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Roxadustat – a representative of hypoxia-inducible factor prolyl hydroxylase inhibitors: mechanism of action, safety, and efficacy

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ABSTRACT

Roxadustat is one of several representatives of a new group of drugs known as HIF-PH inhibitors. It is attempting to gain recognition in medicine, mainly in the treatment of anemia in the course of CKD chronic kidney disease. Still, it may also prove effective in anemic patients with other diseases: MDS (myelodysplastic syndrome), PRCA (pure red cell anemia), or CIA (chronic inflammation anemia) such as RA, SLE, UC. This study aims to present the mechanism of action of roxadustat and its impact on hemoglobin levels. It also aims to compare the effectiveness of roxadustat with that of existing therapies for anemia in patients with CKD (Chronic Kidney Disease) and CIA (Chronic Inflammatory Anemia). A review of the scientific literature related on the use of roxadustat in patients with various stages of CKD and in other diseases such as MDS was conducted. Like ESA, roxadustat, induces an increase in RBC count. However, unlike ESA, which are EPO receptor agonists, roxadustat stimulates endogenous EPO production. This allows it to be more effective in achieving and maintaining Hb levels of 11 ± 1g/dL in inflammatory conditions. It achieves this by inhibiting HIF-PH, thereby increasing the cell's ability to survive in hypoxia conditions and enhancing its antioxidant potential. However, due to its polygenic action, it also affects other gene pathways. Further research is needed to understand the full spectrum of the drug. However, both China and the EMA decided to approve the drug for marketing, while the FDA rejected it.

Keywords: Roxadustat, HIF-PH inhibitor, ESA, Chronic kidney disease, Anemia, Chronic Inflammation Anemia (CIA)

1. INTRODUCTION

Roxadustat belongs to a new group of drugs called HIF-PH inhibitors, alongside along darodustat, vadadustat, molidustat, and desidustat. However this article

focuses specifically on roxadustat. Like ESAs – recombinant EPO analogues, e.g., epoetin alfa, darbepoetin – the identical effect of both groups is an increase in the number of RBCs. However ESAs are already a well-known group of drugs, and their impact is to replace the action of EPO by directly stimulating the EPO receptor in the bone marrow (Zhang et al., 2021; Liu et al., 2023). Unlike ESAs, roxadustat stimulates RBC growth by producing endogenous EPO, as does the entire group of HIF-PH inhibitors. Due to its polygenic mechanism, roxadustat has both opponents and supporters, but the balance of benefits and losses certainly favors the use of this drug. This review article aims to describe the effect of this drug on the myeloid system, compare its efficacy in therapy both in comparison with and in combination with ESA, and highlight the most critical side effects. China was the first country to approve roxadustat for treating chronic anemia in dialysis patients with CKD (Grzeszczak et al., 2021; Żuberek et al., 2023).

This drug affects the aerobic metabolism of cells, switching the metabolic process to anaerobic glycolysis and creating an artificial state of hypoxia in the cell. This indirectly reduces oxidative stress and reducing the number of ROS (Reactive Oxygen Species), thereby protecting against accelerated apoptosis, and thus the destruction of important cells such as liver, bone marrow, immune system cells, and the most important cells in CKD: renal interstitial fibroblasts, renal vascular endothelial cells, and proximal and distal renal tubules. Roxadustat is particularly beneficial for patients with MDS and in red blood cell aplasia with anti-EPO antibodies (Zhang et al., 2019; Tanaka et al., 2020).

