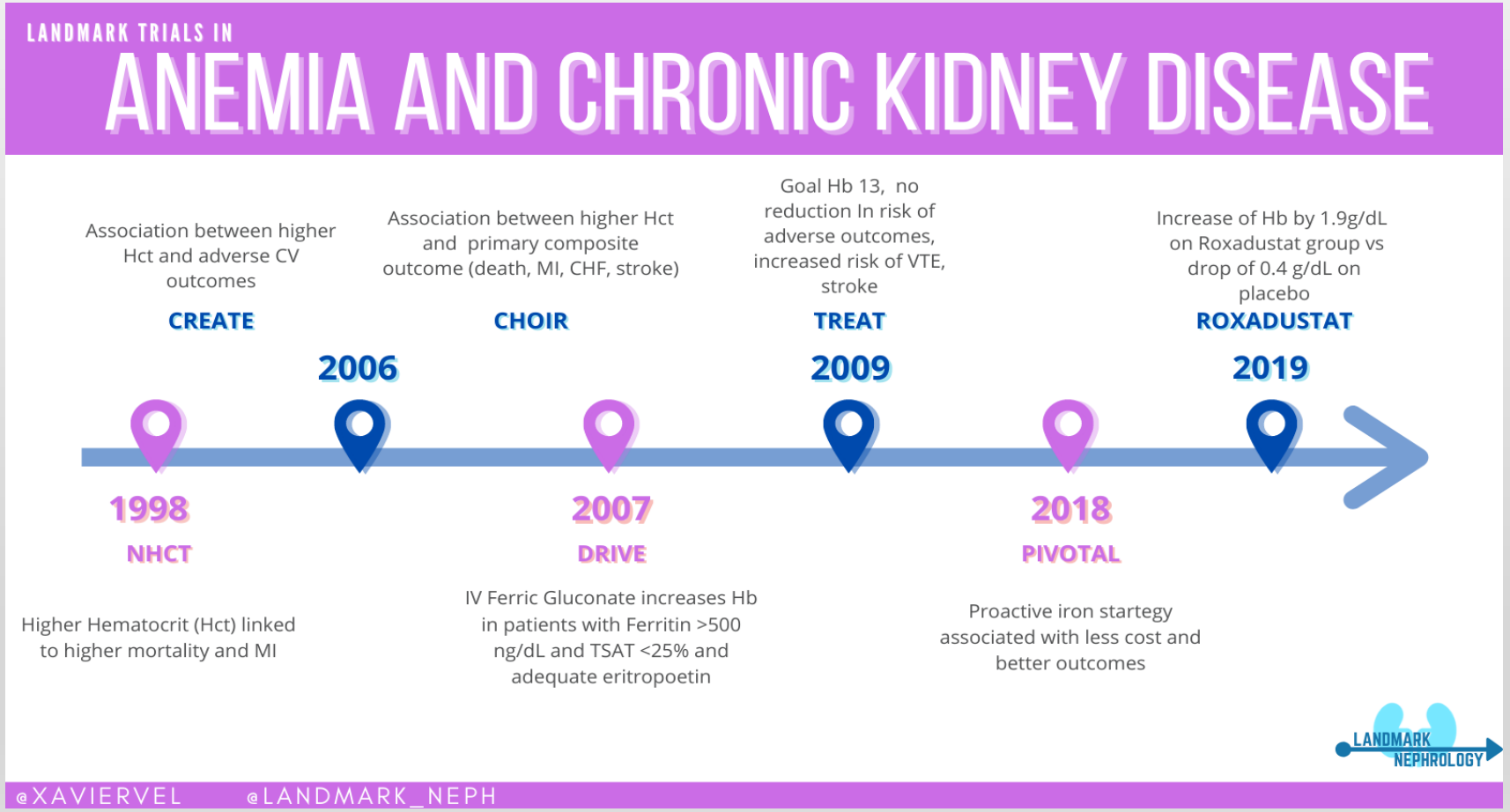
Ο πρώτος αναστολέας HIF- PHI. Από το Κλινικό πρόγραμμα στην κλινική πράξη

Γιώργος Σπανός
Νεφρολόγος - Επιμελητής Α'
ΓΝΘ “Γ. Παπανικολάου”

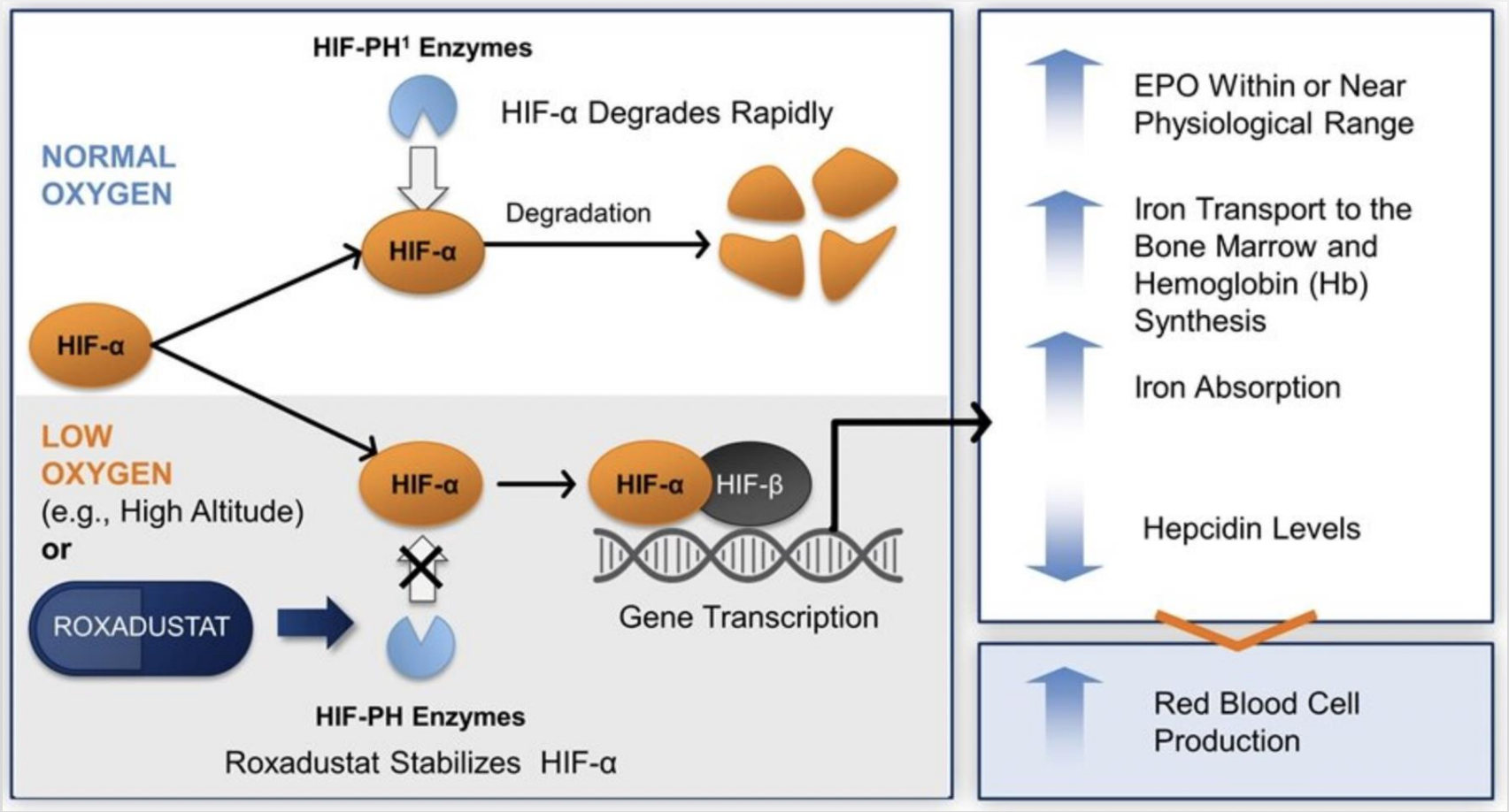
Disclaimer

Για την παρούσα διάλεξη έχω λάβει τιμητική αμοιβή από την εταιρία Astellas

HIF-PHIs Hypoxia-inducible factor prolyl hydroxylase inhibitors



HIF-PHIs Hypoxia-inducible factor prolyl hydroxylase inhibitors



Μελέτες Roxadustat

Table 8
Summary of all the 38 completed clinical trials related Roxadustat.

Sr No.	NCT Number	Interventions	Study Title	Conditions	Sponsor:
1	NCT04076943	Drug: Roxadustat	Evaluation of Efficacy and Safety of Roxadustat for the Treatment of Chemotherapy Induced Anemia Has Results	Chemotherapy Induced Anemia	• FibroGen•AstraZeneca • Astellas Pharma Inc
2	NCT04454879	Drug: Roxadustat	Different Doses of Roxadustat Treatment for Anemia in Peritoneal Dialysis Patients	• Renal Anemia	• FibroGen•AstraZeneca • Astellas Pharma Inc
3	NCT04484857	Drug: Roxadustat	Study of Roxadustat Conversion in Participants Receiving Stable ESA or as Initial Anemia Treatment in Hemodialysis Participants	• Anemia Associated With End Stage Renal Disease	FibroGen • AstraZeneca
4	NCT04410198	Drug: Roxadustat	Study of Roxadustat Conversion in Participants Receiving Stabe Erythropoiesis-Stimulating Agent (ESA) or as Initial Anemia Treatment in Chronic Dialysis Participants	• Anemia Associated With End Stage Renal Disease (ESRD)	• FibroGen • AstraZeneca
5	NCT04655027	Drug: Roxadustat Drug: rHuEPO	A Study to Investigate the Effect of Roxadustat Versus Recombinant Human Erythropoietin (rHuEPO) on Oral Iron Absorption in Chinese Patients with Anemia of Chronic Kidney Disease (CKD)	• Anemia of Chronic Kidney Disease	• AstraZeneca • Parexel
6	NCT02273726	Drug: Epoetin Alfa Drug: Roxadustat	Study to Evaluate the Efficacy and Safety of Roxadustat in the Treatment of Anemia in Participants with ESRD on Stable Dialysis	•CKD Anemia in Stable Dialysis Patients	• FibroGen • Astellas Pharma Europe B.V. • AstraZeneca
7	NCT02965040	Drug: Roxadustat	A Phase 1 Study of Roxadustat in Subjects with Different Degrees of Renal Function	• Normal Renal Function •Impaired Renal Function	• Astellas Pharma Europe B.V. • FibroGen •Astellas Pharma Inc
8	NCT04059913	Drug: Roxadustat	Evaluate the Efficacy and Safety of Multiple Roxadustat Dosing Regimens for the Treatment of Anemia in Dialysis Participants with Chronic Kidney Disease	CKD Anemia in Dialysis Participants	• FibroGen
9	NCT03960489	Drug: Roxadustat	A Study to Assess the Relative Bioavailability of Roxadustat Following a Single Dose of Pediatric Azo Dye-free Tablet Formulation and Pediatric Azo Dye-free Mini-tablet Formulation Compared to a Single Dose of Azo Dye-containing Tablet Formulation in Healthy Adult Subjects	• Healthy Adult Subjects	• Astellas Pharma Global Development, Inc. • FibroGen •Astellas Pharma Inc
10	NCT01887600	Drug: Roxadustat Drug: Placebo	Roxadustat in the Treatment of Anemia in Chronic Kidney Disease Patients Not Requiring Dialysis	Anemia in Chronic Kidney Disease in non-dialysisPatients	• Astellas Pharma Europe B.V. • FibroGen • Astellas Pharma Inc
11	NCT02052310	Drug: Roxadustat Drug: Epoetin Alfa	Safety and Efficacy Study of Roxadustat (FG-4592) for the Treatment of Anemia in End-Stage Renal Disease (ESRD) Newly Initiated Dialysis Participants	Anemia in Incident Dialysis Patients	• FibroGen • Astellas Pharma Europe B.V. •AstraZeneca
12	NCT01630889	Drug: Roxadustat	Open-Label Extension Study for the Long-Term Efficacy and Safety of Roxadustat in Participants with Dialysis and Non-Dialysis Chronic Kidney Disease	• Chronic Kidney Disease • End Stage Renal Disease •Anemia	• FibroGen •AstraZeneca • Astellas Pharma Inc
13	NCT02161224	Drug: FG-4592	A Study to Investigate the Exposure and Safety and Tolerability of a Single Dose of FG-4592 in Subjects With Moderately Diminished Liver Function Compared to Those with Normal Liver Function	• PK of FG-4592 • Hepatic Insufficiency • Healthy Subjects	• Astellas Pharma Europe B.V. • FibroGen •Astellas Pharma Inc
14	NCT02021318	Drug: Roxadustat Drug: Darbepoetin alfa	Roxadustat in the Treatment of Anemia in Chronic Kidney Disease (CKD) Patients, Not on Dialysis, in Comparison to Darbepoetin Alfa	• Anemia in Chronic Kidney Disease in non-dialysis Patients	• Astellas Pharma Europe B.V. •FibroGen • Astellas Pharma Inc
15	NCT02161796	Drug: FG-4592 Drug: Placebo	A Study to Evaluate the Dose proportionality and Effects of FG-4592 in Healthy Young and Elderly Male and Female Subjects	• PK for FG-4592 • Healthy Subjects	• Astellas Pharma Europe B.V. •FibroGen • Astellas Pharma Inc
16	NCT02278341	Drug: Roxadustat	Roxadustat in the Treatment of Anemia in End Stage Renal Disease (ESRD) Patients on Stable Dialysis	Anemia • End Stage Renal	• Astellas Pharma Europe B.V.

