Clinical management, treatment goals and treatment guidelines

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EMA Workshop - Challenges in drug development, regulation and clinical practice in ITP

Virtual, 30th June 2026

Declarations

- Advisory work: Alpine, Amgen, Gliknik, Novartis, Recordati, Sanofi, Sobi and Takeda
- Presentation honoraria: Nova Nordisk
- Travel: Novartis

Guidelines

International consensus 2010 ⟹ **2019**

ASH guideline 2011 ⟹ 2019

Provan D, et al. Blood Advances. 2019;3:3780–817.

Guidelines

Anticipated guidelines

International consensus 2010 ⇒ **2019** ⇒ 2026/7

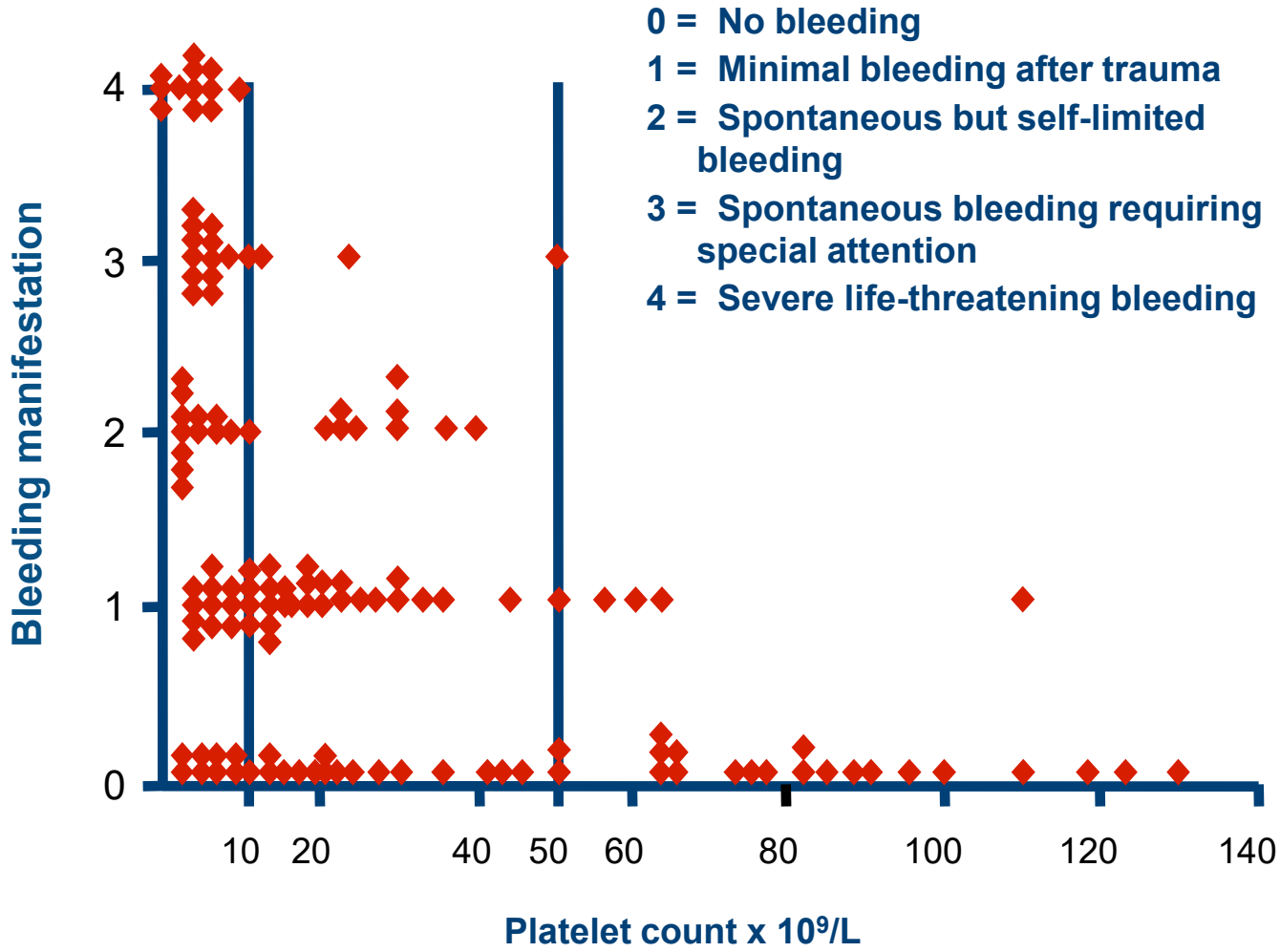
ASH guideline 2011 ⇒ 2019 ⇒ 2026/7

Dutch	2020
Spanish	2021
Italian (adult)	2021
Italian (paediatric)	2022
Central Europe	2023
Germany/Austria/Swiss	2023

