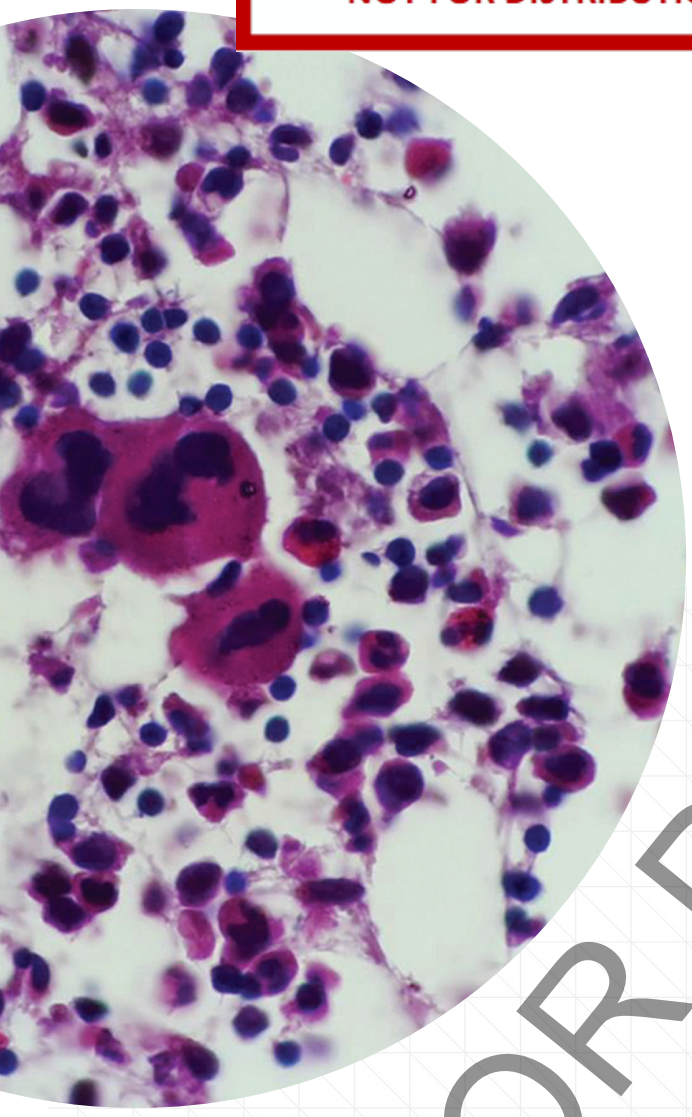
ASH CLINICAL PRACTICE GUIDELINES
IMMUNE THROMBOCYTOPENIA (ITP)

NOT FOR DISTRIBUTION

POCKET GUIDE



Management of Immune Thrombocytopenia (ITP)

A POCKET GUIDE FOR THE CLINICIAN

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The recommendations in this guide are based on the American Society of Hematology 2019 Guideline for Immune Thrombocytopenia

Context

Immune Thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by a low platelet count resulting from platelet destruction and impaired platelet production. The incidence of ITP is estimated to be 2 to 5 per 100,000 persons in the general population and can be an isolated primary condition or it may be secondary to other conditions. The information in this pocket guide is intended to support patients, clinicians, and other health professionals in making evidence-based decisions about first-and second-line management of adults and children with ITP.

Adult

INPATIENT VS. OUTPATIENT MANAGEMENT

Table 1 – Inpatient vs. Outpatient Management

Platelet Count	Status	Management
Platelet count of <20 x10^9/l and asymptomatic or minor mucocutaneous bleeding	Newly diagnosed	Inpatient C
	Established diagnosis	Outpatient[1] C
Platelet count of ≥20 x10^9/l and asymptomatic or minor mucocutaneous bleeding	Newly diagnosed	Outpatient[1] C
	Established diagnosis	Outpatient[1] C

[1] Patients who are refractory to treatment, those 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. The need for admission is also variable across the range of platelet counts represented here (0-20 x10^9/l).

Good Practice Statement

Patients not admitted to the hospital should receive education and expedited follow-up with a hematologist within 24-72 hours.

