Immune Thrombocytopenia

An Educational Slide Set
American Society of Hematology 2019 Guidelines for Immune Thrombocytopenia

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American Society of Hematology 2019 Guideline for Immune Thrombocytopenia

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ASH Clinical Practice Guidelines on ITP

1. Evidence Review and Development of Recommendations
2. How to Use these Guidelines - Interpretation of Strong and Conditional Recommendations
3. Management of newly diagnosed adult patients with immune thrombocytopenia
4. Management of adults with ITP who are corticosteroid dependent or do not have a response to corticosteroids
5. Management of children newly diagnosed with ITP
6. Management of children with ITP unresponsive to first-line therapy
7. Other ITP therapies
8. Priorities for future research
How were these ASH guidelines developed?

**PANEL FORMATION**
Each guideline panel was formed following these key criteria:
- Balance of expertise (including disciplines beyond hematology, and patients)
- Close attention to minimization and management of COI

**CLINICAL QUESTIONS**
10 to 20 clinically-relevant questions generated in PICO format (population, intervention, comparison, outcome)

**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

**Example: PICO question**
"Should adults with newly diagnosed ITP and a platelet count of <30 × 10^9/L who are asymptomatic or have minor mucocutaneous bleeding be treated with corticosteroids or observation?"

**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. Resources, such as this slide set, derived from guidelines that require updating are removed from the ASH website.
How patients and clinicians should use these recommendations

|                      | STRONG Recommendation ("The panel recommends...") | CONDITIONAL Recommendation ("The panel suggests...") |
|----------------------|----------------------------------------------------|------------------------------------------------------|
| **For patients**     | Most individuals would want the intervention.       | A majority would want the intervention, but many would not. |
| **For clinicians**   | Most individuals should receive the intervention.   | Different choices will be appropriate for different patients, depending on their values and preferences. Use shared decision making. |
Objectives

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

1. Describe recommendations for managing adults and children with newly diagnosed ITP

2. Describe recommendations for managing adults with ITP who are corticosteroid dependant or unresponsive to corticosteroids

3. Describe recommendations for managing children with ITP who are unresponsive to first-line therapy
ITP is an acquired autoimmune disorder with heterogeneous presentation and disease severity.

These guidelines are intended to help clinicians make decisions about management of ITP in adults and children.

Recognizing potential risks of ITP and balancing benefits and side effects of available therapies can be complex and requires an evidence-based approach to management.

These guidelines will not cover emergency treatment of ITP.

Additional recommendations regarding the diagnosis of ITP, management of ITP in pregnancy and secondary ITP were carried over from the 2011 ASH guidelines.

Cindy Neunert, Wendy Lim, Mark Crowther, Alan Cohen, Lawrence Solberg, Mark A. Crowther; The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011; 117 (16): 4190-4207. doi: https://doi.org/10.1182/blood-2010-08-302984

What do the ASH ITP guidelines cover?
MANAGEMENT OF NEWLY DIAGNOSED ADULT PATIENTS WITH ITP
Case 1: New thrombocytopenia

26-year-old female seen by her PCP for a routine yearly checkup:

Complete blood count with differential is normal except for a low platelet count of 50 x 10^9/L. She is asymptomatic without any concerns for bleeding.

**Physical Examination:** No additional findings on exam

**Labs:** HIV, Hep C and B are normal and metabolic panel is unremarkable

Peripheral blood smear shows no platelet clumping or other morphologic abnormalities

**Past Medical History:** None

**Medications:** None

**Diagnosis:** ITP
As her hematologist, what is the next best step for treating this patient?

A. Initiate low dose prednisone at 20mg/day for ‘mild ITP’
B. Discharge the patient back to her PCP for annual lab work
C. Monitor her labs closely
D. Initiate dexamethasone at 40mg/day x 4 days for a quick response
Recommendation

In adults with newly diagnosed ITP and a platelet count of ≥30 x 10^9/L who are asymptomatic or have minor mucocutaneous bleeding, the panel recommends *against* corticosteroids rather than management with observation *(Strong recommendation based on very low certainty in the evidence)*.

