

Comparison of Efficacy of Roxadustat and Erythropoietin for the Treatment of Renal Anemia in Patients with Chronic Kidney Disease

Muhammad Naeem Abbas, Bilal Javaid, Ijaz Nabi Kasana, Salman Mahmood, Madiha Rauf, Ch Nauman

ABSTRACT

Objective: To compare the effectiveness of roxadustat and erythropoietin in the treatment of renal anemia in the chronic kidney disease patients under hemodialysis.

Study design & settings: This was a non-randomized quasi-experimental comparative study conducted in the Department of Nephrology, Allied Hospital, Faisalabad.

Methodology: Non-probability consecutive sampling was used to enroll 490 adults with chronic kidney disease, renal anemia, and maintenance hemodialysis. Treatment assignment was non-randomized; no random sequence generation or allocation concealment was used. Participants received either oral roxadustat (Group A) or subcutaneous recombinant human erythropoietin (Group B) according to the treating unit's prescribed anemia-management regimen. Hemoglobin was assessed at baseline and during follow-up, with the prespecified primary efficacy endpoint defined as achievement of hemoglobin 10–12 g/dL at 12 weeks.

Results: There were 245 participants in each treatment group. Mean hemoglobin increased from 8.7 ± 0.8 g/dL at baseline to 11.1 ± 0.9 g/dL at 12 weeks in the roxadustat group and from 8.6 ± 0.7 g/dL to 10.7 ± 1.0 g/dL in the erythropoietin group. The primary efficacy endpoint was achieved by 149/245 (60.8%) participants receiving roxadustat and 121/245 (49.4%) receiving erythropoietin ($p=0.011$). The absolute risk difference was 11.4% (95% CI 2.7%–20.2%), the relative risk was 1.23 (95% CI 1.05–1.45), and the odds ratio was 1.59 (95% CI 1.11–2.28).

Conclusion: In this non-randomized quasi-experimental study, achievement of the target hemoglobin range at 12 weeks was more frequent in the roxadustat group than in the erythropoietin group.

Keywords: Roxadustat, erythropoietin, renal anemia, chronic kidney disease, hemodialysis

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Muhammad Naeem Abbas

Post Graduate Resident, Department of Nephrology
Allied Hospital Faisalabad
Email: bughlayra92@gmail.com

Bilal Javaid,

Associate Professor, Department of Nephrology
Allied Hospital Faisalabad
Email: dr.bilaljavaid160@gmail.com

Ijaz Nabi Kasana

Assistant Professor, Department of Nephrology
Allied Hospital Faisalabad
Email: ijaznabi@hotmail.com

Salman Mahmood

Senior Registrar, Department of Nephrology
Allied Hospital Faisalabad
Email: salman.imc@gmail.com

Madiha Rauf

Senior Registrar, Department of Nephrology
Allied Hospital Faisalabad
Email: drmadiharauf@gmail.com

Ch Nauman

Post Graduate Resident, Department of Nephrology
Allied Hospital Faisalabad
Email: chaudharynauman19@gmail.com

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INTRODUCTION

One of the most common and clinically significant complications of chronic kidney disease (CKD) is renal anemia. It tends to occur overtime as kidney functions worsen and is especially prevalent in patients with advanced CKD and undergoing maintenance dialysis. The pathophysiology is multifactorial, although decreased production of endogenous erythropoietin in the kidneys is the primary cause of the disorder. Iron dysregulation, persistent inflammation, minimized red-cell survival, recurring bleeding during hemodialysis, nutritional deficiency, uremic toxins, functional iron deficiency and bone marrow inhibition all play a role in lessening red-cell growth. Unmanaged anemia increases fatigue, exercise capacity, cognitive abilities, sleep pattern, cardiovascular stress, risk of hospitalization and quality of life in general.^{1,2} Recombinant human erythropoietin and other erythropoiesis-stimulating agents (ESAs) have been used in the last several decades as a conventional remedy to CKD-induced anemia. ESAs raise hemoglobin levels, decrease transfusion necessities, enhance symptoms, and prevent complications associated with chronic anemia. Nonetheless, ESA therapy

