Management of Initial and Second-Line Therapy in Adults with Primary ITP

An Educational Slide Set

American Society of Hematology 2026 Guidelines for Immune Thrombocytopenia (ITP): Initial and Second-Line Therapy in Adults with Primary ITP

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American Society of Hematology 2026 Guidelines for Immune Thrombocytopenia (ITP): Initial and Second-Line Therapy in Adults with Primary ITP

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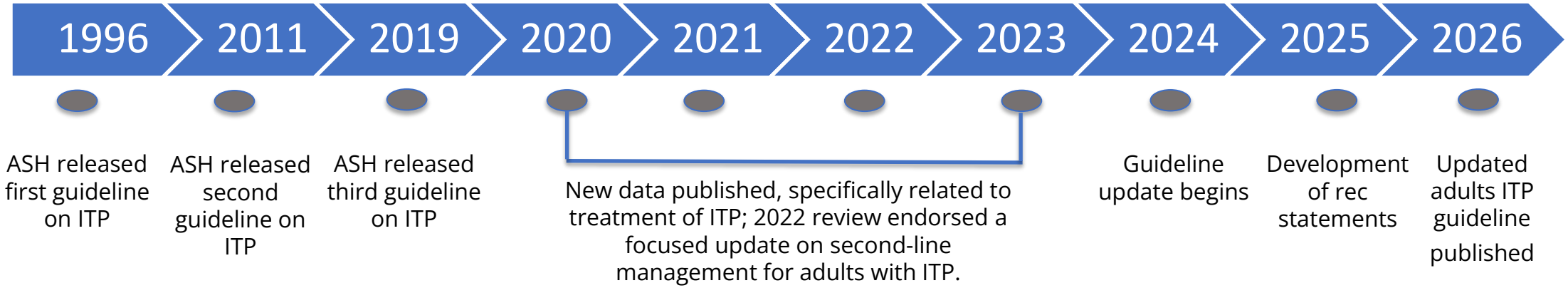
Scope: Initial and Second-Line Therapy in Adults with Primary ITP

1. Adults with primary ITP requiring initial therapy
2. Adults with primary ITP needing additional treatment after initial therapy with corticosteroids (with or without IVIG)
3. Good Practice statements: Splenectomy
4. Good Practice statements: Thrombopoietic agent switching

History of Immune Thrombocytopenia Guideline

ASH first issued guidance on ITP in 1996, followed by comprehensive clinical practice guidelines in 2011 and updated in 2019. In 2026, ASH developed a focused update on the management of adults with primary ITP, based on new evidence accumulated in preceding years.



How were these guidelines updated?

PANEL FORMATION

Guideline panel was formed following these key criteria:

- Balance of expertise (including hematologists and lived experience experts)
- Close attention to minimization and management of conflicts of interest

CLINICAL QUESTIONS

2 **clinically-relevant questions** generated in **PICO format** (population, intervention, comparison, outcome)

Example: Should adults with primary ITP requiring initial therapy, be treated with corticosteroids (with or without IVIG) + additional agent (MMF, thrombopoietic agent, anti-CD20, SYK inhibitor) or corticosteroids (with or without IVIG)?

EVIDENCE SYNTHESIS

Evidence summary generated for each PICO question via systematic review of health effects plus:

- Resource use
- Feasibility
- Acceptability
- Equity
- Patient values and preferences

MAKING RECOMMENDATIONS

Recommendations made by guideline panel members based on evidence for all factors

ASH guidelines are reviewed annually by expert work groups convened by ASH. When a guideline requires updating, resources derived from it, such as this slide set, are removed from the ASH website.

