Boosting Platelets:

Expert Approaches to Adult Immune Thrombocytopenia (ITP)

Saturday 14 June 2025: 8:00am – 9:30am

NP-41521 | June 2025

Disclosures

- This non-promotional symposium is initiated, organised, and sponsored by Sobi
- This symposium contains information about Sobi products. The information is intended for healthcare professionals attending the EHA2025 Congress only, and the content has been developed for an EU audience in Europe
- All opinions expressed reflect the views of the faculty and not those of Sobi

Disclaimer

- Avatrombopag is indicated for the treatment of severe thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo an invasive procedure

- Avatrombopag is indicated for the treatment of primary chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins)

Sobi Ltd. DOPTELET (avatrombopag). Summary of Product Characteristics 2024.

Faculty

Monica Carpenedo (Chair)

Head of the Non-Malignant Haematology Unit at the Department of Hematology, Oncology and Molecular Medicine, Niguarda Hospital, in Milan, Italy

María Luisa Lozano

Professor at the University of Murcia, Spain; Head of the Haematology Department at the Morales Meseguer Hospital, and Director of the Regional Blood Bank, Murcia, Spain

Waleed Ghanima

Head of research and consultant haematologist
at Østfold Hospital, Norway
Professor at the Institute of Clinical Medicine, University of Oslo, Norway

Disclosures of the faculty

- **Monica Carpenedo** has received honoraria or consultation fees from Amgen, Argenx, Grifols, Novartis, Sanofi, Sobi
- **María Luisa Lozano** has received grants or research support from Amgen and Terumo, and has received honoraria or consultation fees from Alexion, Amgen, Argnx, Celgene, GSK, Grifols, Novartis, Sanofi, Sobi and UCB
- **Waleed Ghanima** has received research support from Bayer, Bristol Myers Squibb, Janssen, Pfizer, Sanofi, Sobi and UCB, has received speaker fees from Amgen, Bayer, Bristol Myers Squibb, Grifols, Novartis, Pfizer, Sanofi and Sobi and attended advisory boards for Alpine, Amgen, Argenx, Cellphire Therapeutics, Grifols, HI-Bio, Hutchmed, Kedrion Biopharma, Novartis, Pfizer, Principia Biopharma, Sanofi, Sobi and UCB

Agenda

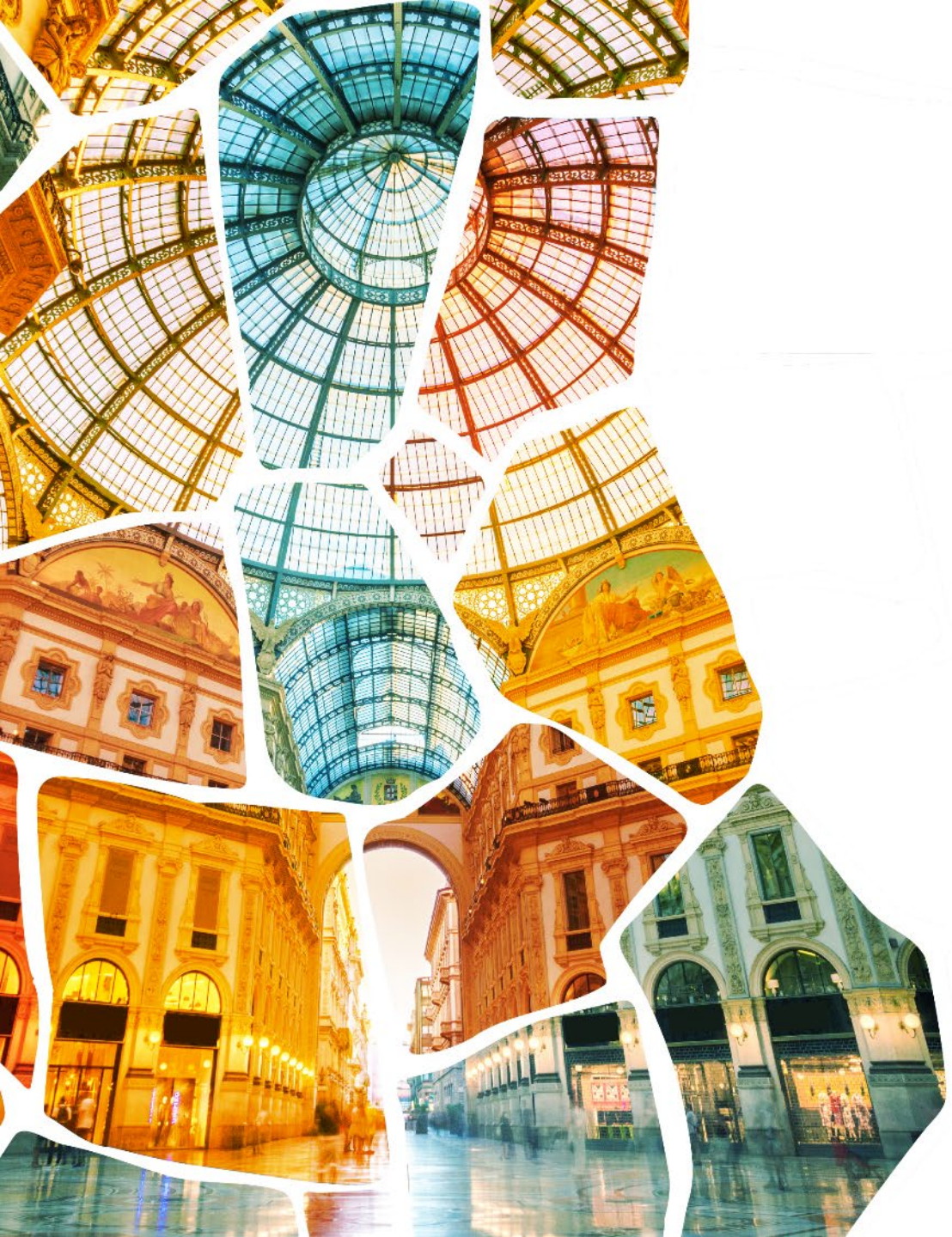
Time (CEST)	Duration (mins)	Title	Faculty
08:00 – 08:05	5	Welcome and introductions	Dr. Carpenedo
08:05 – 08:20	15	Real-world challenges in the care of adults with ITP	
Case conversations: Practical lessons in ITP Management with TPO-RAs			
08:20 – 08:45	25	**Patient case 1:** When, why, and how to treat after first-line	Dr. Lozano
08:45 – 09:10	25	**Patient case 2:** Facing a patient with refractory ITP – when, why, and how to treat	Dr. Ghanima
09:10 – 09:25	15	Q&A session	All faculty
09:25 – 09:30	5	Closing remarks	Dr. Carpenedo

ITP, immune thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.

Learning objectives

- Focus on key challenges in the management of people with ITP
- Discuss real-world evidence on evolving use of TPO-RAs in ITP and how this may impact future guidelines
- Recognise how individualised care, facilitated by SDM, can optimise treatment decisions and help shape treatment approaches for people with ITP

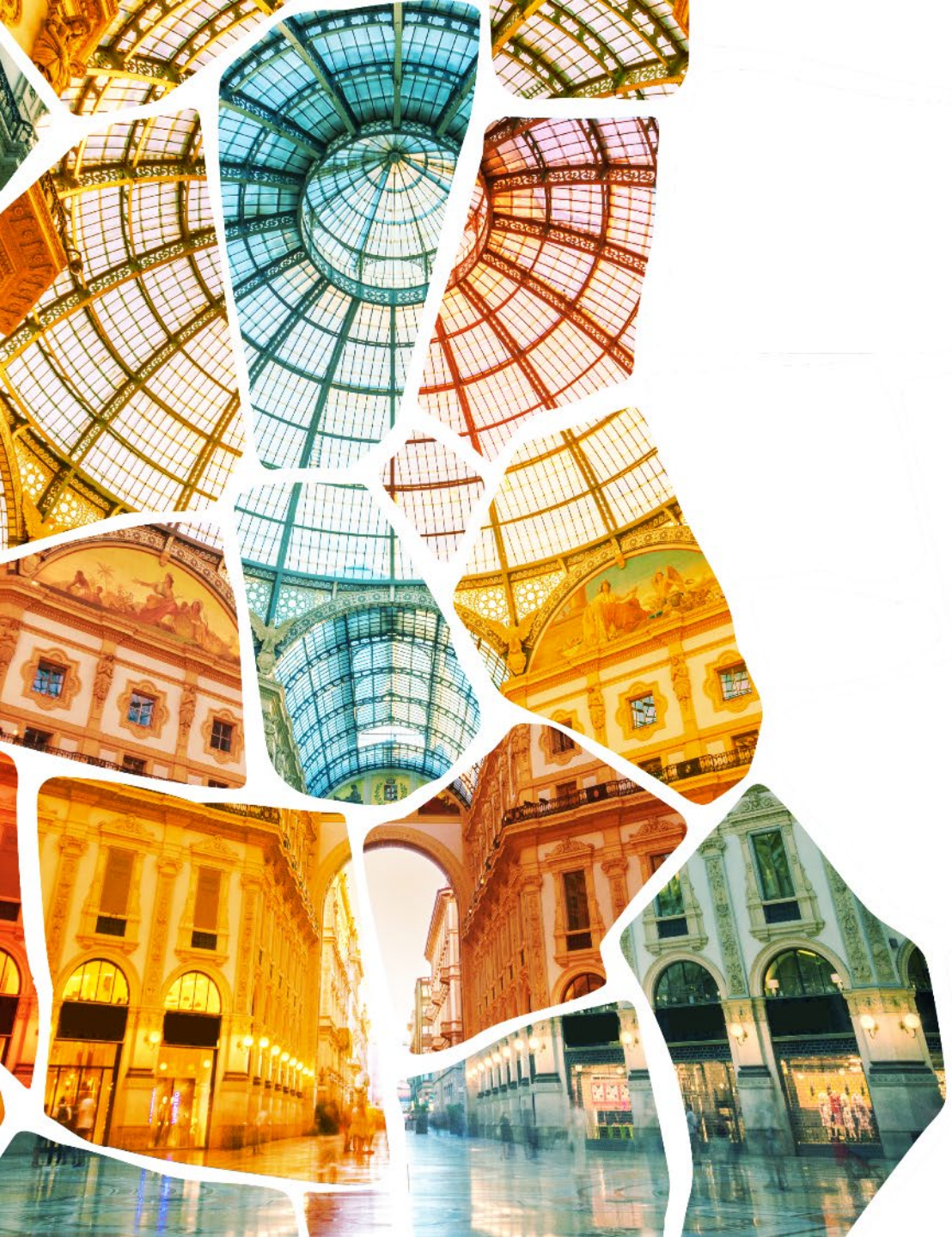
ITP, immune thrombocytopenia; SDM, shared decision making; TPO-RA, thrombopoietin receptor agonist.



Real world challenges in the care of adults with ITP

Dr Monica Carpenedo

Milan, Italy



Real world challenges in the care of adults with ITP

Dr Monica Carpenedo

Milan, Italy

ITP is a dynamic, evolving disease[1–8]

What is ITP?[2–6]

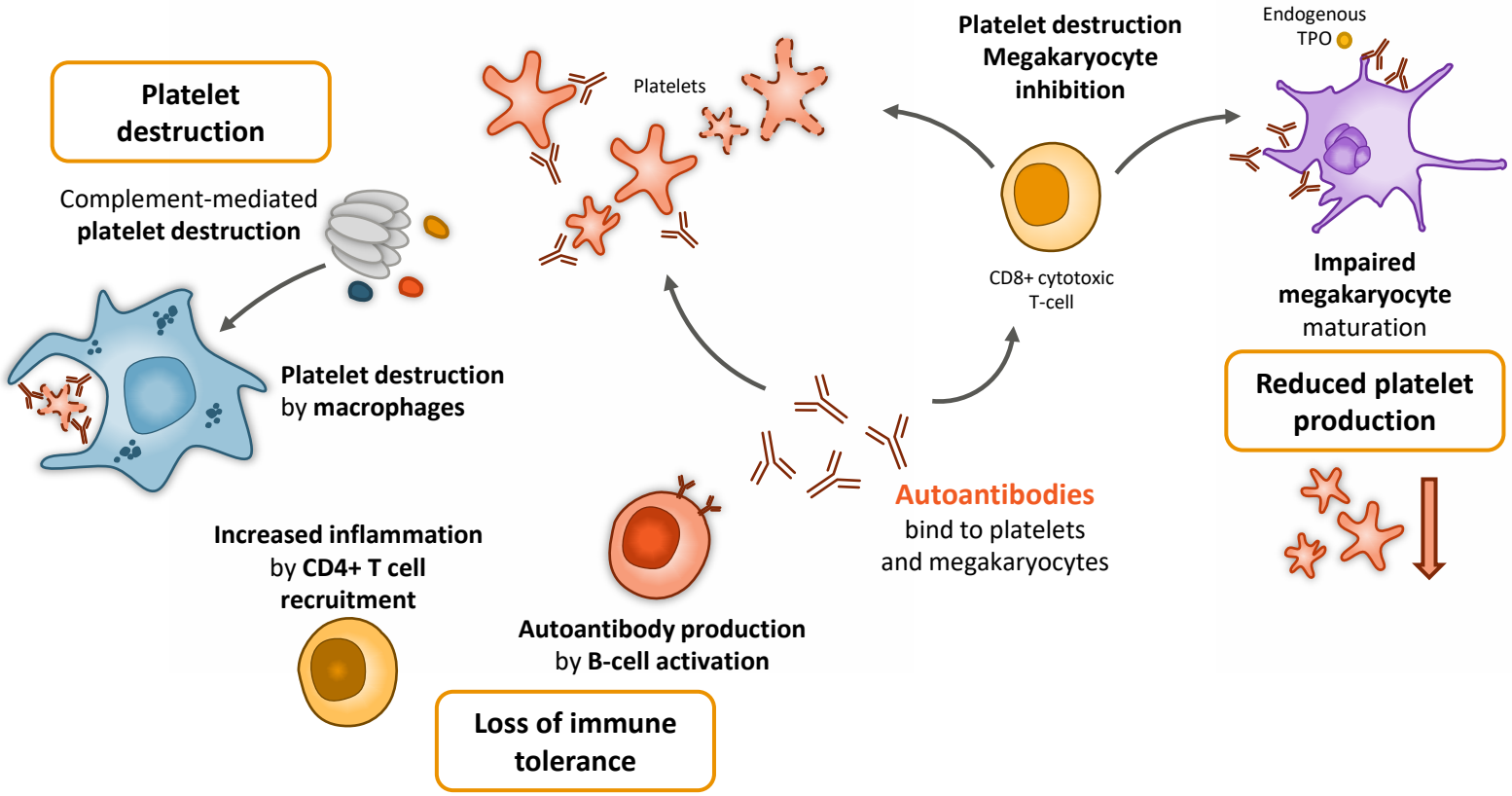
Acquired immune disorder characterised by **isolated thrombocytopenia**

Platelet count of <100 × 10^9/L

Different patients

Different phase of disease in same patients

Different disease burden



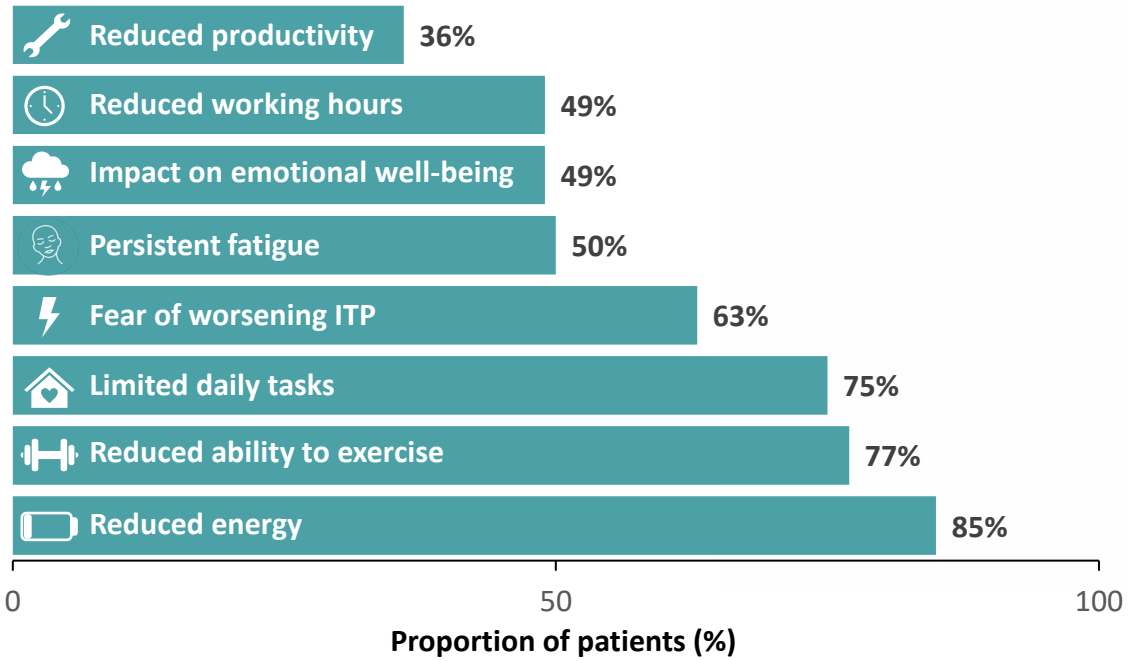
CD, cluster of differentiation; ITP, immune thrombocytopenia; TPO, thrombopoietin.

1. Nugent D et al. *Br J Haematol* 2009;146(6):585–596; 2. National Organization for Rare Disorders. Immune thrombocytopenia. Found at: https://rarediseases.org/rare-diseases/immune-thrombocytopenia/ (Accessed June 2025); 3. Lambert MP & Gernsheimer TB. *Blood* 2017;127(21):2829–2835; 4. Kistanguri G & McCrae KR. *Hematol Oncol Clin North Am* 2013;27(3):495–520; 5. Cooper N & Ghanima W. *N Engl J Med* 2019;381:945–955; 6. Provan D & Semple JW. *EBioMedicine* 2022;76:103820; 7. Zufferey A et al. *J Clin Med* 2017;6(2):16; 8. Martínez-Carballeira D et al. *Hematology Reports* 2024;16:204–219.

ITP has a substantial impact on patients' daily activities and emotional well-being

ITP World Impact Survey (I-WISh)

Patient perspectives (N=1507)



Physician perspectives (N=472)

80% reported ITP symptoms reduced patient HRQoL

66% reported that ITP-related fatigue substantially reduced HRQoL

The multi-dimensional impact of ITP on patients' lives should be **an integral component of disease management**

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

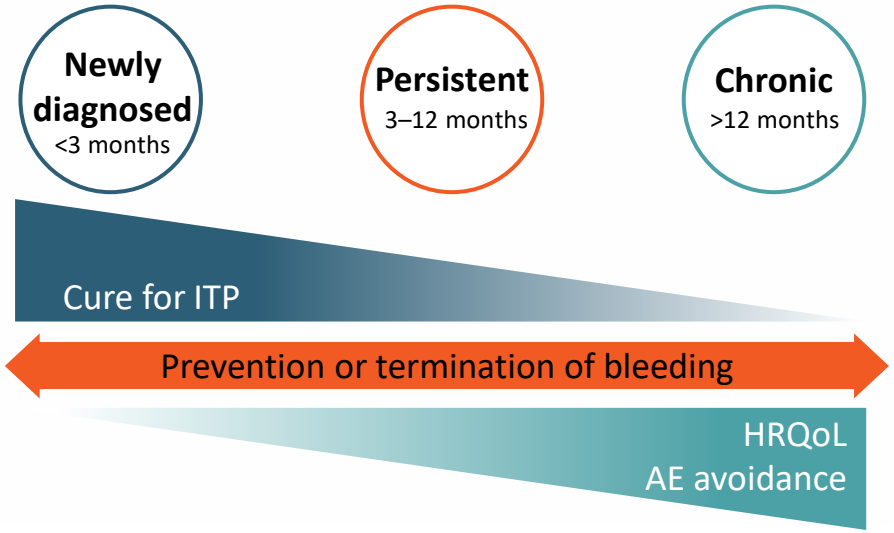
Cooper N et al. *Am J Hematol* 2021;96(2):199–207.

ITP treatment goals aim to individualise treatment, prevent severe bleeding, and improve HRQoL

International consensus treatment goals, 2019[1]

1. Treatment goals should **be individualised to the patient** and the phase of the disease
2. Treatment should **prevent severe bleeding episodes**
3. Treatment should **maintain a target platelet level >20 to 30×10^9/L** at least for symptomatic patients
4. Treatment should be with **minimal toxicity**
5. Treatment should **optimise HRQoL**

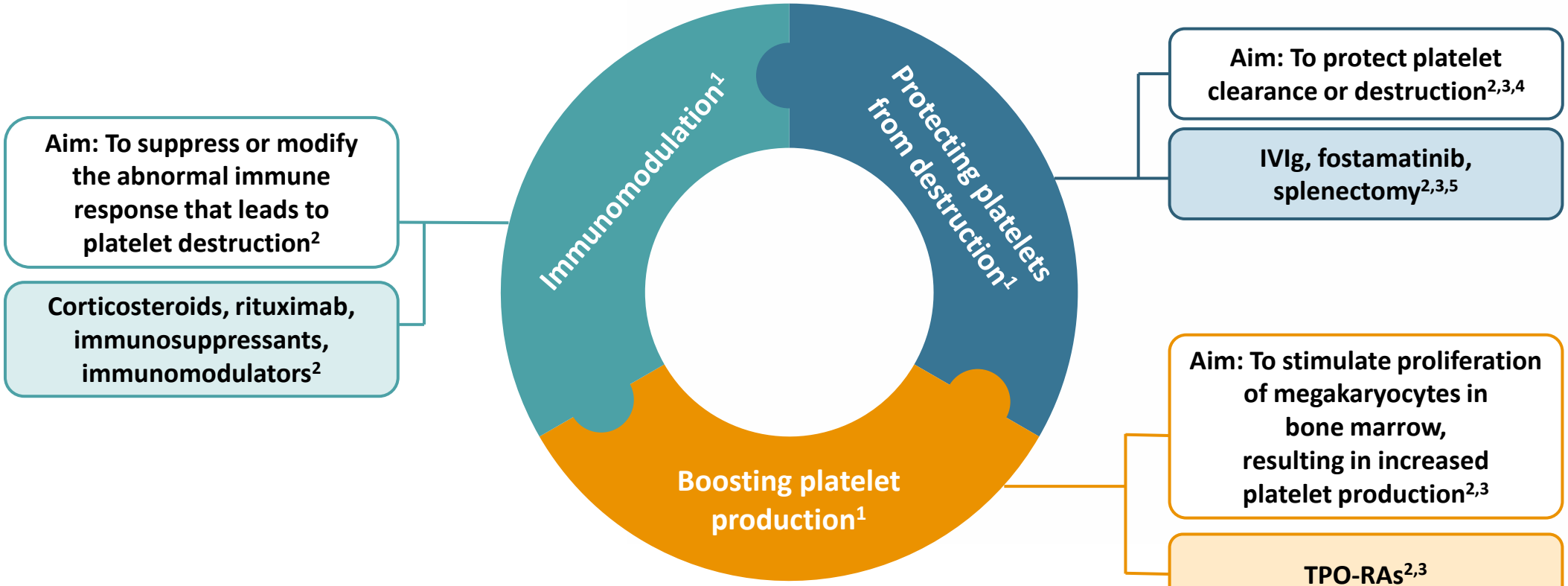
Treatment goals change with ITP duration and severity[2–5]



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

1. Provan D et al. *Blood Adv* 2019;3:3780–3817; 2. National Organization for Rare Disorders. Immune thrombocytopenia. Found at: https://rarediseases.org/rare-diseases/immune-thrombocytopenia/ (Accessed June 2025); 3. Kistanguri G & McCrae KR. *Hematol Oncol Clin North Am* 2013;27(3):495–520; 4. Zufferey A et al. *J Clin Med* 2017;6(2):16; 5. Matzdorff A et al. *Oncol Res Treat* 2018;41 Suppl 5:1–30.