EHA 2027

Provan D, et al. Blood Advances. 2019;3:3780–817.

International consensus 2019: indications for treatment



- No absolute platelet cut-off. Serious bleeding rare if platelets ≥20 x 10^9/L **BUT** individualise:
  - Bleeding symptoms
  - Anticoagulation/antiplatelet drugs
  - Occupational or recreational risk
  - Age
  - Fatigue

Lacey & Penner. Semin Thromb Hemost 1977;3:160–174. Image adapted from Drew Provan with permission

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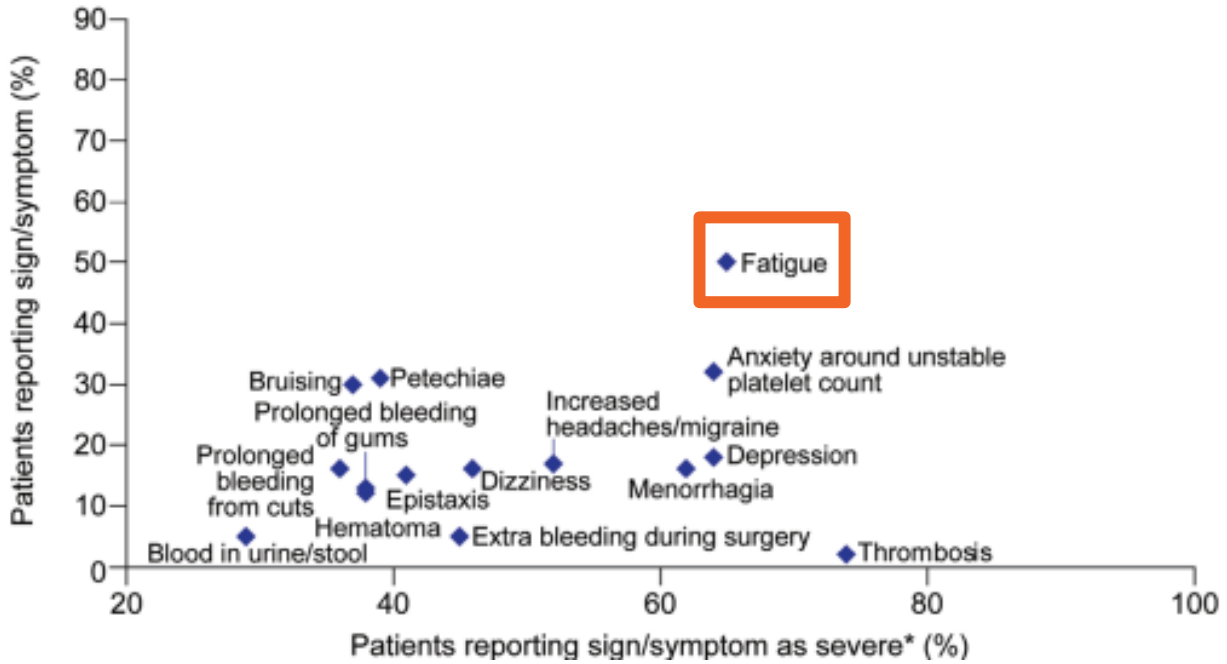
International consensus 2019: goals of treatment



- Maintain platelets >20-30 x 10^9/L

  BUT individualise

- Minimise toxicity & optimise HRQoL

- I-WISh was completed by 1,507 patients and 472 physicians from 13 countries. I-WISh; ITP World Impact Survey

