Evidence-based management of immune thrombocytopenia: ASH guideline update

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In 1996 and 2011, the American Society of Hematology (ASH) supported efforts to create guidelines for the diagnosis and management of patients with immune thrombocytopenia (ITP). These guidelines used different approaches to arrive at recommendations for testing and treatment. Despite differences in methodology, in both cases there was a paucity of randomized trials to inform recommendations. As data on the diagnosis and management of ITP expands, the ASH Committee on Quality is dedicated to maintaining updated guidelines representing recent evidence and guideline methodology. Here, we will review the updated ASH guidelines on ITP with a focus on recommendations with new understanding and future research to close knowledge gaps.

Learning Objectives

- Highlight evidence supporting the management of adult and pediatric patients with newly diagnosed ITP
- Outline an appropriate management strategy for adults and children with persistent or chronic ITP based on recent revisions to the ASH ITP guidelines
- Understand current gaps in knowledge in ITP

Background

In 1996, the American Society of Hematology (ASH) published the first guidelines for the management of immune thrombocytopenia (ITP).[1] At that time, the guidelines were created using a consensus approach resulting in expert opinion. In 2011, ASH updated the guidelines, applying the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology.[2] Utilizing GRADE methodology, 6 panel members developed 7 clinical cases, conducted systematic literature reviews, and formulated 18 recommendations based on the quality of the evidence available. Recommendations are considered strong (grade 1) or weak (grade 2) based on the confidence in the evidence. A letter of A, B, or C then details the strength of the evidence used to support that recommendation. A grade 1A recommendation is the highest level of recommendation, representing extreme confidence in a recommendation based on high-quality evidence. Given the paucity of high-quality literature, many of the 2011 recommendations were of low confidence. Table 1 highlights key concepts and differences between the 1996 and 2011 ASH guidelines.

In an era of rapidly expanding medical knowledge, the ASH Committee on Quality is dedicated to maintaining up-to-date guidelines. The ITP guidelines are currently being revised with emphasis placed on incorporating expert biostatisticians, employing a comprehensive evidence to decision framework (Table 2), determining a priori important outcomes, and involvement of patient representatives. The evidence-to-decision framework provides a full review of the available literature, but it furthers places that evidence within the context of clinical practice identifying potential limitations and/or practical aspects of patient care that may shift the balance between 2 considered treatment approaches. Additionally, the panel reviewed areas of future research based on identified gaps. The panel is composed of individuals with and without conflicts of interest, balanced to favor a majority of unconflicted members. If members had a relevant conflict, then they were recused from the weighing of risks and benefits and any decisions that required a vote from the panel. This is important to note, as it may have influenced certain recommendations in which a vote was required.

The current efforts address both adult and pediatric ITP, and questions focused on the management of ITP, as this is the area with most rapid gain of knowledge since 2011. Table 3 outlines the questions selected for inclusion with complete information on the population of interest, the intervention, the comparator, and the ranked outcomes. This list is in no manner comprehensive of all possible questions encountered in clinical practice; rather, it represents those questions given high priority by the panel either because of new literature since the 2011 guidelines or because of significant controversy. This review will address the updated ASH guidelines on ITP with a focus on recommendations with new information since 2011 and future research to close knowledge gaps. The evidence provided in this review is based desired population and outcomes, study design, and number of patients; therefore, it may not be inclusive of all available data.

Adult ITP

Prioritized questions for adult ITP are shown in Table 3. Corticosteroid selection for adults with newly diagnosed was a highly prioritized question given recent randomized trials comparing dexamethasone to prednisone.[3-6] Based on the available data, remission rates were

Conflict-of-interest disclosure: N.C. is on the Board of Directors or an advisory committee for Amgen, has consulted for Novartis, has been affiliated with the Speakers Bureau for GSK and Amgen, has been a speaker at educational events organized by Novartis and Amgen, and participates in advisory boards for Amgen, and Novartis. C.E.N. declares no competing financial interests.

