Phase 4 ADOPT study: interim analysis of efficacy and safety results of avatrombopag treatment in adult patients with immune thrombocytopenia

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OBJECTIVES

- To describe the real-world effectiveness and safety of the TPO-RA avatrombopag in adult patients with ITP in routine clinical practice in Europe.

METHODS

Multicenter, observational, Phase 4 ADOPT study (NCT04943042)[1]

Patients

Inclusion criteria ✓

- ≥18 years of age
- Established and well documented ITP diagnosis
- Treated with, or initiating treatment with avatrombopag for ITP at enrollment
- Informed consent
- Willing/able to comply with protocol requirements

Exclusion criteria X

- Secondary ITP
- Enrollment in other clinical interventional study or intake of an investigational medicinal product within 3 months prior to this study

Study design

Retrospective period
Data collected from patients' medical records for up to 12 months

Avatrombopag treatment[a]
Prospective period
Data collected at routine clinical visits for 12 months

Interim analysis: data cut-off April 4, 2024[b]

Primary endpoint: Cumulative number of weeks with PC ≥30 × 10^9/L

Key secondary endpoints[c]

- Cumulative number of weeks with PC ≥50 × 10^9/L
- PC ≥30 × 10^9/L for ≥8 consecutive weeks
- PC ≥50 × 10^9/L for ≥8 consecutive weeks
- Rescue medication use
- WHO grade ≥2 bleeding events
- AEs, AEs leading to discontinuation of avatrombopag, SAEs, and AESIs (TEEs or bleeding events)[d]

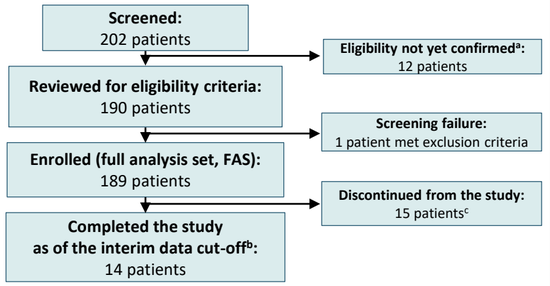
Statistical analyses:

- No formal statistical hypothesis testing; data summarized using descriptive statistics
- Baseline characteristics, prior treatments, and safety analyzed in all enrolled patients
- Effectiveness analyzed in all patients who had 12 months of data in the prospective period

[a]Patients were prescribed avatrombopag according to usual clinical practice and according to investigator judgment. Any concomitant medication was also prescribed at the investigator's discretion and per usual clinical practice.
[b]An updated data cut-off was used versus the abstract (January 2, 2024).
[c]The full list of endpoints is available online[1] and these results will be reported when further patient data are available.
[d]TEEs were any thrombotic or embolic event, whether arterial or venous; bleeding events were any clinically significant blood loss meeting WHO bleeding scale grade ≥3 criteria.

RESULTS

Figure 1: Patient disposition



[a]Details relating to inclusion and exclusion criteria are not yet available.
[b]Patients who had completed their end of study visit.
[c]Reason for discontinuation listed as 'other' (not lost to follow-up, withdrawn consent, or enrollment in another trial).

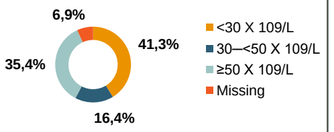
Figure 2: Retrospective period: demographics and clinical characteristics (FAS; N = 189)

Age (years)
Mean (SD): 55.4 (18.0)
Median (min, max): 56 (18, 92)

56.6% female

Time since ITP diagnosis to first avatrombopag treatment
Mean (SD): 483 (598) weeks
Median (min, max): 279 (0.1, 3390) weeks
≥12 months: 81.5%

Baseline PC



Splenectomy: 9.0%

Prior significant bleeding events: 8.5%

Prior TEEs: 10.6%

Table 1. Retrospective period: previous treatments within 12 months prior to initiating avatrombopag (FAS)