(continued on next page)

Table 8 (*continued*)

Sr No.	NCT Number	Interventions	Study Title	Conditions	Sponsor:
		Drug: Epoetin alfa Drug: Darbepoetin alfa Drug: Iron		Disease (ESRD)	• FibroGen • Astellas Pharma Inc
17	NCT01750190	Drug: Roxadustat Drug: Placebo	A Study of Roxadustat for the Treatment of Anemia in Participants With Chronic Kidney Disease and Not Receiving Dialysis	CKD Anemia	• FibroGen • Astellas Pharma Europe B.V. • AstraZeneca
18	NCT01244763	Drug: Roxadustat	Study of Roxadustat in Non- Dialysis Chronic Kidney Disease Participants with Anemia	• Chronic Kidney Disease •Anemia	• FibroGen • Astellas Pharma Inc
19	NCT02252731	Drug: Warfarin Drug: FG-4592	A Study to Evaluate the Effects of Multiple Doses of FG-4592 on the Exposure, Safety and Tolerability and Effect of Warfarin in Healthy Subjects	Pharmacokinetics of FG-4592 • Healthy Subjects	Astellas Pharma Europe B.V. •FibroGen • Astellas Pharma Inc
20	NCT02174731	Drug: Roxadustat Drug: Epoetin alfa	Safety and Efficacy Study of Roxadustat to Treat Anemia in Patients with Chronic Kidney Disease, on Dialysis.	• Anemia	• AstraZeneca • FibroGen
21	NCT01147666	Drug: Roxadustat Drug: Epoetin Alfa Other: Placebo	Study of Roxadustat (FG-4592) in Participants with End-Stage Renal Disease Receiving Maintenance Hemodialysis	End Stage Renal Disease • Anemia	• FibroGen • AstraZeneca •Astellas Pharma Inc
22	NCT02174627	Drug: Roxadustat Drug: Placebo	Safety and Efficacy Study of Roxadustat to Treat Anemia in Patients with Chronic Kidney Disease (CKD), Not on Dialysis	• Anemia	AstraZeneca • FibroGen
23	NCT00761657	Drug: Roxadustat Drug: Placebo	Phase 2 Study of Roxadustat in Participants with Anemia and Chronic Kidney Disease Not Requiring Dialysis	• Chronic Kidney Disease •Anemia	• FibroGen • Astellas Pharma Inc
24	NCT01414075	Drug: Roxadustat Drug: Oral Iron Drug: IV Iron	Study of Roxadustat (FG-4592) to Correct Anemia in Newly Initiated Dialysis Participants Not on Erythropoiesis-Stimulating Agent Treatment	• Dialysis • Anemia	• FibroGen • Astellas Pharma Inc
25	NCT01376063	Drug: FG-4592	Study to Investigate the Interaction Between FG-4592 and Rosiglitazone in Healthy Adult Subjects	• Healthy Adult Subjects	• FibroGen
26	NCT01596855	Drug: FG-4592 Drug: Epoetin Alfa	Study of FG-4592 in Subjects with End-Stage Renal Disease Receiving Maintenance Hemodialysis in China	• Anemia in the End Stage Renal Disease	• FibroGen • Ruijin Hospital
27	NCT01599507	Drug: FG-4592 Drug: Placebo	Study of FG-4592 in Subjects with Chronic Kidney Disease in China	Anemia in Chronic Kidney Disease	• FibroGen
28	NCT02652806	Drug: FG-4592 Drug: Epoetin Alfa	FG-4592 for Treatment of Anemia in Subjects with Chronic Kidney Disease	• Anemia	• FibroGen
29	NCT02652819	Drug: FG-4592 Drug: Placebo	FG-4592 for Treatment of Anemia in Subjects with Chronic Kidney Disease Not on Dialysis	• Anemia	• FibroGen
30	NCT02988973	Drug: Roxadustat Drug: DA	A Study of Intermittent Oral Dosing of ASP1517 in Non-Dialysis Chronic Kidney Disease Patients with Anemia	Chronic Kidney Disease	• Astellas Pharma Inc •FibroGen
31	NCT02780726	Drug: Roxadustat	A Study of Intermittent Oral Dosing of ASP1517 in Peritoneal Dialysis Chronic Kidney Disease Patients With Anemia	Peritoneal Dialysis Chronic Kidney Disease Patients With Anemia	• Astellas Pharma Inc •FibroGen
32	NCT02780141	Drug: Roxadustat	A Study of Intermittent Oral Dosing of ASP1517 in Erythropoiesis Stimulating Agent (ESA)-Naive Hemodialysis Chronic Kidney Disease Patients with Anemia	ESA-naive Hemodialysis Chronic Kidney Disease Patients With Anemia	• Astellas Pharma Inc • FibroGen
33	NCT02964936	Drug: Roxadustat	A Study of Intermittent Oral Dosing of ASP1517 in ESA untreated Chronic Kidney Disease Patients with Anemia	• Chronic Kidney Disease	Astellas Pharma Inc •FibroGen
34	NCT02779764	Drug: Roxadustat	A Long-Term Study of Intermittent Oral Dosing of ASP1517 in Hemodialysis Chronic Kidney Disease Patients with Anemia Converted From Erythropoiesis Stimulating Agent (ESA) Treatment	Hemodialysis Patients With Renal Anemia	Astellas Pharma Inc • FibroGen

(continued on next page)

Table 8 (*continued*)

Sr No.	NCT Number	Interventions	Study Title	Conditions	Sponsor:
35	NCT01083888	Drug: Roxadustat	ASP1517 Pharmacokinetics Study in Anemia Patients on Hemodialysis	• Anemia • Hemodialysis • Renal Impairment	Astellas Pharma Inc
36	NCT02952092	Drug: Roxadustat Drug: Darbepoetin alfa	A Study of Intermittent Oral Dosing of ASP1517 in Hemodialysis Chronic Kidney Disease Patients with Anemia	• Hemodialysis Chronic Kidney Disease Patients With Anemia Healthy Volunteers	• Astellas Pharma Inc • FibroGen Astellas Pharma Inc
37	NCT00978198	Drug: ASP1517 (Roxadustat) Drug: Placebo	Safety, Tolerability, and Pharmacokinetic Study of ASP1517 in Healthy Non-elderly Male Volunteers		
38	NCT01888445	Drug: Roxadustat Drug: darbepoetin alfa	A Study to Investigate the Effect of ASP1517 After Intermittent Oral Dosing in Dialysis Chronic Kidney Disease Patients with Anemia Compared With Darbepoetin as a Reference Drug	• Renal Anemia Associated With Chronic Renal Failure (CRF)	Astellas Pharma Inc

Mahajan R et al. Heliyon 2023 Jun 1;9(6):e16595

Μελέτες Roxadustat

	Non Dialysis CKD	Incident HD CKD*	Stable HD CKD†
ESA-untreated patients	Astellas; Europe ALPS (N = 594)[1,2] AstraZeneca; Global OLYMPUS (N = 2760)[2,3] FibroGen; Global ANDES (N = 916)[2,4] Astellas; Europe DOLOMITES (N = 616)[2,5]	FibroGen; Global HIMALAYAS (N = 1043)[2,6]	
ESA-treated patients		AstraZeneca; Global ROCKIES (N = 2101)[2,7] Astellas; Europe PYRENEES (N = 834)[2,8] FibroGen; USA SIERRAS (N = 741)[2,9]	

Placebo controlled

ESA controlled

1. Shutov E, et al. Nephrol Dial Transplant. 2021;gfab057; 2. EVRENZO SmPC August 2021; 3. Fishbane S, et al. J Am Soc Nephrol. 2021;32(3):737–755; 4. Coyne DW, et al. Kidney Int Rep. 2020;6(3):624–635; 5. Barratt J, et al. Nephrol Dial Transplant. 2021;gfab191; 6. Provenzano R, et al. Nephrol Dial Transplant. 2021;gfab051; 7. ClinicalTrials.gov. NCT02174731. (Accessed: July 2021); 8. ClinicalTrials.gov. NCT02278341. (Accessed: July 2021); 9. Charytan C, et al. Kidney Int Rep. 2021;6(7):1829–1839.

Alps

RCT

Roxadustat for anemia in non-dialysis chronic kidney disease patients

Background

Erythropoietin-stimulating agents and iron therapy are the standard treatment for CKD-related anaemia until novel therapy, HIF-PHIs

Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) effective in treating CKD anaemia

Methods

European multicenter double-blind trial

Age ≥ 18

CKD 3–5 (non-dialysis) n = 594

Roxadustat or placebo × 3 weekly

Randomization 2:1

Roxadustat n = 391

Placebo n = 203

	Primary endpoints	Results (roxadustat vs. placebo)
EMA	Hemoglobin response at 24 weeks	OR 34.74 (20.48–58.93) $p < 0.001$
FDA	Mean changes in hemoglobin over weeks 28–52	+1.692 g/dL (1.52–1.86) $p < 0.001$

Safety profile

Adverse events	87.7% vs. 86.7%

Conclusion

Roxadustat was well tolerated and superior to placebo for the treatment of CKD-related anemia in patients not on dialysis

NEPHROLOGY DIALYSIS TRANSPLANTATION

Shutov E., et al. NDT (2021)
@NDTSocial

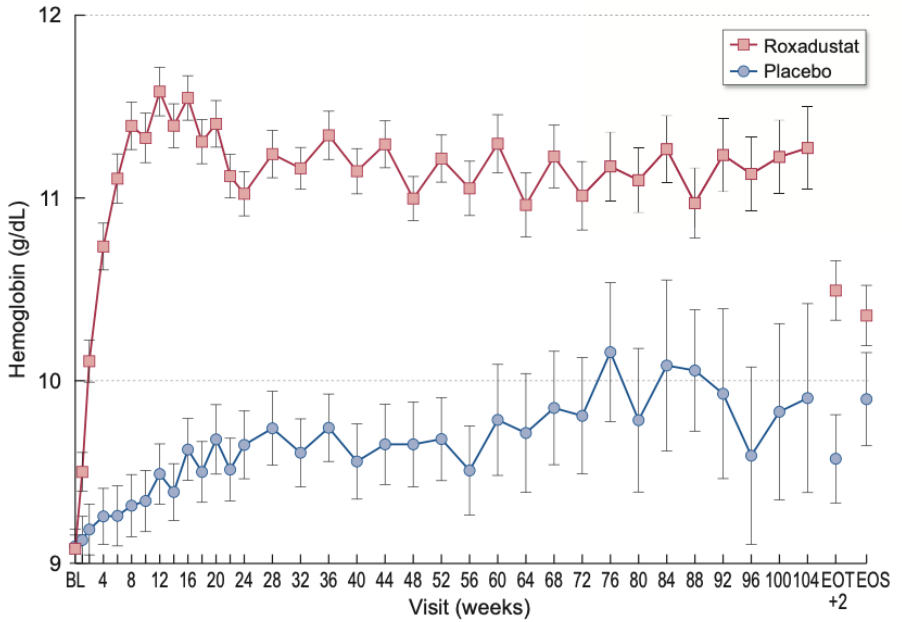


FIGURE 3: Mean Hb over time regardless of rescue therapy use (all randomized patients).

Nephrol Dial Transplant (2021) 36: 1629–1639

Olympus

Roxadustat for Treating Anemia in Patients with CKD Not on Dialysis: Results from the Randomized Phase 3 Study

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

METHODS

2781 patients
- Not on dialysis
- CKD stages 3–5
- Hb <10.0 g/dL

1:1 (R)

70 mg TIW oral roxadustat n=1393

70 mg TIW oral placebo n=1388

Doses were titrated to achieve and maintain Hb 11±1 g/dL

OUTCOMES

Change from baseline in Hb over weeks 28–52

Roxadustat: 1.75 g/dL

Placebo: 0.40 g/dL

Difference +1.35 g/dL with roxadustat versus placebo (*P*<0.001)

Efficacy was independent of:
- Iron repletion
- Evidence of inflammation

Need for RBC transfusion

↓ 63%

With roxadustat versus placebo (*P*<0.001)

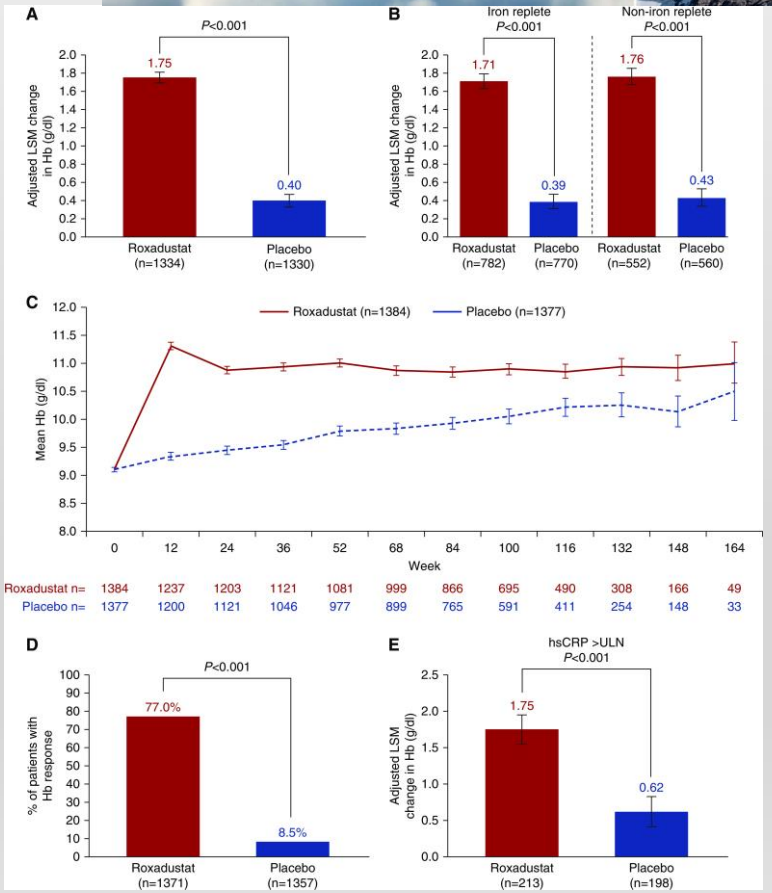
AEs were similar

Roxadustat: 89.8% Placebo: 88.3%

Conclusion

Roxadustat effectively increased Hb in patients with NDD-CKD and reduced the need for RBC transfusion with an adverse event profile comparable to placebo

doi: 10.1681/ASN.2020081150



J Am Soc Nephrol. 2021 Mar; 32(3): 737–755.

Andes

Roxadustat for Chronic Kidney Disease-Related Anemia in Non-Dialysis Patients

PATIENTS

Eligibility: aged ≥18 y, CKD Stage 3–5, not on dialysis

Randomization (2:1)

- Roxadustat (n=616)
- Placebo (n=306)

PRIMARY ENDPOINTS

US: mean (SD) change in hemoglobin over Weeks 28–52

RESULTS

Roxadustat: 2.00 (0.95) g/dL
Placebo: 0.16 (0.90) g/dL
Difference: 1.85 g/dL (*P*<0.0001)

EU: patients (%) with a hemoglobin response (Week 24)

Roxadustat: 86.0%
Placebo: 6.6%
OR: 77.6 (*P*<0.0001)

KEY SECONDARY ENDPOINT

Patients (%) receiving rescue therapy at Week 52

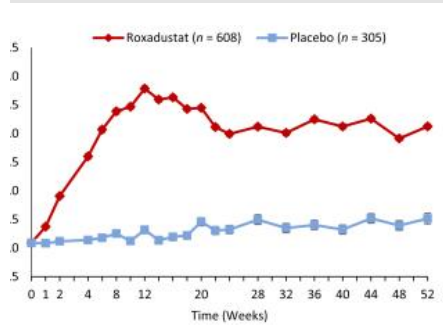
Roxadustat: 8.9%
Placebo: 28.9%
HR: 0.19 (*P*<0.0001)

HR=hazard ratio, OR=odds ratio, SD=standard deviation

CONCLUSION:
In this Phase 3 study, roxadustat corrected and maintained hemoglobin levels, and was well tolerated in patients with CKD-related anemia not on dialysis.

KI REPORTS
KIReports.org

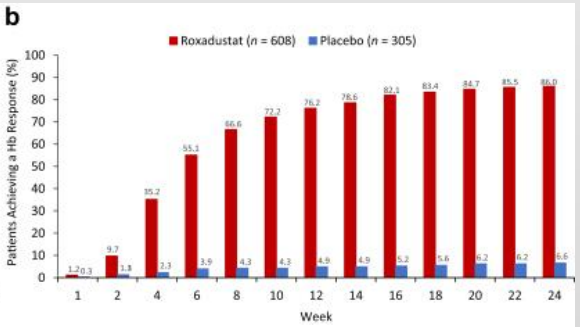
Coyne et al, 2021



anges in Hb (g/dl) from BL over W28–52 regardless of rescue therapy (ITT)

	Roxadustat		Placebo		Treatment
	Hb (O + I)	Hb Δ from BL	Hb (O + I)	Hb Δ from BL	Difference†
*	9.1 (0.8)		9.1 (0.7)		
28–52	11.1 (0.7)	2.00 (0.95)	9.2 (1.1)	0.16 (0.90)	
M (SE)		2.02 (0.04)		0.17 (0.05)	1.85 (0.06)
5% CI)		(1.95, 2.09)		(0.07, 0.27)	(1.74, 1.97)
alue					<0.0001

b



Patients Achieving a Hb Response during first 24 weeks of treatment, censoring for rescue therapy (FAS)

	Roxadustat	Placebo	Difference (95% CI)	OR (95% CI)‡ [Roxadustat/Placebo]
Patients Achieving Response†, n (%)	523 (86.0)	20 (6.6)	79.5 (75.6, 83.4)	77.6 (44.7, 134.5)
(95% CI)§	(83.0, 88.7)	(4.1, 9.9)		
P-value‖				<0.0001

Kidney Int Rep. 2020 Dec 5;6(3):624-635.