Off-label drug use: None disclosed.

increased with dexamethasone (relative risk, 2.96; 95% confidence interval [CI], 1.03-2.96); however, the number of cycles, length of treatment with dexamethasone, and platelet count used to establish remission were not consistent among studies, causing low confidence in the data. The other significant response difference was an increase in overall initial response by day 7 among patients receiving dexamethasone (1.31; 95% CI, 1.11-1.54). Data are missing on health-related quality of life (HRQoL), and there was no significant difference between response at 1 month, durable response, and major bleeding. Therefore, based on preselected outcomes, the balance between desirable and undesirable effects did not appear to favor either approach. Clinically, selection of corticosteroid type is dependent on individual patient characteristics such as comorbidities that would affect the side effect profile. Therefore, either dexamethasone (40 mg/kg × 4 days) or prednisone (0.5-2.0 mg/kg per day) is acceptable initial therapy for adults with newly diagnosed ITP. Physicians should avoid prolonged use of either corticosteroid regimen and be aware of monitoring for important side effects such as hypertension, increased blood glucose, and mood/mental changes.

Since the 2011 guidelines, 2 randomized trials have investigated augmenting initial corticosteroid therapy with rituximab.[7,8] Both trials (n = 177) demonstrated an increase in sustained response (platelet count $\geq 50 \times 10^9$/L after 6 months of treatment), with rates of 35% with dexamethasone monotherapy and 60% with combination therapy ($P = .004$; 95% CI, 0.079-0.455). A fair number of patients in each study group (27% monotherapy and 47% combination) required additional treatment with either corticosteroids or IVIg during the first 28 days of the study trial period. Additional data on prioritized outcomes such as major bleeding and HRQoL were absent. The identified population for the guidelines was treatment-naive patients; however, indirect data on all newly diagnosed patients also exist. Due to concerns about a lack of safety data, wide CIs on prioritized outcomes, increased initial cost, and need for longer-term outcome data, corticosteroids alone continue to be favored as initial treatment of adults with newly diagnosed ITP.

High priority was placed on management of adult patients who have persistent or chronic ITP (≥3 months) and are corticosteroid dependent or have no response to corticosteroids. Based on regional resources and drug access, a number of agents are considered second line. However, the panel limited second-line treatment options to splenectomy, rituximab, and thrombopoietin- receptor agonists (TPO-RAs). In order to compare these 3 different treatment approaches, each was evaluated side by side (Table 3). It is recognized that in clinical practice these 3 approaches are often considered simultaneously. No randomized trials directly compare these 3 options simultaneously, and each is considerably different with regards to route of administration, side effects, and potential impact on patient-related outcomes.

Several key concepts emerged when evaluating one second-line therapy against the other: (1) the 2 US Food and Drug Administration (FDA)–approved TPO-RAs (romiplostim and eltrombopag) were determined to be equally efficacious, with no significant differences beyond the route of administration and potential for hepatobiliary laboratory abnormalities with eltormbopag[9,10]; (2) selection of a treatment approach may be influenced by disease duration; (3) patient preference plays a substantial role in treatment choice; and (4) the calculated risk over time of certain sides effects cannot be ascertained with the current evidence.

General considerations for splenectomy include the desirable effect of high remission rates (77%, range 58% to 91%)[11-15] balanced against undesirable effects of lifelong risk of infection, thromboembolic events, and a pooled incidence of 12.3% for surgical complications,[11,14-17] which are potentially higher in certain populations. There was low confidence in the high remission rates with splenectomy given that these data represented a heterogeneous population of patients and did not represent data from more modern cohorts. Rituximab is a potentially splenectomy-sparing therapy with high initial response rates of ~60%. However, the beneficial effects of rituximab appear to wane over time, with approximately ~24% of patients remaining in remission at 1 year.[18-22] There is a lack of long-term follow-up data with rituximab as well as potential for drug-related side effects. A significant benefit of the TPO-RAs is their favorable safety profile that avoids immunosuppression. While a durable response for the TPO-RAs is seen in ~45% of patients,[23,24] it is mostly thought that patients need long-term use of treatment with limited very long-term (>10 years) safety data. Although recent publications (not included in the evidence tables) report remission following many months of treatment in 20% and 30% of patients with TPO-RA use, these are mostly from single-center retrospective cohorts and one prospective study of use in early disease; therefore, the full impact of TPO-RAs on remission is yet to be fully understood.[25-30] Rates of additional important outcomes such as major bleeding were balanced among the 3 treatments. There was no identified data meeting inclusion criteria on patient-related outcomes such as HRQoL.