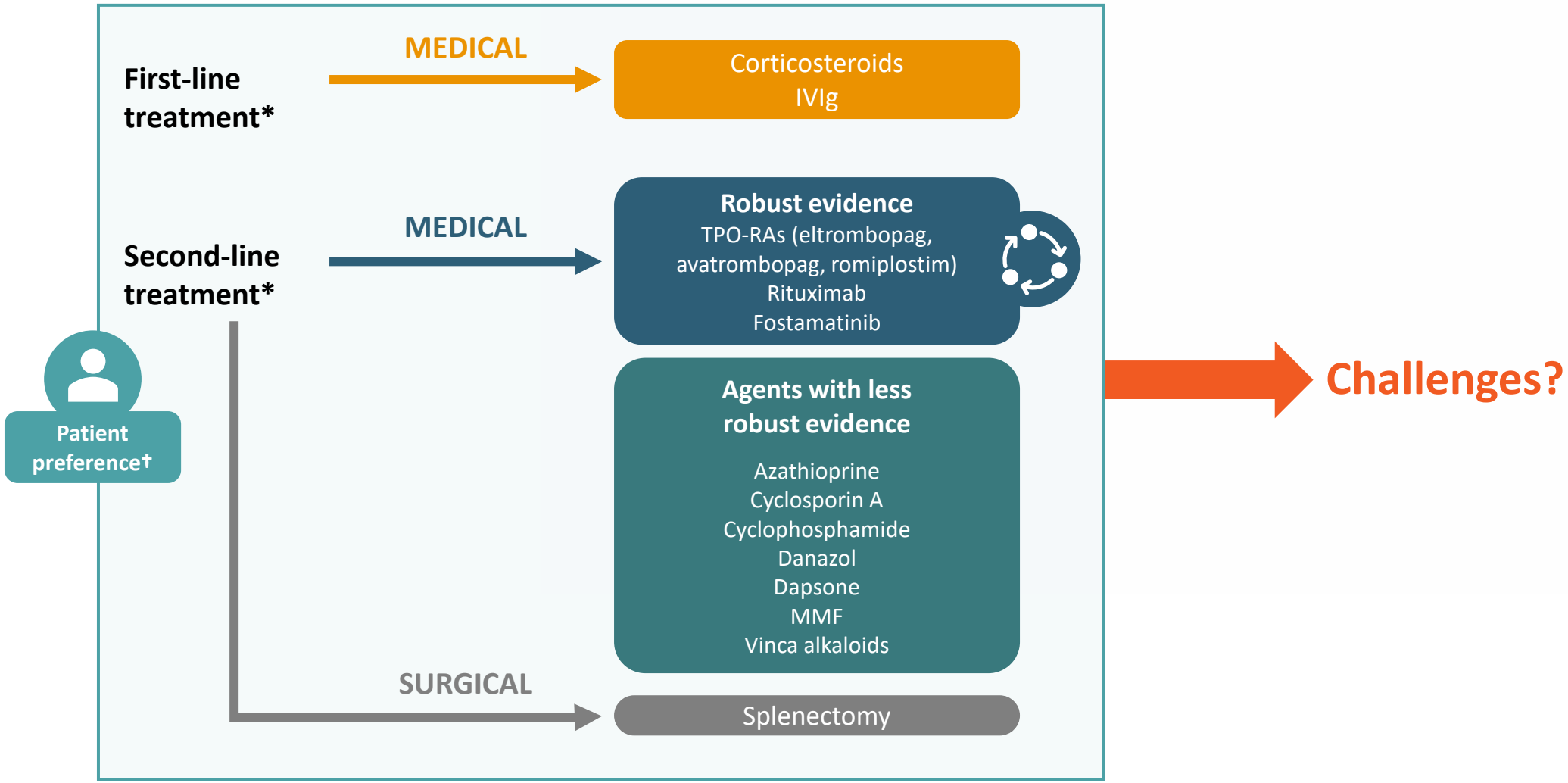
ITP treatment strategies aim to modify, protect, or boost platelet production



ITP, immune thrombocytopenia; IV anti-D, intravenous anti-D immunoglobulin; IVIg, intravenous immunoglobulin; TPO-RA, thrombopoietin receptor agonist.

1. Ghanima W et al. *Hematology Am Soc Hematol Educ Program* 2024;1:678–684; 2. Audia S & Bonnotte B. *J Clin Med* 2021;10:1004; 3. Kuter DJ et al. *Hematol Oncol Clin North Am* 2009;23:1193–211; 4.Chaturvedi S et al. *Blood* 2018;131(11):1172–1182; 5. Grifols UK Ltd. TAVLESSE (Fostamatinib) Summary of Product Characteristics 2023.

Current guidelines recommend a multi-line treatment approach for adult ITP[1–4]



A number of these treatment options are used off-label for the treatment of ITP, but in line with international guidelines.
*Watch and wait only if no or mild bleeding with a platelet count of >20–30 × 10^9/L; †Patient preference must be considered when discussing treatment options in a shared-decision making approach.
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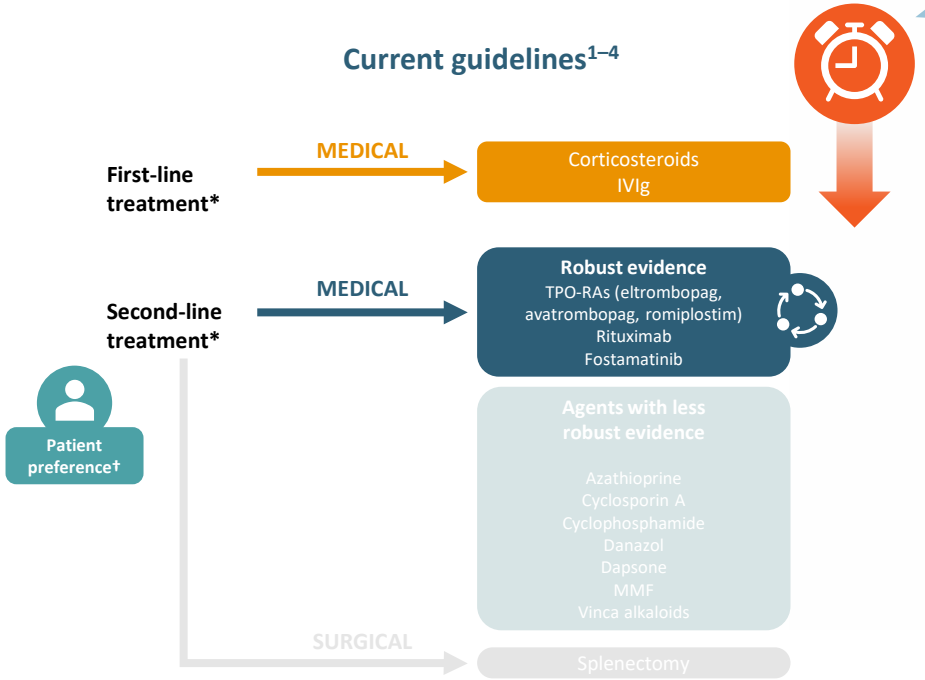
Challenge
When should we switch from protecting platelets to boosting platelets?



Limited guidance on the timing of TPO-RA treatment in ITP guidelines[1,2,5]

First-line treatments are used for newly-diagnosed patients (<3 months)[1,3,4]

Second-line treatments are intended for patients who are refractory to first-line therapy or who have persistent (≥3–<12 months) or chronic (≥12 months) ITP[1–5]

RWE: Early switch to TPO-RAs can improve long-term clinical outcomes[3–6]

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ITP, immune thrombocytopenia; IVIg, intravenous immunoglobulin; MMF, mycophenolate mofetil; RWE, real-world evidence; TPO-RA, thrombopoietin receptor agonist.
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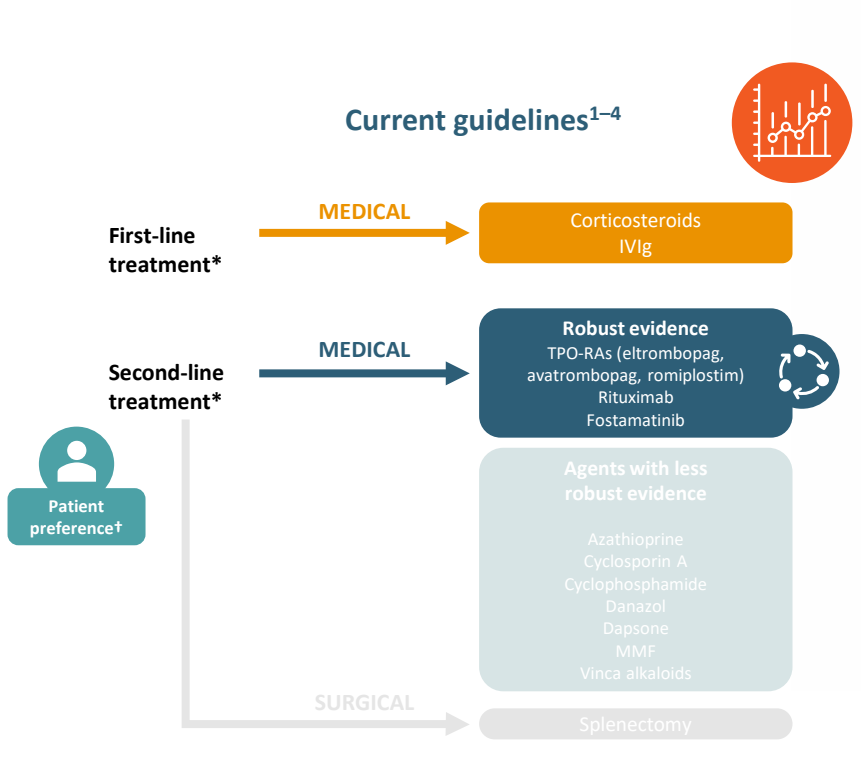
5. Carpenedo M et al. *Ther Adv Hematol* 2021;12:20406207211048361; 6. Cuker A et al. *Ann Hematol* 2023;102:2051–2058.

Challenge
How should we manage platelet count fluctuations and instability?



Limited guidance on how to manage platelet count fluctuations and instability in patients with ITP[1]

There are large individual variations in platelet count between patients[3]

Traditionally, use of platelet thresholds for deciding whether to treat has not been evidence based[3]

The longer ITP persists, platelet counts become less relevant for deciding for or against therapy[3]

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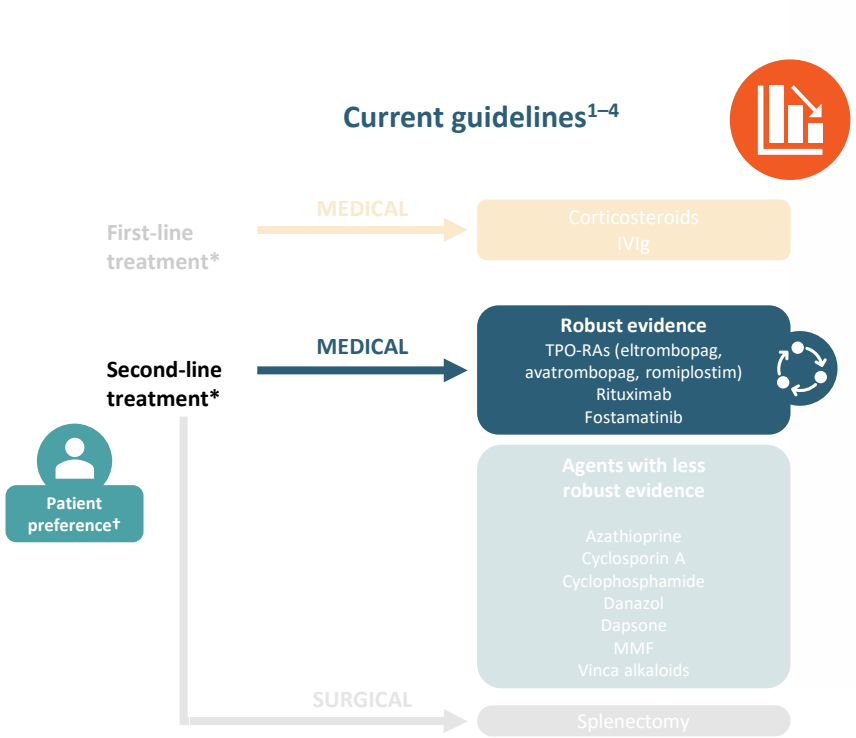
Challenge

How can we taper therapy after platelet count stabilization and achieve remission?



Limited guidance on TPO-RA tapering/discontinuation in ITP guidelines[1]

Up to 30% of patients with ITP maintain a sustained response after TPO-RA dose reduction or discontinuation[1]

Currently guidance is limited to expert opinion[5]

RWE: Optimization of TPO-RA tapering and discontinuation in selected patients can improve QoL[5]

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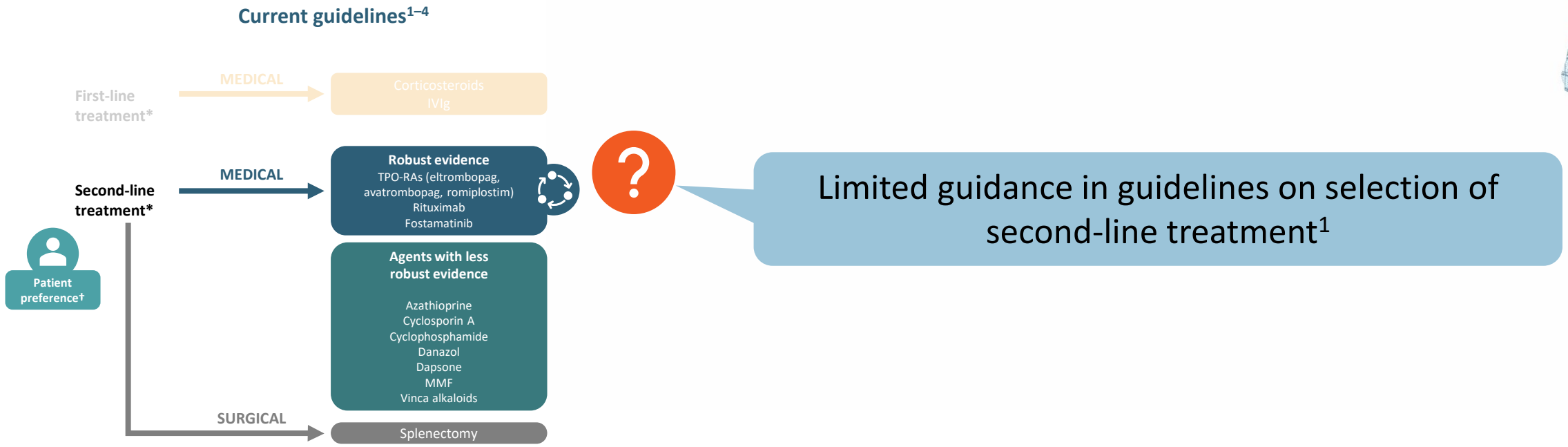
Challenge
How do different needs of patients affect decision-making?



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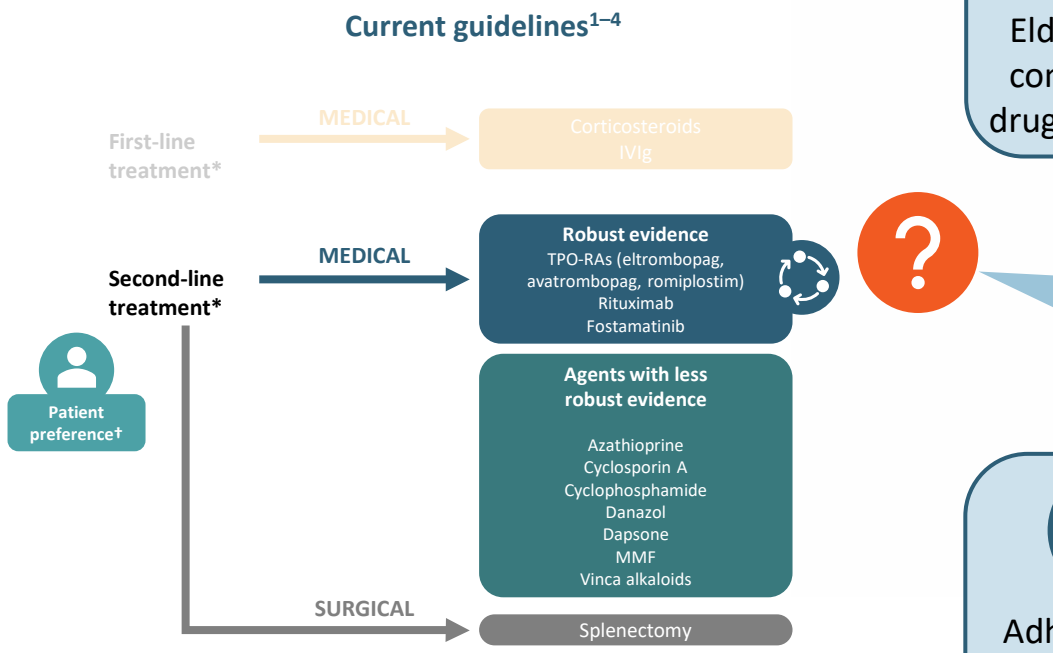
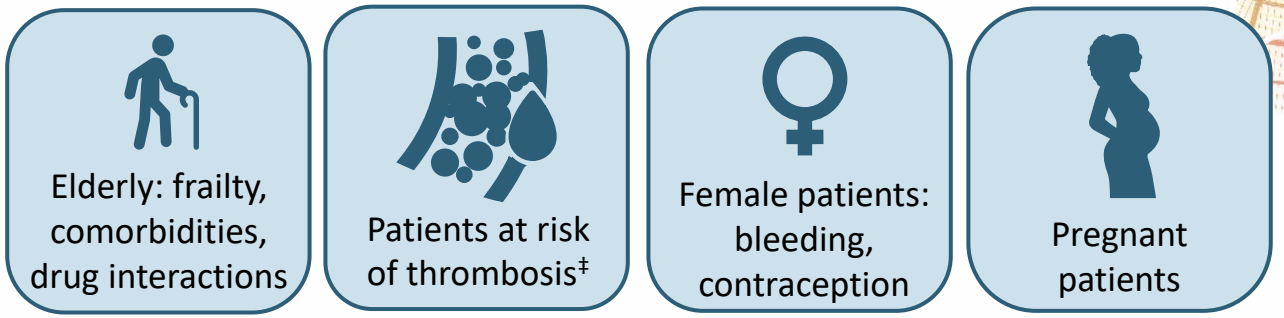
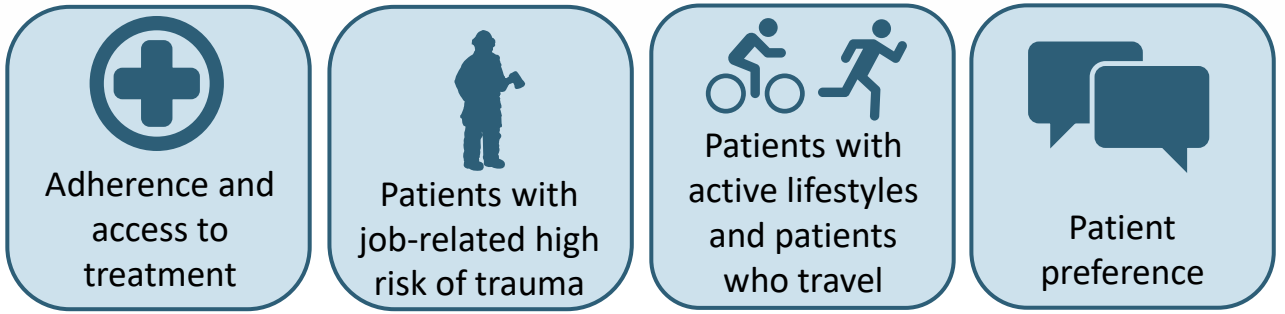


Multiple considerations when determining second-line treatment choice[1–7]





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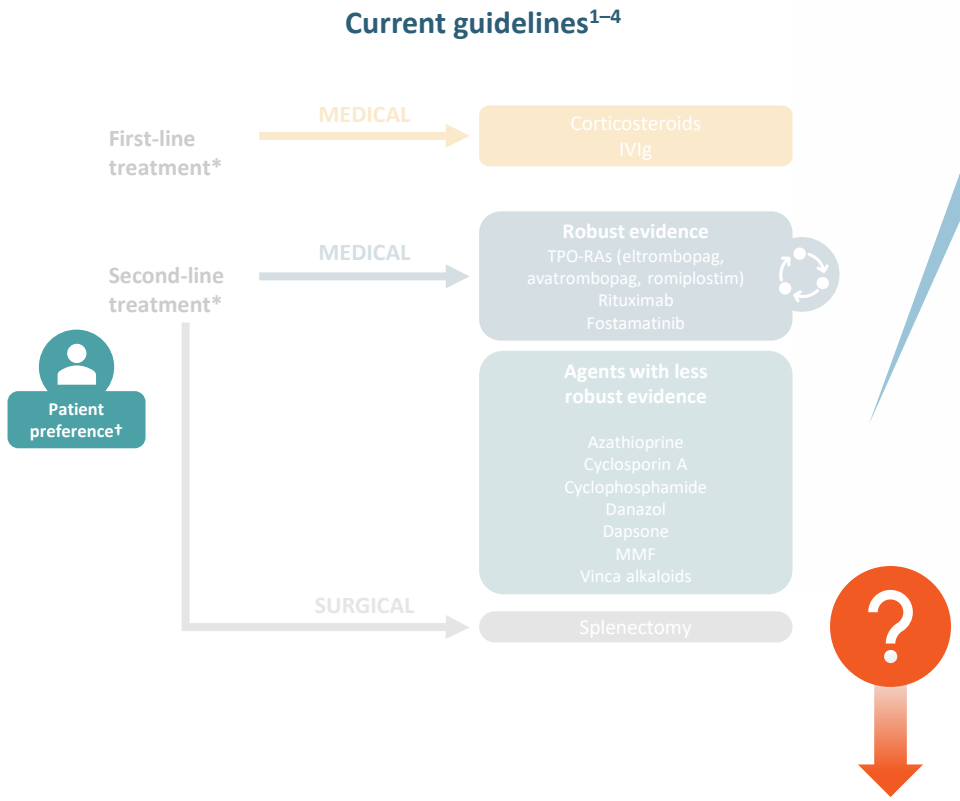
Challenge
How should we manage treatment of a patient with refractory ITP?



Limited guidance on how to manage treatment of a patient with refractory ITP[1,2]

Approximately 15% of patients do not have a durable response after 3 lines of therapy[2]

Patients are usually offered a combination of ITP treatments[3,4]

RWE: Combination therapies and novel agents may be suitable options for patients with refractory ITP[4]

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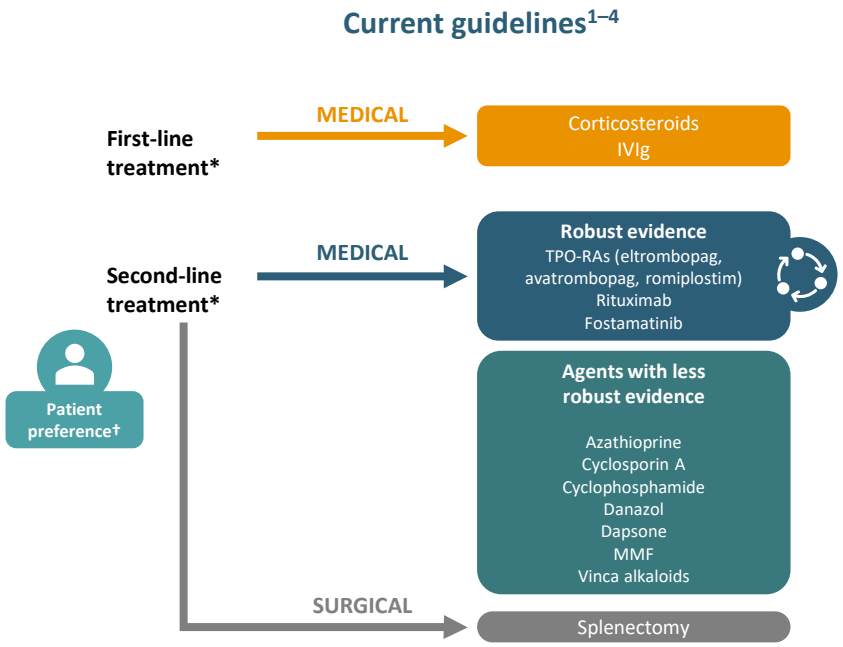
Limited guidance on timing, approach, and patient selection for TPO-RAs



Challenges

1. When should we switch from protecting platelets to boosting platelets?
2. How should we manage platelet count fluctuations and instability?
3. How can we taper therapy and achieve remission?
4. How do we manage patients with individualised needs?
5. How should we manage treatment of a patient with refractory ITP?