How patients and clinicians should use these recommendations

	STRONG Recommendation		CONDITIONAL Recommendation	
	"The panel recommends…"	**"The panel recommends against…"**	**"The panel suggests…"**	**"The panel suggests against…"**
				
For patients	Most individuals would choose the recommended course of action.	Most individuals would choose to avoid the intervention.	A majority would choose the suggested course of action, but many would not.	A majority would choose to avoid the intervention, but many would not.
For clinicians	Most individuals should receive the recommended course of action.	Most individuals should not receive the intervention.	Different choices will be appropriate for different patients, depending on their values and preferences. Use **shared decision making**.	Different choices will be appropriate for different patients, depending on their values and preferences. Use **shared decision making.**

What has changed since 2019?

Two new drugs with novel mechanisms of action have been approved, including inhibitors of spleen tyrosine kinase (SYK) and Bruton tyrosine kinase (BTK).

Several new drug classes are in late-stage clinical development, including B-cell activating factor receptor inhibitors, anti-CD38 agents, neonatal Fc receptor antagonists, and complement inhibitors.

Therapeutic goals are shifting from a primary focus on platelet count–based outcomes to more ambitious aims, including improved health-related quality of life, sustained treatment-free response, and even the possibility of cure.

Patients and clinicians now have more treatment options than ever before, but must determine how best to prioritize and sequence these therapies.

Learning Objectives

By the end of this session, you should be able to

1. Choose appropriate initial treatment for adults with primary ITP.
2. Choose appropriate therapy for adults with primary ITP requiring additional treatment after corticosteroids, with or without IVIG.
3. Determine the role and optimal timing of splenectomy in the modern treatment landscape.
4. Optimize treatment sequencing, including switching between thrombopoietic agents when appropriate.

CASE 1

Adults with Primary ITP Requiring Initial Therapy

Case 1:

- 66-year-old man
- History of hypertension and benign prostatic hyperplasia
- Isolated thrombocytopenia at 15 x10^9/L
- CBC 3 months earlier: normal
- No new therapy started
- No argument for infection

Blood investigations

- Isolated thrombocytopenia on CBC
- Blood film: normal
- Immunoglobulin level: normal
- Viral testing: HIV, HBV, and HCV negative
- Liver enzymes: normal
- Bone marrow examination not required
- Antiplatelet antibodies not required

- No organomegaly
- Petechiae and bruises on the legs
- No mucosal bleeding

Diagnosis of primary ITP

- 66-year-old man
- Primary ITP, untreated, platelets at 15x10^9/L, petechiae/bruises
- History of hypertension and prostate hyperplasia

What should you do?

A. Discuss the different treatment options with the patient
B. Propose treatment with dexamethasone alone
C. Propose combination therapy with dexamethasone and rituximab
D. Propose combination therapy with dexamethasone and TPO-RA
E. Propose combination therapy with dexamethasone and MMF

- 66-year-old man
- Primary ITP, untreated, platelets at $15x10^9/L$, petechiae
- History of hypertension and prostate hyperplasia

What should you do?

A. Discuss the different treatment options with the patient

ASH guidelines are primarily intended to **help clinicians and patients make shared decisions** about diagnostic and treatment alternatives, with the goal of improving quality of patient care. Other purposes are to inform policy, education and advocacy, and to state future research needs. These guidelines are not intended to serve or be construed as a standard of care. **Clinicians must make decisions on the basis of the clinical presentation of each individual patient, ideally through a shared process that considers the patient's values and preferences with respect to the anticipated outcomes of the chosen option.**

Agents considered

Thrombopoietic agent

Anti-CD20

MMF

Corticosteroids

- 66-year-old man
- Primary ITP, untreated, platelets at 15x10^9/L, petechiae/bruises
- History of hypertension and prostate hyperplasia

What should you do ?

