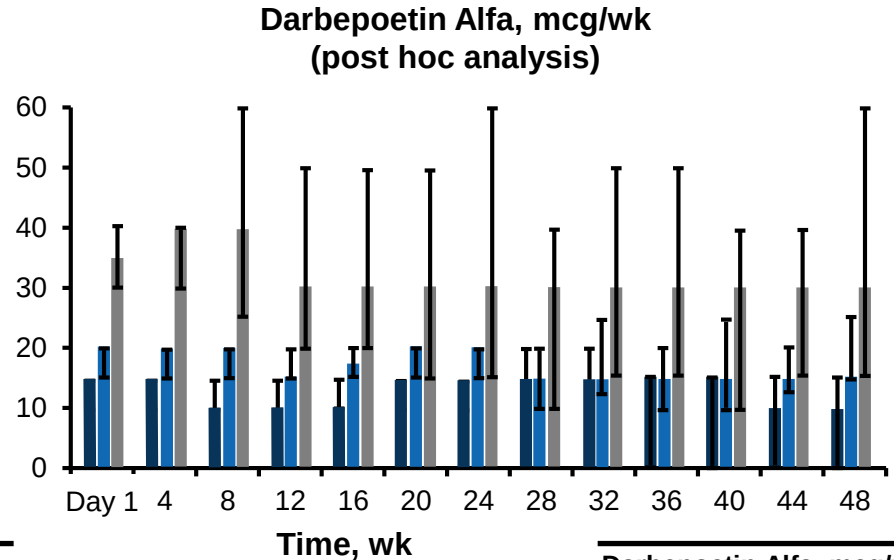
ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; TIW: three times weekly.

1. https://www.pmda.go.jp/files/000234811.pdf.

Dosing in a Conversion/Maintenance Study in Patients With HD-CKD: Daprodustat[1]



Daprodustat, mg/d
4.0 (2.7, 6.0)
6.0 (4.0, 8.7)
6.0 (4.0, 8.0)



Darbepoetin Alfa, mcg/wk
10.4 (4.2, 15)
15.0 (13.3, 22.9)
25.8 (12.5, 46.7)

Median dose (Q1, Q3)

ERI, erythropoietin resistance index; HD-CKD, hemodialysis-dependent chronic kidney disease.

1. Akizawa T et al. *Clin J Am Soc Nephrol*. 2020;15:1155-1165.

Case Studies in CKD-Related Anemia: Could HIF-PH Inhibitors Address Current Challenges?

- **Tonya**
  - 54-year-old woman with longstanding HTN, T2DM, and stage 4 ND-CKD
  - Hb: 8.5 g/dL
  - Oral HIF-PH inhibitors are self-administered
  - Dose adjustments can be made via telephone call with nephrologist or pharmacist
  - Ferritin and TSAT will need to be monitored

- **Richard**
  - 67-year-old man with longstanding HTN, glomerulonephritis, and HD-CKD
  - Hb: 9.5 g/dL
  - Oral HIF-PH inhibitors are self-administered
  - Hb is monitored at dialysis session and doses adjusted accordingly
  - HIF-PH inhibitor may reduce IV iron use

