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Clinical and Hematological Evaluation of Hydroxyurea Therapy in Iraqi Patients with Sickle Cell Anemia

Fatima Manssor ALTaweel[1], Ahmed Salih Sahib[1 2], Shaima Jabbar[1 *], Basim Abdulkareem Alhijaj[3], Raja Abdul Zahra Mohammed Al-Mas'udi[4]

[1]Department of Pharmacology and Toxicology, College of Pharmacy, University of Kerbala, Karbala, Iraq
[2]Department of Pharmacology and Toxicology, College of Pharmacy, Ahl al Bayt University, Karbala, Iraq
[3]Consultant Pediatrician BCHBD, Alzahraa Medical College, IAMRS Vice President
[4]Children's Department, Al-Fayhaa Hospital, Basra, Iraq

***Corresponding Author:**
Shaima Jabbar: shaymaa.a@uokerbala.edu.iq

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Abstract

Background: Sickle cell anemia (SCA) is a chronic inherited hemoglobinopathy associated with severe morbidity and reduced quality of life. Hydroxyurea (HU) is the most effective disease-modifying pharmacological therapy for SCA; however, continuous evaluation of its clinical and hematological impact in different populations is essential.

Objective: To assess the clinical efficacy and hematological effects of hydroxyurea therapy in Iraqi patients with sickle cell anemia.

Materials and Methods: A cross-sectional observational study was conducted on 50 Iraqi patients diagnosed with SCA and treated with hydroxyurea for at least six months. Clinical outcomes included frequency of vaso-occlusive crises and pain intensity. Hematological parameters assessed were hemoglobin concentration and fetal hemoglobin (HbF) percentage. Data were analyzed using descriptive and comparative statistical methods.

Results: Hydroxyurea therapy resulted in a significant increase in HbF levels and total hemoglobin concentration. Additionally, patients experienced a notable reduction in pain intensity and frequency of vaso-occlusive crises. The drug was generally well tolerated, and no severe adverse drug reactions were observed.

Conclusion: Hydroxyurea demonstrates significant clinical and hematological benefits in Iraqi patients with sickle cell anemia. The findings support its role as a safe and effective pharmacological therapy and highlight its importance in routine clinical practice.

التقييم السريري والدموي للعلاج بالهيدروكسي يوريا لدى المرضى العراقيين المصابين بفقر الدم المنجلي

فاطمة منصور الطويل، أحمد صالح صاحب، شيماء جبار

الملخص

المقدمة :يُعد فقر الدم المنجلي (Sickle Cell Anemia, SCA) أحد اضطرابات الهيموغلوبين الوراثية المزمنة، ويرتبط بمعدلات مرتفعة من المراضة وتدنّي جودة الحياة. يُعد الهيدروكسي يوريا (Hydroxyurea, HU) العلاج الدوائي المُعدِّل للمرض الأكثر فاعلية في علاج فقر الدم المنجلي، إلا أن التقييم المستمر لتأثيراته السريرية والدموية في مختلف المجتمعات السكانية يُعد أمرًا ضروريًا.

الهدف :تقييم الفعالية السريرية والتأثيرات الدموية للعلاج بالهيدروكسي يوريا لدى المرضى العراقيين المصابين بفقر الدم المنجلي.

المواد وطرائق العمل :أُجريت دراسة رصدية مقطعية شملت 50 مريضًا عراقيًا مشخصين بفقر الدم المنجلي ويتلقون العلاج بالهيدروكسي يوريا لمدة لا تقل عن ستة أشهر. شملت المؤشرات السريرية المدروسة تكرار نوبات الانسداد الوعائي وشدة الألم. كما تم تقييم المؤشرات الدموية المتمثلة بتركيز الهيموغلوبين ونسبة الهيموغلوبين الجنيني .(HbF) جرى تحليل البيانات باستخدام الطرق الإحصائية الوصفية والمقارنة.

النتائج :أدى العلاج بالهيدروكسي يوريا إلى زيادة معنوية في مستويات الهيموغلوبين الجنيني وتركيز الهيموغلوبين الكلي. إضافةً إلى ذلك، لوحظ انخفاض ملحوظ في شدة الألم وتكرار نوبات الانسداد الوعائي. وقد تميز الدواء بتحمل جيد لدى المرضى، دون تسجيل أي تفاعلات دوائية ضارة شديدة.