This represents a paradigmatic situation when a strong recommendation may be used despite low confidence in the effects. High quality indirect evidence in other patient populations that the likelihood of adverse events were considered large.

For patients with a platelet count at the lower end of this threshold, for those with additional comorbidities that predispose to bleeding, anticoagulant or antiplatelet medications, and upcoming procedures, and for elderly patients (>60 years old), treatment with corticosteroids may be appropriate.
**Recommendation**

In adults with newly diagnosed ITP and a platelet count of $<30 \times 10^9$/L who are asymptomatic or have minor mucocutaneous bleeding, the panel suggests **corticosteroids rather than management with observation** *(Conditional recommendation based on very low certainty in the evidence)*

- The platelet count threshold at which bleeding risk increases and the natural history of newly diagnosed ITP with a platelet count of $<30 \times 10^9$/L managed with observation is not known.
- At higher platelet counts within this population or in younger patients, observation may be reasonable.
- Consideration should be given to additional comorbidities, use of anticoagulants or antiplatelet medications, need for upcoming procedures, and age of the patient.
Good Practice Statement

• The treating physician should ensure the patient is adequately monitored for potential corticosteroid side effects regardless of the duration or type of corticosteroid selected. This includes close monitoring for hypertension, hyperglycemia, sleep and mood disturbances, gastric irritation or ulcer formation, glaucoma, myopathy, and osteoporosis.

• Given the potential impact of corticosteroids on mental health, the treating physician should conduct an assessment of health-related quality of life (depression, fatigue, mental status, etc.) while patients are receiving corticosteroids.
Case 1, Continued:

• Her platelet count continues to be around $50 \times 10^9/L$ on monthly monitoring until 3 months later when she calls your office because of ‘blood blisters’ appearing suddenly in her mouth, large skin bruises on her arms and legs, and menorrhagia.

• She also reports feeling more fatigued than usual.

• Her platelet count is $15 \times 10^9/L$ and her hemoglobin has dropped to 10 g/dL
How should you manage her severe ITP with bleeding?

A. Observation since she has an acute viral illness that will self resolve
B. Initiate low dose prednisone at 20mg/day and return to clinic in a week
C. Admit her to the hospital and start treatment with corticosteroids
D. Start eltrombopag for initial episode of symptomatic severe ITP
Three relevant recommendations:

• In adults with newly diagnosed ITP and a platelet count of <20 x10^9/L who are asymptomatic or have minor mucocutaneous bleeding, the panel suggests admission to the hospital (Conditional recommendation based on very low certainty in the evidence).

• In adults with an established diagnosis of ITP and a platelet count of <20 x10^9/L who are asymptomatic or have minor mucocutaneous bleeding, the panel suggests outpatient management (Conditional recommendation based on very low certainty in the evidence).

• In adults with a platelet count of ≥20 x10^9/L who are asymptomatic or have minor mucocutaneous bleeding, the panel suggests outpatient management (Conditional recommendation based on very low certainty in the evidence).
Remarks and Good Practice Statement

• In any setting, patients refractory to treatment, with social concerns, uncertainty about the diagnosis, significant comorbidities with risk of bleeding, and more significant mucosal bleeding may benefit from admission to the hospital.

• Patients not admitted to the hospital should receive expedited follow-up with a hematologist. The need for admission is also variable across the range of platelet counts represented across the two recommendations.

• The referring physician should ensure that the patient has follow-up with a hematologist within 72 hours of the diagnosis or disease relapse.
Recommendation

In adults with newly diagnosed ITP, the panel recommends **against a prolonged course (>6 weeks) of prednisone rather than a short course (≤ 6 weeks)** *(Strong recommendation based on very low certainty in the evidence)*

- This represents a paradigmatic situation when a strong recommendation may be used despite low confidence in the effects.
- There is no evidence for a benefit with longer duration of corticosteroids and high-quality indirect evidence for adverse events with the use of courses of corticosteroids for > 6 weeks based on.
- Side effects include hypertension, hyperglycemia, sleep and mood disturbances, gastric irritation or ulcer formation, glaucoma, and osteoporosis.
- Corticosteroid course duration of 6 weeks represents a reasonable duration to provide a standard maximum 21 days of treatment plus additional time for the taper.
Recommendation

In adults with newly diagnosed ITP requiring corticosteroids, the panel suggests either prednisone (0.5 to 2.0 mg/kg/day) or dexamethasone (40 mg/day for 4 days) for initial therapy (Conditional recommendation based on very low certainty in the evidence).

