What's new in primary ITP? Key updates from ASH 2024

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Agenda

- How is ITP managed today?
- New treatments for ITP
- The real-world impact of ITP

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How ITP is managed today

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There are several efficacious treatments for ITP[1,2]

Initial therapies

- **Corticosteroids**[2,3]
- IVIg[3]
- Anti-D Ig[3]

Second line onwards[2–4]

- **TPO-RAs**
  - Eltrombopag
  - Romiplostim
  - Avatrombopag
- **Anti-CD20**
  - Rituximab (off label)
- **Syk inhibitor**
  - Fostamatinib
- **Splenectomy**

There are limited options for patients who are refractory/intolerant to standard therapies[1]

CD, cluster of differentiation; Ig, immunoglobulin; ITP, immune thrombocytopenia; IVIg, intravenous Ig; Syk, spleen tyrosine kinase; TPO-RA, thrombopoietin receptor agonist.

1. Al-Samkari H. *Am J Hematol*. 2024;99:2178–90; 2. Neunert C, et al. *Blood Adv*. 2019:3:3829–66; 3. Provan D, et al. *Blood Adv*. 2019;3:3780–817;
4. Prescribing information. Available at www.accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed 8 November 2024).

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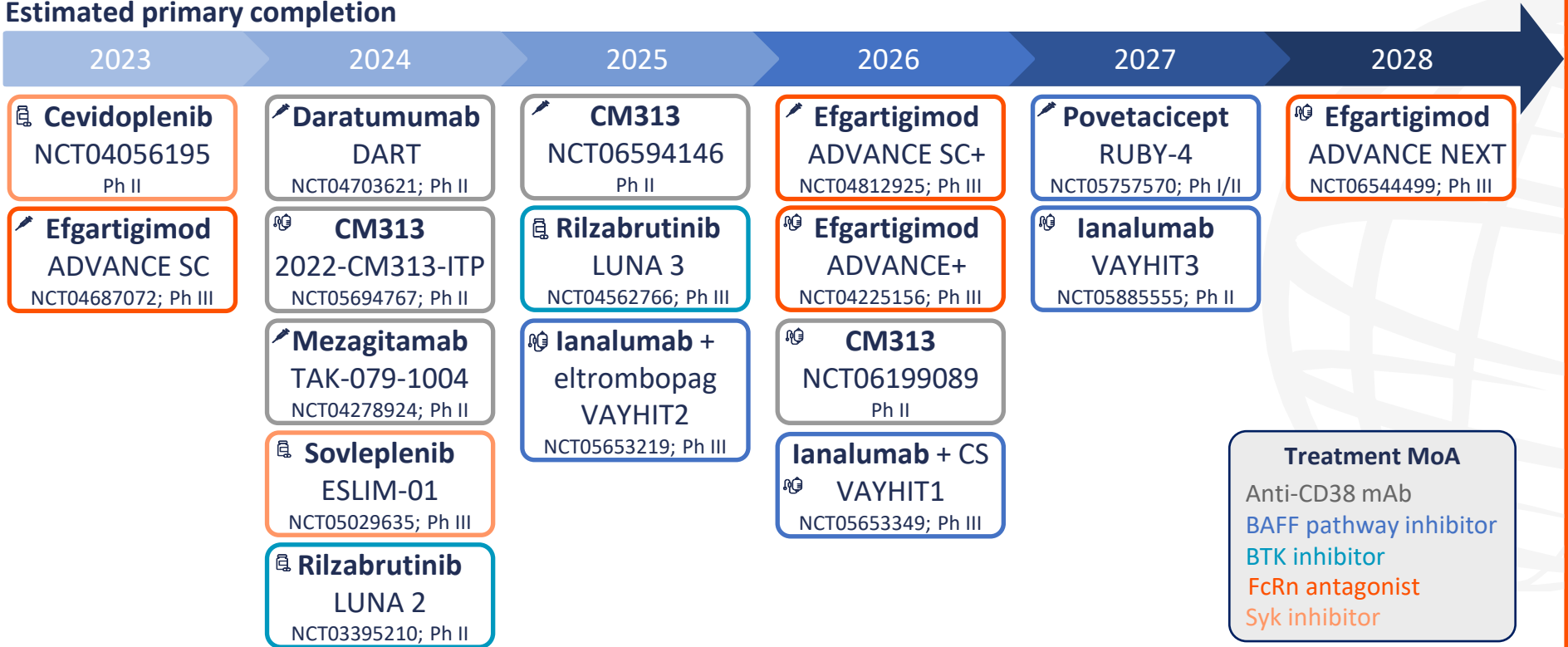
New treatments for ITP

Phase II/III emerging agents for ITP

Estimated primary completion



Trial completion dates are estimates reported by ClinicalTrials.gov. BAFF, B-cell activating factor; BTK, Bruton's tyrosine kinase; CD, cluster of differentiation; CS, corticosteroids; ITP, immune thrombocytopenia; mAb, monoclonal antibody; MoA, mechanism of action; Ph, phase; Syk, spleen tyrosine kinase.

