A European retrospective study to describe real-world outcomes in patients with primary immune thrombocytopenia treated with avatrombopag: Interim results

Poster 02

Francesco Zaja[1,2], Quentin A Hill[3], Francisco Jose Lopez Jaime[4], Rosa Sonja Alesci[5], Wolfgang Miesbach[6], Fatemeh Saberi Hosnijeh[7], Luca Le Treust[8], Elisa Lucchini[2], Milica Putnik[9], Carly Rich[9]

1. DSM, Università degli Studi di Trieste, Trieste, Italy; 2. UCO Ematologia, Azienda Sanitaria Universitaria Giuliano Isontina, Trieste, Italy; 3. Leeds Teaching Hospital NHS Trust, Leeds, UK; 4. Hospital Universitario Regional de Malaga, Malaga, Spain; 5. IMD Gerinnungszentrum Hochtaunus, Bad Homburg , Germany; 6. University Hospital Frankfurt, Frankfurt, Germany; 7, Real-World Evidence, Evidence & Access, OPEN Health, Rotterdam, The Netherlands; 8. Real-World Evidence, Evidence & Access, OPEN Health, London, UK; 9. Sobi, Stockholm, Sweden

CONCLUSIONS

- This interim analysis demonstrates real-world clinical profile of avatrombopag in patients with primary immune thrombocytopenia in Europe and supports data from clinical trials and other post-marketing evidence.
- 68% of the patients had a complete response by week 12, 71% by week 26, and 81% by week 52 after avatrombopag initiation.
- Platelet counts reached the thresholds of ≥50×10^9/L and ≥100×10^9/L in a median of 8 (95% confidence intervals: 7-21) and 21 (9-196) days, respectively, from avatrombopag initiation.
- Of patients who reached to ≥50×10^9/L threshold, around 60% maintained the response at 2 year in overall population and in TPO-RA subgroups.

INTRODUCTION

- Primary immune thrombocytopenia (ITP) is an autoimmune disorder characterised by isolated thrombocytopenia (peripheral blood platelet count (PC) <100×10^9/L) in the absence of other causes or disorders that may be associated with thrombocytopenia.[1,2]
- Avatrombopag (AVA), an oral thrombopoietin-receptor agonist (TPO-RA), is a safe and efficacious treatment approved for patients with ITP (2021 by European Medicines Agency).[3]
- There is limited real-world evidence on AVA's clinical effectiveness in European population treated in routine clinical practice.[5]

OBJECTIVES

- This study aims to report real-world evidence on the clinical outcomes of patients with primary ITP treated with AVA in Europe

METHODS

Study design

- A non-interventional, retrospective, multi-centre chart in six European countries (Belgium, Czech Republic, Germany, Italy, Spain, and United Kingdom)

Study population

- Adult patients with primary ITP treated with AVA
- ***Inclusion criteria:***
  - Confirmed diagnosis of primary ITP documented in medical records
  - Receiving AVA for the treatment of primary ITP within routine clinical practice
  - Medical records available for ≥12 weeks prior to and from AVA initiation
  - Aged ≥18 years at the start of first TPO-RA treatment
  - Providing consent to access patient's medical records in line with country regulations
- ***Exclusion criteria:***
  - Participating in any form of interventional study during follow-up

Study definition

- ***Index date:*** Date of initiation of AVA
- ***Baseline period:*** 26 weeks prior to AVA initiation
- ***Post-index period (follow-up):*** Period after the index date until date of death or date of most recent follow-up visit or PC assessment (whichever was earliest)
- ***Platelet response:*** Defined as achieving a meaningful PC threshold (i.e., ≥ 30×10^9/L or ≥ 50×10^9/L) while they were on AVA in the absence of rescue therapy (date first achieved was date of first response)
- ***Complete platelet response:*** Defined as achieving a PC ≥ 100×10^9/L (date first achieved was date of first response) in the absence of rescue therapy

Primary endpoints

- Proportion of patients achieving meaningful PC thresholds and complete response by week 12, 26, 52 and at any time while on AVA post-index
- Proportion of patients with a ≥50%, ≥75%, and 100% increase in PC from baseline by week 12, 26, and 52 among patients who respond to AVA
- Time from index date to an initial platelet response
- Duration of response

Statistical methods

- Quantitative variables were summarised using mean, standard deviation (SD), medians, and interquartile range (IQR).
- Categorical variables were described with frequencies and percentages. Point estimates for proportions were presented along with associated 95% confidence intervals (CI).
- Time-to-event analyses (based on Kaplan-Meier) were used to estimate the median time to response and duration of response.
- PC counts obtained during rescue therapy was excluded from the analysis.

