MJA
The Medical Journal of Australia

Supporting Information

Supplementary material

This appendix was part of the submitted manuscript and has been peer reviewed.
It is posted as supplied by the authors.

Appendix to: Choi PYI, Merriman E, Bennett A, et al. Consensus guidelines for the management of adult immune thrombocytopenia in Australia and New Zealand. *Med J Aust* 2021; doi: 10.5694/mja2.51284.

Supplementary Box. Methodology of consensus guidance development

- THANZ members with research and clinical interests in ITP were convened by Professor Robert Bird who conceived the idea of a national consensus guideline statement for adult ITP.
- Authors met regularly via videoconference (during the COVID-19 pandemic).
- Key clinical dilemmas and contentious areas within ITP were discussed and agreed upon by consensus for literature review and guideline development.
- Subsections of the manuscript were written by small teams of two to three authors who reviewed the available literature available over at least the preceding 20 years.
- Recommendations were graded as described in Box 1.
- These subsections were then combined for review by all authors to be debated until consensus achieved.
- Statements with no dissent were accepted. Statements with minor dissent were annotated with a weakened (conditional) recommendation if consensus could not be achieved.
- Statements with strong dissent were removed from the manuscript unless consensus agreed there was benefit to the readership to include and describe the dilemma.
- Final complete draft was reviewed by authorship, before distribution to THANZ Council for external peer review.
- Endorsement of the guidelines was subsequently obtained from THANZ and ITP Australia.

COVID-19 = coronavirus disease 2019; ITP = immune thrombocytopenic purpura; THANZ = Thrombosis and Haemostasis Society of Australia and New Zealand.

Table S1. Important differential diagnoses requiring prompt exclusion

Differential diagnosis	Initial features	Further investigation
Myelodysplastic syndrome	Dysplastic features on blood film, macrocytosis	Bone marrow examination, cytogenetics, NGS — if available
Thrombotic thrombocytopenic purpura (TTP)	Anaemia, red cell fragments, renal failure	ADAMTS-13 level
Hereditary thrombocytopenias	No history of previous normal platelet count, positive family history	NGS for platelet disorders — if available
Pregnancy-related thrombocytopenias	History of pregnancy	β-HCG, urgent evaluation for hypertensive disorders of pregnancy if in third trimester
Pseudothrombocytopenia	Platelet count out of keeping with clinical features	Repeat FBC, use citrate tube
Liver disease, hypersplenism	Enlarged spleen, abnormal LFTs	
Antiphospholipid syndrome	History of thromboses, recurrent miscarriage, prolonged APTT	Lupus anticoagulant screen, antiphospholipid antibodies

APTT = activated partial thromboplastin time; FBC = full blood count; LFTs = liver function tests; NGS = Next Generation Sequencing.

Table S2. Target platelet counts for surgeries and invasive procedures*,[1]

Type of surgery or procedure	Target platelet count
Surgery	
Minor surgery (low risk of bleeding)	> 50×10^9/L
Minor surgery at a compressible site	> 20×10^9/L
Major surgery (including abdominal/thoracic surgery and operations in non-compressible sites)	> 80×10^9/L
Neurosurgery	> 100×10^9/L
Surgery at posterior segment of eye	> 100×10^9/L
Dental	
Dental cleaning	> 20×10^9/L
Tooth extraction (simple)	> 30×10^9/L
Tooth extraction (complex, surgical, molar)	> 50×10^9/L
Regional anaesthetic nerve block for tooth extraction	> 30×10^9/L
Procedures	
Lumbar puncture (elective)	> 50×10^9/L
Lumbar puncture (emergency)	> 20×10^9/L
Spinal/epidural anaesthesia	> 70×10^9/L
Central line placement	> 20×10^9/L
Gastroscopy (with biopsy)	> 20×10^9/L
Bronchoscopy, with lavage	> 20×10^9/L
Bronchoscopy, with transbronchial biopsy	> 50×10^9/L
Joint aspiration	> 20×10^9/L
Liver biopsy, transjugular (preferred for thrombocytopenic patients)	> 10×10^9/L
Liver biopsy, transcutaneous	> 50×10^9/L
Bone marrow biopsy	Thrombocytopenia not a contraindication
Other organ biopsies/punctures	> 50×10^9/L

* This is derived from expert recommendations in an international guideline and adapted with permission (S Karger AG, Basel). While they are not supported by direct evidence, they may be of practical use to guide clinicians and proceduralists.

Table S3. National collaborators of clinical research in immune thrombocytopenic purpura

Research centre	Areas of interest	Research priorities	Contact details
National Platelet Research and Referral Centre (https://jcsmr.anu.edu.au/research/centres/nprc)	Disorders of platelet number and function	▪ Surface platelet receptor expression ▪ Platelet immunology ▪ Viscoelastometry in thrombocytopenia ▪ Biobanking	info.nprc@anu.edu.au
Sydney Platelet Group	Inherited disorders of platelet function and/or number	▪ Integrated phenotypic-genetic approach to diagnosis	https://redcap.stvincents.com.au/surveys/?s=3XLLJ97RPL
Royal Adelaide Hospital (RAH)	Disorders of platelet number and/or function	▪ NGS panels for inherited thrombocytopenia or platelet function abnormalities	Outpatient referrals to assess suitability of NGS panel testing can be faxed to RAH Haematology outpatient clinic (08) 7074 6220.
Australian Red Cross Lifeblood Platelet and Neutrophil Laboratory (Queensland)	Immune-mediated platelet disorders		Full contact details for the Platelet and Neutrophil reference laboratories are available at: https://transfusion.com.au/transplantation_services

Table S4. Key points

- As ITP is a diagnosis of exclusion, failure of response to treatment heightens the possibility of an alternative diagnosis.
- We recommend treatment for newly diagnosed ITP when platelet counts are consistently below 20×10^9/L, even in the absence of bleeding (GRADE 1C).
- Splenectomy, rituximab and thrombopoietin receptor agonists (TPO-RAs) have the most robust evidence in terms of efficacy and safety and hence it is recommended that these three options be discussed with patients as suitable second line treatments (GRADE 1C).
- Patient preferences, age, lifestyle, comorbidities, and drug availability are important when considering when to start second line treatment and which treatment modality to adopt (GRADE 1D).
- Splenectomy should be considered in patients aged less than 65 years, with disease duration greater than 12 months, and for whom this option impacts least on their lifestyle (GRADE 2D).
- Rituximab should be considered in patients who have expressed a strong preference to avoid surgery.
- Rituximab should be considered in younger, female patients with short disease duration (< 1–2 years) (GRADE 2C).
- TPO-RAs significantly reduce the incidence of severe bleeding, the need for rescue therapy, and improve health-related quality of life measures.
- Clinical trial enrolment of eligible ITP patients who have not responded to currently available therapies is strongly recommended where available in limited sites around Australia and New Zealand (GRADE 1D).
- For pregnant patients with ITP, it is sometimes useful to rehearse ITP treatment several weeks before term, in order to plan for a neuraxial anaesthesia, where a platelet target of $\geq 70 \times 10^9$/L is reasonable (GRADE 2D).
- It is generally safe to administer antiplatelet therapy if platelet counts are $\geq 30 \times 10^9$/L, and dual antiplatelet therapy if platelet counts are $\geq 50 \times 10^9$/L (GRADE 1D).

Reference

1 Matzdorff A, Meyer O, Ostermann H, et al. Immune thrombocytopenia — current diagnostics and therapy: recommendations of a Joint Working Group of DGHO, OGHO, SGH, GPOH, and DGTI. *Oncol Res Treat* 2018; 41 (Suppl): 1-30.