Terminology in ITP

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History of Terminology and Guidelines

Consensus on Terminology Definitions and Outcome criteria

Evolution of Guidelines and new drugs availability

1996 — 1st to rank evidence - George et al

2001 — Rituximab - Stasi et al, 2001

2008 — Romiplostim - FDA August 2008
EMA November 2008

Eltrombopag - FDA November 2008
EMA December 2008

IWG consensus on terminology, definitions and outcome criteria - Rodeghiero et al

2009 —

2010 — 1st International Consensus Report - Provan et al

2011 — ASH guidelines based on GRADE - Neunert et al

History of Terminology and Guidelines

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Evolution of Guidelines and new drugs availability

	2018	Fostamatinib - FDA April 2018 EMA November 2019
	2019	Avatrombopag - FDA June 2019 EMA December 2020
	2019	Updated International consensus report ASH guidelines
Preliminary ERCI/IWG consensus	2024	
ERCI/IWG consensus	2025	
	2025/26	New drugs on the horizon Updated ASH guidelines Updated EHA/ERCI guidelines

Guidelines

Provide **Evidence** grading and **Recommendation** Strength (statistical approach may be required)

- PICO model (**P**opulation/**P**atient - **I**ntervention **C**omparator – **O**utcome)
- In a specific **P**opulation does **I**ntervention or **C**omparator result in better **O**utcome?

Statistical approach may be required

Terminology

Provide **general definitions** on:

- Patient characteristics
- Distinct goals of treatment
- Distinct outcomes
- Type of interventions
- Class of drugs
- Aspects of the disease

Consensus reached through progressive agreements among experts

Terminology, Definitions, and Outcomes

- Provided clinical context for communication between medical care teams
- Established the importance of disease severity in decision making
- Some gaps exist
  - Newer therapies have shifted practice and influenced relevance
  - Usage of definitions in medication access and clinical trial enrollment
  - Wide differences in application of outcomes in clinical trials

----------INDICATIONS AND USAGE----------

TAVALISSE is a kinase inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

----------INDICATIONS AND USAGE----------

Nplate is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

----------INDICATIONS AND USAGE----------

DOPTELET is a thrombopoietin receptor agonist indicated for the treatment of:

- Thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure. (1.1)
- Thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. (1.2)

PROMACTA is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

PROMACTA should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. PROMACTA should not be used in an attempt to normalize platelet counts. (1)

Outcome Criteria

Table 2. Proposed criteria for assessing response to ITP treatments

Quality of response*†

- CR: platelet count ≥ 100 × 10^9/L and absence of bleeding
- R: platelet count ≥ 30 × 10^9/L and at least 2-fold increase the baseline count and absence of bleeding
- Time to response: time from starting treatment to time of achievement of CR or R‡
- NR: platelet count < 30 × 10^9/L or less than 2-fold increase of baseline platelet count or bleeding
- Loss of CR or R: platelet count below 100 × 10^9/L or bleeding (from CR) or below 30 × 10^9/L or less than 2-fold increase of baseline platelet count or bleeding (from R)

Timing of assessment of response to ITP treatments

- Variable, depends on the type of treatment (see Table 3)