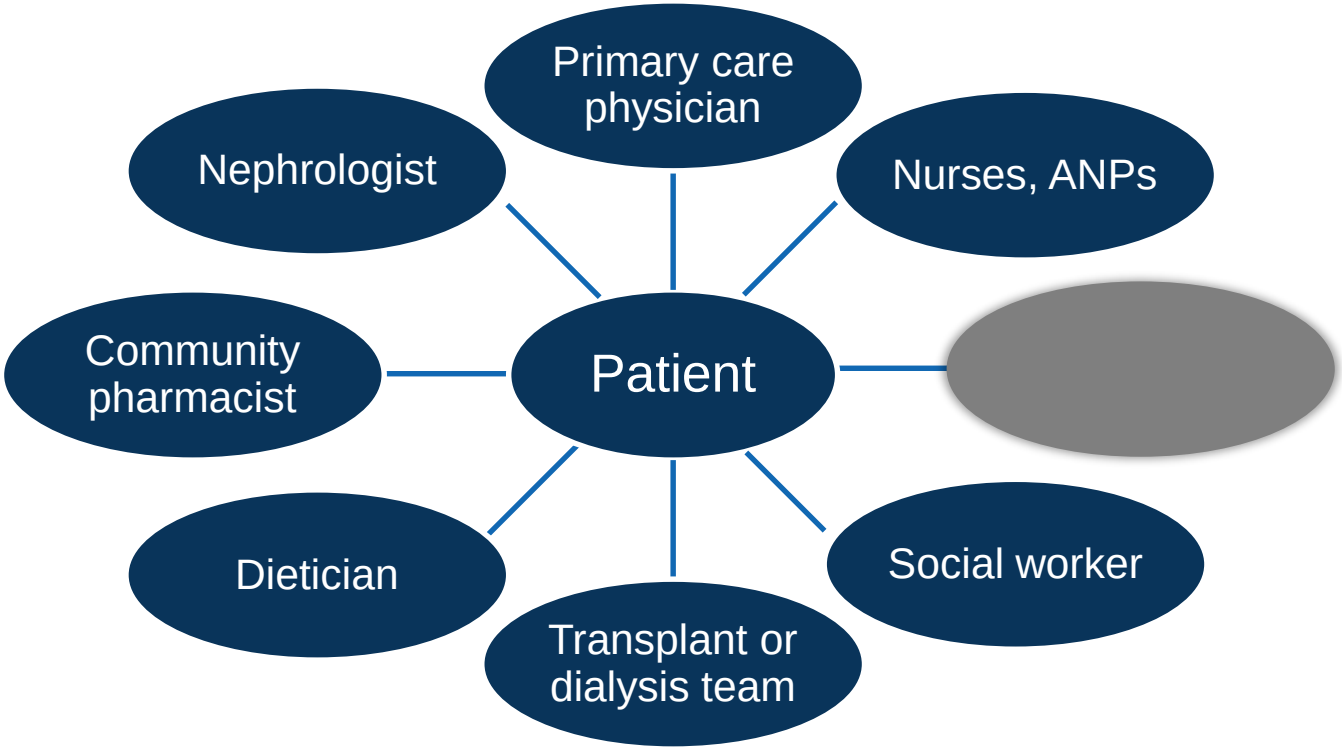
CKD, chronic kidney disease; Hb, hemoglobin; HD-CKD, hemodialysis-dependent chronic kidney disease; HIF-PH, hypoxia-inducible factor prolyl hydroxylase; HTN, hypertension; IV, intravenous; ND-CKD, nondialysis-dependent chronic kidney disease; T2DM, type 2 diabetes mellitus; TSAT, transferrin saturation.

Clinical Implications of HIF-PH Inhibitors for Collaborative Care and the Evolving Role of Health-System Pharmacists

Wendy L. St. Peter, Pharm.D, FCCP, FNKF, FASN
Professor, College of Pharmacy
University of Minnesota
Minneapolis, Minnesota

Go online to access full CPE information, including faculty disclosures.