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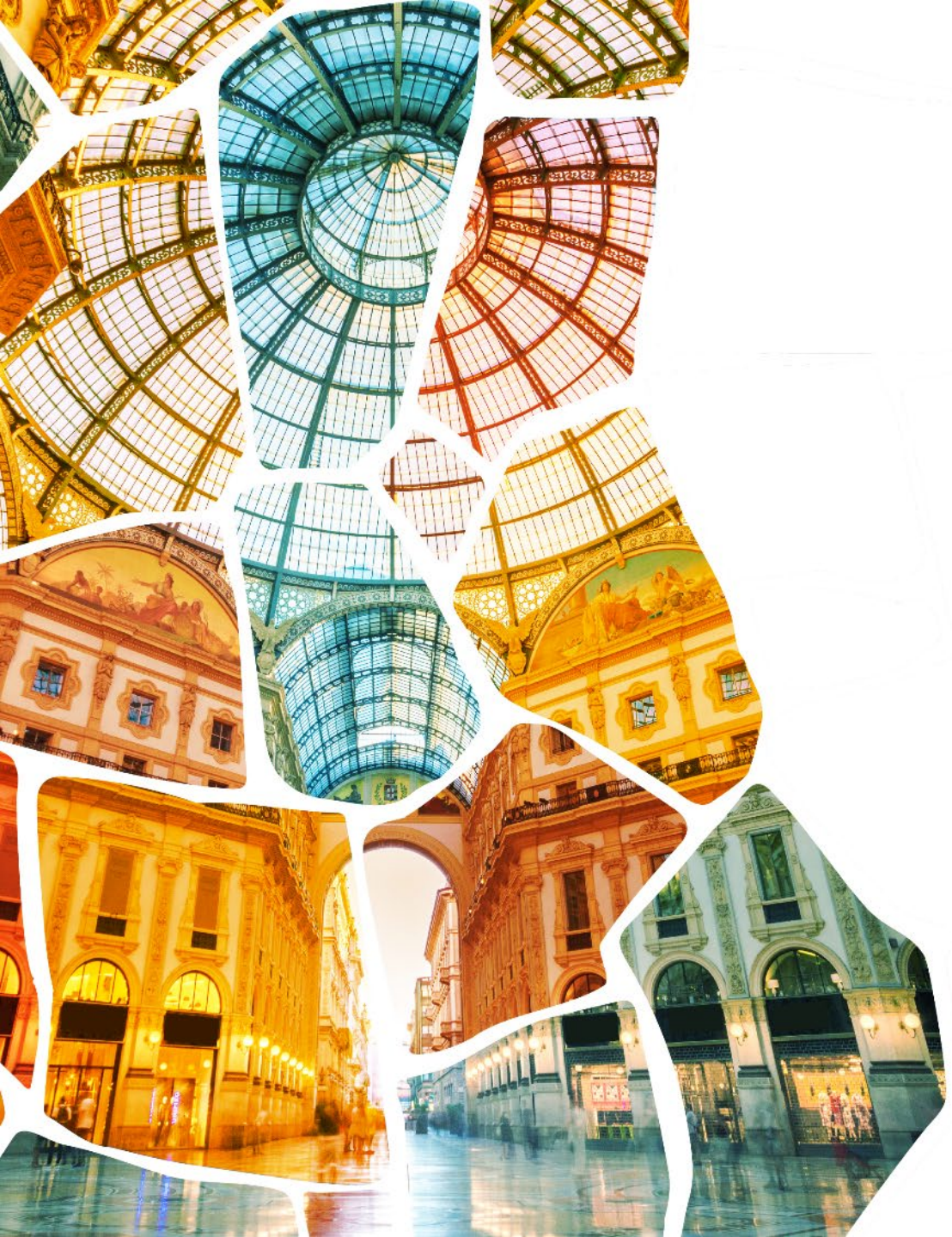
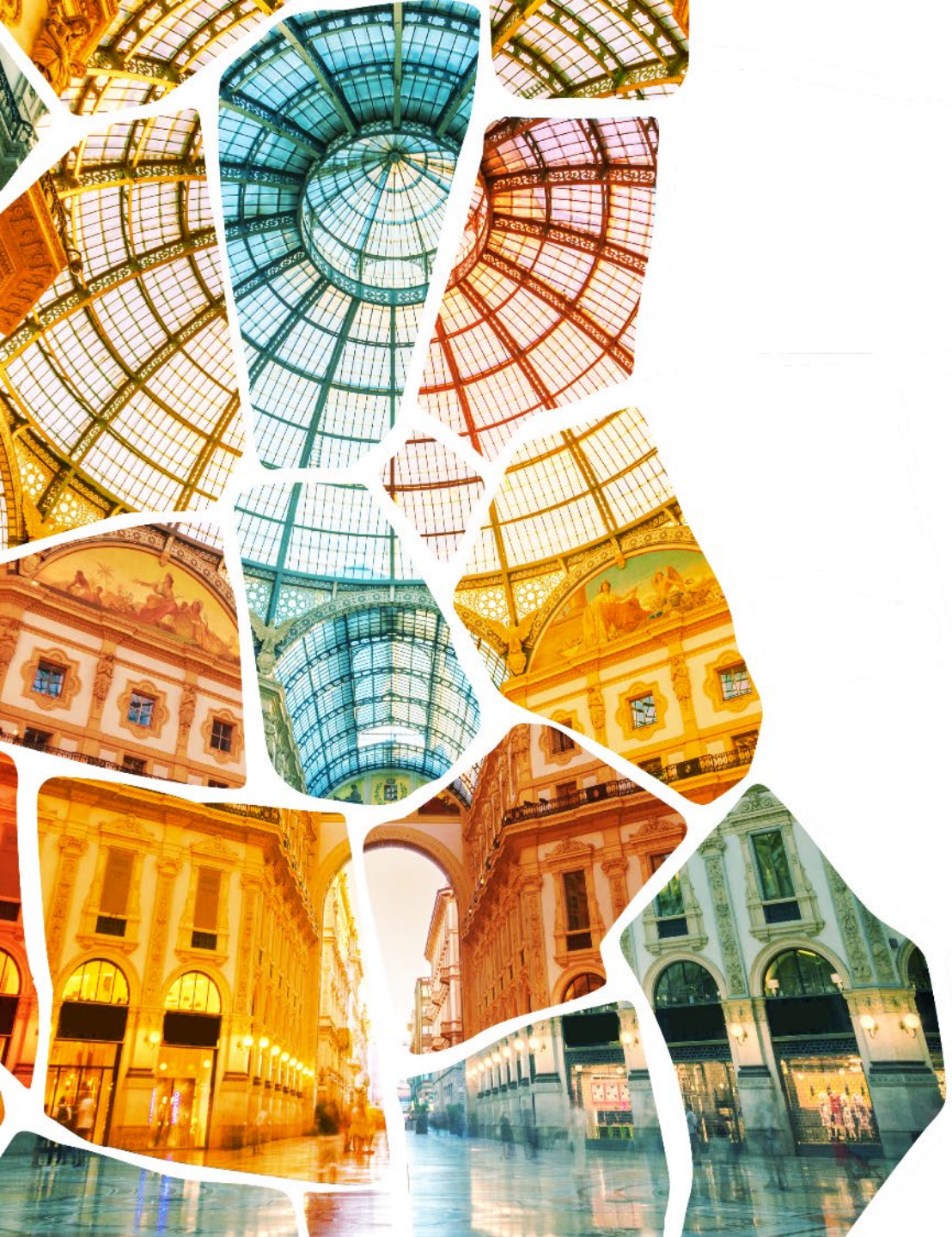


When, why, and how to treat after first-line

Dr María Luisa Lozano

Murcia, Spain



When, why, and how to treat after first-line

Dr María Luisa Lozano

Murcia, Spain

Patient case 1

José

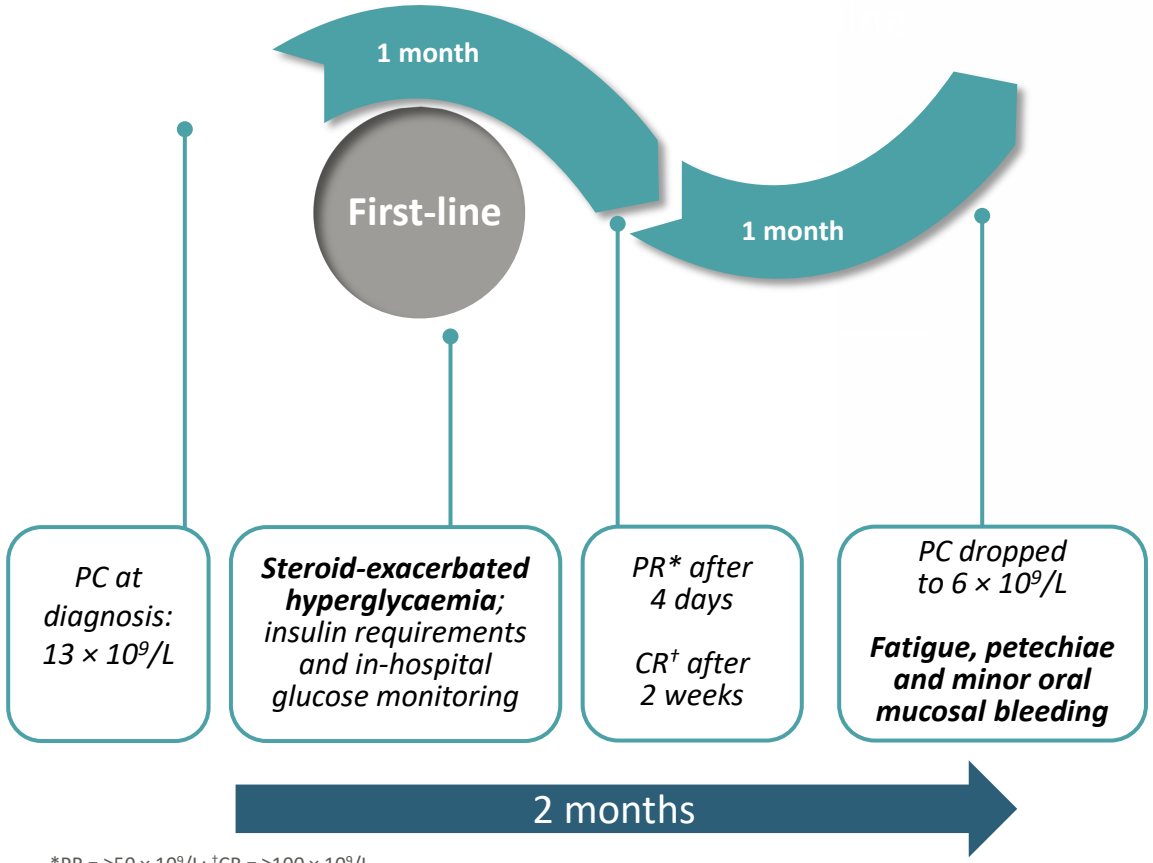
	54-year-old, white, male Landscape gardener, frequent traveller, likes to play tennis
	Long term oral antidiabetic drugs Anti-hypertensive medications
	Isolated thrombocytopenia with platelet count 13 × 10^9/L
	Asymptomatic, no abnormal bleeding
	No lymphadenopathy, or hepatosplenomegaly Sporadic petechiae on lower limbs
	CBC: Isolated thrombocytopenia with no platelet clumping
	Normal kidney, liver and thyroid function Serum immunoglobulins within normal range
	Microbiology: Consistent with past hepatitis B serology

CBC, complete blood count.

José: Treatment timeline

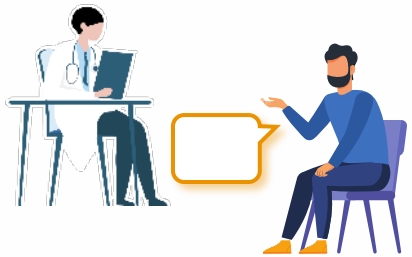
Prednisolone 1 mg/kg/day

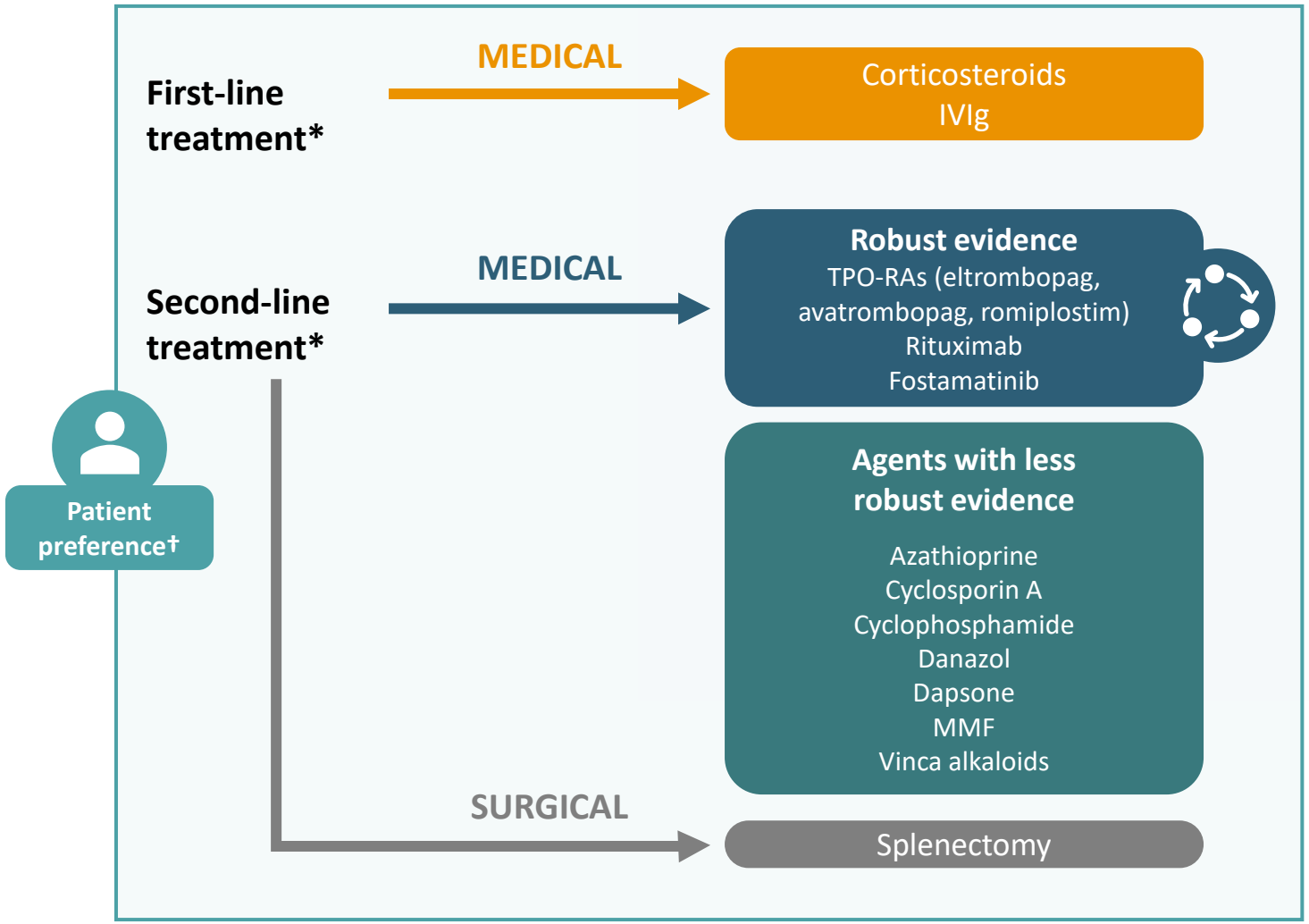
Prednisolone tapered and discontinued



*PR = ≥50 × 10^9/L; †CR = ≥100 × 10^9/L.
CR, complete response; PC, platelet count; PR, partial response.

What second-line therapies do guidelines recommend?





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ASH, American Society of Hematology; G-A-S, Germany, Austria and Switzerland; ICR, International Consensus Report; ITP, immune thrombocytopenia; MMF, mycophenolate mofetil; TPO-RA, thrombopoietin receptor agonist.
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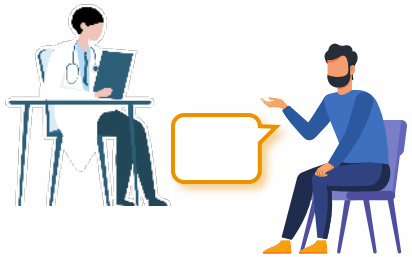
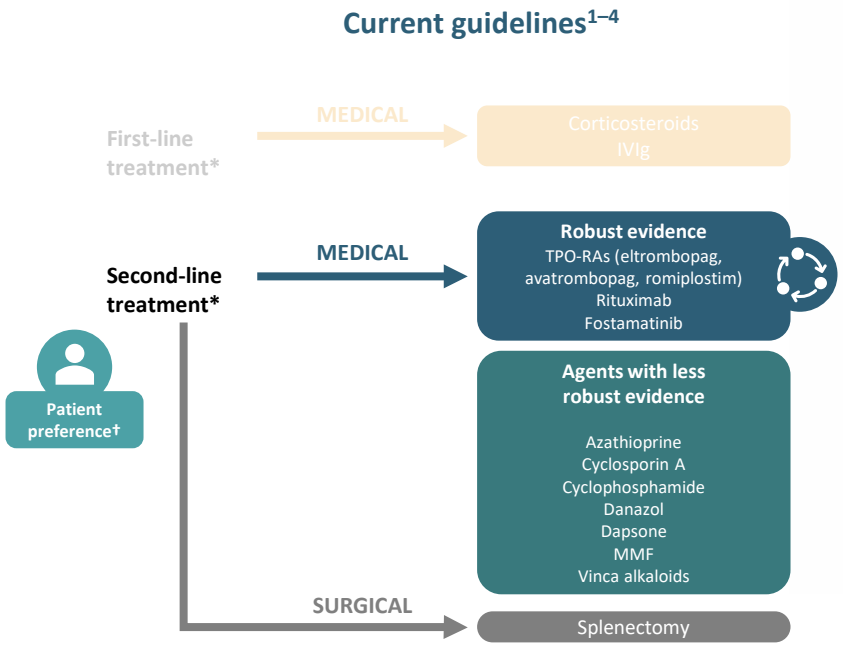




Specific to ICR[1]

Robust evidence: **TPO-RAs**, **fostamatinib**, **rituximab**

Less robust evidence: Azathioprine, cyclosporin A, cyclophosphamide, danazol, dapsone, MMF, vinca alkaloids

Specific to ASH[2]

If the patient places high value on achieving platelet responses: **TPO-RA**

If the patient places high value on avoiding long-term medication: **Rituximab**

Specific to G-A-S[3,4]

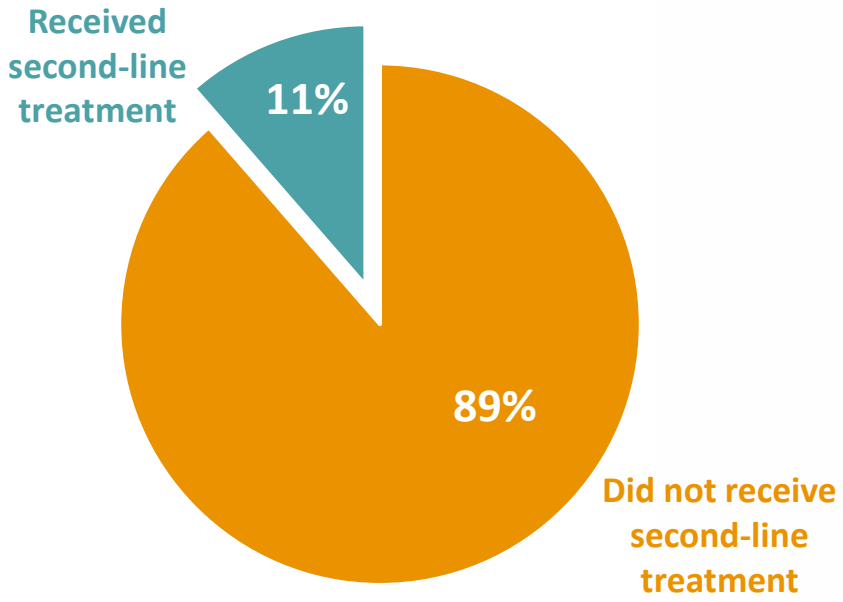
In patients with minimal bleeding consider "**Watch and wait**"*

If therapy is needed: **TPO-RA**

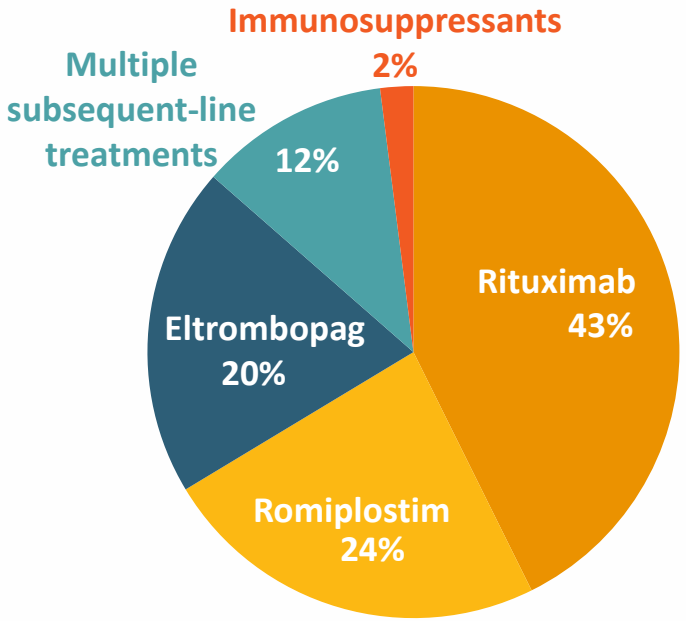
A number of these treatment options are used off-label for the treatment of ITP, but in line with international guidelines.
*Watch and wait only if no or mild bleeding with a platelet count of >20–30 × 10^9/L; †Patient preference must be considered when discussing treatment options in a shared-decision making approach.
ASH, American Society of Hematology; G-A-S, Germany, Austria and Switzerland; ICR, International Consensus Report; ITP, immune thrombocytopenia; MMF, mycophenolate mofetil; TPO-RA, thrombopoietin receptor agonist.
1. Provan D et al. *Blood Adv* 2019;3:3780–3817; 2. Neunert C et al. *Blood Adv* 2019;3:3829–3866; 3. Matzdorff A et al. *Oncol Res Treat* 2018;41 Suppl 5:1–30; 4. Matzdorff A et al. *Oncol Res Treat* 2023;46:5–44.

Early use of second-line treatment has been shown to improve outcomes

Patients (%) who received second-line treatment within 90 days from diagnosis (N=8268)



Second-line treatments (%) used for patients within 90 days from diagnosis (n=941)



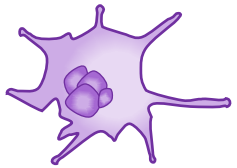
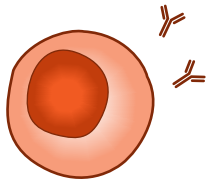
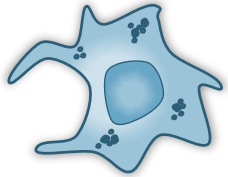
Study period: Jan 2012–Sept 2019

Early use of second-line treatment was associated with:

- **Improved platelet counts and reduced bleeding events** between 3 and 6-months post-treatment initiation
- A **significant reduction in corticosteroid use** at 3 months (39% vs 87%, P<0.001)

Cuker A et al. *Ann Hematol* 2023;102:2051–2058.

Which second-line treatments could be considered for José?

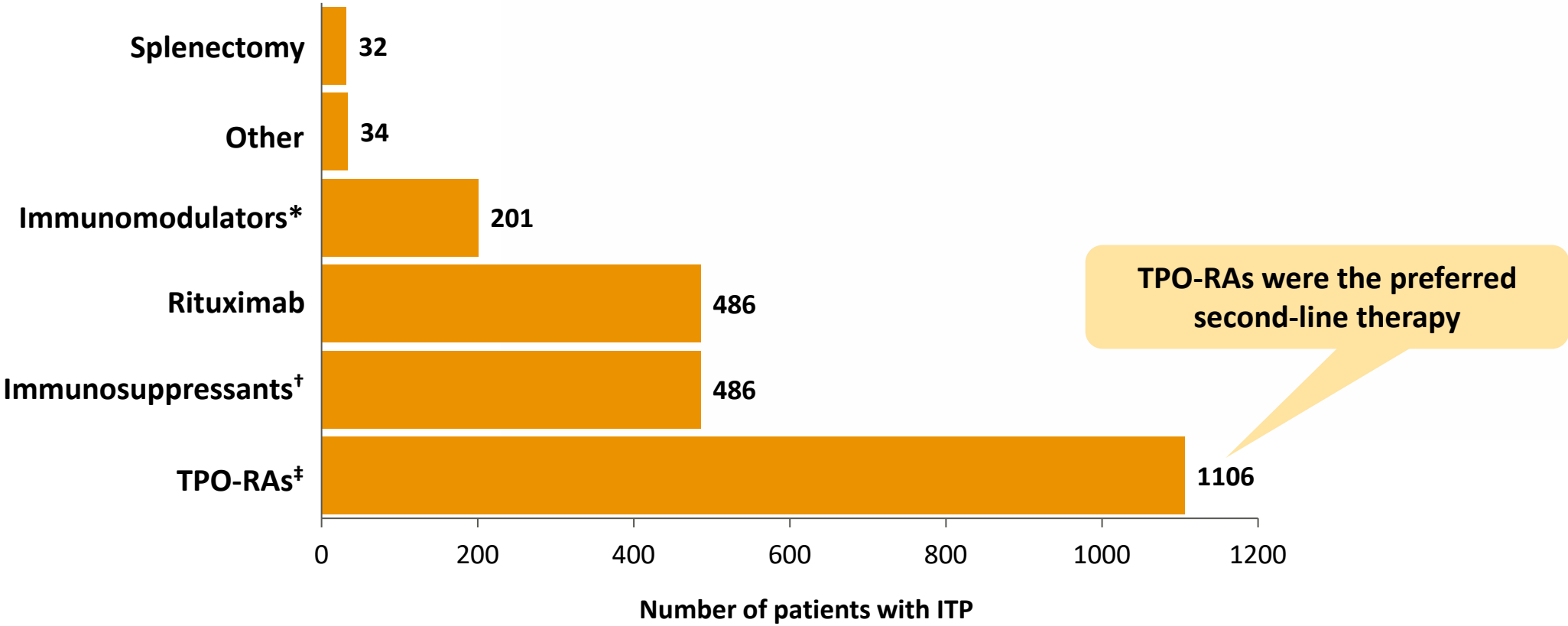
	TPO-RA[1–3] **Boosting platelet production**	Rituximab[1,3] **Immunomodulation**	Fostamatinib[1,3] **Protecting platelets from destruction**	Splenectomy[1–4] **Protecting platelets from destruction**
	 **Megakaryocyte**	 **B-cell**	 **Macrophage**	 **Spleen**
MoA	Proliferation of megakaryocytes resulting in increased platelet production	Suppress or modify the abnormal immune response that leads to platelet destruction	Protect platelet clearance or destruction	Protect platelet clearance or destruction
Evidence	• Phase 3 studies • Response maintained at >80% • SROT rates 20–30%	• Response rate of ~40–60% • Durable response <20%	• Phase 3 studies • Response maintained at 40–75% • Durable response =18%	• Response maintained at >50–70% • Low cost
Special considerations	Frequent monitoring of platelet counts while tapering*	Reactivation of infections; infusion reactions	Hepatotoxicity, hypertension, diarrhoea	Ensure prior vaccination†

*Liver monitoring is needed for some TPO-RAs[5]; †According to recommendations of each country.
MoA, mode of action; SROT, Sustained response off treatment; TPO-RA, thrombopoietin receptor agonist.

1. Audia S & Bonnotte B. *J Clin Med* 2021;10:1004; 2. Kuter DJ et al. *Hematol Oncol Clin North Am* 2009;23:1193–211; 3. Lozano ML et al. *Clinical Medicine* 2020;157(4):191–198; 4. Chaturvedi S et al. *Blood* 2018;131(11):1172–1182;
5. Revolade (eltrombopag) Summary of Product Characteristics 2024. Found at: https://www.ema.europa.eu/en/documents/product-information/revolade-epar-product-information_en.pdf (accessed March 2025).

Which second-line treatments are more commonly used here in Europe?

