Evidence Gap Analysis of the Burden of Illness and Treatment of Primary Immune Thrombocytopenia

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Background

- Primary immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by isolated thrombocytopenia (platelet count < 100 × 10^9/L) in the absence of other causes of thrombocytopenia.[1]
- Most patients present with various bleeding signs.[2,3] Debilitating fatigue is a common symptom, reported in up to 61% of patients as an important issue and identified in clinical trials as among the worst items at baseline evaluation.[4]
- Immunoglobulin G autoantibodies are directly pathogenic in primary ITP. Efgartigimod is engineered for optimal blocking of FcRn, which is central to immunoglobulin G regulation.

Objective

- To identify evidence gaps in the literature on the burden of illness and treatment of adult primary ITP to support the launch of efgartigimod.

Methods

- A targeted literature review was conducted from 1 July 2011 to 26 October 2021 in PubMed, Embase, and the Cochrane Library using a predefined search strategy.
- Articles on disease description; epidemiology; clinical, humanistic, and economic burden; and treatment patterns were included.

Results

Gaps in Epidemiology

Identified evidence	Evidence gaps
• ITP is a rare disease. – Incidence in adults ranges 1.6-5.3 per 100,000 people per year.[2] – Prevalence varied considerably depending on studies[5] and ranges from 17 to ~50 per 100,000 persons.[6-8] • Mortality risk in patients with ITP is higher compared with the general population.[5] – Mortality rates are particularly high among patients who are refractory to treatment,[9] patients who have experienced cardiovascular or bleeding events,[10,a] older patients, and hospitalized patients.[11]	• Robust epidemiology studies with large sample sizes are lacking; evidence is mostly based on review articles and a few dated studies (up to 2015). • No data are available on the number of patients in second- and third-line treatment settings. • Some epidemiology estimates included mixed populations,[b] leading to inaccurate estimation. • There is limited information on the mortality rate. Studies mostly focused on subgroups of patients, such as hospitalized patients or those who experienced cardiovascular or bleeding events.[a]

[a] Bleeding event requiring hospital contact.
[b] Mixed populations of adult and pediatric patients, different disease stages, or other types of thrombocytopenia.

Clinical Burden

Identified evidence	Evidence gaps
• Bleeding events occur frequently in patients with ITP. – The overall rate of bleeding-related episodes was 1.72 per patient-year (95% CI, 1.68-1.75), with rates higher during the first 3 months after ITP onset.[12] – Predictors of severe bleeding include newly diagnosed ITP, severe thrombocytopenia,[a] and previous minor bleeding.[13] • Fatigue is a common morbidity as up to 61% of patients reported it being an important issue.[4] • ITP can also be associated with other clinical manifestations, including thromboembolism events,[b] infection, and bone marrow fibrosis.[2,14-18]	• Predictive factors[c] for the relevant clinical burden are not well studied. • There is a lack of data on when the clinical manifestations occur, particularly regarding disease stage or disease duration. • Most studies focused on rates but lack data on severity of manifestations. • It is not clear how disease severity or platelet count level are associated with the various clinical manifestations. • Fatigue is the only clinical symptom evaluated for its effects on HRQOL. The effects of other clinical symptoms on humanistic and/or economic burden are not assessed. • Clinical manifestations of ITP have not been well assessed as an efficacy outcome in clinical studies.

CI = confidence interval; HRQOL = health-related quality of life.
[a] Severe thrombocytopenia was defined as platelet count < 10 × 10^9/L or < 20 × 10^9/L, depending on different articles cited in the review.
[b] Thromboembolism events include venous thromboembolism, ischemic stroke, or TIA (transient ischemic attack) in different studies.
[c] Associations with either an increased or a reduced risk.