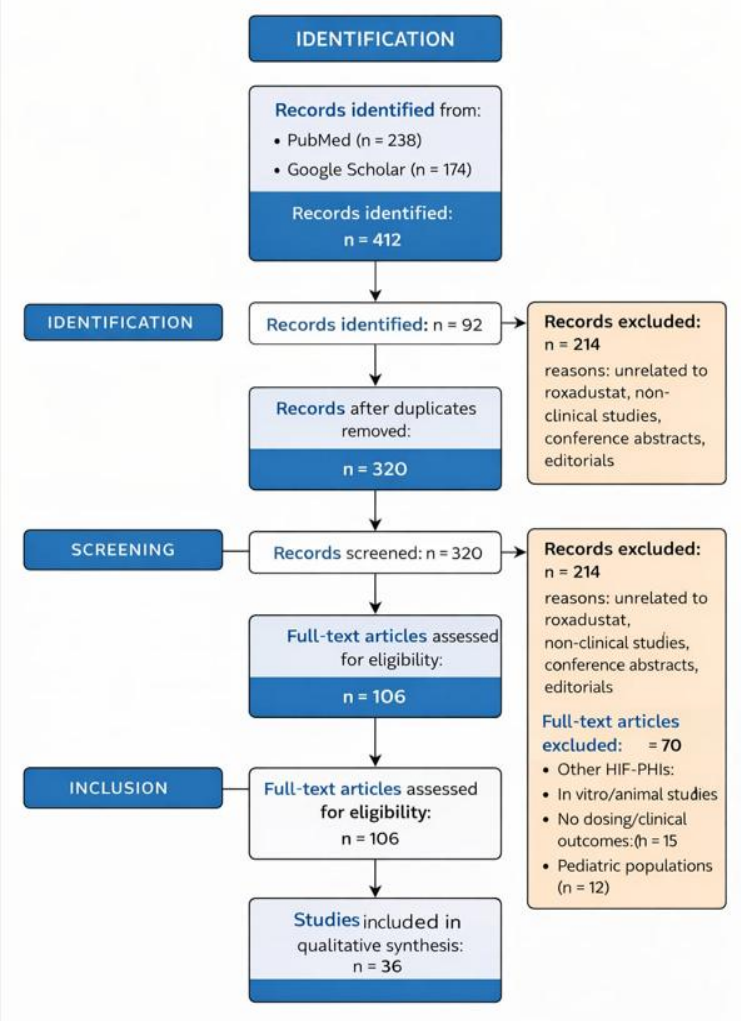

Figure 1. Article selection process according to the PRISMA 2020 flow diagram based on inclusion and exclusion criteria.

2. REVIEW METHODS

This article is a narrative review containing elements of a structured literature search. The searches were performed in accordance with the PRISMA 2020 guidelines by searching the literature in PubMed (MEDLINE) and Google Scholar (Figure 1). The scope of the

searches covered publications between 1st January 2017 and 31st July 2025. This time frame was chosen to include the period before and after the first approval of roxadustat in China in 2018, when large-scale clinical trials of hypoxia-induced prolyl hydroxylase inhibitors (HIF-PHIs) began.

The search strategy included the following keywords and combinations thereof: roxadustat; hypoxia-inducible prolyl hydroxylase inhibitor (HIF-PHI); anaemia; chronic kidney disease; erythropoietin; randomised controlled trial; meta-analysis; and systematic review. Boolean operators ('AND', 'OR') were used where appropriate.

A preliminary search of the databases identified 412 records (PubMed: n = 238; Google Scholar: n = 174). After removing 92 duplicate records, the titles and abstracts of 320 unique articles were analysed. At this stage, 214 records were excluded due to irrelevance, lack of clinical focus or inappropriate publication type. The remaining 106 articles were evaluated against the exclusion criteria. As many as 70 articles met the exclusion criteria, including 24 that described HIF-PHI other than roxadustat, 19 that were performed on in vitro or animal models, 15 that were described without dosing, and 12 that involved studies on children. Ultimately, only 36 articles met all inclusion and exclusion requirements.

The inclusion criteria comprised studies evaluating the use of roxadustat in adult populations (aged ≥18 years), including randomised controlled trials, observational studies, cohort studies, systematic reviews and meta-analyses, particularly those addressing anaemia associated with chronic kidney disease, cancer or erythropoiesis-stimulating agent (ESA) resistance. The inclusion criteria also comprised studies comparing the use of roxadustat with erythropoiesis-stimulating agents.

Studies involving children or adolescents, lacking information on drug dosage or treatment duration, evaluating HIF-PHIs other than roxadustat, or limited to in vivo or in vitro experimental models were excluded. Non-English publications were also excluded.

Due to the narrative nature of this review, no formal risk-of-bias assessment or quantitative meta-analysis was conducted. However, priority was given to high-quality randomised controlled trials and systematic reviews in order to evaluate the mechanism of action, clinical efficacy and safety profile of roxadustat.