Second-line treatments prescribed in Europe 2010–2022 (UK, France, Italy, Norway, Germany; N=2360)[1,2]



*Dapsone, danazol and hydroxychloroquine; †Azathioprine, MMF, cyclophosphamide, fostamatinib and cyclosporin; ‡Avatrombopag, romiplostim and eltrombopag.
MMF, mycophenolate mofetil; TPO-RA, thrombopoeitin receptor agonist.

1. Moulis G. et al. Presented at the European Hematology Association (EHA), June 13–16, 2024, Madrid, Spain; P2239; 2. Moulis G. et al., European Consortium for ITP (ERCI) group (in press).

We have three TPO-RAs available to treat ITP; are there any differences between them?

	Administration	Initial dose	Specific considerations
Romiplostim*[1,2]	SC injection	1 µg/kg once weekly	Administration by HCP or self-administered at home
Eltrombopag*[1,3]	Oral	1 tablet (50 mg) per day	Dietary restrictions: Take 2 hours before or 4 hours after any products such as antacids, dairy products†, or mineral supplements containing polyvalent cations‡ Need for frequent liver function test
Avatrombopag*[1,4]	Oral	1 tablet (20 mg) per day	No dietary restrictions

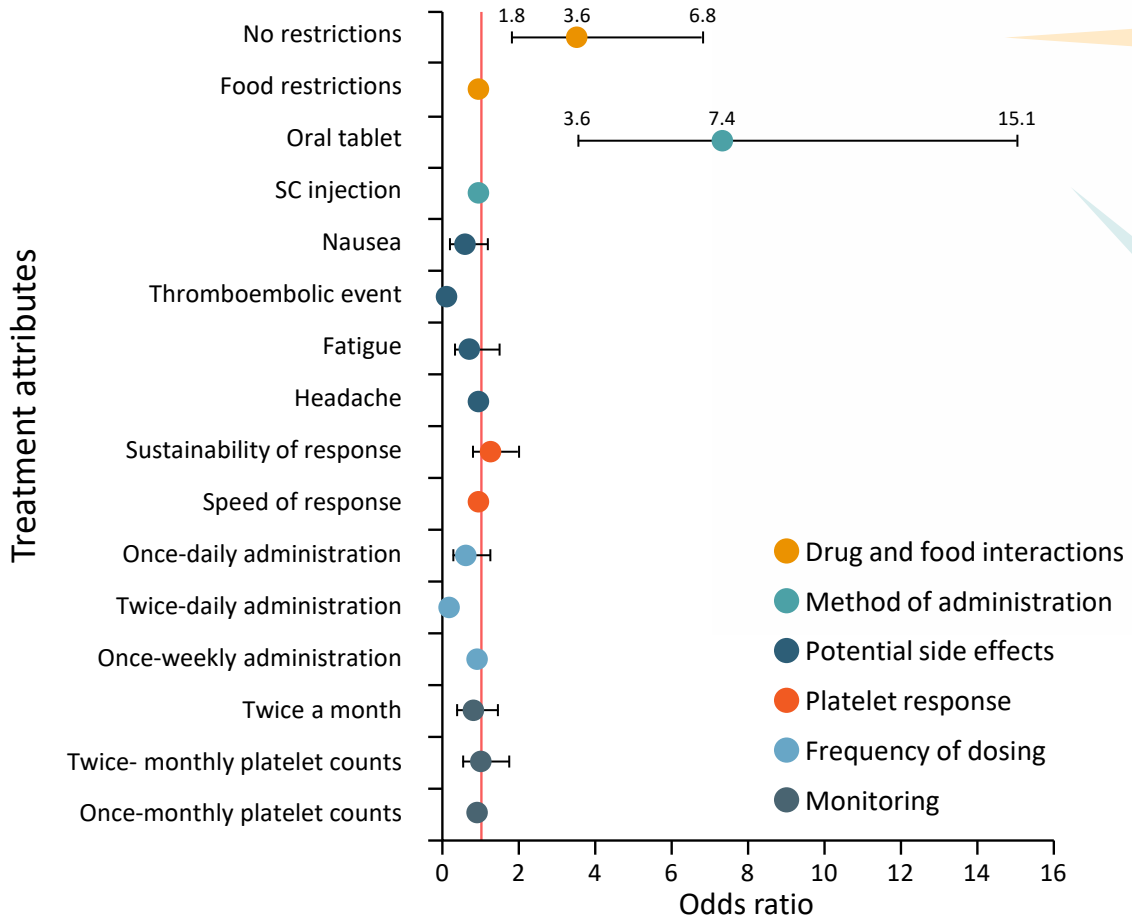
Unknown if response rates differ

Choice is based on efficacy, safety profile, patient preference and comfort/supervision

*TPO-RAs approved in Europe and USA; †Or other calcium containing food products; ‡Such as calcium, iron, magnesium, aluminium, selenium or zinc.
HCP, healthcare professional; ITP, immune thrombocytopenia; SC, subcutaneous; TPO-RA, thrombopoietin receptor agonist.
1. Gilreath J et al. *Drugs* 2021;81:1285–1305; 2. Amgen Ltd. NPLATE (romiplostim). Summary of Product Characteristics 2024; 3. Novartis Pharmaceuticals UK Ltd. REVOLADE (eltrombopag). Summary of Product Characteristics 2024; 4. Sobi Ltd. DOPTELET (avatrombopag). Summary of Product Characteristics 2024.

Patients with ITP typically prefer orally administered treatments that do not require dietary restrictions

Association between TPO-RA attributes and participants' preference for these treatments (n=31)[1]



Patients preferred orally administered treatments versus SC injection

	UK (n=31)[1]	Italy (n=76)[2]	Netherlands (n=76)[3]
OR	7.4	3.8	4.2
95% CI	3.6–15.1	2.5–5.6	2.8–6.5

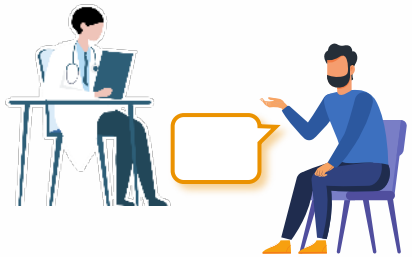
Patients preferred treatments that did not require dietary restrictions versus those that did

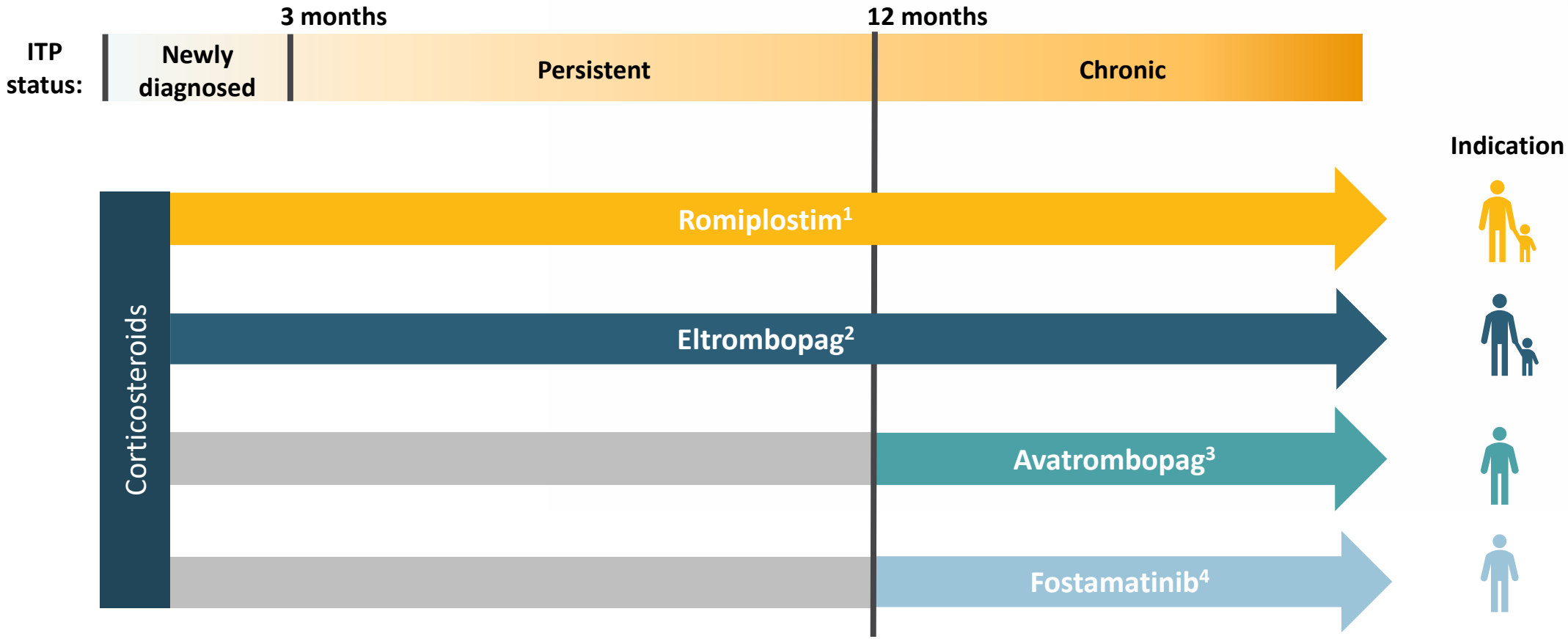
	UK (n=31)[1]	Italy (n=76)[2]	Netherlands (n=76)[3]
OR	3.6	1.6	1.9
95% CI	1.8–6.8	1.2–2.1	1.5–2.4

CI, confidence interval; ITP, immune mediated thrombocytopenia; OR, odds ratio; TPO-RA, thrombopoietin receptor agonist.

1. McDonald Vet al. *Hematology* 2021;26(1):799–808; 2. Lucchesi A et al. *Hematology* 2023;14:1–8; 3. Jansen AJG et al. *Hematology* 2023;28(1):2267942.

Could José start treatment with any TPO-RA?

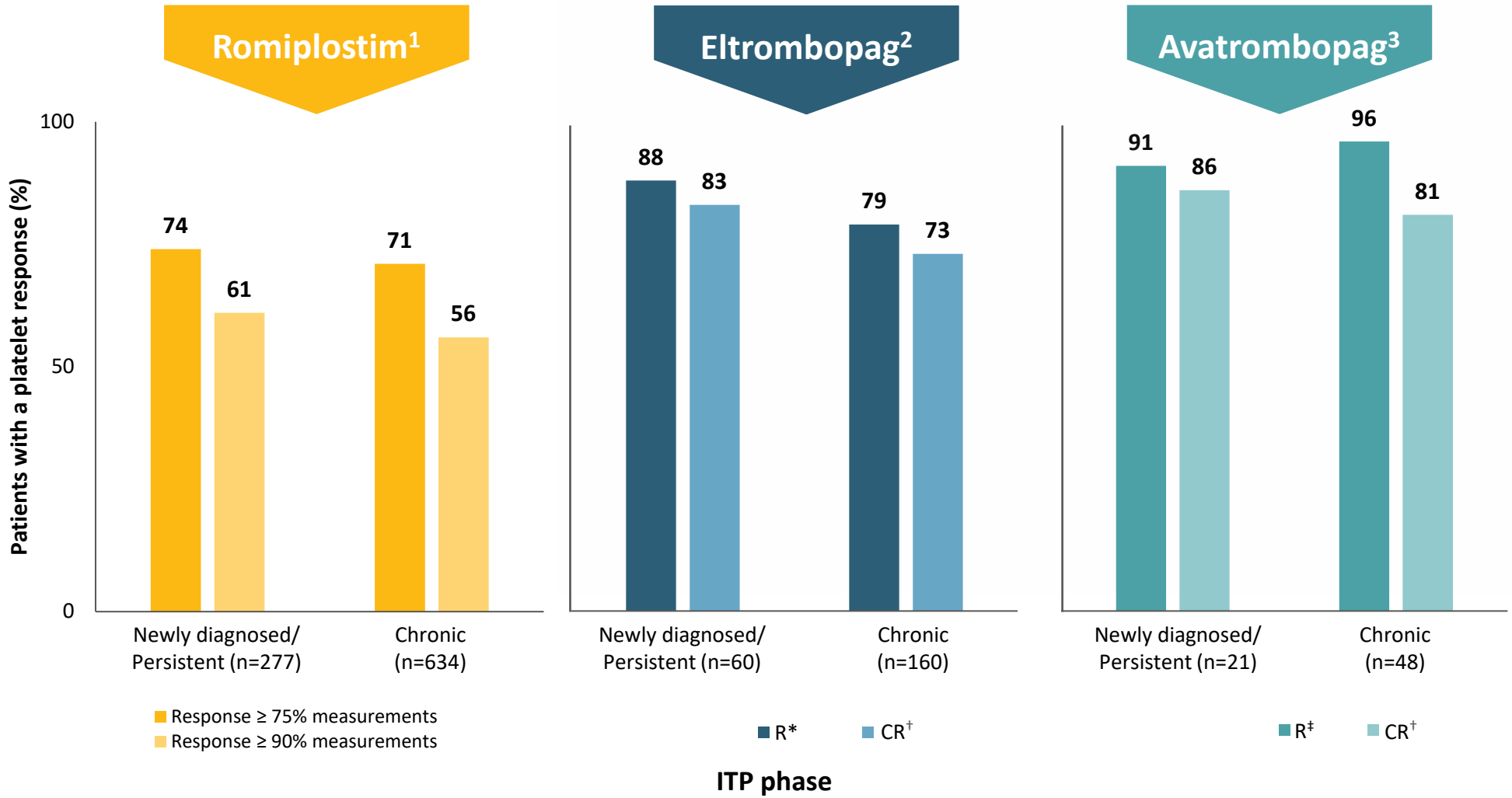




ITP, immune mediated thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.

1. Amgen Ltd. NPLATE (romiplostim). Summary of Product Characteristics 2024; 2. Novartis Pharmaceuticals UK Ltd. REVOLADE (eltrombopag). Summary of Product Characteristics 2024;
3. Sobi Ltd. DOPTELET (avatrombopag). Summary of Product Characteristics 2024. 4. Grifols UK Ltd. TAVLESSE (Fostamatinib) Summary of Product Characteristics 2023.

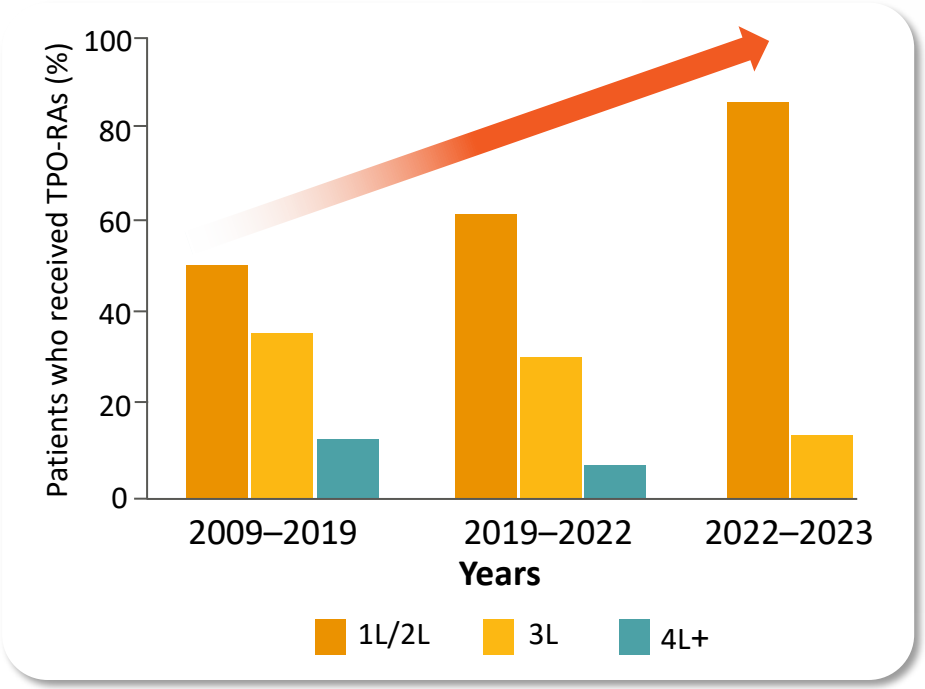
Efficacy and safety profiles of approved TPO-RAs are similar across ITP phases



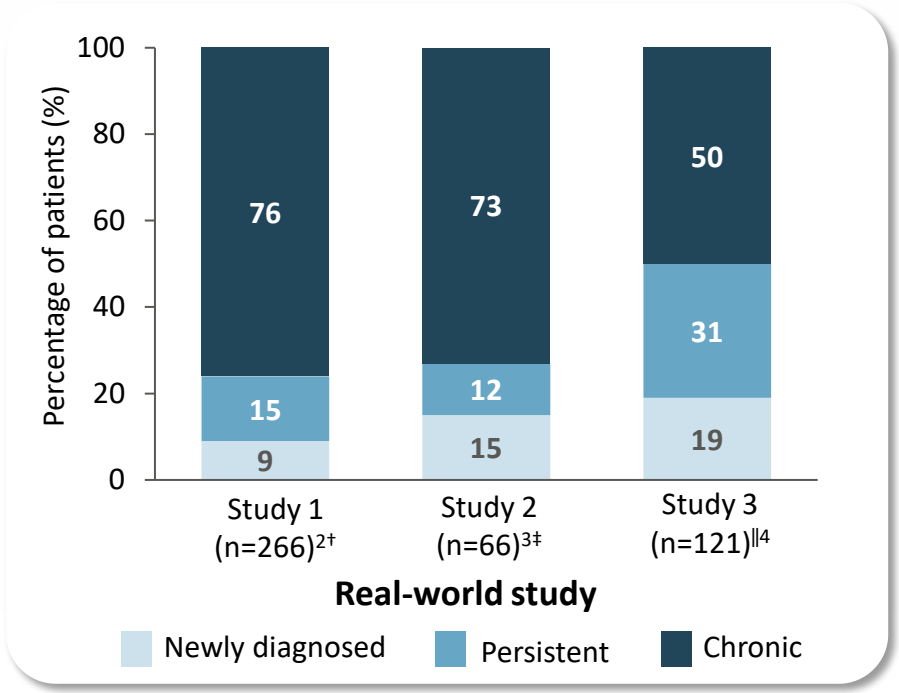
*R = PC ≥30 × 10^9/L; †CR = PC >100 × 10^9/L; ‡R = PC ≥50 × 10^9/L.
CR, complete response; ITP, immune thrombocytopenia; PC, platelet count; R, response; TPO-RA, thrombopoietin receptor agonist.
1. Lozano ML et al. *Expert Rev Hematol* 2020;13:1319–1332; 2. González-López TJ et al. *Int J Hematol* 2017; 106:508–516; 3. Virk ZM et al. *Am J Hematol* 2024;99:155–162.

Are TPO-RAs being used at this stage of ITP?

Line of treatment for first TPO-RA (Norwegian ITP registry)*[1]



ITP phase at avatrombopag initiation in three real-world studies[2–4]



TPO-RAs are increasingly used in first and second-line treatment

*Real-world use, effectiveness and safety of romiplostim, eltrombopag and avatrombopag in patients with ITP: Data from the Norwegian ITP registry; †Real-world study of avatrombopag in patients with ITP: Data from the Spanish ITP Group; ‡A multicentre real-life observational study in Madrid, Spain of avatrombopag in patients with ITP; ‖Real-world study of avatrombopag in patients with ITP who are intolerant or have inadequate response to eltrombopag or hetrombopag.
1/2/3/4L, first/second/third/fourth line; ITP, immune thrombocytopenia; ROM, romiplostim; TPO-RA, thrombopoietin receptor agonist.

1. Tomasello R et al. Presented at ASH 2023, Poster #3952; 2. Pascual-Izquierdo C et al. *Am J Hematol* 2024;99:2328–2339; 3. Pascual-Izquierdo C et al. *Br J Haematol* 2025;206:652–656; 4. Tian H et al. *Br J Haematol* 2024;205:2414–2124.

Are TPO-RAs associated with increased risk of thrombosis?

ITP Despite ITP being associated with bleeding, patients with ITP are also, at increased risk of both venous and arterial TEEs, even in the absence of treatment[1–5]

RCT evidence	Network meta-analysis of 14 multicentre RCTs Probability of TEEs with TPO-RA vs control[6]	Current RWE	TPO-RAs: TEEs per 100 patient-years
Romiplostim	OR 0.92; 95% CI 0.14–6.13; n=279; p = 0.93		**4.2–7.5**[1,7]
Eltrombopag	OR 2.32; 95% CI 0.64–8.47; n=521; p = 0.20		**2.7–5.9**[1,7]
Avatrombopag	OR 4.15; 95% CI 0.20–85.23; n=32; p = 0.36		**1.2**[8]

Further RWE: coming soon

No significant association between thrombosis and TPO-RAs in RCTs[1,6]

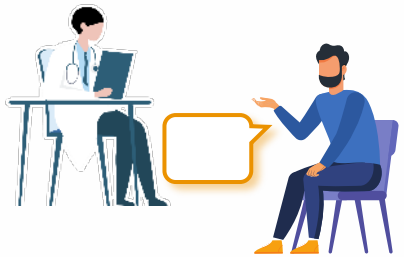
RWE: Low incidence of TEEs

Results of RCTs and RWE suggest there is no difference in the risk of thrombosis between TPO-RAs[1,6–8]
Overall, the risk of TEEs is modestly higher with TPO-RAs than with untreated ITP[1,2,7,8]

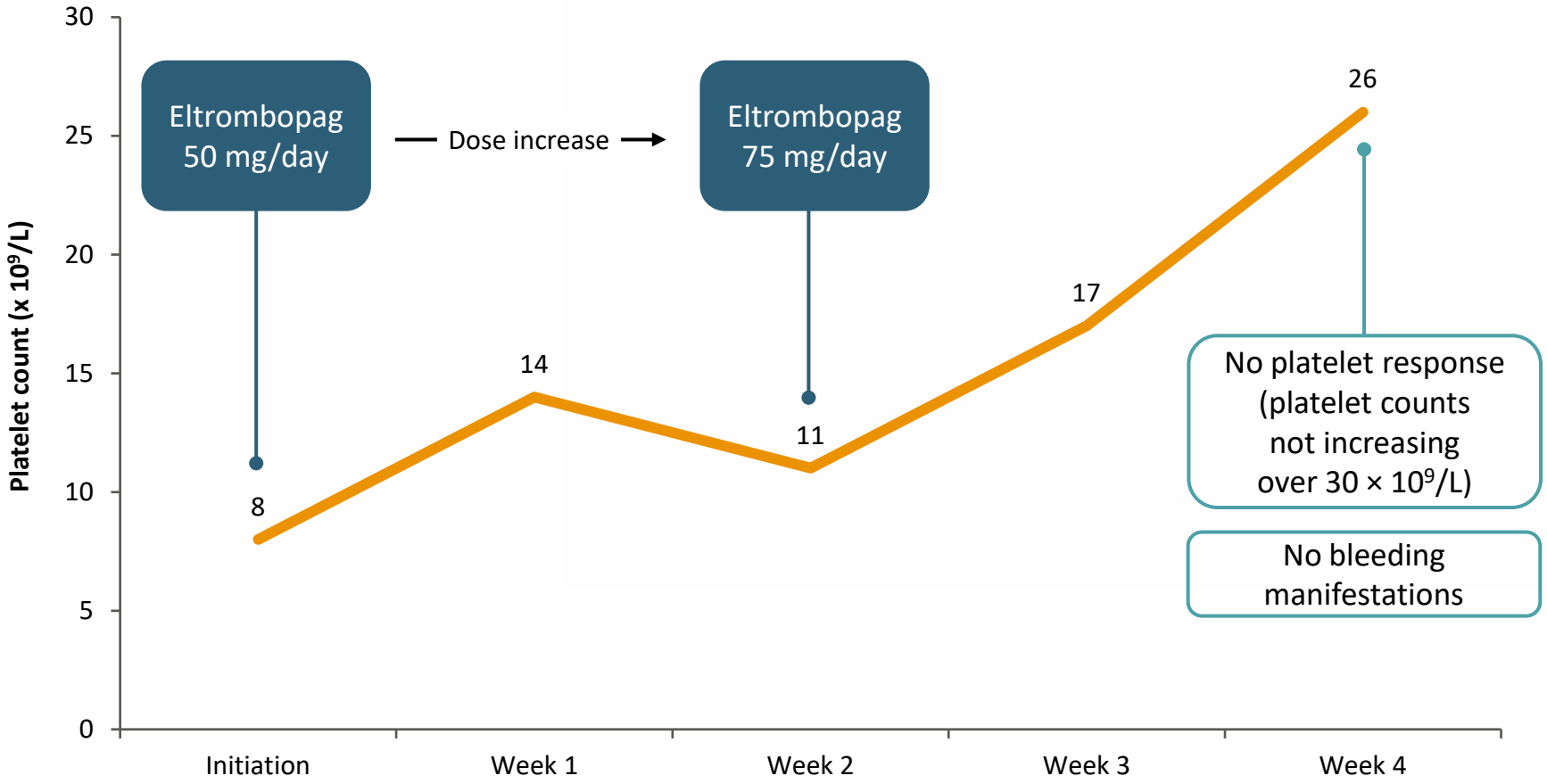
CI, confidence interval; ITP, immune mediated thrombocytopenia; OR, odds ratio; RCT, randomised controlled trial; RWE, real-world evidence; TEE, thromboembolic event; TPO-RA, thrombopoietin receptor agonist.

1. Swan D et al. *Br J Haematol* 2021;194:822–834; 2. Lambert C et al. *Eur Haematol* 2024;112(4):504–515; 3. Ali EA et al. *Cureus* 2022;14(10):e30279; 4. Goncalves I et al. *Res Pract Thromb Haemost* 2024;8(1):102342; 5. Rasheed M et al. *Blood* 2020;136(1):9–10. 6. Shen N et al. *Biomedical Reports* 2024;20(3):44; 7. Lozano ML et al. *Sci Rep* 2019;9:16680; 8. Virk ZM et al. *Am J Hematol* 2024;99(2):155–162.

