

Iron Parameters in Patients Treated with Roxadustat for Anemia of Chronic Kidney Disease

Tomas Ganz, Francesco Locatelli, Mustafa Arici, Tadao Akizawa, and Michael Reusch

Supplementary Material

Table S1. Study Characteristics of Phase 3 Trials in Patients With Non–Dialysis-Dependent (NDD) and Dialysis-Dependent (DD) Chronic Kidney Disease Randomized to Receive Roxadustat

Table S2. Total Iron-Binding Capacity in Patients With Chronic Kidney Disease Randomized to Receive Roxadustat, Erythropoiesis-Stimulating Agent (ESA), or Placebo ($\mu\text{g/dL}$)^a

Table S3. Transferrin Saturation in Patients With Chronic Kidney Disease Randomized to Receive Roxadustat, Erythropoiesis-Stimulating Agent (ESA), or Placebo (%)

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Table S1. Study Characteristics of Phase 3 Trials in Patients With Non–Dialysis-Dependent (NDD) and Dialysis-Dependent (DD) Chronic Kidney Disease Randomized to Receive Roxadustat

	Chen[11]	Chen[10]	CL-0314[7]	CL-0310[6]	CL-0307[5]	CL-0308[9]	CL-0312[9]	CL-0302[8]	ALPS[12]	OLYMPUS[13]	ANDES[14]	DOLOMITES[15]	HIMALAYAS[16]	ROCKIES[17, 20]	PYRENEES[18]	SIERRAS[19]
Region	China	China	Japan	Japan	Japan	Japan	Japan	Japan	Global	Global	Global	Europe	Global	Global	Europe	United States
Comparator	PBO	EA	–	DA	DA	–	–	–	PBO	PBO	PBO	DA	EA	EA	DA or EA	EA
Randomized, <i>n</i>	154	305	100	334	303	75	164 ^a	ESA-N: 13 ESA-C: 43	597	2781	922	616	1043	2106	838	741
NDD, <i>n</i>	154	–	100	334	–	–	–	–	597	2781	922	616	NA	NA	NA	NA
ID-DD, <i>n</i>	–	–	–	–	–	75	–	56	–	–	–	NA	1039	283	–	71
Stable DD, <i>n</i>	–	305	–	–	303	–	164	–	–	–	–	NA	–	1823	838	–
Baseline Hb, g/dL ^{b,c}	7.0-10.0	9.0-12.0	<10.5	10.0-12.0	10.0-12.0	≤10.0	10.0-12.0	ESA-N: <10.5 ESA-C: 10.0-12.0	≤10.0	<10.0	≤10.0	≤10.5	≤10.0	<10.0 or <12.0	9.5-12.0	9.0-12.0
Hb target, g/dL ^c	100-120	100-120	100-120	100-120	100-120	100-120	100-120	100-120	100-120	≥110	≥110	100-120	100-120 ^d	100-120 ^d	100-120	100-120 ^d
Roxadustat starting dose, mg, TIW	70 (pts 40-60 kg) 100 (pts ≥60 kg)	100 (pts 45-60 kg) 120 (pts ≥60 kg)	50 or 70	70 or 100	70 or 100	50 or 70	70 or 100	ESA-N: 50 or 70 ESA-C: 70 or 100	70 (pts 45-70 kg) 100 (pts 70-160 kg)	70	70 (pts 45-70 kg) 100 (pts ≥70 kg)	70 or 100	70 (pts ≤70 kg) 100 (pts 70-160 kg)	70 (pts 45-70 kg) 100 (pts 70-160 kg)	100, 150, or 200 ^e	70, 100, 150, or 200 ^e
Baseline characteristics																
Iron-replete, <i>n</i> (%)	–	–	43 (43.4)	106 (52.7)	44 (29.1)	–	–	ESA-N: 11 (84.6) ESA-C: 19 (44.2)	204 (52.2)	809 (58.5)	373 (60.6)	182 (56.3)	406 (77.8)	–	355 (86.0)	360 (97.3)
Age, <i>y</i> , mean (SD)	54.7 (13.3)	47.6 (11.7)	68.8 (11.3)	69.3 (11.2)	64.6 (11.7)	66.2 (12.1)	62.8 (11.8)	ESA-N: 66.1 (10.9) ESA-C: 63.7 (10.1)	62.0 ^f (20-89)	60.9 (14.7)	64.9 (12.6)	66.8 (13.6)	53.8 (14.7)	53.5 (15.3)	61.0 (13.8)	57.6 (13.6)
eGFR, mL/min, mean (SD)	16.5 (8.0)	–	–	17.7 (7.9)	–	–	–	–	16.5 (10.2)	19.7 (11.7)	21.9 (11.5)	20.3 (11.5)	–	–	–	–
Dialysis vintage (<i>y</i>), mean (SD)	–	4.5 (3.5)	–	–	7.7 (7.5)	0.053 (0.051)	7.5 (6.6)	ESA-N: 3.0 (3.2) ESA-C: 3.2 (3.2)	–	–	–	–	0.2 (0.07)	–	4.4 (4.2)	4.0 (3.5)

