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Insights from EHA and ISTH 2024: How can we optimize care for patients with chronic ITP?

Practice aid for ITP

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How does ITP impact the patient and their HRQoL?

Fatigue

Unmet medical need

- Fatigue **affects HRQoL** and has significant **socioeconomic consequences**[1]
- Fatigue affects 22–45% of patients with ITP[2]
- Causes not fully understood[1]

Monitoring

- Check fatigue is not caused by:[3]
  - **Low iron**
  - **Thyroid function problems**
  - **Depression**
- PRO tool: **FACIT-F** questionnaire[1]

Management[3]

- **Support** from ITP patient groups
- **Psychosocial support** includes:
  - Regular **exercise**
  - **Healthy eating**
  - **Reducing stress**
  - Balancing **home-work-life**
  - Talking to **family/friends**

Venous thromboses

Unmet medical need

- Adults with ITP have **greater risk of TE** vs general population[4]
- Estimated VT incidence in ITP population: **0.41–0.67 per 100 person-years**[5]

Monitoring[5]

- **Monitor platelet count**
- Thrombotic **risk factors** include:
  - **Older age**
  - **Secondary ITP**
  - **Multiple prior ITP therapies**
  - **Use of TPO-RAs**

Management

- **No standard treatment guidelines**[5]
- **Treatments** include:[4]
  - **Antithrombotics** e.g. warfarin, LMWH, DOAC
  - **Anticoagulants + antiplatelet**

Heavy menstrual bleeding

Unmet medical need

- ITP may cause **HMB**, which can **impact QoL**[6]
- Estimated **prevalence of HMB** in patients with ITP is 6–55% at **diagnosis** and 17–79% **during disease**[6]
- **HMB may cause iron deficiency or IDA**[6]

Monitoring[6]

- **Clinical criteria** can include**:** cycle of ≥7 days; changing protection at least every 2 hrs or at night; clots; iron deficiency; impacting social participation
- PRO tools: **PBAC, ITP-PAQ, MMAS**

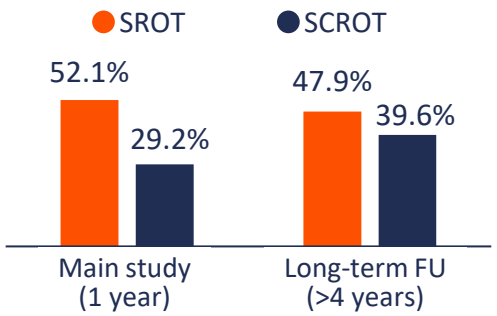
Management

- **Limited options that do not permanently impair fertility:**
  - Antifibrinolytics ± hormonal therapy
- **Options that permanently impair fertility:**
  - Endometrial ablation; hysterectomy[6]
- **Iron supplementation** for iron deficiency/IDA[7]

What are the latest data that inform the use of current treatments for chronic ITP?

Long-term follow-up of the STOPAGO study in persistent/chronic primary ITP (N=48)[18]

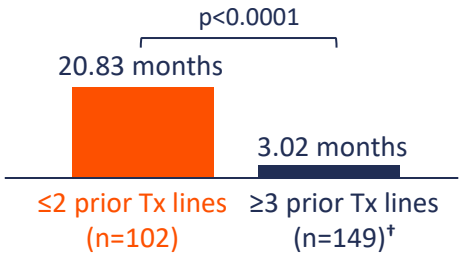
Clinical response after TPO-RA discontinuation



~50% of patients maintained SROT for >4 years after TPO-RA discontinuation

Outcome of splenectomy after the year 2000 in patients with refractory ITP from the UK ITP Registry[20]

Median time to first treatment post-splenectomy*



Probability of splenectomy inducing sustained remission in refractory patients with ITP is considerably lower vs non-refractory patients

First line

Corticosteroids[8]
IVIg / Anti-D Ig[8,9]

Second line onwards

TPO-RAs
Eltrombopag[8,9,10,11]
Romiplostim[8,9,12,13]
Avatrombopag[8,9,14,15]

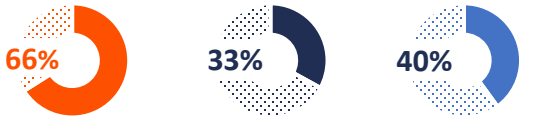
Anti-CD20
Rituximab (*off label*)[8,9]

SYK inhibitor
Fostamatinib[9,16,17]

Other immunosuppresants[8,9]

Splenectomy[8,9]

Italian real-world experience with fostamatinib in adult patients with refractory symptomatic chronic ITP[19]



Overall response within 3 months | **Complete response‡** | **Still receiving Tx at 6 months**

59 **side effects** reported in 38 patients (31 treatment related); most common were: **diarrhoea** (n=13), **hypertension** (n=8), **transaminitis** (n=8), **neutropenia** (n=4)

Data suggest fostamatinib is an effective therapeutic option in real-world practice with an acceptable safety profile

*Median time to first treatment post-splenectomy was a surrogate marker of splenectomy failure.
†Refractory ITP defined as having received ≥3 lines of therapy.
‡According to International Working Group criteria.

What data are there for emerging chronic ITP treatments?