RESULTS

Patients' baseline characteristics

- By July 2024, data relating to 31 patients had been collected: 16 TPO-RA naïve and 15 prior TPO-RA exposed (60% eltrombopag, 13.3% romiplostim, 26.7% both) **(Table 1)**.
- Mean (SD) age of patients at data collection was 58.8 (21.1) years and 52% of patients were female.
- Median (IQR) time from ITP diagnosis until AVA initiation was 5 (0.6-12.1) years and patients were followed for a median time of 37 (25.6-53.4) weeks.
- Median baseline PC was 42.5×10^9/L which is higher than the threshold for initiating treatment (<30×10^9/L).

Table 1: Patients' baseline characteristics

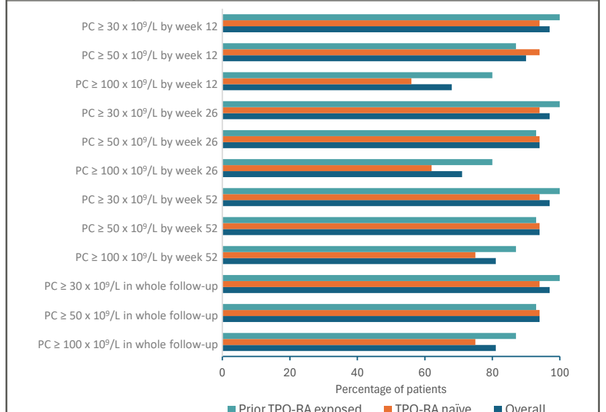
	Overall, N=31	TPO-RA Naïve, N=16	Prior TPO-RA exposed, N=15
Age at data collection, years, Mean (SD)	58.8 (21.1)	56.1 (23.6)	61.6 (18.4)
Female sex, N (%)	16 (52%)	8 (50%)	8 (53%)
Median (IQR) baseline platelet count, ×10^9/L	42.5 (21.5-83.5)	53.5 (23.8-99.8)	42 (14-63.5)
History of splenectomy, N (%)	2 (6%)	0	2 (13%)
Number of prior TPO-RA treatments, N (%)			
0	16 (52%)	16 (100%)	NR
1	11 (35%)	NR	11 (73%)
2	4 (13%)	NR	4 (27%)
Number of prior steroid treatments, N (%)			
0	10 (32%)	4 (25%)	6 (40%)
1	18 (58%)	11 (69%)	7 (47%)
2	3 (10%)	1 (6%)	2 (13%)
Time from diagnosis to index, years, Mean (SD)	10.2 (14)	4 (4.7)	17.4 (17.5)
Median (IQR)	5 (0.6-12.1)	1.6 (0.1-7.9)	11.1 (4.5-26.7)
Follow-up, weeks, Mean (SD)	51.1 (38.5)	41.1 (33.7)	61.7 (41.4)
Median (IQR)	37 (25.6-53.4)	32.2 (22.1-44.9)	47.3 (32.4-80.5)

IQR: interquartile range; NR: not relevant; SD: standard deviation; TPO-RA: thrombopoietin-receptor agonist

Proportion of patients achieving meaningful PC thresholds post-index (Figure 1)