It seems that there is more experience with both eltrombopag and romiplostim; I would prefer to start with eltrombopag



José's platelet response during treatment eltrombopag



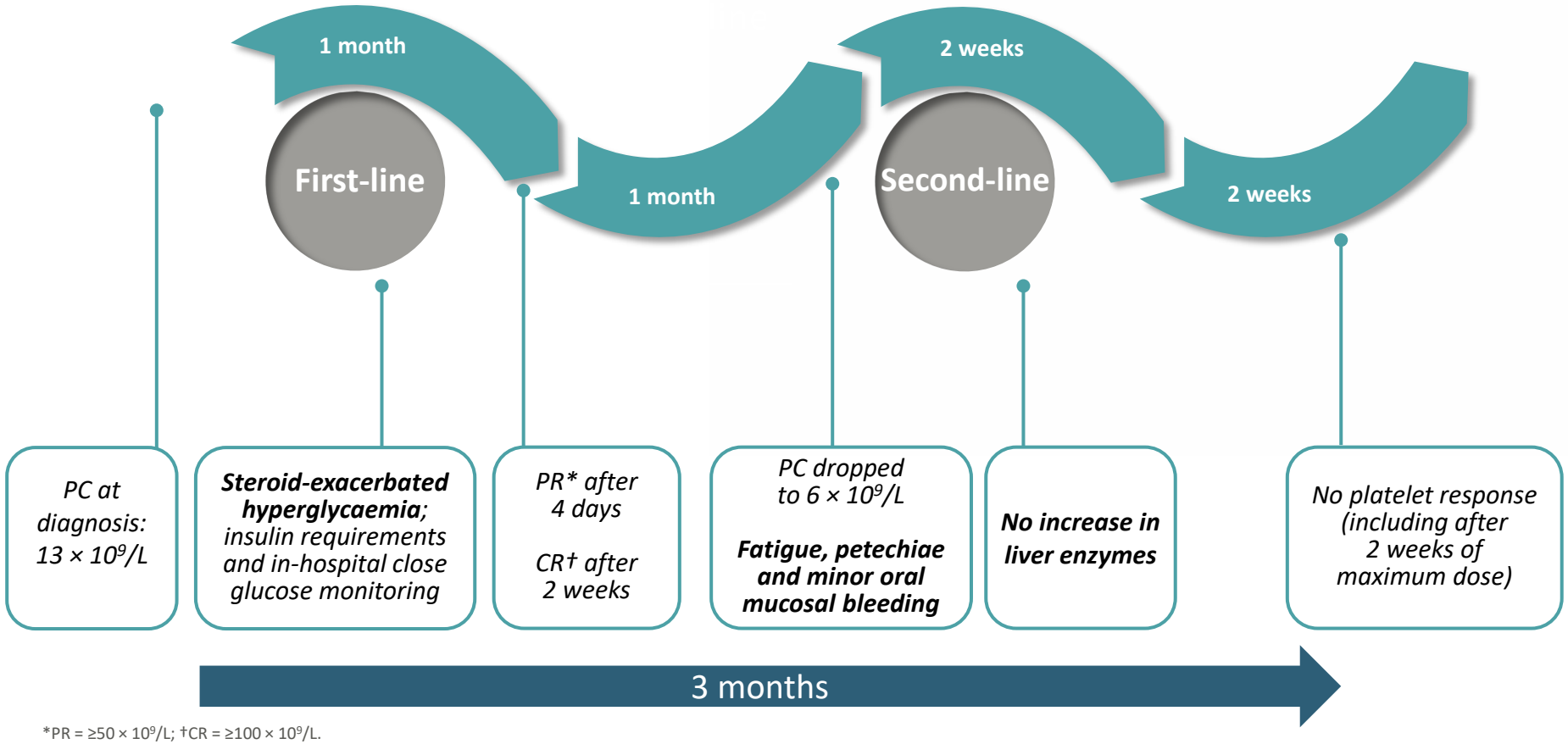
José: Treatment timeline

Prednisolone 1 mg/kg/day

Prednisolone tapered and discontinued

Eltrombopag 50 mg QD

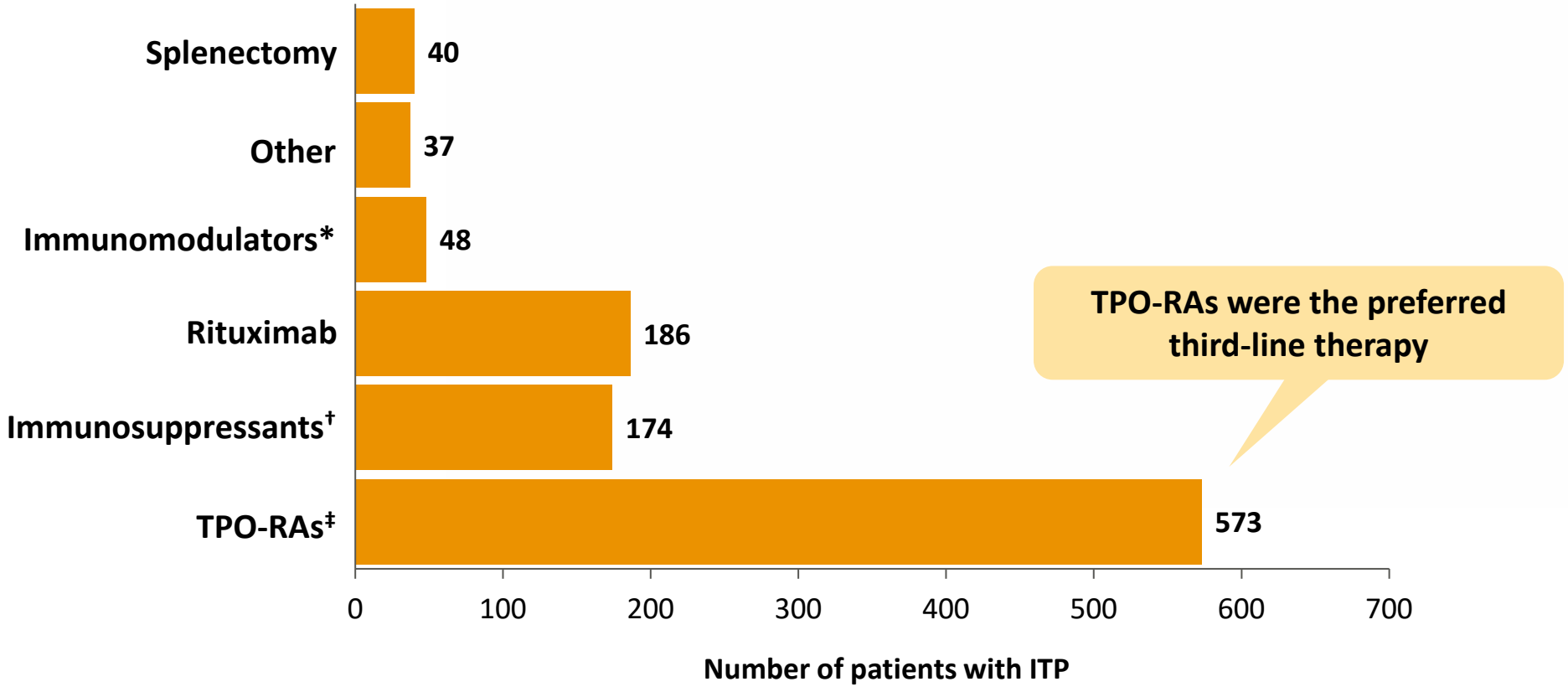
Eltrombopag 75 mg QD



*PR = ≥50 × 10^9/L; †CR = ≥100 × 10^9/L.
CR, complete response; PC, platelet count; PR, partial response; QD, once daily.

Switching to another TPO-RA is the most common subsequent treatment

Third-line treatments prescribed in Europe 2010–2022 (UK, France, Italy, Norway, Germany; N=1060)[1,2]



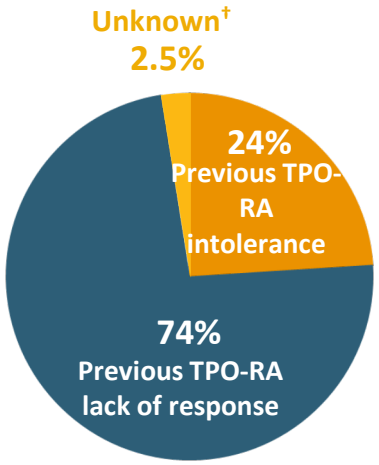
*Dapsone, danazol and hydroxychloroquine; †Azathioprine, MMF, cyclophosphamide, fostamatinib and cyclosporin; ‡Avatrombopag, romiplostim and eltrombopag.
MMF, mycophenolate mofetil; TPO-RA, thrombopoietin receptor agonist.

1. Moulis G. et al. Presented at the European Hematology Association (EHA), June 13–16, 2024, Madrid, Spain; P2239; 2. Moulis G. et al., European Consortium for ITP (ERCI) group (in press).

How likely is José to have a platelet response if I switch to another TPO-RA such as avatrombopag?

RWE: Switch to avatrombopag due to previous TPO-RA failure (n=121)*[1]

Reason for switch



Platelet response rate with avatrombopag

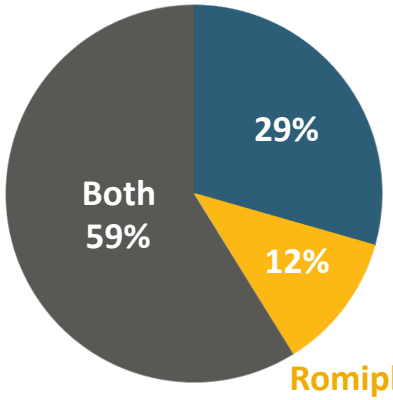
Median duration of treatment:
18 weeks
(range: 2–126)

R: 88%
Platelet count ≥30 × 10^9/L
P=0.002‡

CR: 65%
Platelet count ≥100 × 10^9/L
P=0.974‡

RWE from the Spanish ITP Group: Switch to avatrombopag in ITP (n=85)[2]

Previous TPO-RA



Platelet response rate with avatrombopag

Median prior treatments:
2 (IQR: 1–3)

R: 90%
Platelet count ≥50 × 10^9/L

More than 88% of patients had a platelet response when switched to avatrombopag[1,2]

*Failure due to intolerance or lack of response to treatment; †3 patients had unknown reasons for using avatrombopag, these patients all received first-line steroid therapy. ‡Previous TPO-RA intolerance group versus lack of response to previous TPO-RA group.
CR, complete response; IG, eltrombopag/hetrombopag intolerance group; ITP, immune thrombocytopenia; R, response; RWE, real-world evidence; TPO-RA, thrombopoietin receptor agonist.

1. Tian H et al. *Br J Haematol* 2024;205:2414–2424; 2. Pascual-Izquierdo C et al. *Am J Hematol* 2024;99:2328–2339.

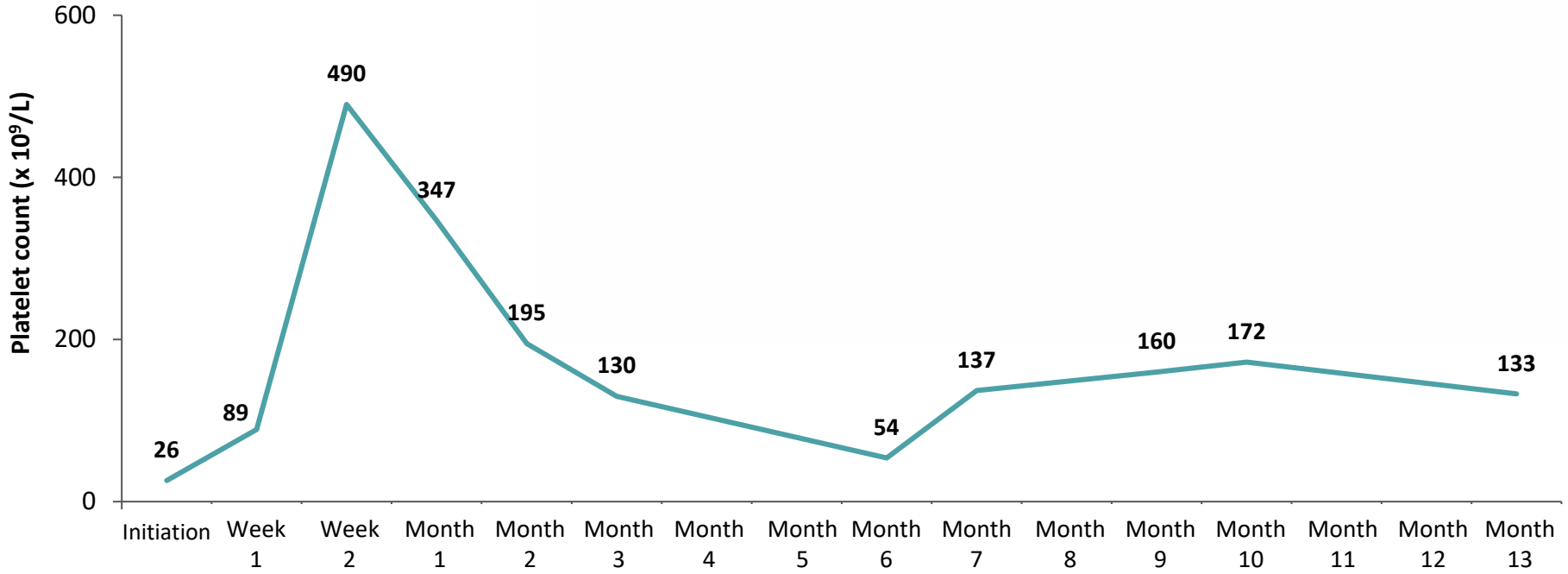
OK. Let's try switching to avatrombopag

José's platelet response with avatrombopag

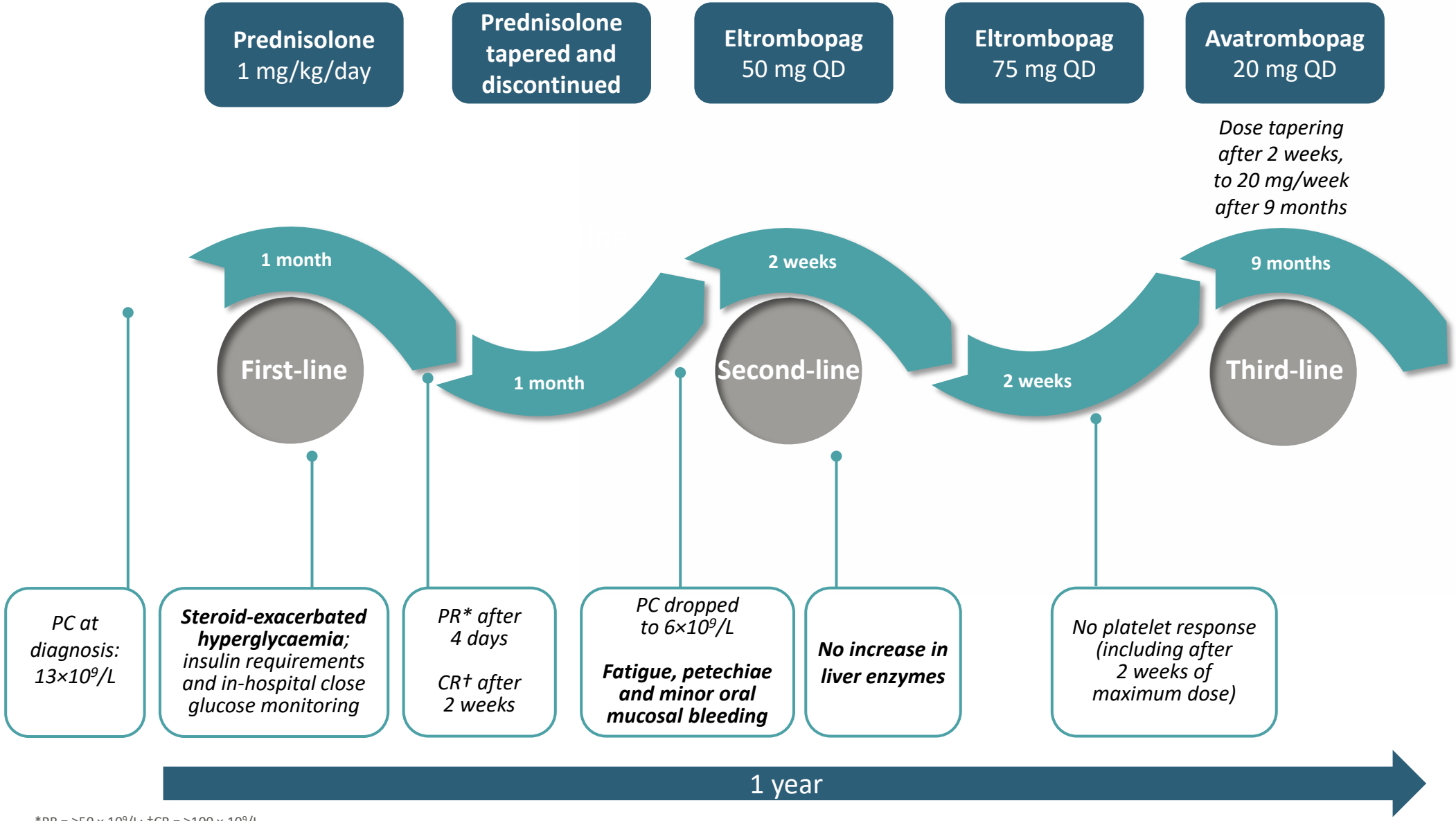
No. of avatrombopag 20 mg tablets per week

7 → 5 → 4 → 3 → 2 → 3 → 2 → 1

Dose tapering
Continued on 20 mg once weekly



José: Treatment timeline



*PR = ≥50 × 10^9/L; †CR = ≥100 × 10^9/L.
CR, complete response; PC, platelet count; PR, partial response; QD, once daily.

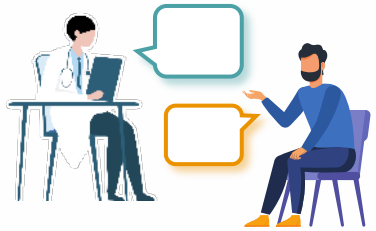
Will José need to take a TPO-RA indefinitely?

A definitive treatment duration has not been established and can be indefinite; it is unclear if remission can be achieved

	Phase 2 study, 2010–2013[1]	Phase 2 ESTIT study, 2016–2018[2]	Phase 2 TAPER study, 2018–2022[3]	Phase 4 STOPAGO study, 2017–2020[4]
Treatment	**Romiplostim**	**Eltrombopag**	**Eltrombopag**	**Eltrombopag/romiplostim**
Patients ≥18 years (n)	75	51	105	48†
ITP duration	≤6 months	≤12 months*	≥3 months	≥3 months
Treatment duration	≤12 months	6 months	Median exposure 5.6 months	Median exposure 1.6 years
SROT definition	PC ≥50 × 10^9/L for 6 months	PC ≥30 × 10^9/L for 6 months	PC ≥30 × 10^9/L until month 12	PC >30 × 10^9/L and no bleeding at Weeks 24 and 52
SROT	**32%**	**25%**	**31%**	**56%** (Week 24) **52%** (Week 52)
Bleeding	BEs in 8% patients with remission BEs in 37% patients without remission **No serious BEs** **Only one BE was considered treatment-related**	5 BEs reported	No BE: 58 patients (55.2%) Grade 1 BE: 7 patients (6.7%) Grade 2, 3 and 4 BE: 1 patient each (1.6%) WHO Grade 4 BE: 1 patient (1.6%)	BEs in 57% patients who relapsed after week 24 BEs in 61% patients who relapsed after week 52 **No severe BEs in patients who relapsed**

*Patients aged ≥18 years with newly diagnosed or persistent ITP;[2] †At TPO-RA initiation, 47% had more than 2 lines of treatment.[4]
BE, bleeding episode; ITP, immune thrombocytopenia; PC, platelet count; SROT, sustained response off treatment; W, week; WHO, World Health Organization.
1. Newland A et al. *Br J Haematol* 2016;172(2):262–273; 2. Lucchini E et al. *Br J Haematol* 2021;193(2):386–396; 3. Cooper N et al. *Am J Hematol* 2024;99:57–67; 4. Guillet S et al. *Blood* 2023;141(23):2867–2877.

How can I reach a point to discontinue TPO-RA treatment?



Factors that may increase the probability of treatment-free responses after discontinuation[1]

1. Shorter disease duration
2. Lower TPO-RA dose
3. No concomitant medication for ITP
4. Robust platelet response to TPO-RA

TPO-RA tapering strategy[1–3]

IF PC is:
>100 × 10^9/L
for 2–3 months
OR
50–100 × 10^9/L
for ≥6 months

→ Start dose tapering*

→ Decrease dose every 2–3 months†

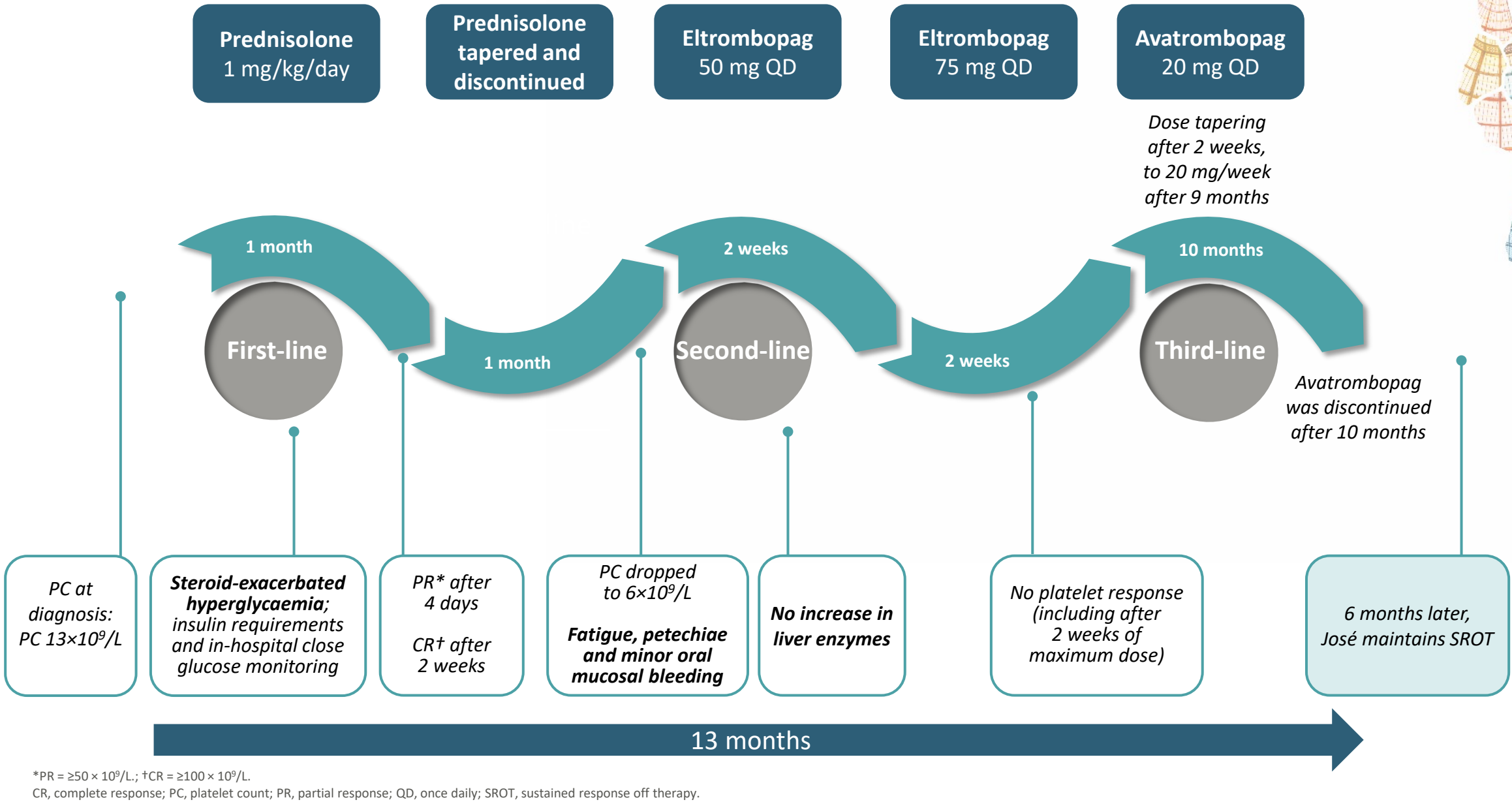
→ **Platelets >50 × 10^9/L:** Reduce dose until withdrawal

→ **Platelets <30–50 × 10^9/L:** Increase dose

Monitoring intervals no longer than 4 weeks

*Taper dose of TPO-RAs for 2–3 months before attempting to discontinue; †Taper dose of eltrombopag by 25 mg every 2 weeks down to a minimum dose of 25 mg, then administer 25 mg EOD for 2 weeks then discontinue, taper the dose of romiplostim by 1 mcg/kg/week every 2 weeks until a dose of 1 mcg/kg/week is reached then administer a 1 mcg/kg dose once every other week before discontinuing.
EOD, every other day; ITP, immune thrombocytopenia; PC, platelet count; TPO-RA, thrombopoietin receptor agonist.
1. Clinical experience of Dr Monica Carpenedo, Dr Maria Lozano and Dr Waleed Ghanima; 2. Zaja F. *Blood Rev* 2020;41:100647; 3. Barlassina A et al. *Platelets* 2023;34(1):2170999.

José: Treatment timeline



*PR = ≥50 × 10^9/L.; †CR = ≥100 × 10^9/L.
CR, complete response; PC, platelet count; PR, partial response; QD, once daily; SROT, sustained response off therapy.