If rapidity of platelet count response is important, an initial course of dexamethasone over prednisone may be preferred given that dexamethasone showed increased desirable effects with regards to response at 7 days.
Good Practice Statement

• The treating physician should ensure the patient is adequately monitored for potential corticosteroid side effects regardless of the duration or type of corticosteroid selected. This includes close monitoring for hypertension, hyperglycemia, sleep and mood disturbances, gastric irritation or ulcer formation, glaucoma, myopathy, and osteoporosis.

• Given the potential impact of corticosteroids on mental health, the treating physician should conduct an assessment of health-related quality of life (depression, fatigue, mental status, etc.) while patients are receiving corticosteroids.
Recommendation

In adults with newly diagnosed ITP, the panel suggests against rituximab and corticosteroids rather than corticosteroids alone for initial therapy (Conditional recommendation based on very low certainty in the evidence)

• If high value is placed on possibility for remission over concerns for potential side effects of rituximab, then an initial course of corticosteroids with rituximab may be preferred.
• The addition of rituximab increases treatment costs; it is unknown if these additional up-front costs are off set by avoidance of later expenses.
MANAGEMENT OF ADULTS WITH ITP WHO ARE CORTICOSTEROID DEPENDENT OR UNRESPONSIVE
Case 1, Continued:

• It has now been 6 months since you initiated corticosteroids for ITP.
• She has responded to prednisone but relapsed following a taper.
• She was subsequently treated with a course of dexamethasone, but invariably relapsed again.
• She presents to your office to discuss options to prevent another relapse
Which of these statements is false about the next best course of action?

A. Rituximab has a durable effect on preventing ITP recurrences for 5 years in 75% with relapsed ITP
B. Either thrombopoietin receptor agonist is an acceptable option for treatment of ITP after failure of corticosteroid therapy
C. Splenectomy is effective for treatment of relapsed ITP, but carries increased risk of long term infections and thrombosis
D. Several immunosuppressive agents like mycophenolate mofetil and azathioprine have activity in adults with relapsed ITP, but are usually reserved for patients who fail second-line therapies
Recommendation

In adults with ITP for ≥ 3 months who are corticosteroid-dependent or unresponsive and are going to be treated with a thrombopoietin receptor agonist, the panel suggests **either eltrombopag or romiplostim** (*Conditional recommendation based on very low certainty in the evidence*)

Individual patient preference may place higher value on use of a daily oral medication (Eltrombopag) or one that requires weekly subcutaneous injection (Romiplostim).
Three relevant recommendations:

- In adults with ITP lasting ≥3 months who are corticosteroid dependent or unresponsive, the ASH guideline panel suggests **either splenectomy or a thrombopoietin receptor agonist** (Conditional recommendations based on very low certainty in the evidence)

- In adults with ITP lasting ≥3 months who are corticosteroid dependent or unresponsive, the panel suggests **rituximab rather than splenectomy** (Conditional recommendations based on very low certainty in the evidence)

- In adults with ITP lasting ≥3 months who are corticosteroid dependent or unresponsive, the panel suggests **a thrombopoietin receptor agonist rather than rituximab** (Conditional recommendations based on very low certainty in the evidence)
Remarks

• The choice of second-line treatment should be individualized based on duration of ITP, frequency of bleeding episodes requiring hospitalization or rescue medication, comorbidities, adherence, medical and social support networks, patient values and preferences, cost, and availability.

• Patient education and shared decision-making are encouraged.

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

• Patients who value avoidance of long-term medication may prefer splenectomy or rituximab.

• Patients who wish to avoid surgery may prefer a thrombopoietin receptor agonist (TPO-RA) or rituximab.