Duration of response§

- 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

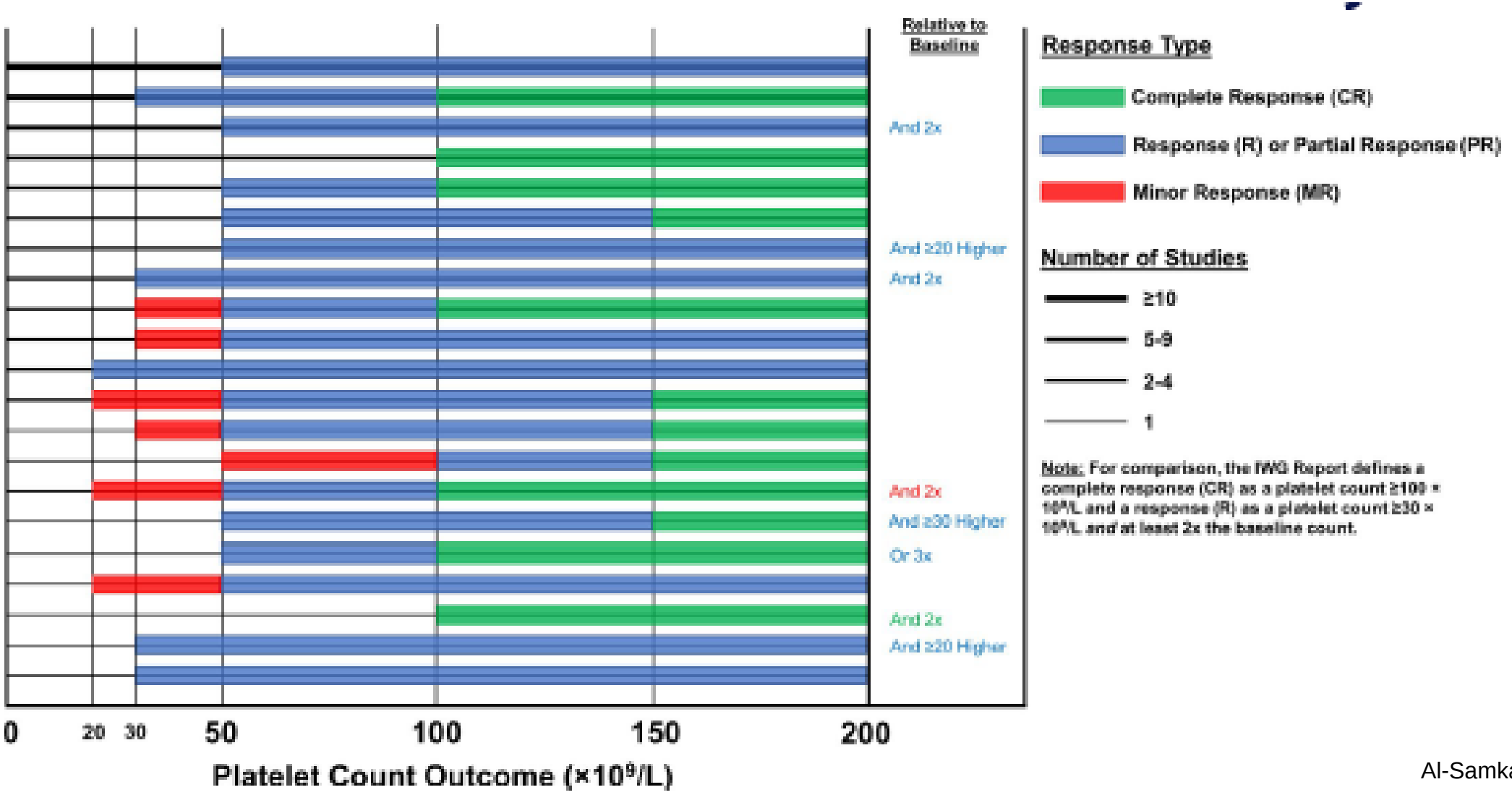
- The need for ongoing or repeated doses administration of corticosteroids for at least 2 months to maintain a platelet count at or above 30 × 10^9/L and/or to avoid bleeding (patients with corticosteroid dependence are considered nonresponders)

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)

