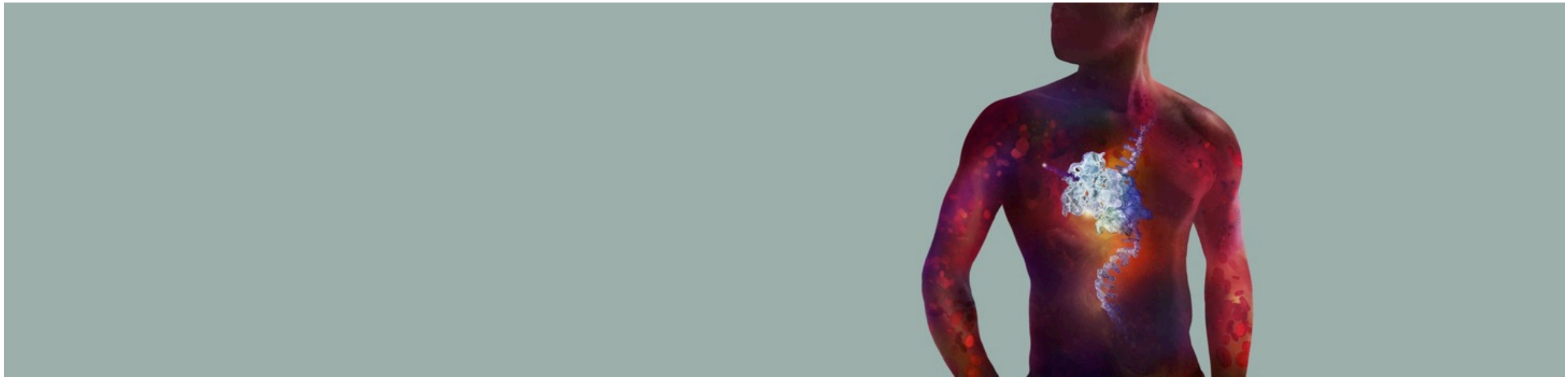
AstraZeneca
What science can do

Investor science call: American Society of Nephrology Kidney Week 2019

Conference call for investors and analysts

10 November 2019



Forward-looking statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement: this document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; effects of patent litigation in respect of IP rights; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure of outsourcing; the risks associated with manufacturing biologics; the risk that R&D will not yield new products that achieve commercial success; the risk of delay to new product launches; the risk that new products do not perform as we expect; the risk that strategic alliances and acquisitions, including licensing and collaborations, will be unsuccessful; the risks from pressures resulting from generic competition; the impact of competition, price controls and price reductions; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the difficulties of obtaining and maintaining regulatory approvals for products; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; the risk of failure of critical processes affecting business continuity; economic, regulatory and political pressures to limit or reduce the cost of our products; failure to achieve strategic priorities or to meet targets or expectations; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; the risk of substantial product liability claims; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; taxation risks; exchange rate fluctuations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the risk of misuse of social medial platforms and new technology; and the risk of failure of information technology and cybercrime. Nothing in this presentation / webcast should be construed as a profit forecast.

Agenda

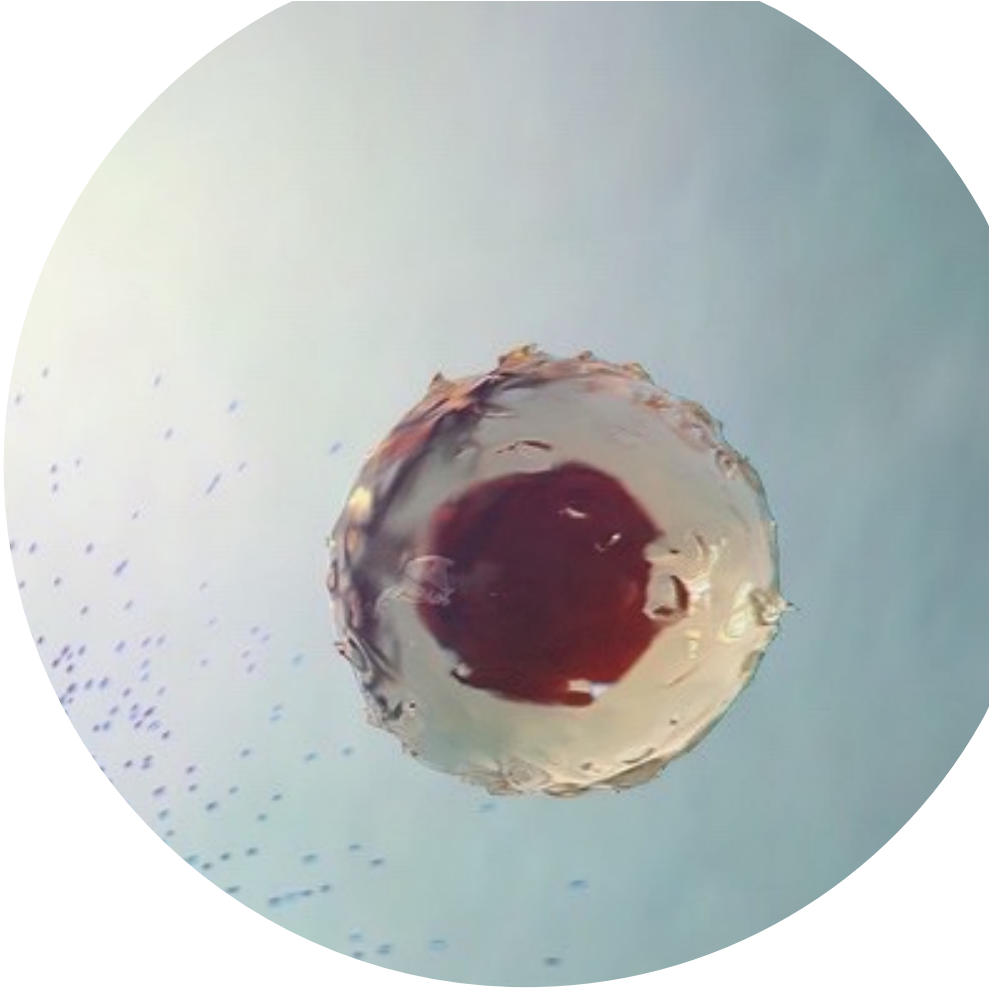
Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

Roxadustat Phase III ‘pooled’ safety and efficacy

Commercial opportunity

Q&A



2019: a very busy year for the pipeline

Investor science events in each therapy area

Oncology

American Society of Clinical Oncology (Jun)

- Meet AZN management event(s)
- Conference call

European Society of Medical Oncology (Sep)

- Meet AZN management event(s)
- Conference call

Cardiovascular, renal and metabolism

European Society of Cardiology (Sep)

- Conference call

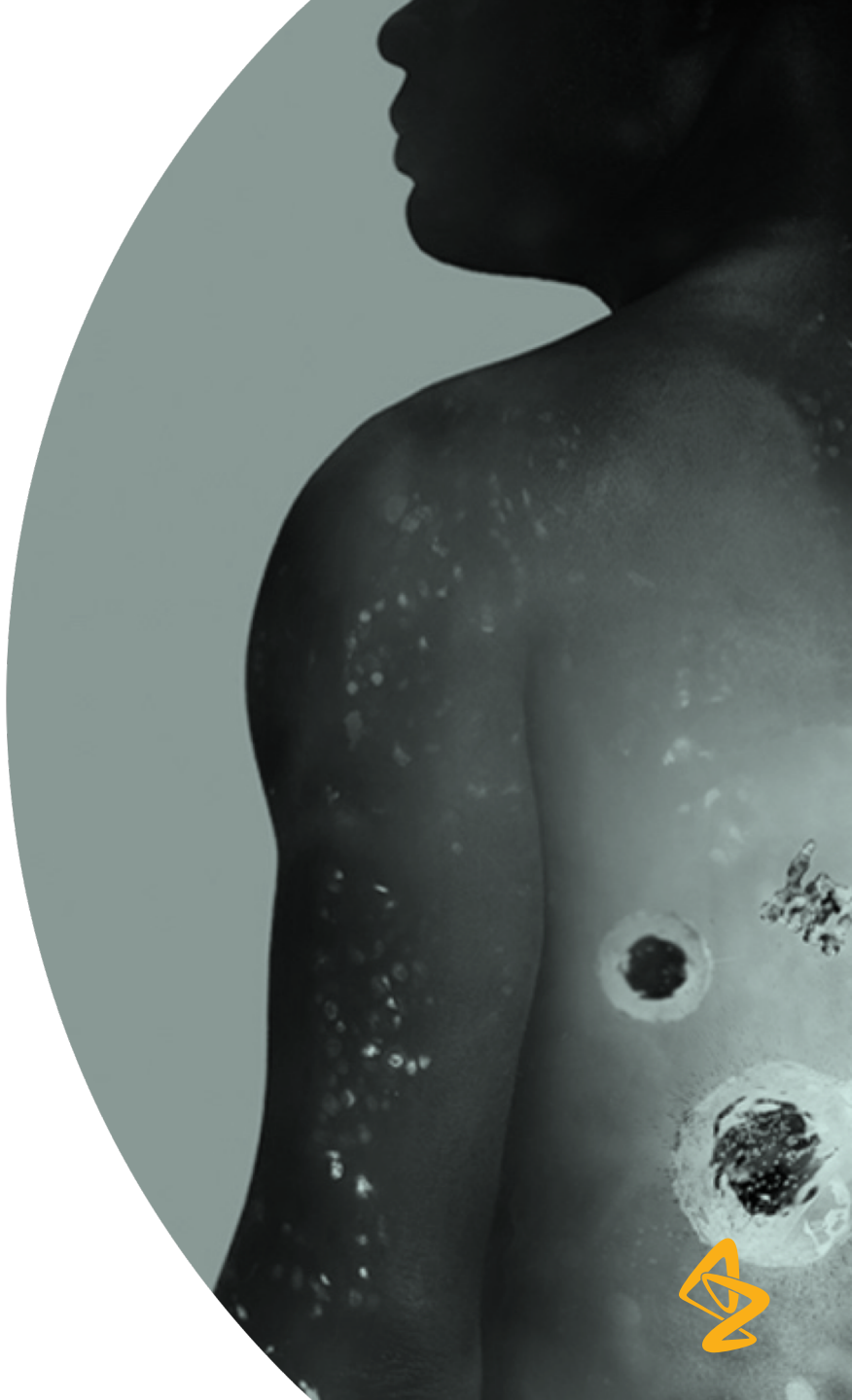
American Society of Nephrology (Nov)

- Conference call

Respiratory (and immunology)

American College of Rheumatology (Nov)

- Conference call



For AstraZeneca investor and analyst events, please visit https://www.astrazeneca.com/investor-relations/results-and-presentations.html.