• Patients who place a high value on achieving a durable response may prefer splenectomy or TPO-RAs.
Algorithm for the selection of second-line therapy in adults with ITP

Figure 1. Selection of second-line therapy in adults with ITP should be individualized based on duration of disease and patient values and preferences. Other factors that may influence treatment decisions include frequency of bleeding sufficient to require hospitalization or rescue medication, comorbidities, compliance, medical and social support networks, cost, and availability of treatments. Patient education and shared decision-making is encouraged.

- **TPO-RA** – thrombopoietin receptor agonist
- All recommendations in Figure 1 are conditional recommendations
Good Practice Statement

• The treating physician should ensure that patients have appropriate immunizations prior to splenectomy and that they receive counseling regarding antibiotic prophylaxis following splenectomy.
• The treating physician should also educate the patient on prompt recognition and management of fever and refer to current recommendations on pre- and post-splenectomy care.
MANAGEMENT OF NEWLY DIAGNOSED CHILDREN WITH ITP
Case 2:

6-year-old male presents with a 24-hour history of bruising and petechiae with no additional bleeding. He was previously healthy and there is no family history of thrombocytopenia.

Physical examination: Scattered petechiae and several bruises to the arms and legs
There is no lymphadenopathy or hepatosplenomegaly

Labs: Complete blood count with a platelet count of $8 \times 10^9/L$ and is otherwise normal
Peripheral blood smear shows a few large platelets and no other morphologic abnormalities

Medications: None

Diagnosis: ITP
As his hematologist, what is the next best step for treating this patient?

A. Initiate prednisone at 20mg/day
B. Discharge the patient back to her PCP for annual lab work
C. Admit to hospital for IVIg
D. Monitor his labs and educate the family about potential bleeding symptoms
Two relevant recommendations:

- In children with newly diagnosed ITP, a platelet count of $< 20 \times 10^9/L$ and no or mild bleeding only, the ASH panel suggests **against admission to the hospital rather than outpatient** *(Conditional recommendations based on very low certainty in the evidence)*

- In children with newly diagnosed ITP, a platelet count of $\geq 20 \times 10^9/L$ and no or mild bleeding only, the ASH panel suggests **against admission to the hospital rather than treatment as an outpatient** *(Conditional recommendations based on very low certainty in the evidence)*

For patients with uncertainty about the diagnosis, those with social concerns, those who live far from the hospital, or those for whom follow-up cannot be guaranteed, admission may be preferable.

The referring physician should ensure that the patient has follow-up with a hematologist within 72 hours of the diagnosis or disease relapse.
Three relevant recommendations:

• In children with newly diagnosed ITP and no or minor bleeding, the panel suggests **observation rather than corticosteroids** *(Conditional recommendation based on very low certainty in the evidence)*

• In children with newly diagnosed ITP and no or minor bleeding, the panel recommends **observation rather than intravenous immunoglobulin** *(Strong recommendation based on moderate certainty in the evidence)*

• In children with newly diagnosed ITP and no or minor bleeding, the ASH panel **recommends observation rather than anti-D immunoglobulin** *(Strong recommendation based on moderate certainty in the evidence)*
Remarks

• Recommendations 12 and 13 represent a paradigmatic situation when a strong recommendation may be used despite low confidence in the effects.

• The likelihood of adverse events were considered large with the use of either IVIg or anti-D immunoglobulin.

• Treating physicians should be mindful of the blackbox warnings associated with IVIG: thrombosis and acute renal failure.

• Treating physicians should be mindful of the blackbox warnings associated with anti-D immunoglobulin: fatal intravascular hemolysis.
Case 2: Continued

- The child’s mother calls you and in addition to a few bruises she notices “wet purpura” in the his mouth.
- She also states that he had a 10 minute episode of epistaxis the day before that stopped with pressure.
- His platelet count is $6 \times 10^9$/L
- You decide to treat him with corticosteroids
What dose of corticosteroids should be prescribed?