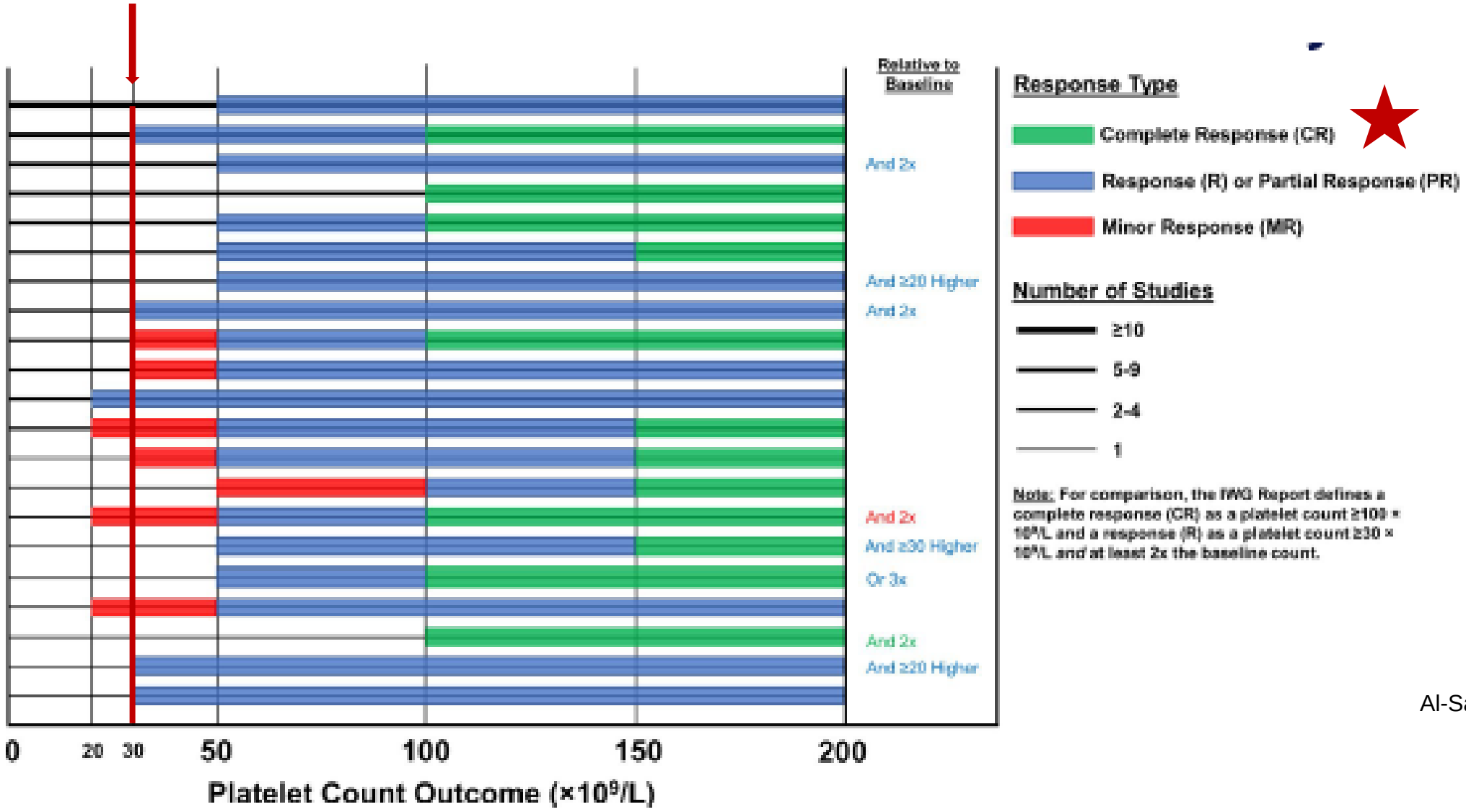
Rodieghiero et al. Blood 2009

Platelet Count Response Criteria



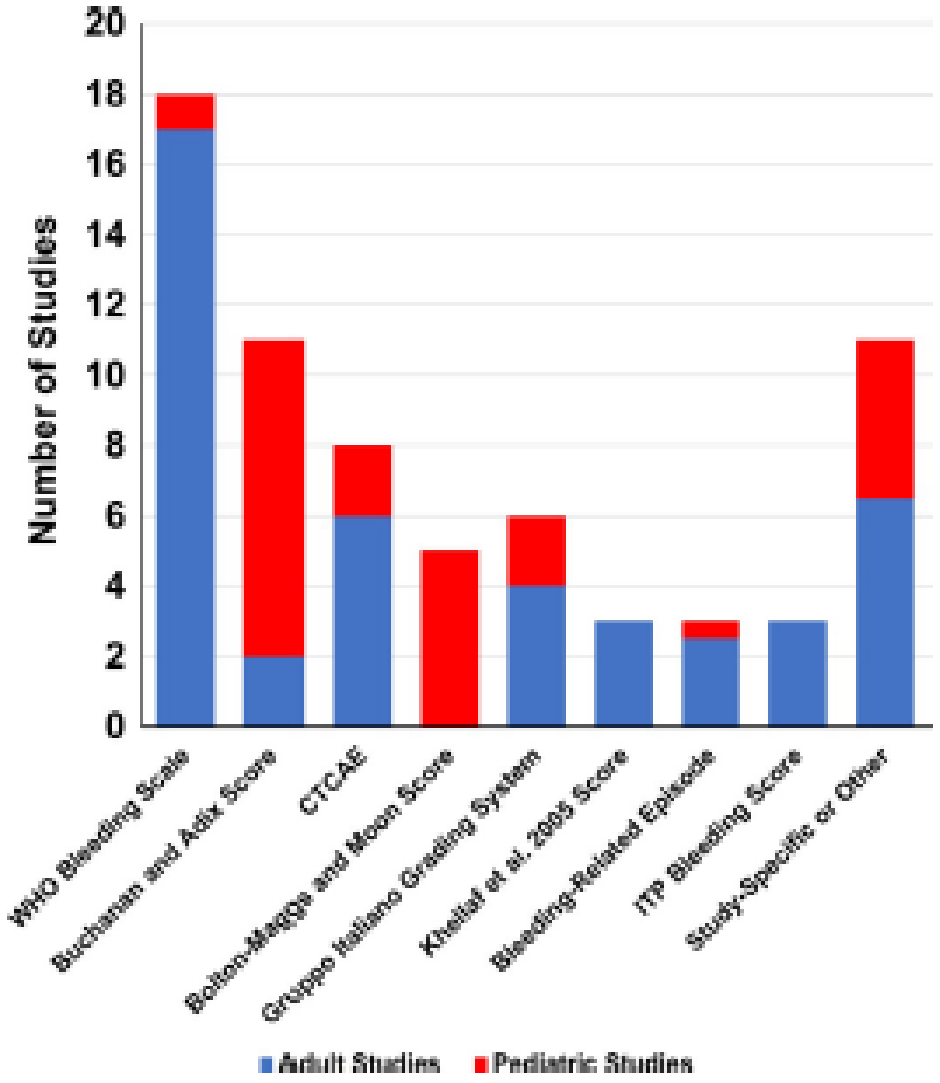
Al-Samkari et al. JTH 2021

Platelet Count Response Criteria



Al-Samkari et al. JTH 2021

Additional Outcomes



Instrument	No. Studies
Adult Instruments	
Medical Outcomes Study Short Form 36 (SF-36v2)	3
Immune Thrombocytopenic Purpura Patient Questionnaire (ITP-PAQ)	2
Motivation and Energy Inventory (MEI-SF)	2
Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)	2
Functional Assessment of Cancer Therapy-Thrombocytopenia Subset (FACT-Th6)	2
EuroQol-5 Dimension (EQ-5D)	1
Pediatric Instruments	
Kids ITP Tool (KIT)	7
Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0)	2

Al-Samkari et al. JTH 2021

IWG Revision

- Refine terminology for modern treatment landscape
- Align terminology with clinical trial design in industry
- Incorporate meaningful patient related outcomes with increased guidance on implementation
- Ensure that terminology best serves the needs of patients and allows for seamless communication among physicians