3. RESULTS & DISCUSSION

3.1. Pharmacodynamics of the drug

Despite its many advantages, caution should be exercised when assessing the value of roxadustat, as its polygenic mechanism may have a broader effect than anticipated. Roxadustat activates multiple signaling pathways, primarily within the hypoxia mechanism, including VEGF, PDGF, GLUT-1, GLUT-3, LDHA, and NQO1. HIF-PH inhibitors induce artificial hypoxia conditions and inhibit the hydroxylation of PHD1, PHD2, and PHD3. This prevents the attachment of proline residues and their detection by the VHL protein, which marks them for destruction by proteasome (Zhang et al., 2019). There are three HIF isoforms: HIF-1α, HIF-2α (the most important from the drug perspective), and HIF-3α. HIF-1α, which is regulated by PHD1/PHD3, has an antioxidant effect increases in anaerobic glycolysis activity in the cells. This transcription factor is found in all cells of the body, and stimulates iron metabolism and regulates programmed cell death (apoptosis). HIF-2α, which is regulated by PHD2, acts exclusively on EPO expression in fibroblast-like renal interstitial cells (Nsiah et al., 2023). This is the main therapeutic effect of Roxadustat, namely an increase in EPO and, consequently, RBC. The function of HIF-3α, which is probably regulated by all three PHD units, is not fully understood. It is predicted to suppress the HIF-1α and HIF-2α subunits (Liu et al., 2023).

3.2. Pharmacokinetics of the drug

Roxadustat is administered orally, but despite this, it does not interact with food products, and its effectiveness is not affected by individual characteristics such as race, age, or gender. It is metabolized by the liver, with a drug half-life of approximately 12 hours in healthy patients and 18 hours in patients with renal impairment. A steady state is reached after 90h in target patients with CKD (Czock & Keller, 2022). Even moderate liver damage has been proven not to significantly affect exposure to the drug, which is metabolized in the liver (Li et al., 2023). The lack of significant differences in pharmacokinetics between healthy and sick patients means the most commonly selected dosage form of roxadustat can be used in studies: 70 mg orally three times a week (Zhu et al., 2022).

3.3. Drug interactions

Studies report that roxadustat reduces the concentration of drugs such as calcium acetate and sevelamar, which are to treat elevated phosphorus levels, which mainly occurs in patients with CKD, therefore requiring monitoring during treatment (Zhu et al., 2022; Li et

al., 2023). In addition, roxadustat increases the concentration of statins in the blood, but this can be resolved by modifying the therapy, taking into account the beneficial effect of roxadustat on lipid metabolism (Angeletti & Cravedi, 2025; Del Balzo et al., 2020).

3.4. Roxadustat versus ESA: Modulation of EPO

The analyzed articles provided specific information on the comparison of ESA drug classes, which were mainly represented in studies by rHuEPO (recombinant human erythropoietin), and the discussed HIF-PH inhibitor. Roxadustat was often used in studies as an alternative to EPO, alongside iron supplementation, as it can act independently of inflammation and can even lower hepcidin levels (which are regulated by IL-6), thereby increasing iron bioavailability. The therapeutic dose range of roxadustat that was studied was 50-100 mg three times a week in patients weighing 45-60 kg and 70-120 mg three times a week for those weighing ≥ 60 kg. However, most available studies use a dose of 70 mg orally three times a week, regardless of body weight, and this is most commonly published in the review literature. Roxadustat has been shown to achieve not only faster, more frequent, and more sustained therapeutic Hb targets of 10–12 g/dL in chronic kidney disease (CKD) patients than rHuEPO does at the same baseline anemia point, when hemoglobin is around 8 g/dL (Ganz et al., 2023).

Patients receiving a HIF-PH inhibitor had lower serum EPO levels with moderate concentration fluctuations compared to patients receiving rHuEPO, who experienced large concentration fluctuations with high peaks. This translates into a lower risk of CVS as a result of point excessive stimulation of RBC proliferation. Roxadustat increases hemoglobin levels even in the presence of elevated hs-CRP (inflammation) (Li et al., 2023).