The drivers for selecting a treatment among TPO-RAs, rituximab, and splenectomy are outlined below:

1. Rituximab and splenectomy. Despite splenectomy having higher overall remission rates (77% vs 25%), rituximab has the potential to be splenectomy sparing in 20% to 30% of patients.[18-22] Both approaches were considered definitive treatments, and there was perceived balanced between undesirable effects. Given the potential benefit of rituximab to potentially spare splenectomy, rituximab was favored over splenectomy by the majority of panel members (75%); however, an additional 25% felt either was an appropriate option, placing higher value on individual patient characteristics and preferences.
2. TPO-RAs and splenectomy. While there are emerging data suggesting that patients with TPO-RAs may undergo remission off treatment, these data are mostly from cohort studies. It is not yet clear from the evidence available the number needed to treat to experience 1 remission. With a paucity of long-term data and lack of control data, the TPO-RAs have generally not been considered to be remission-inducing agents. The need for ongoing therapy with TPO-RAs was balanced against the desirable effects of TPO-RAs in terms of high response rates and relatively few toxicities.[23,24,31-35] Therefore, collectively, the desirable and undesirables were felt to balanced between the 2 therapies.
3. TPO-RAs and rituximab. The balance between desirable and undesirable effects appears to favor the TPO-RAs, largely due to reduced toxicities with TPO-RAs compared with rituximab and similar durable response rates (45% vs 40%). This is especially true earlier in the course of the disease in which patients and providers may still wish to avoid side effects in exchange for the need for ongoing therapy. After considering these aspects, the majority (67%) of the panel favored the TPO-RAs over rituximab; however, a minority thought that either option would be appropriate (33%) and placed higher value on individual patient characteristics and preferences.

Table 1. Differences between the 1996 and 2009 ASH evidence-based practice guidelines for the diagnosis and management of ITP

