Rethink the LYFGENIA Patient

Insights to help identify, evaluate, and discuss LYFGENIA with appropriate patients

Determining which patients with sickle cell disease (SCD) may be appropriate for LYFGENIA requires consideration of multiple factors.

This guide provides a practical framework to help identify patients in your practice who may be eligible for LYFGENIA therapy and support referral conversations.

Actor portrayals

Indication

LYFGENIA is indicated for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events.

Limitations of Use

Following treatment with LYFGENIA, patients with α-thalassemia trait (-α3.7/-α3.7) may experience anemia with erythroid dysplasia that may require chronic red blood cell transfusions. LYFGENIA has not been studied in patients with more than two α-globin gene deletions.

Important Safety Information

Boxed WARNING: HEMATOLOGIC MALIGNANCY

Hematologic malignancy has occurred in patients treated with LYFGENIA. Monitor patients closely for evidence of malignancy through complete blood counts at least every 6 months and through integration site analysis at Months 6, 12, and as warranted.

Please see additional **Important Safety Information** on page 7 and **full Prescribing Information**, including **Boxed WARNING** for LYFGENIA.

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LYFGENIA™: Transformational results. One-time treatment. Lasting impact.

After LYFGENIA infusion, almost all evaluable patients achieved complete resolution of VOEs (VOE-CR) and severe VOEs (sVOE-CR).[1]

Primary Endpoint[1]

Secondary Endpoint[1]

Patient-Reported Outcomes[2]

At 36 months (n=20), more than half of patients reported clinically meaningful improvements in pain intensity (57%), pain interference (64%), and fatigue (64%).

- This exploratory analysis includes a subset of adult Study 1-C patients with available baseline and follow-up HRQOL data (PROMIS-57).
- No efficacy conclusions should be drawn from these data.

The efficacy outcomes were VOE-CR and sVOE-CR, which were defined as the elimination of (s)VOEs between 6 and 18 months post infusion with LYFGENIA.[1]

VOEs were defined as any of the following requiring evaluation at a medical facility: acute pain episode lasting >2 hours with no medically determined cause other than vaso-occlusion, acute chest syndrome, or acute hepatic/splenic sequestration.[1]

sVOEs were also counted as VOEs and were defined as VOEs requiring hospitalization, >1 emergency or urgent care visits, each requiring i.v. medications, within 72 hours, or priapism requiring any medical attention.[1]

After the primary evaluation period to last follow-up, 4 of 28 patients who achieved VOE-CR experienced VOEs while maintaining globin response.[1]

The efficacy of LYFGENIA was studied in a single-arm, 24-month, open-label, multicenter Phase 1/2 study (Study 1-C).[1]

In Study 1-C, 32 patients with a history of at least 4 VOEs in the 24 months prior to informed consent were evaluated for VOEs.[1]

Learn more at LYFGENIAhcp.com.

Consider earlier intervention with LYFGENIA gene therapy which offers the potential to reduce VOEs[1,2]

Important Safety Information (cont'd)

Hematologic Malignancy

Hematologic malignancy has occurred in patients treated with LYFGENIA (Study 1, Group A). At the time of initial product approval, two patients treated with an earlier version of LYFGENIA using a different manufacturing process and transplant procedure (Study 1, Group A) developed acute myeloid leukemia (AML). One patient with α-thalassemia trait (Study 1, Group C) has been diagnosed with myelodysplastic syndrome (MDS).

The additional hematopoietic stress associated with mobilization, conditioning, and infusion of LYFGENIA, including the need to regenerate the hematopoietic system, may increase the risk of a hematologic malignancy.
Patients with sickle cell disease have an increased risk of hematologic malignancy as compared to the general population.

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The Right Patient for LYFGENIA May Already Be in Your Practice

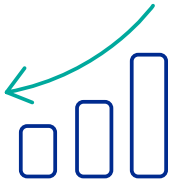
The impact of SCD is not one-size-fits-all

VOEs can vary in frequency and severity, but even patients with fewer events can experience disruptions to their lives.[3,4]

When considering treatment, think beyond the most severe cases:

Younger individuals at least 12 years of age who may benefit from intervention[5-8]

Those **experiencing fewer VOEs** where even limited events can still mean hospitalizations, school/work interruptions, and long-term health risks[3,4]



Individuals looking to **lessen the impact of their VOEs, including crises,** and pursue what matters most in their lives

Those seeking **a different future**, defined less by unpredictable VOEs and more by possibility

Not just for the most severe:
LYFGENIA may be appropriate for more patients than you think

Important Safety Information (cont'd)

Hematologic Malignancy (cont'd)

Patients treated with LYFGENIA may develop hematologic malignancies and should have lifelong monitoring. Monitor for hematologic malignancies with a complete blood count (with differential) at least every 6 months for at least 15 years after treatment with LYFGENIA, and integration site analysis at Months 6, 12, and as warranted.

