Immunomodulation and ITP. Outlook.

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Anti-CD20 agents and thrombopoietin-receptor (TPO-r) mimetics are very effective treatments for immune thrombocytopenia (ITP) and have deeply modified the therapeutic strategy. However, there are still unmet needs and challenges. Concerning rituximab, the main limitation of the treatment except the absence of license is its modest long-term efficacy, with a remission rate at 5 years of only 20% in adults. Maintenance treatment or association with other immunomodulatory drugs such as dexamethasone and ciclosporine may achieve better long-term response. For TPO-r agonists (i.e., romiplostim and eltrombopag), several groups demonstrated that in case of failure of one of the available, another can be used. Switching may be beneficial, with more than 50% chance of response, and could limit the risk of platelet fluctuation occasionally observed with these treatments. In theory, according to the mechanism of action of TPO-r agonists, a rapid relapse of thrombocytopenia should be observed after they are stopped. Several recent studies suggested sustained responses in patients achieving complete response with TPO-r agonists and who stopped the treatments. Sustained response could be related to a restoration of the number and function of T-regulatory lymphocytes. Mechanisms of failure of TPO-r agonists are not well understood. It has been suggested that in case of failure, eltrombopag could stimulate megacaryocyte proliferation and maturation but had no effect on the final steps of platelet production and release. In this situation, adding immunosuppressive drugs such as azathioprine could overcome resistance to TPO-r agonists. Thrombosis in ITP is a concern, particularly with TPO-r agonists, even though the pivotal studies of eltrombopag and romiplostim did not report a higher incidence of thrombosis events with TPO-r agonists than placebo. Despite these reassuring data, the risk of thrombosis with TPO-r agonists remains unanswered. Other unmet needs in ITP is the absence of strong predictive factors for chronic evolution in patient with newly diagnosed ITP and for response to treatments such as rituximab and splenectomy. Finding strong predictive factors for individual decision should be an important topic of research for near future.