Cooper N, *et al. Am J Hematol*. 2021;96:188–98

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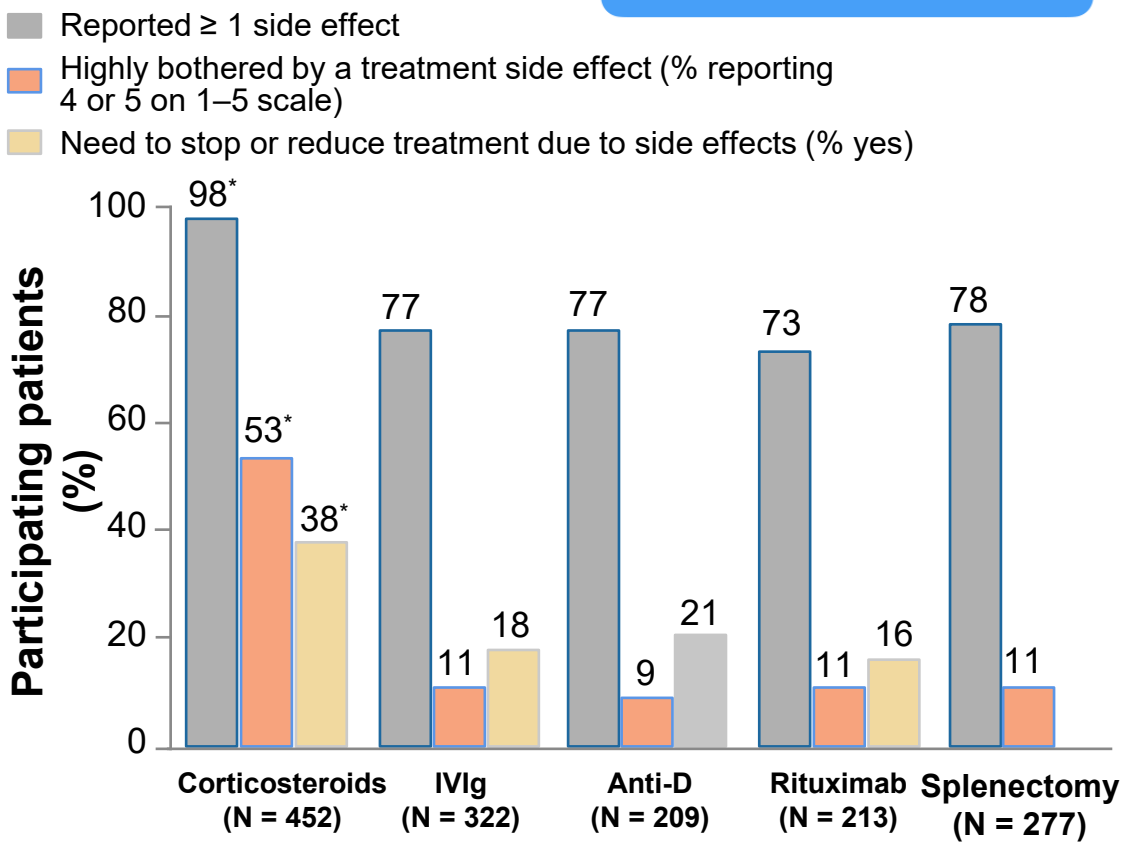
International consensus 2019: initial treatment

Initial treatment

Corticosteroids
- Dexamethasone
- Prednis(ol)one
- Methyprednisolone

IVIg

Anti-D



Corticosteroid dose

- Prednisolone 1 mg/kg
  - 80 mg **max**
- Dexamethasone 40 mg OD 4 days

Corticosteroid duration

- Prednisolone
  - Initial dose 2-3 weeks **max**
    - Taper responders to stop by 8 weeks **max**
    - Taper non responders at 2 weeks **to stop in 1 week**
- Dexamethasone 3 cycles **max**

Brown TM, et al. BMC Blood Disord. 2012;12:2.