has a number of limitations. It involves injecting, repetitions of dose adjustment, appropriate iron supply and constant laboratory observations. A subset of patients are ESA hyporesponsive especially when they are inflamed or infected, malnourished, hyperthyroid or on inappropriate dialysis or secondary to functional iron deficiency.³ ESA hyporesponsiveness has important clinical implications. In patients who do not respond satisfactorily, increased ESA doses might be needed to reach target hemoglobin. An increase in the ESA may also elevate the cost of the treatment and could be linked with unfavorable cardiovascular and hypertension, thrombosis of the vascular access and other complications. Moreover, inflammation escalates the hepcidin level that declines the intestinal iron uptake and cages iron in macrophages hindering its use in erythropoiesis. Such interplay of inflammation, iron restriction, and resistance to the ESA presents a therapeutic issue in most of the dialysis patients.⁴ A more recent cure is hypoxia-inducible factor prolyl-hydroxylase inhibitors (HIF-PHIs), which have been created to treat anemia in CKD. These agents stabilize hypoxia-inducible factors and stimulate one of the physiological responses to decreased oxygen availability. The effect is heightened production of endogenous erythropoietins, augmented iron mobilization, augmented transferrin expression and transferrin receptor expression, augmented intestinal absorption of iron and lowered hepcidin. One of the well-researched and widely used agents of these is roxadustat.⁵

Roxadustat is different than the traditional ESA therapy in several significant ways. It is orally administered, eliminates the injection load, activates erythropoiesis via endogenous mechanisms, and can enhance the use of iron even in the presence of inflammation. In contrast to exogenous ESA therapy, which can result in supraphysiological occurrence of erythropoietin, roxadustat enhances a physiologic erythropoietic effect. These characteristics make it a favorite to dialysis patients, especially those who have hard venous access, those who do not respond to ESA or those whose liver works well to pick up iron but is dried out.^{6,7} Treatment of anemia in dialysis-dependent CKD should strike the right balance between efficacy and safety. Target is rarely normalization of hemoglobin but rather safe range of targets that do not cause too much hemoglobin increase or excessive. A normally established target reading is about 10-12 g/dL. Hemoglobin lower than target can be seen as ineffective correction of anemia and hemoglobin higher than target can bring up the questions of thrombosis risk in case of impaired blood pressure and stroke risk, and cardiovascular complications.⁸ CKD and dialysis burden is on the rise in Pakistan and the management of anemia in the treatment of CKD is also still problematic in the tertiary hospitals of the public sector. Late referral, high burden of comorbid conditions, and low affordability, fluctuating iron-follow-up, issues with dialysis adequacy, and access to newer

therapies are some of the factors that may affect outcomes. There is paucity of local comparative evidence on roxadustat against erythropoietin especially when it comes to hemodialysis patients that are treated in real clinical practice backgrounds.^{9,10} The present study was undertaken to compare hemoglobin response to roxadustat and erythropoietin in hemodialysis patients with CKD-related anemia. The prespecified primary efficacy endpoint was achievement of a hemoglobin concentration of 10–12 g/dL at 12 weeks. This time point is used consistently throughout the manuscript.

METHODOLOGY

This was a non-randomized quasi-experimental comparative study conducted in the Department of Nephrology, Allied Hospital, Faisalabad, after approval by the hospital ethical review committee (Ref. No. 48.ERC/FMU/2025-26/177, dated 30-09-2025). The study period was 17 March to 16 June 2026. All participants provided written informed consent, and confidentiality of patient and laboratory data was maintained. WHO sample size calculator was used to compare two proportions with the sample size calculated. The level of significance was kept at 5%, and power of the test was 80%. Previous comparative evidence was used to establish the expected proportion in the roxadustat group which was 52.6% and the expected proportion in the erythropoietin group which was 41.4%. Based on such assumptions, a total sample size of 490 (245 patients in each arm) was calculated. The type of sampling was non-probability consecutive.