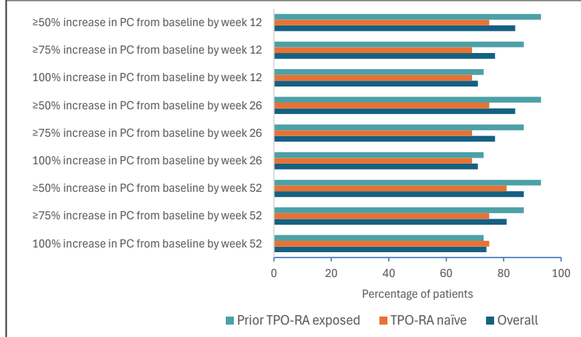
- By week 12, 97% (30 out of 31 patients) and 90% (28/31) of the patients achieved PC threshold of 30×10^9/L and 50×10^9/L, respectively.
- By week 26, 97% (30/31) and 94% (29/31) of the patients achieved PC threshold of 30×10^9/L and 50×10^9/L, respectively.
- 68% (21/31) of the patients had a complete response (≥100×10^9/L) by week 12, 71% (22/31) by week 26, and 81% (25/31) by week 52 post-index.
- 81% (25/31) of the patients (75% [12/16] for TPO-RA naïve patients, 87% [13/15] for TPO-RA exposed patients) had a record of complete response anytime post-index.

Figure 1: Proportion of patients achieving meaningful PC thresholds post-index



PC: platelet count; TPO-RA: thrombopoietin-receptor agonist

Figure 2: Proportion of patients with a ≥50%, ≥75% and 100% increase in PC from baseline



PC: platelet count; TPO-RA: thrombopoietin-receptor agonist

Proportion of patients with a ≥50%, ≥75% and 100% increase in PC from baseline (Figure 2)

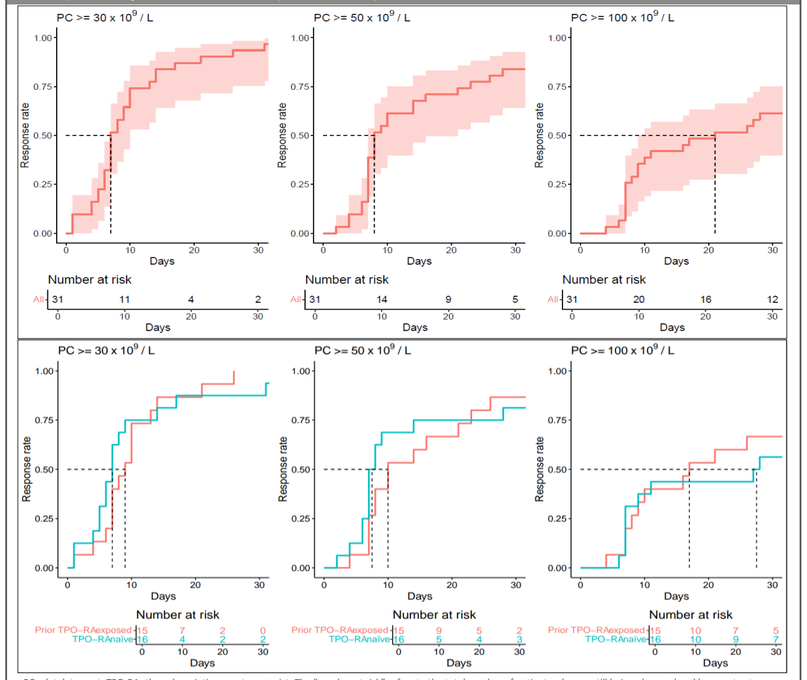
- PC doubled from baseline in 71% (22/31), 71% (22/31), and 74% (23/31) of the patients by week 12, 26, and 52, respectively.
- The proportion of patients with a ≥50%, ≥75%, and 100% increase in PC from baseline by week 12 and 26 was numerically higher in TPO-RA exposed patients compared with TPO-RA naïve patients.

Table 2: Duration of platelet response (in patients who respond)

PC response	Duration of response	Overall	TPO-RA Naïve	Prior TPO-RA exposed
		Proportion [95% CI] (Total N of patients)	Proportion [95% CI] (Total N of patients)	Proportion [95% CI] (Total N of patients)
≥30 × 10^9/L	1 year	76.7% [62.9% - 93.4%] (30)	66.7% [46.6% - 95.3%] (15)	86.7% [71.1% - 100%] (15)
	2 years	76.7% [62.9% - 93.4%] (30)	NE	86.7% [71.1% - 100%] (15)
≥50 × 10^9/L	1 year	60.5% [44.5% - 82.2%] (29)	60.0% [39.7% ; 90.7%] (15)	62.5% [41.0% - 95.3%] (14)
	2 years	60.5% [44.5% - 82.2%] (29)	60.0% [39.7% ; 90.7%] (15)	62.5% [41.0% - 95.3%] (14)
≥100 × 10^9/L	1 year	21.8% [8.5% - 55.8%] (25)	33.3% [12.5% - 88.8%] (12)	13.0% [2.2% - 77.1%] (13)
	2 years	NE	NE	NE