	1997	2009
Methodology	Each article was evaluated independently by 2 panel members, and validity was assessed using published guidelines.	Development of a background consisting of recommendations on nomenclature, diagnosis, and response criteria (largely drawn from a recently published consensus document).
	Most of the literature on the treatment of ITP consists of case series without a control group (level V).	Creation of focused clinical questions that form the basis for systematic literature review.
	For those therapies for which only level V evidence is available, or for which no evidence is available, and for issues on diagnosis that have not been addressed by clinical studies, the opinion of the panel was assessed.	Establishment of evidence tables and the development of recommendations using GRADE methodology.
Nomenclature	Idiopathic thrombocytopenic purpura	Immune thrombocytopenia
Chronic ITP	>6 mo	>12 mo
Pathology	Increased destruction of platelets by antibodies	Reduced production of platelets as well as increased destruction of platelets
Diagnostic tests in adults	The diagnosis of ITP is based principally on the history, physical examination, complete blood count, and examination of the peripheral smear. Further diagnostic studies are generally not indicated in the routine workup of patients with suspected ITP.	History examination, blood smear, and in addition, testing patients for HCV and HIV. Other routine testing only if there is a clinical or biological suggestion.
Is a bone marrow examination recommended?	Children with peristent thrombocytopenia (>6-12 mo)	A bone marrow examination is not necessary irrespective of age in patients presenting with typical ITP (grade 2C)
Platelet count to initiate treatment: children	Children with platelet counts <20 000 and significant mucous membrane bleeding and those with counts <10 000 and minor purpura should be treated with IVIg or glucocorticoids	Children with no bleeding or mild bleeding (defined as skin manifestations only, such as bruising and petechiae) be managed with observation alone regardless of platelet count (grade 1B)
Platelet count to initiate treatment: adults	Patients with platelet counts <20 000 to 30 000, and those with counts <50 000 and significant mucous membrane bleeding (or risk factors for bleeding, such as hypertension, peptic ulcer disease, or a vigorous lifestyle)	Treatment should be administered for newly diagnosed patients with a platelet count 30 109/L (grade 2C)
First-line treatment	IVIg or corticosteroids	IVIg, steroids, or anti-D immunoglobulin*
Splenectomy	Splenectomy is often appropriate if platelet counts remain below 30 000 after 4 to 6 weeks of medical treatment	Splenectomy for adults who fail corticosteroid therapy (grade 1B).
		Splenectomy for children and adolescents with chronic or persistent ITP who have significant or persistent bleeding and lack of responsiveness or intolerance of other therapies such as corticosteroids, IVIg, and anti-D, and/or who have a need for improved quality of life (grade 1B).
		In children, splenectomy or other interventions with potentially serious complications be delayed for at least 12 mo, unless accompanied by severe disease defined by the International Working Group as unresponsive to other measures or other quality of life considerations (grade 2C).

HCV, hepatitis C virus; IVIg, IV immunoglobulin.

* Anti-D immunoglobulin is recommended only in patients who are Rh positive, have a negative direct antiglobulin test result, and have not undergone splenectomy. Additionally, clinicians are cautioned that the FDA has provided a warning and specific monitoring requirements because of reports of fatal intravascular hemolysis reported with anti-D.

Table 1. (continued)

	1997	2009
Alternative second-line treatments		Adults: Thrombopoietin receptor agonists for patients at risk of bleeding who relapse after splenectomy or who have a contraindication to splenectomy and who have failed at least one other therapy (grade 1B); thrombopoietin receptor agonists may be considered for patients at risk of bleeding who have failed one line of therapy such as corticosteroids or IVIg and who have not had splenectomy (grade 2C); rituximab may be considered for patients at risk of bleeding who have failed one line of therapy such as corticosteroids, IVIg, or splenectomy (grade 2C) Children: Rituximab be considered for children or adolescents with ITP who have significant ongoing bleeding despite treatment with IVIg, anti-D, or conventional doses of corticosteroids (grade 2C); rituximab may also be considered as an alternative to splenectomy in children and adolescents with chronic ITP or in patients who do not respond favorably to splenectomy (grade 2C); high-dose dexamethasone may be considered for children or adolescents with ITP who have significant ongoing bleeding despite treatment with IVIg, anti-D, or conventional doses of corticosteroids (grade 2C); high-dose dexamethasone may also be considered as an alternative to splenectomy in children and adolescents with chronic ITP or in patients who do not respond favorably to splenectomy (grade 2C)
ITP in pregnancy	Women with ITP should be delivered by cesarean section in selected circumstances. Women with ITP who are of childbearing age and have counts <10 000 after splenectomy and other treatments should be discouraged from becoming pregnant.	Mode of delivery based on obstetric needs

HCV, hepatitis C virus; IVIg, IV immunoglobulin.
*Anti-D immunoglobulin is recommended only in patients who are Rh positive, have a negative direct antiglobulin test result, and have not undergone splenectomy. Additionally, clinicians are cautioned that the FDA has provided a warning and specific monitoring requirements because of reports of fatal intravascular hemolysis reported with anti-D.

The discrepancy in these 3 points partly reflects the composition of voting members of the committee (4 panelists were recused from TPO-RA–related decisions due to conflicts of interest) but also reflects the lack of published data for long-term outcome in adult ITP (ie, true long-term remission rates of splenectomy, rituximab, and TPO-RAs), the lack of comparative studies on these 3 very different therapeutic strategies, and the divided opinion on the use of splenectomy in adult ITP.

