Treatment of Rare Anemias Shifting Rapidly

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Investigators said several new anemia therapies are in development, and many of them may help wide swaths of patients.

A wave of new therapies is starting to reshape the treatment landscape for people with rare anemias, but the authors of a new review also caution that more research is needed to better understand which therapies are right for which patients.

Writing in *Frontiers in Medicine*, the authors began by reviewing congenital and acquired forms of anemia. Those include sickle cell disease (SCD) and hemolytic anemias (CHAs), both congenital, and autoimmune hemolytic anemias, aplastic anemia, or paroxysmal nocturnal hemoglobinuria (PNH), which are acquired forms of anemia.

Such conditions typically have similar clinical and laboratory characteristics, which the authors said often results in diagnostic errors and delays.

For PNH and congenital anemias, transfusions have historically been the cornerstone of therapy, they noted, while immunosuppressive treatments have been more common for acquired anemias. However, they added that things are changing.

"In the last decade, a deeper understanding of physiopathology, particularly regarding the underlying molecular mechanisms, led to the development of several targeting agents," they said. "The rise of a new era of personalized medicine for rare anemia is ongoing, moving from supportive treatment to disease-modifying agents and the advent of gene therapy."

In their review article, the authors outlined some of those new therapies and strategies, and explained potential future directions for research.

Among the newer therapies, the erythroid maturation agent luspatercept (Reblozyl) and the pyruvate kinase activators mitapivat (Pyrukynd) and etavopivat have been shown to reduce transfusion dependence in both β-thalassemia and pyruvate kinase deficiency (PKD), which in turn reduces the risk of iron overload and attendant long-term complications, the authors said.

Mitapivat, etavopivat, and the hemoglobin S polymerization inhibitor voxelotor (Oxbryta) have emerged as new treatment options for SCD, the authors noted. Gene

therapies have also been studied for both SCD, β-thalassemia, and PKD. They said this approach may hold promise, but that a number of issues remain unresolved.

“Gene therapy represents a fascinating approach, although patient selection, the toxicity of the conditioning regimens, and the possible long-term safety are still open issues,” they wrote.

Turning to acquired anemias, the investigators said novel B-cell/plasma-targeting agents will likely soon be available for patients with warm autoimmune hemolytic anemia (wAIHA), and new complement inhibitors could help patients with wAIHA and cold agglutinin disease.

“PNH treatment is moving from the intravenous anti-C5 eculizumab (Soliris) to its long-term analog ravulizumab (Ultomiris), and to subcutaneous and oral proximal inhibitors (anti-C3 pegcetacoplan [Empaveli], factor D and factor B inhibitors danicopan and iptacopan),” the authors wrote.

In summary, they said the expansion of treatment options for anemia may have a compounding effect, as disease-specific therapies lead to improvements for a broader swath of patients.

“Interestingly, compounds designed for a specific disorder have been considered beneficial also for other anemias in a sort of repurposing process with potentially lower overall development costs and shorter development timelines,” they said. “Importantly, these compounds may also improve patient convenience.”

Yet, they also cautioned that the opportunity for precision medicine creates a need for optimal therapeutic selection.

“Nonresponders to novel therapies are often disregarded in clinical trials and predictors of response are only seldom explored (ie, presence of disruptive genotype in PKD),” they wrote.

The authors said these issues will be important avenues for investigation in anemia. They further noted that these new therapies will likely affect the economics of treating these patients, something they said health plans and national insurers should consider.

Reference

Fattizzo B, Motta I. Rise of the planet of rare anemias: an update on emerging treatment strategies. *Front Med* (Lausanne). Published online January 9, 2023. doi:10.3389/fmed.2022.1097426