الاستنتاج :يُظهر الهيدروكسي يوريا فوائد سريرية ودموية مهمة لدى المرضى العراقيين المصابين بفقر الدم المنجلي. وتدعم هذه النتائج دوره كعلاج دوائي آمن وفعّال، وتبرز أهميته في الممارسة السريرية الروتينية.

1. Introduction

Sickle cell anemia (SCA) is a chronic inherited hemoglobinopathy caused by a structural abnormality in hemoglobin, leading to the formation of hemoglobin S (HbS). Under conditions of low oxygen tension, HbS polymerizes, resulting in erythrocyte deformation, increased hemolysis, and microvascular occlusion (Pavan et al., 2024). These pathological events contribute to chronic anemia, recurrent vaso-occlusive crises, progressive organ damage, and reduced life expectancy. SCA remains a major public health challenge, particularly in developing countries where access to advanced healthcare resources is limited. From a pharmaceutical sciences perspective, the management of sickle cell anemia relies heavily on pharmacological interventions aimed at modifying disease progression and reducing clinical complications (Light et al., 2023; McCormick et al., 2021). Among available therapeutic options, hydroxyurea is recognized as the most effective disease-modifying drug currently approved for the treatment of SCA. Originally developed as an antineoplastic agent, hydroxyurea has demonstrated substantial clinical benefits in patients with sickle cell anemia, leading to its widespread adoption in clinical practice (McGann & Ware, 2015; Ware, 2015). The primary pharmacological mechanism of hydroxyurea involves the induction of fetal hemoglobin (HbF) production. Increased HbF levels interfere with HbS polymerization, thereby reducing erythrocyte sickling and improving red blood cell survival. In addition to HbF induction, hydroxyurea exhibits several secondary pharmacodynamic effects, including reduction of leukocyte and reticulocyte counts, improvement of erythrocyte hydration, and enhancement of nitric oxide bioavailability. These combined effects contribute to decreased vascular inflammation, improved blood flow, and reduced frequency of vaso-occlusive events (López Rubio & Argüello Marina, 2024; Riley et al., 2024; Ware, 2015).

Clinical studies have consistently demonstrated that hydroxyurea therapy leads to a reduction in pain crises, hospital admissions, and transfusion requirements, while improving hematological parameters and overall quality of life in patients with SCA. Despite these documented benefits, variability in patient response to hydroxyurea has been reported. Factors such as dosage regimen, duration of therapy, treatment adherence, and patient-specific biological characteristics may influence therapeutic outcomes (Albohassan et al., 2022; Riley et al., 2024).

In Iraq and neighboring regions, sickle cell anemia represents a significant clinical burden, yet locally generated data evaluating the effectiveness of hydroxyurea therapy remain limited. Differences in healthcare infrastructure, monitoring practices, and patient demographics underscore the importance of assessing the clinical and hematological response to hydroxyurea within the local population. Such evaluations are essential to optimize treatment strategies and support evidence-based pharmaceutical care (Salvia et al., 2013; Subira et al., 2025).

Therefore, the present study was designed to evaluate the clinical efficacy and hematological impact of hydroxyurea therapy in Iraqi patients with sickle cell anemia. By focusing on real-world clinical outcomes and laboratory parameters, this study aims to contribute valuable local evidence supporting the role of hydroxyurea as a cornerstone pharmacological therapy in the management of sickle cell anemia.

2. Patients and Methods

2.1. Study Design and Ethical Approval

This cross-sectional study was conducted after obtaining formal approval from the Scientific and Ethical Committee of the College of Pharmacy, University of Karbala. Written informed consent was obtained from all participants or their legal guardians prior to enrollment.

2.2. Study Population

The study included 50 patients of both sexes diagnosed with sickle cell anemia, with ages ranging from 14 to 65 years. All participants had been receiving hydroxyurea (HU) therapy as part of their routine clinical management.

Hydroxyurea Treatment and Patient Grouping

Patients were categorized into three groups according to the prescribed daily dose of hydroxyurea:

Group I: 22 patients receiving 10 mg/kg/day

Group II: 20 patients receiving 15 mg/kg/day

Group III: 8 patients receiving 20 mg/kg/day

The allocation of patients to these dosage groups was based on individualized clinical evaluation and therapeutic decision-making by the attending medical team. Dose selection followed established pharmacological guidelines for hydroxyurea administration and was tailored to each patient's disease severity, clinical response, and medical history.