Based on the balance of desirables and undesirables previously mentioned, and accounting for the important component of disease duration and patient preference, several treatment considerations emerge.

- If splenectomy is not an option and/or not desired by the patient, then TPO-RAs were preferred to rituximab. This balance was driven primarily by patients earlier in the disease course and might change over time or with patients who place high value on treatment-free remission.
- In the setting where treatment-free remission is desired, rituximab or splenectomy is the preferable option. A trial of rituximab may be desirable prior to splenectomy, as it has potential splenectomy-sparing therapy.
- Evidence suggests that patients who fail rituximab should be treated with either a TPO-RA or splenectomy, depending on patient values.
- As highlighted, implementing these guidelines requires a high level of shared decision making with patients and frequent reassessment patient-related outcomes and treatment plans.

Pediatric ITP

A major difference for the pediatric questions is reflected in the lack of the platelet count as a primary outcome. Rather, high emphasis was placed on patient-related outcomes such as bleeding rates, HRQoL, and side effects. This differs from previous guidelines[1,2] in which the platelet count was the primary outcome reported in clinical trials and the primary outcome assessed for recommendations. Prioritized questions and outcomes for pediatric patients are highlighted in Table 3.

Table 2. Evidence-to-decision framework

Is the problem a priority?
How substantial are the desired effects?
How substantial are the undesirable effects?
What is the overall certainty in the evidence?
Is there important uncertainty about or variability in how people might value the main outcome?
Do the desirable effects outweigh the undesirable effects?
How large are the resource requirements?
What is the certainty of the evidence of resource requirements?
Are the net benefits worth the incremental costs?
What would be in the impact on health equity?
Is the intervention/option acceptable to key stakeholders?
Is the intervention feasible to implement?

Table 3. Prioritized PICO questions and outcomes

Final question(s) in PICO format	Selected outcomes	
Adult ITP		
Should adults with newly diagnosed ITP and a platelet count $<30 \times 10^9$/L who are asymptomatic be treated with corticosteroids or observation?	Major bleeding Overall health-related quality of life	Remission Mortality
Should adults with newly diagnosed ITP and a platelet count $\geq 30 \times 10^9$/L who are asymptomatic be treated with corticosteroids or observation?	Response within 7 d	
Should adults with newly diagnosed ITP and a platelet count $<20 \times 10^9$/L and no or mild bleeding be treated as an outpatient or be admitted to the hospital?	Major bleeding	
Should adults with newly diagnosed ITP and a platelet count $\geq 20 \times 10^9$/L and no or mild bleeding be treated as an outpatient or be admitted to the hospital?	Mortality	
Should adults with newly diagnosed ITP receive a shorter ($\leq$ 8 wk) or prolonged course (including treatment and taper) of corticosteroids for initial therapy?	Durable response Major bleeding Remission	Infection Mortality
Should adults with newly diagnosed ITP be treated with prednisone (0.5-2.0 mg/kg per day) or dexamethasone (40 mg/day $\times$ 4 d) as the type of corticosteroid for initial therapy?	Durable response Overall HRQoL Response within 7 d	Major bleeding Remission Response within 1 mo
Should adults with newly diagnosed ITP be treated with rituximab and corticosteroids or corticosteroids alone for initial therapy?	Durable response Major bleeding Overall HRQoL Response within 1 mo	Infection Mortality Remission
If an adult with ITP is corticosteroid dependent or unresponsive to corticosteroids and is going to be treated with a TPO-RA, should the patient receive eltrombopag or romiplostim?	Durable response Overall HRQoL Response within 1 mo Reduction or discontinuation of corticosteroids	Major Bleeding Remission Thrombosis
Should adults with ITP lasting $\geq$3 mo who are corticosteroid dependent or have no response to corticosteroids undergo splenectomy or be treated with TPO-RAs?	Durable response Major bleeding Overall HRQoL Response within one month Reduction/discontinuation of corticosteroids	Infection Operative complications Remission Thrombosis
Should adults with ITP lasting $\geq$3 mo who are corticosteroid dependent or have no response to corticosteroids be treated with rituximab or TPO-RAs?	Durable response Major bleeding Overall HRQoL Response within one month Reduction/discontinuation of corticosteroids	Infection Thrombosis Remission
Should adults with ITP lasting $\geq$3 mo who are corticosteroid dependent or have no response to corticosteroids undergo splenectomy or be treated with rituximab?	Durable response Major bleeding Overall HRQoL Response within one month Reduction/discontinuation of corticosteroids	Infection Operative complications Remission Thrombosis
Pediatric ITP		
Should children with newly diagnosed ITP and a platelet count $<20 \times 10^9$/L be treated as an outpatient or be admitted to the hospital?	Major bleeding	Mortality
Should children with newly diagnosed ITP and a platelet count $\geq 20 \times 10^9$/L be treated as an outpatient or be admitted to the hospital?	Overall HRQoL	
Should children with newly diagnosed ITP and no or minor bleeding be treated with observation or corticosteroids for initial therapy?	Durable response Overall HRQoL Remission	Major bleeding Mortality
Should children with newly diagnosed ITP and no or minor bleeding be treated with observation or IVIg?	Durable response Overall HRQoL Remission	Major Bleeding Mortality