A. **Discuss the different treatment options with the patient**
B. Propose treatment with dexamethasone alone
C. **Propose combination therapy with dexamethasone and rituximab**
D. **Propose combination therapy with dexamethasone and TPO-RA**
E. Propose combination therapy with dexamethasone and MMF

Recommendation 1:

Recommendation	Strength	Evidence Certainty
In adults with primary ITP requiring initial therapy, the ASH guideline panel ***suggests either*** rituximab plus corticosteroids (with or without IVIG) or a thrombopoietic agent plus corticosteroids (with or without IVIG) rather than mycophenolate mofetil plus corticosteroids (with or without IVIG) or corticosteroids (with or without IVIG) alone [(TPO-RA/TPO; anti-CD20 (recommendation limited to rituximab or its biosimilars))].	Conditional	Low
If rituximab and thrombopoietic agents are not available options, the panel ***suggests*** corticosteroids (with or without IVIG) alone rather than mycophenolate mofetil (MMF) plus corticosteroids (with or without IVIG) [(MMF; corticosteroids alone)].	Conditional	Low

Recommendation 1:

Remarks

- A demonstrable rise in platelet count with corticosteroids and/or IVIG increases confidence in the diagnosis of ITP. Therefore, it is reasonable to treat a patient with a brief course (≤2 weeks) of corticosteroids (with or without IVIG) to increase confidence in the diagnosis of ITP before implementing combination therapy, especially in cases of diagnostic uncertainty.
- Although the most studied corticosteroid component of combination therapy is dexamethasone 40 mg daily × 4 days for 1 to 3 cycles, it is also reasonable to use prednis(ol)one at a starting dose of 0.5-2 mg/kg/day.
- Whether corticosteroids are used as part of combination therapy or alone, it is advisable to limit their administration to 6 weeks or less to minimize toxicity.

Recommendation 1:

Remarks (cont.)

- If combination therapy with rituximab is used, the most studied regimen is 375 mg/m2 × 4 weekly doses. However, other doses and schedules of rituximab may be used according to local practice. Biosimilars to rituximab are suitable substitutes.
- If combination therapy with a thrombopoietic agent is used, any approved thrombopoietic agent at a standard starting dose may be used. The optimal duration of therapy with a thrombopoietic agent is uncertain; it is typically guided by clinical response, toxicity, and platelet count stability. If a thrombopoietic agent and corticosteroids are used together, in a patient who responds, it is advisable to taper the corticosteroids before the thrombopoietic agent.

Case 1: Summary

- 66-year-old man
- Primary ITP, untreated, platelets at $15x10^9$/L, petechia
- History of hypertension and prostate hyperplasia
- **Shared decision making** :
  - Risk factors for thrombosis were considered: male, age
  - Patient prefers infusions rather than daily medication or weekly SC administration

⇒ **Rituximab was thus favored**

  - Risk of infection was then considered:
    - Check for recommended vaccinations: up to date
    - Anti-pneumococcal vaccine: up to date

Case 1: Summary

- **Combination therapy as first-line treatment was chosen**
  - **Dexamethasone 40 mg/day for 4 days** was administered orally, without IVIg
  - After 3 days, platelet count increased to $55x10^9$/L, supporting the diagnosis of ITP
  - Rituximab was started 2 weeks after vaccination
  - In the meantime, platelet count increased up to $110x10^9$/L
  - At the time of rituximab, platelet count was $30x10^9$/L
  - A **new course of dexamethasone 40 mg/day for 4 days** was administered with **rituximab 375 mg/m²/week for 4 weeks**
  - A stable complete response was achieved 3 weeks after D1 (day 1) rituximab
  - The complete response is maintained at 1 year follow-up

CASE 2

Additional Treatment After Initial Therapy with Corticosteroids (with or without IVIG)

Case 2

- 77-year-old woman with persistent ITP
- History of coronary artery disease and 1 unprovoked VTE, now off anticoagulation
- Diagnosed with ITP 3 months ago; initially responded to brief course of corticosteroids ± IVIG
- Relapsed after corticosteroid taper; platelets now <30 x10^9/L
- Prefers to minimize thrombotic risk and avoid rituximab-related immune effects