2.3. Hematological Analysis

Fetal hemoglobin (HbF) percentage was determined using hemoglobin electrophoresis. This parameter was used to evaluate the hematological response to hydroxyurea therapy.

2.4. Clinical Evaluation

Clinical data were obtained through review of patients' medical records and structured patient interviews. The evaluated clinical parameters included:

The frequency of vaso-occlusive crises before and during hydroxyurea therapy

The intensity of pain associated with vaso-occlusive episodes, assessed using the Visual Analog Scale (VAS)

2.5. Hematological Assessment

Venous blood samples were collected under aseptic conditions for hematological investigations. Hemoglobin concentration was measured using automated hematology analyzers. The percentage of fetal hemoglobin (HbF) was determined using standard laboratory methods.

2.6. Safety Evaluation

Patients were routinely monitored for hydroxyurea-related adverse effects throughout the treatment period. Safety assessment focused on the detection of hematological abnormalities, including cytopenia, as well as reported gastrointestinal symptoms.

2.7. Statistical Analysis

Data were analyzed using descriptive statistics. Results were expressed as mean ± standard deviation. Comparative analysis was performed to assess differences in clinical and hematological parameters before and during hydroxyurea therapy. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Demographic and Treatment Characteristics of the Study Population

The demographic and treatment characteristics of the study population are summarized in Table1. The mean age of the patients was 20.14 ± 9.13 years, with an average body weight of 50.37 ± 12.09 kg. The mean daily dose of hydroxyurea administered to the patients was 671.9 ± 237.2 mg/day, reflecting individualized dosing based on clinical assessment.

Table1: Demographic and Treatment Characteristics of The Study Population (N = 50)

Parameter	Mean ± SD
Age (years)	20.14 ± 9.13
Weight (kg)	50.37 ± 12.09
Hydroxyurea dose (mg/day)	671.9 ± 237.2

3.2. Hematological Parameters in Patients Receiving Hydroxyurea

Hematological parameters of patients receiving hydroxyurea therapy are presented in Table2. The mean hemoglobin concentration was 9.43 ± 1.36 g/dL, while the mean fetal hemoglobin (HbF) percentage reached 17.36 ± 7.28%, indicating a favorable hematological response to treatment. Platelet counts remained within the upper normal reference range, with a mean value of 392.2 ± 190.0 ×10⁹/L. Reticulocyte counts were elevated (6.98 ± 3.87%), reflecting active erythropoiesis, whereas neutrophil counts (4.21 ± 1.72 ×10⁹/L) remained within acceptable safety limits.

Table2: Hematological Parameters in Patients Receiving Hydroxyurea

Parameter	Mean ± SD	Reference Range
Hemoglobin (g/dL)	9.43 ± 1.36	12–17
HbF (%)	17.36 ± 7.28	—
Platelet count (×10⁹/L)	392.2 ± 190.0	150–400
Reticulocyte count (%)	6.98 ± 3.87	0.5–1.5
Neutrophil count (×10⁹/L)	4.21 ± 1.72	2–8

3.3. Distribution of Patients According to Hydroxyurea Dosage

The distribution of patients according to hydroxyurea dosage is shown in Table3. Most patients received doses of 10 mg/kg/day (44.0%) or 15 mg/kg/day (40.0%), while a smaller proportion were treated with 20 mg/kg/day (16.0%). Dose selection was individualized based on clinical evaluation and patient response.

Table3: Distribution of Patients According to Hydroxyurea Dosage

Hydroxyurea dose (mg/kg/day)	Number of patients (n)	Percentage (%)
10 mg/kg/day	22	44.0
15 mg/kg/day	20	40.0
20 mg/kg/day	8	16.0
Total	50	100

3.4. Hematological Parameters Before and During Hydroxyurea Therapy

Comparison of hematological parameters before and during hydroxyurea therapy is presented in Table4. Hydroxyurea treatment was associated with a significant increase in hemoglobin concentration (8.1 ± 1.2 vs. 9.6 ± 1.4 g/dL, $p < 0.05$) and a marked elevation in fetal hemoglobin levels (6.4 ± 2.1% vs. 14.8 ± 4.3%, $p < 0.001$).