International consensus 2019: subsequent treatment

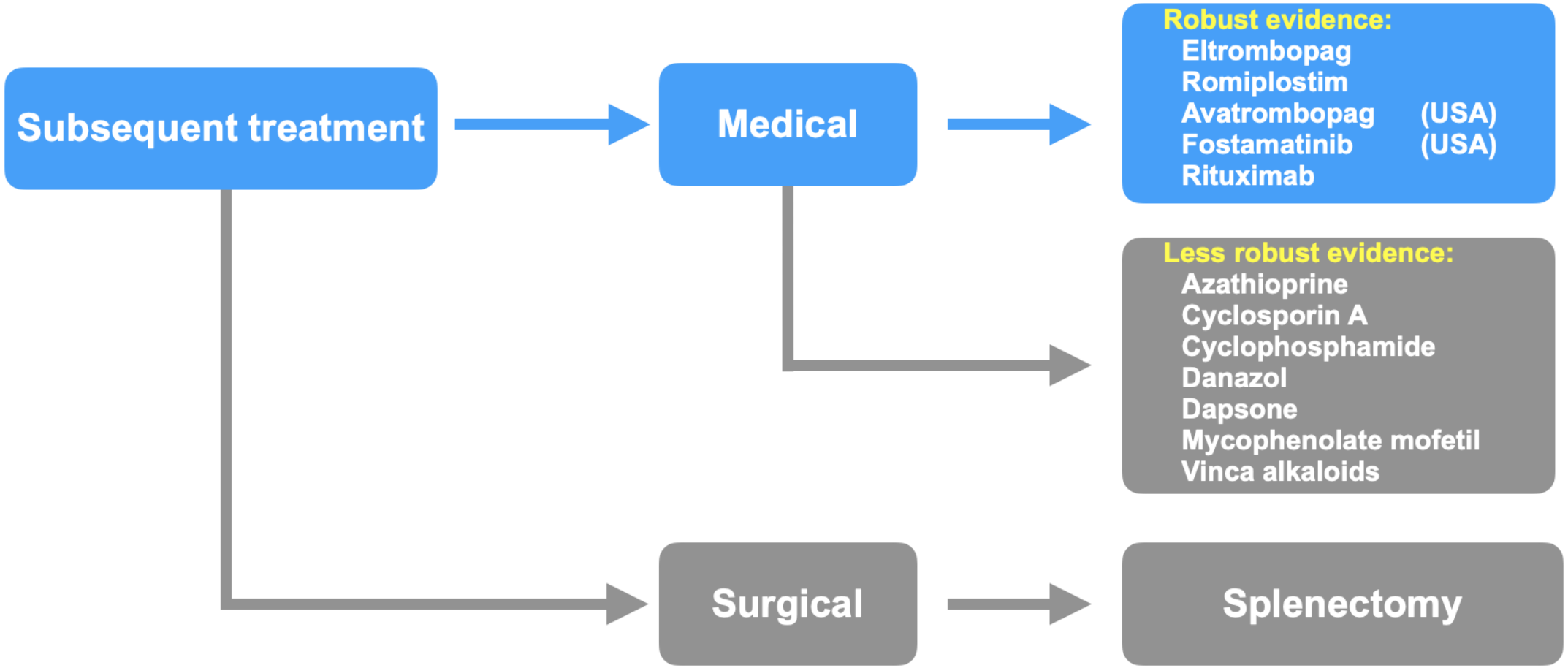


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Image adapted from Drew Provan with permission

International consensus 2019: failing multiple therapies

- Consider specialist review
  - Trials (use HRQoL e.g. ITP-PAQ)
  - Review diagnosis and need for treatment
  - Adequacy of prior therapies
  - Consider splenectomy or search for accessory spleen
  - Consider alternative medical therapies
- Last resort
  - Alemtuzumab
  - Combination chemotherapy
  - Haematopoietic stem cell transplantation