PICO, population, intervention, comparator, and outcome.

Table 3. (continued)

Final question(s) in PICO format	Selected outcomes	
Should children with newly diagnosed ITP and no or minor bleeding be treated with observation or anti-D immunoglobulin for initial therapy?	Durable response Major bleeding Overall HRQoL	Hemolysis Mortality Remission
Should children with newly diagnosed ITP who as determined above require treatment, be treated with anti-D immunoglobulin or corticosteroids for initial therapy?	Durable response Major bleeding Overall HRQoL	Hemolysis Mortality Remission
Should children with newly diagnosed ITP who as determined above require drug therapy receive IVIg or anti-D immunoglobulin for initial therapy?	Durable response Major bleeding Overall HRQoL	Hemolysis Mortality Remission
Should children with newly diagnosed ITP who as determined above require drug therapy receive a course of corticosteroids longer or shorter than 7 d?	Durable response Major bleeding Overall HRQoL Remission	Infection Mood or mental changes Mortality
Should children with newly diagnosed ITP who as determined above require drug therapy receive dexamethasone (0.6 mg/kg per day for 4 d every 4 wk) or prednisone (2-4 mg/kg per day × 5-7 d) as the type of corticosteroid?	Durable response Mortality	Major bleeding Remission
What is the best treatment of children who are unresponsive to first-line treatment? That is, what are the risks and benefits to various treatments: splenectomy, rituximab, and TPO-RAs?	Durable response Major bleeding Overall HRQoL Response within 1 month Reduction/discontinuation of corticosteroids	Infection Thrombosis Remission

PICO, population, intervention, comparator, and outcome.

Consistent with previous guidelines, observation for children with no or mild bleeding is still supported as the primary management for children with ITP regardless of the platelet count. When first-line therapy is necessary, either for bleeding symptoms or to improve HRQoL, comparisons of anti-D immunoglobulin, IVIg, and corticosteroids were conducted. At that time, an FDA black box warning was released regarding fatal disseminated intravascular coagulation–associated hemolysis with anti-D immunoglobulin, impacting perceived risk–benefit balance for anti-D immunoglobulin.

