Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group

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Diagnosis and management of immune thrombocytopenic purpura (ITP) remain largely dependent on clinical expertise and observations more than on evidence derived from clinical trials of high scientific quality. One major obstacle to the implementation of such studies and in producing reliable meta-analyses of existing data is a lack of consensus on standardized critical definitions, outcome criteria, and terminology. Moreover, the demand for comparative clinical trials has dramatically increased since the introduction of new classes of therapeutic agents, such as thrombopoietin receptor agonists, and innovative treatment modalities, such as anti-CD 20 antibodies. To overcome the present heterogeneity, an International Working Group of recognized expert clinicians convened a 2-day structured meeting (the Vicenza Consensus Conference) to define standard terminology and definitions for primary ITP and its different phases and criteria for the grading of severity, and clinically meaningful outcomes and response. These consensus criteria and definitions could be used by investigational clinical trials or cohort studies. Adoption of these recommendations would serve to improve communication among investigators, to enhance comparability among clinical trials, to facilitate meta-analyses and development of therapeutic guidelines, and to provide a standardized framework for regulatory agencies. (Blood. 2009;113:2386-2393)

Introduction

Immune thrombocytopenic purpura (ITP), also known as idiopathic thrombocytopenic purpura, is an immune-mediated acquired disease of adults and children characterized by transient or persistent decrease of the platelet count and, depending upon the degree of thrombocytopenia, increased risk of bleeding.1

A recent review compared the definitions and clinical criteria used in different studies.2 It showed widely discrepant criteria used to evaluate patient characteristics, determine responses, and report clinical outcomes. This heterogeneity makes comparison of the results of clinical trials or cohort description uneven and therefore unreliable and application of practical guidelines troublesome. Many of these difficulties could be minimized by adopting a common set of definitions. The need for standardization and harmonization of response criteria has been recently highlighted by clinical trials of novel targeted therapies, such as thrombopoietin (TPO)–receptor agonists6-9 and anti–CD-20 antibodies,10 which have different mechanisms of action and heterogeneous patterns of response. Furthermore, the importance of this harmonization has become increasingly apparent by the necessity to develop and validate ITP-specific bleeding scales11-13 and quality of life14-16 questionnaires. To address these issues, an International Working Group (IWG) of recognized experts convened a 2-day structured face-to-face consensus conference in Vicenza, Italy (the Vicenza Consensus Conference) in October 2007. This article reports the definitions and recommendations agreed upon by the members of this consensus conference.

Methodology of the conference

The location of the conference, its funding, and the composition of the IWG were decided during the 5th official meeting of the
European Hematology Association (EHA) Scientific Working Group on Thrombocytopenias (EHASWG; http://www.ehaweb.org/eha/about_eha/eha科学发展_group.html) held on June 7, 2007, during the 12th EHA Congress in Vienna. It was decided that the IWG members should include the 7 officers of the current executive committee of the EHASWG and be expanded by the addition of 13 members selected for their recognized clinical expertise and wide geographic representation to provide an international scope. Preliminary agreement regarding the identification of the main topics of the conference and the clarification of its objectives were previously agreed on through 2 rounds of Delphi-like questionnaires circulated among the members. Specific aspects pertinent to pediatrics that had been previously elaborated by the Intercontinental Childhood ITP Study (ICIS) Group (http://pages.unibas.ch/itpbasel/) were also included for further examination. Coordinated by the conference chairman, 5 working parties (WP) covered specific topics, guided the discussion interactively, and prepared serial summaries of each topic. Consensus was reached by several meetings on specific topics by ad hoc subgroups followed by plenary sessions. A second short conference was held during the 49th Annual Meeting of the American Society of Hematology in Atlanta (December 8, 2007) to approve the final draft. Furthermore, 3 experts who did not attend the Vicenza Consensus Conference acted as external reviewers to ensure that the proposal was intrinsically logical, consistent, clear, and reasonably applicable. The final version was finally circulated among all members for minor modifications and explicit approval. None of the IWG members and external reviewers received honoraria.