Information on all clinical trials can be found using the NCT number at clinicaltrials.gov (accessed 20 November 2024). Al-Samkari H. *Am J Hematol*. 2024;99:2178–90.

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ASH data: Phase III RCTs in adults

Rilzabrutinib vs placebo (LUNA 3)[1]

Patients with primary persistent/chronic ITP
(data cut-off: 14 March 2024)

	R (n=133)	P (n=69)	
Primary endpoint Durable response*	23%	0%	p<0.0001
Median time to initial platelet response†	15 days	50 days	
Duration of platelet response†	Longer with R vs P		p<0.0001
Rescue therapy required	Lower with R vs P		p=0.0007
Physical fatigue at week 13 and week 25	Improved with R vs P		
AEs and SAEs	Similar		

Rilzabrutinib treatment was efficacious and tolerable

Long-term sovleplenib vs crossover from placebo (P-Sov) (ESLIM-01 extension stage)[2]

Patients with primary ITP who completed 24 weeks of treatment, or did not respond in first 12 weeks of ESLIM-01
(data cut-off: 31 January 2024)

	All sov (N=179)	P-Sov (n=53)
Overall response‡	81.0%	83.0%
Durable response§	51.4%	43.4%
Long-term durable response¶	59.8%	64.2%
Received rescue therapy	22.9%	18.9%
Most common TRAEs (≥gr 3):		
↑ ALT	2.2%	
↓ neutrophil count	1.7%	
↑ GGT	1.7%	

Long-term sovleplenib treatment was effective in increasing and maintaining PCs with a well-tolerated safety profile

Direct comparisons between trials should not be made due to differences in trial design.

*PC ≥50 x 10^9/L for ≥two-thirds of ≥8 of the last 12 weeks of the 24-week blinded treatment period in the absence of rescue medication; †platelet response: PC ≥50 x 10^9/L or ≥30–<50 x 10^9/L and >2 x BL; ‡≥1 PC ≥50 x 10^9/L with Sov not impacted by rescue treatment; §PC ≥50 x10^9/L at ≥4 of 6 scheduled visits during weeks 14–24 in ESLIM-01 not impacted by rescue treatment, or PC ≥50 x10^9/L at 2 of 3 protocol-defined visits during the second 12 weeks of 24 weeks in the open-label sub-study not impacted by rescue treatment; ¶after receiving Sov for 12 weeks, PC ≥50 x 10^9/L at ≥2 of 3 of any 12-week consecutive protocol defined visits not impacted by rescue treatment. AE, adverse event; ALT, alanine aminotransferase; ASH, American Society of Hematology; BL, baseline; GGT, gamma-glutamyltransferase; gr, grade; ITP, immune thrombocytopenia; P, placebo; P-Sov, received P followed by Sov; PC, platelet count; R, rilzabrutinib; RCT, randomized controlled trial; SAE, serious AE; Sov, sovleplenib; TRAE, treatment-related AE.

1. Kuter DJ, et al. Abstr 5; 2. Hu Y, et al. Abstr 2558. All data presented at: 66th ASH Annual Meeting and Exposition, 7–10 December 2024, San Diego, CA, USA.