Patient case 1

José: Summary

- Patient priority: Maintain an active lifestyle that is minimally impacted by ITP (travel, sports)
- Initially treated with corticosteroids as first-line therapy
- Required TPO-RA in the first 3 months from diagnosis
- No response to maximum-dose eltrombopag, had a complete response to avatrombopag after treatment switch
- Avatrombopag was progressively tapered and discontinued after 10 months of treatment
- Currently, after 6 months off therapy, platelet counts remain stable and no bleeding symptoms have been reported
- Undergoes regular monitoring every 2–3 months, with no impact on his daily activities

ITP, immune mediated thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.

Facing a patient with refractory ITP – when, why, and how to treat

Dr Waleed Ghanima

Oslo, Norway

Facing a patient with refractory ITP – when, why, and how to treat

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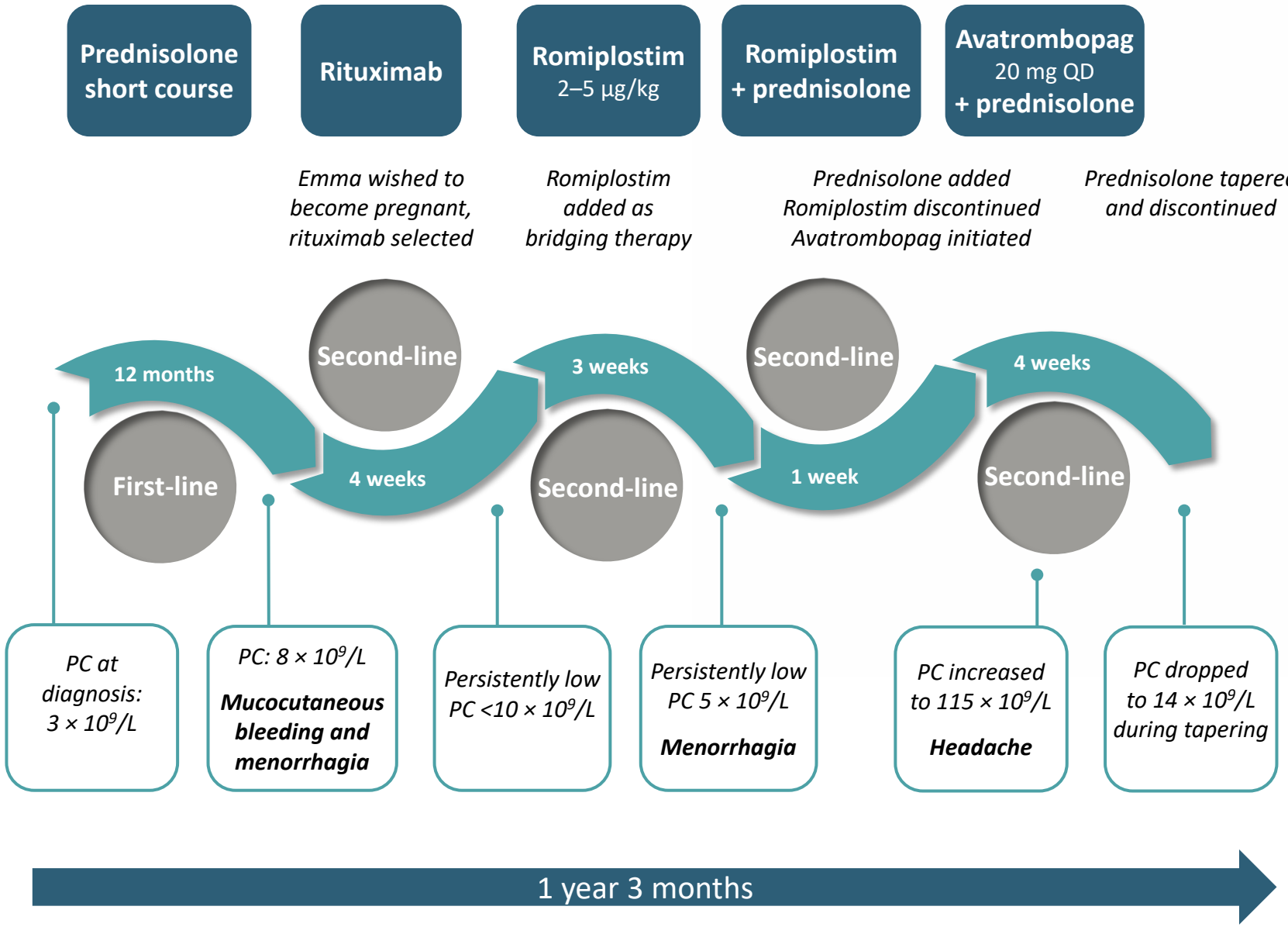
Patient case 2

Emma

- 23-year-old, female, Jehovah's Witness, engineer
- No concurrent medication
- Diagnosed with ITP 12 months ago with a platelet count of 3×10^9 /L
- Mucocutaneous bleeding, heavy menstrual bleeding
- CBC: Hb 11.4 g/dL, WBC 4×10^9/L, Neutrophil 3.3×10^9/L
- Anti platelet GP antibodies: Positive anti IIb/IIIa antibodies
- Microbiology: Negative serology

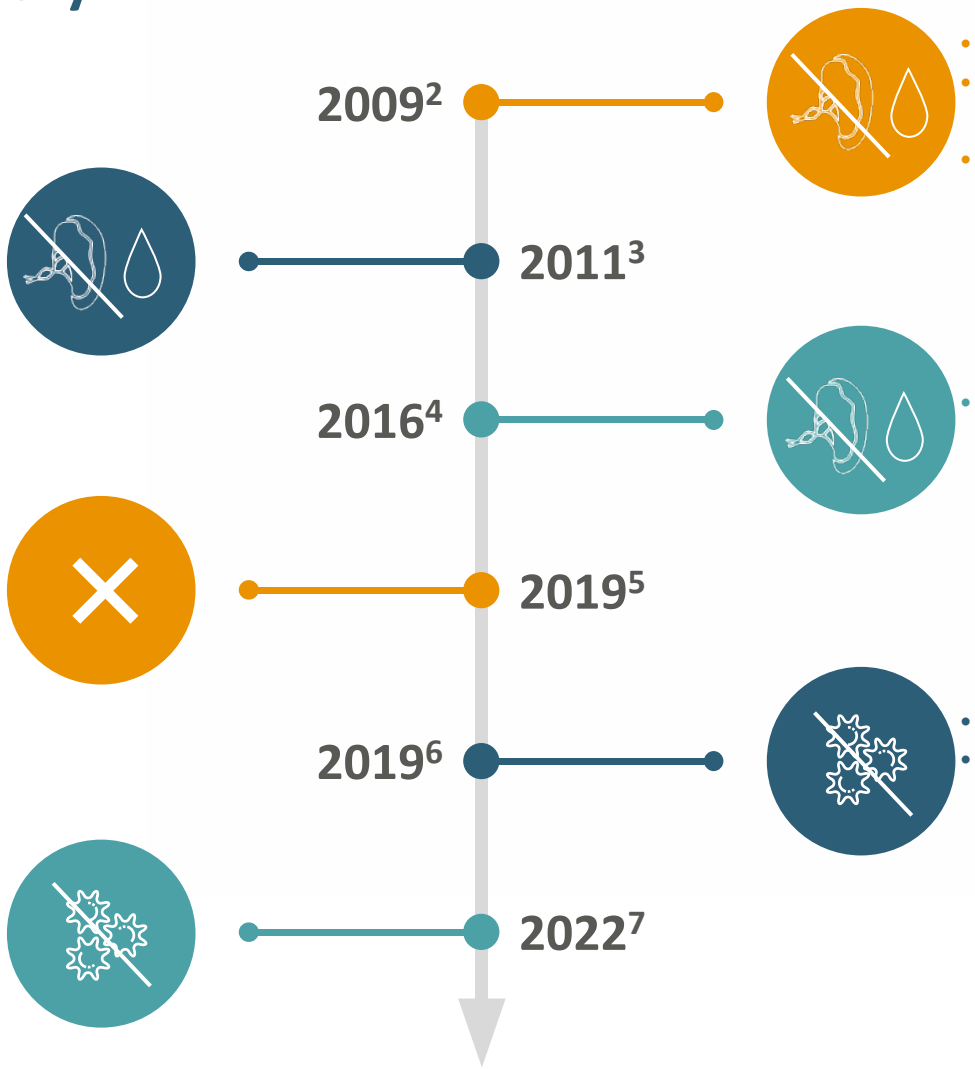
CBC, complete blood count; GP, glycoprotein; Hb, haemoglobin; ITP, immune mediated thrombocytopenia; WBC, white blood cell.

Emma: Treatment timeline



PC, platelet count; QD, once daily.

Does Emma have refractory ITP?[1]



- Failed/relapsed after splenectomy
- Bleeding symptoms/risk of bleeding requiring treatment
- Temporary corticosteroids/IVIg response

- Bleeding risk requiring treatment after splenectomy
- Temporary corticosteroids/IVIg response
- Exclude other causes of thrombocytopenia

- Bleeding risk requiring treatment after splenectomy*

- Refractory ITP was not defined; patients will eventually achieve a haemostatically effective platelet count without splenectomy

- No platelet count response to ≥2 treatments
- No single medication raises platelet count and reduces bleeding

- Persistently 'low'† platelet counts despite all safe conventional therapies, regardless of bleeding

*Or in patients unable/unwilling to undergo splenectomy; †The threshold for 'low' platelet count varies based on age, comorbidities, and therapies.
ITP, immune thrombocytopenia, IVIg, intravenous immunoglobulin; TPO-RA, thrombopoietin receptor agonist.
1. Arnold DM et al. *Br J Haematol* 2023;203:23–27; 2. Rodeghiero F et al. *Blood* 2009;113(11):2386–2393; 3. Neunert C et al. *Blood* 2011;117(16):4190–4207; 4. Cuker A and Neunert C. *Blood* 2016;128(12):1547–1554;
5. Provan D et al. *Blood Advances* 2019;3(22):3780–3817; 6. Miltiadous O et al. *Blood* 2019;135(7):472–490; 7. Vianelli N et al. *Ann Hematol* 2022;101:963–978.

How often are patients with ITP exposed to multiple lines of treatment?

Frequency of exposure to multiple lines of treatment

Patient group	McMaster ITP registry (N=531) (primary ITP n=408; secondary ITP n=123)	Norwegian ITP registry (N=255) (primary ITP n=236; secondary ITP n=19)
First-line + any second-line	225 (42.0%)	116 (45.5%)
First-line + rituximab + TPO-RA	40 (7.5%)	28 (11.0%)
First-line + rituximab + TPO-RA + splenectomy	25 (4.7%)	8 (3.1%)
First-line + rituximab + TPO-RA + any immunosuppressant	30 (5.6%)	4 (1.6%)
First-line + rituximab + TPO-RA + any immunosuppressant + splenectomy	**20 (3.8%)**	**1 (0.4%)**

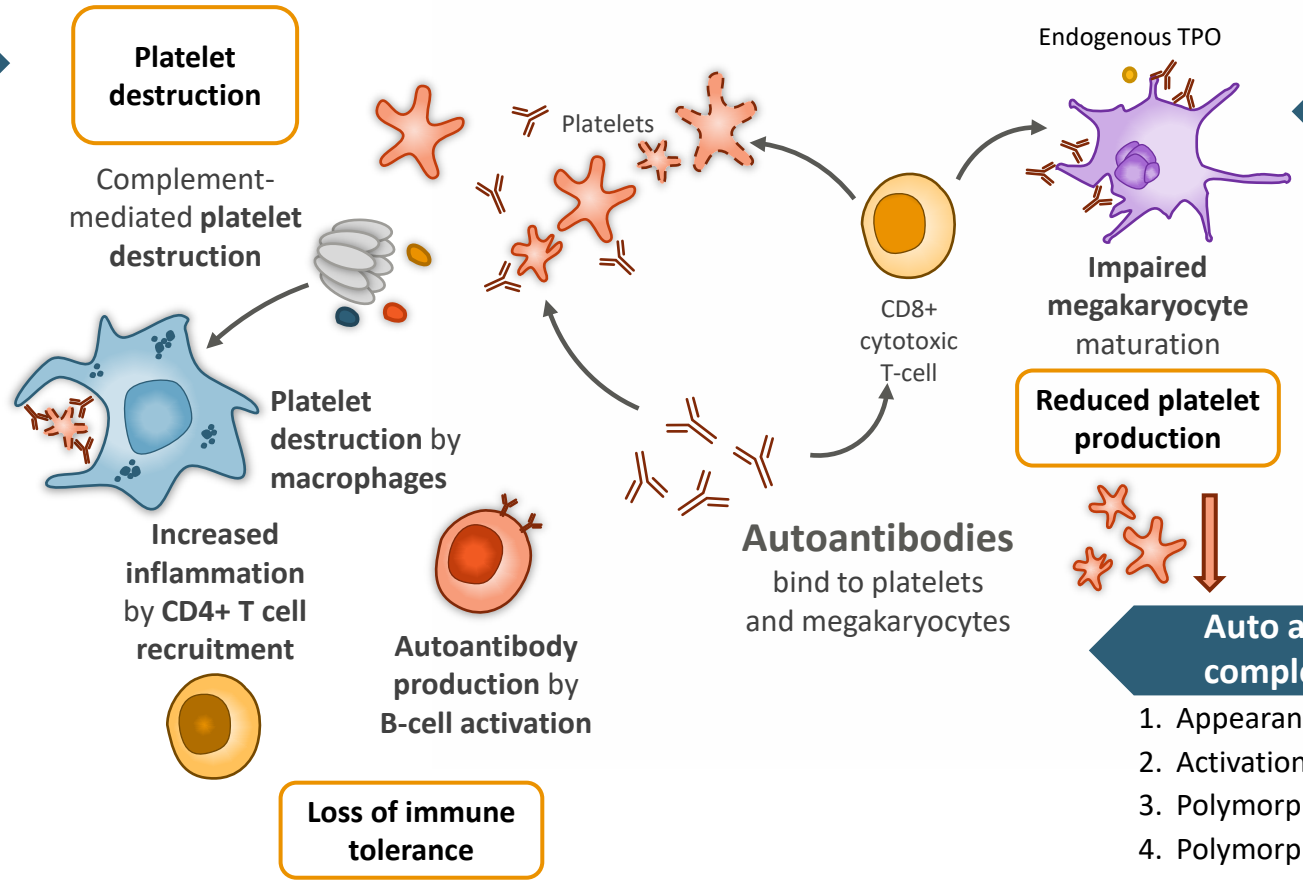
The proportions of patients with refractory ITP who were exposed to multiple lines of treatment were similar across both registries

ITP, Immune thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.
Arnold DM et al. *Br J Haematol* 2023;203:23–27.

Why does ITP become refractory?

T-cell related mechanisms

1. Deficiencies in Treg cell number and suppressor function
2. Increased Th1/Th2 and T-cell 1/T-cell 2 responses, increased Tc17 cells and T-follicular helper cells
3. Reduction in T-cell receptor diversity
4. Expanded clones of activated terminally differentiated CD8+ effector memory cells



Mechanisms related to platelet production

1. Enhanced apoptosis
2. Defects in mesenchymal stem cells that release stromal-derived factor 1, which supports megakaryocyte development

Auto antibodies and complement-related mechanisms

1. Appearance of long-lived plasma cells
2. Activation of complement system
3. Polymorphisms in FcR-γIIb and FcR-γIIIa
4. Polymorphisms in pro-and anti-inflammatory cytokines

There are multiple mechanisms that lead to refractory ITP with patients needing alternative or additional therapies

CD, cluster of differentiation; FcR, Fc receptor; ITP, immune thrombocytopenia; Th, T-helper; Treg, regulatory T cell.
Cines D. *Br J Haematol* 2023;203:10–16.

What do I need to consider when managing a patient with refractory ITP?

Considerations when managing the treatment of patients with refractory ITP

1. Reassessing diagnosis to exclude other causes of ITP[1]
2. Redefining objective (platelet count threshold/bleeding risk)[2]
3. Avoiding over treatment[2]
4. Assessing HRQoL while treating the patient[2]
5. Patient's involvement[2]

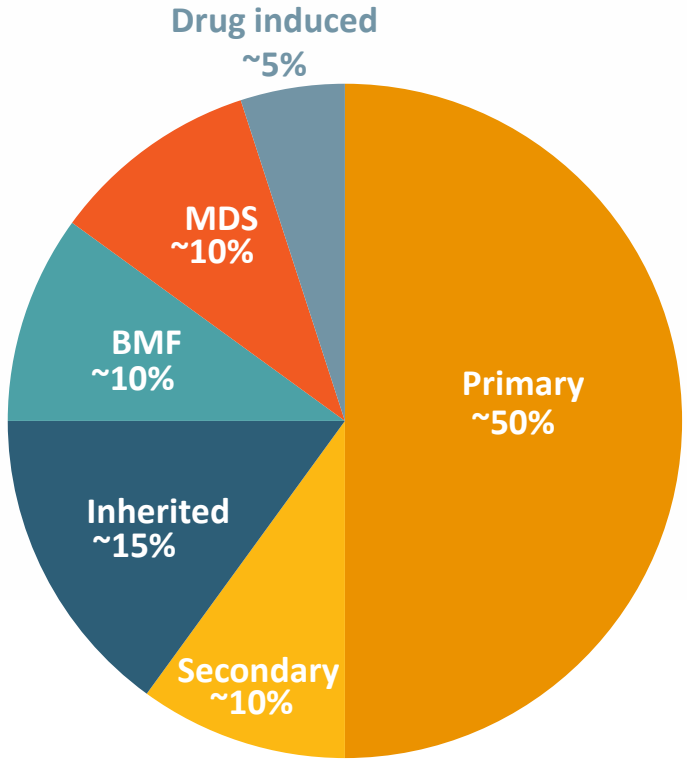
HRQoL, health-related quality of life; ITP, immune thrombocytopenia.

1. Miltiadous O et al *Blood* 2020;135(7):472–490; 2. Al-Samkari H & Neufeld EJ. *Br J Haematol* 2023;203:65–78.

What additional investigations could I include for Emma?[1,2]

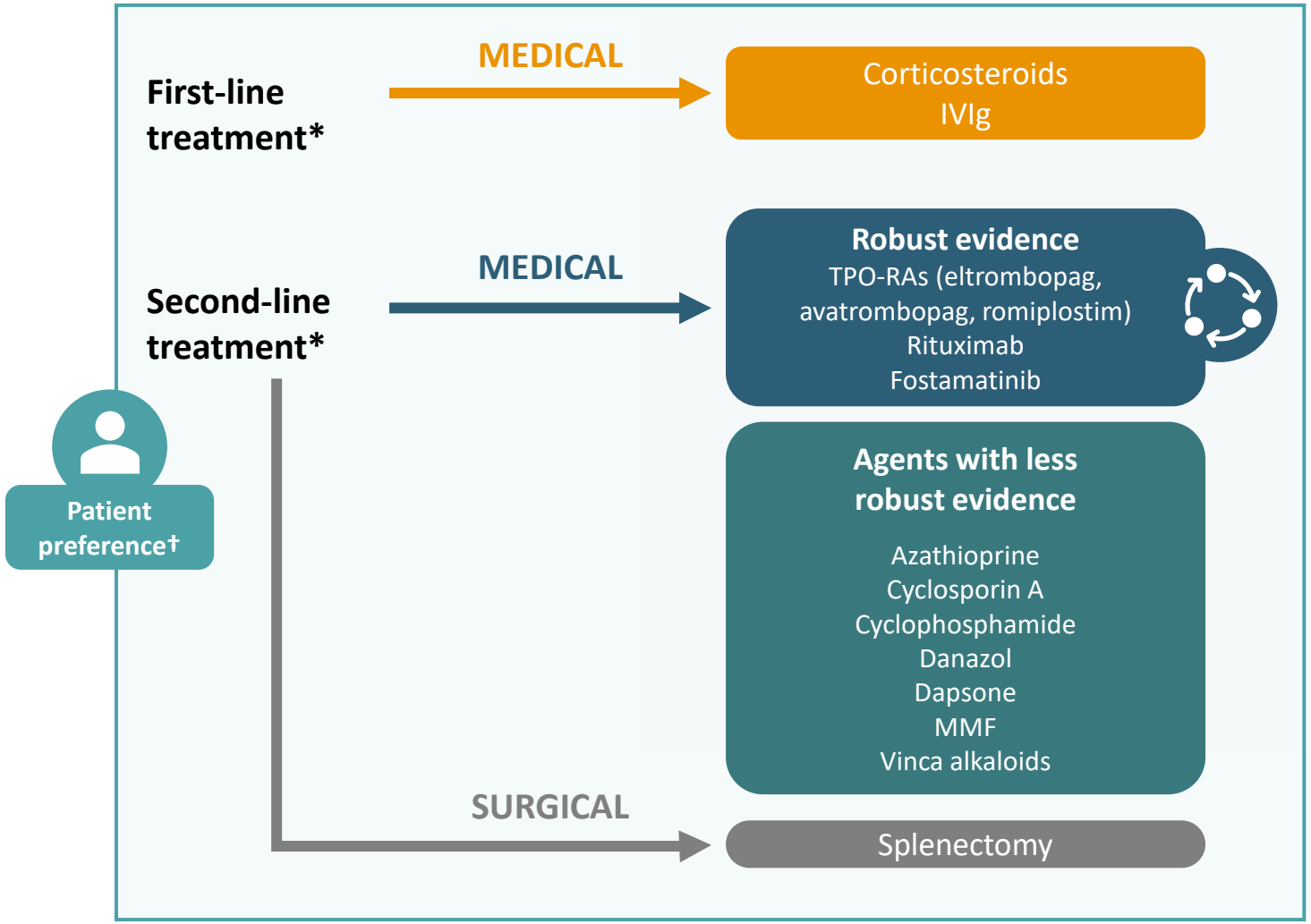
1. Immunoglobulins (IgM, IgG, IgA) and electrophoresis
2. Infectious work-up: CMV, HCV, HIV PCR
3. *Helicobacter pylori* stool antigen or urea breath test
4. ANA
5. Bone marrow aspirate/biopsy, flow cytometry and cytogenetics
6. Genetic testing (inherited thrombocytopenia and/or bone marrow failure syndromes)

Estimated incidence of ITP types in patients with refractory ITP[1]



ANA, anti-nuclear antibody; BMF, bone marrow failure; CMV, cytomegalovirus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; ITP, immune thrombocytopenia; MDS, myelodysplastic syndrome; PCR, polymerase chain reaction.
1. Miltiadous O et al *Blood* 2020;135(7):472–490; 2. Clinical experience of Dr Waleed Ghanima.

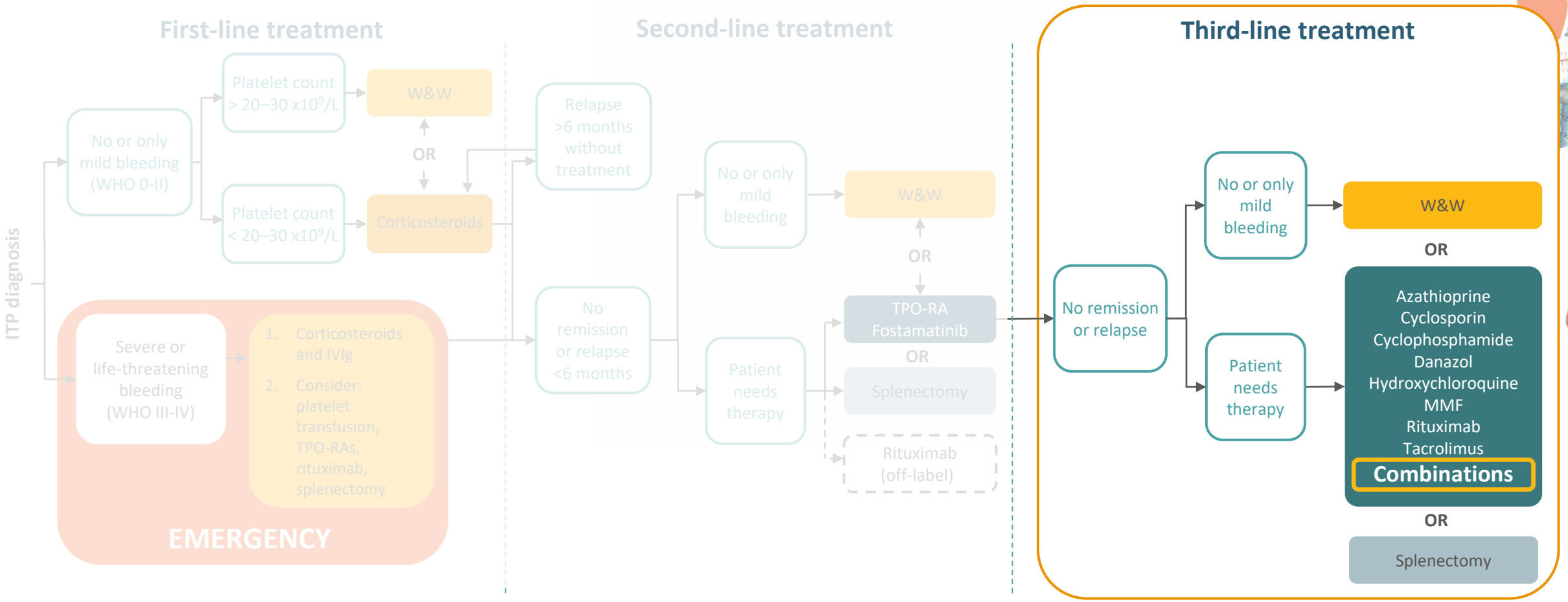
Current guidelines recommend a multi-line treatment approach for adult ITP[1–4]



A number of these treatment options are used off-label for the treatment of ITP, but in line with international guidelines.
*Watch and wait only if no or mild bleeding with a platelet count of >20–30 × 10^9/L; †Patient preference must be considered when discussing treatment options in a shared-decision making approach.
ITP, immune thrombocytopenia; IVIg, intravenous immunoglobulin; MMF, Mycophenolate mofetil; TPO-RA, thrombopoietin receptor agonist.
1. Provan D et al. *Blood Adv* 2019;3:3780–3817; 2. Neunert C et al. *Blood Adv* 2019;3:3829–3866; 3. Matzdorff A et al. *Oncol Res Treat* 2018;41 Suppl 5:1–30; 4. Matzdorff A et al. *Oncol Res Treat* 2023;46:5–44.