DA, darbepoetin alfa; EA, epoetin alfa; eGFR, estimated glomerular filtration rate; ESA, erythropoiesis-stimulating agent; ESA-N, ESA-naive; ESA-C, ESA-converted; Hb, hemoglobin; ID-DD, incident-to-dialysis dialysis-dependent; NA, not applicable or not available; PBO, placebo; pts, patients; SD, standard deviation; TIW, 3 times per week.

^aPatients were registered to 1 or 2 roxadustat groups, not randomized.

^bBaseline hemoglobin varied by ESA use at time of randomization.

^cTo convert to SI units (g/L), multiply numbers by 10.

^dHemoglobin maintenance target in ESA-treated patients followed local guidelines and labeling.

^eDependent on initial ESA dose 4 weeks prior to randomization.

^fMedian (range).

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Table S2. Total Iron-Binding Capacity in Patients With Chronic Kidney Disease Randomized to Receive Roxadustat, Erythropoiesis-Stimulating Agent (ESA), or Placebo ($\mu\text{g/dL}$)^a

Study	Roxadustat			ESA			Placebo			LSMD (95% CI)	P Value
	n	Mean Baseline	LSM CFB (95% CI)	n	Mean Baseline	LSM CFB (95% CI)	n	Mean Baseline	LSM CFB (95% CI)		
Chen[11]	85	305.25	101.68 (66.82) ^b	–	–	–	43	290.95	-1.84 (54.30) ^b	105.53 (82.63, 128.38)	–
Chen[10]	BL: 204 Wk 24: 160	264.80	53.07	BL: 100 Wk 24: 94	269.83	-6.70	–	–	–	59.78 (45.25, 74.30)	–
CL-0314[7]	99	268.72	32.96 (40.22) ^b	–	–	–	–	–	–	–	–
CL-0310[6]	201	265.92	–	131	259.78	–	–	–	–	–	–
CL-0307[5]	150	242.46	43.58 (45.25) ^b	151	243.02	8.94 (31.84) ^b	–	–	–	–	–
CL-0308[9]	74	236.3	75.4 (60.9) ^b	–	–	–	–	–	–	–	–
CL-0312[9]	163	248.6	55.9 (53.6) ^b	–	–	–	–	–	–	–	–
CL-0302[8]	–	–	–	–	–	–	–	–	–	–	–
ALPS[12] ^c	–	–	–	–	–	–	–	–	–	–	–
OLYMPUS[13]	BL: 1384 Wk 24: 1200	230.44	30.79 (28.08, 33.50)	–	–	–	BL: 1377 Wk 24: 1050	232.46	-3.82 (-6.65, -0.99)	34.61 (31.29, 37.93)	<0.001
ANDES[14]	BL: 608 Wk 44: 476	257.18	35.07 (30.13, 40.01)	–	–	–	BL: 305 Wk 44: 185	262.30	-3.58 (-10.33, 3.17)	38.65 (31.86, 45.45)	<0.0001
DOLOMITES[15] ^c	–	–	–	–	–	–	–	–	–	–	–
HIMALAYAS[16]	BL: 522 Wk 44: 364	241.04	37.70 (33.28, 42.12)	BL: 513 Wk 44: 383	238.06	1.65 (-2.73, 6.02)	–	–	–	36.05 (30.23, 41.87)	<0.0001
ROCKIES[17]	BL: 1051 Wk 24: 874	208.16	34.98 (31.77, 38.18)	BL: 1055 Wk 24: 946	208.64	-2.41 (-5.50, 0.68)	–	–	–	37.38 (33.82, 40.95)	<0.001
PYRENEES[18]	–	–	55.75 (49.38) ^b	–	–	15.31 (35.70) ^b	–	–	–	–	–
SIERRAS[19]	BL: 369 Wk 52: 235	201.88	47.21 (43.06, 51.37)	BL: 370 Wk 52: 272	202.89	10.94 (6.95, 14.92)	–	–	–	36.28 (31.73, 40.82)	<0.0001

Note: n numbers are the same for baseline and CFB unless otherwise specified.