Non-HD (vs placebo)

Efficacy and Cardiovascular Safety of Roxadustat for Treatment of Anemia in Patients with Non–Dialysis-Dependent CKD
Pooled Results of Three Randomized Clinical Trials

Robert Provenzano,[1] Lynda Szczech,[2] Robert Leong,[2] Khalil G. Saikali,[2] Ming Zhong,[2] Tyson T. Lee,[2] Dustin J. Little,[3] Mark T. Houser,[3] Lars Frison,[4] John Houghton,[3] and Thomas B. Neff[2,a]

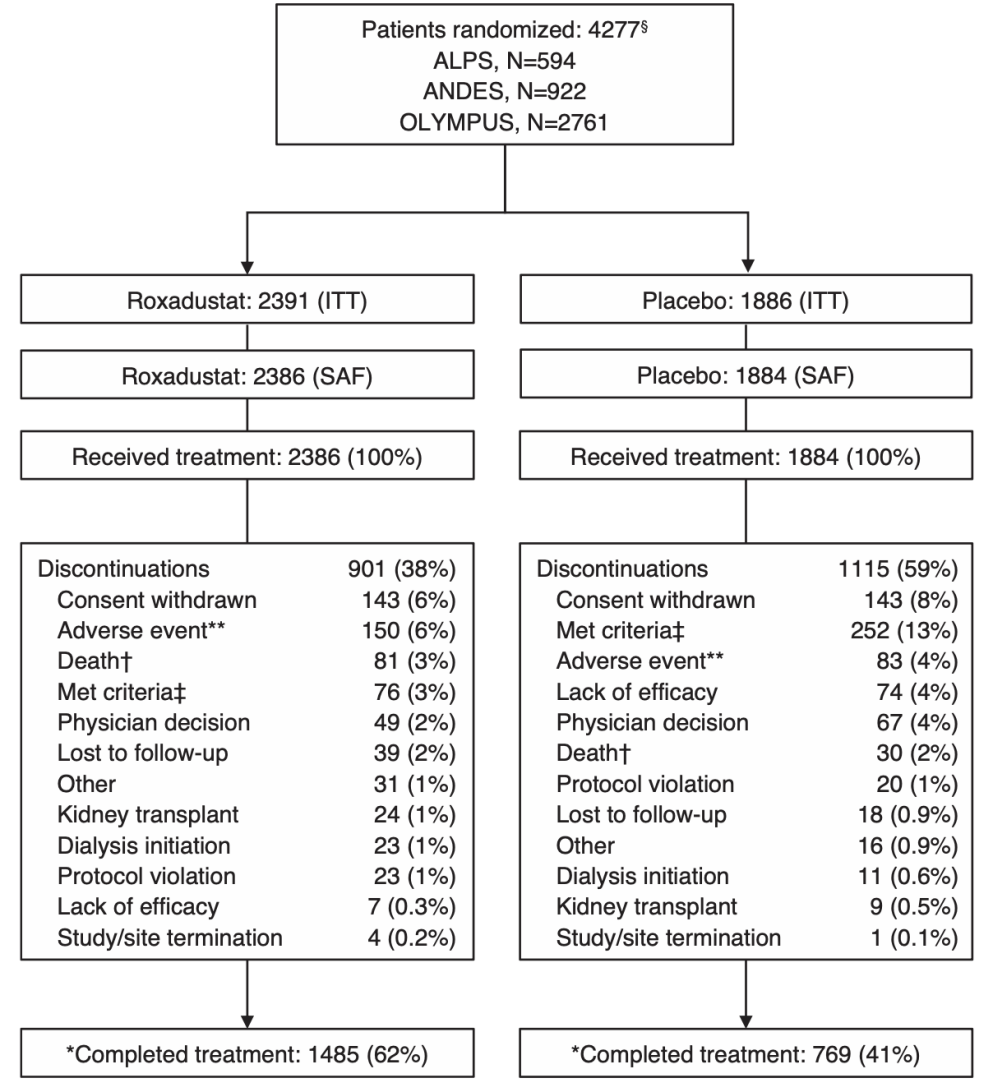


Table 1. Baseline characteristics of participants in three phase 3 studies of roxadustat with non–dialysis-dependent CKD (ITT)

Characteristics	Roxadustat (n=2391)	Placebo (n=1886)
Age (yr), mean (SD)[a]	62 (14)	63 (14)
Male sex, *n* (%)	974 (41)	832 (44)
Weight (kg), mean (SD)	71 (18)	71 (19)
Hemoglobin (g/dl), mean (SD)	9.1 (0.7)	9.1 (0.7)
<8.0, *n* (%)	204 (9)	164 (9)
≥8.0, *n* (%)	2187 (92)	1722 (91)
eGFR (ml/min per 1.73 m^2), mean (SD)	20 (12)	20 (12)
<10.0, *n* (%)	481 (20)	359 (19)
10.0 to <15.0, *n* (%)	526 (22)	452 (24)
15.0 to <30.0, *n* (%)	954 (40)	724 (38)
≥30.0, *n* (%)	430 (18)	351 (19)
hs-CRP (mg/L), mean (SD)[b]	7.4 (17.4)	7.2 (16.7)
Median (min–max)	2.2 (0.1–338)	2.2 (0.1–187)
Greater than upper limit of normal, *n* (%)	526 (22)	357 (19)
LDL cholesterol (mg/dl), mean (SD)	99 (44)	95 (42)
Iron repletion status, *n* (%)		
Ferritin ≥100 ng/ml and TSAT ≥20%	1433 (60)	1127 (60)
Diabetes mellitus, *n* (%)	1337 (56)	1096 (58)

ITT, intention-to-treat population; hs-CRP, high-sensitivity C-reactive protein; min, minimum; max, maximum; TSAT, transferrin saturation.
[a]Age was calculated in years from birth date to date of informed consent or first-dose date.
[b]Upper limit of normal for hs-CRP was defined as 4.6 mg/l.

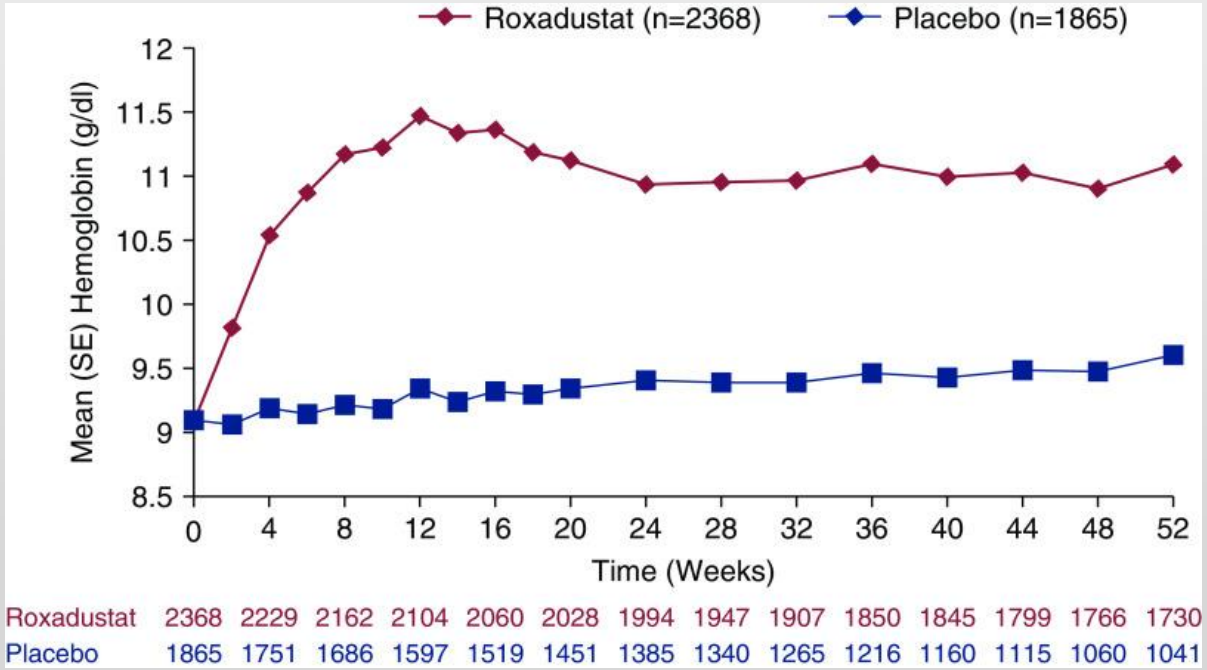
NDD pool vs placebo
ALPS
ANDES
OLYMPUS

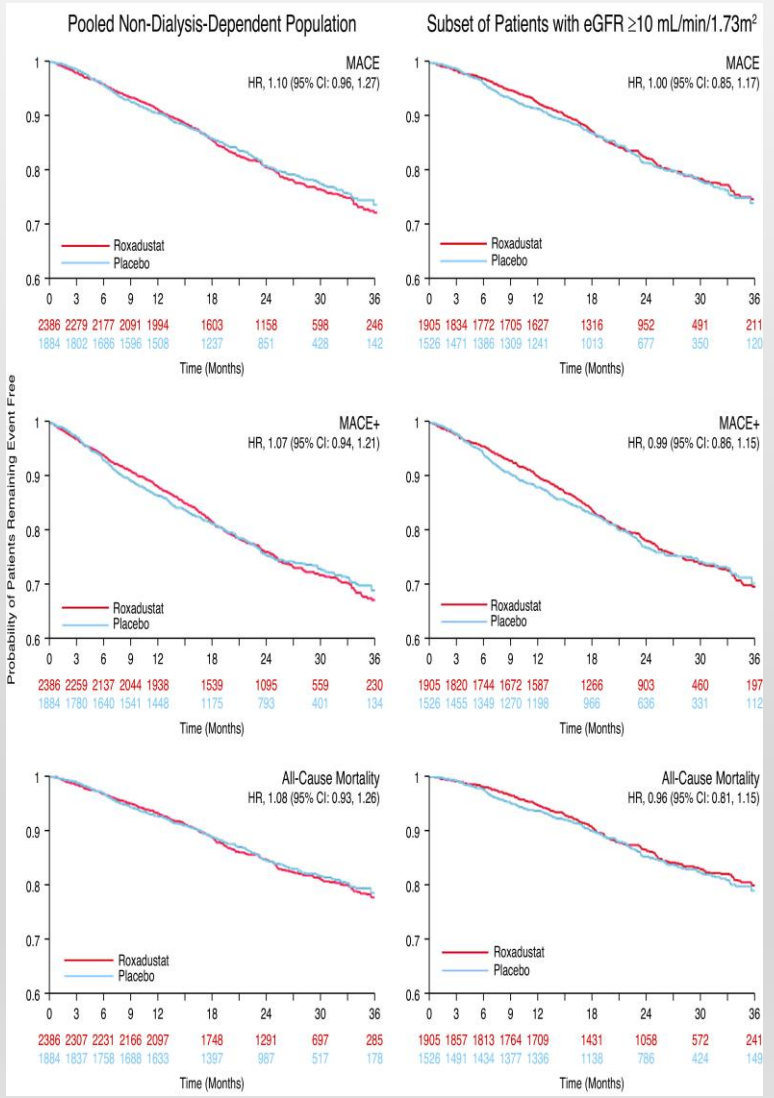
Clin J Am Soc Nephrol. 2021 Aug;16(8):1190-1200.

Non-HD (vs placebo)

Efficacy and Cardiovascular Safety of Roxadustat for Treatment of Anemia in Patients with Non–Dialysis-Dependent CKD
Pooled Results of Three Randomized Clinical Trials

Robert Provenzano,[1] Lynda Szczech,[2] Robert Leong,[2] Khalil G. Saikali,[2] Ming Zhong,[2] Tyson T. Lee,[2] Dustin J. Little,[3] Mark T. Houser,[3] Lars Frison,[4] John Houghton,[3] and Thomas B. Neff[2,a]





NDD pool vs placebo
ALPS
ANDES
OLYMPUS

Clin J Am Soc Nephrol. 2021 Aug;16(8):1190-1200.

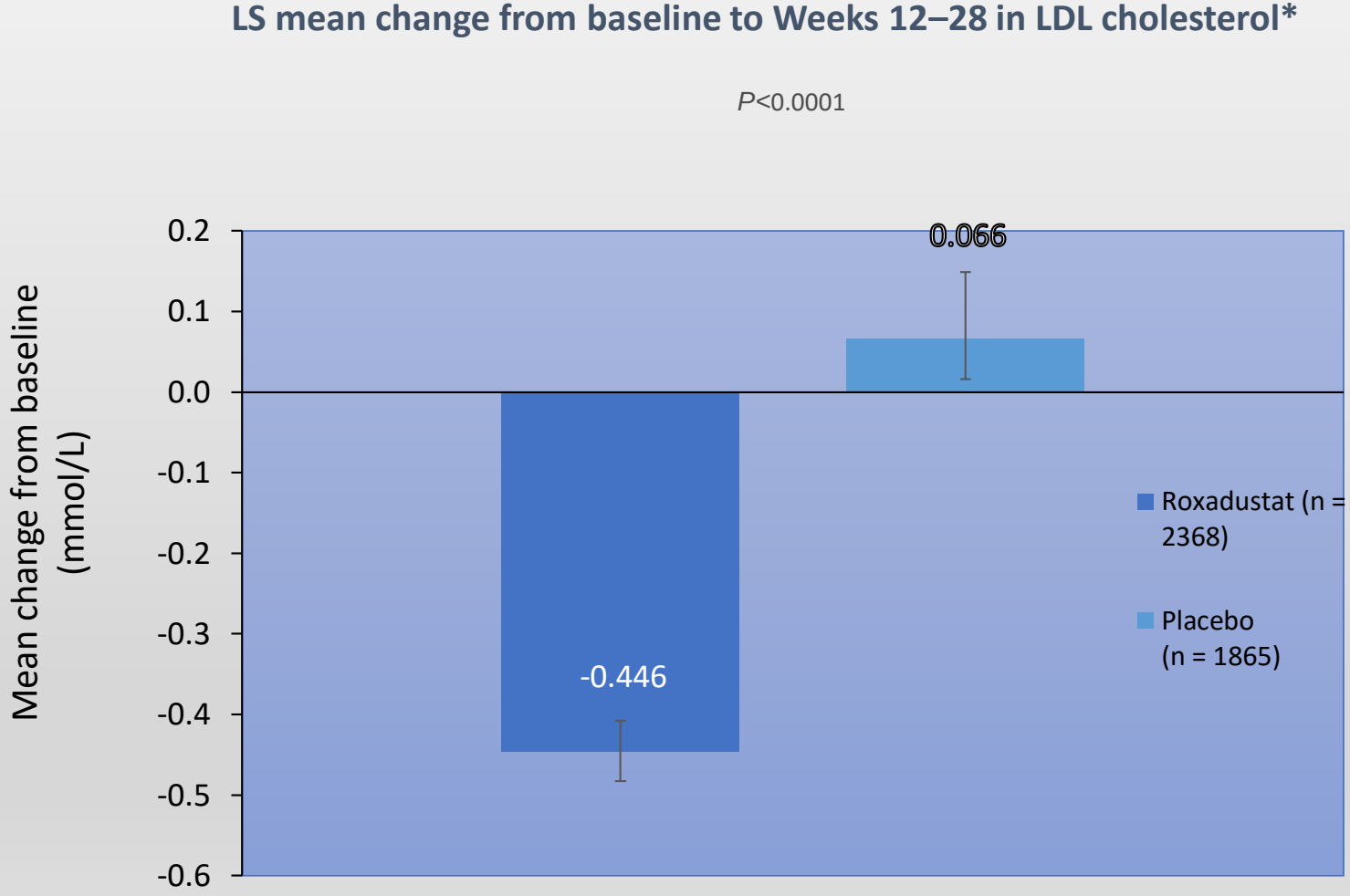
Non-HD (vs placebo)

Efficacy and Cardiovascular Safety of Roxadustat for Treatment of Anemia in Patients with Non–Dialysis-Dependent CKD
Pooled Results of Three Randomized Clinical Trials

Robert Provenzano,[1] Lynda Szczech,[2] Robert Leong,[2] Khalil G. Saikali,[2] Ming Zhong,[2] Tyson T. Lee,[2] Dustin J. Little,[3] Mark T. Houser,[3] Lars Frison,[4] John Houghton,[3] and Thomas B. Neff[2,a]

NDD pool vs placebo
ALPS
ANDES
OLYMPUS

LS mean change from baseline to Weeks 12–28 in LDL cholesterol*



Clin J Am Soc Nephrol. 2021 Aug;16(8):1190-1200.