ERCI-IWG ITP Standardized Definitions

Francesco Rodeghiero, Cindy Neunert, Hanny Al-Samkari, Rachael Grace Donald M. Arnold, James B. Bussel, Nichola Cooper, Marc Michel, Waleed Ghanima, Francesco Zaja, Drew Provan, Tomás Josè González-López, Thomas Kühne, Marisa Lozano, Guillaume Moulis

IWG Revision

- IWG working to revise the 2009 standardization
  - 3 working groups
  - 1 working meeting
  - Regulatory agencies, patient representatives, and expert panelists
  - Pediatric representation

Guiding Principles

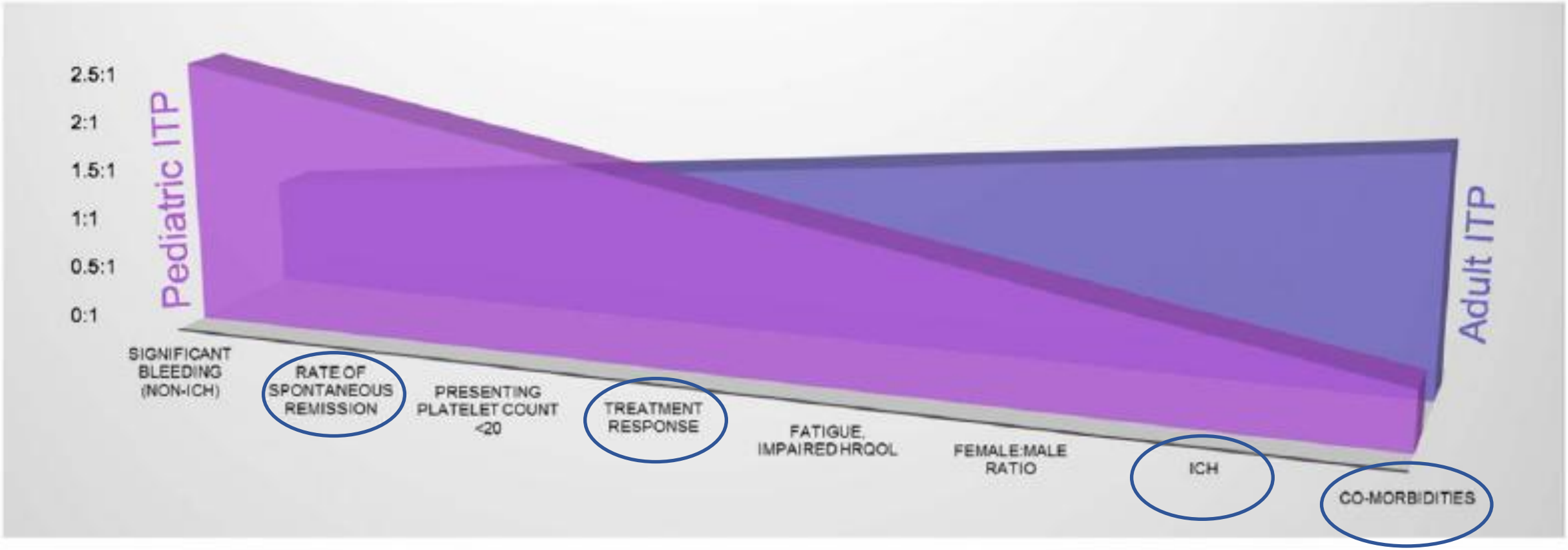
- Standardized terminology is closely linked with guideline development but should not be providing treatment guidance

- Cure is the ideal goal in treating any disease, however….
  - Most available therapies generally do not offer a cure
  - Platelet count outcomes may not be the same as patient goals
  - The primary treatment goal is to control and prevent clinically important bleeding and other reported symptoms

- It is crucial to minimize treatment toxicity
  - Our terminology should be in line with this