OBSERVATION VS. TREATMENT

Determining whether a patient with newly diagnosed ITP should be observed or requires pharmacological treatment depends on the degree of thrombocytopenia, patient comorbidities, medications, and age – all of which impact the risk of bleeding. Management approaches vary based on disease duration, access to care, quality-of-life implications, and patient and provider preferences, among other factors.

Table 2 - Observation vs. Treatment (Newly Diagnosed ITP)

Platelet count ≥30 x 10^9/l and asymptomatic or minor mucocutaneous bleeding	Management with observation[1] ✓
Platelet count <30 x 10^9/l and asymptomatic or minor mucocutaneous bleeding	Treatment with corticosteroids[2] C

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

[2] This should include consideration of the severity of thrombocytopenia, additional comorbidities, use of anticoagulant or antiplatelet medications, need for upcoming procedures, and age of the patient.

TREATMENT

First-Line Therapies for Adults

In adults with newly diagnosed ITP, the ASH guideline panel recommends against a prolonged course (>6 weeks) of prednisone in favor of a short course (≤6 weeks) ✓ and suggests either prednisone (0.5 - 2.0 mg/kg/day) or dexamethasone (40 mg/day for 4 days) as the type of corticosteroid for initial therapy[1] C. The ASH guideline panel suggests corticosteroids alone rather than rituximab and corticosteroids for initial therapy[2] C.

[1] If a high value is placed on rapidity of platelet count response, an initial course of dexamethasone may be preferred over prednisone, given that dexamethasone increases the likelihood of a platelet count response at 7 days.

[2] 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.

Good Practice Statement

For patients receiving corticosteroids, the treating physician should ensure the patient is adequately monitored for potential 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 (HRQoL) (depression, fatigue, mental status etc.) while patients are receiving corticosteroids.

Second-Line Therapies for Adults

In adults with ITP lasting ≥3 months who are corticosteroid-dependent or have no response to corticosteroids, the ASH guideline panel **suggests** the following as potential second-line therapies C (see Figure 1):

- Thrombopoietin receptor agonist (eltrombopag or romiplostim)[1]
- Rituximab
- Splenectomy[2]

Follow the algorithm in Figure 1 to determine the most suitable second-line therapies based on presentation and patient preferences.

[1] Individual patient preference may place a higher value on the use of a daily oral medication (eltrombopag) or one that requires weekly subcutaneous injections (romiplostim).

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

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.

Each of the these second-line treatments may be effective therapy and therefore the choice of 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. For example, patients who place a high value on achieving a durable response may prefer splenectomy or thrombopoietin receptor agonists (TPO-RAs), patients who value avoidance of long-term medication may prefer splenectomy or rituximab, and patients who wish to avoid surgery may prefer a TPO-RA or rituximab. Patient education and shared decision-making are encouraged.