Furthermore, the efficacy of roxadustat has been found to be independent of iPTH levels (elevated in CKD), which reduce bone marrow sensitivity to EPO (Angeletti & Cravedi, 2025).

3.5. Roxadustat versus ESA: Effect on CVS

Roxadustat has been shown to have a beneficial effect on patients' lipid profiles, lowering LDL and TG. However, data on its beneficial effect on HDL are inconclusive, and ESAs have no effect on this profile. However, rHuEPO has been shown to increase albumin levels, whereas roxadustat has no effect on them.

EPO has been shown to increase the risk of CVS disease, including thrombosis, and arteriovenous fistulas, in dialysis patients. In addition, excessive administration of rHuEPO can lead to AH arterial hypertension, vascular remodeling and tumor growth. By stimulating receptor EPO and increasing cell division, EPO also increases VEGF expression and can activate pro-survival pathways such as JAK2/STAT5 and PI3K/AKT (Cygulska et al., 2024).

An important pathology caused by chronic anemia in CKD is LVH (left ventricular hypertrophy). This can be reversed if hemoglobin levels are restored quickly enough – it has also been shown that hemoglobin levels are an important factor in cardiac remodeling. LVMI (left ventricular mass index), as measured by ECHO, allows the extent of cardiac remodeling to be determined. The beneficial effects of both roxadustat and ESA have been demonstrated independently of each other. LVMI decreased by approximately 10–20 g/m² over six months of therapy. However, changes in other cardiac parameters, such as LVEDd (left ventricular end-diastolic diameter) and LVPWT (left ventricular posterior wall thickness), were observed only with ECHO and the additional use of roxadustat. Improvement in these three parameters leads to an increase in cardiac EF in patients (Tan et al., 2024).

It was also confirmed that, in patients from the roxadustat treatment group, both SBP (systolic blood pressure) and DBP (diastolic blood pressure) decreased by 10-12 mmHg. In contrast, there were no significant changes in BP (blood pressure) in the EPO treatment group. (Li et al., 2023)

3.6. Roxadustat in the treatment of ESA hyporesponsiveness

There are many causes of ESA hyporesponsiveness. These include insufficiently effective dialysis (despite the fact that most studies involving patients undergoing hemodialysis three to four times a week or daily peritoneal dialysis), low albumin levels, low muscle mass, low body fat and chronic inflammation with elevated CRP, IL-6, TNF-α causing an increase in hepcidin. This blocks access to natural iron stores and prevents iron from being absorbed from food (functional iron deficiency). Deficiencies in in vitamin B12 and folic acid are also cause (Cai et al., 2021).

Roxadustat offers hope to patients who develop erythropoietin hyporesponsiveness (ERI), which is defined as an ESA dose of ≥ 1 IU/kg/w/g/L. In studies, the ESA dose was increased by 20 IU/kg each time when the desired hemoglobin level was not achieved, provided the maximum dose did not exceed twice the stable dose (Tang et al., 2024).

Furthermore, the most successful ESA hyporesponsiveness treatment were observed in patients with anti-EPO antibody production as the underlying mechanism. These antibodies can block erythrocyte maturation, leading to PRCA pure red cell aplasia, while maintaining normal blood cell counts in other lines (Liu et al., 2024).

Immunisation with the formation of anti-EPO antibodies most often occurs as a result of prolonged contact between APC (Antigen-Presenting Cell) cells and the polyethylene glycol chain of rHuEPO in subcutaneous tissues, which is a consequence of the method of ESA administration (subcutaneous or intravenous). In addition to being ease and comfortable for the patient to administer, the efficacy of roxadustat should also be sought without inducing immunization. Furthermore, polycarbonate chain of rHuEPO is sensitive to breaks in the cold chain (2–8°C) during transport to the patient, and breaking it may lead to a change in its conformation and increased immunization. Currently, there is no evidence that either the α- or β-isoform of rHuEPO is more immunogenic (Xu et al., 2024).