Table4: Hematological Parameters Before and During Hydroxyurea Therapy

Parameter	Before HU (Mean ± SD)	During HU (Mean ± SD)	p-value
Hemoglobin (g/dL)	8.1 ± 1.2	9.6 ± 1.4	< 0.05
HbF (%)	6.4 ± 2.1	14.8 ± 4.3	< 0.001

3.5. Pain Crisis Characteristics

The frequency of vaso-occlusive crises before and during hydroxyurea therapy is summarized in Table5. Prior to treatment, more than half of the patients (**52%**) experienced three or more painful crises per year. Following hydroxyurea therapy, this proportion markedly decreased to **14%**, while the percentage of patients reporting no painful crises increased from **8% to 36%**, indicating a substantial clinical improvement. Pain intensity assessment using the Visual Analog Scale (VAS) is presented in Table6. Hydroxyurea therapy resulted in a significant reduction in pain severity, with mean VAS scores decreasing from **7.6 ± 1.1** before treatment to **3.9 ± 1.3** during treatment (**p < 0.001**).

Table5: Frequency of Vaso-Occlusive Crises per Year

Frequency	Before HU n (%)	During HU n (%)
None	4 (8%)	18 (36%)
Once	6 (12%)	15 (30%)
Twice	14 (28%)	10 (20%)
≥ 3 times	26 (52%)	7 (14%)

Table6: Pain Intensity (VAS Score)

Parameter	Mean ± SD
VAS score before HU	7.6 ± 1.1
VAS score during HU	3.9 ± 1.3
p-value	< 0.001

3.6. Safety Profile of Hydroxyurea Therapy

The safety profile of hydroxyurea therapy is presented in Table 7. Most patients (**76%**) did not experience any adverse effects during treatment. Mild cytopenia was observed in **10%** of patients, while gastrointestinal symptoms and other minor effects were reported in **8%** and **6%** of patients, respectively. No severe or life-threatening adverse drug reactions were recorded.

Table7: Safety Profile of Hydroxyurea Therapy

Adverse Effect	Number Of Patients (N)	Percentage (%)
Mild cytopenia	5	10
Gastrointestinal symptoms	4	8
Other minor effects	3	6
No adverse effects	38	76

4. Discussion

Hydroxyurea remains the most widely accepted disease-modifying pharmacological therapy for sickle cell anemia, with proven benefits in reducing disease severity and improving patient quality of life. The present study demonstrates that hydroxyurea therapy is associated with significant clinical and hematological improvement in Iraqi patients with sickle cell anemia, supporting its continued use in routine clinical practice (López Rubio & Argüello Marina, 2024).

One of the most important findings of this study is the marked increase in fetal hemoglobin (HbF) levels following hydroxyurea treatment. Increased HbF production is a well-established pharmacological effect of hydroxyurea and plays a central role in inhibiting hemoglobin S polymerization. By reducing erythrocyte sickling, elevated HbF contributes to improved red blood cell deformability and prolonged erythrocyte survival, ultimately leading to better oxygen delivery and reduced hemolysis. This mechanism explains the observed improvement in total hemoglobin concentration among treated patients (Charache et al., 1992; Dc et al., 1992; S. et al., 1992).

In addition to hematological benefits, hydroxyurea therapy resulted in a significant reduction in the frequency and intensity of vaso-occlusive pain episodes. Pain crises are the most common and debilitating complication of sickle cell anemia and are a major cause of hospitalization. The reduction in pain severity observed in this study may be attributed not only to increased HbF levels but also to additional pharmacodynamic effects of hydroxyurea, including decreased leukocyte count and reduced endothelial adhesion. These effects collectively reduce vascular inflammation and microvascular obstruction (Ifeanyi Obeagu, 2024; Jang et al., 2021).

From a pharmaceutical perspective, hydroxyurea exerts multiple mechanisms of action that extend beyond HbF induction. The drug has been shown to enhance nitric oxide bioavailability, which contributes to vasodilation and improved blood flow. Nitric oxide also plays a role in reducing platelet aggregation and endothelial activation, further limiting vaso-occlusive events. These pleiotropic effects reinforce the importance of hydroxyurea as a multifunctional therapeutic agent in sickle cell disease management (Gupta & Kumar, 2024).