Blood investigations

- Isolated thrombocytopenia on CBC
- Blood film: normal
- Immunoglobulin level: normal
- Viruses : HIV, HBV, HCV negative
- Liver enzymes: normal
- Bone marrow examination not required
- Antiplatelet antibodies not required

- No organomegaly
- Petechia and bruises on the legs
- No mucosal bleeding

Primary ITP requiring additional treatment after corticosteroids/IVIG

- 77-year-old woman with persistent ITP after initial corticosteroid-based therapy
- Initial response to brief corticosteroids ± IVIG, followed by relapse after taper
- History of coronary artery disease and 1 unprovoked VTE, now off anticoagulation
- Prefers to minimize thrombotic risk and avoid rituximab-related immune effects

What should you do ?

A. Discuss the different treatment options with the patient
B. Propose treatment with TPO-RA
C. Propose treatment with rituximab
D. Propose therapy with BTK inhibitor or MMF or SYK inhibitor
E. Propose therapy with azathioprine

- 77-year-old woman with persistent ITP after initial corticosteroid-based therapy
- Initial response to brief corticosteroids ± IVIG, followed by relapse after taper
- History of coronary artery disease and 1 unprovoked VTE, now off anticoagulation
- Prefers to minimize thrombotic risk and avoid rituximab-related immune effects

What should you do ?

A. Discuss the different treatment options with the patient

ASH guidelines are primarily intended to **help clinicians and patients make shared decisions** about diagnostic and treatment alternatives, with the goal of improving quality of patient care. Other purposes are to inform policy, education and advocacy, and to state future research needs. These guidelines are not intended to serve or be construed as a standard of care. **Clinicians must make decisions on the basis of the clinical presentation of each individual patient, ideally through a shared process that considers the patient's values and preferences with respect to the anticipated outcomes of the chosen option.**

Agents considered

- Thrombopoietic agent
- Anti–CD20
- MMF
- SYK inhibitor
- BTK inhibitor
- Azathioprine

- 77-year-old woman with persistent ITP after initial corticosteroid-based therapy
- Initial response to brief corticosteroids ± IVIG, followed by relapse after taper
- History of coronary artery disease and 1 unprovoked VTE, now off anticoagulation
- Prefers to minimize thrombotic risk and avoid rituximab-related immune effects

What should you do ?

A. **Discuss the different treatment options with the patient**
B. Propose treatment with TPO-RA
C. Propose treatment with rituximab
D. Propose therapy with BTK inhibitor or MMF or SYK inhibitor
E. Propose therapy with azathioprine

Recommendation 2a:

Recommendation	Strength	Evidence Certainty
In adults with primary ITP needing additional treatment after initial therapy with corticosteroids (with or without IVIG), the ASH guideline panel recommends a thrombopoietic agent (strong recommendation based on moderate certainty in the evidence of effects ⊕⊕⊕◯)	Strong	Moderate
or suggests rituximab (conditional recommendation based on low certainty in the evidence ⊕⊕◯◯).	Conditional	Low

Recommendation 2a:

Remarks

- If a thrombopoietic agent is used, any approved thrombopoietic agent at a standard starting dose may be used. Duration of therapy is typically guided by clinical response, toxicity, and platelet count stability.

- Rituximab may be preferable for patients who value avoiding chronic medication, or who have a contraindication to, are unable to access, or cannot tolerate thrombopoietic agents.

- If rituximab is used, the most studied regiment is 375 mg/m2 × 4 weekly doses. However, other doses and schedules of rituximab may be used according to local practice. Biosimilars to rituximab are suitable substitutes.

