

# Management of Adult Patients with Primary Immune Thrombocytopenia (ITP) in Clinical Practice: A Consensus Approach of the Spanish ITP Expert Group, Comment about Thrombopoietin Analogs

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## DESCRIPTION

Different scientific societies and expert groups have developed guidelines and consensus documents with recommendations for the diagnosis and treatment of adult patients with ITP [1-4]. However, agreement between recommendations and their application in real clinical practice continues to be insufficient [5,6]. There are clinically relevant aspects in the current practice scenarios not included in guidelines, for which expert consensus could be useful. Many of them are related to the use of Thrombopoietin Analogs (TPO-RA). There is no clear evidence about their early use in persistent ITP, TPO-RA tapering, the convenience of switching to a different TPO-RA drug in the event of previous TPO-RA failure, the possibility of using these agents in the context of surgery, secondary ITP, or in combination with immunosuppressant drugs in multi-refractory patients. To help with these questions, Delphi methodology could be an option to describe expert opinion in situations without clear scientific evidence to take decisions [7-10].

Regarding to the use of TPO-RA in persistent ITP, Spanish and Italian [7,8]. Delphi, clearly describe how they agree in the early use of TPO-RA as a way to improve the chance of achieving partial or complete response and better quality of life [8]. The most common second line treatment option are TPO-RA for close to 90% of physicians [5-7], starting in persistent ITP, without waiting 6 to 12 months to start. This looks like a routine clinical practice only suggested by guidelines [1-4]. There are two studies evaluating the use of TPO-RA in newly diagnosed and persistent ITP with results of sustained remission close to 30%-54% [11,12] better results than the ones found in chronic ITP.

Other important question is related to TPO-RA tapering. There is no solid evidence about when, how and in which patient tapering could be done. All the Delphi consensus published, agree on reduce dose of TPO-RA in patients with a stable response and platelet count  $>100 \times 10^9/L$  maintained for at least 6 months in the absence of concomitant treatments [7,8].

Cooper, et al. [9], suggest tapering if platelets  $>50 \times 10^9/L$  in more than 75% of controls for 6 to 12 months. This other option is only considered for about 54% of Italian and Spanish experts [7,8]. On the other hand, they do not recommend tapering if there is a history of severe, life-threatening bleeding and no effective rapid rescue therapy, history of large fluctuations in platelet count, the presence of comorbidities that increase bleeding risk, concomitant use of anticoagulant or antiplatelet medications, and a history of rapid relapse after dose reduction [9,10]. Continuing on a minimum dose or applying a step-wise titration over a longer period may be an appropriate tapering strategy for patients with fluctuating responses to treatment or in patients in whom responses to dose reductions need to be monitored relatively frequently. The ITP experts believe this will reduce the risk of withdrawal effects and maintain stability for the patient [7-10]. Their no clear schemes of tapering and predictors of sustained response in this setting remain unclear.

Other relevant topics like switching between TPO-RA, concomitant use with immunosuppressive drugs to get better sustain remission or to rescue refractory patients and finally the use of TPO-RA for surgery. Only Mingot-Castellano, et al. have reviewed these topics in their Delphi project [7]. In case of treatment failure with a TPO-RA, 90% of hematologist considers to switch to another TPO-RA. We know this can be effective between 33%-59% of patients [13]. Despite of this, 40% of specialists use the combination of immunosuppressive drugs and TPO-RA in multi refractory patients. Regarding to combination therapy, there are case reports and a retrospective series of Mahévas, et al. [14]. with a favorable response in 70% of patients. In Spanish Delphi, 62% of hematologists consider the use of TPO-RA to prepare ITP patients for surgery to maintain platelets level in absence of steroids toxicity in this situation. There are only few reference and case reports with regard of the use of TPO-RA in surgery [15].

Delphi method allowed exploring systematically the management of adult patients with ITP based on the qualified

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opinion of physicians routinely treating these patients. Delphi survey study conducted in expertise hematologists may offer a framework of the real management of adult patients with ITP in clinical practice and they could design the new lines of investigation to be explored to answer real clinical practice necessities. With regard to TPO-RA, highlighted areas where further studies are needed, are tapering in patients with response, the potential benefits of early treatment, how to switch between them or the usefulness of their combination with immune suppressive drugs. Long-term prospective studies are warranted to determine whether this approach is indeed optimal, and predictive markers are needed to identify patients with ITP who may successfully stop TPO-RA treatment.

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