The American Perspective: "Teaching a New Dog a New Trick"
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In recent years physicians and researchers in most fields of medicine have become increasingly specialized. Especially at university settings, physicians not only focus on one area of medicine (hematology, cardiology, etc), but also focus on one particular disease in their field of specialty. While this focus on one disease can be very productive and lead to many advances, to the outside observer it might appear to prevent people with different interests from communicating ideas and research projects. The annual American Society of Hematology (ASH) meeting will be held virtually in early December this year. Each year, hematologists from around the world get together to share information, ideas, and discuss research from within their specific field or disease of expertise. The exchange of ideas that will occur between different groups of researchers may focus on seemingly different and distinct diseases, but invariably this exchange leads to new ideas and studies that may apply to their own disease. These types of exchanges likely have contributed to the development of the three novel treatments for ITP that will be discussed in this essay that had their "start" in other diseases.

IgG antibodies bind to the platelets of ITP patients leading to their clearance and destruction, and the clinical picture of low platelet counts and bleeding that characterizes ITP. Efgartigimod (say that quickly three times) is a fragment of the human IgG antibody that binds to what is known as the FcRn receptor, leading to the premature clearance of the IgG antibodies that lead to ITP. Efgartigimod was originally studied in myasthenia gravis, another antibody-mediated disease like ITP, that can lead to severe muscle weakness. The thought behind the development of the drug is that treatment with efgartigimod will lead to lower levels of the anti-platelet IgG antibodies and improvements in the platelet count by decreasing the amount of anti-platelet antibodies that are present to degrade or clear platelets. Indeed, the initial studies of this drug have shown a rapid reduction of these antibodies does occur after treatment, and this drop in the antibodies was accompanied by increases in the platelet count. A larger, multicenter study is presently underway to study the effectiveness and safety of this treatment in chronic ITP.

There is a relatively new class of drugs called Bruton tyrosine kinase (BTK) inhibitors that have been approved for the treatment of different forms of chronic lymphocytic leukemia (CLL) and lymphomas. This class of drugs can lead to decreased survival of malignant B cells in patients with these conditions, but may also lead to a decrease in the B cells responsible for production of anti-platelet antibodies that target platelets in ITP. At this year's upcoming ASH meeting the results of a study of the oral medication rilzabrutinib will be presented. In this study of chronic ITP (many of which that had already failed prior ITP treatments), nearly half of patients showed an improvement in their platelet counts. While further study is needed with rilzabrutinib and other similar medications, there is hope that this medication may soon be able to help patients with chronic ITP.

The complement system is part of our normal immune system that helps to protect us from infection, inflammation, and other threat to our bodies. There are three different

components of the complement system that are activated in different ways and for different reasons. These include the classical pathway, the lectin pathway, and the alternative pathway. Impaired function in any one of these components can be associated with several diseases, and there are different treatments targeted to each specific pathway. In the specific case of ITP, there has been evidence for the activation of the classical pathway of complement by platelet antibodies contributing to the destruction of platelets. Sutimlimab is an antibody that targets C1s, one of the proteins involved in the classical pathway of complement. This medication has been shown to be an effective treatment of a rare blood disease called cold agglutinin disease that leads to the immune destruction of red cells by the same classical complement pathway. At last year's annual ASH meeting sutimlimab was reported to lead to a sustained increase in the platelet count in patients with chronic ITP patients that had failed at least two prior therapies. This study provided evidence for an additional mechanism of destruction of platelets in ITP, and provides hope for new treatment options for those patients that have not responded to prior therapies for chronic ITP.

The upcoming 62nd Annual Meeting of the American Society of Hematology will without question be different this year due to the ongoing pandemic. However, the exchange of ideas among researchers that is the most important part of the meeting will remain the same. It will just happen on a computer, an in a colder climate for many of us who look forward to the locations of this meeting and a little bit of sun each December.