**Recommendations**

**Definition of primary and secondary immune thrombocytopenia (primary and secondary ITP) and platelet count threshold**

The panel decided to avoid the term “idiopathic,” preferring “immune,” to emphasize the immune-mediated mechanism of the disease and to choose “primary” (as opposed to idiopathic) to indicate the absence of any obvious initiating and/or underlying cause. The term “purpura” was felt inappropriate, because bleeding symptoms are absent or minimal in a large proportion of cases. The acronym ITP (now proposed to stand for “immune,” to emphasize the immune-mediated mechanism of the disease) was preserved because of its widespread and time-honored use and taking into account its utility for literature searches. A platelet count less than $100 \times 10^9/L$ was established as the threshold for diagnosis. A uniform predefined cutoff, instead of local normal ranges or other thresholds based on frequency distribution, is more convenient for practical use and comparisons across studies. This threshold was preferred to the more commonly used level of less than $150 \times 10^9/L$, based upon a prospective cohort of otherwise healthy subjects with a platelet count between 100 and $150 \times 10^9/L$, showing that the 10-year probability of developing more severe thrombocytopenia (persistent platelet count below $100 \times 10^9/L$) is only $6.9\%$ (95\% confidence interval [CI], 4.0\%–12.0\%). Moreover, in some non-Western populations, platelet count values between 100 and $150 \times 10^9/L$ are frequently found in apparently healthy people. The new cutoff level will also avoid inclusion of most women with pregnancy-related thrombocytopenia, a well known physiologic phenomenon not requiring specific follow-up in the absence of additional clinical features (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Proposed definitions of disease</th>
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<tr>
<td><strong>Primary ITP</strong></td>
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<tr>
<td><strong>Secondary ITP</strong></td>
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<tr>
<td><strong>Phases of the disease</strong></td>
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<tr>
<td>&amp; Persistent ITP: between 3 to 12 months from diagnosis. Includes patients not reaching spontaneous remission or not maintaining complete response off therapy.</td>
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<tr>
<td>&amp; Chronic ITP: lasting for more than 12 months</td>
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<tr>
<td>&amp; Severe ITP: Presence of bleeding symptoms at presentation sufficient to mandate treatment, or occurrence of new bleeding symptoms requiring additional therapeutic intervention with a different platelet-enhancing agent or an increased dose</td>
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*The acronym ITP should be followed by the name of the associated disease (for thrombocytopenia after exposure to drugs, the terms “drug-induced” should be used) in parentheses: for example, “secondary ITP (lupus-associated),” “secondary ITP (HIV-associated),” and “secondary ITP (drug-induced).” For manuscript titles, abstracts, and so on, definitions such as lupus-associated ITP or HIV-associated ITP can also be used. The term “secondary immune thrombocytopenia” or “secondary ITP” has been proposed to broadly include all forms of immune-mediated thrombocytopenias except primary ITP. Secondary forms include thrombocytopenias that are due to an underlying disease or to drug exposure. Some rare secondary immune thrombocytopenias, such as fetal and neonatal alloimmune thrombocytopenic purpura and posttransfusion purpura, would maintain their standard designation. For the other secondary forms of ITP, the name of the associated disease should follow the designation in parentheses. For example: “secondary ITP (systemic lupus erythematosus-associated or SLE-associated)” and “secondary ITP (human immunodeficiency virus or HIV-associated).” For cases possibly initiated by or associated with *Helicobacter pylori* infection, considering the high prevalence of the infection in some countries, a diagnosis of “secondary ITP (*Helicobacter pylori*–associated)” would require the demonstration of complete resolution of ITP after proven eradication of the bacteria. In the case of thrombocytopenia related to drug exposure (with the exclusion of myelosuppressive chemotherapy), the term “drug-induced” was preferred. The name of the incriminated drug should be indicated when known. For example: “Secondary ITP (quinine-induced).” Heparin-induced thrombocytopenia will maintain its designation and acronym (HIT) because of its unique features.