Presenters

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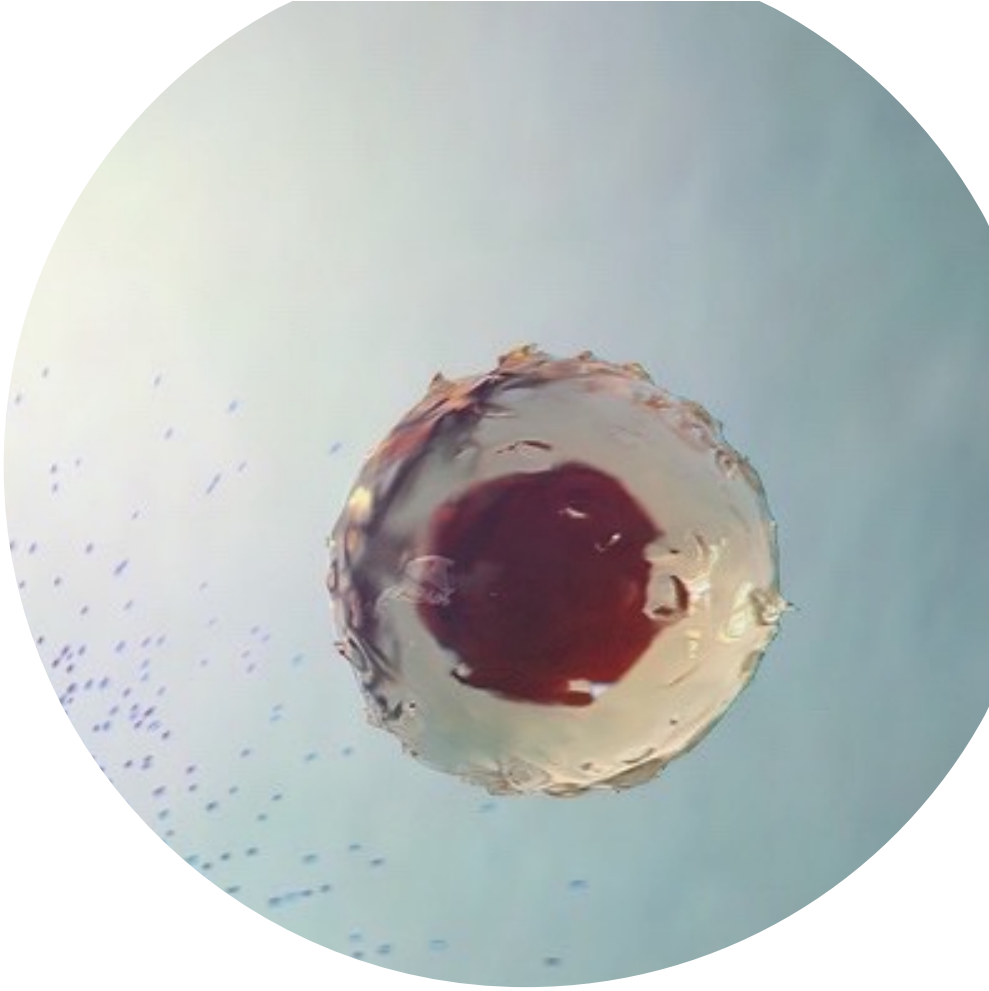

Anaemia can be a serious medical condition; it is associated with increased risk of hospitalisation, cardiovascular (CV) complications and death

200 million

adult patients have chronic kidney disease (CKD) worldwide

Past

Roxadustat is a first in class hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor

Past

Patients were previously treated with transfusion-only care when iron supplementation was insufficient

Present

CKD anaemia is currently characterised as erythropoietin (EPO) and iron deficiency

Patients receive EPO supplements and extra iron to encourage erythrocyte production

Treating CKD anaemia enables the
body to stimulate complete erythropoiesis

Future

Roxadustat has the potential to revolutionise the treatment paradigm of patients with anaemia from CKD

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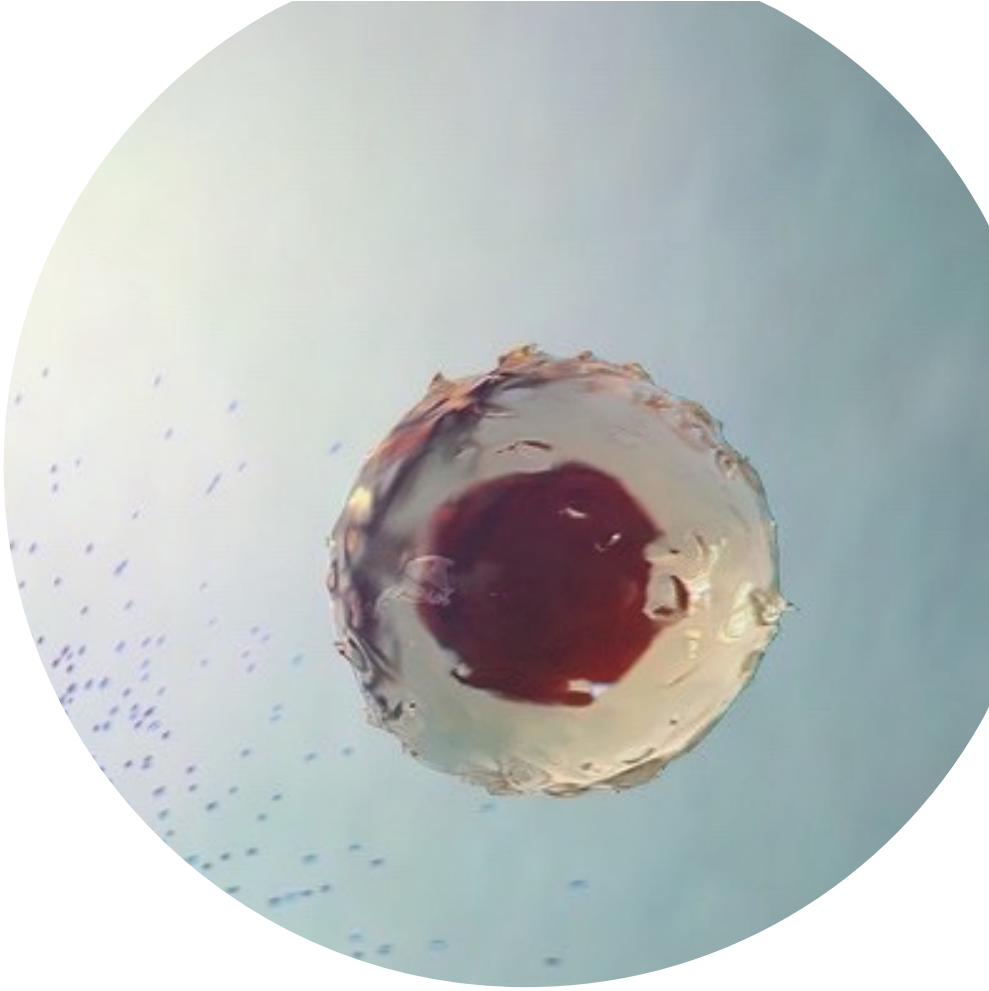
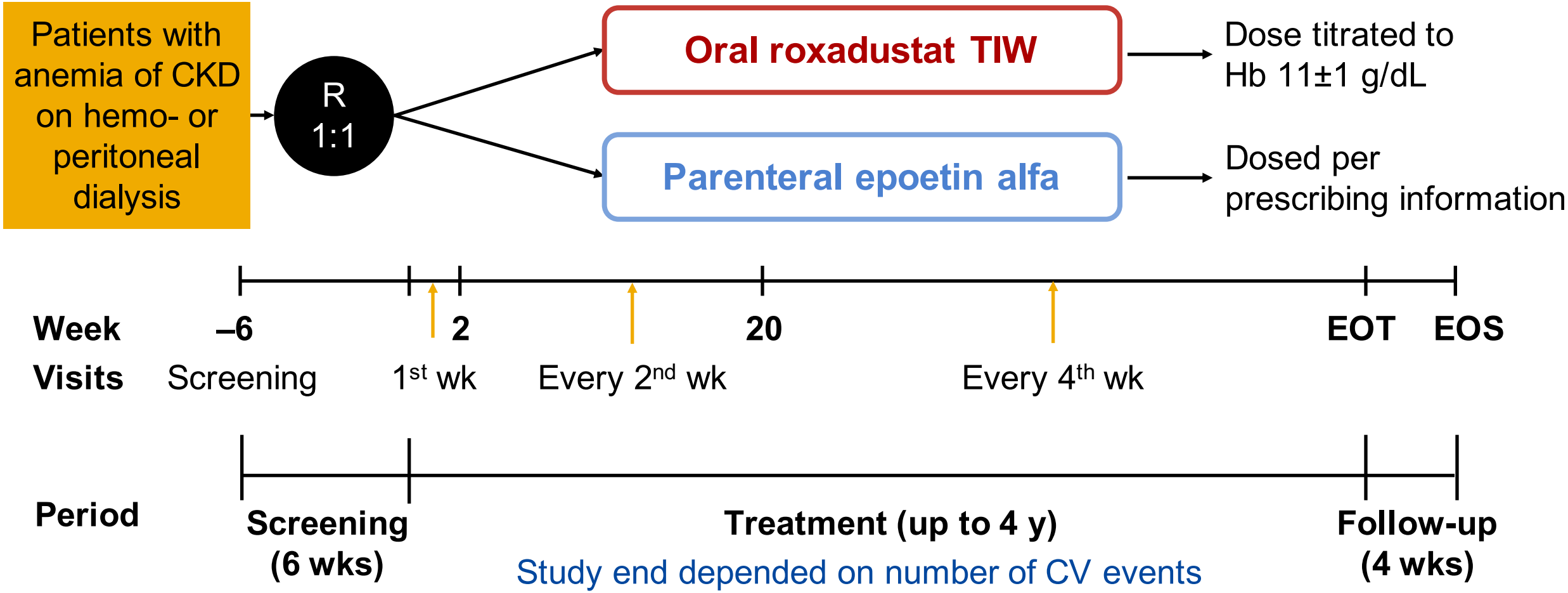