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ASH data: Phase II RCT in adults

Ianalumab (VAYHIT3)

Patients with primary ITP previously treated with at least a CS and a TPO-RA, with no prior splenectomy, and a PC <30 x 10^9/L (data cut-off: 12 June 2024; N=10)

Patient characteristics: median no. of prior treatment lines 6.5 (CS and TPO-RAs 100%; IVIg/anti-D Ig 90%; rituximab 40%; other immunosuppressants 60%)

Primary endpoint ConfR*	n=5	(n=4 received ianalumab + TPO-RA; n=1 ianalumab monotherapy)
Achieved ConfR* and stable response†	n=4	
Median best post-BL PC, x 10^9/L	129.0	
Patients experiencing AEs / grade ≥3 AEs	n=10 / n=3	
Patients experiencing SAEs / grade ≥3 SAEs	n=2 / n=2	
AEs	Infections (n=6); potential signs of IRRs (n=4)	

These first data demonstrated that a short course of ianalumab shows promising efficacy in heavily pre-treated patients with primary ITP, and is well tolerated

*PC ≥50 x 10^9/L at two or more consecutive assessments at least 7 days apart between week 1 and week 25, in the absence of rescue treatment for ≥4 weeks prior to PC assessment and start of new ITP treatment before reaching a ConfR; †proportion of patients with ≥75% PCs collected between study days 121 and 183 ≥50 x 10^9/L in the absence of rescue treatment/new ITP treatment. AE, adverse event; ASH, American Society of Hematology; BL, baseline; ConfR, confirmed response; CS, corticosteroid; Ig, immunoglobulin; IRR, infusion-related reaction; ITP, immune thrombocytopenia; IVIg, intravenous Ig; PC, platelet count; RCT, randomized controlled trial; SAE, serious AE; TPO-RA, thrombopoietin receptor agonist. Kuter DJ, et al. Presented at: 66th ASH Annual Meeting and Exposition, 7–10 December 2024, San Diego, CA, USA. Abstr 710.

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ASH data: Phase III RCT in children

Avatrombopag vs placebo (AVA-PED-301)

Children aged 1–17 years with primary ITP ≥6 months with mean of two PCs <30 x 10^9/L with no single PC >35 x 10^9/L

	A (n=54)	P (n=21)	
Achieved CMR*	92.6%	19.1%	
Mean % of time with CMR	62.5%	16.7%	
Achieved CMR* in the final 3–7 out of 8 weeks of core phase	31.5–83.3%	0%	p<0.0001 for 3–6/8 weeks; p=0.0019 for 7/8 weeks
Achieved R† at any time in core phase	88.9%	9.5%	
Mean % of time with R†	51.0%	8.1%	
Achieved R† in the final 3–6 out of 8 weeks of core phase	13.0–75.9%	0%	p<0.0001 for 3 and 4/8 weeks; p=0.0002 for 5/8 weeks; p=0.0077 for 6/8 weeks

Avatrombopag demonstrated a significant and consistent durable response during the core phase regardless of how the response was measured

*PC ≥30 x 10^9/L; †PC ≥50 x 10^9/L. A, avatrombopag; ASH, American Society of Hematology; CMR, clinically meaningful response; ITP, immune thrombocytopenia; P, placebo; PC, platelet count; R, platelet response; RCT, randomized controlled trial.

Grace RF, et al. Presented at: 66th ASH Annual Meeting and Exposition, 7–10 December 2024, San Diego, CA, USA. Abstr 1191.

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The real-world impact of ITP

ITP can have a large burden on patient HRQoL[1]

Symptomatic bleeding affects **60–70%** of patients with **chronic ITP** and **70–80%** of patients with **newly diagnosed ITP**[2]

Patients may have **concerns over the risk of bleeding**[3] and **may have to alter their lifestyles** to reduce bleeding risk[2]

Heavy menstrual bleeding is common in female patients with ITP and **often impacts daily life**[4]

Patients can experience **fatigue and cognitive impairment** that can **decrease participation in activities and work**[1,5]

ITP **impacts** patients' **psychological** and **emotional wellbeing**[1,6]

Adults living with chronic ITP have an **increased risk of thrombosis and thromboembolism** compared with the general population[7,8]

Platelet count does not fully correlate with disease burden[9]

HRQoL, health-related quality of life; ITP, immune thrombocytopenia.

1. Cooper N et al. *Am J Hematol*. 2021;96:199–207; 2. Matzdorff A, et al. *Oncol Res Treat*. 2018;41:1–30; 3. Kruse C, et al. *Ann Blood*. 2021;6:9;
4. van Dijk WEM, et al. *Br J Haematol*. 2022;198:753–64; 5. Kuter DJ, et al. *Br J Haematol*. 2024;205:291–9; 5. Kruse A, et al. *Blood*. 2019;134(Suppl. 1):2362;
7. Wang L, et al. *Blood*. 2022;140(Suppl. 1):55–6; 8. Saldanha A, et al. *Thrombosis Research*. 2024;241:109109; 9. Maitland H, et al. *Hematology*. 2024;29:2375177.

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