Figure 1: Second-Line Therapies for Adults

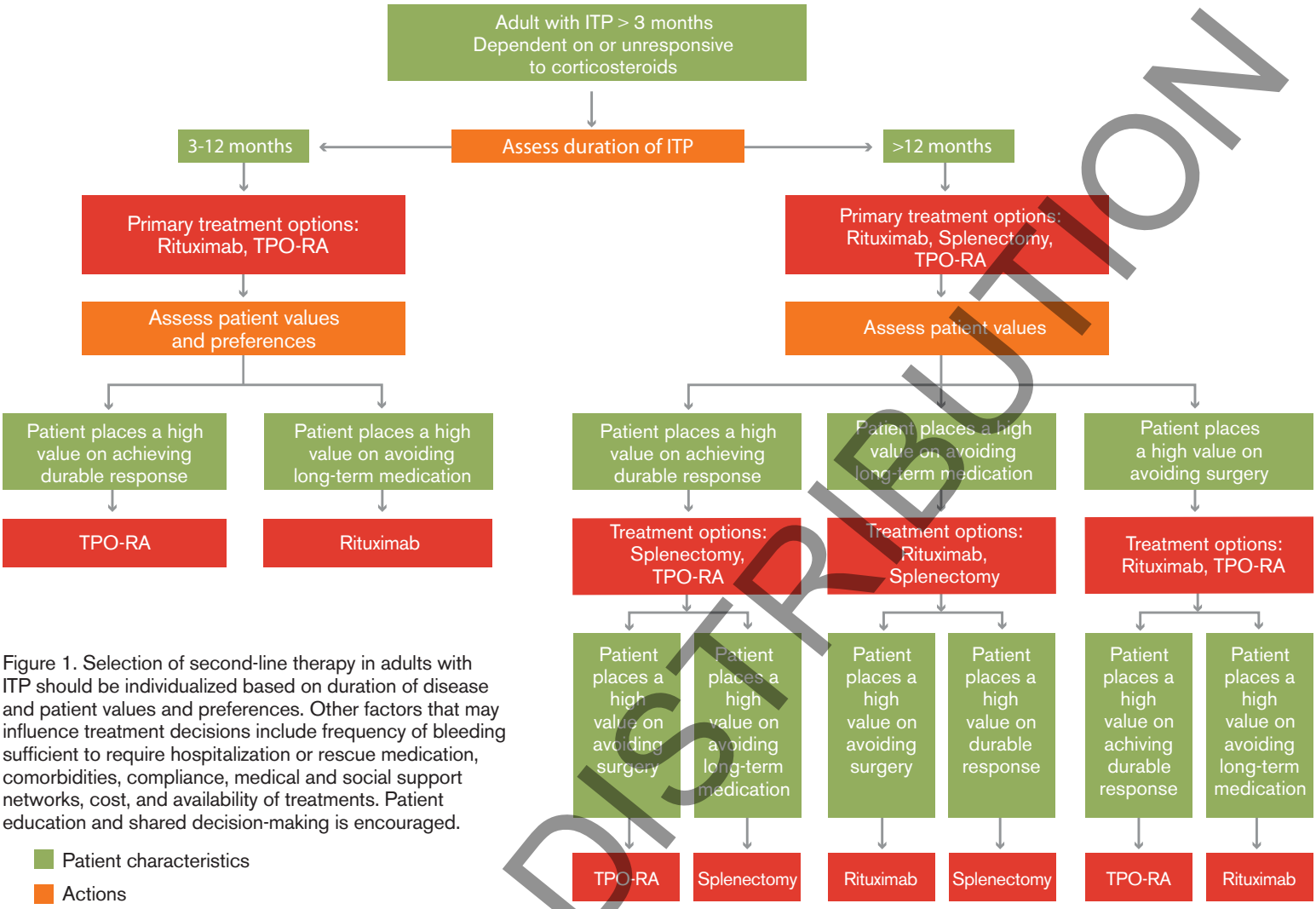

Figure 1. Selection of second-line therapy in adults with ITP should be individualized based on duration of disease and patient values and preferences. Other factors that may influence treatment decisions include frequency of bleeding sufficient to require hospitalization or rescue medication, comorbidities,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

- Patient characteristics
- Actions
- Treatment options

TPO-RA – thrombopoietin receptor agonist

All recommendations in Figure 1 are conditional recommendations C

Pediatric

INPATIENT VS. OUTPATIENT MANAGEMENT

Table 3 – Management of Newly Diagnosed ITP

Platelet Count	Management
Platelet count of <20 x10^9/l and no or mild bleeding (skin manifestations) only	Outpatient[1] C
Platelet count of ≥20 x10^9/l and no or mild bleeding (skin manifestations) only	Outpatient[1] C

[1] 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 to the hospital may be preferable.

Good Practice Statement

Patients not admitted to the hospital should receive education and expedited follow-up with a hematologist within 24-72 hours.

OBSERVATION VS. TREATMENT

In children with newly diagnosed ITP who have no or minor bleeding, the ASH guideline panel **recommends** observation over both intravenous immunoglobulin and anti-D immunoglobulin ☑, and **suggests** observation over corticosteroids C.