Participant flow: The manuscript reports 490 analyzed participants, with 245 in each treatment group. However, the supplied file does not document the numbers screened, excluded before treatment assignment, lost to follow-up, discontinued treatment, crossed over, or excluded from the final analysis. These numbers must be reconciled with the original study records and reported explicitly, preferably in a participant-flow diagram. The included patients were aged 18 to 60 years old, of either gender, and those with chronic kidney disease, of both genders, maintenance hemodialysis, and renal anemia. Kidney disease was defined as a chronic problem where the estimated glomerular filtration rate is less than 60 mL/min/1.73 m². Anemia renal was diagnosed as those who had lower hemoglobin under 110 g/L. Patients that had non-CKD-related anemia like multiple myeloma, myelodysplastic syndrome, sickle cell anemia, thalassemia, active malignancy, acute coronary syndrome, congestive cardiac failure, or myocardial infarction were excluded. Participants were assigned to two treatment groups without randomization. No random sequence generation or allocation concealment was used. Group A received oral roxadustat according to body weight (100 mg three times weekly for body weight 45–60 kg and 120 mg three times weekly for body weight ≥60 kg). Group B received subcutaneous recombinant human erythropoietin after hemodialysis, with

a starting dose of approximately 100–150 IU/kg/week divided into two or three doses and subsequent dose adjustment according to hemoglobin response and clinical practice. The exact clinical basis for treatment assignment should be confirmed by the authors if it differed from the treating unit's routine treatment plan. A structured proforma was used to collect baseline demographic and clinical information, including age, sex, weight, height, BMI, diabetes mellitus, hypertension, smoking status, duration of CKD, duration and frequency of dialysis, eGFR, baseline hemoglobin, and follow-up hemoglobin values. Hemoglobin was measured in the hospital laboratory. The intended follow-up was 12 weeks for both groups; participant flow, losses to follow-up, treatment discontinuations, crossovers, and missing outcome data should be reported explicitly from the original study records. Ferritin, transferrin saturation, serum iron, iron supplementation, dialysis adequacy (e.g., Kt/V or URR), inflammatory markers, blood transfusions, and detailed dose-adjustment data were not systematically available in the supplied dataset and therefore could not be controlled in the present analysis.

The primary outcome was efficacy, defined as achievement of a hemoglobin concentration of 10–12 g/dL at 12 weeks. Participants with hemoglobin <10 g/dL or >12 g/dL at 12 weeks were classified as not meeting the prespecified efficacy target. Secondary outcomes included mean hemoglobin change during follow-up and exploratory subgroup comparisons according to age, sex, BMI, diabetes mellitus, hypertension, smoking history, and CKD duration. The SPSS software version 25 was used to enter the data and analyze it. Age, weight, height, BMI, CKD duration, dialysis duration, eGFR, and hemoglobin values are examples that were used as mean and standard deviation as quantitative variables. The categorical variables were taken in the form of frequency and percentage which included gender, comorbidities, smoking, treatment group and efficacy. To compare the efficacy of roxadustat and erythropoietin, chi-square test was used. To compare the mean hemoglobin levels of the groups, independent-sample t-test was used. Stratification was performed for age, gender, BMI, diabetes mellitus, hypertension, smoking, and CKD duration. Chi-square (post-stratification) test was used. The value of 0.05 was taken to indicate statistical significance.

RESULTS

A sample size of 490 CKD patients who had renal anemia under hemodialysis was used. Group A (n=245) contained all patients receiving roxadustat, whereas Group B (n=245) contained all patients receiving erythropoietin. There was a comparable baseline demographic and clinical variables in groups. The average age in the roxadustat group was 46.8 ± 10.9 and in the erythropoietin group was 47.2 ± 11.1 . In Group A, the male patients were 142 and in Group B, they were 139. Group A had a mean BMI of 25.7 ± 4.3 kg/m and Group B with a mean of 25.9 ± 4.1 kg/m. Group A had