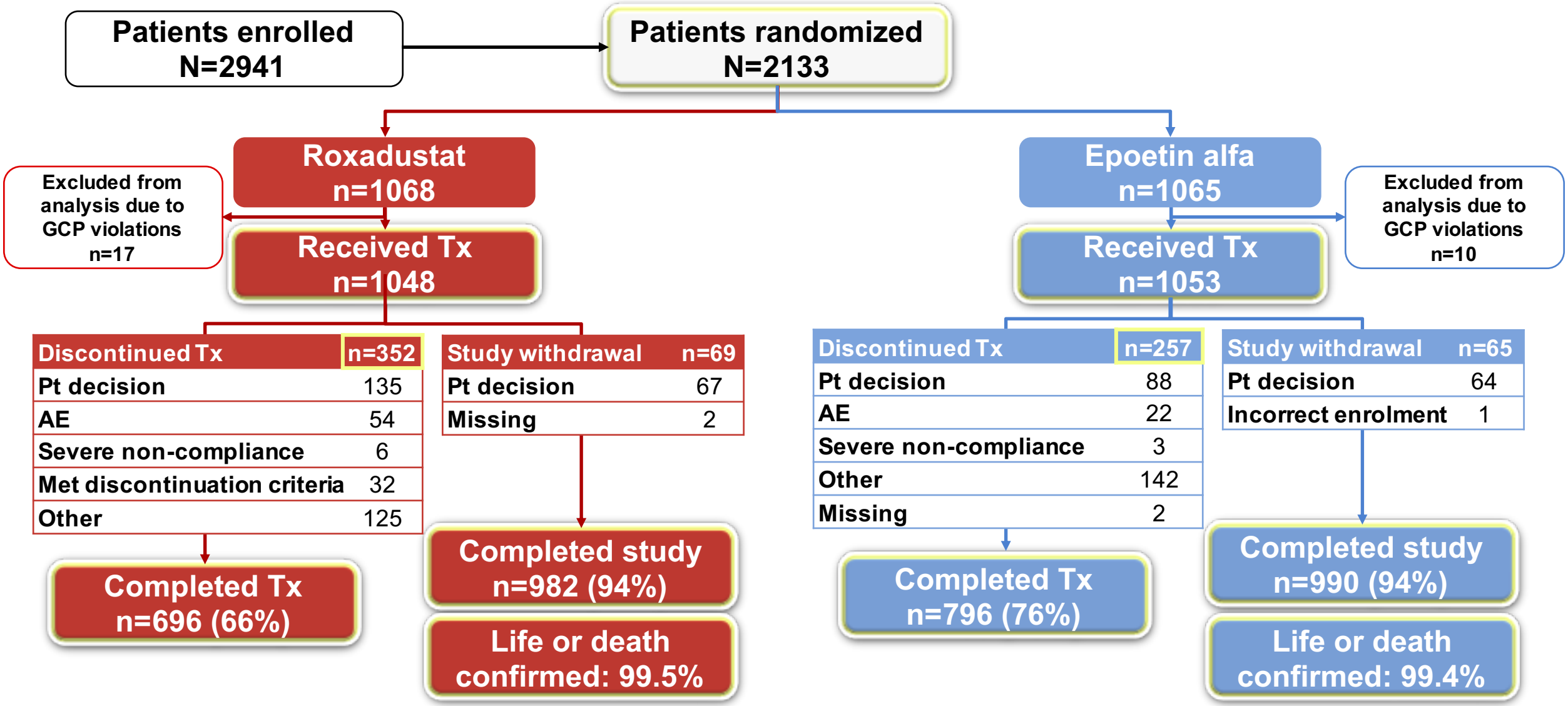
Roxadustat Phase III ROCKIES trial

Design: Phase 3, Randomized, Open Label, Active Controlled



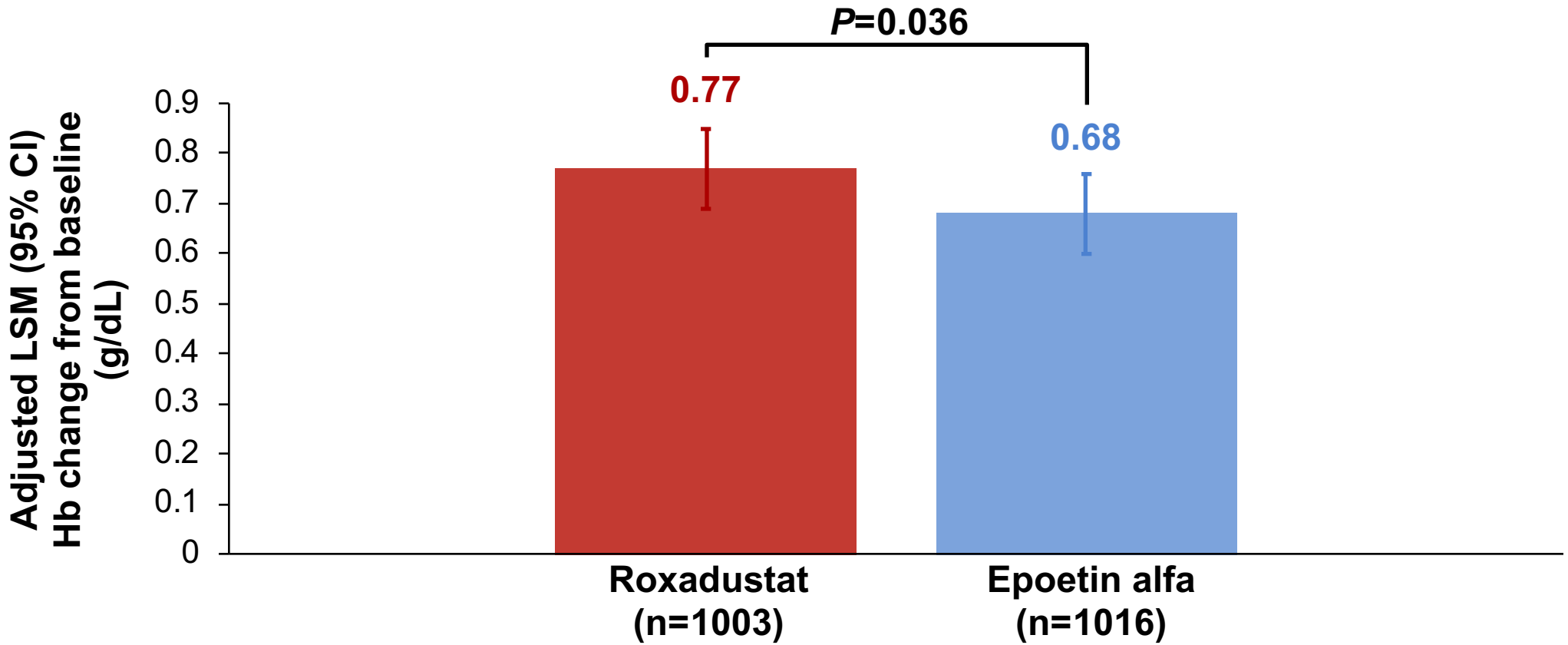
CKD, chronic kidney disease; CV, cardiovascular; EOS, end of study; EOT, end of treatment; Hb, hemoglobin; R, randomization; TIW, three times weekly; wk, week(s)

Patient Disposition



AE, adverse event; GCP, good clinical practice; Pt, patient; Tx, treatment

Primary Efficacy Endpoint for US: Hb Change from Baseline to Average Hb in Weeks 28–52



Intent-to-treat analysis set. Error bars are 95% confidence intervals

CI, confidence interval; Hb, hemoglobin; LSM, least squares mean; US, United States

Adverse Events in the Population*

AE category	Roxadustat (N=1048)			Epoetin alfa (N=1053)		
	N pts w/ event	%	N per 100 P-Y	N pts w/ event	%	N per 100 P-Y
Any AE	891	85.0	**168.2**	890	84.5	**132.5**
Any AE leading to discontinuation of drug	57	5.4	**3.1**	26	2.5	**1.2**
Any serious AE	604	57.6	**49.2**	606	57.5	**43.5**
All-cause mortality	167	15.9	**9.0**	187	17.8	**8.9**

*Followed on-treatment and for 28 days off-treatment

AE, adverse event; pts, patients; P-Y, patient years; w/, with

Common AEs and SAEs in the Population*

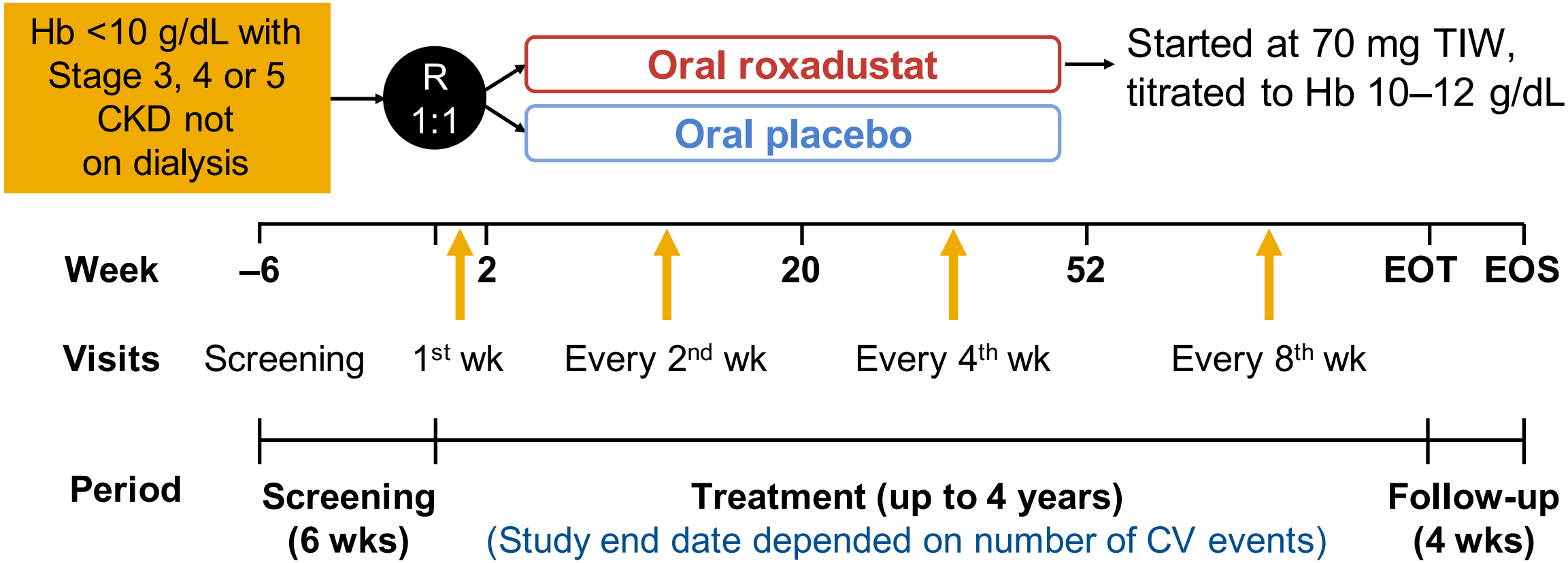
AE category	Roxadustat (N=1048)			Epoetin alfa (N=1053)		
	N pts w/ event	%	N per 100 P-Y	N pts w/ event	%	N per 100 P-Y
Most reported AEs						
Diarrhea	117	11.2	**6.8**	107	10.2	**5.5**
Hypertension	92	8.8	**5.3**	94	8.9	**4.8**
Pneumonia	91	8.7	**5.1**	101	9.6	**5.0**
Headache	82	7.8	**4.7**	57	5.4	**2.8**
Arteriovenous fistula thrombosis	78	7.4	**4.4**	57	5.4	**2.8**
Most reported SAEs						
Pneumonia	70	6.7	**3.9**	78	7.4	**3.8**
Sepsis	40	3.8	**2.2**	40	3.8	**1.9**
Acute MI	39	3.7	**2.1**	41	3.9	**2.0**
Arteriovenous fistula thrombosis	37	3.5	**2.0**	31	2.9	**1.5**

*Followed on-treatment and for 28 days off-treatment

AE, adverse event; FAIR, follow-up adjusted incidence rate; MI, myocardial infarction; pts, patients; P-Y, patient years; SAE, serious adverse event, w/, with