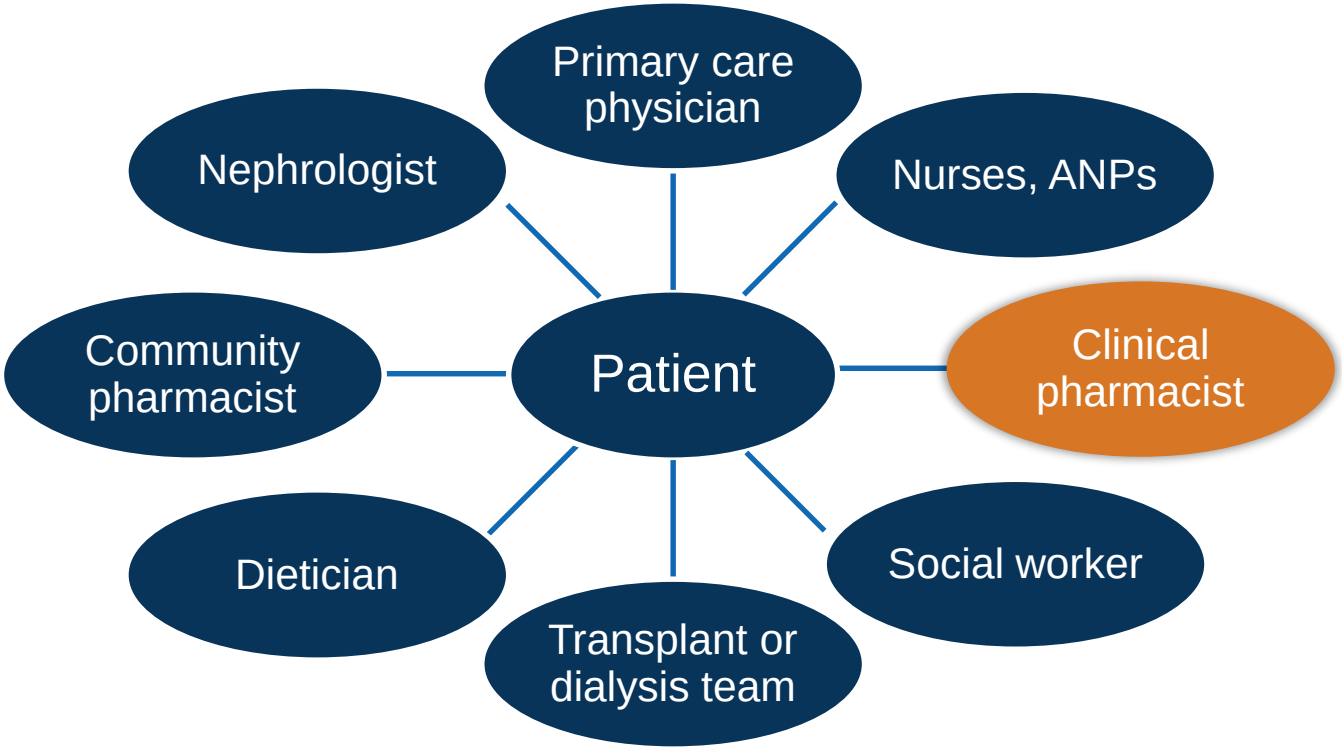
A Multidisciplinary Approach to CKD Care: What Is Missing?[1,2]



ANP, advanced nurse practitioner; CKD, chronic kidney disease.

1. Joy MS et al. *Am J Kidney Dis*. 2005;45:1105-1118. 2. Meaney CJ et al. *J Am Coll Clin Pharm*. 2020 Jul 23 [Epub ahead of print].

A Multidisciplinary Approach to CKD Care: What Is Missing?[1,2]



ANP, advanced nurse practitioner; CKD, chronic kidney disease.

1. Joy MS et al. *Am J Kidney Dis*. 2005;45:1105-1118. 2. Meaney CJ et al. *J Am Coll Clin Pharm*. 2020 Jul 23 [Epub ahead of print].

Patients' Experience of Anemia in CKD: Results From a Recent Survey of 500 Patients in the United States[1]

Attribute many AEs to anemia in CKD; reported feeling a lack of energy, sadness and/or depressed, as well as pain, difficulty sleeping, and worrying about worsening anemia

Struggle to recall key information about anemia in CKD or didn't know or couldn't recall their Hb levels

Many did not correctly identify the symptoms of anemia, including paleness, headaches, or difficulty breathing as common symptoms associated with severe anemia in CKD

Feel more confident about the management of their condition after their doctor had spoken to them about treatment options

Most likely to look for information about anemia in CKD either online or via social media

AEs, adverse events; CKD, chronic kidney disease.