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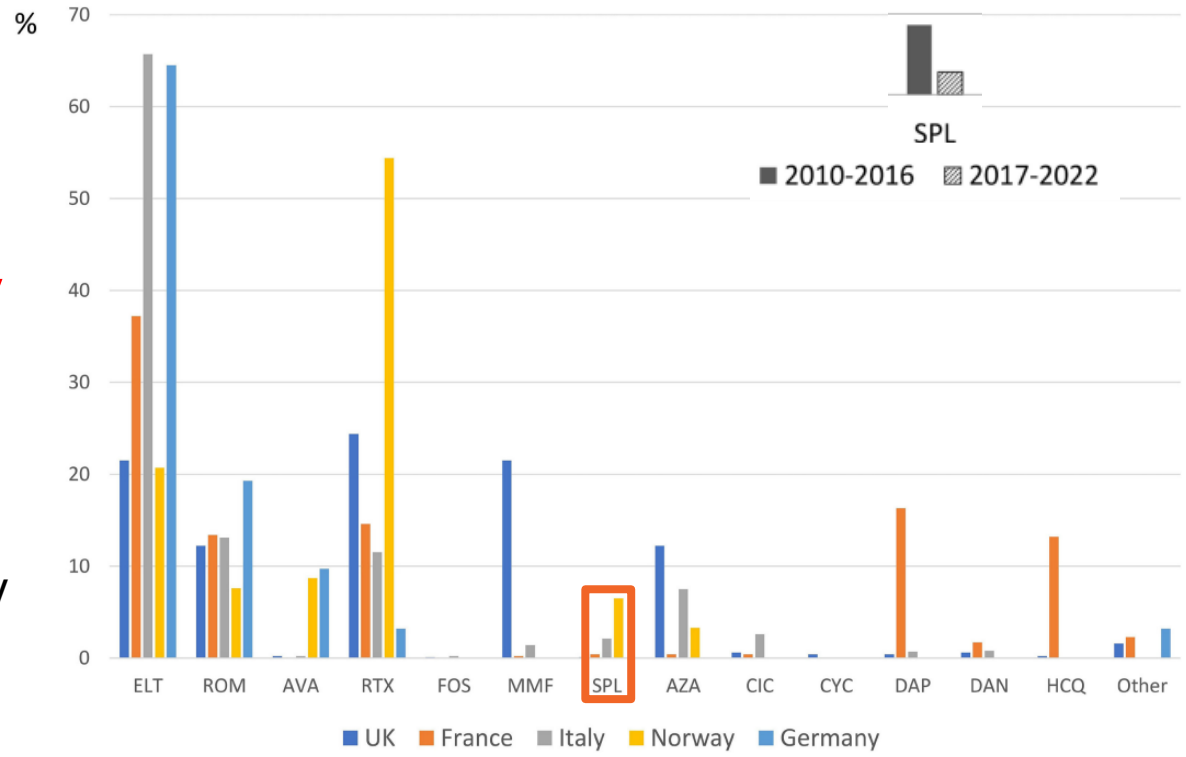
Clinical practice since 2019

- Broadly similar practice but treatment trends:
  - **Diminishing role of splenectomy**
    - **Later and less frequently**
    - **Reduced efficacy in refractory setting?***
      - TPO RA or rituximab before splenectomy (n=185), sustained response 65%*
      - >4 prior treatments predicted worse outcome
      - >6 prior treatments, sustained response 42% (5/16)



Moulis et al Haematologica. 2025 Dec 1;110(12):3094-3098; *Mageau et al Am J Hematol 2022 Jan 1;97(1):10-17

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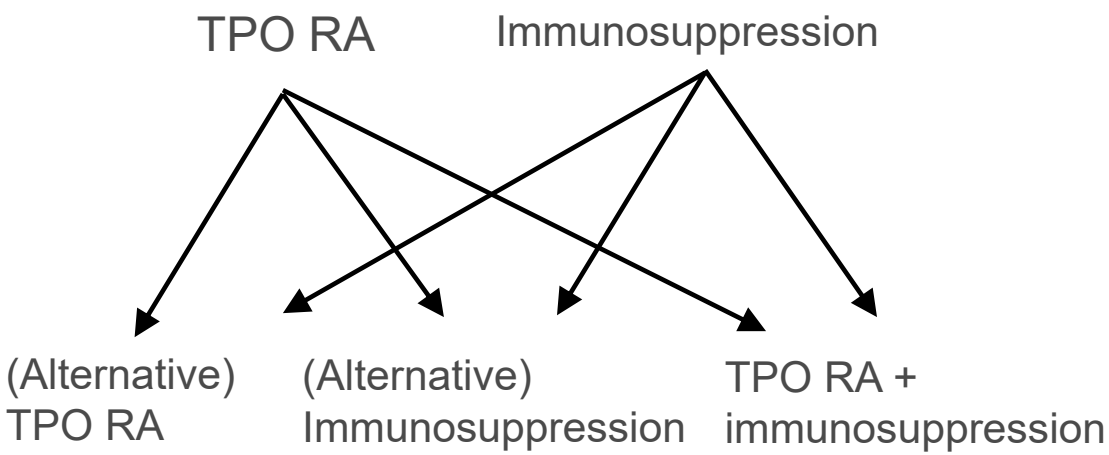
Clinical practice since 2019