In the event that a malignancy occurs, contact Genetix Biotherapeutics at 1-833-999-6378 for reporting and to obtain instructions on collection of samples for testing.

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Rethink Your Patients. Reimagine What's Possible With LYFGENIA.

Consider these key categories to help identify potential candidates in your practice

Demographics[1]

- Confirmed diagnosis of severe sickle cell disease
- Managed in pediatric (≥12 years of age) or adult care, with no specific age cap
- Appropriate for autologous hematopoietic stem cell (HSC) transplantation

Clinical History[1]

- History of VOEs

Current Treatments[1,9,10]

- Inadequate response to disease-modifying therapies
- Dependence on chronic transfusion therapy

Lifestyle and Psychosocial Factors[1-3]

- Significant time spent managing disease, leading to interruptions of daily life
- Frequently missing school or work because of VOEs
- Availability of caregiver/family support for treatment and recovery
- Willingness and capacity to undergo myeloablative conditioning and long-term monitoring

Additional Considerations[1,11]

- Patient understanding of risks and potential long-term benefit
- Motivation for a one-time, potentially transformative therapy vs. continued chronic management
- Access to a QTC

While patients may not need to meet all criteria, LYFGENIA eligibility requires age ≥12 and a history of VOEs[1]

Important Safety Information (cont'd)

Hematologic Malignancy (cont'd)

Post-Marketing Long Term Follow-Up Study: Patients who intend to receive treatment with LYFGENIA are encouraged to enroll in the study, as available, to assess the long-term safety of LYFGENIA and the risk of malignancies occurring after treatment with LYFGENIA by calling Genetix Biotherapeutics at 1-833-999-6378. The study includes monitoring (at pre-specified intervals) for clonal expansion.

Delayed Platelet Engraftment

Delayed platelet engraftment has been observed with LYFGENIA. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia. Two patients (4%) required more than 100 days post treatment with LYFGENIA to achieve platelet engraftment.

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Help Patients Make Informed Decisions

Additional considerations to support patients as they explore treatment with LYFGENIA

Affording LYFGENIA treatment

Once enrolled in Patient Support Services, patients will have a dedicated Patient Navigator to help them understand their insurance coverage and out-of-pocket costs. Additionally, patients who qualify can be connected with financial assistance programs that are available.

Future family planning

Due to the chemotherapy component of LYFGENIA treatment, patients may not be able to become pregnant or father a child. Patients should be advised of this risk and their options for fertility preservation.[1]

Long-term treatment readiness

Although LYFGENIA is a one-time therapy, patients must understand the overall timeline associated with the treatment process and be able to demonstrate a willingness to adhere to the length of time the process requires.[1]

For additional support, patients can enroll in the Genetix Patient Support Program and connect with a Patient Navigator today, at no cost.

www.GenetixPatientSupport.com | patientsupport@genetixbiotx.com | 1-833-888-6378

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Reframe the Sickle Cell Conversation With Your Patients

Help patients move beyond management by discussing the broader impact of sickle cell disease

Discussion Questions

- "How much time do you spend trying to manage pain crises?"
- "How often are pain crises affecting your life, school, or work?"
- "How do hospital visits caused by VOEs affect your daily routine?"
- "What are the hardest parts of living with pain, fatigue, or VOEs caused by sickle cell disease?"
- "What would life look like if you could potentially reduce or eliminate VOEs?"
- "What concerns, if any, do you have about the potential side effects, risks, or overall treatment process for a gene therapy?"
- "What questions do you have around the long-term monitoring requirements, such as follow-up visits, lab tests, or ongoing assessments?"

LYFGENIA is administered only at Qualified Treatment Centers—contact a Representative to initiate the referral process

Important Safety Information (cont'd)

Delayed Platelet Engraftment (cont'd)
Patients should be made aware of the risk of bleeding until platelet recovery has been achieved. Monitor patients for thrombocytopenia and bleeding according to standard guidelines. Conduct frequent platelet counts until platelet engraftment and platelet recovery are achieved. Perform blood cell count determination and other appropriate testing whenever clinical symptoms suggestive of bleeding arise.

Neutrophil Engraftment Failure
There is a potential risk of neutrophil engraftment failure after treatment with LYFGENIA. Neutrophil engraftment failure is defined as failure to achieve three consecutive absolute neutrophil counts (ANC) ≥ 0.5×10^9 cells/L obtained on different days by Day 43 after infusion of LYFGENIA. Monitor neutrophil counts until engraftment has been achieved. If neutrophil engraftment failure occurs in a patient treated with LYFGENIA, provide rescue treatment with the back-up collection of CD34+ cells.

