



No. 40 – TPO-Like Drugs for Children and

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Title: **The Promise of TPO-Like Drugs for Children and Adolescents with ITP**

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In the last issue of *The Platelet* my colleague Dr. Jim George discussed advances in the development of so-called thrombopoietin (TPO)-like agents in ITP. Unlike other treatments, these drugs stimulate platelet production by a direct effect on the bone marrow cells which are the source of our platelets. TPO is the natural hormone in our body that regulates platelet production. Attempts to simply give the hormone itself to people with ITP were unsuccessful because of the development of antibodies against it, which paradoxically reduced rather than increased the platelet count. This problem does not occur with the new TPO-like drugs for ITP.

Two TPO-like agents have been approved for persons over 18 years of age, one of them (romiplostim) administered by injection under the skin once weekly and the other (eltrombopag) taken orally once daily. As Dr. George pointed out in the last issue of *The Platelet*, both of these agents raise the platelet count and reduce bleeding in most adults with severe refractory ITP. However, the drugs are costly, require continued treatment to maintain an increased platelet count (that is, the drugs don't "cure" ITP), and have potential adverse effects. Several other TPO-like agents are being developed and are currently under investigation.

So what about TPO-like agents in children, recalling that about one-third of all cases of ITP occur in infants, children, and adolescents? Consistent with the usual approach of studying benefits and side effects of new drugs in adults before testing them in children, romiplostim and eltrombopag have been evaluated in children only recently. In fact, the first published results of romiplostim appeared in the journal *Blood* just several months ago. I had the opportunity to be one of the primary investigators in the study, which included 22 patients with "refractory" ITP under age of 18 years. All but two of the 17 children receiving romiplostim responded nicely (while none of the 5 children receiving placebo responded), with platelets rising to over 50,000 per mm³. There were no unusual side effects experienced by these children. Three of my own patients with chronic ITP continue to receive the drug as part of a follow-up study and prefer it as an alternative to splenectomy. The next step is study of a much larger group of children to validate the initial favorable results with the aim of gaining licensing approval from the regulatory authorities. Initial studies of eltrombopag in children are still in progress and have not yet been published.

So what does all this mean for children with ITP? Well, it is an encouraging step in the right direction. However, the same limitations apply in children as in adults. This treatment is not a cure. TPO-like agents have side effects. Although the adverse effects appear to be mild and tolerable, there are uncertainties about long term use in young patients.

Most pediatric hematologists are quite positive about the use of TPO-like agents in selected children with ITP. One potential use for such medications would be in children with ITP and persistently low platelet counts that are not responsive to the initial drugs administered to raise the platelet count. For instance, a 5 year old child with sudden onset of ITP, worrisome bleeding, but no or minimal response to steroids or IVIG might possibly benefit from short term use of a TPO-like agent to increase the platelet count until the ITP resolves on its own (as is usually the case). This would be an example of limited temporary use of one of these drugs rather than the indefinite treatment as is nearly always the case now when they are used in adults with severe refractory ITP. This use of TPO-like agents has, of course, not yet been tested in clinical trials but could be something to explore in the future if current research continues to generate positive results.

In conclusion, the use TPO-like agents in children with ITP, although less well studied than in adult patients, appears promising but warrants additional careful study.