Gene Therapy in Hematology: What Explains the Uptake Gap?

Authors:

Dr. Haydar Frangoul, MD
Department Pediatric Hematology/Oncology, Transplant and Cellular Therapy Program
TriStar Medical Group Children's Specialists
Sarah Cannon Research Institute
Nashville, TN 37203

Dr. Steven Pipe, MD
Department of Pediatric Hematology/Oncology, Hemophilia & Coagulation Disorders
C.S. Mott Children's Hospital
University of Michigan
Ann Arbor, MI 48109

Sarah Hendry, MBA
Franchise Head, Hematology/Oncology
Spherix Global Insights
Exton, PA 19341

Bridging the Gap Between Promise and Practice

Gene therapy has ushered in a new era for patients with inherited blood disorders, offering the promise of a one-time, potentially curative treatment. With regulatory approvals for multiple therapies such as Casgevy (exa-cel, Vertex) and Lyfgenia (lovo-cel, Genetix Bioherapeutics) in Sickle Cell Disease (SCD), Zynteglo (beti-cel, Genetix Biotherapeutics) and Casgevy (exa-cel, Vertex) in transfusion-dependent beta-thalassemia (TDT), and Roctavian (val-rox, BioMarin), Hemgenix (etranacogene dezaparvovec, CSL Behring), and Beqvez (fidanacogene elaparvovec, Pfizer – discontinued) in hemophilia, the therapeutic landscape is more dynamic than ever before. Yet while the scientific foundation is solid, the real-world story of gene therapy adoption is far more nuanced. Clinical uptake has not been uniform across indications, and in fact, uptake has been moving at a faster pace in SCD and TDT compared to hemophilia A and B. In this whitepaper, we examine the reasons why.

As clinicians and researchers deeply embedded in these respective fields, we have witnessed firsthand the clinical promise and logistical realities of gene therapy adoption. In collaboration with Spherix Global Insights, this whitepaper draws from physician surveys, patient experiences, and direct reflections to explore how policy, infrastructure, and psychology collectively shape gene therapy's trajectory across different hematologic diseases.

Different Diseases, Different Drivers

In the realm of SCD and thalassemia, the momentum behind gene therapy is fueled by urgency. According to a recent survey of 51 treating hematologists conducted by Spherix Global Insights, transfusion dependent thalassemia and sickle cell disease are consistently rated among the highest for unmet need of any classical hematology condition, with physicians citing as many as 47% of SCD and 51% of TDT patients with suboptimal disease control.[1] As Dr. Frangoul, who has overseen numerous gene therapy treatments, explains, "For many of our sickle cell disease patients, the status quo is unacceptable—repeated vaso-occlusive crises, iron overload, chronic fatigue. These patients are not just open to a curative approach; they're actively looking for one." Further, recent research published at the University of South Carolina reports that deaths from sickle cell disease have actually increased in adults from 2008 to 2023[2], meaning there is much work to be done to improve the outlook for these patients.

Hemoglobinopathies: Sickle Cell Disease and Transfusion-Dependent Thalassemia

TDT patients similarly face relentless transfusion schedules and the burden of chelation therapy, leading many to explore alternatives. Patient populations in both SCD and TDT often include younger individuals who are eager to regain autonomy, particularly when supported by engaged caregivers and experienced transplant centers. Many of these institutions already have infrastructures in place from nurses trained in conditioning regimens to social workers adept at coordinating post-treatment support, which accelerates clinical readiness for gene therapy.

Getting to the transplant center, however, creates its own unique hurdle for patients. Referrals to a specialty center for assessment have not been as widespread as hoped, particularly among SCD patients. According to a Spherix study of 187 individual patient charts supplied by 109 unique treating US hematologists, a vast majority of patients are seen as possible candidates for gene therapy. In fact, only 12% of patients are considered poor candidates, and physicians estimate that up to 29% of patients may ultimately receive gene therapy for sickle cell disease. This candidacy has not yet translated into active treatment, though; only 1% of patients are reported to have received approval and just another 6% have started the process for acquiring prior authorization.[3] Anecdotal experiences suggests that once patients and their families know about curative options like gene therapy, they are very interested in learning more – but hematologists may not have the time or ability to share detailed information with every patient, leaving many individuals unaware of their options. While gene therapy may not be the right choice for every patient, they all deserve the opportunity to be assessed and given a full view of their options.