- Broadly similar practice but treatment trends:
  - Diminishing role of splenectomy
  - **TPO RA switching**
  - **Access to generic TPO RA**
  - **Monotherapy vs. combinations**
  - **TPO RA and TE**
- TPO RA + immunosuppression**
  - Failure to rituximab and TPO RA and splenectomy
  - 77% (30/39) responded, median 15 months (range 4-63)



Annualised incidence of thromboembolism/100 person years

	Romiplostim	Eltrombopag	ITP	Gen Pop
Arterial*	2.8-2.6	-	0.96 - 1.15	0.67 - 0.91
Venous*	4.3-1.5	-	0.41 - 0.67	0.28 - 0.42
All TEE	7.5-4.2	3.2-2.5		

**Crickx Br J Haematol. 2023 Aug;202(4):883-889; *Rodeghiero Am J Hematol 2016 Jan;91(1):39-45

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Clinical practice since 2019

- Broadly similar practice but treatment trends:
  - Diminishing role of splenectomy
  - TPO RA trends
  - **Rilzabrutinib approved**
    - **EMA 12/2025**
    - **MHRA 05/2026**

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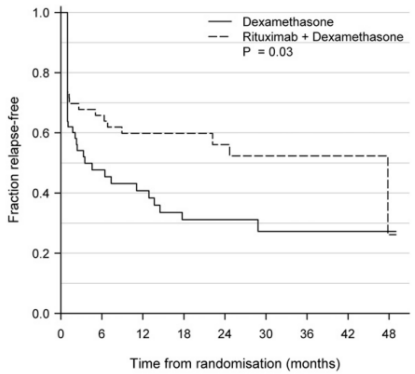
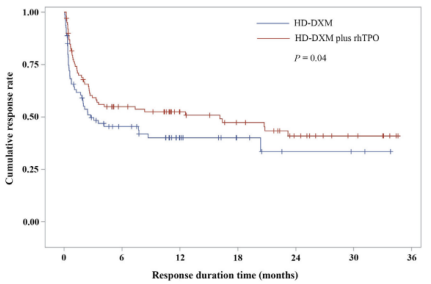
Unmet need

- Diagnostic test for ITP
- Biomarkers to predict treatment response
- Reduce steroid dependence and improve HRQoL
  - Upfront treatment to improve sustained remission off treatment

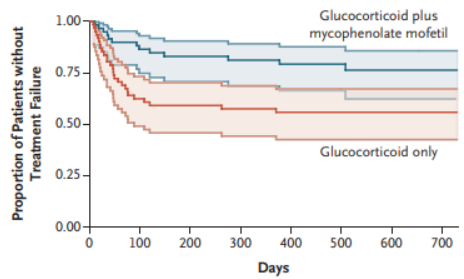
Upfront randomised controlled trials



*Rituximab Dex vs. Dex
6 m primary end point:
58% vs 37% (P = 0.02)



**rHuTPO Dex vs. Dex
6 m primary end point:
51% vs 37% (P = 0.04)



***MMF steroid vs. steroid. Treatment failure 22% vs 44% (p<0.001)

*Gudbrandsdottir Blood. 2013;121(11):1976-1981; **Yu Am J Hematol. 2020;95:1542–1552; ***Bradbury N Engl J Med. 2021 Sep 2;385(10):885-895

Unmet need

- Diagnostic test for ITP
- Biomarkers to predict treatment response
- Reduce steroid dependence and improve HRQoL
  - Upfront treatment to improve sustained remission off treatment
- Treatments for refractory difficult to treat patients

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Unmet need

- Non-commercial adaptive trials to optimise sequencing of existing medications
- Study inclusion/exclusion permissive for patient's representative of those we treat
  - Secondary ITP e.g. Evans syndrome, co-morbidity
  - Patient diversity e.g. patient information translated, patient friendly visits (frequency, remove reviews)

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Why might guidelines differ?