Current guidelines for the treating of ESA hyporesponsiveness recommend suppressive therapy and transfusions in cases of immunization involving the formation of anti-EPO antibodies. However, this approach does not achieve the desired therapeutic effect of Hb level of 10-11 g/dL, even when iron, vitamin B12, and folic acid levels are adequately balanced. Only the addition of roxadustat to this treatment enables the desired hemoglobin level to be achieved. The use of roxadustat has been studied in patients who have undergone immunosuppression, as well as in those who have opted out due to the undesirable side effects of chronic steroid therapy. Roxadustat has been shown to be effective in both groups (Tanaka et al., 2020).

3.7. Simultaneous administration of roxadustat and ESA

Studies have also attempted to combine roxadustat therapy with ESA treatment. This combination reduces both the cost of roxadustat treatment and the side effects of ESAs. This combination was commonly used in patients undergoing hemodialysis 3-4 times a week as part of CKD-5d treatment. Throughout the study, hemoglobin increased steadily, as did STfR, while ferritin and TIBC also decreased steadily. In some cases, hemoglobin did not reach the target range; however, authors speculate that this may have been due to initial Hb levels being too low in patients (below 6.5 g/dL), the study period being too short (only 16 weeks), or roxadustat doses being too low (Xu et al., 2024).

3.8. A new role in CKD Therapy – Causes of kidney Damege

The basis for treating CKD is not only avoiding nephrotoxic drugs (NSAIDs, aminoglycosides, cisplatin, cyclosporine, tacrolimus, or high doses of MTX), but also measures aimed at reducing proteinuria through the use of: ACE inhibitors, ARBs, SGLT2 inhibitors, GLP-1 agonists, tirzepatide, and finarenone, as well as treating comorbidities such as hypertension and hyperlipidemia (through the use of statins, ezetimibe, and PCSK-9 inhibitors). In addition, renal therapy should maintain adequate circulating blood volume, combat acidosis, and treat disorders of calcium-phosphate metabolism (Li et al., 2023).

One of the most common causes of kidney damage is ischemia followed by sudden reperfusion. Roxadustat enables metabolically very active cells to temporarily obtain energy through anaerobic glycolysis in conditions of lack of perfusion, allowing them to perform their function and meet their own needs, thereby preventing cell death and fibrosis (Xu et al., 2024; Liu et al., 2024; Chen et al., 2023).

Roxadustat was most commonly initiated in patient with stage G3 renal impairment, defined as a GFR 30-59 (mL/min/1.73 m^2) according to the KDIGO guidelines, or in patients who were about to start renal replacement therapy, defined as a GFR 15-29 (ml/min/1.73 m^2) according to KDIGO. Its use continued during dialysis regardless of the method, whether it was hemodialysis, peritoneal dialysis, or even simultaneously with transplantation. Administering roxadustat at a dose of 70 mg orally three times a week has been proven to allow patients to maintain Hb levels of 11 ± 1 g/dl throughout the entire study period (Akizawa et al., 2020; Fishbane et al., 2022).

3.9. Effects of roxadustat in patients with diabetes

In addition, weakening the inflammatory response in patients with diabetes will prevent the excessive activation of oxidative stress factors to some extent, including production of ROS and the subsequent damage caused by free radicals reacting with first structure they encounter and damaging it, or even causing apoptosis. Although, roxadustat does not affect glycemia, it may indirectly lower ROS levels, and weaken the formation of AGEs (advanced glycation end products) and the activation of the NF-κB pathway protein family by doing so (Zhang et al., 2022).

It has been established that roxadustat, tested in patients with diabetic kidney disease, affects two insulin-independent glucose transporters – GLUT-1 and GLUT-3, which are present in both the kidney and the eye. Roxadustat was tested in patients with diabetic

kidney disease. The former is stimulated more strongly. Both transporters have a common effect of protecting against glucotoxicity and hypoxia. However, it should be noted that roxadustat also stimulates neoangiogenesis by increasing the expression of pro-angiogenic factors such as VEGF, which may exacerbate diabetic microangiopathy. This proven mechanism of stimulating vascular proliferation is both beneficial in patients with ROP retinopathy of prematurity, which mainly results from retinal vascular immaturity and hypoxia, but negative in patients with AMD Age-related Macular Degradation and diabetic retinopathy (Li et al., 2023; Fang et al., 2023).