1. Palaka E et al. Kidney Week 2019. Poster 232.

New Models of CKD Care Including Pharmacists: Improving Medication Reconciliation and Medication Management[1]

Patients with CKD are at a high risk for medication-therapy problems (MTPs) and have demonstrated poor adherence to key CV medication

Current pharmacist training is focused on providing patient-centered care, identifying and resolving MTPs, and improving adherence

Medication management provided by pharmacists has been shown to reduce MTPs and improve medication adherence in patients with CKD

Growing evidence supports pharmacy services, and pharmacists in clinical care models, to slow GFR decline, reduce hospitalizations and mortality, and decrease LOS, but more robust translational research is needed

Scalable clinical care and reimbursement models are needed to fully address the complex medication-related needs of patients with CKD

CKD, chronic kidney disease; CV, cardiovascular; GFR, glomerular filtration rate; LOS, length of stay.

1. St Peter WL et al. *Curr Opin Nephrol Hypertens*. 2013;22:656-662.

Review of Pharmacist-Managed CKD Clinics[1]

International systematic review of pharmacists' interventions in CKD; included 37 studies with 4,743 patients

Of the eight controlled studies, including 744 patients with CKD, pharmacist interventions were associated with

- Reduced composite of ESRD and mortality in patients with diabetes 14.8 vs 28.2 per 100 patient-years ($P < .001$; adjusted relative risk 60%)
- Reduced all-cause hospitalizations: 1.8 ± 2.4 vs 3.1 ± 3.0 ($P = .02$)
- Improved anemia management (target Hb; $P = .0001$)

Four studies reported improved health outcomes

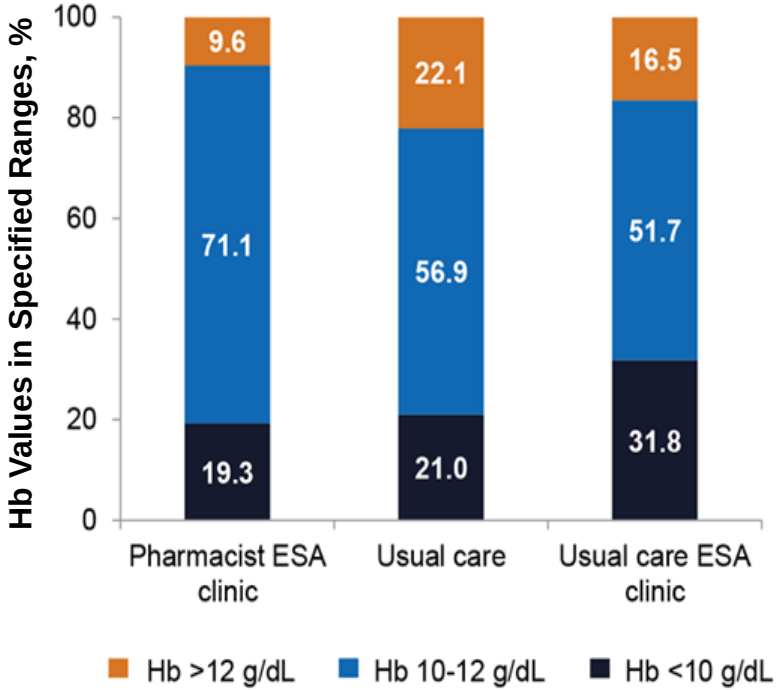
- Improved HRQOL in dimensions of general health (28% improvement, $P < .001$) and social functioning (26% improvement, $P < .001$)

CKD, chronic kidney disease; ESRD, end-stage renal disease; Hb, hemoglobin; HRQOL, health-related quality of life.

1. Salgado TM et al. *Nephrol Dial Transplant*. 2012;27:276-292.

Review of Pharmacist-Managed Anemia CKD Clinics[1]

- Review of 16 VAMC clinics (2009)
- 572 patients with CKD over 6 months
- Pharmacist-based care
  - More likely to achieve target Hb level
  - Reduced ESA use by up to 36%
  - More likely to get a serum iron and TIBC (TSAT) test



CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; TIBC, total iron binding capacity; TSAT, transferrin saturation; VAMC, Veterans Affairs Medical Center.