TREATMENT

First-Line Therapies for Children

In children with newly diagnosed ITP who have non-life-threatening mucosal bleeding and/or diminished health-related quality of life, the ASH guideline panel **suggests** corticosteroids rather than intravenous immunoglobulin or anti-D immunoglobulin[1] C. For patients where corticosteroids are contra-indicated or otherwise not preferred, the ASH guideline panel **suggests** either intravenous immunoglobulin or anti-D immunoglobulin[2] C.

In children with newly diagnosed ITP who have non-life-threatening mucosal bleeding and/or diminished health related quality of life, the ASH guideline panel **recommends *against*** courses of corticosteroids longer than 7 days in favor of courses 7 days or shorter ☑, and **suggests** prednisone (2 - 4 mg/kg/day; maximum, 120 mg daily, for 5-7 days) rather than dexamethasone (0.6 mg/kg/day; maximum, 40 mg/kg/day, for 4 days) C.

[1] This recommendation assumes corticosteroid dosing as outlined in the following paragraph. This recommendation is reserved only for children with non-major mucosal bleeding.

[2] This recommendation is reserved only for children with non-major mucosal bleeding

Good Practice Statement

For patients receiving corticosteroids, the treating physician should ensure the patient is adequately monitored for potential 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 (HRQoL) (depression, fatigue, mental status etc.) while patients are receiving corticosteroids.

Second-Line Therapies for Children

In children with ITP lasting ≥3 months who have non-life-threatening mucosal bleeding and/or diminished health-related quality of life and do not respond to first-line treatment, the ASH guideline panel **suggests** the following options for second-line therapies presented in the order they should be pursued C:

1. Thrombopoietin receptor agonist (eltrombopag or romiplostim)[1]
2. Rituximab
3. Splenectomy[2]

[1] Individual patient preference may place a higher value on the use of a daily oral medication (eltrombopag) or one that requires weekly subcutaneous injections (romiplostim). For pediatric patients, eltrombopag dosing should avoid consumption of calcium containing foods such as dairy products by four hours. This may limit the ability of some children to take this medication.

[2] If possible, splenectomy should be delayed as long as possible after diagnosis because of the potential for spontaneous remission in the first year.

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.

Each of the these second-line treatments may be effective therapy and therefore the choice of 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.

Strength of Recommendations and Quality of Evidence

The methodology for determining the strength of each recommendation and the quality of the evidence supporting the recommendations was adapted from GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Guyatt GH, et al; GRADE Working Group. 2008;336(7650):924–926. More details on this specific adaptation of the GRADE process can be found in American Society of Hematology 2019 Guideline for Immune Thrombocytopenia.[1]

Strength of Recommendation	
✓	**Strong recommendations** - Most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences.
C	**Conditional recommendations** - Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values and preferences.

How to Use This Pocket Guide

ASH pocket guides are primarily intended to help clinicians make decisions about diagnostic and treatment alternatives. The information included in this guide is not intended to serve or be construed as a standard of care. Clinicians must make decisions on the basis of the unique clinical presentation of an individual patient, ideally though a shared process that considers the patient's values and preferences with respect to all options and their possible outcomes. Decisions may be constrained by realities of a specific clinical setting, including but not limited to institutional policies, time limitations, or unavailability of treatments. ASH pocket guides may not include all appropriate methods of care for the clinical scenarios described. As science advances and new evidence becomes available, these pocket guides may become obsolete. Following these guidelines cannot guarantee successful outcomes ASH does not warrant or guarantee any products described in these guidelines.

The complete 2019 ASH Clinical Practice Guideline for Immune Thrombocytopenia[1] include additional remarks and contextual information that may affect clinical decisionmaking. To learn more about these guidelines, visit ***hematology.org/ITPguidelines***.

Conflict of interest information for Drs. Neunert, Vesely, Mithoowani, and Kim may be found at ***hematology.org/pocketguidesCOI***.

[1] Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guideline for immune thrombocytopenia. Blood Adv. 2019. In press.

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For expert consultation on immune thrombocytopenia and other hematologic questions, submit a request to the ASH Consult a Colleague program at ***www.hematology.org/consult*** (ASH members only).