The safety profile of hydroxyurea observed in this study was favorable, with no severe adverse drug reactions reported. Mild and transient side effects, when present, were manageable through routine clinical monitoring. This finding is particularly important in resource-limited healthcare settings, where access to alternative advanced therapies may be restricted. The good tolerability of hydroxyurea supports its long-term use, provided that patients undergo regular hematological monitoring to minimize the risk of cytopenia (Khargekar et al., 2024; Strouse et al., 2008; Vick et al., 2021). The findings of this study are consistent with previously published international and regional studies, which have reported similar improvements in HbF levels, hemoglobin concentration, and clinical outcomes among patients receiving hydroxyurea therapy. However, data focusing on Iraqi populations remain limited. Therefore, the present study contributes valuable local evidence that reinforces global recommendations for hydroxyurea use in sickle cell anemia (Al-Shami et al., 2025).

Despite the encouraging results, some variability in patient response was observed, which may be influenced by factors such as treatment adherence, dosage regimen, duration of therapy, and individual biological differences. Although genetic factors were not evaluated in this study, non-genetic determinants such as nutritional status, comorbidities, and access to healthcare services may also affect therapeutic outcomes. Future studies incorporating these variables

may provide a more comprehensive understanding of treatment response (Al-Shami et al., 2025; Gupta & Kumar, 2024; Khargekar et al., 2024; Vick et al., 2021).

Overall, the expanded clinical and pharmaceutical evaluation presented in this study highlights the multifaceted benefits of hydroxyurea therapy. Its ability to improve hematological parameters, reduce clinical complications, and maintain an acceptable safety profile underscores its role as the cornerstone of pharmacological management for sickle cell anemia.

5. Conclusion

The findings of this study demonstrate that hydroxyurea therapy leads to significant clinical and hematological improvement in Iraqi patients with sickle cell anemia. Treatment was associated with a marked increase in fetal hemoglobin levels and total hemoglobin concentration, along with a substantial reduction in pain intensity and frequency of vaso-occlusive crises. In addition, hydroxyurea was generally well tolerated, with no severe adverse drug reactions observed. These results support the role of hydroxyurea as a safe and effective disease-modifying pharmacological therapy for sickle cell anemia and highlight its importance in routine clinical practice. Continuous monitoring and individualized dosing remain essential to optimize therapeutic outcomes and ensure long-term safety.

References

Albohassan, H., Ammen, M., Alomran, A. A., Bu Shehab, H., Al Sakkak, H., & Al Bohassan, A. (2022). Impact of Hydroxyurea Therapy in Reducing Pain Crises, Hospital Admissions, and Length of Stay Among Sickle Cell Patients in the Eastern Region of Saudi Arabia. *Cureus*. https://doi.org/10.7759/cureus.31527

Al-Shami, A., Maad, A., Al-Saban, A., & Al-Mekhlafi, A. (2025). Impact of Hydroxyurea on Liver, Kidney, and Hematological Parameters in Sickle Cell Anemia Patients Above 15 Years Old in Sana'a City. *International Journal of General Medicine*, *Volume 18*. https://doi.org/10.2147/ijgm.s554130

Charache, S., Dover, G. J., Moore, R. D., Eckert, S., Ballas, S. K., Koshy, M., Milner, P. F. A., Orringer, E. P., Phillips, G., Platt, O. S., & Thomas, G. H. (1992). Hydroxyurea: Effects on hemoglobin F production in patients with sickle cell anemia. *Blood*, *79*(10).

Dc, W., Charache, B. S., Dover, G. J., Moore, R. D., Eckert, S., Ballas, S. K., Koshy, M., Milner, P. F. A., Orringer, E. P., Jr, G. P., Platt, O. S., & Thomas, G. H. (1992). Hydroxyurea: effects on hemoglobin F production in patients with sickle cell anemia [see comments]. *Blood*, *79*.