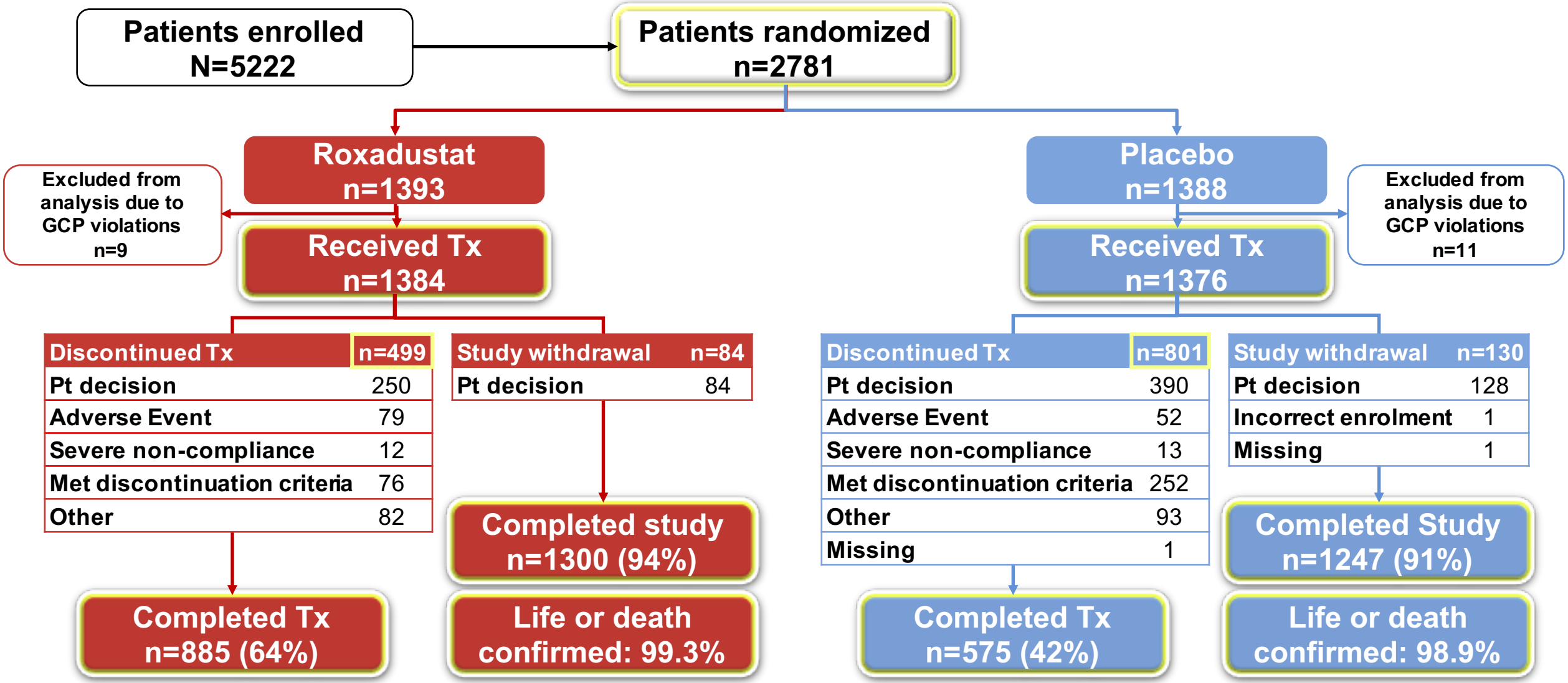
Roxadustat Phase III OLYMPUS trial

Design: Phase 3, Double-Blind, Randomized



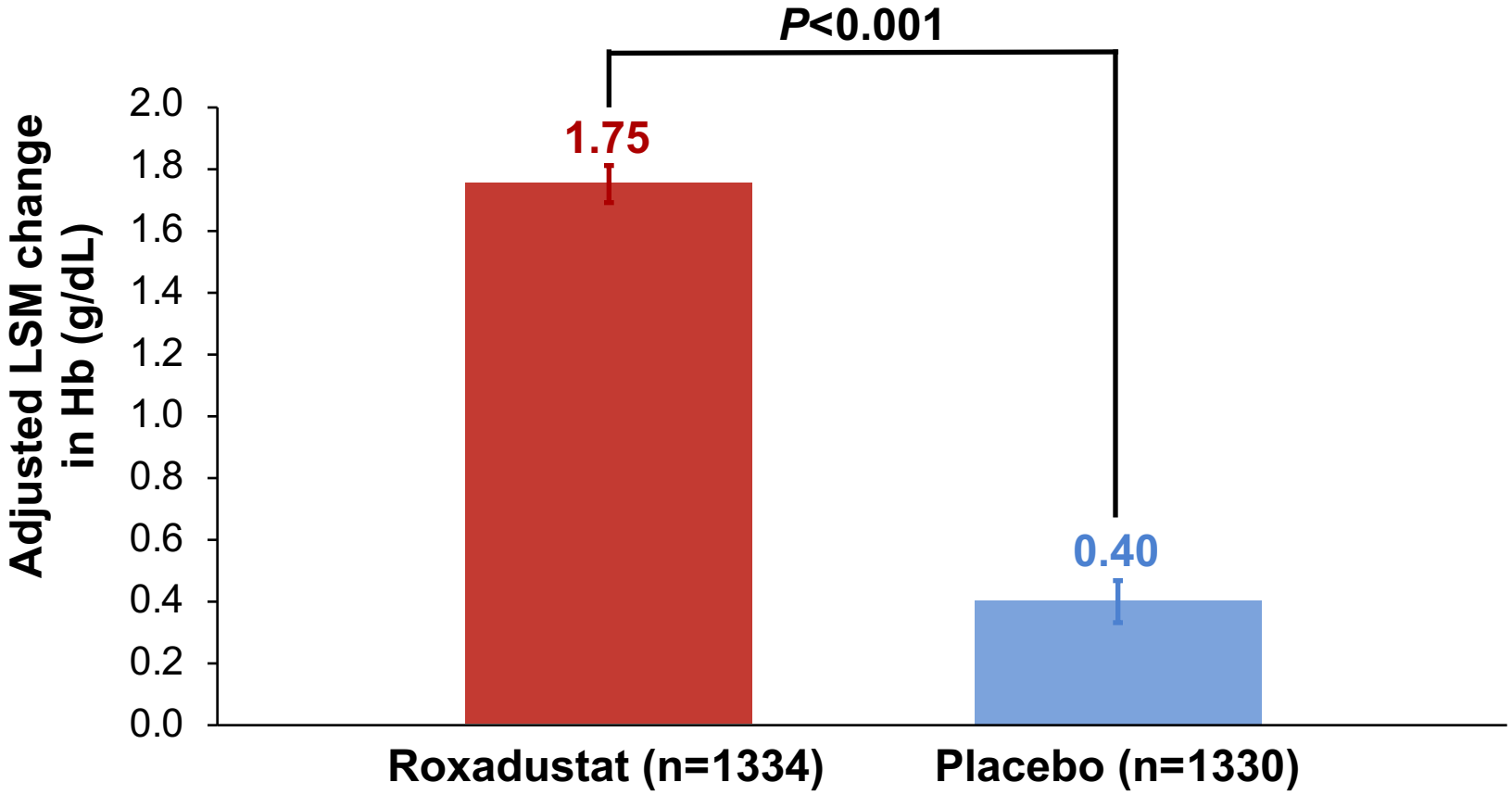
CKD, chronic kidney disease; CV, cardiovascular; EOS, end of study; EOT, end of treatment; Hb, hemoglobin; R, randomization; TIW, three times weekly; wk, week(s)

Patient Disposition



Patients who discontinued treatment were followed for concomitant medications, adverse events, vital status and hospitalization. GCP, good clinical practice; Pt, patient; Tx, treatment

Primary Efficacy Endpoint for US: Change in Hemoglobin from Baseline to the Average Over Weeks 28–52



Intent-to-treat analysis set. Error bars are 95% confidence intervals

Hb, hemoglobin; LSM, least squares mean

Adverse Events (ITT*)

OLYMPUS Events	Roxadustat (N=1384)			Placebo (N=1377)		
	N pts w/ event	%	N per 100 P-Y†	N pts w/ event	%	N per 100 P-Y†
Any AE	1243	89.8	**182.9**	1216	88.3	**171.9**
Any AE leading to discontinuation of drug	78	5.6	**2.8**	57	4.1	**2.1**
Any serious AE	795	57.4	**42.1**	749	54.4	**40.0**
All-cause mortality‡	284	20.5	**9.6**	245	17.8	**8.4**
Pooled data from non-dialysis patients (Phase 3: OLYMPUS, ANDES, ALPS)						
	Roxadustat (N=2386)			Placebo (N=1884)		
All-cause mortality‡	400	16.8	**8.3**	301	16.0	**8.1**

*ITT analysis; includes events on-treatment + off-treatment until study end date. †N per 100 P-Y calculated by FAIR
‡Includes deaths from adverse events and public record searches

AE, adverse event; FAIR, follow-up adjusted incidence rate; ITT, intent-to-treat; pts, patients; P-Y, patient years; w/, with

Common Adverse Events (ITT*)

AE category	Roxadustat (N=1384)			Placebo (N=1377)		
	N pts w/ event	%	N per 100 P-Y†	N pts w/ event	%	N per 100 P-Y†
Most reported AEs						
End stage renal disease	209	21.0	**11.7**	282	20.5	**11.8**
Urinary tract infection	177	12.8	**6.8**	110	8.0	**4.2**
Pneumonia	165	11.9	**6.2**	130	9.4	**4.9**
Hypertension	159	11.5	**6.1**	125	9.1	**4.8**
Most reported SAEs						
End stage renal disease	199	14.4	**7.7**	201	14.6	**8.1**
Pneumonia	113	8.2	**4.1**	88	6.4	**3.3**
Azotemia	61	4.4	**2.2**	60	4.4	**2.2**
Sepsis	49	3.5	**1.8**	23	1.7	**0.8**
Acute kidney injury	41	3.0	**1.5**	32	2.3	**1.2**
Hyperkalemia	41	3.0	**1.5**	25	1.8	**0.9**

*ITT analysis; includes events on-treatment + off-treatment in long term follow-up until study end date

†N per 100 P-Y calculated by FAIR

AE, adverse event; FAIR, follow-up adjusted incidence rate; ITT, intent-to-treat; pts, patients; P-Y, patient years; w/, with

Conclusions for both trials

ROCKIES

- Compared with epoetin alfa, roxadustat:
  - Increased Hb at least as effectively in dialysis patients with anaemia
  - Increased Hb more effectively in those with inflammation
  - Required significantly less monthly IV iron use
  - Lowered hepcidin to a greater extent
- Common adverse events with roxadustat were generally similar to those of epoetin alfa and commonly found in dialysis-dependent patients

OLYMPUS

- Compared with placebo, roxadustat treatment:
  - Significantly increased Hb levels
    - regardless of iron-repletion
    - regardless of inflammation
  - Reduced the need for rescue therapy, including red blood cell (RBC) transfusion
- More patients on placebo discontinued study drug earlier than roxadustat, especially in patients with more advanced CKD (lower eGFR[1])
- Overall safety findings are generally consistent with the patient population
- Risks and benefits of roxadustat will be determined across all trials in the development program

Source: Oral Presentation #TH-OR022, ROCKIES: An International, Phase 3, Randomized, Open-Label, Active-Controlled Study of Roxadustat for Anemia in Dialysis-Dependent CKD Patients, ASN Kidney Week 2019, Washington D.C., US.

Oral Presentation #TH-OR023, OLYMPUS: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, International Study of Roxadustat Efficacy in Patients with Non-Dialysis-Dependent (NDD) Chronic Kidney Disease (CKD) and Anemia, ASN Kidney Week 2019, Washington D.C., US. 1. glomerular filtration rate

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Roxadustat Phase III ‘pooled’ safety and efficacy

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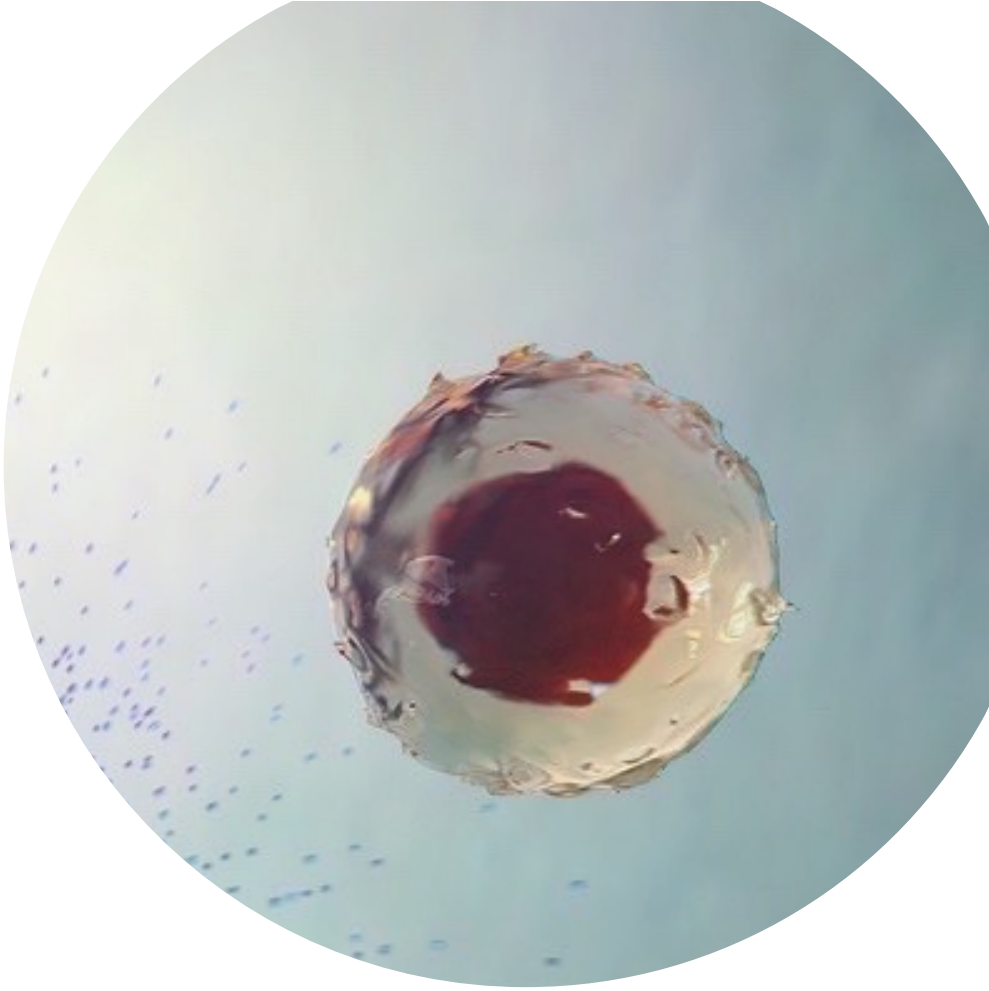


