European Delphi panel to build consensus on the tapering and discontinuation of thrombopoietin receptor agonists in immune thrombocytopenia

Barlassina A[1], Cooper N[2], González-López TJ[3], Somenzi O[4], Zaja F[5–6]

[1]OPEN Health Evidence & Access; [2]Imperial College London; [3]Hospital Universitario de Burgos; [4]Novartis Pharmaceuticals; [5]Dipartimento Clinico di Scienze Mediche, Chirurgiche e della Salute, Università degli Studi di Trieste; [6]UCO Ematologia, Azienda Sanitaria Universitaria Giuliano Isontina

INTRODUCTION

- Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder characterized by accelerated platelet destruction and inadequate platelet production.[1,2]
- Thrombopoietin receptor agonists (TPO-RAs), such as eltrombopag, avatrombopag, and romiplostim, have been shown to induce proliferation and differentiation of megakaryocytes, thereby improving patients' platelet count and preventing severe bleedings.[3]
- Evidence indicates that up to 30% of patients receiving romiplostim or eltrombopag maintain a sustained response for months after treatment is discontinued.[4,5]
- To date, randomized studies on the tapering and discontinuation of TPO-RAs are lacking.
- A three-round Delphi panel was held to gain expert consensus on tapering and discontinuation of TPO-RAs among European experts.

OBJECTIVES

1. To develop consensus among European experts on clinical practices for tapering and discontinuing TPO-RAs.
2. To identify knowledge gaps and clinical practice discrepancies in tapering and discontinuing TPO-RAs to highlight areas where further evidence-based research is needed.

METHODS

- A 3-step Delphi panel was conducted (Figure 1). The survey's statements were developed from a literature review and input from a Steering Committee (SC) of three experienced haematologists.
- Thirteen haematologists with at least two years of experience working with patients with ITP and/or at least one scientific publication in this disease area were invited to participate in the Delphi panel (target sample size of 12 KOLs[6]).
- The first round of the Delphi panel was carried out via one-to-one video-conference interview and the subsequent two rounds via electronic surveys.
- Several analysis rules determined whether a statement could progress to the next round and specified the level of agreement required to achieve consensus or dissensus (Figure 2).
- Measures of central tendency (mode, mean) and variability (interquartile range) were reported back to help panellists look at their previous responses considering the overall group responses.

Figure 1. Delphi panel framework

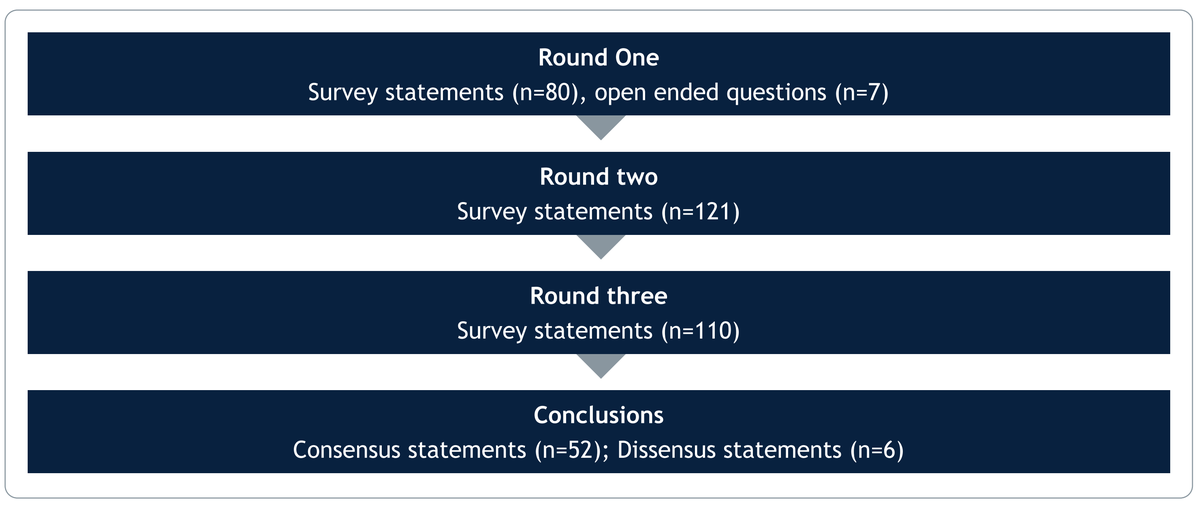
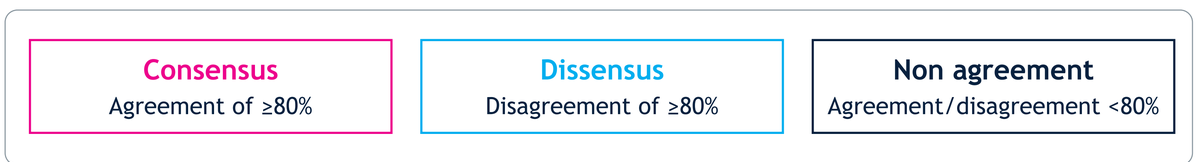


