J Pediatr Res 2025;12(3):165-166
DOI: 10.4274/jpr.galenos.2025.63139

Letter to the Editor

Ruxolitinib as a Bridge to Avoid Splenectomy in Young Children with β-Thalassemia Major

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To the Editor,

β-thalassemia major remains one of the most challenging inherited hemoglobinopathies in pediatric hematology. Despite advances in transfusion protocols and chelation therapy, massive splenomegaly continues to represent a critical clinical problem in young children. Splenectomy, while effective in alleviating hypersplenism, carries significant lifelong risks and is generally deferred until after the age of five due to the danger of overwhelming post-splenectomy infection (1,2). In this context, the use of targeted pharmacologic approaches to reduce splenic extramedullary hematopoiesis and preserve splenic function has become the subject of increasing clinical interest.

The Janus kinase 2 (JAK2) pathway plays a central role in erythropoietin-driven erythroid proliferation in the spleen and liver. Ruxolitinib, a JAK1/2 inhibitor originally developed for myeloproliferative disorders, has been shown in experimental models to reduce splenomegaly by attenuating this signaling cascade (3,4). Early-phase clinical studies have suggested that ruxolitinib may be a safe and effective therapeutic option in transfusion-dependent thalassemia, though its use in pediatrics remains off-label (5).

We recently managed two young children with transfusion-dependent β-thalassemia major who presented with massive splenomegaly unresponsive to conventional management. Both patients were girls under five years of age, receiving regular transfusions and iron chelation, yet continued to demonstrate progressive spleen enlargement. Multidisciplinary consensus strongly recommended avoiding splenectomy at this age, prompting the initiation of low-dose ruxolitinib (5 mg twice daily).

Clinical response was rapid and favorable. Within the first month, both patients demonstrated significant reductions in spleen and liver size on imaging, accompanied by decreased transfusion requirements. For the first case, annual transfusion needs decreased from 185 mL/kg to 95 mL/kg, while in the second, from 190 mL/kg to 105 mL/kg. Importantly, treatment was well tolerated, with no observed adverse events including hypoglycemia, cytopenias, or infectious complications. Over one year of follow-up, both children maintained improved transfusion intervals (every 3-4 weeks), and splenectomy was successfully deferred.

Our clinical experience adds to the growing evidence that ruxolitinib may serve as a feasible bridge therapy for young children with refractory splenomegaly secondary to β-thalassemia major. Notably, the effective use of a lower dose than reported in phase 2a studies (5) highlights the potential for tailored dosing in younger populations, balancing efficacy with safety. While these results are encouraging, they must be interpreted cautiously given the limited number of patients and retrospective nature of the observation.

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Received: 11.06.2025 **Accepted:** 27.08.2025 **Publication Date:** 03.10.2025

Cite this article as: Tufan Taş B, Koç A. Ruxolitinib as a bridge to avoid splenectomy in young children with β-thalassemia major. J Pediatr Res. 2025;12(3):165-166

Nevertheless, our findings raise important considerations for pediatric hematologists. Firstly, ruxolitinib may provide a therapeutic window in cases where splenectomy is indicated but contraindicated due to young age. Secondly, it demonstrates that even lower doses may confer significant clinical benefit. Finally, this report underscores the urgent need for prospective pediatric trials in order to establish standardized dosing regimens, long-term safety profiles, and validated clinical endpoints in this vulnerable population.

In conclusion, ruxolitinib represents a promising therapeutic option in deferring splenectomy in children with transfusion-dependent β-thalassemia major and massive splenomegaly. Larger multicenter studies are warranted in order to confirm these preliminary observations and to define the role of ruxolitinib in routine pediatric practice.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.T.T., A.K., Concept: B.T.T., Design: B.T.T., A.K., Data Collection or Processing: B.T.T., Analysis or Interpretation: B.T.T., Literature Search: B.T.T., A.K., Writing: B.T.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors received no financial support for the research, authorship, and/or publication of this article.

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