Humanistic Burden

Identified evidence	Evidence gaps
• ITP has a significant and negative effect on various aspects of HRQOL in patients, both with and without interventions.[19] • More than 60% of patients reported ITP having a negative effect on functioning, with energy level and ability to exercise being the most affected areas. Nearly half of patients felt that ITP negatively affected their psychological and emotional well-being, with concerns about worsened condition and platelet counts being the most affected issues.[20] • Fatigue has a significant effect on a considerable proportion of patients (range, 12.5%-61%) and has been assessed separately from the general HRQOL evaluation.[4,20] Patients with persistent ITP had the worst fatigue in all measured dimensions in fatigue instruments, and the severity of fatigue correlated with worsened HRQOL outcomes.[21]	• Despite evidence that patients with ITP have significant impairment in HRQOL, recent data on humanistic burden are limited. • Most studies on HRQOL used the generic SF-36 instrument. • The disease-specific instrument ITP-PAQ has been used only in studies with romiplostim. • Fatigue is considered a significant morbidity of ITP. However, current literature lacks robust analysis on fatigue, both in terms of a standardized definition and well-accepted/validated measurement. • Most humanistic burden studies were cross-sectional. Given that ITP is a chronic disease, robust longitudinal analysis is needed. • No data are available on the factors that are associated with or predict impaired HRQOL. • No study assessed caregiver burden. • Utility data are limited to 1 study in Italy and 1 multinational survey.

ITP-PAQ = Immune Thrombocytopenia Patient Assessment Questionnaire.

Economic Burden

Identified evidence	Evidence gaps
• 4 studies analyzed direct costs and HCRU in patients with ITP; all studies showed significant medical costs and hospital utilization due to ITP.[6,8,11,22] • Costs of bleeding were specifically evaluated and shown to be significant.[23,24] • Patients with ITP reported significantly reduced productivity, particularly among those with high symptom burden and those aged 18-49 years.[20]	• Analyses of HCRU and costs were mostly based on a 12-month follow-up period; therefore, data on the long-term economic burden of chronic ITP are lacking. • Data from the I-WISh survey mainly include patients with chronic ITP[20]; therefore, it is not clear how ITP affects productivity and employment status during the early phases of ITP. • No articles assessed loss of productivity among caregivers of patients with ITP. • Most studies were US-focused analyses. Therefore, data are scarce in other countries.

HCRU = healthcare resource utilization; I-WISh = ITP World Impact Survey; US = United States.

Current Treatment Landscape and Treatment Patterns

Treatment for ITP	Evidence gaps
First-line options • Corticosteroids: only effective in the initial few days in 85% of cases; frequent relapses reported after discontinuation.[25] • IVIG: 1-3 days for initial response and 2-7 days for peak response[26]; associated with various side effects, including an increased risk of thrombosis.[27] • Anti-D immunoglobulin: not approved as a licensed treatment of ITP in some countries.[27] **Second- and third-line options** • TPO-RAs: widely used and approved for chronic and refractory ITP; associated with various side effects and/or administration restrictions.[27-29] Avatrombopag was recently approved and, unlike eltrombopag, has no food restriction or hepatotoxicity.[28,29] • Immunomodulators: rituximab is used in the second line, although not approved for ITP.[25] Fostamatinib is approved to treat only chronic and refractory ITP and is used in the third-line setting.[27] • Splenectomy: reserved for refractory and chronic ITP; challenging to predict patient response and associated with various risks and complications.[25,27]	• Treating ITP is challenging; current available treatments have limitations and are associated with various risks and complications. • Data for therapies beyond the second line are limited; there is no clear treatment paradigm, with patients switching from one therapy to another.
Treatment patterns	**Evidence gaps**
• Across different studies, treatment patterns were similar in the first line, with corticosteroids being the most commonly used treatment. • Variation exists across different studies in the second-line setting.	• Data on treatment patterns are mainly based on studies in the US and a few European countries.

IVIG = intravenous immunoglobulin; TPO-RA = thrombopoietin receptor agonist.

Conclusions

- Data on ITP are not all consistent or up to date. Uncertainty about treatment response and a lack of effective treatment remain unmet needs for patients with ITP; efgartigimod has the potential to offer a new treatment for patients with ITP. Several gaps have been identified, and closure of these gaps could help support the launch of efgartigimod in ITP.

Disclosures

Clémence Arvin-Berod, Glenn Phillips, Marie Godar, and Jaume Ayguasanosa are employees of argenx. Mehul Desai is a former employee of argenx. Jin Yang and Catherine Masaquel are employees of RTI Health Solutions.

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