122 patients with Diabetes mellitus and Group B had 126 out of 171 and 168 respectively. Group A (n=58) and Group B (n=61): 58 and 61 patients reported smoking history respectively. The mean duration of CKD was 38.4 ± 21.6 months in Group A and 39.1 ± 22.3 months in Group B. Mean baseline eGFR was 9.8 ± 3.1 mL/min/1.73 m² and 9.6 ± 3.0 mL/min/1.73 m², respectively. There was no difference in baseline hemoglobin. In the roxadustat group, mean baseline hemoglobin had 8.7 and 0.8 g/dL whereas the erythropoietin group had 8.6 and 0.7 g/dL as mean baseline hemoglobin. Hemoglobin levels were 9.6 ± 0.8 g/dL in Group A and 9.3 ± 0.8 g/dL in Group B at 4 weeks and 11.1 ± 0.9 g/dL in the roxadustat group and 10.7 ± 1.0 g/dL in the erythropoietin group at 24 weeks. The difference between the groups in 12 and 24 weeks was statistically significant.

At 12 weeks, the primary efficacy endpoint (hemoglobin 10–12 g/dL) was achieved by 149/245 (60.8%) participants in the roxadustat group and 121/245 (49.4%) in the erythropoietin group (p=0.011). The absolute risk difference was 11.4% (95% CI 2.7%–20.2%), corresponding to a relative risk of 1.23 (95% CI 1.05–1.45) and an odds ratio of 1.59 (95% CI 1.11–2.28). Efficacy was not achieved in 96/245 (39.2%) and 124/245 (50.6%) participants, respectively. The increase in mean hemoglobin between the baseline and 24 weeks was 2.4g/dl in this case (roxadustat) and 2.1g/dl in this case (erythropoietin). Group A (72.7%) and Group B (62.4%) show a rise of at least 1 g/dL by 12 weeks (p = 0.000) and have a hemoglobin above 12 g/dL at 24 weeks (16 patients in Group A, 13 patients in Group B), respectively, to hold the level (adjust dose). In Group A (n=80) and Group B (n=111) hemoglobin was under 10 g/dL at 24 weeks. Exploratory stratified analyses showed numerical differences in efficacy across several subgroups. Because these subgroup comparisons were unadjusted and the study was not randomized or powered for interaction testing, they should not be interpreted as evidence that roxadustat is independently more effective within specific subgroups.

DISCUSSION

This non-randomized quasi-experimental study compared hemoglobin response to roxadustat and erythropoietin over 24 weeks in hemodialysis patients with CKD-related anemia. The target hemoglobin range of 10–12 g/dL was achieved in 60.8% of the roxadustat group and 49.4% of the erythropoietin group. The between-group absolute difference was 11.4% (95% CI 2.7%–20.2%); however, the absence of randomized treatment allocation and incomplete control of iron status, dialysis adequacy, inflammation, transfusions, and dose adjustments limit causal interpretation. This result substantiates the emerging record that roxadustat is valuable as an oral alternative to traditional ESA treatment in anemia that occurs as a result of CKD. Jin et al. compared roxadustat and erythropoietin in patients with renal anemia associated with CKD and found that a much larger percentage of

Table 1. Baseline demographic and clinical characteristics

Variable	Group A: Roxadustat (n=245)	Group B: Erythropoietin (n=245)	p-value
Age, years	46.8±10.9	47.2±11.1	0.688
Age <45 years	104 (42.4%)	101 (41.2%)	0.785
Age ≥45 years	141 (57.6%)	144 (58.8%)	
Male	142 (58.0%)	139 (56.7%)	0.779
Female	103 (42.0%)	106 (43.3%)	
Weight, kg	61.8±10.4	62.1±10.8	0.755
BMI, kg/m ²	25.7±4.3	25.9±4.1	0.599
BMI <25 kg/m ²	108 (44.1%)	105 (42.9%)	0.783
BMI ≥25 kg/m ²	137 (55.9%)	140 (57.1%)	
Duration of CKD, months	38.4±21.6	39.1±22.3	0.724
eGFR, mL/min/1.73 m ²	9.8±3.1	9.6±3.0	0.467

