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Title: Immune Suppressive Therapy & ITP: Is There Still a Place for This in the Treatment of Chronic ITP? Professor Spero Cataland, M.D., Wexner Medical Center, Ohio State University

Without question, the development of the thrombopoietin receptor agonists (TPO agonists) for the treatment of chronic ITP represent one of the most significant advances in hematology in recent years. Eltrombopag (Promacta in the US; Revolade in the UK) is the oral TPO agonist that has been approved for the treatment of chronic ITP, and romiplostim (Nplate) is a similar agent that is given via subcutaneous injection. Both medications have been shown to increase the production of platelets and improve the platelet counts in the majority patients with chronic ITP who require treatment to prevent bleeding. Both agents are more effective and have fewer side effect than medicines that suppress the immune system (for example, cyclosporine, azathioprine, and mycophenolate) that were commonly used to treat chronic ITP before the TPO drugs became available. Therefore you might ask if there is still a role for medicines that suppress the immune system.

This exact question was raised by a patient that I have cared for with chronic ITP for more than 10 years. She had a splenectomy more than 25 years ago and then did very well for many years, not requiring any treatment of her ITP until recently. Her platelet count was stable in the 20-30 range and she had no bleeding symptoms. Over the past 2-3 years though her platelet count began to slowly drift down, to the range of 10-15. Her platelet count occasionally dropped to less than 10 with some bleeding symptoms, which required short courses of steroids. We began to discuss starting some continuing treatment and the discussion appropriately started with the TPO agents. She preferred an oral medicine over having to come to the clinic to receive the subcutaneous doses of romiplostim. Over the course of the next 1-2 weeks, she showed early signs of responding to eltrombopag, but unfortunately she had gastrointestinal upset that began after she started the eltrombopag. Stopping the eltrombopag for a short period of time followed by re-starting it confirmed that her symptoms were indeed caused by the eltrombopag. I discussed with her that switching to romiplostim might be the next rational step, but she was not thrilled with the idea of having to return to the clinic each week for the injection. She went on to ask, "Isn't there something else that I can take by mouth so that I do not have to come back to the clinic each week?" Her question caused me to think back to how we managed chronic ITP in the days before the TPO medicines were available. While the TPO medicines are more reliable and may have fewer side effects compared to some of the immune suppressive medicines, could they be considered reasonable options for her?

My patient's question led to a discussion about the use of azathioprine, cyclosporine, or mycophenolate mofetil to treat her ITP. I felt that there was enough experience to support their use, and that the potential side effects were acceptable. There are data that suggest approximately 30-40% of patients may respond to these medicines with an increase in their platelet count. After a discussion of the side effects of each agent, she decided on azathioprine. Over the next 4-6 weeks she was able to increase her platelet count and has continued azathioprine since that time – now for 10 months.

In general, I believe that the TPO medicines are superior to the immune suppressive medications. However, these immune suppressive medicines may still be reasonable options for many patients. Intolerable side effects and patient preference to avoid coming to the clinic for weekly injections have been reasons for some of the chronic ITP patients I care for to choose therapy with one of the immune suppressive medications. While not first choice for chronic ITP, these immune suppressive medicines are still useful for some patients to manage and control their chronic ITP.