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Considerations on Study Population - Immune Thrombocytopenia -

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Disclaimer

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Importance of Study Population Selection in ITP

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- **Target population:** all ITP or a specific (well defined) subgroup of ITP (common traits)
- **Study population:** sample of target population used to draw conclusion on the target population

→ should be <u>in support of clear study conclusions and representative of target population</u>

- Balance between **homogenous study population** and **external validity**

→ Heterogenicity in functional (aetiology) and symptomatic aspects of ITP

- Well-defined study population: variability ↓ assay sensitivity and validity ↑
- Appropriate study population is **crucial for clinical trial success**

Guidelines as harmonised framework

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- **Consistency and scientific validity**

e.g. standardize population definitions across chronic ITP clinical trials

- **Homogeneity in study populations across trials via harmonized criteria**

(regulatory/scientific/practical GLs)

Core Population Definition According to EMA-GL

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Key inclusion

- Platelet count $<30\times10^9$/L (up to $<50\times10^9$/L under specific conditions and stratification).
- Typically with prior/concomitant treatment (corticosteroids, IvIg, splenectomy, second-line therapies); Dose, duration, and response to be documented

Key exclusion criteria

- Secondary ITP cases and significant comorbidities to avoid confounding

Stratification

- Splenectomy status, baseline platelet count, concomitant therapies, refractory or unresponsive to prior treatment

Diagnostic Considerations for Study Population

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- **Full blood count:** isolated thrombocytopenia, with bleeding symptoms at least Hb >9 g/dL
- **Helicobacter pylori:** testing encouraged as association currently unclear
- **Screening for anti-nuclear antibodies (ANA) and anti-phospholipid antibodies (APLA):** positive test does not as qualify for secondary ITP
- **Bone marrow examination:** not required (e.g. for non-typical ITP, lack of response to treatments)
- **Biomarkers:** to be considered to describe and explore patient characterization

Inclusion based on time since diagnosis

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Newly diagnosed: 0-3 months

Persistent: 3-12 months

Chronic: ≥12 months since diagnosis

- Longer time since diagnosis linked to less likely spontaneous remission

- Mechanistically no difference in response to treatment expected based on these categories
- Representativeness of study population for target ITP population
- Assay sensitivity might be reduced, stratification to be considered

Heterogeneity in treatment response

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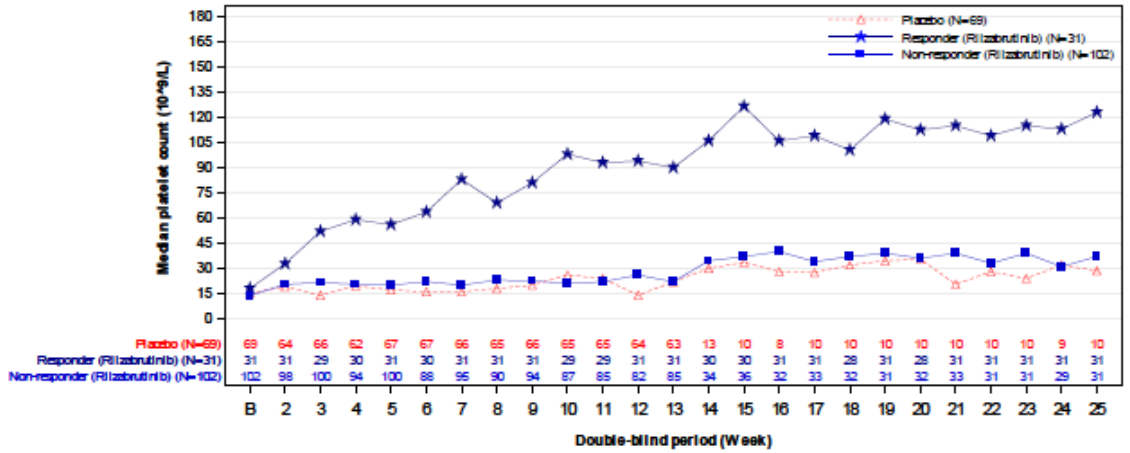
- High rate of patients without substantial platelet response
- Exploration and identification of **predictive factors/traits**
- Comprehensive diagnostic profile could support such identification of factors/traits

- Rate of non-response ↓
- Target population ↓
- Precision in treatment ↑
- Study success ↑

Figure: Median platelet count by visit during the 24-week blinded treatment period



B: Baseline
Baseline platelet count is defined as average of 1st, 2nd qualifying screening platelet counts, and Week 1 (Study day 1) platelet count
Durable platelet response is defined as the proportion of participants able to achieve platelet counts at or above 50,000/μL for >=two-thirds of at least 8 non-missing weekly scheduled platelet measurements during the last 12 weeks of the 24-week blinded treatment period in the absence of rescue therapy, provided that at least 2 non-missing weekly scheduled platelet measurements are at or above 50,000/μL during the last 6 weeks of the 24-week blinded treatment period
Based on all available platelet counts

Taken from EPAR WAYRILZ EMA/348131/2025

Special population

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- **Pediatric Cohorts:** often self-limiting (in ~2/3), persistent/chronic form more likely with increasing age – later-line treatment options also required (rarely splenectomy)

- **Elderly:** Comorbidities and concomitant medications, closely monitor thrombotic events

Encouraged to be included and adequately reflected in clinical studies

Summary Regulatory Perspective on Study Population

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- Clear definition of target and study population
- Platelet threshold typically <30 x10^9/L
- Exclusion of secondary causes and confounders
- Stratification (splenectomy, baseline platelets, concomitant therapy)
- **Balance between internal and external validity**

Future Considerations:

- Relevance of characterisation based on time since diagnosis
- Exploration of potential prognostic factors to link response to specific mechanisms

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THANK YOU!

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