Iron Parameters in Patients Treated With Roxadustat for Anemia Associated With Chronic Kidney Disease: Post Hoc Analysis of the Non-Dialysis-Dependent or Incident Dialysis Population From Four Phase 3 Studies

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Background: Anemia is a common complication in patients with chronic kidney disease (CKD) who are non–dialysis-dependent (NDD) or incident dialysis-dependent (ID-DD) (ie, initiated dialysis within the last 4 months). This post hoc analysis examined iron metabolism parameters in patients with anemia of CKD who were NDD/ID-DD and treated with either roxadustat or an erythropoiesis-stimulating agent (ESA).

Endpoint/parameter	Non–Dialysis-Dependent/Incident to Dialysis (NDD/ID-DD)	
	Roxadustat (n=1078)	ESA (n=1051)
CFB in hemoglobin (g/dL) to Weeks 28-52, regardless of rescue therapy		
Baseline, mean (SD)	9.04 (1.15)	9.05 (1.12)
CFB, mean (SD)	2.06 (1.36)	1.90 (1.31)
LS mean (95% CI)	1.85 (1.734, 1.966)	1.65 (1.534, 1.765)
LSMD (95% CI)	0.20 (0.038, 0.362)	
P-value	0.0153	
CFB in serum iron (µg/dL) to Week 20		
Baseline, mean (SD)	65.39 (26.56)	64.21 (26.76)
CFB, mean (SD)	5.04 (32.93)	-0.37 (32.76)
LS mean (95% CI)	6.93 (4.122, 9.735)	-0.29 (-3.065, 2.486)
LSMD (95% CI)	7.22 (3.337, 11.099)	
P-value	0.0003	
CFB in ferritin (µg/L) to Week 20		
Baseline, mean (SD)	384.75 (352.97)	373.63 (312.13)
CFB, mean (SD)	-139.92 (244.26)	-107.57 (230.93)
LS mean (95% CI)	-118.57 (-138.008, -99.140)	-108.50 (-127.885, -89.114)
LSMD (95% CI)	-10.07 (-37.031, 16.881)	
P-value	0.4837	
CFB in TIBC to Week 20		
Baseline, mean (SD)	44.62 (8.97)	44.57 (8.61)
CFB, mean (SD)	7.55 (8.03)	0.56 (6.05)
LS mean (95% CI)	6.77 (5.894, 7.651)	0.49 (-0.370, 1.358)
LSMD (95% CI)	6.28 (5.074, 7.484)	
P-value	<0.0001	
CFB in TSAT (%) to Week 20		
Baseline, mean (SD)	27.35 (10.91)	27.17 (10.40)
CFB, mean (SD)	-1.44 (12.47)	-0.66 (10.95)
LS mean (95% CI)	-0.17 (-1.176, -0.828)	-0.37 (-1.364, 0.617)
LSMD (95% CI)	0.20 (-1.184, 1.593)	
P-value	0.7774	
Proportion of patients using IV iron as rescue therapy up to Week 52		
IV iron, n (%)	36.5%	49.1%
95% CI	0.34, 0.39	0.46, 0.52
Odds ratio (95% CI)	0.52 (0.42, 0.63)	
P-value	<0.0001	

Methods or Case description: The results of four phase 3, randomized, open-label studies (NDD [DOLOMITES]; ID-DD [HIMALAYAS, SIERRAS, ROCKIES]) comparing oral roxadustat to an ESA (darbepoetin alfa or epoetin alfa) for patients with anemia of CKD were pooled in this post hoc exploratory analysis. Iron metabolism parameters (serum iron, ferritin, total iron binding capacity [TIBC], transferrin saturation [TSAT]), hemoglobin, and proportion of patients using intravenous (IV) iron supplementation were measured at various intervals within the 52-week efficacy evaluation period in patients with NDD or ID-DD CKD. The Table displays change from baseline (CFB), least squares mean difference (LSMD), 95% confidence interval (95% CI), and P-value for each iron metabolism parameter.

Results or Learning points: In total, 2129 patients were evaluated (1078 roxadustat, 1051 ESA). Hemoglobin levels increased from baseline to Weeks 28-52 for patients receiving roxadustat with NDD/ID-DD CKD compared to ESA active control (P = 0.0153). Treatment with roxadustat was associated with increased serum iron (P = 0.0003) and TIBC (P <0.0001) from baseline to Week 20 compared to treatment with ESA. Ferritin and TSAT did not significantly change from baseline to Week 20 in patients with NDD/ID-DD CKD receiving roxadustat. Fewer patients receiving roxadustat received IV iron supplementation at Week 52 (P <0.0001).

Conclusions: Compared with ESA, roxadustat treatment was associated with improvement in iron metabolism while achieving a statistically significant increase in hemoglobin levels in patients with anemia of NDD or ID-DD CKD.

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SARS-CoV-2 breakthrough infections in patients with a history of anti-CD20 therapy during the Omicron variant waves in Switzerland (RituxiVac 3.0)

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Background: Patients with B-cell depleting therapies show inferior immune responses to vaccines, including mRNA vaccines against SARS-CoV-2. Here, we investigated the incidence of SARS-CoV-2 breakthrough infections in the RituxiVac study cohort during the Omicron waves in Switzerland.

Methods or Case description: Using a questionnaire, we assessed vaccination history, self-reported adherence to protective measures, SARS-CoV-2 exposure, SARS-CoV-2 infection and COVID-19 complications in patients with a history of anti-CD20 therapies and healthy controls. Primary outcome was the hazard of self-reported positive SARS-CoV-2 PCR or antigen tests in patients vs. controls in association with protective measures, additional SARS-CoV-2 vaccine doses and biomarkers of vaccine-driven immunogenicity. Secondary outcomes were COVID-19 related hospitalizations and COVID-19 related mortality.

Results or Learning points: The present analysis included 81 patients with a history of anti-CD20 drugs and 24 healthy controls. The median follow-up duration was 3.5 months. Adherence to protective measures and rates of exposure to SARS-CoV-2 were similar among patients and healthy controls, as were self-reported SARS-CoV-2 infections (25/81 [31%] vs. 9/24 [38%], p = 0.54). Severe COVID-19 occurred in 8.6% (7/81) of patients and COVID-19 related mortality was 5.9% (4/81) whereas no severe or fatal cases occurred in the control group (p = 0.3 and 0.6, respectively). Neither vaccine elicited antibody levels nor the extent of the cell-mediated immune response (as by ELIspot assay) after the second vaccine dose were associated with the risk for SARS-Cov-2 infection. However, having had a third vaccine dose was associated with a reduced risk for SARS-CoV-2 infections among anti-CD20 treated patients (HR 0.19, 95%CI: 0.05-0.7, p <0.05).