The distinction between primary and secondary immune thrombocytopenia is clinically relevant because of their different natural histories and distinct treatments. For thrombocytopenias secondary to an ongoing medical condition, treatment is often targeted toward the underlying disorder. On the other hand, drug-induced ITP often remits quickly after the withdrawal of the inciting drug, and most severe cases may require transfusion of platelets alone as initial treatment, as opposed to the application of immunomodulation often used in primary ITP. The coexistence of anti-nuclear
antibodies and/or anti-phospholipid antibodies (aPL) on their own, in the absence of distinctive clinical manifestations suggestive of SLE\textsuperscript{27} and/or antiphospholipid syndrome,\textsuperscript{28} does not qualify these cases as secondary ITP. The increased risk of thrombosis in aPL antibody-positive cases reported in some studies is controversial,\textsuperscript{24} and in our opinion, the available evidence does not warrant consideration of the coexistence of thrombocytopenia with aPL antibodies as a distinct clinical entity. We are aware that a different consensus was reached by the experts who updated previous Sapporo criteria for the classification of definite antiphospholipid syndrome,\textsuperscript{28} which might contribute to confusion rather than harmonization. However, in the updated criteria, the presence of aPL antibodies has no impact on the clinical management of patients with ITP, bearing relevance only for patient stratification in clinical trials. The impact of these associated laboratory abnormalities should be further investigated in studies of the natural history of ITP. The IWG agreed that the proposed definitions, therapeutic goals, and outcome assessment should be applied only to primary ITP.

**Definition of the different phases and severity of the disease**

Only those terms relevant for treatment and/or prognosis were retained to describe the phases of ITP. The panel recommended that the term “acute,” which has been used to describe a self-limited form of the disease (eg, secondary to viral illness in children) be avoided because of both its vagueness and its post hoc or retrospective definition. In the absence of reliable predictive clinical or laboratory parameters of disease duration, the term “newly diagnosed ITP” was suggested for all cases at diagnosis. A new category, called “persistent ITP,” was introduced for patients with ITP to define the period lasting between 3 and 12 months from diagnosis. This category includes patients not achieving spontaneous remission or not maintaining their response after stopping treatment between 3 and 12 months from diagnosis. The chances of spontaneous remissions are still significant during this period,\textsuperscript{29,31} making deferral of more aggressive therapeutic approaches (such as splenectomy) worthy of consideration. The term “chronic ITP” is to be reserved for patients with ITP lasting for more than 12 months (Table 1).

To date, disease severity (mild, moderate, severe) has been correlated with the degree of thrombocytopenia, which is taken as a surrogate for risk of bleeding. However, the panel agreed that, regardless of the phase of the disease, the term “severe” ITP should be used only in patients who have clinically relevant bleeding. This is defined by the presence of bleeding symptoms at presentation sufficient to mandate treatment, or by the occurrence of new bleeding symptoms requiring additional therapeutic intervention with a different platelet-enhancing agent or an increased dose. For example, using the proposed schema, a patient with chronic ITP, a platelet count of $2 \times 10^9$/L, and just a few petechiae and ecchymoses would not be classified as having “severe” disease. Unfortunately, the few bleeding assessment tools specifically developed for ITP\textsuperscript{11,13,32,33} have not been validated in large prospective studies and so a more precise definition of “clinically relevant” bleeding cannot be given. This is an area of research that merits further development.

**Therapeutic goals**

The major goal for treatment of ITP is to provide a safe platelet count (eg, one that prevents major bleeding) rather than correcting the platelet count to normal levels.\textsuperscript{3,3,34,35} Treatment of patients with ITP should take into account the severity of the illness and the age of the patient, because the bleeding risk and the hemorrhagic fatality rate increase with age\textsuperscript{36} and are the lowest in children of post-toddler age. Most fatal bleeding has been reported to occur in adults with ITP who have platelet counts lower than $30 \times 10^9$/L.\textsuperscript{37}

Because of the real and potential toxicity of currently available treatments, a critical concept is to avoid unnecessary treatment of asymptomatic patients with milder degrees of thrombocytopenia. Current guidelines\textsuperscript{3,34} suggest that treatment should be initiated in the presence of bleeding symptoms. Treatment decisions based on platelet count threshold remains controversial. Although most guidelines suggest that treatment should be considered with counts less than $30 \times 10^9$/L, in adults, the ICIS group recommended that children without bleeding may not require therapy regardless of their platelet count, with the exception of “on-demand therapy.” This deserves further evaluation, including better attempts at individualization.