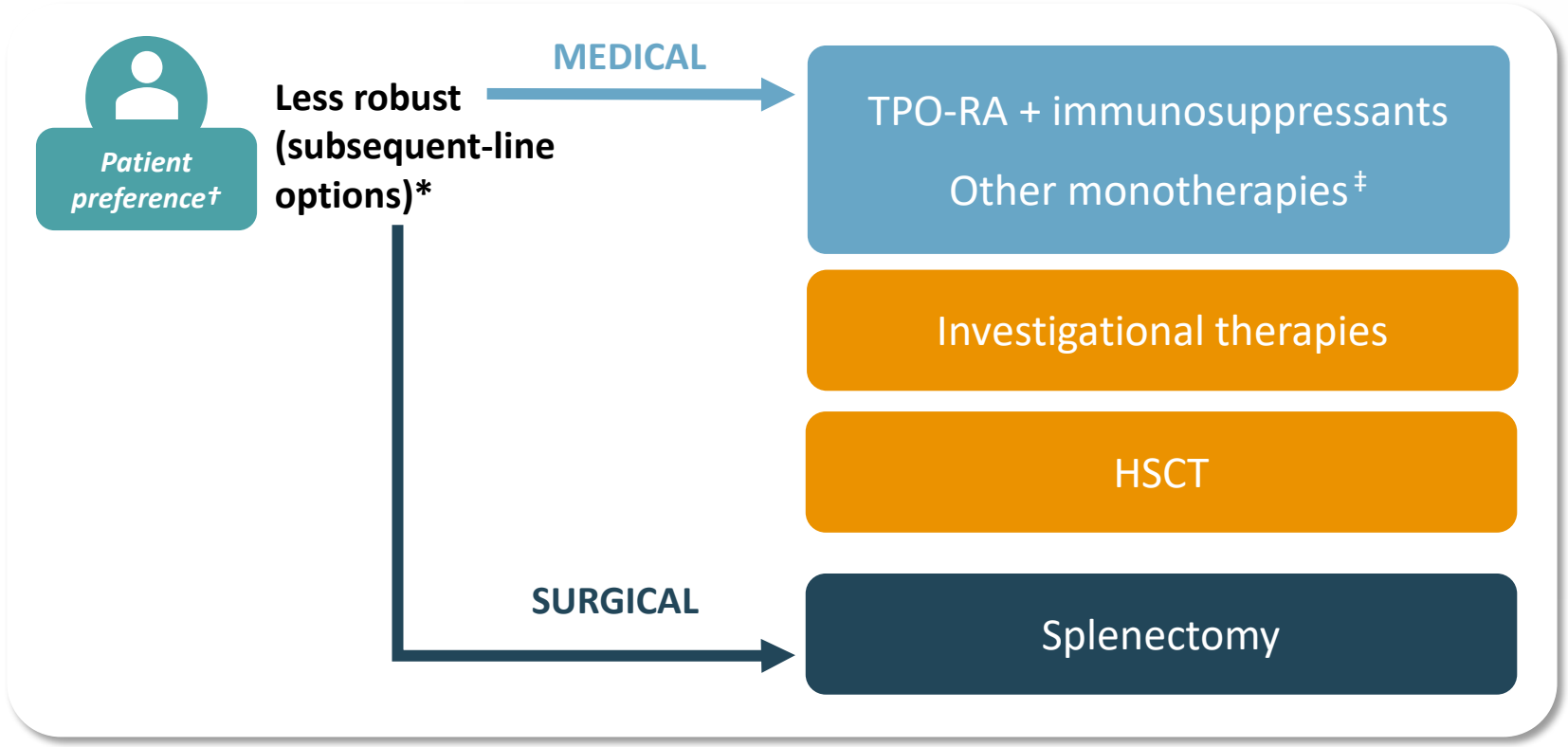
There are many third-line therapies available, and one option is to use combination therapies

Expert report on ITP: Current diagnostics and treatment recommendations in Austria, Germany, and Switzerland



ITP, immune thrombocytopenia; MMF, mycophenolate mofetil; TPO-RA, thrombopoietin receptor agonist; W&W, Watch and Wait; WHO, World Health Organization.
Matzdorff A et al. *Oncol Res Treat* 2023;46:5–44.

Current guidelines and multi-line approach to treatment of adult ITP: Refractory therapies[1–4]



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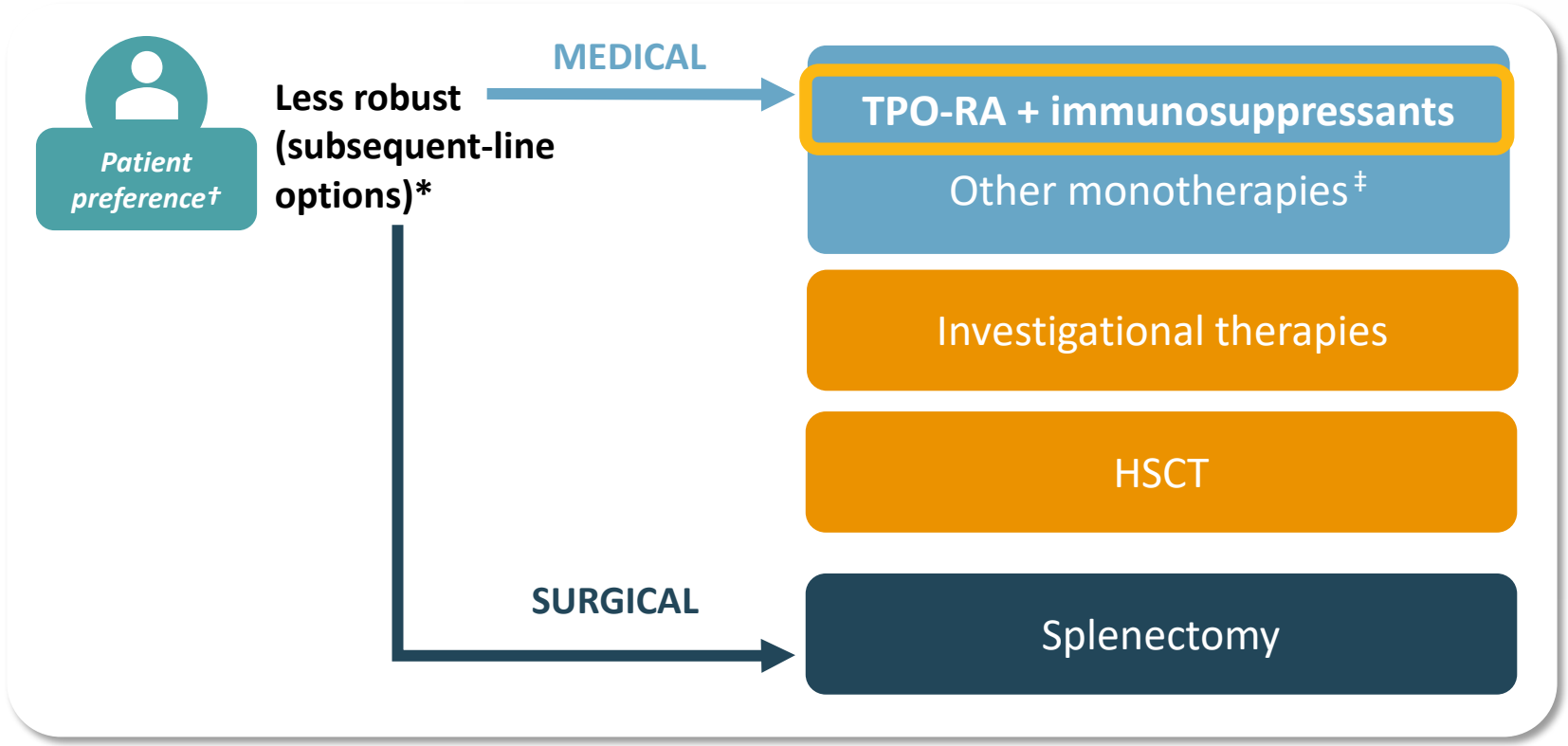
HSCT, Hematopoitic stem-cell transplantation; ITP, immune thrombocytopenia; MMF, mycophenolate mofetil; TPO-RA, thrombopoietin receptor agonist.
1. Provan D et al. *Blood Adv* 2019;3:3780–3817; 2. Neunert C et al. *Blood Adv* 2019;3:3829–3866; 3. Matzdorff A et al. *Oncol Res Treat* 2018;41 Suppl 5:1–30; 4. Matzdorff A et al. *Oncol Res Treat* 2023;46:5–44.

Current guidelines and multi-line approach to treatment of adult ITP: Combination therapies[1–4]



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What evidence exists to support combining TPO-RAs + immunosuppressants?

French multicentre retrospective study, 1990–2014[1]

Multi-refractory ITP: Severe, chronic ITP not responding to rituximab, splenectomy*, and TPO-RAs available in France (eltrombopag and romiplostim) at maximal approved dose

- IVIg, corticosteroid or no treatment (n=12) → 12 NR, 3 deaths
- Immunosuppressant† (n=14) → **1 CR;** 13 NR, 2 deaths
- **TPO-RA + immunosuppressant (n=10)** → **5 CR; 2 R**, 3 NR
- TPO-RA + IVIg/corticosteroid (n=5) → 5 NR

Single agent: 1/14 (7%) responded

Combination: 7/10 (70%) responded

Single centre retrospective study (French update), 2009–2021[2]

Multi-refractory ITP: Persistent/chronic ITP not responding to rituximab, splenectomy*, and TPO-RAs available in France (eltrombopag and romiplostim) at maximal approved dose

TPO-RA + immunosuppressant (N=39) → **24 CR; 6 R**, 9 NR

TPO-RAs
- Eltrombopag (n=20)
- Romiplostim (n=19)

Immunosuppressants
- MMF (n=21)
- Azathioprine (n=14)
- Cyclophosphamide (n=2)
- Cyclosporin A (n=1)
- Everolimus (n=1)

30/39 (77%) responded

Median follow-up of 21 months:
19/30 (63%) responded
11/30 (37%) relapsed

19 patients‡ stopped combination therapy§

Some patients with multi-refractory ITP can **experience long-lasting responses with this combination therapy**

*Except if splenectomy was contraindicated or refused by the patient; †Cyclophosphamide, n=1; azathioprine, n=4; cyclosporine, n=1; mycophenolate mofetil, n=2; alemtuzumab, n=1; high-dose cyclophosphamide followed by autologous HSCT, n=1; ‡9 CR, 2 R, 8 NR; §Therapy was stopped because of failure/relapse in 11 patients, CR in 5 patients, adverse event in 1 patient, pregnancy in 1 patient and Waldenstrom's macroglobulinemia progression in 1 patient.
CR, complete response; HSCT, hematopoitic stem-cell transplantation; ITP, immune thrombocytopenia; IVIg, intravenous immunoglobulin NR, no response; R, response; TPO-RA, thrombopoietin receptor agonist.
1. Mahévas M et al. *Blood* 2016;128:1625–1630; 2. Crickx E et al. *Br J Haematol* 2023;202:883–889.

Avatrombopag + fostamatinib can be effective in patients with multi-refractory ITP

Retrospective study of avatrombopag + fostamatinib in patients with multi-refractory ITP (N=18*)

TPO-RA + immunosuppressant:
Avatrombopag
280 mg/week
+ fostamatinib
2100 mg/week

8 CR; 7 R†

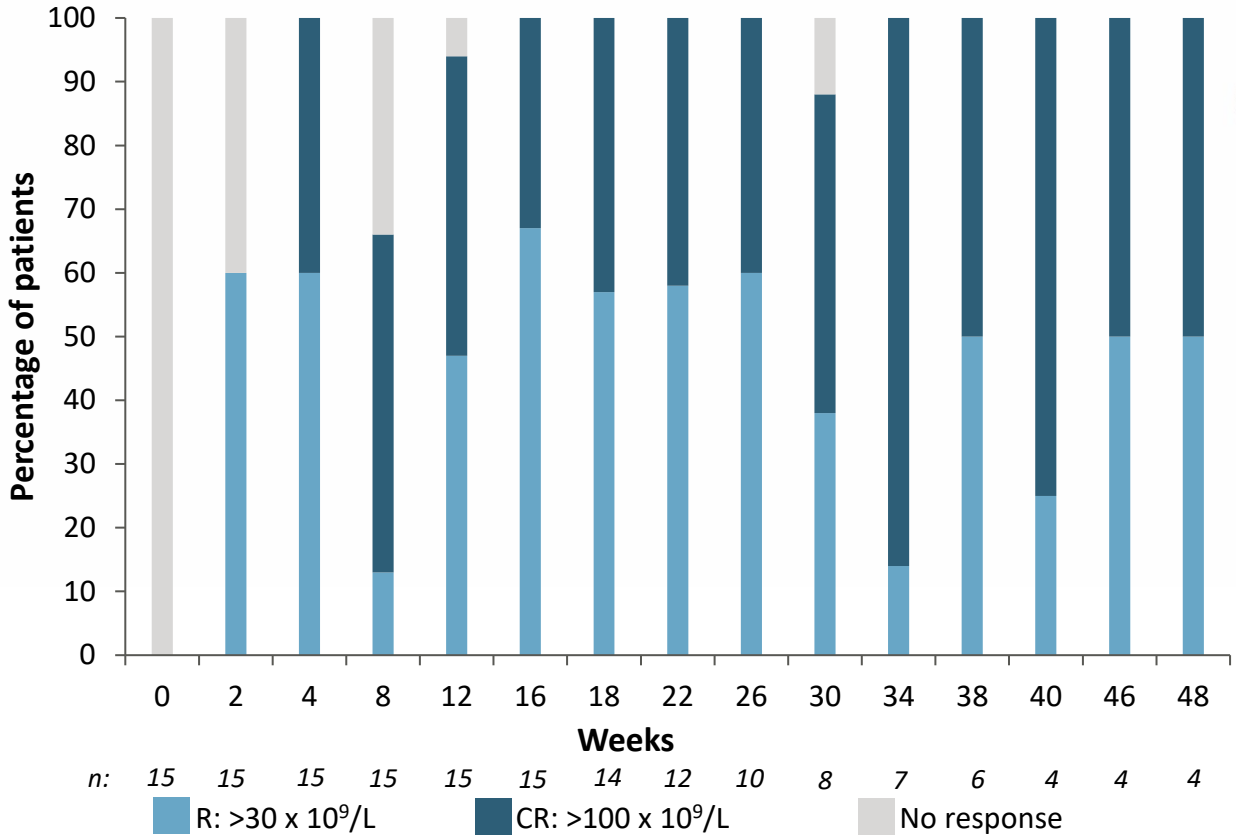
15/18 (83%) achieved response

Mean prior treatments **5** (IQR: 4–7)

Median time to CR **15 days** (IQR: 8–35)

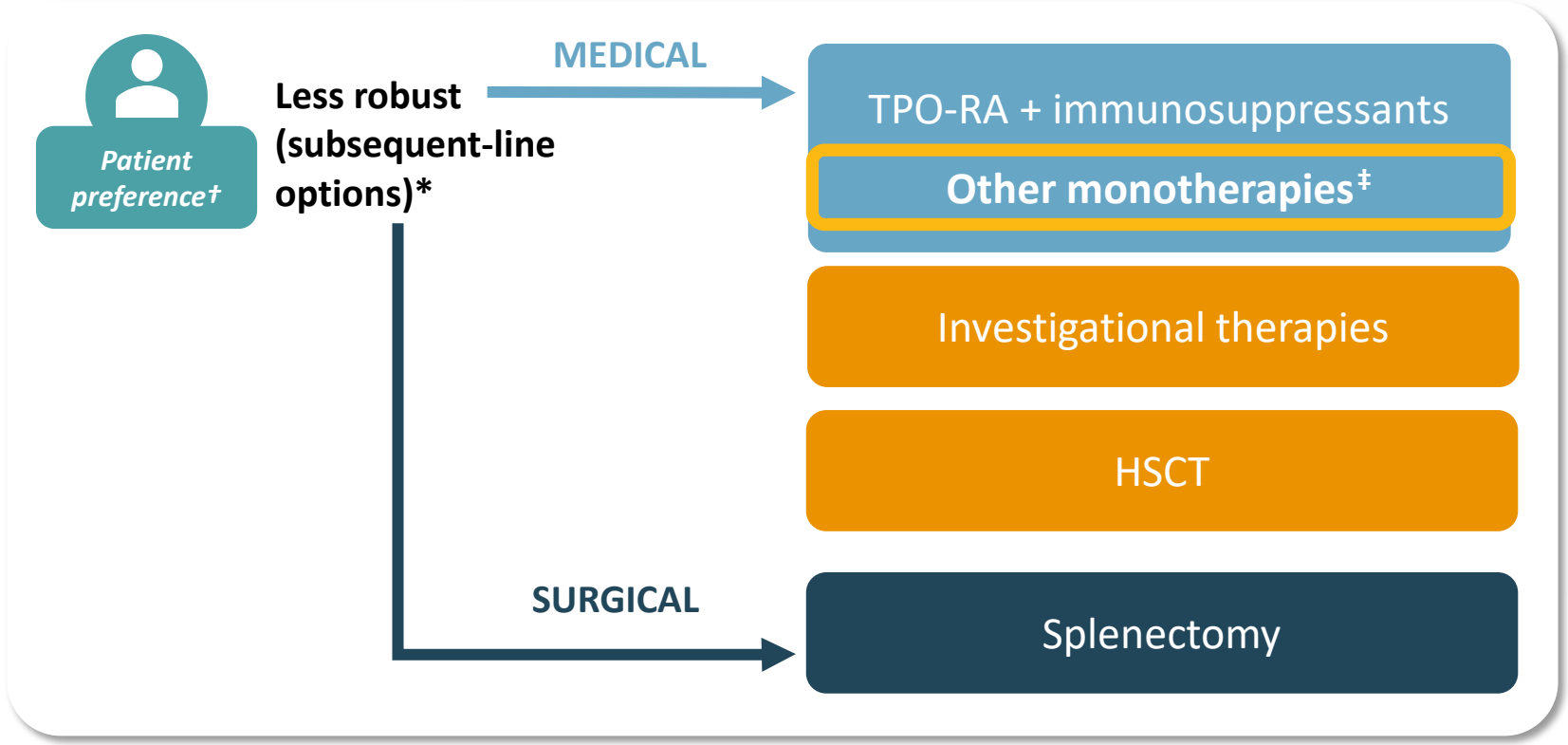
5/15 (27%) relapsed during dose tapering

Platelet count in patients who experienced response (N=15)



*12 patients with chronic ITP, 5 patients with persistent ITP and 1 patient with newly diagnosed ITP; †R was defined as a platelet count = 30–100 × 10^9/L and CR was defined as a platelet count >100 × 10^9/L.
CR, complete response; IQR, interquartile range; ITP, immune thrombocytopenia; OR, odds ratio; R, response.
Mingot-Castellano ME et al. *Br J Haematol* 2024;205(4):1551–1555.

Current guidelines and multi-line approach to treatment of adult ITP: Other monotherapies[1–4]



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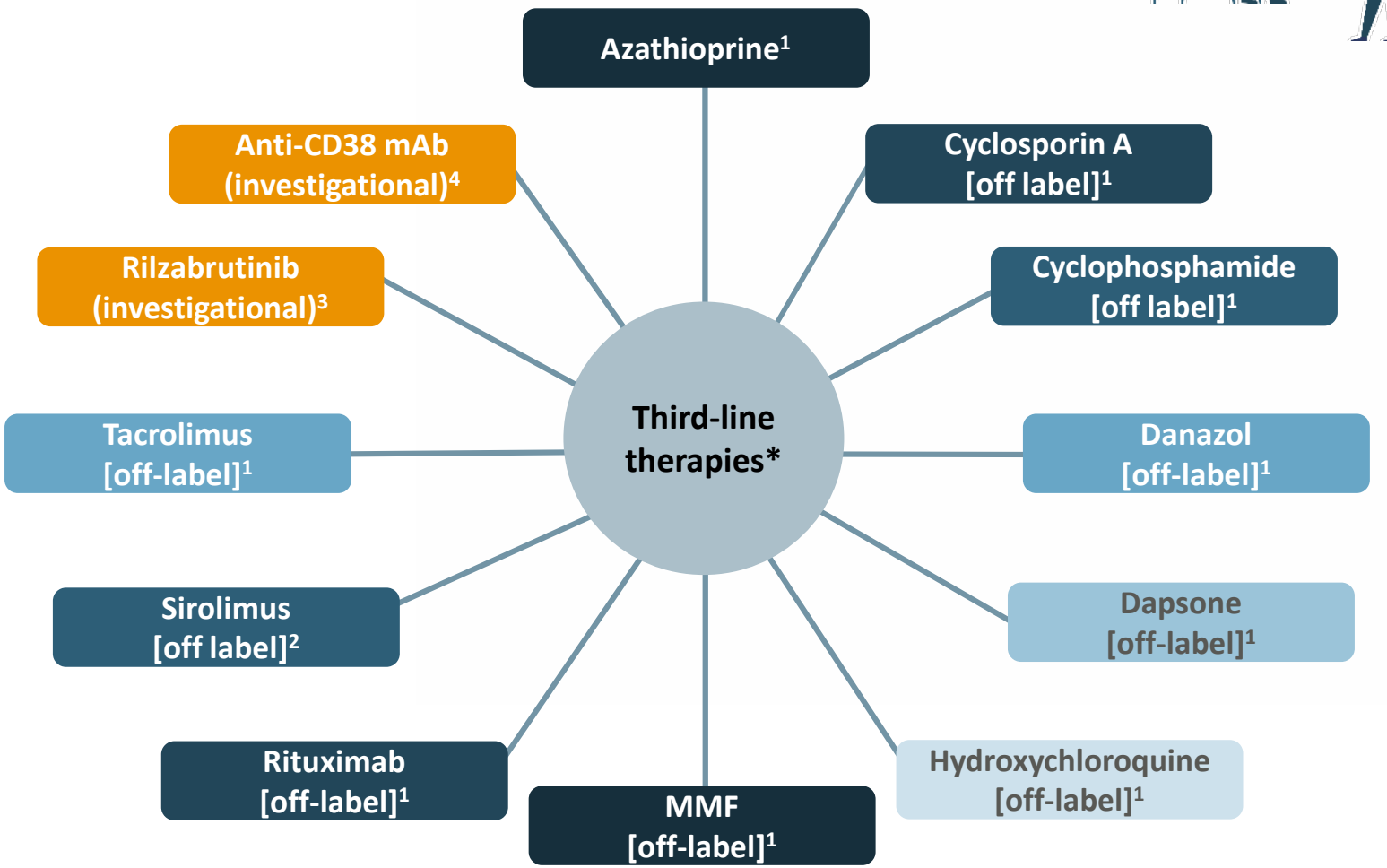
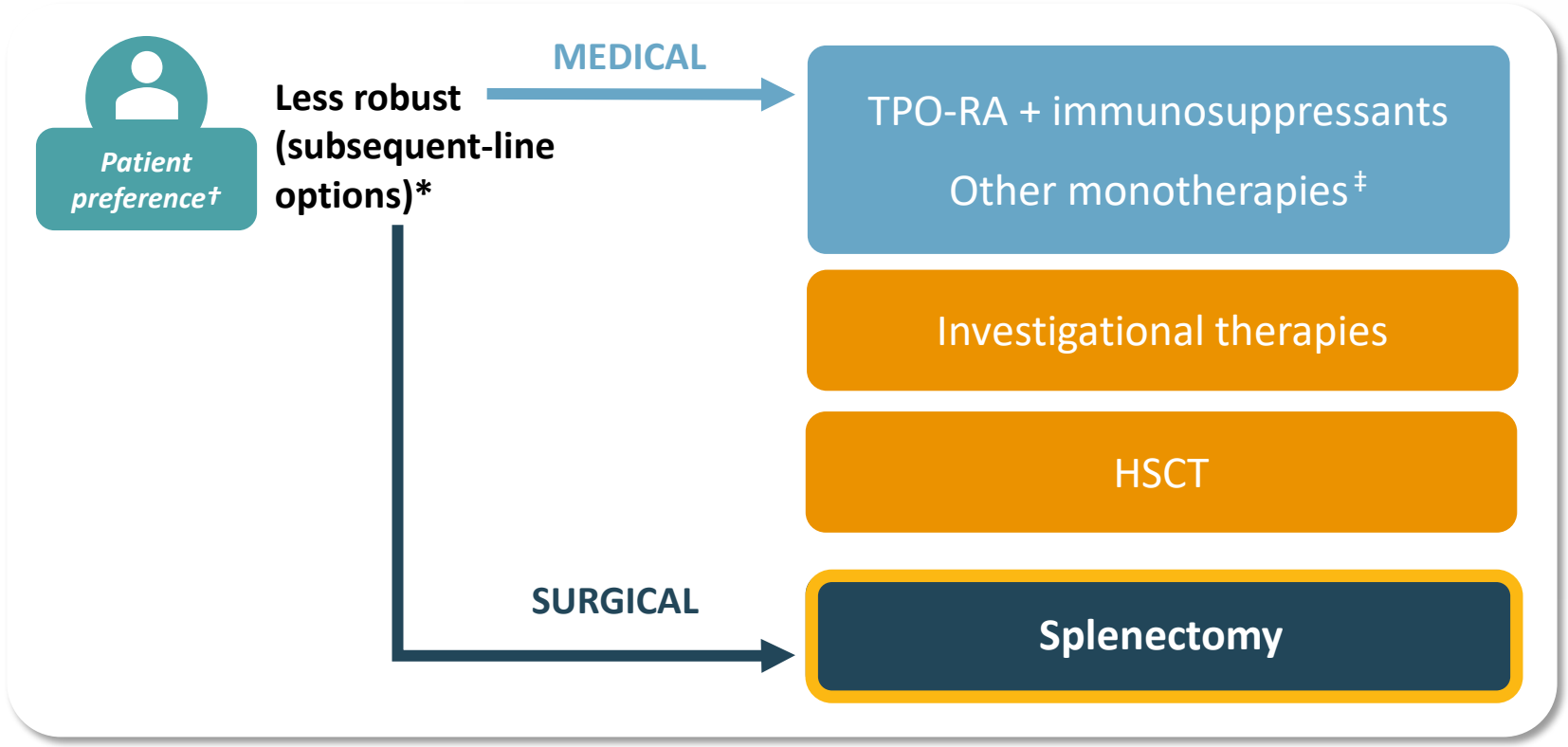
What other third-line monotherapies are available?