There are many reasons why gene therapy may not come up in a visit, the most obvious being that there are already so many topics to cover in limited time. When asked about visits with thalassemia and sickle cell disease patients, most frequent topics discussed include patient quality of life (66% of visits), managing fatigue (40% of visits), and medication side effects (38% of visits)[4], leaving little room for discussing longer-term

strategies and other therapeutic options. Further, hematologists often have in their mind who is a 'good' candidate for gene therapy, which likely impacts the targets for such discussions. According to a Spherix study of 71 unique treating US hematologists, in order to be a 'good' or 'appropriate' candidate, physicians report that patients must be appropriately motivated – a metric that is hard to quantify or demonstrate.[5]

Perhaps the greatest barrier to gene therapy uptake in SCD today, and one that can be improved with greater access to information, is patient awareness and education.

Bleeding Disorders: Hemophilia

By contrast, hemophilia patients have more therapeutic options today than ever before – and awareness is not the issue. As Dr. Pipe notes, "We've seen an explosion of innovation in hemophilia, particularly with non-factor therapies like Hemlibra (emicizumab, Genentech). For patients who are well-controlled, the perceived benefit of switching to gene therapy, especially one that requires immunosuppression, is often not worth the unknown." This is especially true in hemophilia A, where prophylactic corticosteroids are typically required, dampening both patient interest and physician enthusiasm.

Moreover, gene therapy's positioning as a one-time solution can be psychologically daunting. "There's a real concern among patients," Dr. Pipe continues, "that by accepting gene therapy now, they're closing the door on future, potentially better treatments. That's a much bigger factor than many realize." The bleeding disorders community objects to the idea that lack of uptake for gene therapy means there is no need or desire for curative therapies – though Spherix data shows that as many as 45% of hematologists believe that there is no need for gene therapy because non-gene modifying products on the market are treating patients effectively.[6] The landscape is in constant flux, with therapies entering and exiting clinical trials, some of which faced delayed approvals (Roctavian) or were pulled from the market post-launch (Beqvez), which can lead to additional trepidation and a desire to "wait and see". Hematologists do expect as many as one-in-three patients may ultimately be treated with gene therapy, the thought is simply that there is value in seeing what comes next.

Operational Readiness and Institutional Capacity

Even when physicians and patients are aligned, gene therapy adoption is contingent on systemic readiness. In the SCD and TDT spaces, years of experience with bone marrow transplantation have created a culture of multidisciplinary coordination. As Dr. Frangoul puts it, "We're not starting from scratch. These systems are already in place, and we're just adapting them."

However, existing systems do not always translate to a streamlined process. Recent Spherix survey data reveal that 82% of hematologists believe the demand for gene therapy among hemoglobinopathy patients is higher than their facility can accommodate, with many citing administrative burden with prior-authorization and single-case agreements as

well as facility expenses and coordination of services playing a key role in slowing the process.[7]

In hemophilia, the story is different. Many hemophilia treatment centers (HTCs) have only recently received internal approval to administer gene therapy commercially. Staffing, payer negotiations, and institutional risk management processes have created delays. "We're just now getting through those administrative hurdles," says Dr. Pipe. "And we still need to scale infrastructure to support everything from patient screening to long-term monitoring."