Treatment of newly diagnosed adult patients or of patients requiring treatment for the first time (initial treatment) is aimed at rapidly obtaining a safe platelet count to prevent or stop hemorrhages and to ensure an acceptable quality of life with minimal treatment-related toxicity. A minority of patients are expected to obtain spontaneous durable remission after initial treatment with

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**Table 2. Proposed criteria for assessing response to ITP treatments**

<table>
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<tr>
<th>Quality of response$\dagger$</th>
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<tr>
<td>CR: platelet count $\geq 100 \times 10^9$/L and absence of bleeding</td>
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<tr>
<td>R: platelet count $\geq 30 \times 10^9$/L and at least 2-fold increase the baseline count and absence of bleeding</td>
</tr>
<tr>
<td>Time to response: time from starting treatment to time of achievement of CR or R$\ddagger$</td>
</tr>
<tr>
<td>NR: platelet count $&lt; 30 \times 10^9$/L or less than 2-fold increase of baseline platelet count or bleeding</td>
</tr>
<tr>
<td>Loss of CR or R: platelet count below $100 \times 10^9$/L or bleeding (from CR) or below $30 \times 10^9$/L or less than 2-fold increase of baseline platelet count or bleeding (from R)</td>
</tr>
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**Duration of response$\ddagger$**

- Measured from the achievement of CR or R to loss of CR or R
- Measured as the proportion of the cumulative time spent in CR or R during the period under examination as well as the total time observed from which the proportion is derived

**Corticosteroid-dependence**

- The need for ongoing or repeated doses administration of corticosteroids for at least 2 months to maintain a platelet count at or above $30 \times 10^9$/L and/or to avoid bleeding (patients with corticosteroid dependence are considered nonresponders)

**Supplemental outcomes (whenever possible)**

- Bleeding symptoms measured by a validated scale (requires additional studies)
- Health-related quality of life assessment measured by a validated instrument (requires additional studies)

For response criteria in refractory ITP, see Table 4. HRQoL indicates health-related quality-of-life assessment. $\dagger$Platelet counts should be confirmed on at least 2 separate occasions (at least 7 days apart when used to define CR, R) or 1 day apart when used to define NR or loss of response. $\ddagger$Baseline platelet count refers to platelet count at the time of starting of the investigated treatment; for post-splenectomy response evaluation, basal platelet count refers to the platelet count before patient was first treated (initial treatment). $\ddagger$Late responses not attributable to the investigated treatment should not be defined as CR or R (see Table 3). $\dagger$The 2 definitions are not mutually exclusive: the first definition, collectively represented using Kaplan-Meyer analysis, is more suitable for short-course treatments aimed at inducing prolonged remission of the disease, whereas the second one is more suitable to evaluate the overall benefit of continuous or intermittent repeated administration of agents requiring dose adjustments with anticipated temporary losses of CR or R.
standard commonly used corticosteroid-based regimens. However, with the availability of new therapies, increasing the rate of long-lasting responses becomes a realistic aim of early intervention. The goal of treatment in persistent or chronic ITP is less well defined and is often inspired by the desire to defer or avoid the risks of more toxic treatments such as splenectomy or immunosuppression. Thus “on-demand” treatment at the time of or in anticipation of high-risk bleeding situations or surgical procedures is another approach that is often warranted. Minimal corticosteroid exposure is a tenet of therapy for chronic ITP. As with initial treatment, the rate of long-lasting responses may become an achievable goal based on investigational studies. On the other hand, the goal of splenectomy is long-term response (in terms of several years) to avoid more toxic treatments, to establish or to increase health-related quality of life, and to save costs.

**Definition of response**

The panel acknowledged that the definition of a treatment response should ideally reflect clinically important endpoints including bleeding and quality of life, rather than rely exclusively on surrogate end points (platelet count) with arbitrary thresholds. Nevertheless, the platelet count is a useful measure of response that is objective, clinically relevant, and easily compared (Table 2).