CFB, change from baseline; LSM, least squares mean; LSMD, least squares mean difference.

^aTo convert to SI unit ($\mu\text{mol/L}$), multiply numbers by 0.179.

^bChange from baseline rather than least squares mean change from baseline.

^cSource provides no values for this parameter.

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Table S3. Transferrin Saturation in Patients With Chronic Kidney Disease Randomized to Receive Roxadustat, Erythropoiesis-Stimulating Agent (ESA), or Placebo (%)

Study	Roxadustat			ESA			Placebo			LSMD (95% CI)	P Value
	n	Mean Baseline	LSM CFB (95% CI)	n	Mean Baseline	LSM CFB (95% CI)	n	Mean Baseline	LSM CFB (95% CI)		
Chen[11]	85	20.6	-5.2 (10.4) ^a	–	–	–	43	23.2	-1.7 (9.2) ^a	-4.3 (-7.4, -1.1)	–
Chen[10]	BL: 204 Wk 27: 160	33.8	-4.5	BL: 100 Wk 27: 94	30.0	-8.7	–	–	–	4.2 (1.5, 6.9)	–
CL-0314[7]	99	27.9	1.0 (10.5) ^a	–	–	–	–	–	–	–	–
CL-0310[6]	201	34.1	–	131	32.7	–	–	–	–	–	–
CL-0307[5]	150	28.3	-1.1 (13.8) ^a	151	29.0	-2.4 (13.8) ^a	–	–	–	–	–
CL-0308[9]	74	28.5	-5.0 (14.8) ^a	–	–	–	–	–	–	–	–
CL-0312[9]	163	29.1	-3.9 (15.4) ^a	–	–	–	–	–	–	–	–
CL-0302[8]	ESA-N: 13 ESA-C: 43	ESA-N: 45.8 ESA-C: 35.9	ESA-N: -14.6 (15.8) ^a ESA-C: -8.1 (14.1) ^a	–	–	–	–	–	–	–	–
ALPS[12]. ^b	–	–	–	–	–	–	–	–	–	–	–
OLYMPUS[13]	BL: 1384 Wk 224: 1199	29.9	-0.8 (-1.4, -0.2)	–	–	–	BL: 1377 Wk 24: 1047	29.5	-0.3 (-0.9, 0.4)	-0.6 (-1.3, 0.2)	0.13
ANDES[14]	BL: 606 Wk 44: 476	26.3	0.4 (-0.8, 1.7)	–	–	–	BL: 304 Wk 44: 185	26.2	0.5 (-1.2, 2.3)	-0.1 (-2.0, 1.7)	0.90
DOLOMITES ^c	323	24.0	1.3 (11.8) ^a	293	23.3	5.2 (13.2) ^a	–	–	–	–	–
HIMALAYAS[16]	BL: 522 Wk 44: 364	27.0	-2.7 (-3.9, -1.5)	BL: 513 Wk 44: 383	27.6	-2.2 (-3.4, -1.1)	–	–	–	-0.5 (-2.0, 1.1)	0.54
ROCKIES[17]	BL: 1051 Wk 24: 866	36.0	-1.9 (-2.8, -1.1)	BL: 1055 Wk 24: 939	35.0	-2.4 (-3.3, -1.6)	–	–	–	0.5 (-0.4, 1.5)	0.29
PYRENEES ^c	413	33.4	-7.3 (17.2) ^a	257	33.2	-5.7 (15.0) ^a	–	–	–	–	–
SIERRAS[19]	BL: 369 Wk 52: 236	33.6	-6.6 (-8.4, -4.8)	BL: 370 Wk 52: 272	33.7	-8.8 (-10.5, -7.0)	–	–	–	2.2 (0.2, 4.2)	0.034

Note: n numbers are the same for baseline and CFB unless otherwise specified.

CFB, change from baseline; ESA, erythropoiesis-stimulating agent; ESA-N, ESA-naive; ESA-C, ESA-converted; LSM, least squares mean; LSMD, least squares mean difference.

^aChange from baseline (standard deviation) rather than least squares mean change from baseline.

^bSource provides no values for this parameter.

^cAstellas data on file.

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