3. 10. Role of roxadustat in the treatment of other anemia—associated diseases - MDS

Roxadustat also offers hope to patients with MDS myelodysplastic syndrome due to the dependence of hemoglobin levels on combination therapy consisting of ESAs, iron preparations, and continuous transfusions, which become ineffective over time (Lu et al., 2025; Zhou et al., 2022; Hou et al., 2022). Although it was not possible to completely eliminate the need for blood transfusions in most double-blind meta-analysis studies, this was due not only to the fact that the desired haemoglobin levels were not achieved, but also to a lack of consent from study participants. Several case studies report the efficacy of roxadustat monotherapy without transfusions. The effective therapeutic dose for patients with MDS undergoing monotherapy with roxadustat and no other ESAs, with the possibility of transfusions, was set at 2.5 mg/kg. Compared to lower doses, it was not possible to maintain a satisfactory haemoglobin level. It is worth noting that this is a much higher dose than that used for roxadustat in CKD: 70 mg orally (Fishbane et al., 2021; Barratt et al., 2021).

Due to concerns about adverse effects (thromboembolic prophylaxis) in oncology patients, daily platelet counts and low-dose aspirin were used to prevent adverse events in this patient group. In studies lasting up to 52 months, there was also no progression of myelodysplastic syndrome (MDS) to acute myeloid leukaemia (AML), but more accurate prospective studies with longer follow-up times are required to confirm this (Glaspy et al., 2023; Coyne et al., 2021). Furthermore, careful monitoring of solid tumour progression should be introduced in the group of oncology patients, as off-target effects of HIF-PH inhibition mechanisms may stimulate their growth (Mittelman et al., 2024; Henry et al., 2022; Ikenoue et al., 2025).

3. 11. Side Effects: beneficial and adverse

The positive effects of roxadustat include not only a reduced risk of osteoporosis, but also depression, neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, thyroid hormone resistance, COVID-19, pulmonary fibrosis, alcoholic liver disease, ischaemic-reperfusion injury of the liver, bronchopulmonary dysplasia, and renal anaemia.

The most thoroughly described effect is on AMI (acute myocardial infarction) by switching cardiomyocytes from aerobic mechanisms, where oxygen supply is insufficient due to narrowed or even closed cardiac vessels, to anaerobic glycolysis, which is more energy-efficient in conditions of limited oxygen supply anaerobic glycolysis, which allowed cardiomyocytes affected by the narrowed artery to survive, in addition, it promoted the development of collateral circulation at the cellular level and AKI (acute kidney injury) in which roxadustat inhibits the fibrosis process and maintains the antioxidant balance of the cell by stimulating the regeneration of renal vessels and preventing the risk of ischemia/rapid reperfusion. Uncertain established effects include inflammatory bowel disease (IBD), chronic kidney disease (CKD), reduced risk of myelodysplastic syndrome (MDS), pneumonia, urinary tract infections (UTIs), arterial hypertension (AH), and hypoxic brain injury.

Roxadustat has a narrow therapeutic window: under conditions of mild or localized hypoxia, it promotes anti-apoptotic pathways, whereas under severe hypoxia it may activate the pro-apoptotic protein p53 (Table 1). Consequently, the most commonly studied dosing regimen is 70 mg orally three times per week. Undesirable effects include diarrhoea, vomiting, peripheral oedema, headache, back pain, fatigue, tumour progression, hepatitis B virus (HBV) replication, colorectal cancer, mitochondrial disorders, Wilson's disease, impaired wound healing, rhabdomyolysis, and polycystic kidney disease (PKD). The most frequently reported and best-characterized adverse effects are described below:

- Pulmonary hypertension, Case report from Łódź, Poland, states that a patient who experienced sudden deterioration in exercise tolerance was diagnosed with severe PAH pulmonary arterial hypertension during treatment in a phase III clinical trial of roxadustat. After immediate discontinuation of roxadustat and replacement with erythropoietin, as well as initiation of typical PAH treatment (sildenafil p.o. and treprostinil s.c.), the symptoms of PAH partially subsided, but it was not possible to achieve as good control of anemia as with the original drug (Tan et al., 2024; Cygulska et al., 2024).