1. Aspinall SL et al. *Am J Kidney Dis*. 2012;60:371-379.

Review of Pharmacist-Managed Anemia CKD Clinics[1] (Cont'd)

Retrospective longitudinal study comparing pharmacist-managed CKD to usual care (N = 101)

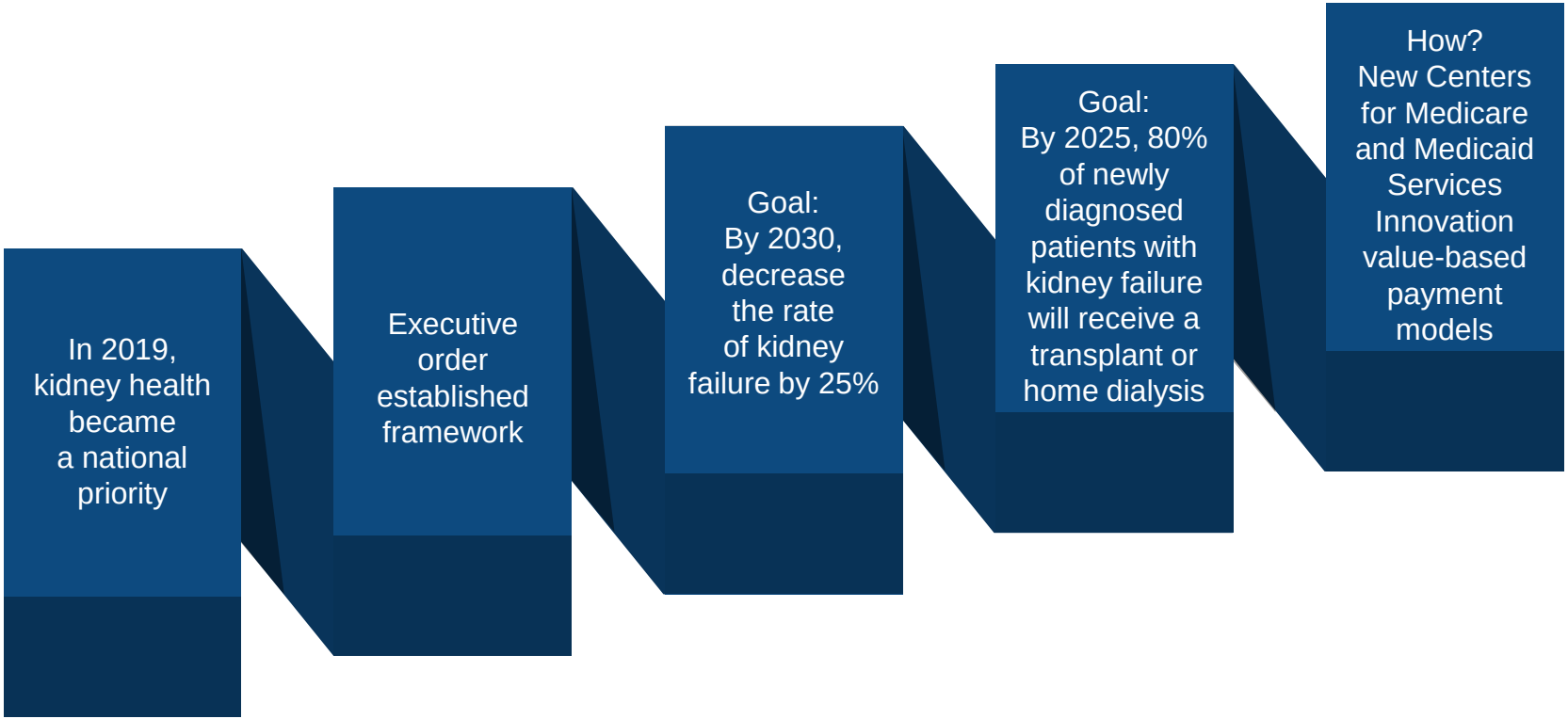
Improved outcomes in pharmacist vs usual care group

- 28 vs 41 days to achieve target Hb
- Iron parameter monitoring and iron therapy initiation better (75% vs 46%)
- 20% reduction in average weekly ESA dose
- $1,288/y annual savings per patient

CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin.