*Many of these agents are off-label or have old approvals, and should be given only when contemporary, more thoroughly studied agents are not effective.
CD, cluster of differentiation; mAb, monoclonal antibody; MMF, mycophenolate mofetil.
1. Matzdorff A et al. *Oncol Res Treat* 2023;46:5-44; 2. Feng Y et al. *Blood Coagulation and Fibrinolysis* 2024;35:155–160; 3. Kuter DJ et al. *Blood* 2025; doi:10.1182/blood.2024027336. Online ahead of print;
4. Chen Y et al. *NEJM* 2024;390:2178–2190.

Current guidelines and multi-line approach to treatment of adult ITP: Splenectomy[1–4]



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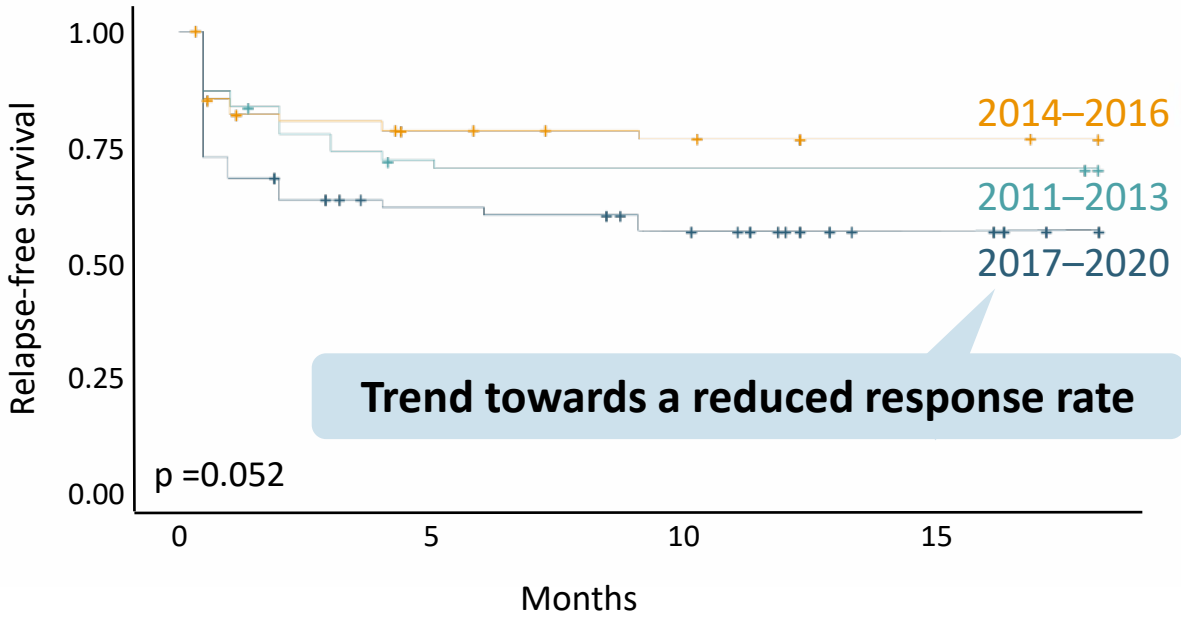
Is splenectomy still relevant during TPO-RA era?

Splenectomy in patients with ITP* (N=185), 2011–2020

Splenectomy

- Median prior treatments **4** (3–6)†
- **144/185 (77.8%)** achieved response
- **121/185 (65.4%)** achieved overall sustained response
- **23/185 (12.4%)** relapsed

Relapse-free survival by time of splenectomy

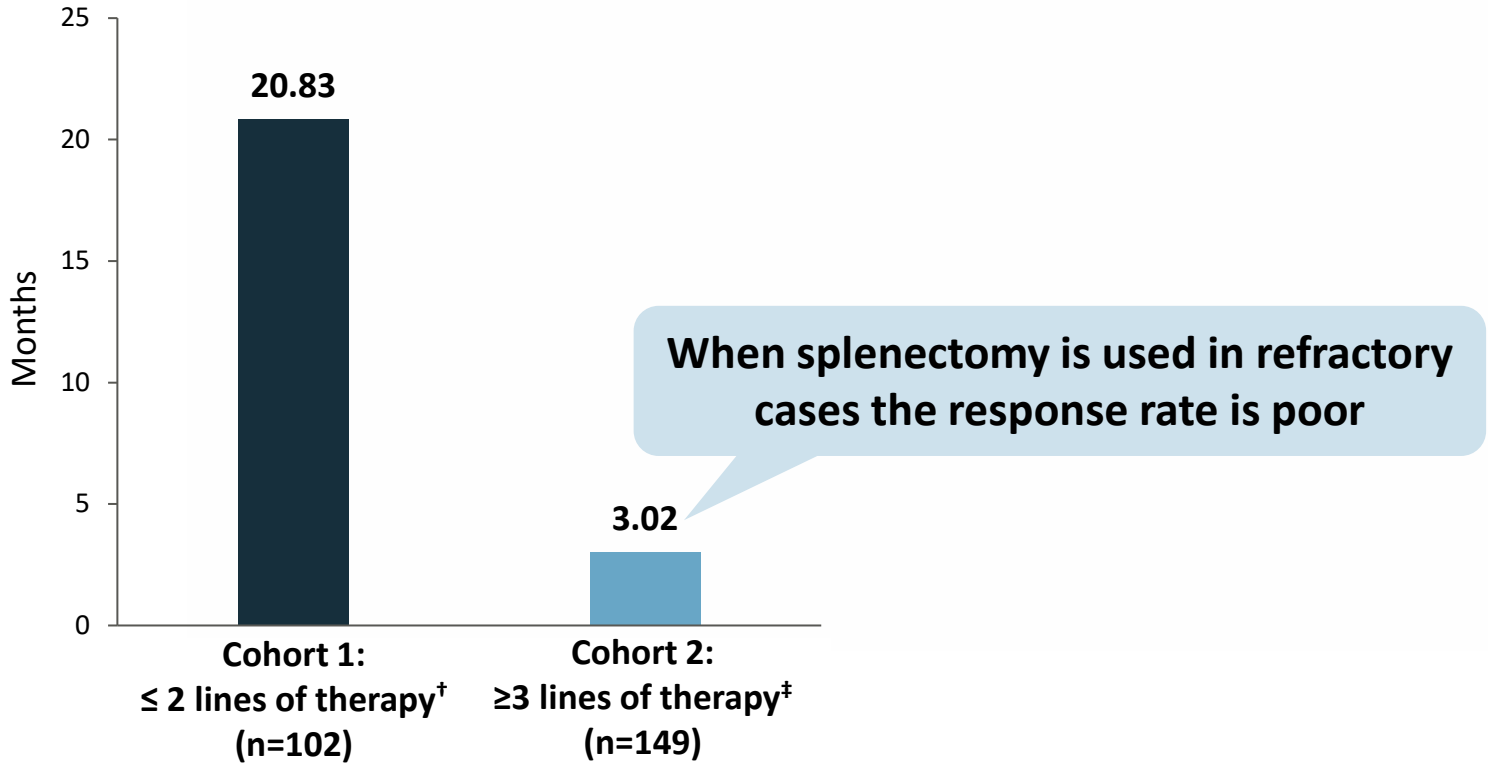


Sustained response to splenectomy was reported in:
50% of patients who **had an inadequate response to TPO-RAs;**
46% of patients who **had an inadequate response to TPO-RAs and rituximab**

*Most patients underwent splenectomy at the chronic ITP phase (n=150), and only two had undergone splenectomy within 3 months of ITP onset; †100 (54.1%) and 135 (73.0%) of patients received at least one TPO-RA and/or rituximab prior to splenectomy.
ITP, immune thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.
Mageau A et al *Am J Hematol* 2022;97(1):10–17.

Outcomes of splenectomy in patients with refractory ITP are poor: An analysis of real-world UK-ITP registry data

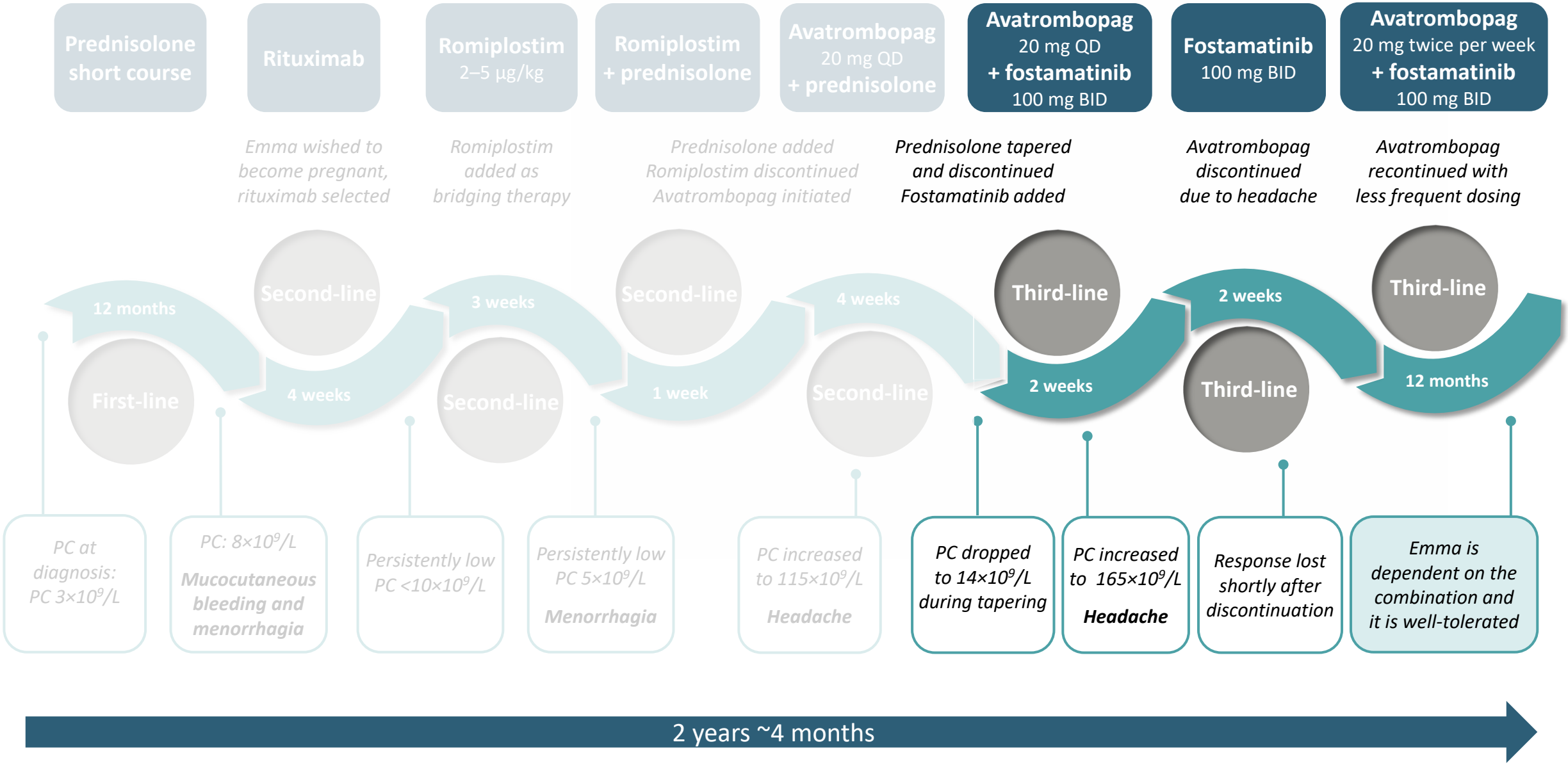
RWE: Median time-to-first treatment after splenectomy* (N=251)



Probability of sustainable remission in refractory cases is extremely low

*after year 2000; †Treatment received prior to splenectomy included corticosteroids ± IVIg (n=47), no treatment (n=48), rituximab (n=2) and MMF (n=2); ‡The last treatment received before splenectomy were corticosteroids ± IVIg (n=104), TPO-RA (n=13), rituximab (n=9), MMF (n=6), danazol (n=4), azathioprine (n=7) and cyclosporin (n=12).
ITP, immune thrombocytopenia; IVIg, intravenous immunoglobulin; MMF, mycophenolate mofetil; TPO-RA, thrombopoietin receptor agonist.
Chen et al. EHA 2024: Abstract: P1626.

Emma: Treatment timeline

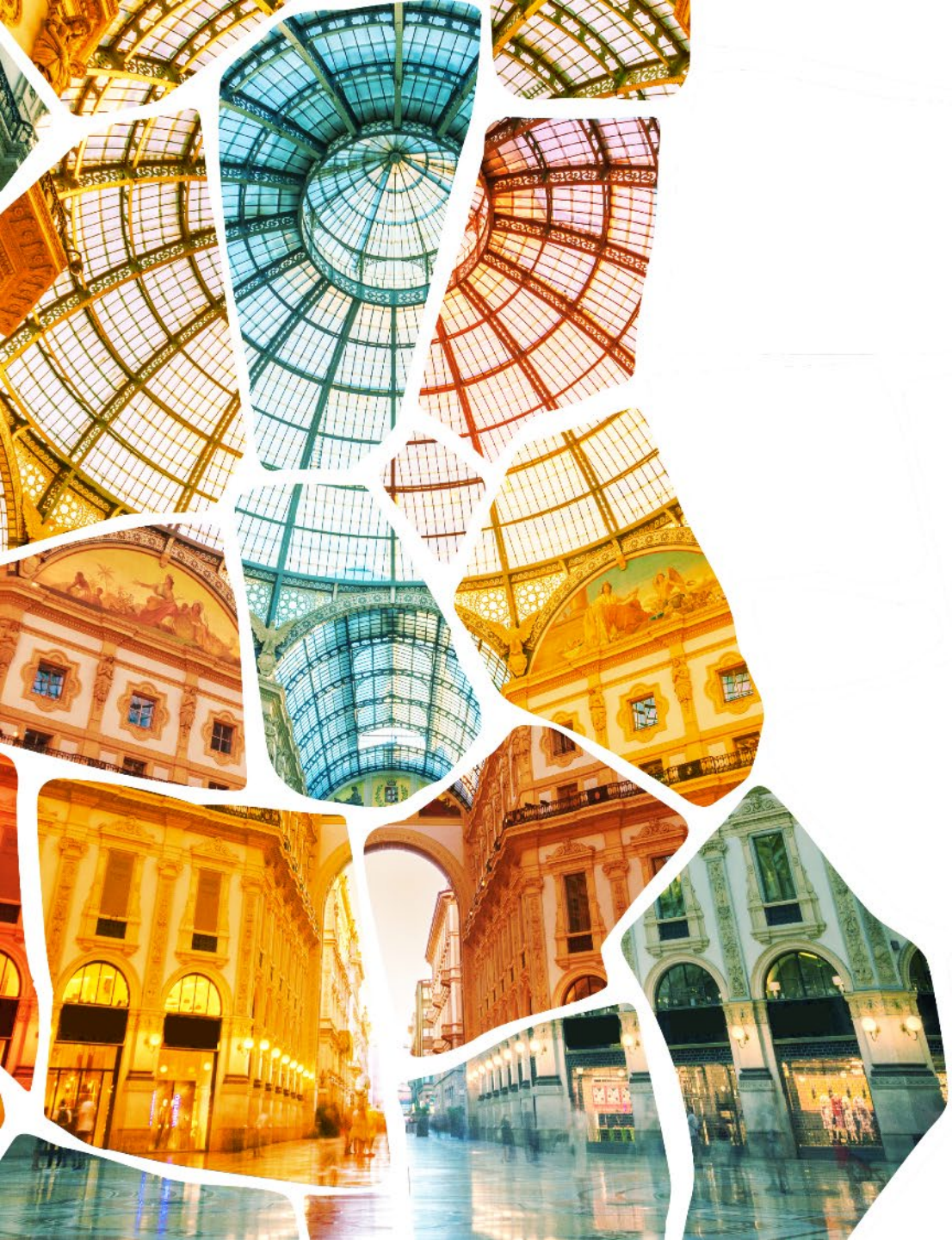


BID, twice daily; PC, platelet count; QD, once daily.

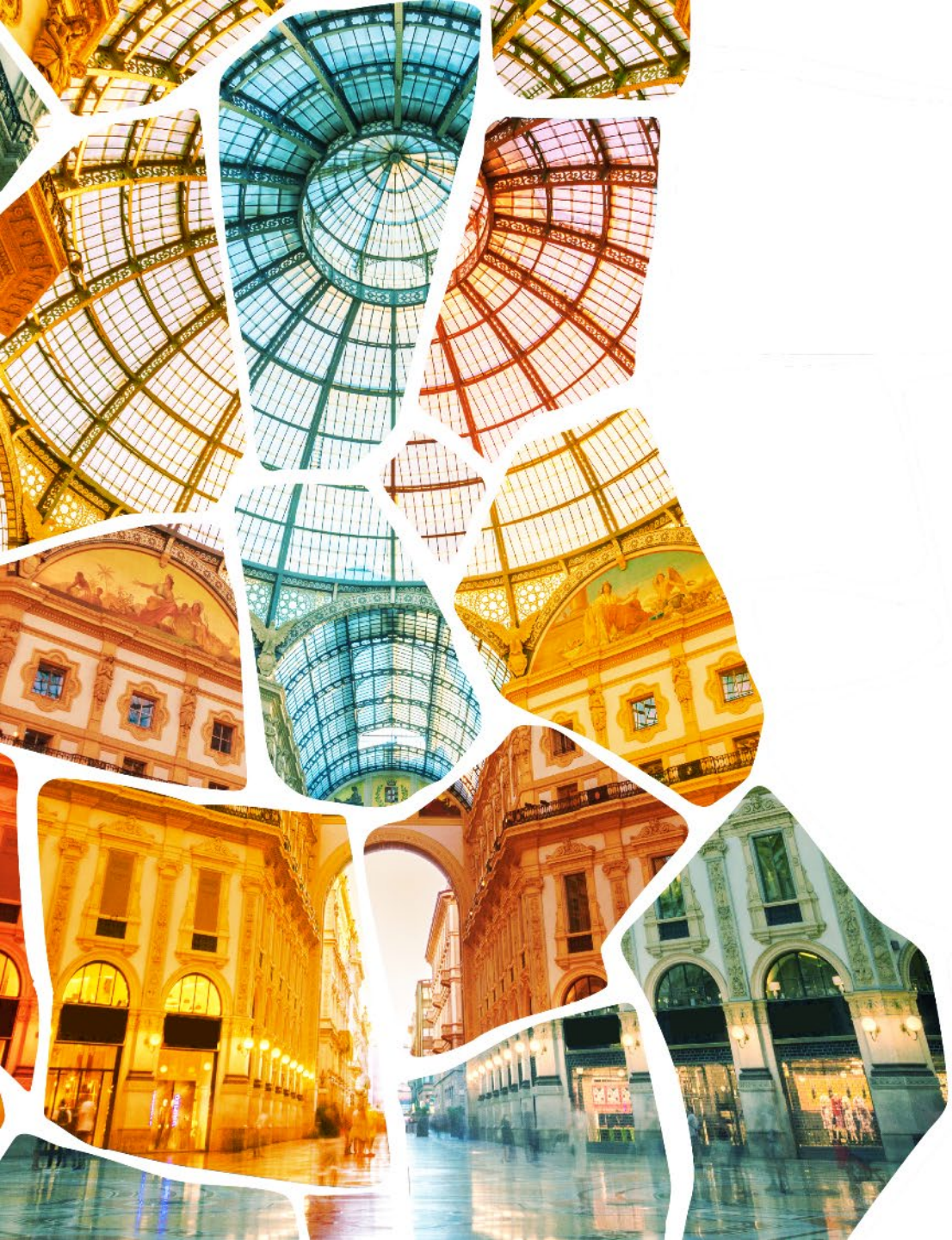
Patient case 2

Emma: Summary

- Emma was refractory after three lines of treatment, including romiplostim + prednisolone combination
- Switched to avatrombopag + prednisolone and had a platelet response after 1 week, but experienced headache
- Tapering of prednisolone to manage headache, but lost platelet response
- Fostamatinib added to avatrombopag and achieved a response, but still experiencing headache
- Avatrombopag discontinued to manage headache, but lost platelet response
- Avatrombopag recontinued at less frequent dosing
- Emma has been on the less frequent avatrombopag + fostamatinib combination for 1 year now
- She is dependent on the combination treatment and it is well tolerated



Key conclusions



Key conclusions

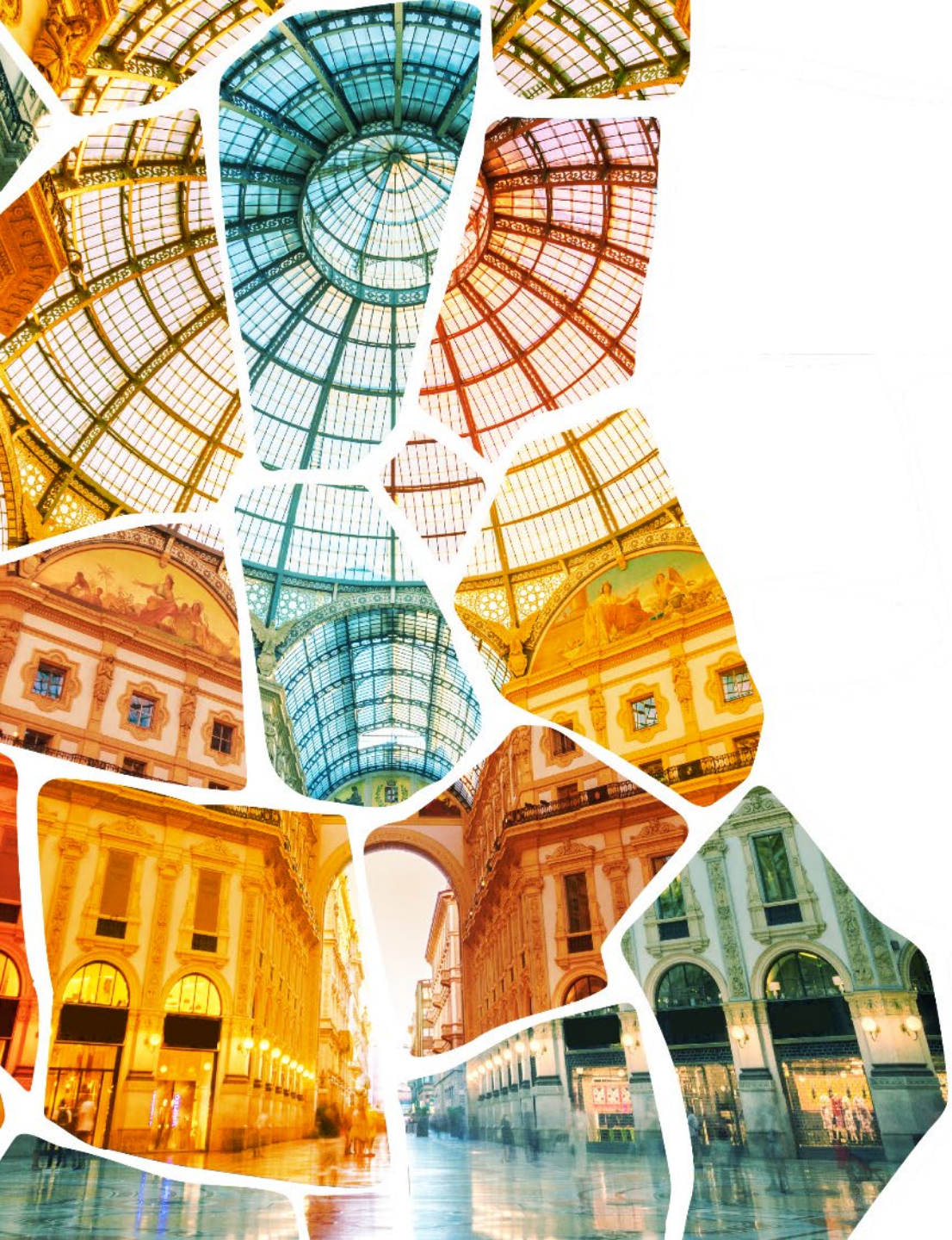
Conclusions

- Currently, guidance on timing of, approach to, and patient selection for TPO-RAs is limited
  - Early initiation of second-line treatment improves patient outcomes
  - Individual patients have different needs which may affect treatment choice
- TPO-RAs are increasingly being used earlier in treatment of ITP
- The efficacy and safety profiles of approved TPO-RAs are similar, with no significant association with thrombosis
- TPO-RA combination therapy in patients with refractory ITP can be effective

Choice of TPO-RA is influenced by efficacy, safety, patient preference and regulatory indications (newly diagnosed vs chronic/refractory ITP)

An update to ITP terminology, definitions and guidelines is needed

ITP, immune thrombocytopenia; TPO-RA, thrombopoietin-receptor agonist.



Thank you

Please remember to fill in the evaluation form via the QR code below before you leave