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Thrombopoietin receptor agonists: ten years later

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Abstract

The two thrombopoietin receptor agonists (TPO-RA), eltrombopag and romiplostim, were licensed in the US for treatment of immune thrombocytopenia (ITP) in 2008 and, since then, their use has progressively increased around the world; they are currently used in more than 100 countries. The six largest randomized controlled trials conducted in ITP have used one of these two agents. All studies have demonstrated a platelet response rate between 50-90%, depending on the criteria used, with good safety and tolerability. TPO-RA were shown to be effective in reducing bleeding and the need for concomitant or rescue medication. Many other investigations of their mechanism of effect, prospective and retrospective trials, and studies focusing on toxicity have been performed widening our knowledge of these two agents. Initial concerns on issues such as myelofibrosis have not been confirmed. Only a small number of patients develop moderate-severe reticulin fibrosis and/or collagen fibrosis; however, these are usually reversed after discontinuation of TPO-RA. Studies indicate, however, that TPO-RA may increase the risk of venous thromboembolism. Both TPO-RA are currently approved in patients with chronic ITP aged >1-year who are refractory to at least one other treatment. Eltrombopag has acquired two additional indications: severe aplastic anemia refractory to first-line treatment and hepatitis C patients undergoing treatment with interferon-ribavirin. Despite these wide-ranging studies, important questions still need to be answered. This summary review on TPO-RA will summarize what is known regarding efficacy in ITP, evaluate safety concerns in more depth, and focus on the questions that remain.