A. Dexamethasone 0.6mg/kg/day (maximum of 40 mg/day) for 4 days
B. Prednisone 2-4mg/kg/day (maximum 120 mg daily) for 5-7 days
C. Prednisone 0.5-1.0 mg/kg/day for 10 days
D. Prednisone 2-4mg/kg/day for 21 days with a taper based on platelet count
In children with newly diagnosed ITP with non-life-threatening bleeding and/or diminished health related quality of life, the panel recommends **against courses of corticosteroids longer than 7 days rather than courses 7 days or shorter** *(Strong recommendation based on very low certainty in the evidence)*

- This represents a paradigmatic situation when a strong recommendation may be used despite low confidence in the effects.
- There is no evidence for a benefit with longer duration of corticosteroids and high-quality indirect evidence for adverse events with the use of courses of corticosteroids for > 7 days in children.
- Side effects associated with prolong corticosteroid exposure include hypertension, hyperglycemia, sleep and mood disturbances, gastric irritation or ulcer formation, glaucoma, and osteoporosis.
Recommendation

In children with newly diagnosed ITP and non life-threatening mucosal bleeding and/or diminished health-related quality of life, the ASH guideline panel suggests prednisone (2 to 4 mg/kg/day; maximum, 120 mg daily, for 5-7 days) rather than dexamethasone (0.6 mg/kg/day; maximum, 40 mg/day, for 4 days) (Conditional recommendation based on very low certainty in the evidence)
Three relevant recommendations:

- In children with newly diagnosed ITP and non-life-threatening mucosal bleeding and/or diminished health-related quality of life (HRQOL), the panel suggests **corticosteroids rather than anti-D immunoglobulin** *(Conditional recommendations based on low certainty in the evidence)*

- In children with newly diagnosed ITP who have non–life-threatening mucosal bleeding and/or diminished HRQoL, the panel suggests **either anti-D immunoglobulin or IVIG** *(Conditional recommendations based on low certainty in the evidence)*

- In children with newly diagnosed ITP who have non–life-threatening mucosal bleeding and/or diminished HRQoL, the panel suggests **corticosteroids rather than IVIG** *(Conditional recommendations based on low certainty in the evidence)*

  - These recommendations are based on the corticosteroid dosing outlined above
  - These recommendations are reserved only for children with non-life-threatening mucosal bleeding that is not severe
MANAGEMENT OF CHILDREN WITH ITP UNRESPONSIVE TO FIRST-LINE THERAPY
Case 2: Continued

- 6 months later the child continues to have a platelet count of $20 \times 10^9$/L
- He responds to IVIg every 3 weeks
- He has had a decline in response to Anti-D immunoglobulin and corticosteroids
- Suffers from recurrent epistaxis and as a result is being sent home from school
- Parents are wondering whether the child can return to soccer practice and report that his quality of life suffering
Case 2: Continued

What treatment should you offer the child now?

A. Continue with IVIg every 3 weeks
B. Splenectomy
C. Romiplostim in combination with corticosteroids
D. Discuss treatment with either rituximab or a thrombopoietin receptor agonist
E. No therapy
Three relevant recommendations:

- In children with ITP who are unresponsive to first-line treatment, the panel suggests **the use of thrombopoietin receptor agonists rather than rituximab** *(Conditional recommendation based on very low certainty in the evidence)*

- In children with ITP who are unresponsive to first-line treatment, the panel suggests **the use of thrombopoietin receptor agonists rather than splenectomy** *(Conditional recommendation based on very low certainty in the evidence)*

- In children with ITP who are unresponsive to first-line treatment, the panel suggests **the use of rituximab rather than splenectomy** *(Conditional recommendation based on very low certainty in the evidence)*
Good Practice Statements and Remarks

- The treating physician should ensure that patients have appropriate immunizations prior to splenectomy and that they receive counseling regarding antibiotic prophylaxis following splenectomy.

- The treating physician should also educate the patient on prompt recognition and management of fever and refer to current recommendations on pre- and post-splenectomy care.

- The choice of second-line treatment should be individualized based on duration of ITP, frequency of bleeding episodes requiring hospitalization or rescue medication, comorbidities, adherence, medical and social support networks, patient values and preferences, cost, and availability.

- Patient education and shared decision-making are encouraged.