CI: confidence intervals; NE: not estimable; TPO-RA: thrombopoietin-receptor agonist; Proportion and 95% confidence intervals were calculated using the Kaplan-Meier estimator, based on the number of events and the number at risk at specific time points.

Figure 3: Median time from index date to an initial platelet response, overall (upper row) and by TPO-RA status (lower row)



PC: platelet count; TPO-RA: thrombopoietin-receptor agonist; The "number at risk" refers to the total number of patients who are still being observed and have not yet experienced the event of interest (PC response) at the beginning of each time period. This number decreases over time as events occur or as patients are censored.

Time from index date to an initial platelet response (Figure 3)

- The median (95% CI) time to achieve a PC count of ≥50×10^9/L and ≥100×10^9/L was 8 (7-21) days and 21 (9-196) days, respectively, from index date.
- The median time to achieve a complete response was numerically longer in naïve TPO-RA patients compared to those previously exposed to TPO-RA.

Duration of response (Table 2)

- Of patients who reached to ≥50×10^9/L and ≥100×10^9/L threshold, 60.5% (95% CI: 44.5%-82.2%) and 21.8% (8.5%-55.8%) maintained the response at 1 year, respectively.
- Of patients who reached to ≥50×10^9/L threshold, 60.5% (44.5%-82.2%), 60.0% (39.7%-90.7%), and 62.5% (41.0%-95.3%) maintained the response at 2 year in overall population, TPO-RA naïve, and prior TPO-RA exposed group, respectively.

References

1. Markham A. Avatrombopag: a review in thrombocytopenia. Drugs. 2021;81(16):1905–13.
2. Rodeghiero F, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009;113(11):2386–93.
3. Prescribing-information.pdf [Internet]. [cited 2023 Apr 7]. Available from: https://www.ema.europa.eu/en/documents/product-information/doptelet-epar-product-information_en.pdf
4. Álvarez Román MT, et al. Phase 4 ADOPT Study: interim analysis of efficacy and safety Results of avatrombopag treatment in adult patients with immune thrombocytopenia EHA 2024 P2235. https://library.ehaweb.org/eha/2024/eha2024-congress/420322/mara.eva.mingot.castellano.phase.4.adopt.study.interim.analysis.of.efficacy.html

Acknowledgements

This study was sponsored by Sobi and conducted by OPEN Health company. This study was an observational study that had no impact on patients except for collection of written informed consent for researcher access to patients' medical records for the purposes of this study. REC approvals, competent authority and local management approvals for the conduct of this study and the sharing of pseudonymised patient data were sought according to applicable local regulations.

Disclosures

FZ: Sobi, Argenx, Novartis, Amgen, Grifols (research funding, honoraria for participation to advisory board; speaker honoraria); **QAH:** has consulted for Alpine, Amgen, Argenx, Gliknik, Incyte, Immunovant, Janssen, Novartis, ReAlta, Sanofi and Sobi; and received speaker honoraria from Grifols and Novartis; **FJLJ:** Speaker & Advisory: Amgen, Bayer, CSL Behring, Novartis, Novo Nordisk, Octapharma, Pfizer, Rovi, Sobi, Takeda; **RSA:** Sobi, Argenx, Novartis, Amgen, Grifols, Octapharma, Sanofi (adboard, grant for participation on congresses, speaker); **WM:** Bayer, Biomarin, Biotest, CSL Behring, Chugai, Freeline, LFB, Novo Nordisk, Octapharma, Pfizer, Regeneron, Roche, Sanofi, sobi, Takeda/Shire, uniQure; **FSH** and **LLT**: Employees of OPEN Health; **EL:** The author has no conflict of interest; **MP** and **CR:** Sobi employees and/or shareholders.

Corresponding author name: Carly Rich, Email: Carly.Rich@sobi.com