- Atherosclerosis, studies indicate that HIF stabilisation by roxadustat, combined with elevated calcium and phosphate levels typical of chronic kidney disease (CKD) and cellular stress, promotes calcification of smooth muscle cells in arteries by altering the function of RUNX2 to an osteoblastic function.
- TSH suppression, off-target effect of Roxadustat is THR-β agonism, which acts on the hypothalamic-pituitary-thyroid axis through negative feedback (Zheng et al., 2023).
- Hyperkalemia is caused by roxadustat as a result of reduced potassium excretion by the kidneys and decreased aldosterone concentration, which affects the RAA system. In addition, HIF activation enhances anaerobic glycolysis, which in turn increases lactate concentration in cells and promotes the transfer of potassium from cells to plasma.

Table 1. Comparison of the effects of roxadustat and ESA therapy.

Parameter	Roxadustat	ESA (rHuEPO)
Mechanism of action	HIF-PH inhibition, stimulation of endogenous EPO, iron metabolism modulation	Exogenous EPO receptor stimulation
EPO serum levels	Lower, stable concentrations	High peaks with wide fluctuations
Hemoglobin response	Faster and more sustained (10–12 g/dL)	Slower, less stable
Effect on inflammation (↑CRP)	Preserved efficacy	Reduced efficacy
Effect in ESA hyporesponsiveness	Effective, including anti-EPO antibody–associated PRCA	Ineffective
Iron metabolism	Decreased hepcidin levels; increased iron bioavailability	No effect on hepcidin
Cardiovascular effects	Reduced blood pressure; decreased LVMI; improved EF	No BP reduction, limited cardiac effects
Lipid profile	Decreased LDL and triglycerides	No effect
Risk of CVS complications	Lower (stable EPO exposure)	Higher (EPO peaks)
Route of administration	Oral	Subcutaneous / intravenous

3.12. Evrenzo (roxadustat) on global markets

Roxadustat was developed and patented by the biopharmaceutical company FibroGen. It is distributed by AstraZeneca in China and by Astellas in the EU, EEA and Japan. It is currently approved for use in China, where it was approved in 2018, and in Japan, where it was approved in 2019 for dialysis patients and in 2020 for non-dialysis patients. It was also approved in the EU+EEA in 2021, simultaneously for both groups. In justifying its approval, the EMA highlighted the overall balance of benefits and risks associated with roxadustat.

Much to the surprise of the pharmaceutical markets, the FDA did not approve the drug for the US market for either dialysis or non-dialysis patients. This was due to worrying data on the drug's side effects, such as blood clots. However, the FDA did not question the drug's efficacy. This decision was based on data from studies involving over 8,000 patients. Suspending registration, the FDA requested additional clinical trials to justify approval, but FibroGen did not express an interest in conducting them.

The product is currently available in the form of coated tablets in doses of 20 mg, 50 mg, 70 mg, 100 mg and 150 mg. It can be taken regardless of mealtimes, but at least one hour after taking phosphate-binding medications. The recommended dosage is three times a week. Currently, the drug is contraindicated during the third trimester of pregnancy and while breastfeeding (Lau & Seifert, 2025).

4. CONCLUSION

Roxadustat has proven to be an effective drug in clinical trials and scientific studies, which is confirmed by its international acceptance and market approval. Although its polygenic mechanism raises concerns, the availability of an increasing number of studies on its side effects, both beneficial and adverse, may be reassuring. And despite reports of some serious adverse events, the balance of benefits and risks shows more advantages to using this drug.

Its beneficial effects have been demonstrated when administered alone, regardless of iron supplementation, and in combination with ESA and iron supplementation, as well as with low-dose ESA supplementation. Patients also find the oral administration of the drug satisfactory. Its superiority in patients with systemic inflammation and ESA hyporesponsiveness, particularly with regard to the anti-EPO antibody production mechanism, is also indisputable.

Scientists are keenly interested in the effectiveness of roxadustat in treating patients receiving chemotherapy for malignant non-myeloid cancers, which may expand the therapeutic indications for this drug in the future.

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Data and materials availability
All data associated with this study will be available based on reasonable request to the corresponding author.

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