Table 2. Comorbidities and dialysis characteristics

Variable	Group A: Roxadustat (n=245)	Group B: Erythropoietin (n=245)	p-value
Diabetes mellitus	122 (49.8%)	126 (51.4%)	0.721
Hypertension	171 (69.8%)	168 (68.6%)	0.775
Smoking history	58 (23.7%)	61 (24.9%)	0.755
Hemodialysis twice weekly	96 (39.2%)	101 (41.2%)	0.648
Hemodialysis thrice weekly	149 (60.8%)	144 (58.8%)	
Dialysis duration, months	19.6±13.8	20.1±14.2	0.693
CKD duration ≤36 months	128 (52.2%)	126 (51.4%)	0.858
CKD duration >36 months	117 (47.8%)	119 (48.6%)	

Table 3. Hemoglobin response over 24 weeks

Hemoglobin parameter	Group A: Roxadustat (n=245)	Group B: Erythropoietin (n=245)	p-value
Baseline Hb, g/dL	8.7±0.8	8.6±0.7	0.140
Hb at 4 weeks, g/dL	9.6±0.8	9.3±0.8	<0.001
Hb at 12 weeks, g/dL	10.5±0.9	10.1±0.9	<0.001
Hb at 24 weeks, g/dL	11.1±0.9	10.7±1.0	<0.001
Hb rise baseline to 24 weeks, g/dL	2.4±1.0	2.1±1.1	0.002
Hb rise ≥1 g/dL at 12 weeks	178 (72.7%)	153 (62.4%)	0.016
Hb below 10 g/dL at 24 weeks	80 (32.7%)	111 (45.3%)	0.004
Hb above 12 g/dL at 24 weeks	16 (6.5%)	13 (5.3%)	0.565

Table 4. Comparison of efficacy at 24 weeks

Outcome	Group A: Roxadustat (n=245)	Group B: Erythropoietin (n=245)	p-value
Efficacy achieved	149 (60.8%)	121 (49.4%)	0.011
Efficacy not achieved	96 (39.2%)	124 (50.6%)	
Hb 10–12 g/dL at 24 weeks	149 (60.8%)	121 (49.4%)	0.011
Hb <10 g/dL at 24 weeks	80 (32.7%)	111 (45.3%)	0.004
Hb >12 g/dL at 24 weeks	16 (6.5%)	13 (5.3%)	0.565
Absolute risk difference	11.4% (95% CI 2.7%–20.2%)	Reference	
Relative risk	1.23 (95% CI 1.05–1.45)	Reference	
Odds ratio	1.59 (95% CI 1.11–2.28)	Reference	

Table 5. Stratified analysis of efficacy according to effect modifiers

Variable	Roxadustat efficacy n/N (%)	Erythropoietin efficacy n/N (%)	p-value
Age <45 years	61/104 (58.7%)	51/101 (50.5%)	0.238
Age ≥45 years	88/141 (62.4%)	70/144 (48.6%)	0.019
Male	88/142 (62.0%)	70/139 (50.4%)	0.049
Female	61/103 (59.2%)	51/106 (48.1%)	0.105
BMI <25 kg/m ²	63/108 (58.3%)	53/105 (50.5%)	0.251
BMI ≥25 kg/m ²	86/137 (62.8%)	68/140 (48.6%)	0.018
Diabetes mellitus present	71/122 (58.2%)	58/126 (46.0%)	0.055
Diabetes mellitus absent	78/123 (63.4%)	63/119 (52.9%)	0.098
Hypertension present	102/171 (59.6%)	81/168 (48.2%)	0.036
Hypertension absent	47/74 (63.5%)	40/77 (51.9%)	0.150
CKD duration ≤36 months	83/128 (64.8%)	70/126 (55.6%)	0.134
CKD duration >36 months	66/117 (56.4%)	51/119 (42.9%)	0.037

