Platelet Response to Avatrombopag Among Patients with Primary Immune Thrombocytopenia Who Switched from Eltrombopag or Romiplostim: the REAL-AVA 2.0 Real-World Study

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Shruti Chaturvedi,[1] M Y Levy,[2] Scott Kolodny,[3] Abiola Oladapo,[3] Chelsea Bernheisel,[3] Elyse Swallow,[4] Debbie Goldschmidt,[4] Alexandra Greatsinger,[4] Loren Ormenaj,[4] Sinia Sareen,[4] Michael Vredenburg,[3] Srikanth Nagalla[5]

[1] Johns Hopkins School of Medicine, Division of Medicine-Hematology, Baltimore, USA; [2] Baylor Charles A. Sammons Cancer Center, Texas Oncology, Dallas, USA; [3] Sobi Inc., Morrisville, USA; [4] Analysis Group, Boston, USA; [5] Miami Cancer Institute, Miami, USA

CONCLUSIONS

- The majority of patients who switched from another TPO-RA to AVA for the treatment of primary ITP achieved or maintained a PC response with AVA at every threshold examined.
- Robust responses were seen after switching to AVA from ELT or ROMI, underscoring AVA's effectiveness regardless of the prior TPO-RA agent used.
- Durable responses to AVA were observed regardless of the reason for switching- whether due to lack of efficacy, convenience, safety, or personal preference - supporting AVA as a versatile and effective option for previously treated ITP.

INTRODUCTION

- Thrombopoietin receptor agonists (TPO-RAs) such as eltrombopag (ELT), romiplostim (ROMI), and avatrombopag (AVA) are FDA- and EMA-approved treatments in patients with immune thrombocytopenia (ITP), an autoimmune disease characterized by low platelet counts (PC), who have had an insufficient response to prior treatments.[1-6]
- As low PCs can impair blood clotting and increase the risk of acute bleeding events,[7] TPO-RA treatments aim to reduce this risk through raising PC levels above target PC thresholds.[8]
- Patients may switch between TPO-RA agents to improve PC response or for tolerability, adherence, or convenience reasons, and prior research has found that switching among TPO-RA therapies can be an effective treatment strategy in patients with primary ITP.[9]
- Additional real-world data are needed to further characterize TPO-RA switches and subsequent treatment response among patients who used ELT or ROMI prior to initiating AVA.

AIM

- Assess PC response to AVA among patients who switched from ELT or ROMI to AVA for primary ITP treatment.

METHODS

Study Design and Population

- REAL-AVA 2.0 was a retrospective multi-site chart review study across medical centers in the US.
- Adult patients with primary ITP who initiated AVA between July 1, 2019 and June 30, 2024 and who were treated with ELT or ROMI in the 3 months prior to AVA initiation were included in this analysis.
- The index date was defined as the date of AVA initiation. The baseline period was the 3 months pre-index. Patients were followed until the earliest of end of data availability, death, or study end (December 31, 2024).
- Patients were assigned to either the "Prior ELT" or "Prior ROMI" cohort based on the most recent treatment received in the baseline period prior to AVA initiation.
- Patients were further stratified into subgroups by reason for AVA initiation:
  1. Lack of efficacy with prior treatment
  2. Other reasons (e.g., convenience, lower adverse event risk, patient preference, other)

Statistical Analyses

- Response to AVA was defined as having at least one PC above the threshold (PC≥30k/μL, ≥50k/μL, and PC≥100k/μL) at any time during AVA treatment.
- PC measurements were excluded from response assessments if they were obtained during or soon after the use of rescue therapy.
  - Rescue therapy was defined as initiation of immunosuppressants or steroids; increase in steroid dose; or receipt of a platelet transfusion, intravenous immunoglobulin (IVIG), or anti-D immunoglobulin.
  - PCs were ineligible to be categorized as a response if they fell within the following time periods after the rescue therapy: immunosuppressants or steroids: 8 weeks; IVIG or anti-D immunoglobulin: 4 weeks; platelet transfusions: 1 week.
- Days between PC measurements were considered a response or nonresponse based on the most recent preceding PC observation after the index date.
- Durability of response was assessed in patients who achieved or maintained a response to AVA and was defined as the percentage of the total AVA treatment duration during which the patient experienced response.