Roxadustat Phase III ‘pooled’ safety and efficacy

Roxadustat NDD and DD Program

Phase 3 CKD non-dialysis-dependent (NDD) Pool				
D5740C00001	FGCL-4592-060	1517-CL-0608	**NDD Pooled**	
OLYMPUS	**ANDES**	**ALPS**		
AstraZeneca	FibroGen	Astellas	**Roxa**	**Placebo**
N=2761	**N=922**	**N=594**	**N=2391**	**N=1886**
R 1:1	R 2:1	R 2:1	**1.62 Avg PEY**	**1.23 Avg PEY**

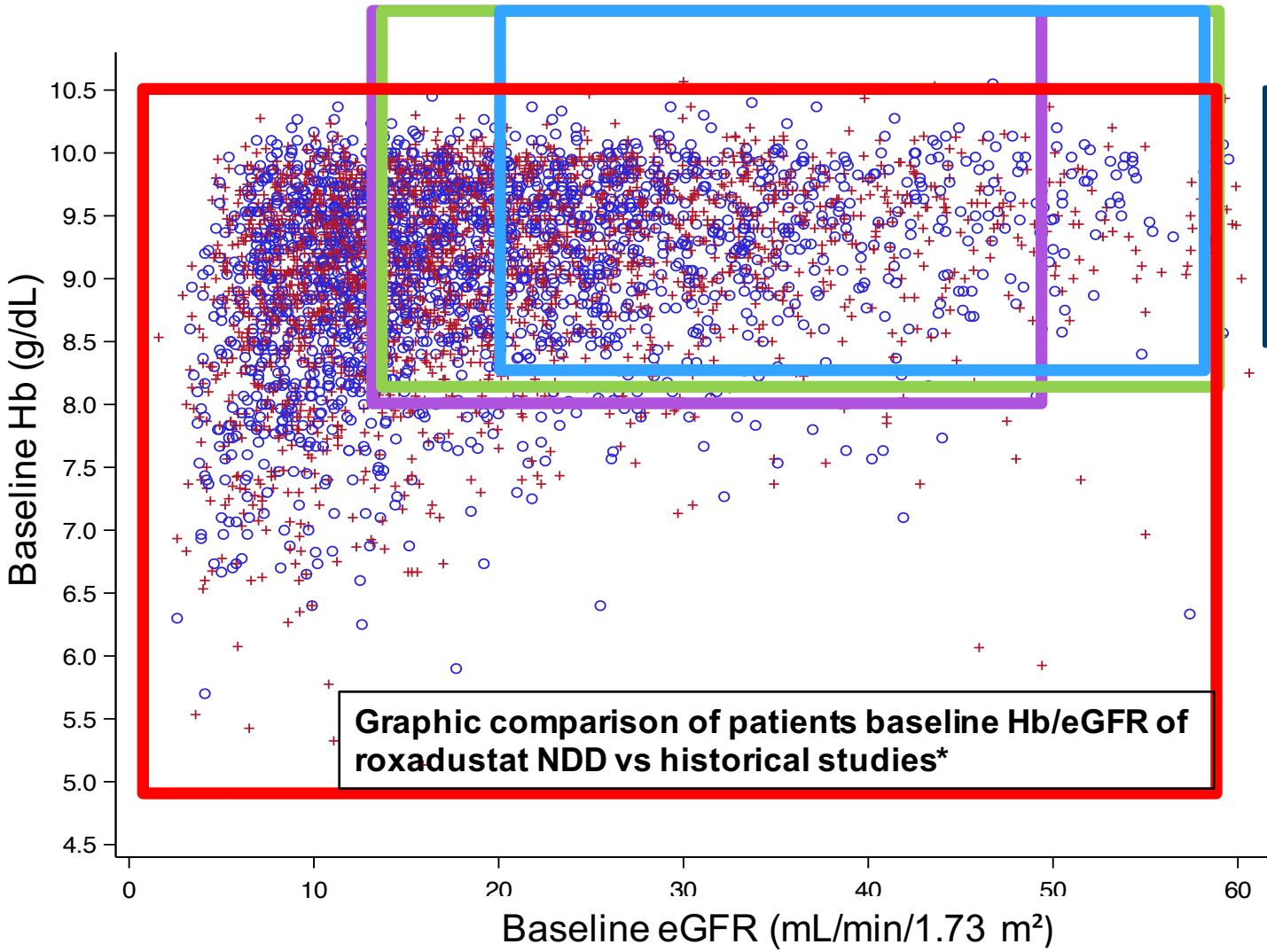
Number of patients: 4277
Patient exposure years: 6194

Phase 3 CKD dialysis-dependent (DD) Pool				
D5740C00002	FGCL-4592-064	FGCL-4592-063	**DD Pooled**	
ROCKIES	**SIERRAS**	**HIMALAYAS**		
AstraZeneca	FibroGen	FibroGen	**Roxa**	**EPO**
Global	US only	Global		
N=2106	**N=741**	**N=1043**	**N=1943**	**N=1947**
R 1:1	R 1:1	R 1:1		
Correction & maintenance Early & Stable DD	Maintenance Early & Stable DD	Correction DD Vintage<4mos Only (Early)	**1.71 Avg PEY**	**1.92 Avg PEY**

Number of patients: 3880
Patient exposure years: 7059

 EPO, epoetin alfa; Hb, hemoglobin; PEY, patient exposure year; R, Randomization, Roxa, roxadustat

Roxadustat NDD Program: Evaluation of Anemia Therapy In A Broad Range of Patients Not Included In Prior CKD Anemia Trials



Roxadustat NDD Patient Features

Advanced CKD: 42% CKD 5

Low Iron stores: 40% non-iron replete

Low Mean Baseline Hb: 9.1

CHOIR (2006)

ARCTOS Mircera (2008)

TREAT (2009)

Roxadustat NDD

Actual Pooled Treatment 1 for Period
o Placebo + Roxadustat

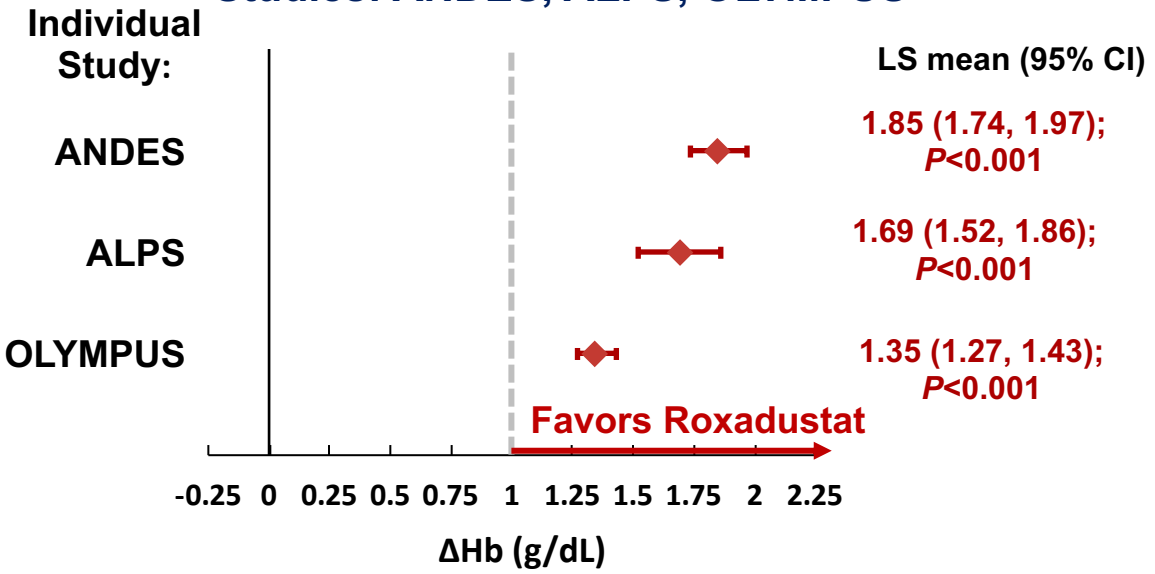
*Historical study patients baseline Hb & eGFR characteristics in figure is based on approximations from published manuscripts
eGFR, estimated glomerular filtration rate

NDD Efficacy: Met Primary Efficacy Endpoint

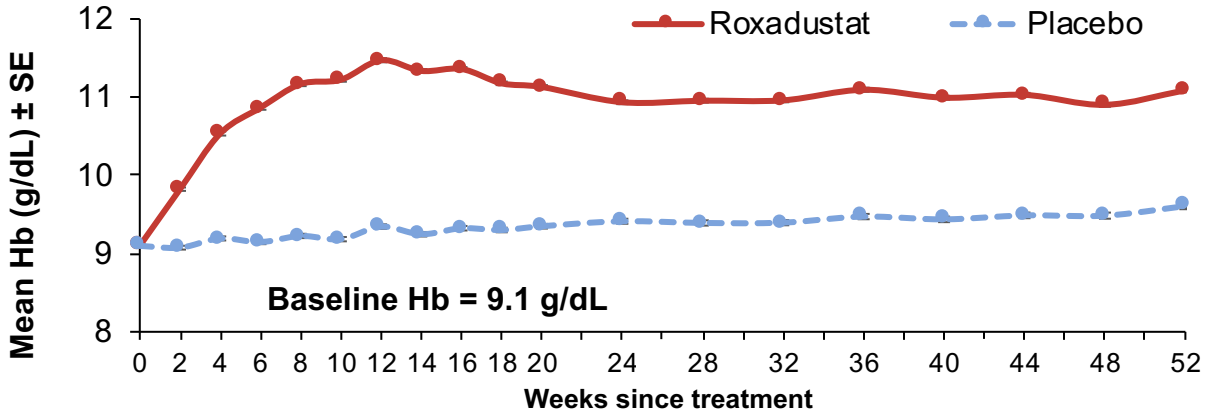
Roxadustat is superior to placebo, regardless of iron-repletion

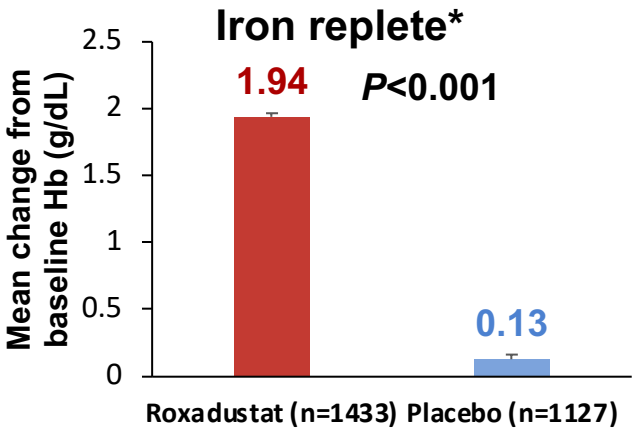
Primary efficacy endpoint (change in Hb from baseline to Hb averaged over Weeks 28–52) was met in individual studies and pooled analyses

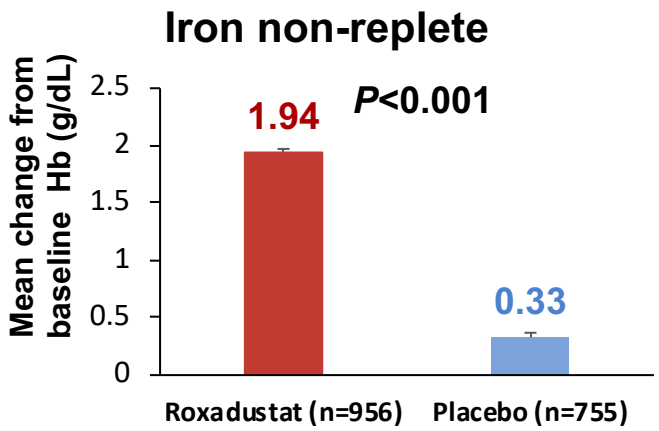
Hb change from baseline to Week 28–52
Studies: ANDES, ALPS, OLYMPUS



NDD (N=4277): Mean Hb over time up to Week 52 (g/dL)
Hb change to Week 28–52: 1.85 (Roxa) vs 0.13 (Placebo) *P<0.001*