- Children are not just little adults

ITP: Children and Adults

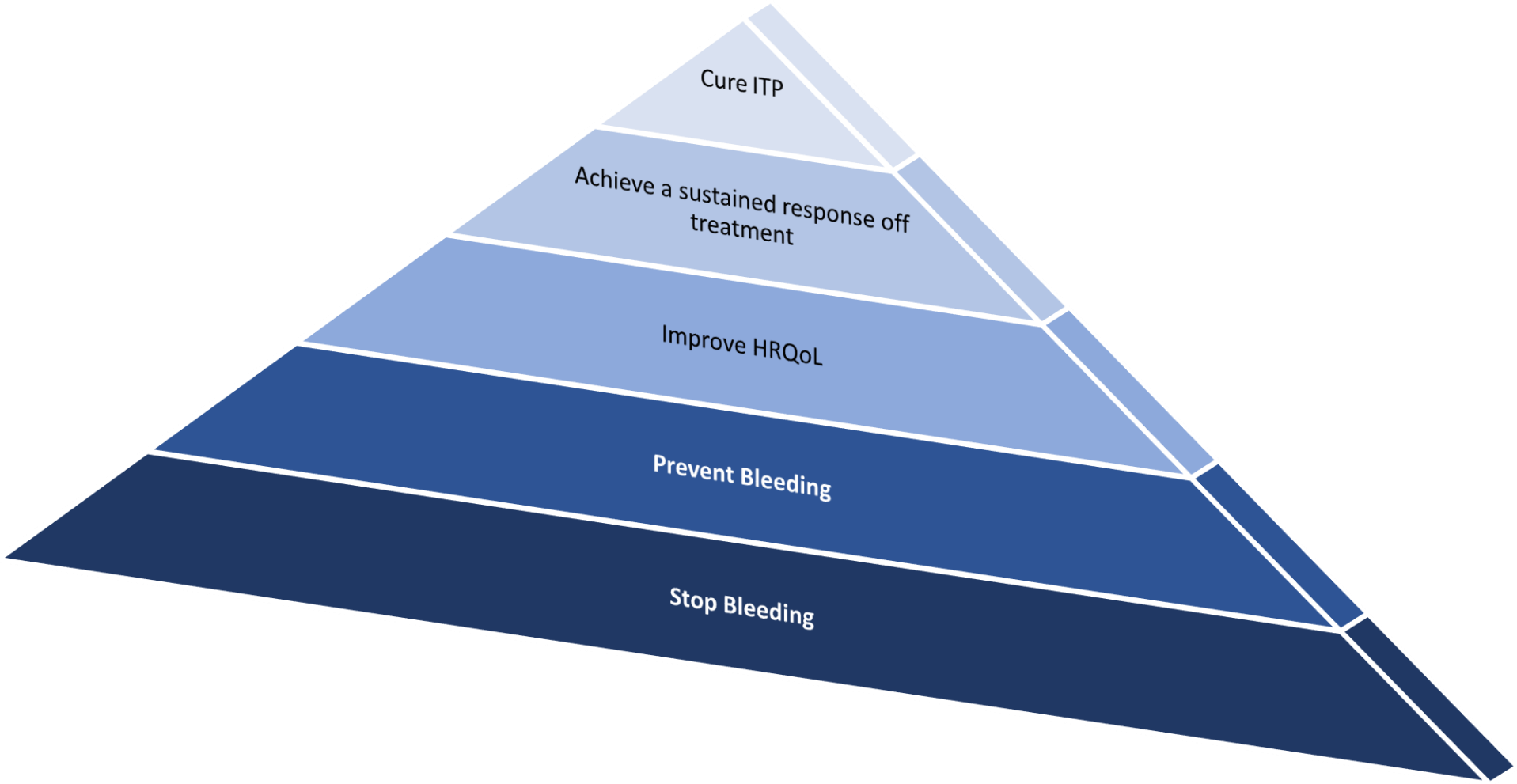


Despotovic et al. Hematology Am Soc Hematol Educ Program 2018.