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Core outcome priorities

Survival analysis
Overall survival (mortality)
Relapse-free survival (or duration of response)
Response assessment
Sustained response (at 6 mts)
Sustained response (at 12 mts)
Time-to-response
Quality of life
Disease-specific QoL (total score)
Overall QoL (total score)
Symptom-specific QoL
Morbidity
Serious bleeding (mWHO ≥ 2, or equivalent)
Any bleeding events
Adverse events
Severe adverse events (CTCAE ≥ 3, or serious adverse events if not reported otherwise); any adverse events if severe are not reported
Severe infectious complications (CTCAE ≥ 3); lower respiratory tract infection if not reported
Thromboembolism (DVT, PE)
Hospitalisations

GRADE guidance: ideally limit number of patient-important outcomes to < 7

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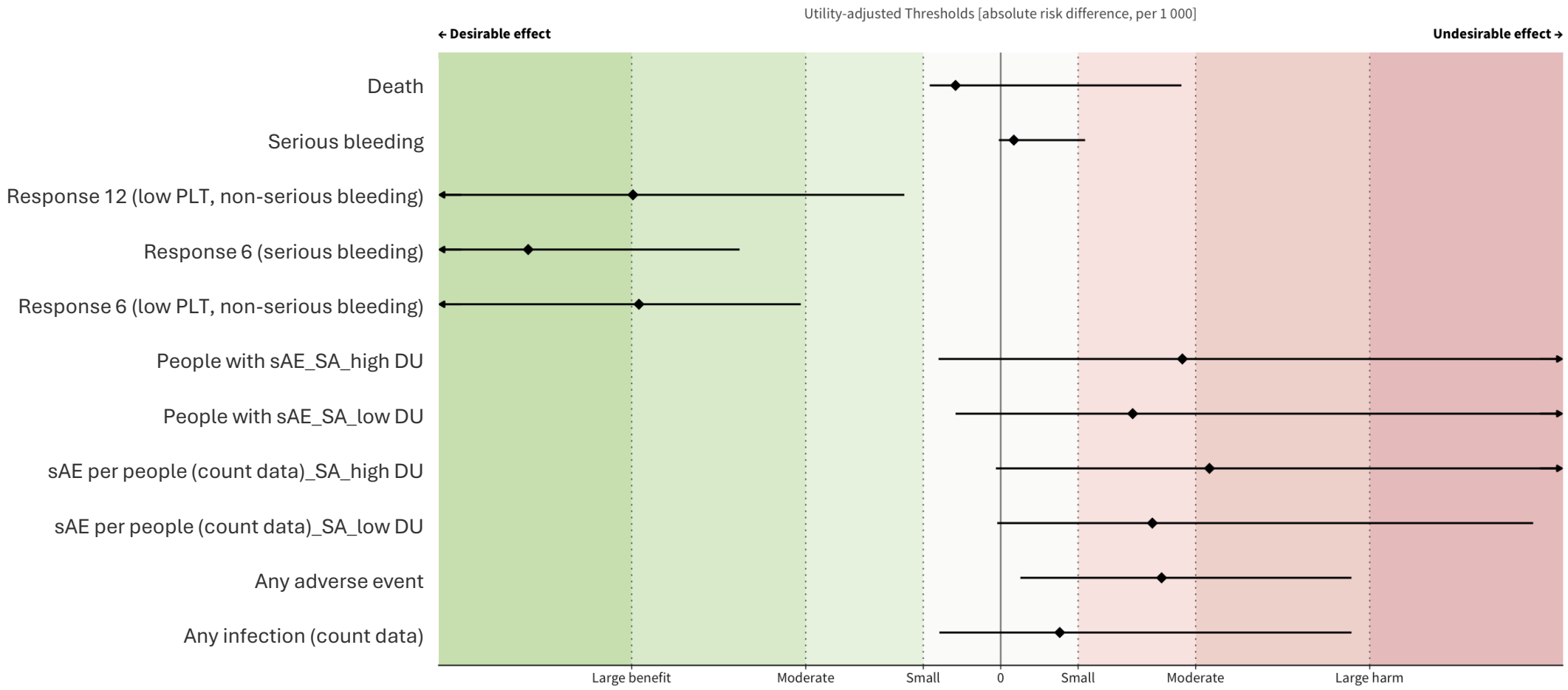
First-line treatment