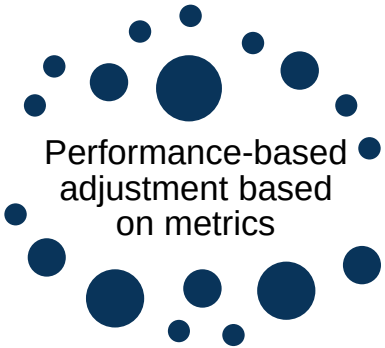
1. Debenito JM et al. *J Manag Care Spec Pharm*. 2014;20:715-720.

Advancing American Kidney Health (AAKH)[1]



1. Patel S et al. *Clin J Am Soc Nephrol.* 2019;14:1789-1791.

Value-Based Kidney Care Choices
Payment Model Incentives[1,2]



- Patient activation
- Depression remission and controlling BP
- Hospital and total per capita costs
- Future: delay kidney disease progression

Transplant bonus: keep patients and their kidneys healthy

Various levels of shared savings/losses

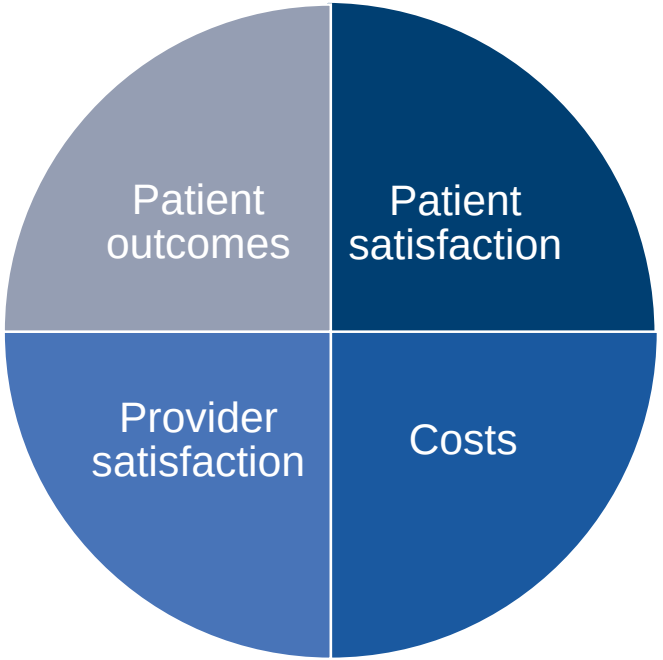
Encourages coordinated team care delivery

BP, blood pressure.

1. Garimella PS, Weiner DE. *J Am Soc Nephrol.* 2019;30:2282-2284. 2. Meaney CJ et al. *J Am Coll Clin Pharm*. 2020 Jul 23 [Epub ahead of print].

Pharmacists Can Enhance Nephrology Practices and Help Meet the Quadruple Aim[1]

- Allow nephrologists to see more patients with stage 4/5 CKD
- Improve patient activation and medication adherence
- Provide kidney disease education (KDE) and post-discharge home visits
- Utilize telehealth provisions



CKD, chronic kidney disease.

1. Meaney CJ et al. *J Am Coll Clin Pharm*. 2020 Jul 23 [Epub ahead of print].

AAKH Through Optimal Medication Management Initiative[1]

Vision

Every person with kidney disease receives optimal medication management through team-based care including a pharmacist to ensure their medications are safe, effective, and convenient for them to use

Mission

Engage pharmacists and key stakeholders to develop partnerships for optimal medication management in persons with kidney disease to improve health outcomes and reduce healthcare costs

AAKH, Advancing American Kidney Health.

1. Meaney CJ et al. *J Am Coll Clin Pharm*. 2020 Jul 23 [Epub ahead of print].

AAKH Through Optimal Medication Management Initiative (Cont'd)

Initiative Leaders
Wendy St. Peter, PharmD, FASN, FNKF, FCCP Rebecca Maxson, PharmD, BCPS

Sub-Initiative	Leaders
Nephrology Pharmacy Practice Standards	Katie Cardone, PharmD, BCACP, FCCP Marisa Battistella, BScPharm, PharmD
Nephrology Pharmacy Education Standards	Joanna Hudson, PharmD, BCPS, FCCP, FASN Calvin Meaney, PharmD, BCPS
Kidney Care Model Roadmap	Harold Manley, PharmD, FCCP, FASN Daniel E. Weiner, MD, MS, FASN
Stakeholder Engagement	Wendy St. Peter, PharmD, FCCP, FASN, FNKF Amy Barton Pai, PharmD

Want more information? Contact Wendy St. Peter: stpet002@umn.edu

AAKH, Advancing American Kidney Health.