Dolomites

RCT

Roxadustat for the treatment of anaemia in chronic kidney disease patients not on dialysis (DOLOMITES)

Background

Erythropoietin-stimulating agents are the standard treatment for anaemia in CKD

Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) effective in treating CKD anaemia

Methods

European: Multicentre, randomised, open-label

18+ Age ≥ 18 years
CKD 3–5 (non-dialysis)

Baseline Hb ≤ 10.5 g/dL

Hb targets over 104 weeks

Correction Hb levels to ≥ 11.0 g/dL and Hb change from baseline ≥ 1.0 g/dL

Maintenance Hb levels 10.0–12.0 g/dL

Results

1:1

	Primary endpoint (per protocol set)	Safety profile (safety analysis set) ⚠	
	Hb response week 24	Adverse events (TEAEs)	MACE
Roxadustat n = 323	89.5% (85.4–92.8)	91.6%	11.8%
Dose titrated to Hb target	Non-inferior		HR 0.81 (0.52, 1.25)
Darbepoetin alfa n = 293	78.0% (72.6–82.8)	92.5%	14.0%

Hb response definition: Baseline Hb > 8 g/dL: Hb ≥ 11.0 g/dL and Δ Hb ≥ 1.0 g/dL
Baseline Hb ≤ 8 g/dL: Δ Hb ≥ 2.0 g/dL

MACE: major adverse cardiovascular event

Secondary endpoints

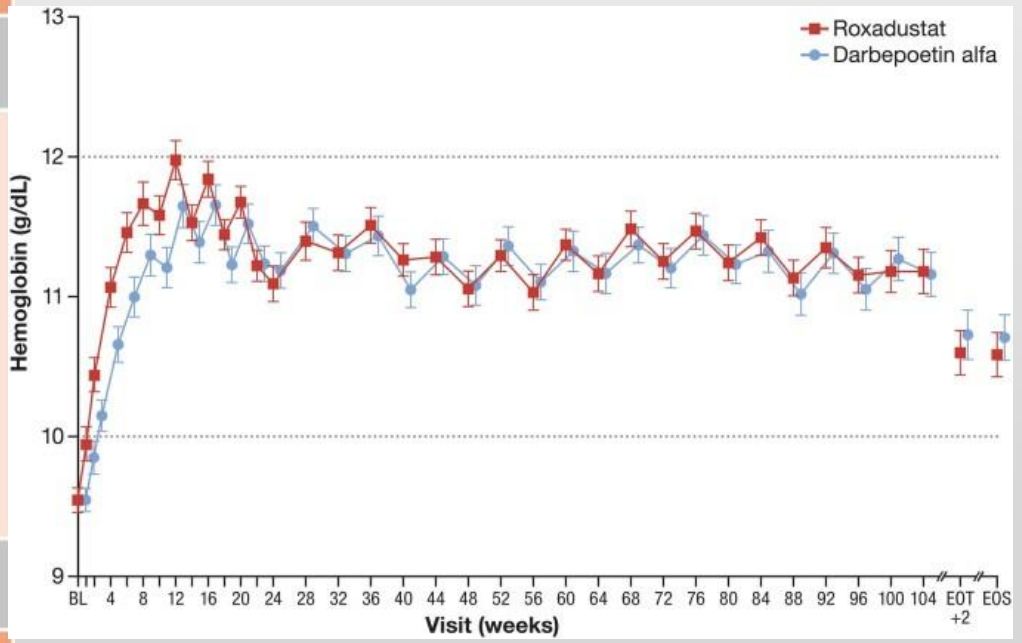
ΔLDL-C
BL to weeks 12–28
Superior
−0.403 mmol/L
(−0.510, −0.296)

Time to use of IV iron
weeks 1–36
Superior
HR 0.45
(0.26, 0.78)

Conclusion

Roxadustat was non-inferior to darbepoetin alfa in the treatment of anaemia in CKD patients not on dialysis. Roxadustat maintained haemoglobin levels for up to 2 years.

Barratt J., et al. NDT (2021)
@NDTSocial



Nephrol Dial Transplant (2021) 36:1616–1628

Himalayas

Randomized Clinical Trial

Roxadustat for Anemia in Patients with End-Stage Renal Disease Incident to Dialysis

Methods

1043 patients
- On dialysis for 2 weeks to ≤4 months prior to randomization
- Hb ≤ 10.0 g/dL
- No ESA for > 3 weeks within preceding 12 weeks

1:1 R

70 mg or 100 mg TIW oral roxadustat
n=522
Dose titrated to Hb 11±1 g/dL

Parenteral epoetin alfa
n=521
Dosed per local prescribing information

Outcomes

Mean change from baseline in Hb over weeks 28–52

Roxadustat	Epoetin alfa
2.57 g/dL	2.36 g/dL

Difference +0.18 g/dL with roxadustat vs. epoetin alfa
P=0.0005*
*For superiority testing

AE rates were comparable between treatment groups

Hb response† during first 24 weeks without rescue therapy

Roxadustat	Epoetin alfa
88.2%	84.4%

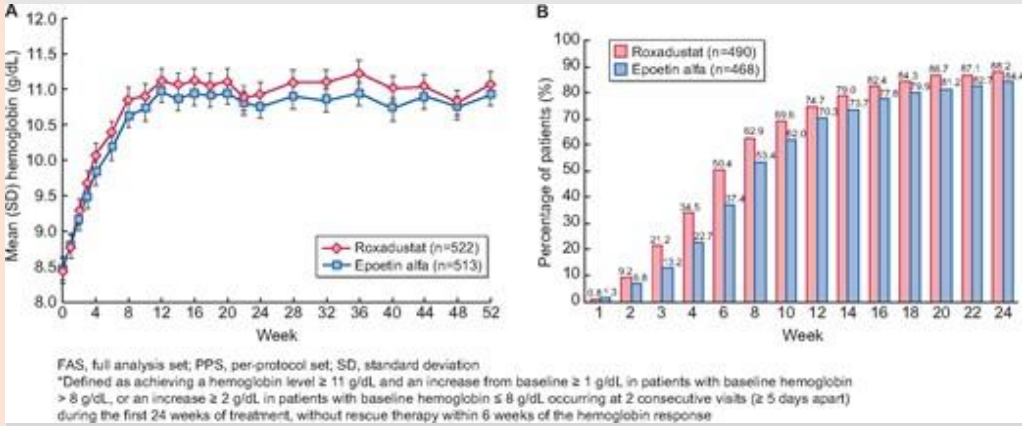
Roxadustat was non-inferior to epoetin alfa

†Hb response defined as Hb ≥ 11.0 g/dL and an increase of ≥ 1.0 g/dL in patients with baseline > 8.0 g/dL, or ≥ 2.0 g/dL in patients with baseline ≤ 8.0 g/dL

Conclusion

Roxadustat was efficacious in correcting and maintaining hemoglobin levels compared with epoetin alfa. Roxadustat had an acceptable safety profile.

Provenzano R., et al. NDT (2021)
@NDTSocial



FAS, full analysis set; PPS, per-protocol set; SD, standard deviation
*Defined as achieving a hemoglobin level ≥ 11 g/dL and an increase from baseline ≥ 1 g/dL in patients with baseline hemoglobin > 8 g/dL, or an increase ≥ 2 g/dL in patients with baseline hemoglobin ≤ 8 g/dL occurring at 2 consecutive visits (≥ 5 days apart) during the first 24 weeks of treatment, without rescue therapy within 6 weeks of the hemoglobin response

Nephrol Dial Transplant (2021) 36:1616–1628

Rockies

Roxadustat Versus Epoetin Alfa for Treating Anemia in Patients with Chronic Kidney Disease on Dialysis: Results from the Randomized Phase 3 ROCKIES Study

JASN® JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

METHODS

2133 patients
- On dialysis for ≥2 weeks
- Hb <10 g/dL if ESA-untreated **or** Hb <12 g/dL if ESA-treated

R 1:1

70–200 mg TIW oral roxadustat
n=1068
Dose titrated to Hb 11±1 g/dL

Parenteral epoetin alfa
n=1065
Per local prescribing information

OUTCOMES

Mean change from baseline in Hb over weeks 28–52

Roxadustat:	Epoetin alfa:
0.77 g/dL	0.68 g/dL

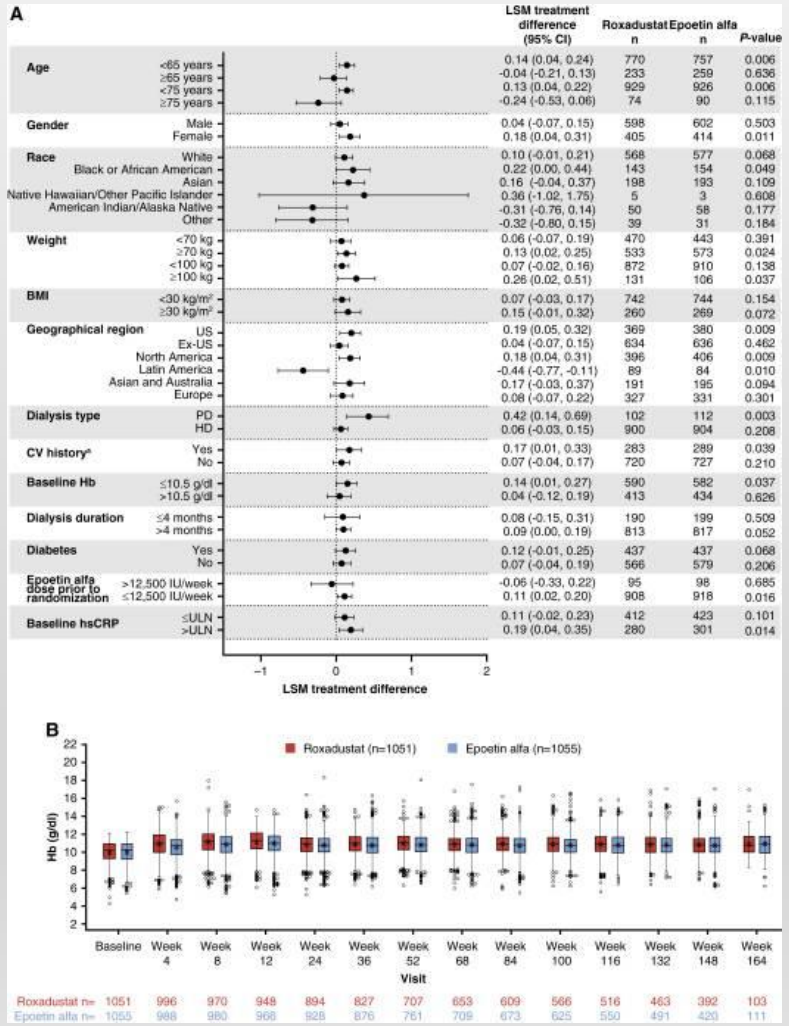
Difference +0.09 g/dL with roxadustat versus epoetin alfa (*P*<0.001 for noninferiority)

Proportion of patients experiencing ≥1 SAE

Roxadustat:	Epoetin alfa:
57.6%	57.5%

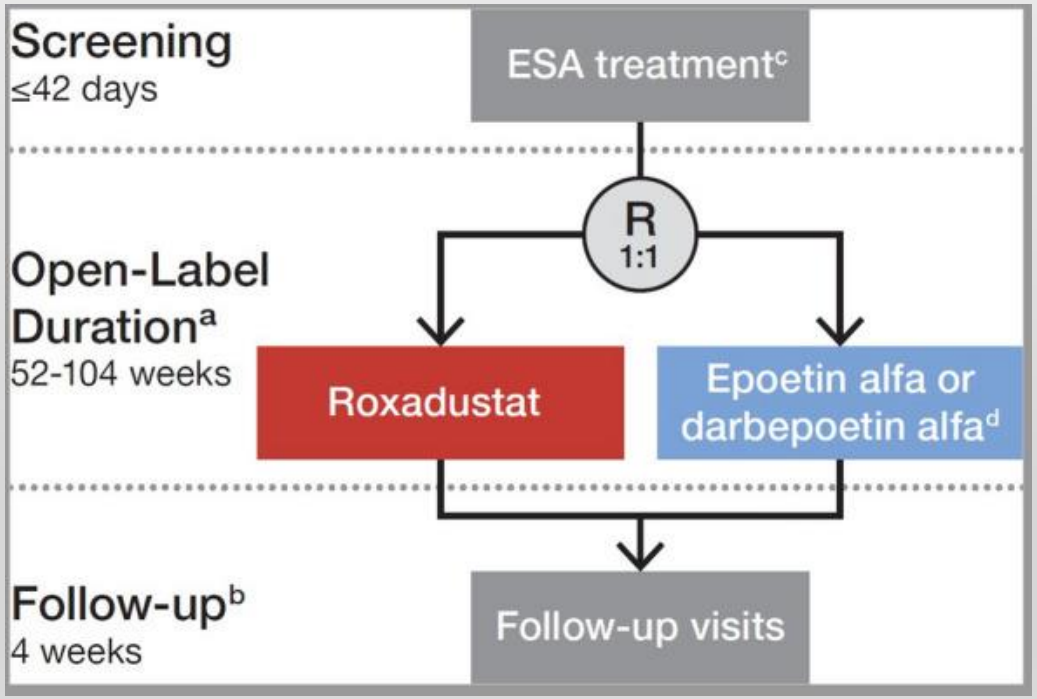
Conclusion
Roxadustat effectively increased hemoglobin in patients with CKD on dialysis with an AE profile comparable to epoetin alfa.