~1 in 5 patients with ITP fail to achieve a platelet count >50 x 10^9/L after treatment with available therapies or may encounter loss of response or intolerance. A significant disease burden remains with an unmet medical need to find a well-tolerated, targeted disease-modifying therapy[21]

	Sovleplenib	Rilzabrutinib	Avatrombopag (paediatric use)	Mezagitamab
Treatment and MoA	SYK inhibitor[22]	BTK inhibitor[23]	TPO-RA[25]	CD38 inhibitor[21]
Phase	Phase III	Phase II	Phase III	Phase II
Treatment arms	Randomized 2:1 sovleplenib (n=126) vs placebo (n=62) 300 mg QD	Rilzabrutinib (N=71) 400 mg BID	Randomized 3:1 avatrombopag (n=54) vs placebo (n=21) 10 or 20 mg QD (age dependent)	Randomized mezagitamab (n=28) vs placebo (n=13) 100, 300 or 600 mg QW
Key efficacy results	**DRR:** 48% vs 0% (p<0.0001)* **ORR** (all p<0.0001) • **≥1 PC ≥50 x 10^9/L:** 71% vs 16%† • **Two consecutive PCs ≥30 x 10^9/L and double from BL:** 73% vs 6% • **PC ≥30 x 10^9/L and increased ≥20 x 10^9/L from BL:** 75% vs 22%‡	**Pooled outcomes[23]** • **Durable response:** 28%§ • **Overall response:** 41%‖ • **Complete response:** 35%¶ **Long-term outcomes[24]** • n=8/17 discontinued ≥1 or↓ concomitant ITP therapy • Visits reaching median PC of ≥50 x 10^9/L: 90%	• **DPR:** 27.8% vs 0% of patients (p=0.0077)** • **PR:** 81.5% vs 0% of patients (p<0.0001)*† • **PC ≥50 x 10^9/L:** 48.9% vs 1.2% of weeks (p<0.0001)*‡ • **PC ≥50 and ≤150 x 10^9/L:** 29.2% vs 1.2% of weeks (p<0.0001)*‡	**Mezagitamab 100/300/600 mg vs placebo** • **PR:** 66.7/62.5/90.9% vs 23.1%*§ • **Complete PR:** 55.6/50.0/81.8% vs 0%*‖ • **Clinically meaningful PR:** 66.7/75.0/90.9% vs 30.8%*¶ • **Haemostatic PR:** 40.0/25.0/100% vs 0%***
Key safety results	**TEAEs: 99% vs 85%** **Grade 3/4 TEAEs: 25% vs 24%** **Most common TEAEs:** URTI, COVID-19, ↑ blood LDH **GI toxicities**: Nausea 1.6% vs 3.2%; vomiting 1.6% vs 1.6%; diarrhoea 1.6% vs 0% **Thromboembolic events:** 0%	**All AEs:** 86%[23] (LT data: 81%)[24] **TRAEs:** 61%[23] (LT data: 41%)[24] **Grade ≥3 AEs:** 17% (all TRAEs grade 1/2)[23] **Most common TRAEs:** Diarrhoea; nausea; headache; fatigue; vomiting[23] **Thromboembolic events:** 0%[23,24]	**TEAEs:** 92.6% vs 76.2% **TRAEs:** 13.0% vs 4.8% **Most common TEAEs:** Petechiae; epistaxis; bruising; headache **Thromboembolic events:** 0%	**TEAEs:** 67.9% vs 69.2% **TRAEs:** 32.1% vs 38.5% **Grade ≥3 TEAEs:** 17.9% vs 23.1%

*PCs ≥50 x 10^9/L at 4–6 visits during 14–24 weeks, not impacted by rescue treatment. †Not impacted by rescue treatment. ‡For patients with a PC <15 x 10^9/L at BL. §≥8 of the last 12 PCs ≥50 x 10^9/L. ‖≥2 consecutive PCs ≥50 x 10^9/L and increased ≥20 x 10^9/L from BL. ¶PCs ≥100 x 10^9/L. **PC ≥50 x 10^9/L in ≥6 of the last 8 weeks of the core phase in absence of rescue therapy. *†≥2 consecutive PC ≥50 × 10^9/L in 12-week core phase in the absence of rescue therapy. *‡During 12-week core phase in absence of rescue therapy. *§PC ≥50 x 10^9/L and ≥20 x 10^9/L above BL on ≥2 visits. *‖PC ≥100 x 10^9/L on ≥2 visits. *¶PC ≥20 x 10^9/L above BL on ≥2 visits. ***PC ≥30 x 10^9/L and ≥20 x 10^9/L above BL on ≥2 visits.

Abbreviations and references

Abbreviations

AE, adverse event; BID, twice daily; BL, baseline; BTK, bruton tyrosine kinase; CD, cluster of differentiation; DOAC, direct oral anticoagulant; DPR, durable PR; DRR, durable response rate; EHA, European Hematology Association; EMA, European Medicines Agency; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FDA, United States Food and Drug Administration; FU, follow-up; GI, gastrointestinal; HMB, heavy menstrual bleeding; HRQoL; health-related QoL; IDA, iron deficient anaemia; Ig, immunoglobulin; ISTH, International Society on Thrombosis and Haemostasis; ITP, immune thrombocytopenia; IVIg, intravenous Ig; LDH, lactate dehydrogenase; LMWH, low molecular weight heparin; LT, long term; MoA, mechanism of action; MMAS, menorrhagia multi-attribute scale; ORR, overall response rate; PAQ, Patient Assessment Questionnaire; PBAC, pictorial blood loss assessment chart; PC, platelet count; PR, platelet response; PRO, patient-reported outcome; QD, once daily; QoL, quality of life; QW, once weekly; SCROT, sustained complete response off treatment; SROT, sustained response off treatment; SYK, spleen tyrosine kinase; TE, thromboembolism; TEAE, treatment-emergent AE; TPO-RA, thrombopoietin receptor agonist; TRAE, treatment-related AE; Tx, treatment; URTI, upper respiratory tract infection; VT, venous thrombosis.

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