Revisiting the data surrounding hemolysis, ~15% patients suffer from hemolysis, defined differently among studies, following anti-D immunoglobulin.[36-38] Less clear, however, is the severity of hemolytic episodes as well as the clinical impact, since magnitude of anti-D immunoglobulin–associated hemolysis is unclassified in the majority of reports. Further, there is a paucity of reported data on prioritized patient-related outcomes, making full determination of balance between desirable and undesirables unknown. Even in the absence of substantial data, the lowest perceived risk is treatment with a short course of corticosteroids, as anti-D immunoglobulin and IVIg have more significant side effects profiles as well as increased cost and no long-term benefit compared with corticosteroids.

High priority was placed on management of children who were unresponsive to first-line therapy with new publications on the TPO-RAs since 2011. Similar to adult ITP, only splenectomy, rituximab, and the TPO-RAs were considered for evaluation.[39-50] Many components of the evidence-to-decision framework align with those for adults with several distinctions: (1) splenectomy is less desirable overall for children because of the lifelong risk of sepsis starting at a young age and prior to full immunity for vaccines; (2) there are concerns regarding the effects of rituximab on a developing immune system; and (3) the ongoing likelihood of spontaneous remission in children. The balance in overall desirable and undesirable effects favored TPO-RAS and rituximab rather than splenectomy. The dominating treatment was TPO-RAs, followed by rituximab, with splenectomy reserved for those who have failed previous therapies. This hierarchy was based mostly on the high rate of spontaneous remission in children. For this reason, less emphasis was placed on the durable remission rates of therapy, and greater importance was placed on avoidance of potential lifelong risks. Parallel to adults, this was accompanied by recognition that this decision will be impacted by the duration of disease and patient and parent values and preference.

Future directions

It is apparent that the majority of recommendations are based on very low-quality evidence regardless of the question being posed or the population of interest. Several important knowledge gaps were identified that should be explored.

First, investigators are encouraged to use common reporting language based on accepted criteria for complete and partial response.[51] Universal adoption of these definitions will assist with pooling of data and comparison of treatments outside of randomized clinical trials. One weakness of these definitions is the lack of ability to account for the need for ongoing treatment to maintain increased platelet counts. Therefore, this should be taken into account when assessing patient values and preferences. Long-term data were lacking on most treatments and are highly desired.

Beyond platelet count response, clinical trials should emphasize patient-related outcomes. Both HRQoL and fatigue are endorsed as being important to patients, and effective treatment should positively influence both. Reliance solely on the platelet count fails to recognize an important exchange in terms of the balance between desirable and undesirable effects of treatment. Greater information is necessary regarding side effects of therapy, reflecting the degree of events and details about the resultant morbidity and mortality. In parallel to this,

long-term safety data are desired for all treatments. Ideally collection of this data alongside patient-related outcomes data would lead to the ability to perform comparative effectiveness trials in the absence of randomized trials. Longer-term outcome data for patients with ITP are also needed. The data assessed in decision making for this gridlines assumed infrequent remissions outside of splenectomy in adult ITP compared with pediatric ITP, yet longer-term follow-up in clinical trials and cohort data are challenging this concept. Rather than concentrating on remission data, information on tolerability and impact on HRQoL, through specifically designed clinical trials, is needed.

While average medication cost can be established from clinical resources, this does not account for all cost variables. More robust cost analysis accounting for the cost of drug administration, requirement for hospitalization, and time lost from work as well as downstream costs of treatment of toxicities and relapse would greatly aid the evidence to decision framework.

Lastly, it was evident that most decisions require strong attention to patient preference and shared decision making. In order for effective shared decision making to occur, providers need research guided tools to assist with assessment of patient values and preferences. This can occur through exploratory qualitative methods, involvement with patient support groups, and inclusion of patient representatives on guideline and similar panels.

Conclusions

Ongoing efforts to maintain guidelines that reflect the most current evidence are underway for ITP. In order to ensure that the guidelines represent a full assessment of desirable and undesirable outcomes of therapies, rigorous methodology must be employed. Applying a priori outcomes, conducting comprehensive appraisals of the evidence quality, and utilizing an inclusive evidence to decision framework will ensure that guidelines represent evidence as well as account for essential aspects of clinical care.

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