Recommendation 2b:

Recommendation	Strength	Evidence Certainty
For adults with primary ITP needing additional treatment after initial therapy with corticosteroids (with or without IVIG), who are either ineligible for or choose not to receive a thrombopoietic agent or rituximab, the ASH guideline panel suggests a BTK inhibitor, MMF, or a SYK inhibitor (conditional recommendation based on very low certainty in the evidence ⨁◯◯◯).	Conditional	Very low

Remarks

- The panel concluded that current evidence in the population of interest is too indirect to definitively rank BTK inhibitors, MMF, or SYK inhibitors. Side effect profiles, cost, availability, and shared decision-making may be considered in selecting an agent.
- The panel concluded that azathioprine has a less favorable benefit to harm ratio; therefore, it is not equivalent to the other suggested treatment options. Nevertheless, azathioprine may be useful in some settings due to its low cost, global availability, and safety profile in pregnancy.

Case 2: Summary

- 77-year-old woman with persistent ITP after initial corticosteroid-based therapy
- Initial response to brief corticosteroids ± IVIG, followed by relapse after taper
- History of coronary artery disease and 1 unprovoked VTE, now off anticoagulation
- Prefers to minimize thrombotic risk and avoid rituximab

- **Shared decision making**:
  - Thrombotic risk factors considered: age, prior unprovoked VTE, and CAD
  - Preferred to **avoid TPO-RA** because of thrombotic concerns and **rituximab** because of concerns about prolonged immunosuppression.
  - **Pros and Cons of BTK-inhibitor vs. MMF vs. SYK-inhibitor** were discussed
- **Decision:** Patient chose treatment with **MMF**
  - A stable response (Platelets >70x10^9/L) was achieved 8 weeks after initiating MMF
  - Response is maintained at 1 year follow-up

CASE 3

Splenectomy

Objectives (Splenectomy)

- Identify appropriate candidates for splenectomy among adults with primary ITP
- Understand timing according to guidelines (delay ≥1 year after diagnosis when feasible)
- Balance efficacy versus surgical and long-term risks

Guideline Context

Splenectomy remains an appropriate consideration for select adults with primary ITP. This includes patients who have failed or are intolerant to multiple lines of medical therapy at optimal doses and durations, wish to avoid long-term medical treatment, or require emergent treatment for severe thrombocytopenia after inadequate response to medical therapies.

Case 3: Splenectomy

- 64-year-old male patient weighing 165 lbs (75 kg)
- Key comorbidities:

  Peripheral polyneuropathy secondary to radiofrequency-treated renal carcinoma (Sept 2011), Raynaud disease, dysphonia, osteoporosis, avascular necrosis of the femoral head, gastroesophageal reflux disease
- Key treatments:

  Omeprazole, duloxetine, clonazepam, vitamin D supplementation

Case 3: Splenectomy

- February 2023: diagnosis of immune thrombocytopenia (ITP); platelet count 22 × 10^9/L; no bleeding.
  - Treated with prednisone 1 mg/kg/day × 7 days: complete response (CR)
- October 2023: relapse; platelet count 14 × 10^9/L; no bleeding
  - Treated with prednisone 1 mg/kg/day × 7 days: response (R) (peak platelet count: 78 × 10^9/L)
- March 2024: second relapse; platelet count 2 × 10^9/L; skin bleeding (ecchymoses)
  - Treated with prednisone 1 mg/kg/day × 7 days + IVIG 1 g/kg/day × 2 days: no response (NR)

Case 3: Splenectomy

- April 2024: eltrombopag initiated at 50 mg/day: no response (NR)
- May 2024: eltrombopag escalated up to 75 mg/day: no response (NR)
- June 2024: romiplostim initiated at 1 µg/kg/week SC and titrated weekly to the maximum approved dose of 10 µg/kg/week (750 µg): no response (NR)
- July 2024: avatrombopag initiated at 40 mg/day: no response (NR)
- August 2024: rituximab 600 mg (375 mg/m^2) weekly × 4 doses: no response (NR)
- September 2024: azathioprine 150 mg/day: no response (NR)
- October 2024: danazol 200 mg/day: no response (NR)

Case 3: Splenectomy

- November 2024: cyclosporine 100 mg/day: no response (NR)
- December 2024: vinblastine 6 mg IV daily × 3 days: no response (NR)
- January 2025: dapsone: no response (NR)
- February 2025: oseltamivir, 2 cycles: minimal, unsustained platelet response; peak platelet count 38 × 10^9/L
- March 2025: platelet relapse 2 weeks after response

Question

What is the best next step?