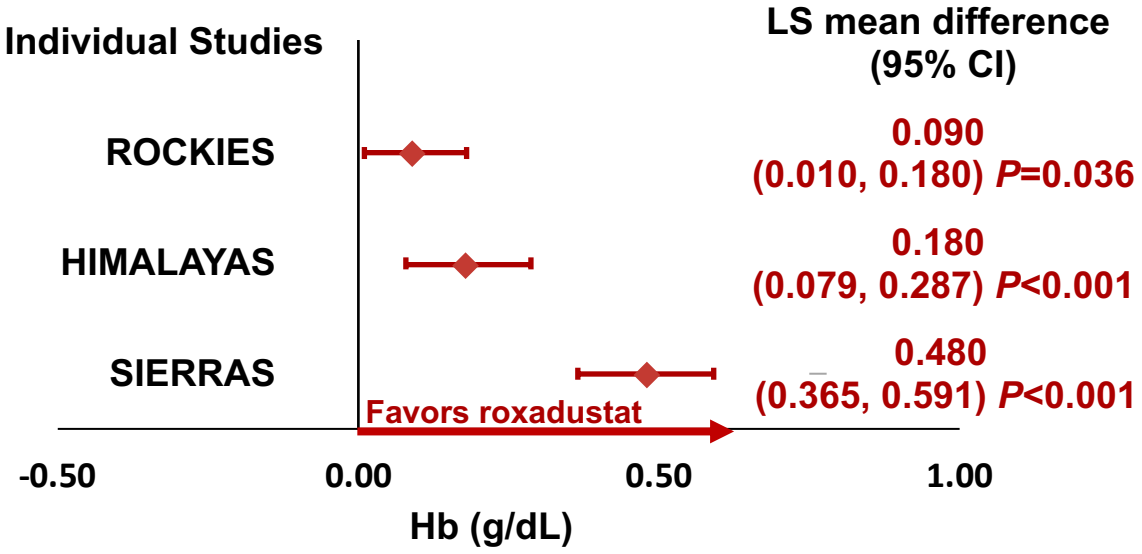
*Iron Replete: TSAT ≥20% and ferritin ≥100 ng/mL

CI, confidence interval; LS, least squares; SE, standard error

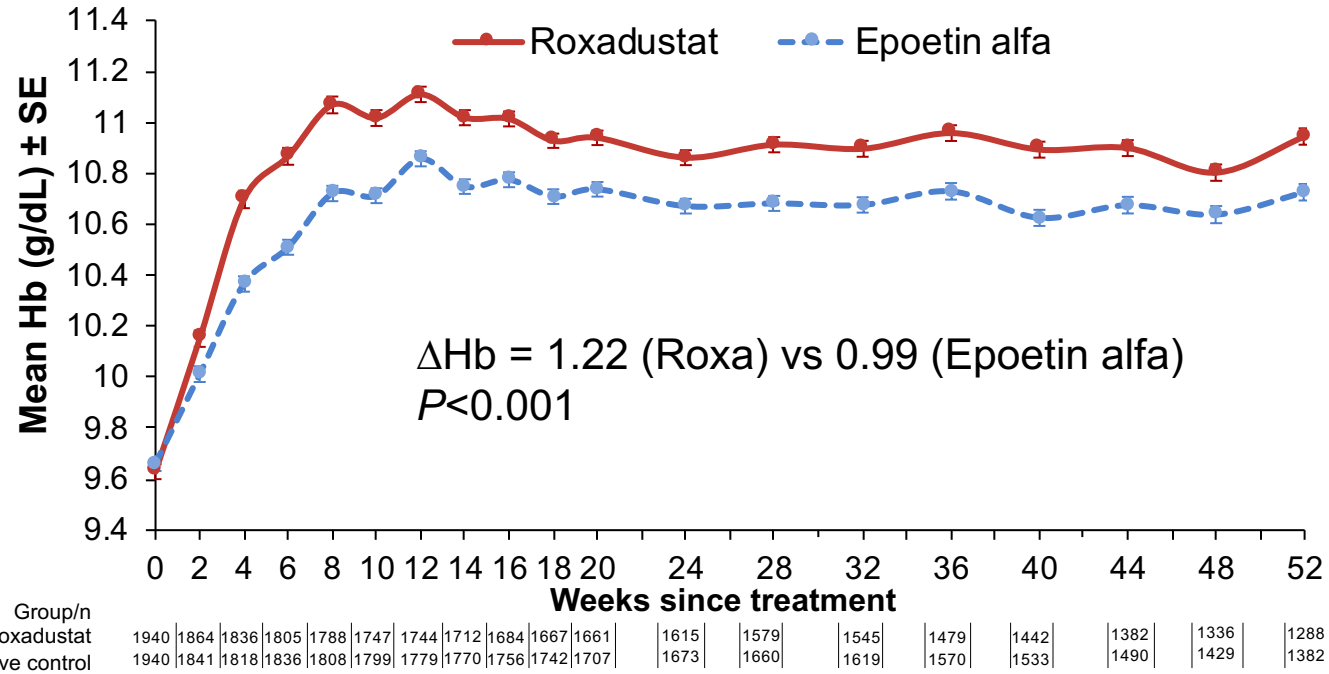
DD: Roxadustat Efficacious, Larger Hb Increase Than EPO in Individual Studies & In Pooled Analysis

Primary efficacy endpoint (change in Hb from baseline to Hb averaged over Weeks 28 to 52): Roxadustat achieved larger Hb increase over epoetin alfa in individual studies & in pooled DD

Hb (g/dL) change from baseline to Week 28–52



DD (N=3857): mean Hb (g/dL) over time

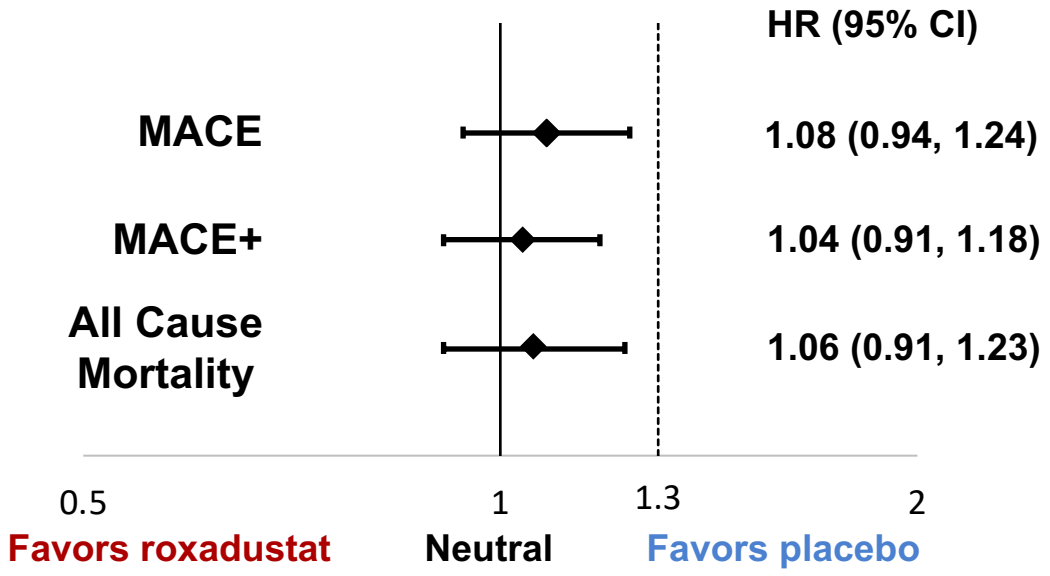


 CRP, C-reactive protein; EPO, epoetin alfa

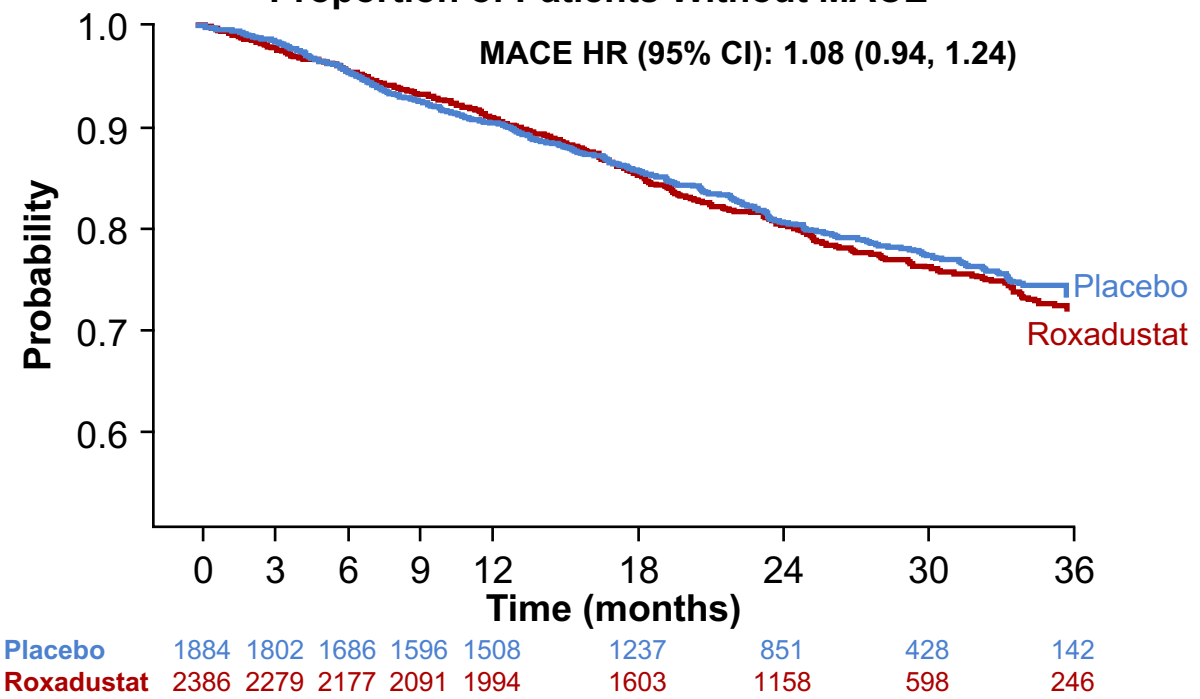
NDD Pool: Cardiovascular Safety Endpoints MACE, MACE+, All-cause Mortality

Risks of MACE, MACE+, or all-cause mortality in roxadustat patients were comparable to placebo in NDD patients*

Time to event endpoints using Cox model, ITT analysis
NDD (OLYMPUS, ANDES, ALPS), N=4270



Proportion of Patients Without MACE**

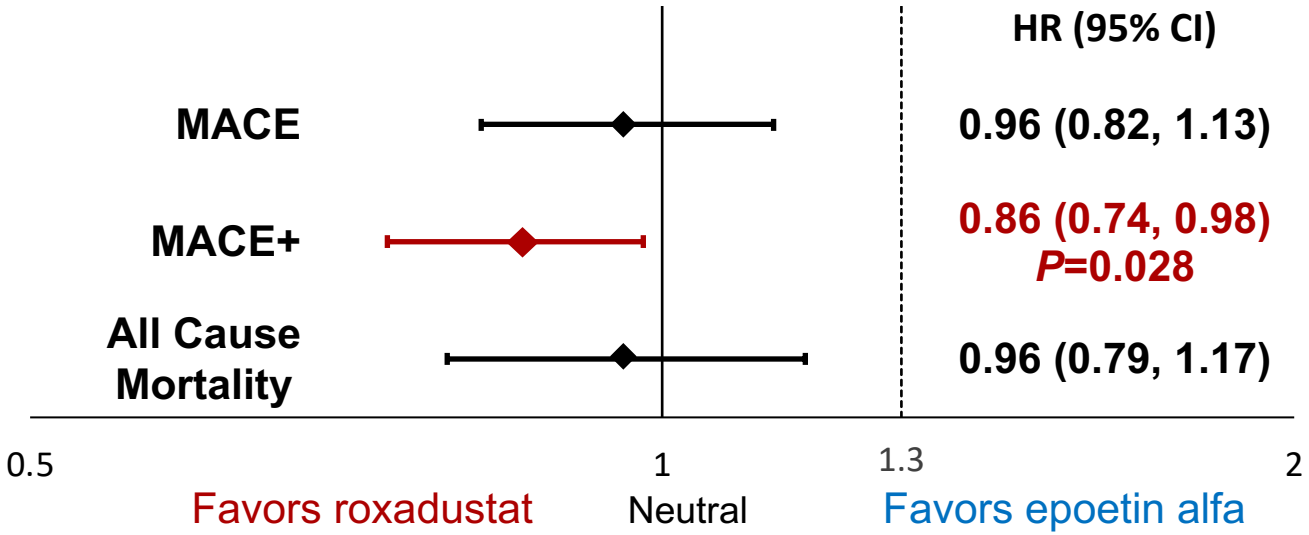


*"comparable" based on hazard ratio (HR) upper bound of 95% confidence interval (95%CI) below reference non-inferiority margin of 1.3
**ITT analysis = Intent to treat analysis evaluation period to include on-treatment and off-treatment long term follow-up, until end of study

