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TO THE EDITOR:

Pediatric refractory ITP, a definition to be defined

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We read with great interest the recent paper by Nakano et al,[1] "What is in a name: defining pediatric refractory ITP," published online on 27 September 2024, in which pediatric hematologists from the United States, Canada, Mexico, and France discuss the necessary framework for accurately defining children with symptomatic immune thrombocytopenia (ITP) who are challenging to treat.

In 2023, the Coagulation Disorder Working Group of the Pediatric Hematology-Oncology Italian Association published a consensus document,[2] aimed at updating previous Italian guidelines and providing recommendations to support pediatricians in the diagnostic workup and treatment of newly diagnosed children with ITP.

Regarding the definition of refractory ITP, we fully agree with the authors that the term is frequently applied to complex cases,[3] which may still be naive to certain treatments and may require a more comprehensive diagnostic evaluation to rule out secondary immune-mediated thrombocytopenias or other causes of thrombocytopenia.

The Italian consensus panel emphasized that the International Working Group criteria[4] for defining refractory ITP (lack of response to splenectomy) are unsuitable for newly diagnosed and persistent ITP in children, given the decline in splenectomy rates in pediatric ITP. Splenectomy is rarely indicated in pediatric ITP and should only be considered in children aged >5 years who have failed all available medical therapies, are experiencing thrombocytopenia-related bleeding, and are at risk of life-threatening complications or a significantly impaired health-related quality of life.

As a unified definition of "refractory" in ITP has yet to be established, the Italian panel reserved the term "refractory ITP" for pediatric patients with more severe and difficult-to-treat disease, specifically:

- Children with persistent, clinically significant active bleeding and consistently low platelet counts (no response according to International Working Group criteria) despite first-line treatments (ie, intravenous immunoglobulin and steroids) or rescue therapies (other immunosuppressive agents, thrombopoietin receptor agonists, or splenectomy);
- Children who are not entirely unresponsive to first-line treatments but require frequent therapeutic interventions to maintain a sustained clinical response, experiencing disease worsening and medication-induced toxicities.

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We believe that both our definition and the definition suggested by Nakano et al[1] clearly delineate a subset of pediatric patients with ITP with acutely symptomatic cases that may require prompt identification for expanded evaluation. This approach can also help define a group of children who should be considered for clinical trials to identify optimal or novel therapies and to deepen understanding of their disease biology.

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