A. Resume oseltamivir monotherapy
B. Add immunosuppression to oseltamivir
C. Add romiplostim to oseltamivir
D. Splenectomy

Answer

What is the best next step?

A. Resume oseltamivir monotherapy
B. Add immunosuppression to oseltamivir
C. Add romiplostim to oseltamivir
D. **Splenectomy**

In a patient refractory to multiple therapies with ITP duration >1 year, splenectomy is likely the best therapeutic option.

Background (cont.)

Splenectomy is an appropriate consideration in adults with primary ITP in the following circumstances: 1) patients who are intolerant to or have failed multiple lines of medical therapy at optimal doses and durations, 2) patients who wish to avoid long-term medical treatment, and 3) patients with severe thrombocytopenia who need emergent treatment and have an inadequate response to medical therapies.

Background

Indium-labeled autologous platelet scintigraphy (ILAPS) predicts the likelihood of response to splenectomy. In a systematic review and meta-analysis, the response rate was 87.1%, 47.1%, and 25.5% in patients with a splenic, mixed, and hepatic sequestration pattern, respectively. ILAPS is currently only offered at a small number of centers around the world.

Normalization of the platelet count following splenectomy does not prevent transplacental passage of maternal anti-platelet antibodies during pregnancy, which can cause neonatal thrombocytopenia.

Case 3: Summary & Treatment Decision

- November 2024: Cyclosporine, 100 mg/d → NR
- December 2024: Vinblastine 6 mg iv, 3 days → NR
- January 2025: Dapsone → NR
- February 2025: Oseltamivir (2 cycles) → Minimum not sustained platelet response (peak 38 × 10^9/L)
- March 2025: Platelet relapse (2 weeks after response)
- **March 2025: Laparoscopic splenectomy → CR**

Good practice statements:

If possible, splenectomy should be delayed for at least one year after diagnosis because of the potential for remission.

The treating clinician should ensure that patients receive appropriate immunizations at least two weeks prior to splenectomy, when feasible, and counseling regarding antibiotic prophylaxis and lifelong risk of sepsis and thrombosis following splenectomy. The treating clinician should educate the patient on prompt recognition and management of fever with antibiotics. After splenectomy, patients should be followed at least annually for platelet count monitoring, counseling, and to ensure adherence to recommended immunization schedules.

CASE 4

Switching thrombopoietic agents

Objectives (Switching TPO-RAs)

- Apply guideline recommendations in practice
- Understand TPO-RA switching

Guideline Context

- TPO-RAs are recommended second-line therapy
- Optimizing their use (including the switching among these drugs) is essential in clinical practice

Case 4: Switching TPO-RAs

- 80-year-old woman with chronic ITP
- Overweight (5'5" tall, 154 pounds)
- Geographic distance (~53 miles) potentially limits access to care
- **Key comorbidities:** Type 2 diabetes mellitus, osteoporosis, iron deficiency anemia (on iron supplementation), rheumatoid arthritis, peptic ulcer disease
- **Key treatments:** Metformin, oral iron supplementation, omeprazole, benzodiazepine (lorazepam), acetaminophen, alendronate, vitamin D

Case 4: Switching TPO-RAs

- May 2024: diagnosis of immune thrombocytopenia (ITP); platelet count 14 × 10^9/L; no bleeding
- May 2024: prednisone 1 mg/kg/day × 7 days: complete response (CR)
- August 2024: relapse; platelet count 3 × 10^9/L; skin bleeding/petechiae; prednisone 1 mg/kg/day × 7 days + IVIG 1 g/kg/day × 2 days: complete response (CR)
- November 2024: second relapse; platelet count 7 × 10^9/L; skin bleeding/petechiae and ecchymoses; prednisone 1 mg/kg/day × 7 days + IVIG 1 g/kg/day × 2 days: complete response (CR); corticosteroid dependence confirmed following second ITP relapse