- If possible, splenectomy should be delayed for as long as possible after diagnosis because of the potential for spontaneous remission.
## Other ITP therapies

| Drug                  | No. of studies | Response within 7 days | Response within 1 month | Durable Response | Remission |
|-----------------------|----------------|------------------------|-------------------------|------------------|-----------|
|                       |                | Unweighted | Weighted (95% CI)       | Unweighted | Weighted (95% CI) | Unweighted | Weighted (95% CI) | Unweighted | Weighted (95% CI) |
| Azathioprine          | 3              | 27%        | 30% (1-95%)             | 59%        | 58% (45-70%)     | 40%        | 21/53 | NA |
|                       |                | N=2        | N=2                     | N=2        | N=2              | N=1        | N=1              | N=1        | N=1              |
| Cyclophosphamide      | 4              | 34%        | 34% (3-91%)             | 58%        | 57% (46-68%)     | 48%        | 19/40 | 45% (25-67%) |
|                       |                | N=2        | N=2                     | N=2        | N=2              | N=2        | N=2              | N=2        | N=2              |
| Cyclosporine A        | 5              | 48%        | 48% (38-58%)            | 32%        | 32% (21-47%)     | 27%        | 21/79 | 27% (18-37%) |
|                       |                | N=4        | N=4                     | N=3        | N=3              | N=3        | N=3              | N=3        | N=3              |
| Danazol               | 9              | 33%        | 38% (26-52%)            | 59%        | 57% (38-74%)     | 5%         | 1/21 | NA |
|                       |                | N=7        | N=7                     | N=5        | N=5              | N=1        | N=1              | N=1        | N=1              |
| Dapsone               | 5              | 50%        | 50% (39-60%)            | 22%        | 21% (7-47%)      | 13%        | 12/89 | 13% (6-27%) |
|                       |                | N=5        | N=5                     | N=3        | N=3              | N=2        | N=2              | N=2        | N=2              |
| Mycophenolate mofetil | 4              | 48%        | 48% (37-60%)            | 61%        | 61% (49-71%)     | 23%        | 16/71 | 22% (8-48%) |
|                       |                | N=4        | N=4                     | N=3        | N=3              | N=3        | N=3              | N=3        | N=3              |
| Vinca alkaloids       | 14             | 71%        | 71% (52-85%)            | 65%        | 65% (57-72%)     | 25%        | 52/206 | 26% (20-33%) |
|                       |                | N=3        | N=3                     | N=6        | N=6              | N=5        | N=5              | N=5        | N=5              |
## Adult ITP Summary

| Recommendation | Population                                                                 | Intervention         | Comparator   | Strength  | Certainty in the evidence |
|----------------|----------------------------------------------------------------------------|----------------------|--------------|-----------|---------------------------|
| 1a             | Newly Diagnosed Platelet Count $< 30 \times 10^9/l$ Asymptomatic or minor bleeding | Corticosteroids      | Observation  | Conditional | Very low                  |
| 1b             | Newly Diagnosed Platelet Count $> 30 \times 10^9/l$ Asymptomatic or minor bleeding | Corticosteroids      | Observation  | Strong     | Very low                  |
| 2a             | Newly diagnosed Platelet Count $< 20 \times 10^9/l$ Asymptomatic or minor bleeding | Inpatient (new patient) | Outpatient (established patient) | Conditional | Very low                  |
| 2b             | Newly Diagnosed Platelet Count $> 20 \times 10^9/l$ Asymptomatic or minor bleeding | Inpatient            | Outpatient   | Conditional | Very low                  |
## Adult ITP Summary

| Recommendation | Population                        | Intervention               | Comparator                        | Strength | Certainty in the evidence |
|----------------|-----------------------------------|---------------------------|----------------------------------|----------|---------------------------|
| 3              | Newly diagnosed Requiring corticosteroids | Prolonged corticosteroids | Short course of corticosteroids | Strong   | Very low                  |
| 4              | Newly diagnosed Requiring corticosteroids | Prednisone                | Dexamethasone                     | Conditional | Very low                  |
| 5              | Newly diagnosed                   | Corticosteroids           | Corticosteroids plus rituximab    | Conditional | Very low                  |
## Adult ITP Summary