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Insertional Oncogenesis

There is a potential risk of lentiviral vector-mediated insertional oncogenesis after treatment with LYFGENIA.

Hypersensitivity Reactions

Allergic reactions may occur with the infusion of LYFGENIA. The dimethyl sulfoxide (DMSO) or dextran 40 in LYFGENIA may cause hypersensitivity reactions, including anaphylaxis.

Anti-retroviral Use

Patients should not take prophylactic HIV anti-retroviral medications for at least one month prior to mobilization and until all cycles of apheresis are completed. There are some long-acting anti-retroviral medications that may require a longer duration of discontinuation for elimination of the medication. If a patient is taking anti-retrovirals for HIV prophylaxis, confirm a negative test for HIV before beginning mobilization and apheresis of CD34+ cells.

Hydroxyurea Use

Patients should not take hydroxyurea for at least 2 months prior to mobilization and until all cycles of apheresis are completed. If hydroxyurea is administered between mobilization and conditioning, discontinue 2 days prior to initiation of conditioning.

Iron Chelation

Drug-drug interactions between iron chelators and the mobilization process and myeloablative conditioning agent must be considered. Iron chelators should be discontinued at least 7 days prior to initiation of mobilization or conditioning. Do not administer myelosuppressive iron chelators (e.g., deferiprone) for 6 months post-treatment with LYFGENIA. Non-myelosuppressive iron chelation should be restarted no sooner than 3 months after LYFGENIA infusion. Phlebotomy can be used in lieu of iron chelation, when appropriate.

Interference with PCR-based Testing

Patients who have received LYFGENIA are likely to test positive by polymerase chain reaction (PCR) assays for HIV due to integrated BB305 LVV proviral DNA, resulting in a possible false-positive PCR assay test result for HIV. Therefore, patients who have received LYFGENIA should not be screened for HIV infection using a PCR-based assay.

Adverse Reactions

The most common adverse reactions ≥ Grade 3 (incidence ≥ 20%) were stomatitis, thrombocytopenia, neutropenia, febrile neutropenia, anemia, and leukopenia.

Three patients died during LYFGENIA clinical trials; one from sudden cardiac death due to underlying disease and two from acute myeloid leukemia who were treated with an earlier version of LYFGENIA using a different manufacturing process and transplant procedure (Study 1, Group A).

Pregnancy/Lactation

Advise patients of the risks associated with myeloablative conditioning agents, including on pregnancy and fertility.

LYFGENIA should not be administered to women who are pregnant, and pregnancy after LYFGENIA infusion should be discussed with the treating physician.

LYFGENIA is not recommended for women who are breastfeeding, and breastfeeding after LYFGENIA infusion should be discussed with the treating physician.

Females and Males of Reproductive Potential

A negative serum pregnancy test must be confirmed prior to the start of mobilization and re-confirmed prior to conditioning procedures and before LYFGENIA administration.

Women of childbearing potential and men capable of fathering a child should use an effective method of contraception (intra-uterine device or combination of hormonal and barrier contraception) from start of mobilization through at least 6 months after administration of LYFGENIA.

Advise patients of the options for fertility preservation.

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Refer Your Patients for LYFGENIA Today

Connect with a LYFGENIA Representative to discuss patient eligibility and the treatment process

Find a Qualified Treatment Center to initiate the referral process

References:

1. LYFGENIA [prescribing information], Sommerville, MA; Genetix Biotherapeutics, Inc.; December 2023. **2.** Kanter J, et al. Presented at American Society of Hematology 2023; Abstract 1051. **3.** Coco M, et al. *Res Nurs Health*. 2023;46(3):299-312. **4.** van Beers EJ, et al. *Haematologica*. 2008;93(5):757-760. **5.** Abdel-Hadi L, et al. *Am J Blood Res*. 2023;13(2):61-70. **6.** Ware RE, et al. *Lancet*. 2017;390(10091):311-323. **7.** Leonard A, Tisdale JF. *Hematology Am Soc Hematol Educ Program*. 2023;2023(1):542-547. **8.** Powars DR, et al. *Medicine (Baltimore)*.2005;84(6):363-376. **9.** Rifkin-Zenenberg S, et al. Presented at American Society of Hematology 2024; Abstract 511. **10.** Kanter J, et al. *N Engl J Med*. 2022;386(7):617-628. **11.** Mahadevia H, et al. *Ann Hematol*.2025;104(2):881-893.

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