Gupta, P., & Kumar, R. (2024). Nitric oxide: A potential etiological agent for vaso-occlusive crises in sickle cell disease. In *Nitric Oxide - Biology and Chemistry* (Vol. 144). https://doi.org/10.1016/j.niox.2024.01.008

Ifeanyi Obeagu, E. (2024). Adhesion Molecules and Endothelial Dysfunction in Vaso-Occlusive Crisis. *General Medicine and Clinical Practice*, *7*(14). https://doi.org/10.31579/2639-4162/209

Jang, T., Poplawska, M., Cimpeanu, E., Mo, G., Dutta, D., & Lim, S. H. (2021). Vaso-occlusive crisis in sickle cell disease: a vicious cycle of secondary events. In *Journal of Translational Medicine* (Vol. 19, Issue 1). https://doi.org/10.1186/s12967-021-03074-z

Khargekar, N., Banerjee, A., Athalye, S., Mahajan, N., Kargutkar, N., Tapase, P., & Madkaikar, M. (2024). Role of hydroxyurea therapy in the prevention of organ damage in sickle cell disease: a systematic review and meta-analysis. *Systematic Reviews*, *13*(1). https://doi.org/10.1186/s13643-024-02461-z

Light, J., Boucher, M., Baskin-Miller, J., & Winstead, M. (2023). Managing the Cerebrovascular Complications of Sickle Cell Disease: Current Perspectives. In *Journal of Blood Medicine* (Vol. 14). https://doi.org/10.2147/JBM.S383472

López Rubio, M., & Argüello Marina, M. (2024). The Current Role of Hydroxyurea in the Treatment of Sickle Cell Anemia. In *Journal of Clinical Medicine* (Vol. 13, Issue 21). https://doi.org/10.3390/jcm13216404

McCormick, M., Osei-Anto, H. A., & Martinez, R. M. (2021). Complications of Sickle Cell Disease and Current Management Approaches. In *Addressing Sickle Cell Disease*.

McGann, P. T., & Ware, R. E. (2015). Hydroxyurea therapy for sickle cell anemia. In *Expert Opinion on Drug Safety* (Vol. 14, Issue 11). https://doi.org/10.1517/14740338.2015.1088827

Pavan, A. R., Terroni, B., & Dos Santos, J. L. (2024). Endothelial dysfunction in Sickle Cell Disease: Strategies for the treatment. In *Nitric Oxide - Biology and Chemistry* (Vol. 149). https://doi.org/10.1016/j.niox.2024.05.003

Riley, C., Kraft, W. K., & Miller, R. (2024). Hydroxyurea in the sickle cell disease modern era. In *Expert Review of Clinical Pharmacology* (Vol. 17, Issue 9). https://doi.org/10.1080/17512433.2024.2390915

S., C., G.J., D., R.D., M., S., E., S.K., B., M., K., P.F.A., M., E.P., O., G., P. Jr., O.S., P., & G.H., T. (1992). Hydroxyurea: Effects on hemoglobin F production in patients with sickle cell anemia. *Blood*, *79*(10).

Salvia, A. C. R. D., Figueiredo, M. S., Braga, J. A. P., Pereira, D. F. A., Brighenti, F. L., & Koga-Ito, C. Y. (2013). Hydroxyurea therapy in sickle cell anemia patients aids to maintain oral fungal colonization balance. *Journal of Oral Pathology and Medicine*, *42*(7). https://doi.org/10.1111/jop.12029

Strouse, J. J., Lanzkron, S., Beach, M. C., Haywood, C., Park, H., Witkop, C., Wilson, R. F., Bass, E. B., & Segal, J. B. (2008). Hydroxyurea for sickle cell disease: A systematic review for efficacy and toxicity in children. *Pediatrics*, *122*(6). https://doi.org/10.1542/peds.2008-0441

Subira, M. I., Ambrose, E. E., & Konje, E. (2025). Adherence to Hydroxyurea Therapy for Pediatric Sickle Cell Anemia in Tanzania: Evidence from Bugando Medical Centre. *International Journal of Environmental Research and Public Health*, *22*(4). https://doi.org/10.3390/ijerph22040616

Vick, L., Potts, M., Jaskowiak, M., & Gibson, R. W. (2021). Hydroxyurea adherence strategies for persons with sickle cell disease: A systematic review. In *Journal of Health Care for the Poor and Underserved* (Vol. 32, Issue 1). https://doi.org/10.1353/hpu.2021.0011

Ware, R. E. (2015). Optimizing hydroxyurea therapy for sickle cell anemia. *Hematology (United States)*, *2015*(1). https://doi.org/10.1182/asheducation-2015.1.436