| Recommendation | Population                                                                 | Intervention    | Comparator     | Strength  | Certainty in the evidence |
|----------------|-----------------------------------------------------------------------------|-----------------|----------------|-----------|---------------------------|
| 6              | ITP > 3 months                                                               | Eltrombopag     | Romiplostim    | Conditional| Very low                  |
|                | No response or unresponsive to corticosteroids                              |                 |                |           |                           |
| 7              | ITP > 3 months                                                               | Splenectomy     | TPO-RA<sup>1</sup> | Conditional| Very low                  |
|                | No response or unresponsive to corticosteroids                              |                 |                |           |                           |
| 8              | ITP > 3 months                                                               | Rituximab       | Splenectomy    | Conditional| Very low                  |
|                | No response or unresponsive to corticosteroids                              |                 |                |           |                           |
| 9              | ITP > 3 months                                                               | TPO-RAs<sup>1</sup> | Rituximab     | Conditional| Very low                  |
|                | No response or unresponsive to corticosteroids                              |                 |                |           |                           |

<sup>1</sup> TPO-RA: Thrombopoietin receptor agonist
# Pediatric ITP Summary

| Recommendation | Population | Intervention | Comparator | Strength | Certainty in the evidence |
|----------------|------------|--------------|------------|----------|---------------------------|
| 10a/b          | Newly diagnosed | Inpatient | Outpatient | Conditional | Very low |
| 11             | Newly diagnosed No or mild bleeding | Corticosteroids | Observation | Conditional | Very low |
| 12             | Newly diagnosed No or mild bleeding | IVIg | Observation | Strong | Moderate |
| 13             | Newly diagnosed No or mild bleeding | Anti-D immunoglobulin | Observation | Strong | Moderate |
| 14             | Newly diagnosed Non-life-threatening mucosal bleeding or impaired HRQoL | Prolonged corticosteroids | Short course corticosteroids | Strong | Very low |
| 15             | Newly diagnosed Non-life-threatening mucosal bleeding or impaired HRQoL | Prednisone | Dexamethasone | Conditional | Very low |
## Pediatric ITP Summary

| Recommendation | Population | Intervention   | Comparator | Strength     | Certainty in the evidence |
|----------------|------------|----------------|------------|--------------|---------------------------|
| 16             | Newly diagnosed Non-life-threatening mucosal bleeding or impaired HRQoL | Corticosteroids | Anti-D immunoglobulin | Conditional | Low                       |
| 17             | Newly diagnosed Non-life-threatening mucosal bleeding or impaired HRQoL | Anti-D immunoglobulin | IVIg | Conditional | Low                       |
| 18             | Newly diagnosed Non-life-threatening mucosal bleeding or impaired HRQoL | Corticosteroids | IVIg | Conditional | Low                       |
| 19             | Unresponsive to first-line therapy | TPO-RA<sup>1</sup> | Rituximab | Conditional | Very low                 |
| 20             | Unresponsive to first-line therapy | TPO-RA<sup>1</sup> | Splenectomy | Conditional | Very low                 |
| 21             | Unresponsive to first-line therapy | Rituximab | Splenectomy | Conditional | Very low                 |

<sup>1</sup>TPO-RA: Thrombopoietin receptor agonist
Future Priorities for Research

- Although the need for randomized control trials in ITP is not debated, the conduct of these trials is challenging. The panel recommends that collaborative cohort studies (retrospective and prospective), registries, and other observational studies addressing these issues could contribute much to improve the current levels of evidence and are likely more feasible.

- Studies should apply standard dosing regimens and definitions, report on patient-reported outcomes including health-related quality of life and side effects. Long-term follow-up data should be reported.

- Collaborative engagement of patients in order to best understand how to apply these guidelines within the context of shared-decision making.

- Many of the agents covered in these recommendations are unavailable in certain countries, therefore global cost-effective strategies should also be assessed.
Acknowledgments

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See more about the ASH ITP guidelines at www.hematology.org/ITPguidelines
Don’t miss our updated ITP Pocket Guide!