“Complete response” (CR) is defined as any platelet count of at least 100 × 10^9/L. “Response” (R) is defined as any platelet count between 30 and 100 × 10^9/L and at least doubling of the baseline count. “No response” (NR) is defined as any platelet count lower than 30 × 10^9/L or less than doubling of the baseline count. The definition of response requires concurrent resolution of bleeding symptoms. The panel decided to avoid “partial” or “minimal response” categories, often used in scientific articles, because of the wide heterogeneity in the criteria used in these definitions. CR and R could be with or without concomitant administration of the investigated agent, and this should be specified. In a clinical trial, when, in addition to the treatment being investigated, any ongoing concomitant ITP-specific treatment is given, this latter, or the time of its discontinuation, should be provided. Often, corticosteroids are administered together with other ITP-specific agents. In this setting, as defined in Table 2, corticosteroid dependence is defined as the ongoing need for continuous corticosteroid administration or frequent courses of corticosteroids to maintain a platelet count at or above 30 × 10^9/L and/or to avoid bleeding. Corticosteroid- or other treatment-dependent patients should be considered non-responders. Specific mention can be made of lessened dose or frequency of this agent as indicative of at least some effect of the investigated agent, even if below the level of a response.

Time to platelet count response is an important facet of management and should be reported in clinical studies. It varies depending on the mechanism of action of the specific agent (Table 3). The frequency of monitoring of platelet counts and the timing of response assessment should be prespecified and will depend on the expected kinetics of platelet increase after each treatment. After splenectomy, the timing to assess the response in terms of platelet count should be within 1 to 2 months after surgery and removed from any treatment. Late responses not attributable to the investigated treatment ("spontaneous remission"), according to Table 3, should not be defined as CR or R.

Duration of the response should be calculated from the time of CR or R until loss of CR or R. Two different scenarios are envisioned: (1) short-course treatments aimed at curing the disease, or at least at achieving prolonged remissions (eg, high-dose pulse dexamethasone, rituximab, splenectomy) and (2) treatments requiring continuous or repeated administrations (eg, TPO-receptor agonists, IVlg, anti-D, etc), for which it is anticipated that platelet count could fail temporarily below or increase above the desired threshold.

For short-course treatments, the overall response duration in a patient cohort should be calculated using a time-dependent analysis, such as the Kaplan-Meier product limit estimate, event rate per person-years, or similar approaches. For treatments requiring continuous prolonged or repeated administrations of the same agent, one should calculate the cumulative time spent in CR or R. This approach is also useful to evaluate the whole impact of a particular treatment plan, including different sequential treatments, allowing a more clinically meaningful estimation of response duration. When response duration includes time receiving treatment, this should be specified, and CR or R with or without concomitant treatment should be calculated and reported separately.

Identical response criteria are proposed for splenectomy. Assessment of response should occur within 1 to 2 months and after withholding concomitant treatment(s), if any, for a time sufficient to reasonably exclude a persistence of their effect (Table 3).

**Refractory ITP: definition, therapeutic goals, and response assessment**

Refractory patients should fulfill 2 criteria. First, they should have failed splenectomy or have relapsed thereafter. Second, they should...
Table 4. Refractory ITP

Definition (all should be met)

- Failure to achieve at least R or loss of R after splenectomy
- Need of treatment(s) (including, but not limited to, low dose of corticosteroids) to minimize the risk of clinically significant bleeding. Need of on-demand or adjunctive therapy alone does not qualify the patient as refractory.
- Primary ITP confirmed by excluding other supervised causes of thrombocytopenia.

Definition of on-demand therapy

- Any therapy used to temporarily increase the platelet count sufficiently to safely perform invasive procedures or in case of major bleeding or trauma.

Definition of adjunctive therapy

- Any non-ITP specific therapy that may decrease bleeding (eg, antifibrinolytic agents, hormonal agents, DDAVP, recombinant factor VIII, fibrin sealants). Platelet transfusion is also included.

Definition of response to therapy in refractory ITP

- Ability to maintain a platelet count sufficient to prevent clinically significant bleeding.
- Ability to decrease toxic therapy (eg, corticosteroids) does not qualify for response but should be reported.

Definition of response to on-demand therapy

- Control of bleeding in the specific situation.
- Achievement of a platelet count sufficient to perform procedure or minimize bleeding from trauma.

DDAVP indicates deamino arginine vasopressin.