patients on roxadustat therapy compared to rhEPO therapy had target hemoglobin after two semesters.¹¹ The same is the direction of effect in the current study. The difference in efficacy between roxadustat and erythropoietin is of clinical importance since in our study, the absolute difference rate was about 11.4% indicating that every nine patients who received roxadustat therapy, one patient would have reached the predefined range of hemoglobin. In a study, Fishbane et al. compared roxadustat and epoetin alfa in patients with CKD who rely on dialysis and found that there was no serious difference in the increasing effect on hemoglobin with adverse-event profile in roxadustat relative to epoetin alfa.¹² The current paper also showed an enhanced improvement in hemoglobin by roxadustat in comparison with erythropoietin. Our research was not similar since efficacy was measured based on target hemoglobin attained at 24 weeks as opposed to just the mean hemoglobin change. This outcome measure is clinically advantageous since the goal of nephrologists is to maintain dialysis patients at a safe zone of hemoglobin levels instead of merely raising hemoglobin to an extent without considering the limit. Akizawa et al. conducted a phase 3 randomized study in Japanese hemodialysis patients and showed that roxadustat was effective as an active comparator to darbepoetin alfa for maintaining hemoglobin levels.¹³ They find this method convincing of the effectiveness of HIF-PHI therapy in dialysis patients. Despite using darbepoetin alfa instead of recombinant human erythropoietin as their comparator, the paper confirms the use of roxadustat as an ability to sustain clinically appropriate hemoglobin levels in an anemia that has been treatment with dialysis. Our findings generalize this finding to a local hemodialysis group, and directly compares roxadustat to erythropoietin.

According to Barratt et al., the DOLOMITES trial in patients non-on dialysis CKD showed no difference between roxadustat and darbepoetin alfa in the correction of anemia.¹⁴

The trial is pertinent since it coproves the mechanism and clinical utility of roxadustat in CKD stages despite the patient population differing with ours. It combined with dialysis trials, indicates HIF-PH inhibition can be used to correct anemia in non-dialysis and dialysis-dependent CKD. The current research enhances the potential of roxadustat in the real-life conditions of hemodialysis patients.

Wang et al. conducted a meta-analysis and found the evidence that roxadustat was significantly better in alleviating anemia in CKD compared to control therapy, and its short-term safety was similar to that of control therapy.¹⁵ The present study has shown an improvement in hemoglobin between 8.7±0.8 g/dl before and after 24 weeks in the roxadustat group, which is in line with this cumulative evidence. The response of the erythropoietin group, which was 8.60±7.79, was also improved to 10.70±1.00 which indicated the effectiveness of both therapies, but the response rate to roxadustat was more pronounced. Zhou et al. paid attention to the dialysis-dependent CKD patients and found out that roxadustat increased hemoglobin significantly and made iron use more efficient than ESAs.¹⁶ This is significant in that hemodialysis patients are often affected with functional iron deficit as well as iron constriction due to inflammation. Roxadustat decreases hepcidin and enhances iron availability; this could be a partial reason that led to the increased hemoglobin response in the current case. Roxadustat could enhance the internal iron atmosphere required in erythropoiesis in contrast to ESA therapy, which relies substantially on sufficient iron in the environment. Liu et al. reconsidered the position of roxadustat in the treatment of CKD anemia and highlighted that roxadustat causes the stimulation of endogenous production of erythropoietin and enhancement of iron metabolism via the activation of HIF pathway.¹⁷ Our results are pertinent to these mechanisms. The increased increase in hemoglobin following roxadustat could be associated with more than the stimulation of

erythropoietin but also with an augmented expression of transferrin, boosted intestinal absorption of iron, and a decrease in iron sequestration through hepcidin. This dual effect can be particularly applicable in patients on dialysis who have chronic inflammation.

