

Poeitins Prepare Platelets For Lift-Off

By Margaret Ragni, MD

Today's Education Session on Thrombocytopenia (7:30 – 9:00 a.m. and 2:00 – 3:30 p.m.) features updates on management of ITP, HIT, and TTP, including the exciting new thrombopoietin agents that enhance platelet counts in antibody-mediated thrombocytopenia.

Diana Beardsley, MD, PhD, Yale University, will highlight the current approach to clinical management of ITP. Despite the lack of evidence-based studies to define clinical management of immune (idiopathic) thrombocytopenic purpura (ITP), a disorder characterized by platelet destruction caused by antiplatelet antibodies, practice guidelines have emerged. In general, although observation is appropriate for mild thrombocytopenia, the child with a platelet count below 10,000/uL and/or mucous membrane bleeding should receive treatment, although no single agent is recommended from among the initial options, including IVIG, anti-D, steroids, or a combination. For those with refractory ITP, a platelet count below 30,000/uL after six-to-12 months of treatment, new trials are in planning through the NHLBI-sponsored Transfusion Medicine Hemostasis Network (TMH CTN). Finally, recent advances to improve platelet production, which is suboptimal in over two-thirds of patients with ITP, are focused on stimulating thrombopoiesis with recombinant thrombopoietins. For upcoming presentations on the role of oral thrombopoietins in the management of ITP, be sure to catch abstract #475 by Bussell et al. on the oral platelet growth factors eltrombopag in ITP and abstract #477 by Desjardins et al. on the oral agent AKR-501 in normals.

Theodore Warkentin, MD, McMaster University, Ontario, next will provide information about inferential detection of HIT antibodies for early diagnosis of HIT, the major key along with early initiation of treatment, to prevent poor outcomes. Because the diagnostic criteria may be variable, depending on the initial platelet count and platelet recovery, "delayed-onset HIT" is increasingly being recognized. This refers to HIT that occurs after stopping heparin. Other atypical clinical scenarios include the patient whose thrombosis *precedes* thrombocytopenia, which may occur in up to 60 percent of those with HIT, or the patient who may develop thrombosis up to 30 days after heparin use, in the setting of a normal platelet count. In addition to the usual lepirudin and argatroban therapies for HIT, fondaparinux is uncommonly used for treatment despite its lack of cross-reactivity with HIT antibodies. Most importantly, stopping heparin alone is insufficient treatment of HIT. Since up to 50 percent may develop thrombosis, anticoagulation is essential and should be started even before HIT antibody results are available. Importantly, coumadin should be avoided until the platelet count returns to normal, because it may lead to microvascular thrombosis by impairing the protein C pathway. Vitamin K may reduce microvascular thrombosis in those receiving coumadin at the time of a HIT diagnosis. Finally, despite the problem of missing the diagnosis, HIT may actually be over-diagnosed as frequently as one of every two suspected patients. This may be avoided by using a cutoff ELISA platelet IgG absorbance above 1 unit for a diagnosis of HIT.

Evan Sadler, MD, PhD, Washington University, St. Louis, will close the session with a talk on TTP, attempting to consider several clinical problems in diagnosis and treatment. TTP is a thrombotic microangiopathy with low (<20 percent) ADAMTS13 activity. Up to one-third of patients treated with plasma exchange, the treatment of choice, show persistent ADAMTS13 antibodies despite clinical response. There are also patients with thrombosis and ADAMTS13 deficiency, but without signs of TTP, clouding the concept of ADAMTS13 as a true biomarker of disease. Moreover, ADAMTS13 does not appear to explain variations in treatment duration, relapse frequency or duration, or presence of microangiopathy. Despite these difficult issues as a biomarker of TTP disease activity, ADAMTS13 testing should be used when the clinical presentation is atypical or in the setting of microangiopathy such as in an autoimmune disease or with pregnancy, and to help identify refractory patients or those who might benefit from immunosuppression. Although the monoclonal antibody to CD20 on B cells, rituximab, shows promise in early TTP, not all patients respond, and thus plasma exchange is still considered first-line treatment. The TMH CTN will study whether combining rituxan with plasma exchange will result in better outcomes in idiopathic TTP, and whether persistent ADAMTS13 deficiency would benefit from prophylactic treatment.