DD Pooled: Cardiovascular Safety Endpoints

- Risk of MACE and all cause mortality in roxadustat patients were not increased compared to epoetin alfa in DD patients*
- Roxadustat patients had a lower risk of MACE+ than epoetin alfa patients

Time to event endpoints using Cox model, on-treatment analysis DD (ROCKIES, HIMALAYAS, SIERRAS), N=3880



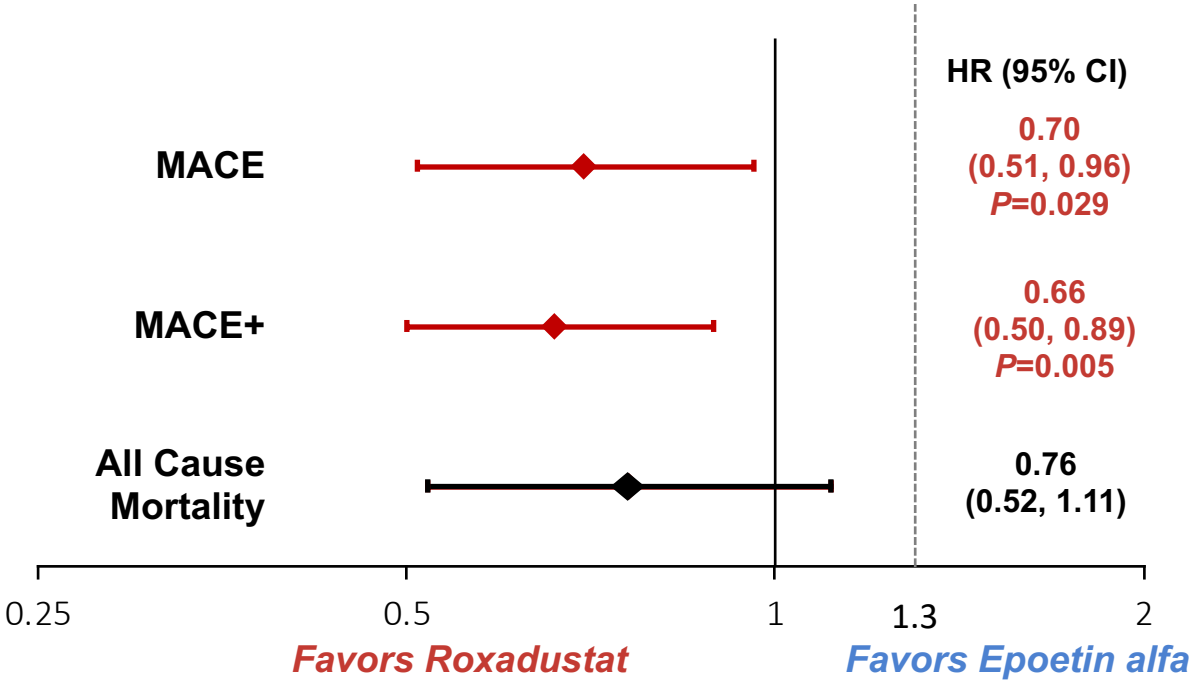
MACE+ Components Incidence Rates, N (%)		
Events	Roxadustat	Epoetin alfa
n	1940	1940
Death (all-cause mortality)	207 (10.7%)	232 (12.0%)
Myocardial infarction	103 (5.3%)	109 (5.6%)
Stroke	45 (2.3%)	50 (2.6%)
Unstable angina	18 (0.9%)	22 (1.1%)
Congestive heart failure	120 (6.2%)	166 (8.6%)

*"risk not increased" based on hazard ratio (HR) upper bound of 95% confidence interval (95%CI) below reference non-inferiority margin of 1.3

Incident Dialysis Pool: Cardiovascular Safety Endpoints

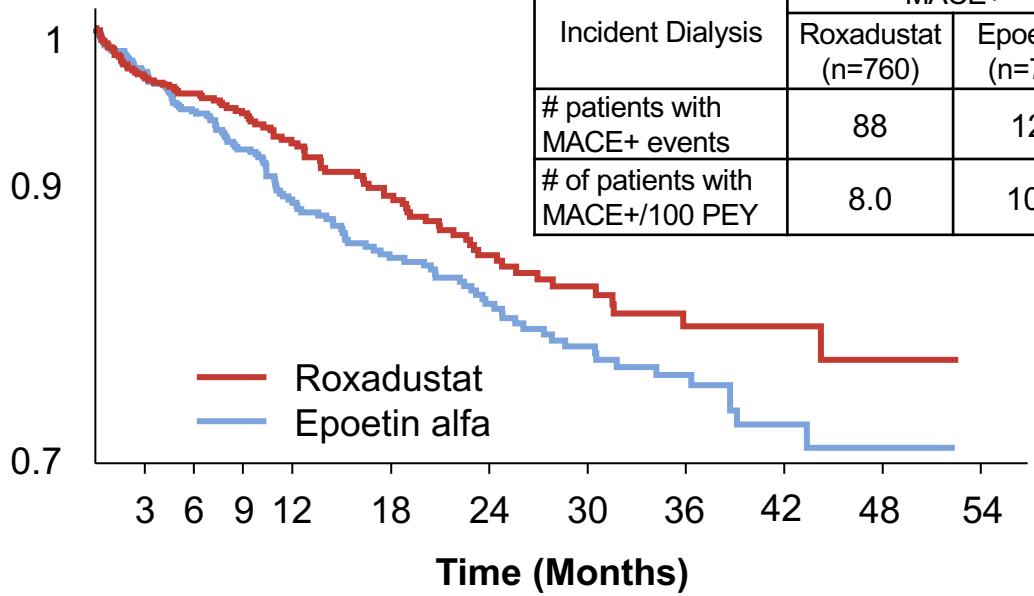
Roxadustat had 30% lower risk of MACE and 34% lower risk of MACE+ than epoetin alfa* and with a trend towards lower all-cause mortality relative to epoetin alfa, in incident dialysis patients

Time to event endpoints using Cox model ID (ROCKIES, HIMALAYAS, SIERRAS), N=1526



Proportion of Patients Without MACE+ Over Time

Incident Dialysis	MACE+	
	Roxadustat (n=760)	Epoetin α (n=766)
# patients with MACE+ events	88	121
# of patients with MACE+/100 PEY	8.0	10.2



Epoetin alfa	699	605	511	401	316	246	171	111	50	24	0
Roxadustat	673	594	495	389	304	223	137	87	43	16	0

*Lower MACE & MACE+ risks – based on incident dialysis

Conclusions: *Efficacy*

- **Roxadustat efficacy was demonstrated**
  - **Achieved primary efficacy endpoint (change in Hb) in individual studies and pooled analyses**
    - **NDD:** roxadustat was superior to placebo and efficacious regardless of iron-repletion
    - **DD:** roxadustat achieved larger mean Hb increase than epoetin alfa, especially in inflamed patients, and less IV iron was required in roxadustat arm than in epoetin alfa.
  - **Lower RBC transfusion risk**
    - **NDD:** In roxadustat patients compared with placebo
    - **DD:** In roxadustat patients compared with epoetin alfa
  - **Other potential benefits in NDD**
    - Reduced LDL cholesterol
    - Less decline in eGFR

Conclusions: *Roxadustat CV Safety*

- **CV safety was demonstrated in all study populations**
  - **Non-dialysis:** Risk of MACE, MACE+, and all-cause mortality in roxadustat patients were comparable to placebo in NDD patients
  - **Incident dialysis:** Roxadustat had 30% lower risk of MACE and 34% lower risk of MACE+ than epoetin alfa, and with a trend towards lower all-cause mortality relative to epoetin alfa
  - **Dialysis-dependent:**
    - Roxadustat patients had a lower risk of MACE+ than epoetin alfa patients
    - Risk of MACE and all-cause mortality in roxadustat patients were not increased compared to epoetin alfa in DD patients

Agenda

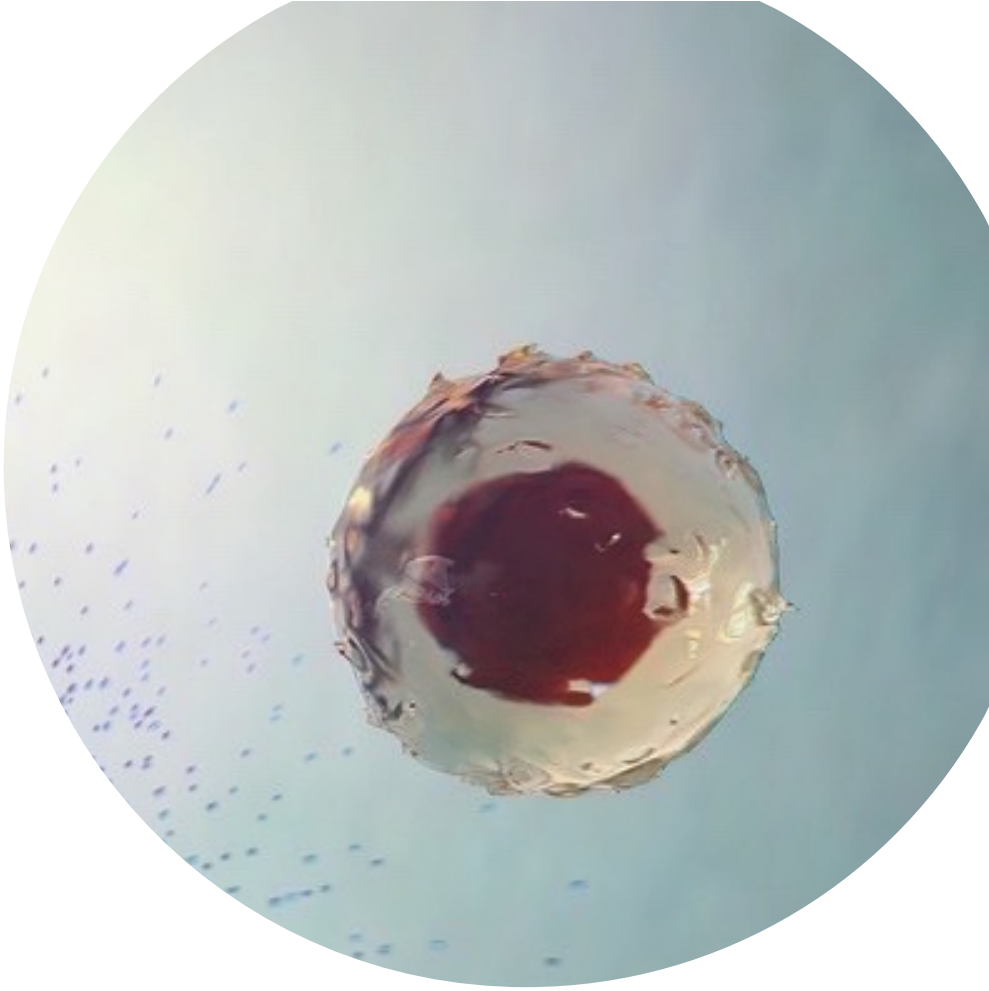
Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

Roxadustat Phase III ‘pooled’ safety and efficacy

Commercial opportunity

Q&A



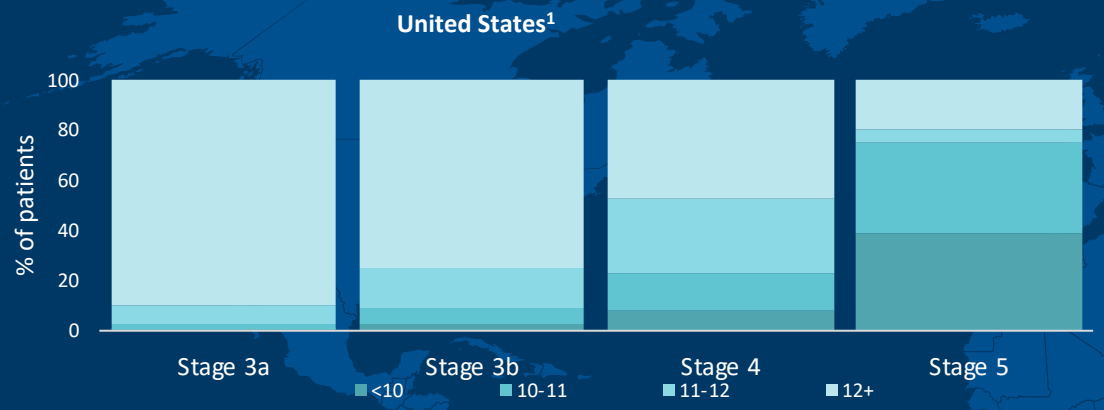
How does roxadustat compare to currently approved treatments for anaemia from CKD in NDD or DD patients?