*May not be applicable in children or in patients with accessory spleen.
†Bleeding symptoms measured by a validated scale whenever possible (requires further studies).
§Specific platelet thresholds cannot be provided, but in most instances, a platelet count of 50-70 × 10⁹/L would fulfill this criterion.
¶A strict definition of response in terms of predefined platelet count cannot be given and may not be appropriate when considering the risk/benefit ratio in refractory ITP, because the trade-off between efficacy of a specific treatment and its short- and long-term toxicity varies among patients.

There have been several randomized clinical trials performed in adults with ITP,⁴¹,⁴２,⁴４,⁴６,⁵⁰ and their results can be compared only with great difficulty because of differences in the characteristics of the patient populations included (newly diagnosed vs persistent or chronic/refractory), study designs and end points, as well as the heterogeneous mechanisms of action and patterns of response to the various investigational treatments. Some of the problems of comparison are attributable not only to these differences but also to the lack of description of key features (eg, patient-related parameters). Even the more numerous controlled studies in children⁷,⁶１-⁷５ present similar problems of interpretation, particularly regarding the end points and definition of outcomes. In summary, the results of clinical trials conducted to date with old or new agents, including studies with anti-CD20 antibodies conducted using uncontrolled designs,¹⁰ are not easily comparable for clinically meaningful response rates and response duration and do not allow the drawing of definite conclusions in all instances. In turn, it is difficult to determine how they should be introduced into current clinical practice.

To avoid these limitations in future trials, the panel recommended minimal standardized criteria and definitions to be used in intervention studies (specifically for phase II and III studies) in order that heterogeneity in study subjects and in result reporting can be minimized (Table 5).

Conclusions

The IWG was developed to harmonize current definitions and terminology in primary ITP, recognizing that current nomenclature is outdated, is limited by heterogeneity, and has not been critically analyzed.² The members of the IWG agreed that the unavoidable arbitrary nature of any proposal should be tempered by obtaining the greatest possible consensus and by choosing only clinically sound definitions. Thus, the strength of this proposal lies in the achievement of consensus from an international group of experts in ITP after a series of face-to-face meetings and discussions. Consensus was reached through rational discussion in a structured plan including collection of opinions through questionnaires and a 2-day conference. Unanimous agreement was obtained in all issues within the present report (with the exception of the definition of refractory ITP in children). Definitions were designed to reflect clinical practice and to standardize clinical trial design. The proposal is not intended to represent guidelines for diagnosis or treatment, but it may be a valuable construct for new clinical guideline development. A limitation is represented by the lack of...
Table 5. Trial-adapted criteria for eligibility and outcome assessments in ITP

Eligibility (all should be met)

- Previously treated or untreated patients fitting within one of the different phases of the disease (in Table 1). Refractory patients defined as in Table 4.
- Entry platelet count: at least 3 x 10^9/L. At least 5 x 10^9/L in specific clinical settings or patients on steroids, or in the presence of bleeding symptoms
- Patients should be on a stable treatment or off any treatment for a time sufficient to exclude a late effect (see Table 3)

Supplemental specifications

- Pediatric and adult patients analyzed separately
- Response to previous treatment(s), if any, should be reported

End points

Primary end points:

- CR or R based on platelet count as in Table 2*

Secondary end points:

- Adverse events (safety), need for rescue interventions, corticosteroids/concomitant treatment reduction, rate of splenectomies.
- Could become primary end points according to the design of the clinical trial or patient characteristics.
- Bleeding scale, HRQoL assessment and, whenever possible, pharmacoeconomic analysis should be included

Timing of assessment of primary end points and duration of response

- Depends on the type of treatment
- Patients enrolled while on a stable treatment with one or more agents must be no longer receiving these treatments for a time sufficient to exclude any protracted effect
- Duration could be calculated as follows depending on study design:
  - The time from CR or R as defined in Table 2 to loss of response
  - The cumulative time spent in CR or R or cumulative time spent without meeting a predefined end point(s)

Adverse events

- Bleeding episodes, rescue interventions, frequency of splenectomy, and treatment-related side effects occurring during or after the time of exposure to the experimental agent always reported. Duration of side effects monitoring time after the end of experimental treatment should be provided.
- For assessment of rebound thrombocytopenia or bleeding, the immediate period after the suspension of the agent up to the attainment of a stable platelet count§ or institution of a new treatment should be considered. This treatment should be recorded.
- A predefined exceedingly high platelet count induced by treatment could be considered an adverse event, depending on the agent under investigation

HRQoL indicates health-related quality of life.