Patients, n (%)[a]	Avatrombopag N = 189
TPO-RA	101 (53.4)
Eltrombopag	57 (30.2)
Romiplostim	58 (30.7)
Corticosteroids	71 (37.6)
Prednisolone	61 (32.3)
Dexamethasone	20 (10.6)
Other	42 (22.2)
IVIg	22 (11.6)
Rituximab	3 (1.6)
Fostamatinib	22 (11.6)

Figure 3: Interim effectiveness (patients with 12 months of prospective data as of the interim data cut-off date, N = 16)

PC ≥30 × 10^9/L

- Over the 12-month follow-up period, the **cumulative number of weeks with a PC ≥30 × 10^9/L** was: **mean** (SD) **48.5 (9.0) and median (min, max) 51.2** (28.3, 61.1)
  - In subgroup analyses, findings did not substantially differ when patients were grouped by baseline PC (<30, 30–<50, and ≥50 × 10^9/L), concomitant ITP medication use (yes, no), or previous TPO-RA use (yes, no); however, interpretation was limited by the small sample size
- **PC ≥30 × 10^9/L was maintained for ≥8 consecutive weeks in 16 patients**

PC ≥50 × 10^9/L

- Over the 12-month follow-up period, the **cumulative number of weeks with a PC ≥50 × 10^9/L** was **mean 43.6 (SD 14.5) and median 47.0 (min 0.0, max 61.1)**
- **PC ≥50 × 10^9/L was maintained for ≥8 consecutive weeks in 15 patients**

1 (6.3%) patient had a WHO grade ≥2 bleeding event

8 (50%) patients required rescue medication

Table 2. Interim safety as of the data cut-off date (FAS)

Patients with events, n (%) [number of events (e)][a]	Avatrombopag N = 189
All AEs	28 (14.8) [55]
AEs related to avatrombopag	9 (4.8) [12][b]
AEs leading to discontinuation of avatrombopag	2 (1.1) [4][c]
SAEs	13 (6.9) [17][d]
AESIs	5 (2.6) [7][e]

[a]The number of events is greater than the number of patients with events, as some patients experienced more than one event.
[b]Abdominal pain, e = 1; bone pain, e = 1; dyspepsia, e = 1; fatigue, e = 1; thrombocytosis, e = 1; toxic skin eruption, e = 1; uncoded, e = 6.
[c]Abdominal pain, e = 1; fatigue, e = 1; uncoded, e = 2.
[d]Acute myocardial infarction, e = 1; atheroembolism, e = 1; cerebral venous thrombosis, e = 1; death, e = 1; embolism, e = 1; empyema, e = 1; epistaxis, e = 1; facial paresis, e = 1; lumbar spinal stenosis, e = 1; meningitis, e = 1; platelet count decreased, e = 1; pulmonary embolism, e = 1; thrombocytopenia, e = 2; thrombosis, e = 1; uncoded, e = 2.
[e]Atheroembolism, e = 1; cerebral venous thrombosis, e = 1; deep vein thrombosis, e = 2; embolism, e = 1; pulmonary embolism, e = 1; thrombosis, e = 1.

CONCLUSIONS

- This first interim analysis of the ADOPT study provides real-world evidence for the effectiveness and safety profile of avatrombopag in adult patients with ITP in European routine practice.
- Future ADOPT study analyses will provide further data on the real-world effectiveness and safety of avatrombopag over a longer time duration than in clinical trials, and in patient subgroups not previously included in the clinical program (newly diagnosed/persistent ITP,[2] prior TEEs).[3,4]

Abbreviations

AE, adverse event; **AESI**, adverse event of special interest; **FAS**, full analysis set; **ITP**, immune thrombocytopenia; **IVIg**, intravenous immunoglobulin; **PC**, platelet count; **SAE**, serious adverse event; **SD**, standard deviation; **TEE**, thromboembolic event; **TPO-RA**, thrombopoietin receptor agonist; **WHO**, World Health Organization.

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