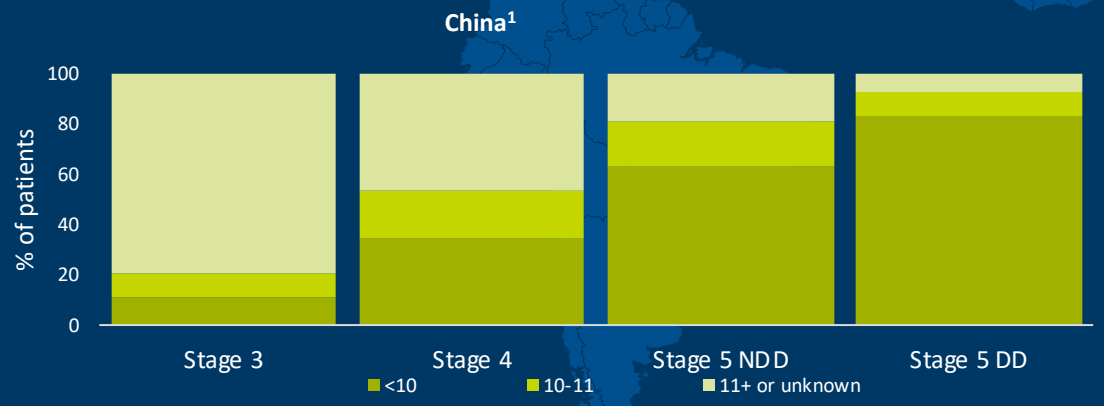
How do you see roxadustat fitting into or potentially changing the CKD treatment paradigm?

What factors will enable more patients, who require treatment of anaemia from CKD in NDD or DD, to benefit from roxadustat in the future?

Chronic kidney disease

The prevalence of anaemia increases as the disease progresses





30 million[2]
US prevalence of patients with CKD

19 million[2]
US prevalence of patients with CKD (Stage 3-5)

4 million[2]
US diagnosed patients with anaemia[3] from CKD

2 million[2]
US treated[4] patients with anaemia from CKD

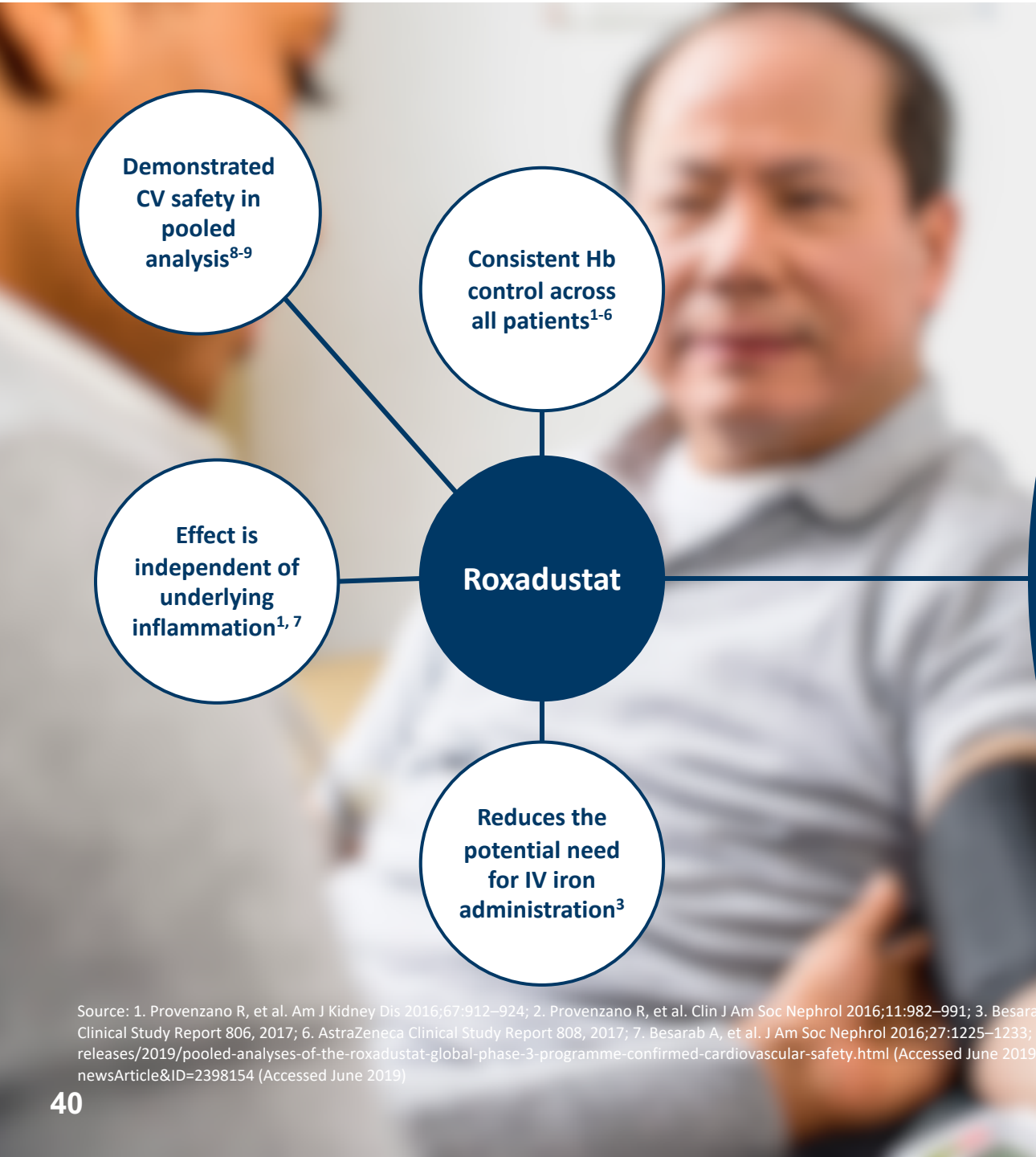
120 million[2]
China prevalence of patients with CKD

39 million[2]
China prevalence of patients With CKD (Stage 3-5)

3 million[2]
China diagnosed patients with anaemia[5] from CKD

1.5 million[2]
China treated[4] patients with anaemia from CKD

Source: 1. National Health and Nutrition Examination Survey (NHANES), AstraZeneca. 2. NHANES, United States Renal Data System (USRDS), Decision Resources, Adelphi DSP, IMS data analysis and Beijing Renmin Hospital. 3. Stage 3-5. 4. Iron or ESA. 5. Hb <11 g/dL



US regulatory submission in Q4 2019

Source: 1. Provenzano R, et al. Am J Kidney Dis 2016;67:912–924; 2. Provenzano R, et al. Clin J Am Soc Nephrol 2016;11:982–991; 3. Besarab A, et al. J Am Soc Nephrol 2016;27:1225–1233; 4. Chen N, et al. Nephrol Dial Transplant 2017;32:1373–1386; 5. AstraZeneca Clinical Study Report 806, 2017; 6. AstraZeneca Clinical Study Report 808, 2017; 7. Besarab A, et al. J Am Soc Nephrol 2016;27:1225–1233; 8. AstraZeneca Press Release, May 2019. Available at: https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2019/pooled-analyses-of-the-roxadustat-global-phase-3-programme-confirmed-cardiovascular-safety.html (Accessed June 2019); 9. FibroGen Press Release, May 2019. Available at: http://phx.corporate-ir.net/phoenix.zhtml?c=253783&p=irol-newsArticle&ID=2398154 (Accessed June 2019)

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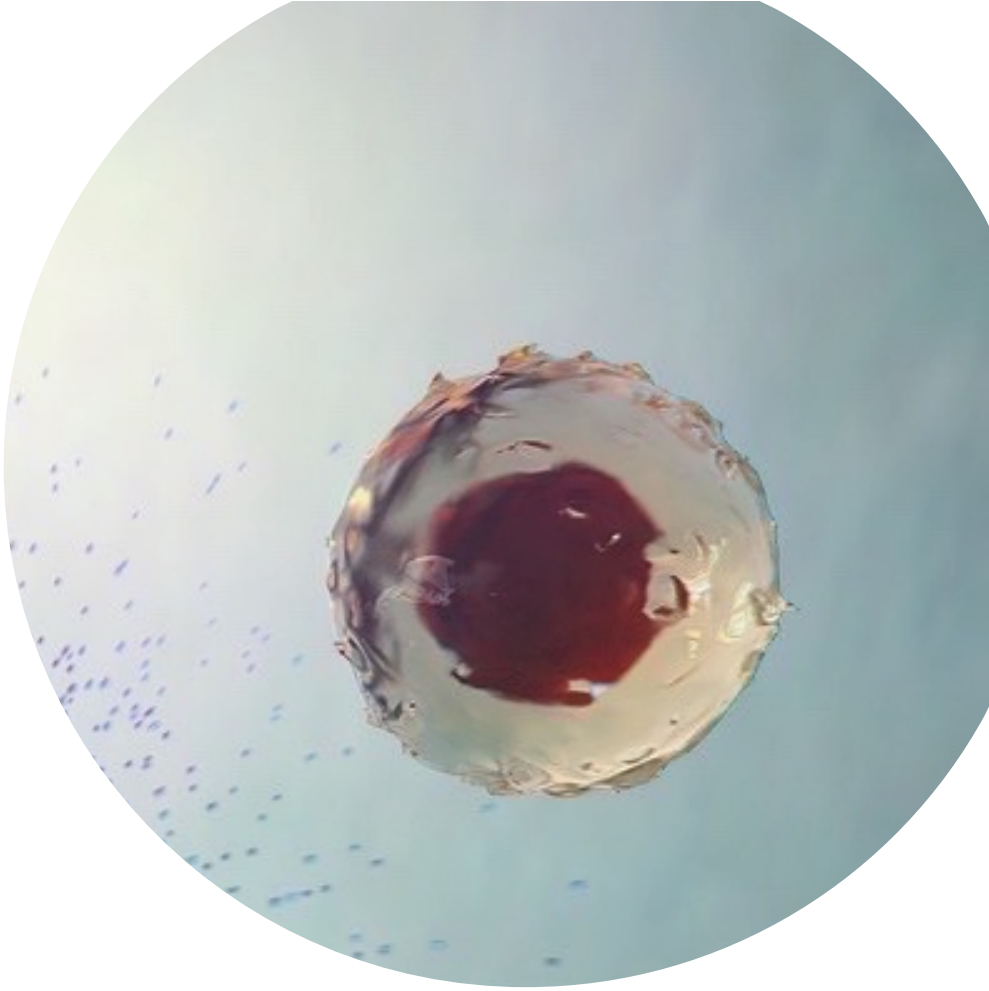


Q&A

Use of AstraZeneca conference call, webcast and presentation slides