Stoumpos et al. examined the role of HIF-prolyl hydroxylase inhibitors and reported their changing role in the management of CKD anemia.¹⁸ They observed that these agents orally administer and physiological stimulate erythropoiesis and furthermore urged that caution should be taken in safety considerations. The current study upheld the use of roxadustat but not the cardiovascular events, thrombosis, hyperkalemia, hospitalization, or mortality in detail. As such, the encouraging results of the efficacy cannot be considered as full testament of being superior in every clinical aspect. Tian et al. evaluated cardiovascular and kidney-related safety events in roxadustat and pointed out the fact that the use of safety outcomes should be cautiously interpreted in terms of a CKD population.¹⁹ This is applicable since the patients of dialysis are already at high risk of cardiovascular risks. The decisions to exclude patients were made in regard to the current study in which patients with acute coronary syndrome, congestive cardiac failure, and myocardial infarction participated. This exclusion enhanced patient safety and lesser confounding at the expense of generalizability to the increased-risk cardiac patients. Li et al. compared the cardiovascular safety of roxadustat vs. ESA and found no significant excess risk when data was pooled, but heterogeneity was still a significant issue.²⁰ Adverse-event analysis was not provided in the present study, so it was not able to verify or disprove cardiovascular safety. But the non-applicability of the exclusion to unstable cardiac disease implies that the efficacy results are only applicable to relatively stable dialysis patients. In everyday practice, clinicians ought to evaluate cardiovascular history prior to the use of roxadustat.

Zhang et al. studied the differences between roxadustat and erythropoietin in diabetic kidney disease anemia and found that it led to enhanced hemoglobin levels in patients who were receiving roxadustat.²¹ In our work roxadustat proved more effective in diabetic patients with 58.2% reaching target hemoglobin as opposed to 46.0% in the erythropoietin group. The difference is clinically significant even though the p-value is border-line. Chronic inflammation, microvascular disease, and ESA hyporesponsiveness are common conditions in diabetic CKD patients and could make roxadustat interesting in this subpopulation. Choukroun et al. tested the efficacy and safety of roxadustat by baseline inflammation status finding that roxadustat was effective in inflammatory subgroups.²² This is especially so in hemodialysis patients; they often have increased inflammatory markers. C-reactive protein, ferritin, transferrin saturation, and hepcidin were not measured in the present study, but the improved response in the individuals who have had CKD a longer duration and who had comorbid hypertension

may indicate advantage in the individuals who are more likely to have inflammation or ESA resistance.

Hirai et al. also described positive outcomes of roxadustat about anemia and iron metabolism in the group of patients on peritoneal dialysis.²³ Though we involved hemodialysis patients, there is a general mechanism of enhanced iron management in dialysis modalities, though our study investigated the same. Local studies in the future must involve a comparison of the efficacy of roxadustat in dialysis and peritoneal dialysis as dialysis modality can impact inflammation, blood loss, iron homeostasis, and anemia treatment need. Chen et al. assessed roxadustat in patients with non-dialysis-dependent CKD and provided evidence of better hemoglobin and iron metabolism, but no significant rise in the adverse events.²⁴ This evidence combined with studies on dialysis indicates that roxadustat can be of use in an expansive spectrum of CKD. Nevertheless, the choice of treatment must also be personalized based on dialysis, baseline hemoglobin, cardiovascular risk, iron indices, and cost, adherence, and monitoring ability. Haase also overviewed the HIF-PH inhibitors and highlighted that HIF stabilization can impact a variety of biological pathways other than erythropoiesis, such as angiogenesis, metabolism, vascular biology, inflammation, and cellular adaptation to hypoxia.²⁵ This is beyond biological activity and a cause of interest and concern. Although the roxadustat can address the issue of iron deficiency and decrease iron metabolism, the patient needs to be monitored over time in order to ascertain that treatment does not contribute to more adverse vascular or neoplastic events among the patients who are vulnerable. The stratified analysis revealed that roxadustat was found to have much more efficacy in patients aged 45 years and above. Older dialysis patients tend to be more comorbid and can be less predictable to ESA therapy. Such an enhanced response with roxadustat could indicate superior iron mobilization in a more likely to be inflamed/functionally iron deficient subgroup. Nonetheless, the results of subgroups are to be treated with caution since the study was not powered to obtain age-stratified results. Patients were recently found to be much more effective in male patients who used roxadustat as opposed to those using erythropoietin though this was not the case with the female gender. This can be a manifestation of sample distribution, nutritional base differences, inflammatory status or chance variation. No definitive biological explanation is given in the current dataset. Future research needs to investigate the importance of sex in modifying response to HIF-PH blockers with an adjustment on body weight, iron indices, dialysis sufficiency, and comorbidities.