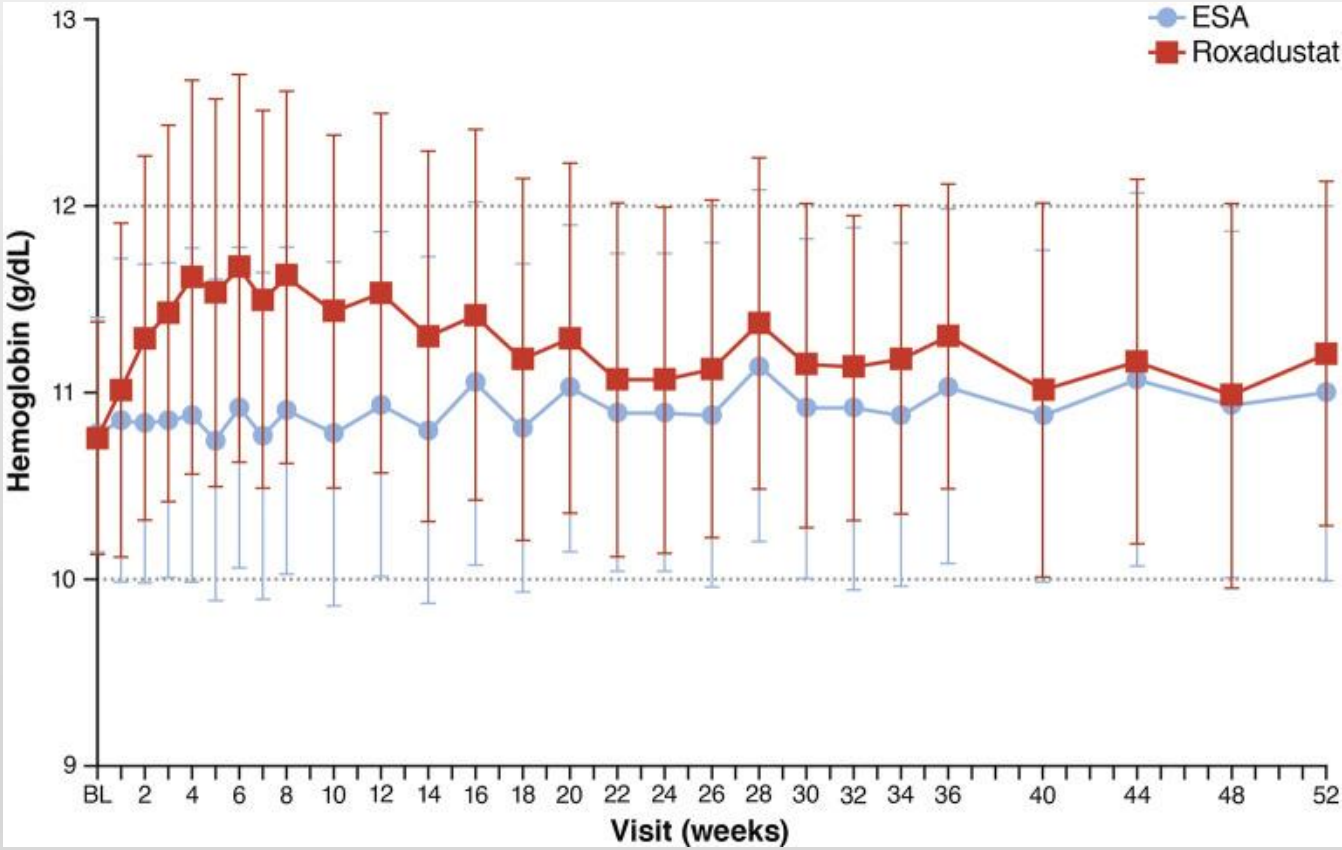
doi: 10.1681/ASN.2020111638



J Am Soc Nephrol. 2022 Apr;33(4):850-866.

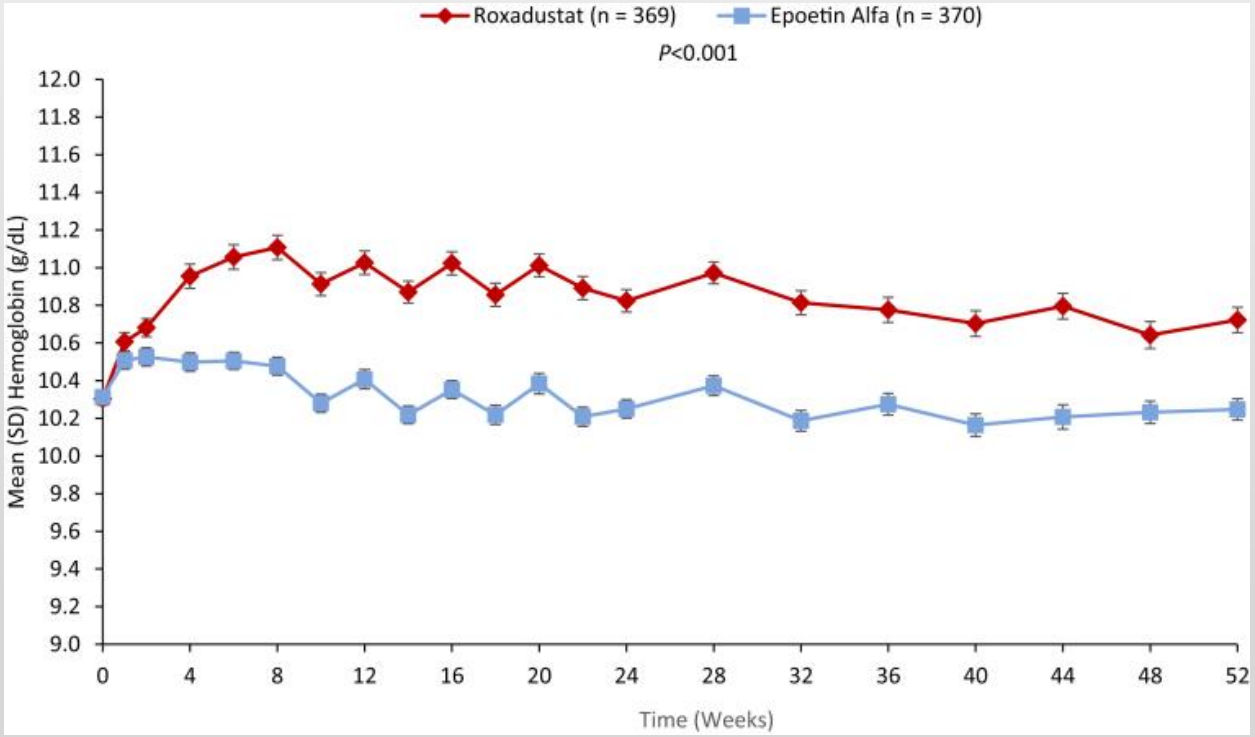
Pyrenees

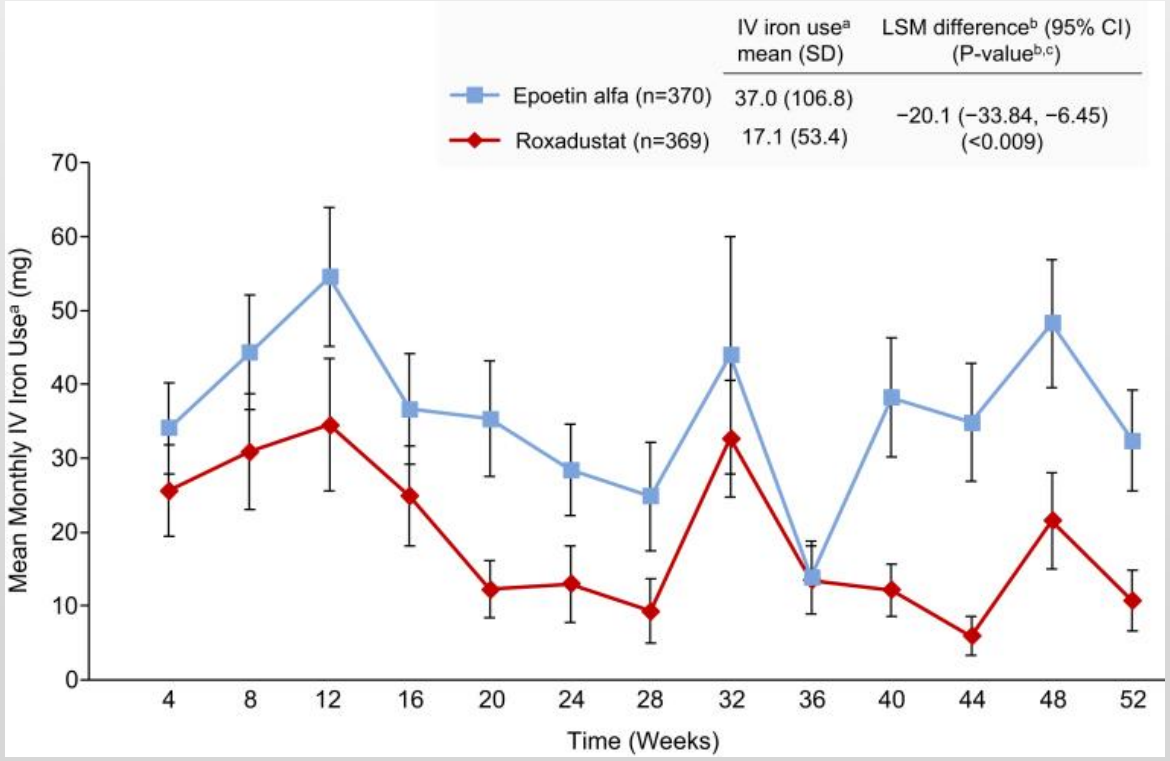




Adv Ther (2021) 38:5361–5380 .

Sierras





Kidney Int Rep. 2021 Apr 17;6(7):1829-1839.

HD (vs EPO)

ORIGINAL RESEARCH

Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies

Jonathan Barratt · Wladyslaw Sulowicz · Michael Schömig · Ciro Esposito · Michael Reusch · James Young · Botond Csiky

Table 1 Component studies for inclusion in pooled analysis

Design feature	1517-CL-0613	FGCL-4592-064	FGCL-4592-063	D5740C00002
Study name	PYRENEES	SIERRAS	HIMALAYAS	ROCKIES
Sponsor company	Astellas	FibroGen	FibroGen	AstraZeneca
Region	Europe	United States	Global	Global
Randomization	1:1	1:1	1:1	1:1
Open-label	X	X	X	X
Comparator	EPO-α or DA	EPO-α	EPO-α	EPO-α
Patients randomized, *n*	836	741	1043	2106
Incident dialysis subgroup	0	71[a]	1043	283
Stable dialysis subgroup	836	670	0	1823
Baseline hemoglobin (g/dl)	≥ 9.5 to ≤ 12.0	≥ 9.0 to ≤ 12.0	≤ 10.0	< 10.0[b] or < 12.0[c]
Hemoglobin target (g/dl)	10.0 to 12.0	10.0 to 12.0[d]	10.0 to 12.0[d]	10.0 to 12.0[d]

DA darbepoetin alfa, *EPO-α* epoetin alfa, *ESA* erythropoiesis-stimulating agent
[a] These were incident dialysis patients on ESA for ≥ 4 weeks prior to screening
[b] For patients in the incident dialysis subgroup
[c] For patients in the stable dialysis subgroup
[d] Hemoglobin maintenance target in ESA-treated patients followed local guidelines and labeling

Table 3 Pooled sample demographics and baseline characteristics (SAF)

Parameter	Pooled sample	
	Roxadustat (*n* = 2354)	ESA (*n* = 2360)
Sex (m), *n* (%)	1365 (58.0)	1379 (58.4)
Age (years), mean (SD)	55.5 (14.9)	56.3 (14.6)
Race, *n* (%)		
White	1581 (67.2)	1584 (67.1)
Black or African American	356 (15.1)	370 (15.7)
Asian	271 (11.5)	266 (11.3)
American Indian or Alaska Native	61 (2.6)	73 (3.1)
Native Hawaiian or Other Pacific Islander	6 (0.3)	6 (0.3)
Other	79 (3.4)	61 (2.6)
Weight (kg), mean (SD)	77.0 (20.2)	77.4 (20.1)
Hemodialysis at baseline, *n* (%)	2137 (90.8)	2156 (91.4)
Time since dialysis initiation (months), mean (SD)	33.9 (42.7)	33.1 (40.9)
Baseline hemoglobin (g/dl), mean (SD)	9.83 (1.28)	9.86 (1.28)
Iron replete at baseline, *n* (%)	2042 (86.7)	2052 (86.9)
LDL at baseline (mg/dl), mean (SD)	95.5 (40.0)	94.7 (39.5)
Most likely CKD etiology, *n* (%)		
Diabetic nephropathy	799 (33.9)	813 (34.4)
Hypertensive nephropathy	684 (29.1)	707 (30.0)
Other	1155 (49.1)	1126 (47.7)

CKD chronic kidney disease, *ESA* erythropoiesis-stimulating agent, *LDL* low-density lipoprotein, *mo* month(s), *SAF* safety analysis set, *SD* standard deviation

Adv Ther (2021) 38:5345–5360

HD (vs EPO)

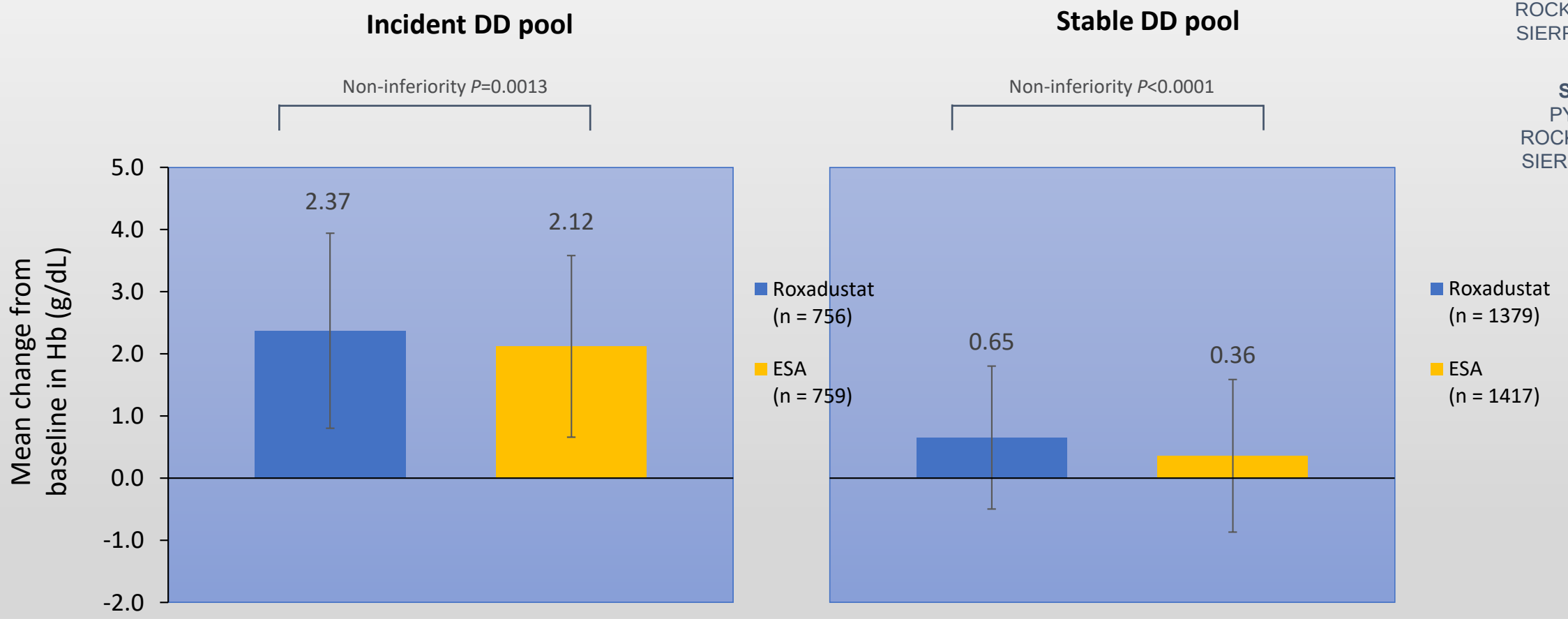
ORIGINAL RESEARCH

Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies

Jonathan Barratt · Wladyslaw Sulowicz · Michael Schömig · Ciro Esposito · Michael Reusch · James Young · Botond Csiky