In SCD, hematologists report greatest concern with prior authorization and single-case agreements.[8] But for those working in HTCs, availability and coordination of services is the greatest concern, followed by length of overall process per patient. In fact, in a recent Spherix study of 56 hematologists who regularly see hemophilia patients, 43% strongly agree that the burden placed on them and their staff by the process of referring a patient for gene therapy makes them hesitant to refer hemophilia patients for evaluation. That, coupled with the fact that 52% of hematologists consider access to a gene therapy center an extremely high barrier for patients suggests that this progress will continue to move at a very slow pace if significant changes are not made at both the systemic and individual institutional level.[9]

Looking Ahead: Tailoring Solutions to Patient Realities

Access has been a major barrier, particularly for Medicaid populations. The Centers for Medicare & Medicaid Services (CMS) introduced the Cell and Gene Therapy Access Model in 2025, enabling states to enter outcomes-based agreements with manufacturers and providing a framework to mitigate upfront financial risks. This program intends to move more patients through the system, but real-world impact remains to be seen.

Early anecdotal data from a recent Spherix survey of 71 hematologists with a focus on hemoglobinopathies suggests that those in states not aligned with the model are more concerned that demand will be greater than what their facilities can reasonably accommodate compared to those in participating states.[10] This could further disincentivize physicians from educating and referring patients – if they believe their patients are unlikely to receive gene therapy because of systemic barriers, they may avoid broaching the topic altogether.

The path forward will depend on aligning innovation with the specific needs and contexts of each disease area. For SCD and thalassemia, the focus should be on increasing awareness, streamlining referrals, and ensuring post-treatment support. For hemophilia, future progress may hinge on the arrival of non-viral delivery systems, redosing strategies, and gene editing platforms with more favorable safety profiles.

Still, it is clear that gene therapy represents a transformational shift in hematology. As Dr. Frangoul notes, "The outcomes we're seeing in real-world patients are not just clinical,

they're life-changing." And as Dr. Pipe adds, "We're in the early innings. But the long-term potential remains vast, as long as we continue addressing the barriers head-on."

Conclusion

In the story of gene therapy, one-size-fits-all does not apply. Success will depend on understanding the human, institutional, and economic contexts in which therapies are delivered. By combining scientific rigor with empathetic implementation, we can bridge the gap between promise and practice: bringing the curative potential of gene therapy to the patients who need it most.

Author Bios

Haydar Frangoul, MD is a Professor of Pediatrics and Medical Director of Pediatric Hematology/Oncology at the Sarah Cannon Research Institute. He is internationally recognized for his work in sickle cell disease and thalassemia and was among the first investigators to administer gene therapy in these populations.

Steven Pipe, MD is a Professor of Pediatrics and Pathology at the University of Michigan and Director of the Pediatric Hemophilia and Coagulation Disorders Program. A global expert in hemophilia, he has served as principal investigator for numerous clinical trials and led early research into AAV gene therapies.

Sarah Hendry, MBA is Franchise Head for Hematology/Oncology at Spherix Global Insights, specializing in physician insights and the commercialization of breakthrough therapies in rare hematologic conditions.

---

[1] Spherix Market Dynamix: Sickle Cell Disease and Thalassemia (US) 2025

[2] Abraha HE, Thoma M, Boghossian NS. Mortality Rate Trends for Sickle Cell Disease and Cystic Fibrosis in the US. JAMA Pediatr. Published online September 08, 2025. doi:10.1001/jamapediatrics.2025.2997

[3] Spherix Patient Chart Dynamix: Sickle Cell Disease (US) 2025

[4] Spherix Patient Chart Dynamix: Sickle Cell Disease (US) 2025

[5] Spherix Market Dynamix: Sickle Cell Disease and Thalassemia (US) 2025

[6] Spherix Market Dynamix: Hemophilia (US) 2025

[7] Spherix Market Dynamix: Sickle Cell Disease and Thalassemia (US) 2025

[8] Spherix Market Dynamix: Sickle Cell Disease and Thalassemia (US) 2025

[9] Spherix Market Dynamix: Hemophilia (US) 2025

[10] Spherix Market Dynamix: Sickle Cell Disease and Thalassemia (US) 2025