IWG Revision

Summary

Treatment Goals



Phase and Severity of ITP

Newly Diagnosed	Diagnosis to 3 months
Persistent	3 -12 months
Chronic	>12 months
Remission	Stable (confirmed by multiple counts) improvement in platelet count to pre-ITP or normal level (>150 x 10^9/L) in the absence of treatment for 12 months
Recurrence	New presentation of ITP in a patient with a previous history of ITP remission
Exacerbation	Worsening patient-related symptoms sufficient to mandate emergency therapy or the introduction of new therapy
Severe ITP	Recurrent clinically relevant bleeding manifestations who requiring treatment
Mild ITP	Not yet requiring treatment for clinical manifestation (at diagnosis or for an exacerbation

Response Criteria

Response	**>30K** and at least double from baseline
Complete Response	>100K without bleeding
Time to Response	The time after which a patient is expected to have a platelet response if using the drug within the reported dose range
Non-response to treatment	No response after treatment administration at maximum dose based on expected time to response
Loss of response	A confirmed drop of platelet < 30K on two occasions following drug titration to max dose May be transient
Sustained response off treatment	Platelet count response to drugs that require **continuous administration** after stopping all ITP treatments for at least 6 months Absence of clinically important bleeding
Clinical Improvement	Clinically relevant improvement in patient symptoms

Multi-drug refractory ITP

A subset of ITP which is non-responsive to at least 3 classes of maintenance ITP therapies

- Not including initial/emergency therapies

Standard Maintenance Therapies (Considered for Multi-Drug Refractoriness)	
Thrombopoietic agents	Includes thrombopoietin receptor agonists (TPO-RAs) and recombinant human thrombopoietin (rhTPO)
SYK inhibitors	Fostamatinib, sovleplenib*, cevidoplenib*
Anti-CD20 monoclonal antibodies	Rituximab†
B-cell activating factor pathway antagonists	Ianalumab*, belimumab†
BTK inhibitors	Rilzabrutinib*
Neonatal Fc receptor antagonists	Efgartigimod*
Complement inhibitors	Sutimlimab†
Anti-CD38 monoclonal antibodies	Daratumumab†, mezagitamab*, CM313*
Other Immune-Acting Therapies (Considered for Multi-Drug Refractoriness)	
Other immunosuppressants/immunomodulators†	Mycophenolate mofetil, azathioprine, cyclosporine, vincristine‡, vinblastine‡, danazol, progestins, dapsone, sirolimus
Splenectomy‡	While not a drug, is considered a “drug class” for the purposes of defining a patient as multi-drug refractory

Primary and Secondary ITP

Primary ITP

Autoimmune
Phenotype

With Inborn
Error in Immunity

Secondary ITP

Bleeding Symptoms

Critical Bleeding	Bleeding that pose **immediate risk** for the patient's life causing hemodynamic instability or respiratory compromise and require immediate management.
Major Bleeding	• At risk to become life-threatening in a matter of hours or is organ-threatening • Capable of causing long-term functional impairment • Associated with a significant decrease in hemoglobin levels (≥2 g/dL)
Moderate Bleeding	• Induces significant pain or discomfort • Interferes with daily activities, • Necessitates medical intervention, or • Is otherwise deemed important by the treating physician
Minor Bleeding	Any bleeding not meeting above criteria

Clinically Relevant

Not clinically Relevant

Outcomes for Clinical Trials

- Response
- Concomitant and emergent ITP treatments
- Safety
  - Infections,Thrombosis, Hepatotoxicity, GI toxicity, Hypertension
- Bleeding events
- Reason for study completion failure
- Health-related quality of life (HRQoL)
- Fatigue

Summary

- Terminology and guidelines can be used to improve patient care
- Need to work alongside patient groups and regulatory agencies
- Likely an iterative process
- Final report coming shortly