IDD pool
HIMALAYAS
ROCKIES (subset)
SIERRAS (subset)

SDD pool
PYRENEES
ROCKIES (subset)
SIERRAS (subset)



Adv Ther (2021) 38:5345–5360

Νέοι HD pts (vs EPO)

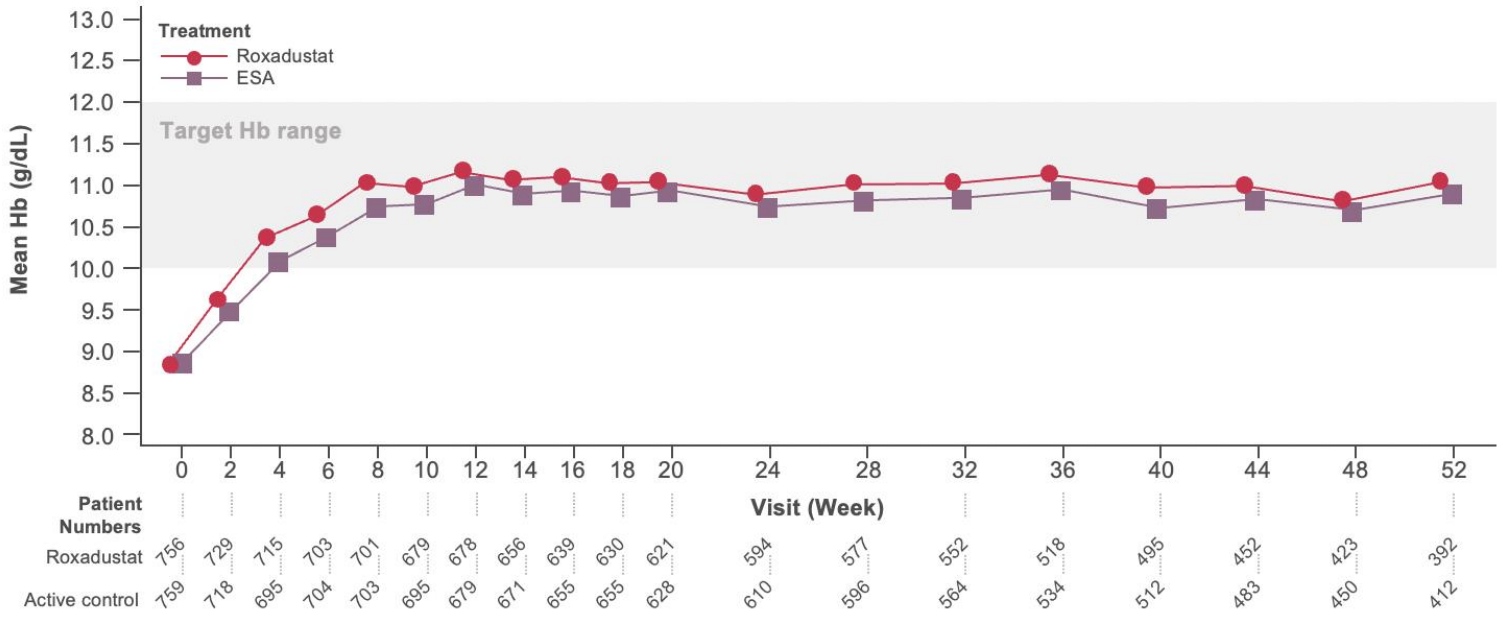
ORIGINAL RESEARCH

Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies

Jonathan Barratt · Wladyslaw Sulowicz · Michael Schömig · Ciro Esposito · Michael Reusch · James Young · Botond Csiky

Mean Hb (g/dL) over 52 weeks (FAS)

IDD pool
HIMALAYAS
ROCKIES (subset)
SIERRAS (subset)



Mean Hb was comparable over time with roxadustat vs ESA treatment in incident DD-CKD patients

Adv Ther (2021) 38:5345–5360

HD >4m (vs EPO)

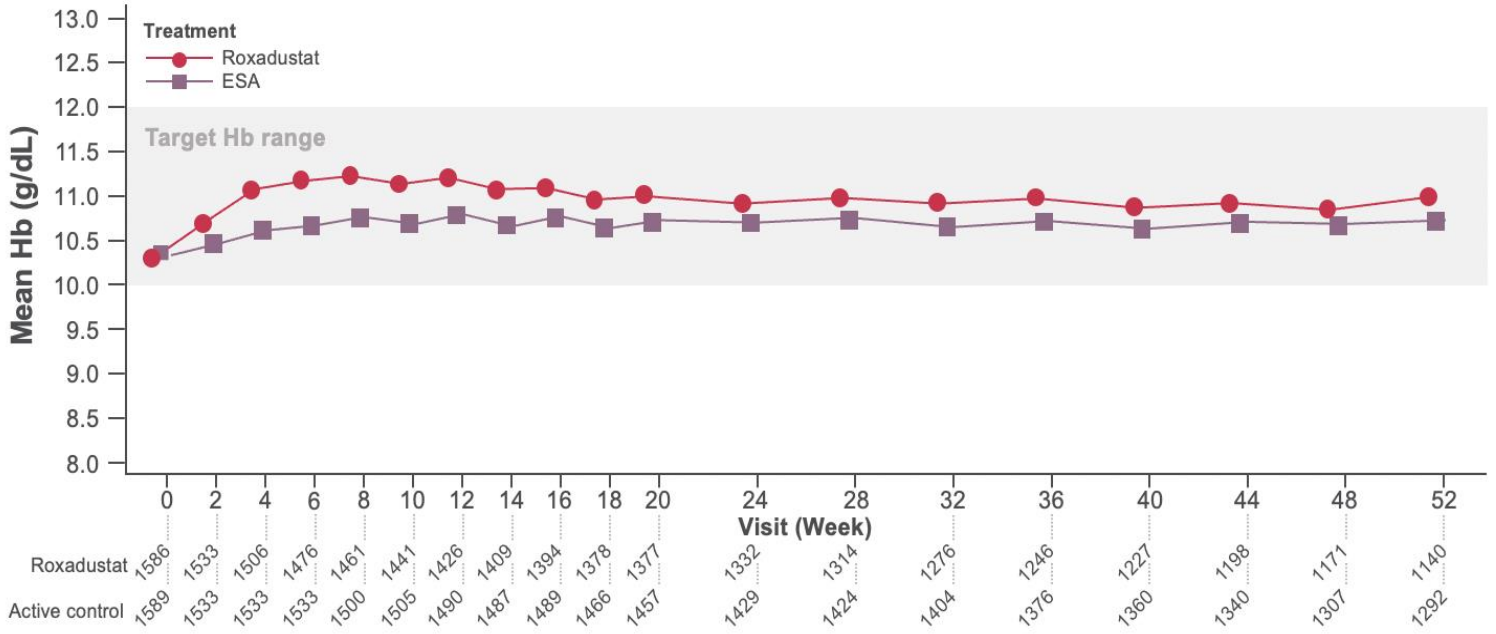
ORIGINAL RESEARCH

Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies

Jonathan Barratt · Wladyslaw Sulowicz · Michael Schömig · Ciro Esposito · Michael Reusch · James Young · Botond Csiky

Mean Hb (g/dL) over 52 weeks (FAS)

SDD pool
PYRENEES
ROCKIES (subset)
SIERRAS (subset)



Mean Hb was comparable over time with roxadustat vs ESA treatment in stable DD-CKD patients previously treated with ESA

Adv Ther (2021) 38:5345–5360

HD (vs EPO)

ORIGINAL RESEARCH

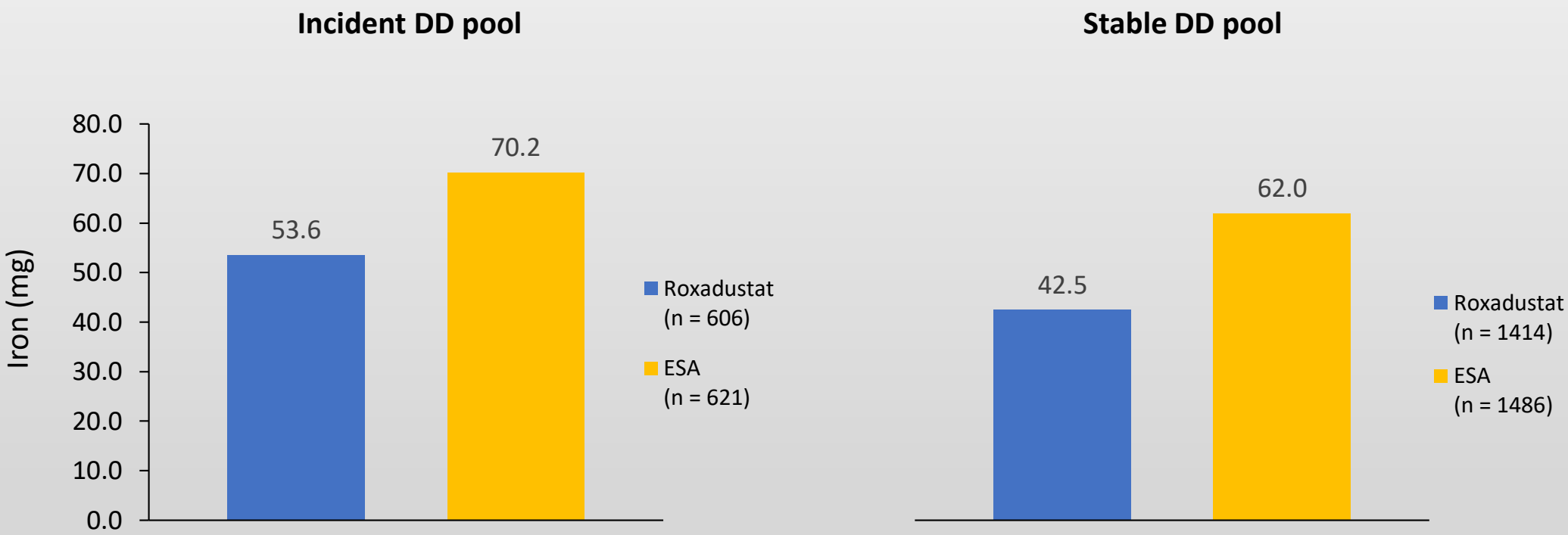
Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies

Jonathan Barratt · Wladyslaw Sulowicz · Michael Schömig · Ciro Esposito · Michael Reusch · James Young · Botond Csiky

- Mean monthly IV iron (mg) over Weeks 28–52

IDD pool
HIMALAYAS
ROCKIES (subset)
SIERRAS (subset)

SDD pool
PYRENEES
ROCKIES (subset)
SIERRAS (subset)



Adv Ther (2021) 38:5345–5360

HD (vs EPO)

ORIGINAL RESEARCH

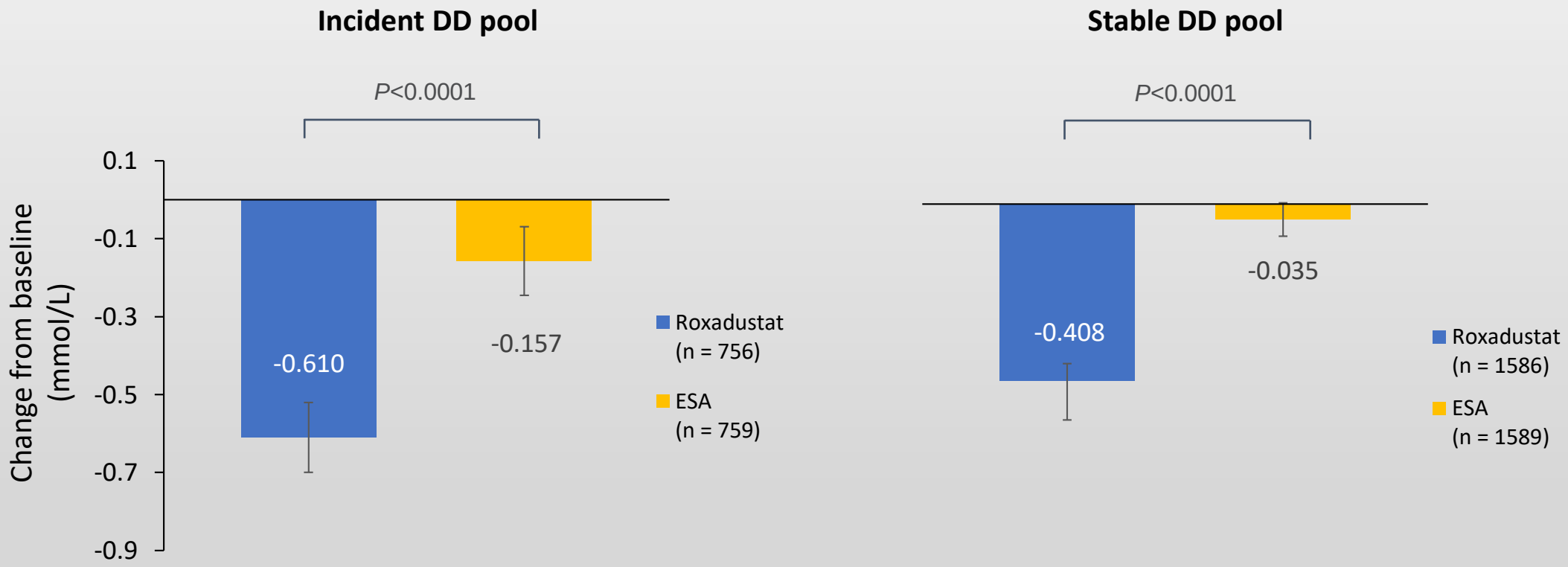
Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies

Jonathan Barratt · Wladyslaw Sulowicz · Michael Schömig · Ciro Esposito · Michael Reusch · James Young · Botond Csiky

- LS mean change from baseline to Weeks 12–28 in LDL cholesterol

IDD pool
HIMALAYAS
ROCKIES (subset)
SIERRAS (subset)

SDD pool
PYRENEES
ROCKIES (subset)
SIERRAS (subset)



Adv Ther (2021) 38:5345–5360

HD (vs EPO)