Case Studies in CKD-Related Anemia: How Might HIF-PH Inhibitors Alter the Pharmacist's Role in Team-Based Care?

- **Tonya**
  - 54-year-old woman with longstanding HTN, T2DM, and stage 4 ND-CKD
  - Hb: 8.5 g/dL
  - Assure anemia-related drugs are safe, effective, and convenient to use
  - Use evidence-based approach (watch for KDIGO guideline updates)
  - Perform point-of-care Hb testing
  - Integrate pharmacist services into nephrology and primary care practices

- **Richard**
  - 67-year-old man with longstanding HTN, glomerulonephritis, and HD-CKD
  - Hb: 9.5 g/dL
  - HIF-PH inhibitors may reduce need for IV iron use
  - Assure anemia-related drugs are safe, effective, and convenient to use
  - Integrate pharmacist services within dialysis care team

Hb, hemoglobin; HD-CKD, hemodialysis-dependent chronic kidney disease; HTN, hypertension; IV, intravenous; KDIGO, Kidney Disease Improving Global Outcomes; ND-CKD, nondialysis-dependent chronic kidney disease; T2DM, type 2 diabetes mellitus.

Symposium Summary

- Anemia is a burdensome complication of CKD for individual patients, as well as the healthcare system
- HIF-PH inhibitors are oral treatments for CKD-related anemia and are noninferior to ESAs for raising Hb
- Emerging evidence suggests that some HIF-PH inhibitors may be safer than ESAs in terms of CV outcomes
- Clinical pharmacists play an increasingly important role in managing patients with CKD

CKD, chronic kidney disease; CV, cardiovascular; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; HIF-PH, hypoxia-inducible factor prolyl hydroxylase.

Audience Q&A

Steven Fishbane, MD
Chief, Division of Nephrology
Northwell Health
Great Neck, New York

Wendy L. St. Peter, Pharm.D, FCCP, FNKF, FASN
Professor, College of Pharmacy
University of Minnesota
Minneapolis, Minnesota

Go online to access full CPE information, including faculty disclosures.

Audience Q&A: Question 1

In the inpatient setting, intensivists refuse to use iron replacement therapy in patients with stage 4/5 CKD, even when getting EPO; they say it increases the risk of infection. UpToDate does list this risk with iron supplementation. Is this the case?

CKD, chronic kidney disease; EPO, epoetin alfa.

Audience Q&A: Question 2

What are the arguments that HIF-PH inhibitors would be cost effective in the ND-CKD arena?

HIF-PH: hypoxia-inducible factor prolyl hydroxylase; ND-CKD, nondialysis-dependent chronic kidney disease.

Audience Q&A: Question 3

Is the clinical advantage of HIF-PH inhibitors over ESAs that these agents do not increase the risk of CVD because of the difference in MOA?

CVD, cardiovascular disease; ESAs, erythropoiesis-stimulating agents; HIF-PH: hypoxia-inducible factor prolyl hydroxylase; MOA, mechanism of action.

Audience Q&A: Question 4

What are your thoughts on administering iron therapy every other day in comparison with twice or three times a day?

Audience Q&A: Question 5

For a patient with ESRD who is on dialysis with serum ferritin >1,000 mcg/L; TSAT <30%; Hb <10 g/dL, what management strategies would you recommend? And what strategies would you recommend if the serum ferritin is 5,000 mcg/L?

ESRD, end-stage renal disease, Hb, hemoglobin, TSAT, transferrin saturation.

Audience Q&A: Question 6

When would roxadustat be used to target higher Hb levels (more normalized) to examine reducing CV risks and better preservation of kidney function?

CV, cardiovascular; Hb, hemoglobin.