Corticosteroids + rituximab



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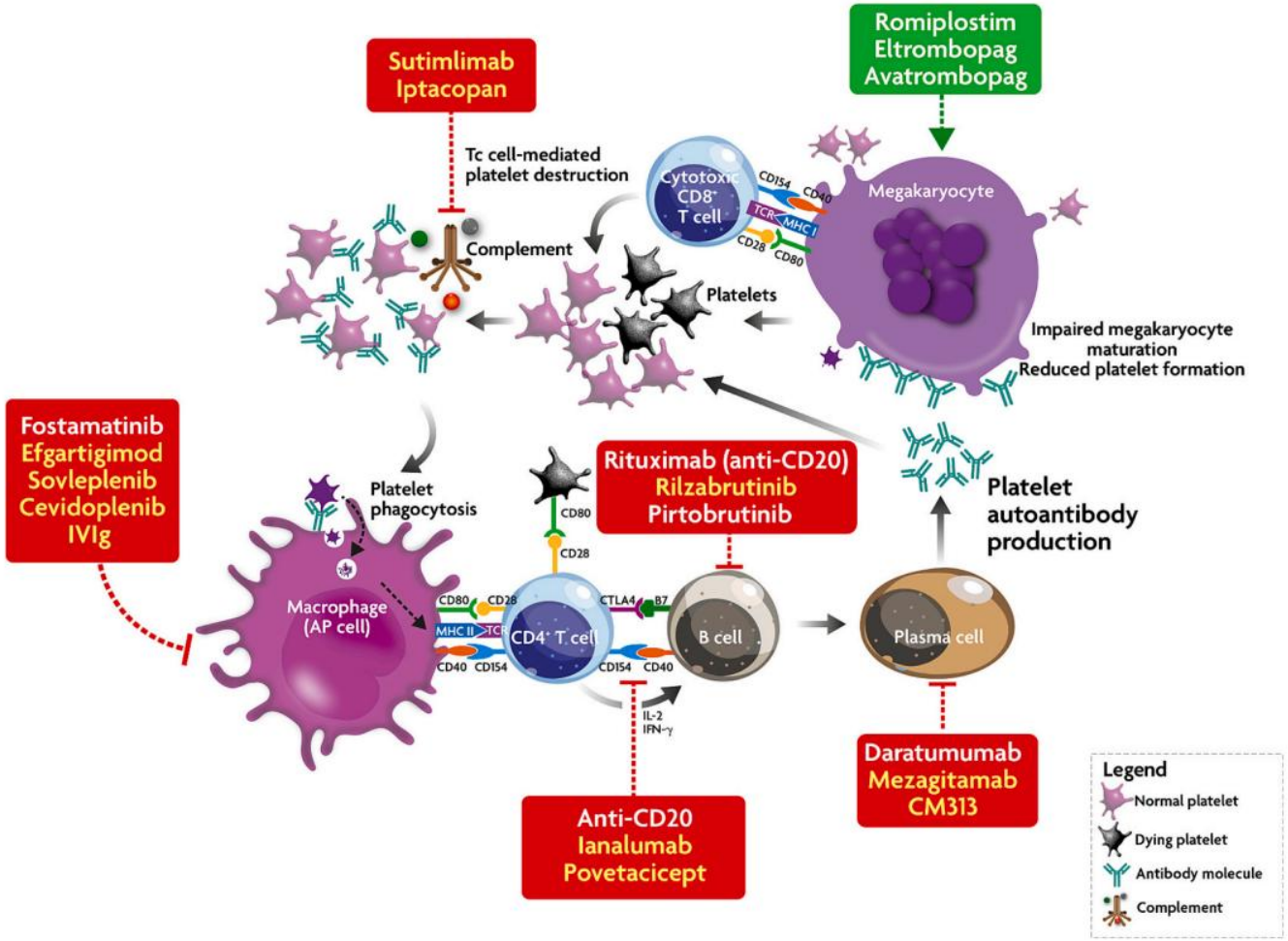
Future prospects



- Rare, complex pathogenesis
- ITP may not be “one disease”
- Some new classes under development
  - Complement inhibition
  - Recombinant Immunoglobulin
  - FcRn inhibitors
  - BAFF inhibitors
  - Plasma cell inhibitors
  - CAR-T (CD19)
  - Bispecific T cell Engager (BiTE)

Image from Gonzalez-Lopez.& Provan Blood Reviews 2025; Aug:73:101300