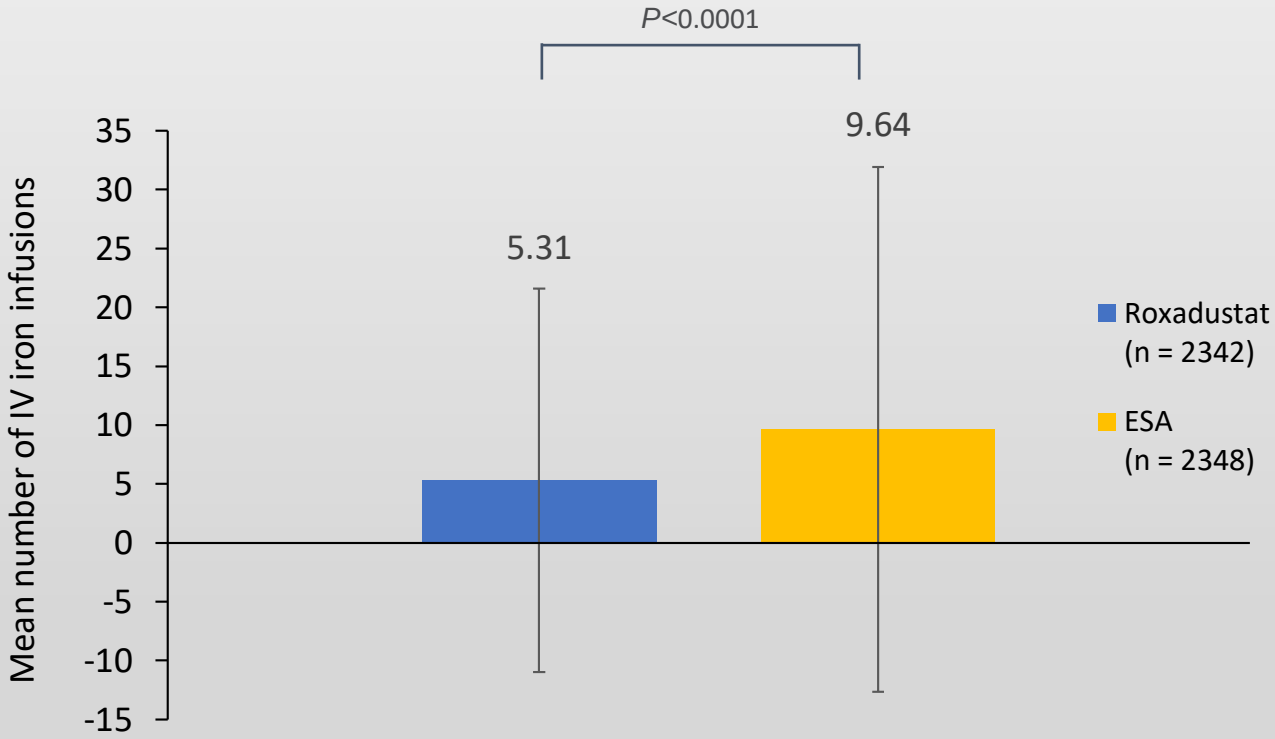
ORIGINAL RESEARCH

Efficacy and Cardiovascular Safety of Roxadustat in Dialysis-Dependent Chronic Kidney Disease: Pooled Analysis of Four Phase 3 Studies

Jonathan Barratt · Wladyslaw Sulowicz · Michael Schömig · Ciro Esposito · Michael Reusch · James Young · Botond Csiky

Overall DD pool
HIMALAYAS
ROCKIES
PYRENEES
SIERRAS

Mean number of IV iron infusions administered per PEY during Weeks 1–52



Adv Ther (2021) 38:5345–5360

Placebo-controlled Non-HD CKD

NDD pool vs placebo
OLYMPUS
ANDES
ALPS

The on-treatment analysis (pre-specified analysis) in the placebo-controlled NDD-CKD pool used a Cox model weighted inversely for the probability of censoring and produced bias. The intent-to-treat analysis was included to mitigate this bias with regard to MACE

	MACE		MACE+		ACM	
	Roxadustat N = 2386	**Placebo N = 1884**	**Roxadustat N = 2386**	**Placebo N = 1884**	**Roxadustat N = 2386**	**Placebo N = 1884**
On-treatment						
Number of events, n (%)	344 (14.4)	166 (8.8)	448 (18.8)	242 (12.8)	260 (10.9)	122 (6.5)
FAIR	8.7	6.8	11.6	10.1	6.4	5.0
HR (95% CI)	1.26 (1.02, 1.55)		1.17 (0.99, 1.40)		1.16 (0.90, 1.50)	
ITT						
Number of patients with events, n (%)	480 (20.1)	350 (18.6)	578 (24.2)	432 (22.9)	400 (16.8)	301 (16)
FAIR	10.6	10.3	13.2	13.2	8.3	8.1
HR (95% CI)	1.10 (0.96, 1.27)		1.07 (0.94, 1.21)		1.08 (0.92, 1.26)	

ESA-controlled HD pts

NDD and IDD pool vs ESA
DOLOMITES
HIMALAYAS
ROCKIES (subset)
SIERRAS (subset)

Baseline characteristics and treatment discontinuation rates were comparable between the pooled roxadustat and pooled ESA patients. The on-treatment analyses support no evidence of increased cardiovascular or mortality risk with roxadustat compared with ESA in patients with symptomatic anaemia of CKD.

OT population	MACE		MACE+		ACM	
	Roxadustat N = 1083	ESA N = 1059	Roxadustat N = 1083	ESA N = 1059	Roxadustat N = 1083	ESA N = 1059
Number of events, n (%)	105 (9.7)	136 (12.8)	134 (12.4)	171 (16.1)	74 (6.8)	99 (9.3)
IR	6.5	8.2	8.3	10.3	4.6	6.0
HR (95% CI)	0.79 (0.61, 1.02)		0.78 (0.62, 0.98)		0.78 (0.57, 1.05)	

Adverse drug reactions

NonHD-CKD

	Roxadustat in NDD-CKD* (n = 3542)	Placebo or ESA in NDD-CKD (n = 1344)
Sepsis	2.1%	0.4%
DVT	1.0%	0.2%
Seizure	1.1%	0.2%
Pulmonary embolism	0.4%	0.2%

DD-CKD

	Roxadustat in DD-CKD† (n = 3351)	ESA in DD-CKD (n = 1363)
Sepsis	3.4%	3.4%
VAT	12.8%	10.2%
DVT	1.3%	0.3%
Seizure	2.0%	1.6%
Pulmonary embolism	0.6%	0.5%

NDD pool vs placebo
OLYMPUS
ANDES
ALPS

NDD vs active comparator
DOLOMITES

Overall DD pool
HIMALAYAS
ROCKIES
PYRENEES
SIERRAS

Meta-analysis HDx

Study or Subgroup	Roxadustat Mean	Roxadustat SD	Roxadustat Total	ESAs Mean	ESAs SD	ESAs Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cao B 2022	26.66	207.66	27	23.18	113.05	28	5.7%	0.02 [−0.51, 0.55]
Chen N 2022	164.26	20.59	40	96.66	19.65	40	5.6%	3.33 [2.64, 4.01]
Duan C 2021	137.04	25.05	48	60.37	22.66	48	5.7%	3.18 [2.57, 3.79]
Gao W 2016	96.63	14.82	20	62.79	13.46	20	5.5%	2.34 [1.52, 3.17]
Hong M 2022	168.51	35.44	31	209.72	27.06	30	5.7%	−1.29 [−1.84, −0.73]
Huang Y 2022	37.28	2.83	45	25.46	3.71	45	5.7%	3.55 [2.88, 4.22]
Li H 2020	167.92	35.07	28	95.6	27.5	28	5.7%	2.26 [1.58, 2.94]
Li J 2021	100.8	43.63	35	63.96	43.15	35	5.8%	0.84 [0.35, 1.33]
Liu W 2021	175.31	5.5	38	84.38	4.69	37	3.2%	17.59 [14.66, 20.52]
Li W 2021	99.63	42.03	20	58.11	41.88	20	5.7%	0.97 [0.31, 1.63]
Shi Y 2020	−277.13	461.9	28	−152.02	521.99	27	5.7%	−0.25 [−0.78, 0.28]
Tan P 2021	168.1	23.18	34	96.28	23.62	36	5.6%	3.03 [2.34, 3.73]
Wang Y 2021	101.7	41.95	35	58.7	42.5	35	5.8%	1.01 [0.51, 1.51]
Wen C 2022	166.3	35	62	92.81	27.4	62	5.8%	2.32 [1.87, 2.78]
Xu W 2021	65.62	12.53	15	49.75	10.77	15	5.6%	1.32 [0.52, 2.12]
Zhang W 2021	−168.56	154.76	25	−41.72	158.69	25	5.7%	−0.80 [−1.37, −0.22]
Zhang X 2021	167.07	14.95	43	138.3	14.35	43	5.8%	1.95 [1.43, 2.46]
Zhang Y 2022	34.15	112.38	20	−7.3	144.14	20	5.7%	0.31 [−0.31, 0.94]
Total (95% CI)			**594**			**594**	**100.0%**	**1.94 [1.15, 2.72]**

Heterogeneity: $Tau^2 = 2.72$; $Chi^2 = 499.58$, df = 17 ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: $Z = 4.83$ ($P < 0.00001$)

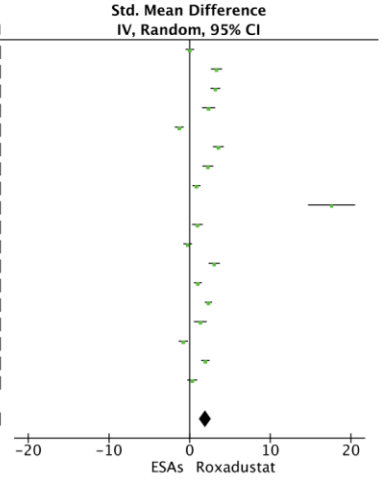


Figure 7. Forest plot for the outcome change in ferritin levels (Δferritin).

Study or Subgroup	Roxadustat Mean	Roxadustat SD	Roxadustat Total	ESAs Mean	ESAs SD	ESAs Total	Weight	Mean Difference IV, Random, 95% CI
Cao B 2022	2.3	12.83	27	1.64	8.25	28	4.6%	0.66 [−5.06, 6.38]
Chen N 2022	19.7	3.58	40	10.97	3.94	40	6.3%	8.73 [7.08, 10.38]
Duan C 2021	4.24	2.37	48	1.57	2.24	48	6.5%	2.67 [1.75, 3.59]
Geng Y 2022	7.42	2.92	30	1.63	2.92	30	6.4%	5.79 [4.31, 7.27]
Hong M 2022	16.53	3.33	31	6.72	3.32	30	6.3%	9.81 [8.14, 11.48]
Li H 2020	15.97	3.32	28	7.51	3.23	28	6.3%	8.46 [6.74, 10.18]
Li J 2021	20.88	1.79	35	17.08	1.86	35	6.5%	3.80 [2.94, 4.66]
Liu W 2021	17.97	3.58	38	8	3.15	37	6.3%	9.97 [8.44, 11.50]
Li W 2021	11.68	2.04	20	5.47	1.89	20	6.4%	6.21 [4.99, 7.43]
Shi Y 2020	0.014	0.22	28	−0.043	0.19	27	6.5%	0.06 [−0.05, 0.17]
Tan P 2021	15.9	3.5	34	8	3.31	36	6.3%	7.90 [6.30, 9.50]
Wen C 2022	16.03	3.71	62	7.37	3.21	62	6.4%	8.66 [7.44, 9.88]
Xu W 2021	12.23	3.26	15	8.09	3.08	15	6.1%	4.14 [1.87, 6.41]
Zhang W 2021	10.11	2.93	25	1.99	2.48	25	6.4%	8.12 [6.62, 9.62]
Zhang X 2021	16.29	2.86	43	10.81	2.8	43	6.4%	5.48 [4.28, 6.68]
Zhang Y 2022	9.4	4	20	1.77	2.57	20	6.2%	7.63 [5.55, 9.71]
Total (95% CI)			**524**			**524**	**100.0%**	**6.21 [3.93, 8.48]**

Heterogeneity: $Tau^2 = 20.56$; $Chi^2 = 1194.12$, df = 15 ($P < 0.00001$); $I^2 = 99\%$
Test for overall effect: $Z = 5.35$ ($P < 0.00001$)

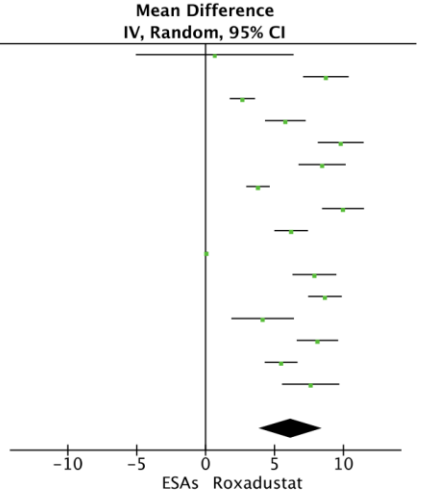
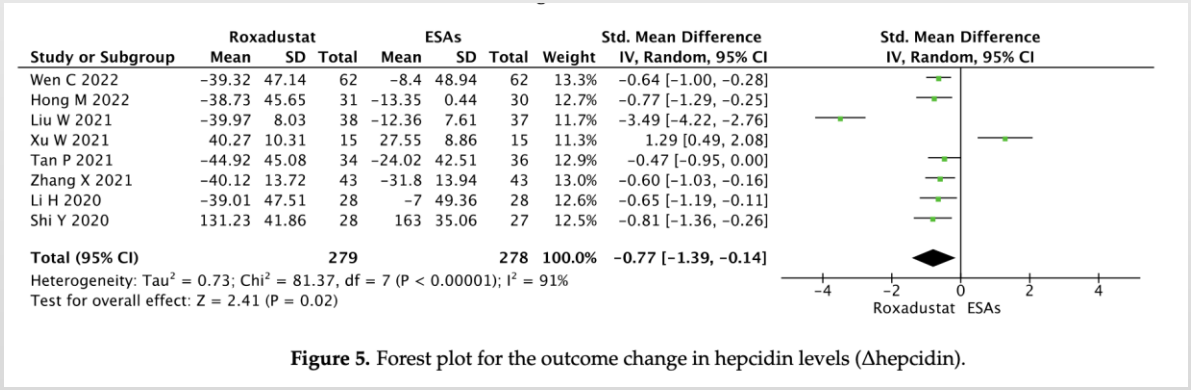


Figure 6. Forest plot for the outcome change in TSAT% levels (ΔTSAT%).