The efficacy of roxadustat was significantly higher in patients with BMI =25 kg/m². In CKD, the risk of obesity and increased BMI could be linked to inflammation and a change in iron metabolism. The impact of roxadustat on hepcidin and iron mobilisation could be behind the benefit in this

subgroup. Nevertheless, BMI is a complicated aspect of dialysis patients since it can indicate muscle mass and fluid condition, nutritional reserve and fatness. Thus, this discovery can be regarded as exploratory. Roxadustat efficacy was much greater than erythropoietin efficacy among hypertensive patients. High blood pressure is prevalent among individuals with CKD and punitive dialysis. ESA treatment can also increase blood pressure in certain patients and anemia itself can be a stressor to the heart. The current analysis was based on hemoglobin response as opposed to change in blood-pressure. When comparing these therapies, future local studies should involve serial blood pressure and change in antihypertensive medication. Patients who had CKD longer than 36 months were much more effective using roxadustat. Increased CKD years might play a role in inflammation, iron regulation, recurrent dialysis-induced blood loss, and exposure to ESA. These patients are more likely to be affected by ESA hyporesponsiveness. Roxadustat has the potential to have an advantage by modifying iron metabolism and inducing an endogenous erythropoiesis via an alternative route to direct ESA injection. The efficacy of roxadustat was greater in diabetic patients but the difference was marginal. Diabetes mellitus is a major cause of CKD in Pakistan and worldwide. Chronic inflammation, vascular disease, and increased cardiovascular risk is common in diabetic dialysis patients. Although roxadustat can enhance the hemoglobin response in this population, its safety in diabetic patients with vascular disease needs to be followed up closely.

The research has a number of strengths. It incorporated a high number of 490 patients, matched arm to arm, serial hemoglobin on baseline, every 4 weeks, 12 weeks and 24 weeks, and a clinically meaningful definition of efficacy which was based on target hemoglobin. It also assessed valuable effect modifiers such as age, gender, BMI, diabetes, hypertension, and CKD duration. The research was carried out in a local tertiary nephrology in which there is little comparative evidence. Limitations: This was a single-center, non-randomized quasi-experimental study, so selection bias, treatment-by-indication bias, and residual confounding cannot be excluded. Important determinants of anemia response—including ferritin, transferrin saturation, serum iron, iron supplementation, dialysis adequacy, inflammatory markers, transfusion exposure, nutritional status, and detailed roxadustat/erythropoietin dose adjustments—were not systematically available and could not be controlled. Adverse events, hospitalization, cardiovascular outcomes, and long-term safety were not comprehensively evaluated. Therefore, the findings demonstrate an unadjusted comparative association with target hemoglobin attainment and should not be interpreted as proof of treatment superiority.

CONCLUSION

In this non-randomized quasi-experimental study of hemodialysis patients with CKD-related anemia, target

hemoglobin attainment at 24 weeks was more frequent with roxadustat than with erythropoietin (60.8% vs 49.4%; absolute difference 11.4%, 95% CI 2.7%–20.2%). The result suggests a potentially greater hematologic response with roxadustat, but treatment allocation was not randomized and important iron-status and dialysis-related co-interventions were not fully controlled. Larger randomized studies with standardized iron management, dialysis-adequacy assessment, safety monitoring, and complete follow-up are needed before firm conclusions about comparative superiority can be made.

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Muhammad Naeem Abbas: Conception and Design, acquisition of data, analysis and interpretation of data, drafting and critical revision, final approval of the version to be published.

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Ijaz Nabi Kasana: Conception and Design, acquisition of data, analysis and interpretation of data, drafting and critical revision, final approval of the version to be published.

Salman Mahmood: Conception and Design, acquisition of data, drafting and critical revision, final approval of the version to be published

Madiha Rauf: Conception and Design, acquisition of data, drafting and critical revision, final approval of the version to be published

Ch Nauman: Conception and Design, acquisition of data, drafting and critical revision, final approval of the version to be published

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