*At variance with Table 4, these definitions should be also adopted for refractory cases, considering the experimental nature of clinical trials requiring objective measurements.
†Specify the duration that a subject should be off other treatments and/or the time elapsed after any rescue medication at the time of response evaluation, see also Table 3. For patients enrolled while on a stable concomitant treatment, still requiring it at the time of response evaluation, only secondary end points can be assessed
§For some agents requiring continuous treatment like TPO agonists an upper limit of acceptable platelet count should be predefined and thus cumulative time spent within a therapeutic window is most suitable
||Defined as a platelet count not requiring treatment or dosage modification for at least 15 days.

Acknowledgments

This project was endorsed by the Scientific Working Group on Thrombocytopenias of the European Hematology Association (EHA) and the Intercontinental Childhood ITP Study (ICIS) Group. Critical revision of the manuscript by Paula Bolton-Maggs (United Kingdom), George Buchanan (United States), and David Kuter (United States) was highly appreciated. We thank Mrs Claudia Guzzoni and Dr Stefania Fortuna for their excellent organizing and secretarial assistance.

The conference was made possible thanks to the financial and logistic support of Fondazione Progetto Ematologia (Vicenza), which received unrestricted grants from Amgen Europe and GlaxoSmithKline Europe to partially cover the costs of the project. None of the IWG members and external reviewers received honoraria.

Authorship

Contribution: F.R. coordinated the project, chaired the conference, and wrote the manuscript; D.P., R.S., T.G., M.M., and P.J. chaired the working parties during the conference and wrote the manuscript; M.R. acted as scientific secretariat of the conference and wrote the manuscript; and D.M.A., V.B., J.B.B., D.B.C., B.H.C., N.C., B.G., T.K., M.G.M., R.M., M.A.S., and J.N.G. were active members of the International Group and reviewed and gave their approval to the final manuscript.

Conflict-of-interest disclosure: F.R., R.S., M.M., and R.M. have been members of scientific advisory boards for Amgen and GlaxoSmithKline. T.G. has received research support from Amgen and GlaxoSmithKline and has been a member of advisory boards for Amgen, GlaxoSmithKline, and Baxter Pharmaceuticals. D.P. has received research support from Baxter, GlaxoSmithKline and Amgen, has consulted for Baxter, GlaxoSmithKline, Amgen, and Symphogen, is on the speakers bureau for Baxter and Amgen, and he owns shares in GlaxoSmithKline (basic employee entry package). D.M.A. has received an operating grant from Hoffman-LaRoche and has been a consultant for Amgen. J.B.B. has received research grants from Amgen, Biogen-IDEC, Cangene, Genentech, GlaxoSmithKline, Genzyme, Immunomedics, MGI Pharma, and Sysmex, has received lecture fees from Baxter, has received consulting fees from Amgen, Symphogen, GlaxoSmithKline, and Baxter, has been a member of scientific advisory boards for Amgen, GlaxoSmithKline, Ligand, and Baxter, and has equity ownership in Amgen and GSK, D.B.C. has been a member of scientific advisory boards for Amgen, GlaxoSmithKline, and Symphogen. B.H.C. has received travel assistance to attend the meeting by GlaxoSmith-Kline and has been a consultant to CSL and Amgen. N.C. has been a member of scientific advisory boards for GlaxoSmithKline. B.G. received support from and is consultant for Roche, Sanofi Pasteur (not for ITP), Amgen, and LFB (Laboratoire Français de fractionnement et de biotechnologie). V.B. has been a member of scientific advisory boards for Baxter and Bayer. T.K. has received unrestricted grants from Hoffman-LaRoche and Amgen. J.N.G. has been a consultant for and also has received research support from Amgen, Inc, related to their development of romiplostim for ITP. The other authors declare no competing financial interests.

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