J. Clin. Med. 2023, 12, 2450.

Meta-analysis HDx



Study or Subgroup	Roxadustat Mean	SD	Total	ESAs Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Wen C 2022	−39.32	47.14	62	−8.4	48.94	62	13.3%	−0.64 [−1.00, −0.28]
Hong M 2022	−38.73	45.65	31	−13.35	0.44	30	12.7%	−0.77 [−1.29, −0.25]
Liu W 2021	−39.97	8.03	38	−12.36	7.61	37	11.7%	−3.49 [−4.22, −2.76]
Xu W 2021	40.27	10.31	15	27.55	8.86	15	11.3%	1.29 [0.49, 2.08]
Tan P 2021	−44.92	45.08	34	−24.02	42.51	36	12.9%	−0.47 [−0.95, 0.00]
Zhang X 2021	−40.12	13.72	43	−31.8	13.94	43	13.0%	−0.60 [−1.03, −0.16]
Li H 2020	−39.01	47.51	28	−7	49.36	28	12.6%	−0.65 [−1.19, −0.11]
Shi Y 2020	131.23	41.86	28	163	35.06	27	12.5%	−0.81 [−1.36, −0.26]
Total (95% CI)			**279**			**278**	**100.0%**	**−0.77 [−1.39, −0.14]**

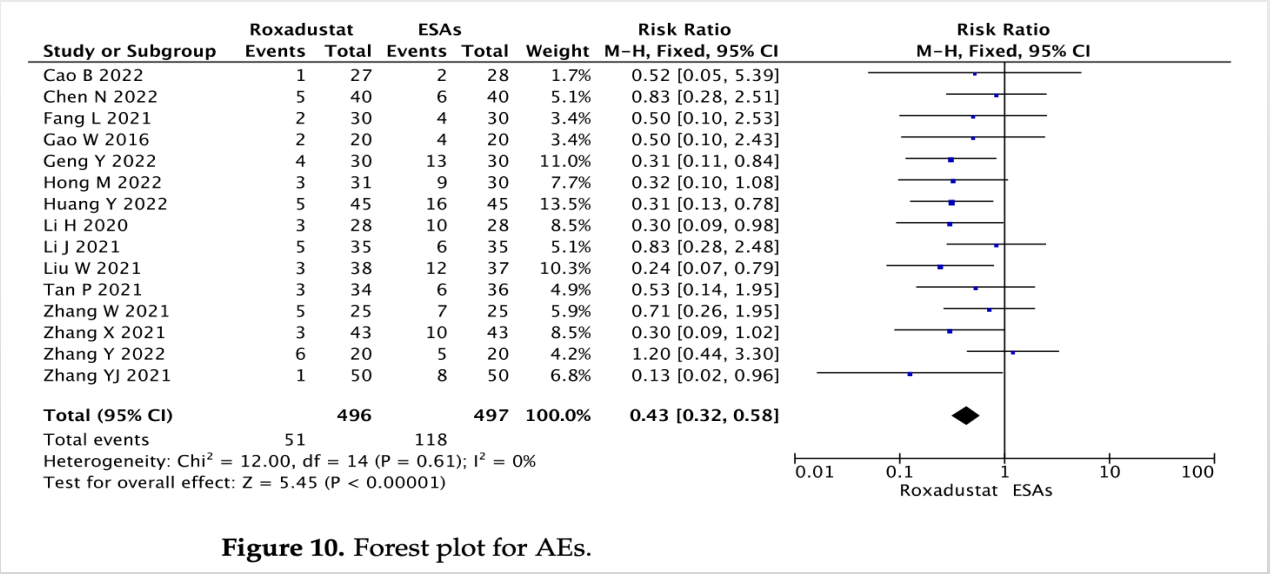
Heterogeneity: $Tau^2 = 0.73$; $Chi^2 = 81.37$, df = 7 ($P < 0.00001$); $I^2 = 91\%$
Test for overall effect: $Z = 2.41$ ($P = 0.02$)

Std. Mean Difference IV, Random, 95% CI

−4 −2 0 2 4

Roxadustat ESAs

Figure 5. Forest plot for the outcome change in hepcidin levels (Δhepcidin).



Study or Subgroup	Roxadustat Events	Total	ESAs Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cao B 2022	1	27	2	28	1.7%	0.52 [0.05, 5.39]
Chen N 2022	5	40	6	40	5.1%	0.83 [0.28, 2.51]
Fang L 2021	2	30	4	30	3.4%	0.50 [0.10, 2.53]
Gao W 2016	2	20	4	20	3.4%	0.50 [0.10, 2.43]
Geng Y 2022	4	30	13	30	11.0%	0.31 [0.11, 0.84]
Hong M 2022	3	31	9	30	7.7%	0.32 [0.10, 1.08]
Huang Y 2022	5	45	16	45	13.5%	0.31 [0.13, 0.78]
Li H 2020	3	28	10	28	8.5%	0.30 [0.09, 0.98]
Li J 2021	5	35	6	35	5.1%	0.83 [0.28, 2.48]
Liu W 2021	3	38	12	37	10.3%	0.24 [0.07, 0.79]
Tan P 2021	3	34	6	36	4.9%	0.53 [0.14, 1.95]
Zhang W 2021	5	25	7	25	5.9%	0.71 [0.26, 1.95]
Zhang X 2021	3	43	10	43	8.5%	0.30 [0.09, 1.02]
Zhang Y 2022	6	20	5	20	4.2%	1.20 [0.44, 3.30]
Zhang YJ 2021	1	50	8	50	6.8%	0.13 [0.02, 0.96]
Total (95% CI)		**496**		**497**	**100.0%**	**0.43 [0.32, 0.58]**
Total events	51		118			

Heterogeneity: $Chi^2 = 12.00$, df = 14 ($P = 0.61$); $I^2 = 0\%$
Test for overall effect: $Z = 5.45$ ($P < 0.00001$)

Risk Ratio M-H, Fixed, 95% CI

0.01 0.1 1 10 100

Roxadustat ESAs

Figure 10. Forest plot for AEs.

J. Clin. Med. 2023, 12, 2450.

Η εμπειρία των τελευταίων μηνών

- 12 ασθενείς έλαβαν roxadustat (2 άνδρες, 10 γυναίκες)

- 6 ασθενείς σε υπό εξωνεφρική κάθαρση
  - 4 πρόσφατη ένταξη,
  - 1 HD,
  - 1 PD
- 6 ασθενείς non-HD CKD, με μέσο eGFR CKD EPI = 27±8.7ml/min/1.73m2, [διάμεσο eGFR :26(IQR 11)]
  - 2 ασθενής σταδίου III
  - 4 ασθενείς σταδίου IV

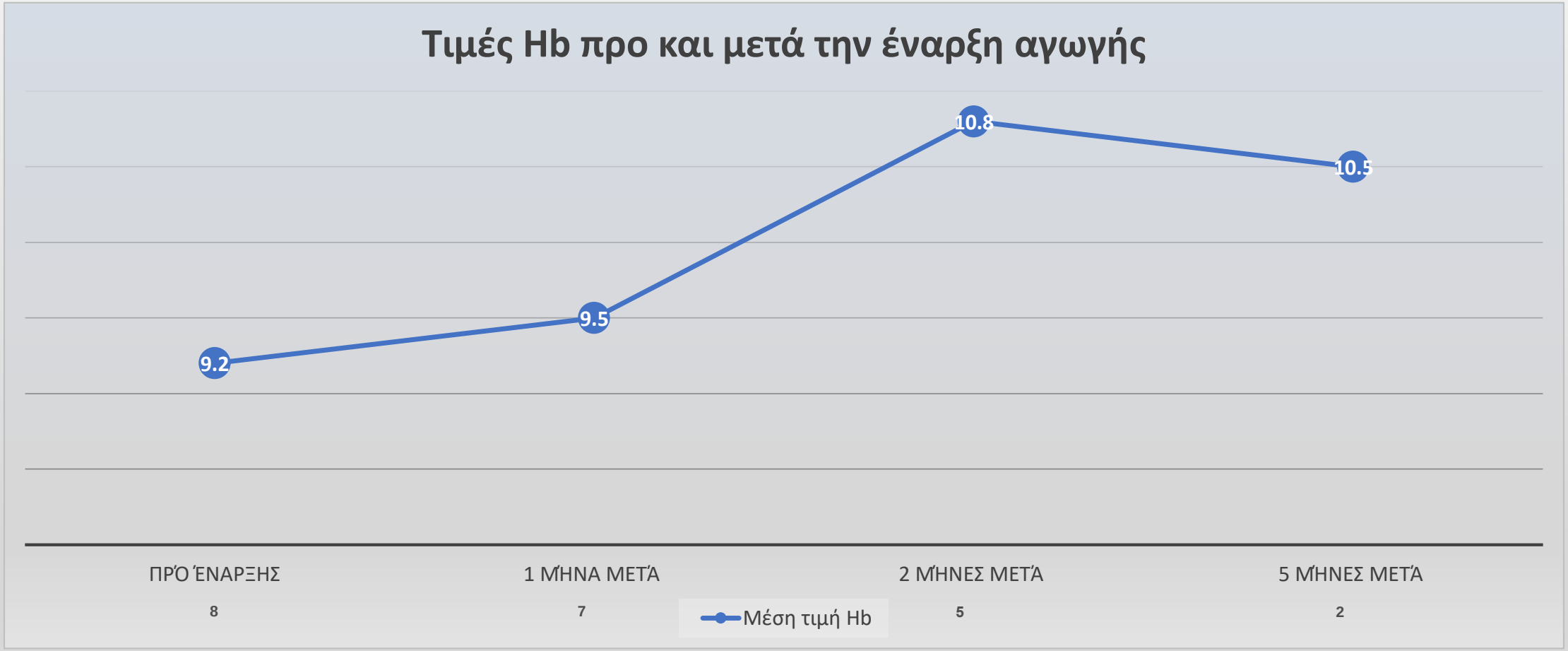
Χαρακτηριστικά ασθενών

Άνδρες / γυναίκες	2/10	Σπειραματονεφρίτιδα	3/12
		Διαβητική Νεφροπάθεια	2/12
Μέση ηλικία	74,63 ± 12.31 έτη	Καρδιονεφρικό	2/12
		Υπερτασική Νεφροσκλήρυνση	1/12
		Άγνωστη	4/12
Μέση διάρκεια παρακολούθησης	56 ± 41 ημέρες		
Μέσο eGFR	27.0±8.7ml/min/1.73m^2		

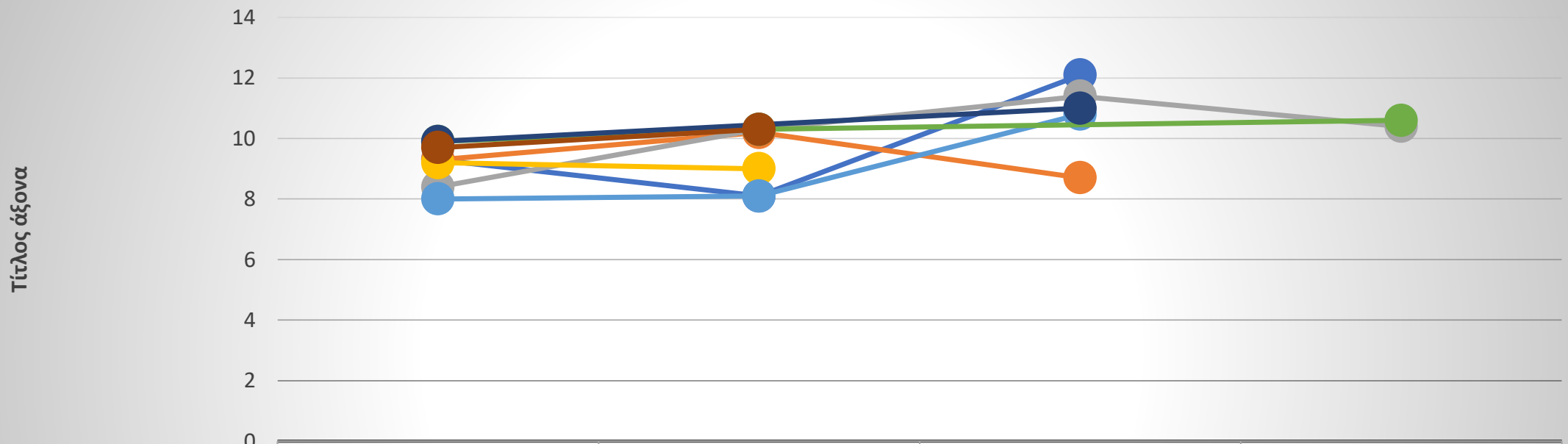
Αποτελέσματα περιστατικών

- 2 ασθενείς διέκοψαν τη θεραπεία με roxadustat
  - 1 ασθενής nonHDx, λόγω λοίμωξης (σπλαχνική λεϊσμανίαση)
  - 1 ασθενής overshooting (Hb>13mg/dL)
- 2 ασθενείς lost follow up
- 2 ασθενείς άλλαξαν ΜΤΝ και άλλαξε σε EPO

Αποτελέσματα 8 περιστατικών



Αποτελέσματα 8 περιστατικών



	πρό έναρξης	1 μήνα μετά	2 μήνες μετά	5 μήνες μετά
Ασθενής 1 (400mg x3)	9.3	8.1	12.1	
Ασθενής 2 (250mg x3)	9.3	10.2	8.7	
Ασθενής 3 (300mg x3)	8.4	10.3	11.4	10.4
Ασθενής 4 (70mg x3)	9.2	9		
Ασθενής 5 (70mg x3)	8	8.1	10.8	
Ασθενής 6 (70mg x3)	9.9	10.3		10.6
Ασθενής 7 (70mg x3)	9.9		11	
Ασθενής 8 (70mg x3)	9.7	10.3		

Συμπεράσματα

- Το roxadustat έδειξε παρόμοια αποτελεσματικότητα σε σύγκριση με ESA σε ασθενείς ΧΧΝ προ ένταξης αλλά και σε αιμοκαθαιρόμενους ασθενείς
- Οι ασθενείς που έλαβαν θεραπεία με roxadustat παρουσίασαν μείωση της χρήσης iv σιδήρου και μεταγγίσεων
- Παρόμοιο προφίλ ασφάλειας σε σύγκριση με ESA

Για ασθενείς που ξεκινούν θεραπεία για την αναιμία **και δεν λαμβάνουν τη δεδομένη στιγμή ESA,** η συνιστώμενη δόση έναρξης του roxadustat είναι:

Σωματικό βάρος	Δόση roxadustat
< 100 kg	70 mg, 3 φορές την εβδομάδα
≥ 100 kg	100 mg, 3 φορές την εβδομάδα

Οι ασθενείς που λαμβάνουν τη δεδομένη στιγμή θεραπεία με ESA μπορούν να μεταβούν στο roxadustat. Η συνιστώμενη δόση έναρξης του roxadustat βασίζεται στη μέση συνταγογραφηθείσα δόση του ESA εντός των 4 εβδομάδων πριν από τη μετάβαση:

EPO-α ή -β (IU/εβδομάδα)	Δαρμπεποετίνη άλφα (μg/εβδομάδα)	Μεθοξυπολυαιθυλενογλυκολο-εποετίνη βήτα (μg/μήνα)	Δόση roxadustat (mg/δόση) τρεις φορές την εβδομάδα
< 5.000	< 25	< 80	70
5.000-8.000	25 έως < 40	80–120	100
> 8.000–16.000	40-80	> 120–200	150
> 16.000	> 80	> 200	200

Φωσφοδεσμευτικά: Το Evrenzo θα πρέπει να λαμβάνεται τουλάχιστον 1 ώρα μετά τη χορήγηση των δεσμευτικών του φωσφόρου ή άλλων φαρμακευτικών προϊόντων ή συμπληρωμάτων που περιέχουν πολυσθενή κατιόντα

Στατίνες: Όταν γίνεται συγχορήγηση με το roxadustat, λάβετε υπόψη αυτήν την αλληλεπίδραση και παρακολουθήστε τις ανεπιθύμητες ενέργειες που συσχετίζονται με τις στατίνες και την ανάγκη μείωσης της δόσης στατίνης.

ESAs: Δεν συνιστάται να συνδυάζεται η χορήγηση του roxadustat με ESA, καθώς ο συνδυασμός δεν έχει μελετηθεί.


ΝΕΦΡΟΛΟΓΙΚΟ ΤΜΗΜΑ
Γ. Ν. "Γ. ΠΑΠΑΝΙΚΟΛΑΟΥ"


ΕΠΙΣΤΗΜΟΝΙΚΗ ΕΚΔΗΛΩΣΗ
Εγκέφαλος
και Νεφρός
10-11 Νοεμβρίου 2023

Ευχαριστώ