Figure 2. Consensus/dissensus rules



RESULTS

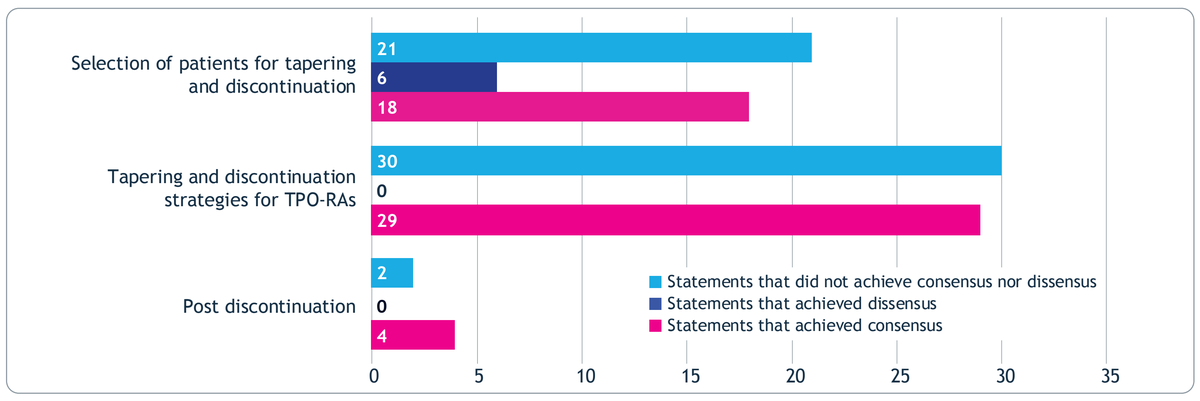
Panel composition

- The panel was composed of 12 HCPs from nine European countries (Belgium, Czech Republic; France, Germany, Norway, Spain, Slovenia, Switzerland, the United Kingdom).

Survey results

- A total of 52 statements of the 121 (43%) achieved consensus, and six statements achieved dissensus (Figure 3).

Figure 3. Number of statements that achieved and did not achieve consensus/dissensus at Round 3



Selection of patients for tapering and discontinuation

- The panel agreed on several criteria for the selection of patients for tapering and discontinuing TPO-RAs and recognized the importance of their involvement in the decision-making process (Figure 4).

Figure 4. Patients eligibility criteria for tapering and discontinuation of TPO-RAs

- **Clinically stable**
- **Platelet count >100 × 10^9 /L**
- **Time on TPO-RAs treatment: >6 months**
- **Lifestyle that does not expose them to physical risks**
- **Motivated to attempt discontinuation**

Tapering and discontinuation strategies

- Several tapering regimens for TPO-RAs and schedules for patient monitoring achieved consensus and differ slightly compared to previously agreed ones (Table 1).[7,8]
- Monitoring intervals during tapering should not be longer than 4 weeks.

Table 1. Tapering regimens that achieved consensus for eltrombopag and romiplostim

Eltrombopag	Romiplostim
Taper the dose of eltrombopag by 25 mg every 2 weeks down to a minimum dose of 25 mg. Administer 25 mg every other day for 2 weeks, then discontinue.	Taper the dose of romiplostim of 1 mcg/kg/week every 2 weeks until a dose of 1 mcg/kg/week is reached and: (*Regimen 1*) administer a 1 mcg/kg dose once every other week before discontinuing treatment. (*Regimen 2*) administer 1 mcg/kg dose every other week for 2 or 3 administrations, before discontinuing treatment. (*Regimen 3*) taper down until a dose of 0.5mcg/kg/week is reached, then discontinue.

Post discontinuation

- In alignment with available evidence, the panel could not determine whether disease duration, treatment history, or patient's age can predict sustained response off treatment after TPO-RA discontinuation.[4,5,9]
- Panellists were not aligned on the percentage of patients who successfully discontinue a TPO-RA and achieve a sustained response off treatment. Prospective and/or real-world evidence studies with large data sets should robustly provide clinical evidence on the rate of successful discontinuation.

CONCLUSIONS

- To our knowledge, this is the first study that presents the aggregated consensus of experts across multiple European countries on tapering and discontinuing TPO-RAs.
- The findings echo those of previous consensus studies on several patients' characteristics that play a role in the decision to taper and discontinue TPO-RAs.
- Also aligned with recommendations from previous studies is the panel's recognition of the importance of the patient's motivation to discontinue, which calls for further patient-centered research to understand patients' perspective on tapering and discontinuing.
- Key knowledge gaps include: (1) the role of several patient characteristics in deciding to taper and discontinue (incl., age, vaccinations status, TPO-RA dose required to maintain a response); (2) schedule for monitoring patients during tapering and after discontinuation; (3) predictors of successful discontinuation; and (4) overall rates of successful discontinuation.
- The persistence of knowledge gaps and discrepancies in clinical practices identified by this Delphi panel highlights the need to conduct prospective, real-world evidence studies to develop guidelines that can provide the basis for a pan-European, evidence-based approach to tapering and discontinuing TPO-RAs.

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DISCLOSURES

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