Case 4: Switching TPO-RAs

- December 2024: type 2 diabetes mellitus requiring insulin; eltrombopag initiated at 50 mg/day: response (R); peak platelet count 53 × 10^9/L
- February 2025: eltrombopag dose escalated up to 75 mg/day to maintain platelet response
- April 2025: relapse on eltrombopag; platelet count 9 × 10^9/L; no bleeding

Question

Best next step?

A. Continue eltrombopag
B. Add immunosuppression
C. Switch TPO-RA
D. Splenectomy

Answer

Best next step?

A. Continue eltrombopag
B. Add immunosuppression
C. Switch TPO-RA
D. Splenectomy

- Best next step: **switch TPO-RA, from eltrombopag to romiplostim**
- In this patient, eltrombopag has proven ineffective as monotherapy, and immunosuppressive agents require time to achieve a response, while the patient's condition is urgent.
- Given the possibility of spontaneous remission in ITP, splenectomy is traditionally reserved, including in these guidelines, for patients with disease duration of at least 1 year.

Case 4: Summary & Treatment Decision

- December 2024: type 2 diabetes mellitus requiring insulin; eltrombopag treatment initiation: response (R); peak platelet count 53 × 10^9/L
- February 2025: escalating eltrombopag doses up to 75 mg/day to maintain platelet response
- April 2025: relapse on eltrombopag; platelet count 9 × 10^9/L; no bleeding
- Romiplostim initiated at 1 µg/kg/week SC and titrated weekly to 3 µg/kg (250 µg), the minimum dose required to achieve a stable platelet count of 70–80 × 10^9/L
- **Sustained response achieved**

Good practice statements:

Background: Patients differ in their response to and tolerance of individual thrombopoietic agents. Patients who have failed to respond to one agent may respond to a different one.

Switching to a different thrombopoietic agent may be considered based on insufficient response, adverse effects, comorbidities, poor adherence, or patient preference.

Shared decision-making with the patient, documentation of the rationale for switching, avoidance of treatment gaps, and close monitoring around the time of switching are good practices to ensure optimal outcomes and continuity of care.

Future Priorities for Research

- Determination of the optimal initial therapy (modality, dose, and duration of treatment), including corticosteroids alone vs. combination regimens with rituximab or thrombopoietic agents
- Impact of the interval between diagnosis and start of initial therapy on outcomes, and long-term follow-up to determine SRoT beyond 12 months after initial combination therapy (do these regimens "cure" some patients or mainly postpone relapse?)
- Determination of the optimal second-line therapy (modality and timing), and generation of more and higher-quality evidence on agents such as azathioprine, MMF, BTK inhibitors, and SYK inhibitors, including their use in refractory disease and in combination regimens
- Identification of clinical predictors and/or biomarkers to guide prioritization and sequencing of specific therapies in individual patients
- Evaluation of the safety of ITP therapies in pregnancy and other vulnerable populations, with attention to long-term outcomes

In Summary: Back to our Learning Objectives

By the end of this session, you should be able to

1. Choose appropriate initial treatment for adults with primary ITP **(Case 1)**
2. Choose appropriate therapy for adults with primary ITP requiring additional treatment after corticosteroids (with or without IVIG) **(Case 2)**
3. Determine the role and optimal timing of splenectomy in the modern treatment landscape **(Case 3)**
4. Optimize treatment sequencing, including switching between thrombopoietic agents when appropriate **(Case 4)**

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See more about the **ASH ITP guidelines** at https://www.hematology.org/immune-thrombocytopenia-guidelines.