RESULTS:

Patient Characteristics (Table 1; Figure 1)

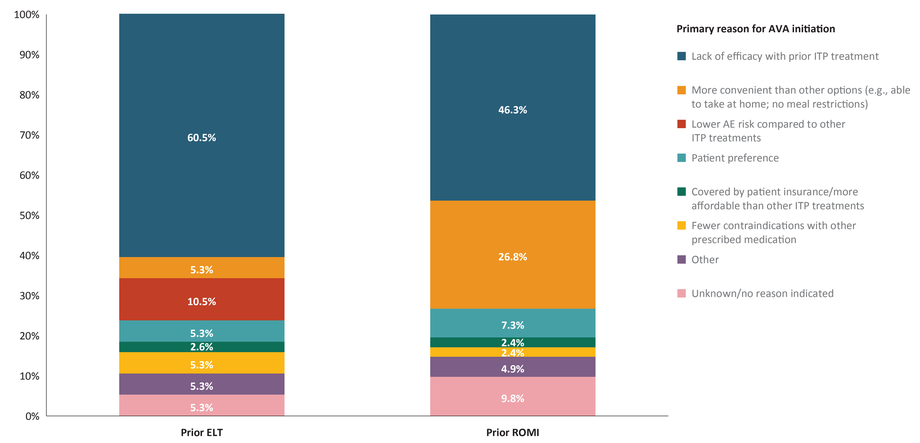
- Charts from 11 medical centers were included in the study: 6 academic institutions and 5 community practice centers.
- A total of 79 patients were included in the analysis: 38 patients who switched from ELT to AVA and 41 patients who switched from ROMI to AVA.
- Among the 38 patients in the Prior ELT cohort, 23 (61%) switched to AVA due to lack of efficacy and 15 (39%) switched for other reasons. Among the 41 patients in the Prior ROMI cohort, 19 (46%) switched due to lack of efficacy and 22 (54%) switched for other reasons. The most common other reasons were convenience and patient preference (**Figure 1**).
- The mean (SD) age at index ranged from 55.5 (17.2) to 62.5 (17.2) years among patients who switched from ELT to AVA, and from 59.2 (23.0) to 61.3 (18.7) years among those who switched from ROMI to AVA.
- The median [IQR] ITP disease duration was 2.3 [0.5-3.6] years among patients who switched from ELT to AVA due to lack of efficacy and 6.4 [0.4-14.0] years among patients who switched for other reasons. In the Prior ROMI cohort, disease duration was 4.5 [1.3-8.4] years in the lack of efficacy subgroup and 2.2 [0.5-6.2] years in the other reasons subgroup.
- Patients who switched to AVA from ELT received ELT for a median of 88 days prior to discontinuation, whereas patients who switched to AVA from ROMI received ROMI for a median of 295 days.
- Median baseline PC was 48.0k/μL and 80.0k/μL for patients who switched to AVA from ELT and ROMI, respectively.
- The median [IQR] duration of follow-up after AVA initiation ranged from 18.7 to 29.8 months, and the median [IQR] duration of AVA treatment ranged from 8.9 to 18.4 months across the four subgroups.

Table 1. Patient demographic and clinical characteristics

	ELT as most recent TPO-RA prior to AVA			ROMI as most recent TPO-RA prior to AVA		
	Overall N = 38	Reason for AVA initiation: Lack of efficacy N=23	Reason for AVA initiation: Other N=15	Overall N = 41	Reason for AVA initiation: Lack of efficacy N=19	Reason for AVA initiation: Other N=22
Demographic Characteristics During Baseline						
Age at index date, Mean ± SD years	58.3 ± 17.3	55.5 ± 17.2	62.5 ± 17.2	60.3 ± 20.5	59.2 ± 23.0	61.3 ± 18.7
Female, n (%)	21 (55.3%)	12 (52.2%)	9 (60.0%)	25 (61.0%)	9 (47.4%)	16 (72.7%)
Race/ethnicity, n (%)[1]						
White	28 (73.7%)	15 (65.2%)	13 (86.7%)	35 (85.4%)	16 (84.2%)	19 (86.4%)
Hispanic, Latino or Spanish origin	3 (7.9%)	1 (4.3%)	2 (13.3%)	3 (7.3%)	1 (5.3%)	2 (9.1%)
Black or African American	4 (10.5%)	4 (17.4%)	0 (0.0%)	3 (7.3%)	1 (5.3%)	2 (9.1%)
Other/Unknown	4 (10.5%)	3 (13.0%)	1 (12.5%)	1 (2.4%)	1 (5.3%)	0 (0.0%)
Insurance type, n (%)[1]						
Commercial/private insurance	20 (52.6%)	14 (60.9%)	6 (40.0%)	19 (46.3%)	8 (42.1%)	11 (50.0%)
Medicare	11 (28.9%)	5 (21.7%)	6 (40.0%)	22 (53.7%)	11 (57.9%)	11 (50.0%)
Medicaid	8 (21.1%)	5 (21.7%)	3 (20.0%)	7 (17.1%)	4 (21.1%)	3 (13.6%)
None	2 (5.3%)	1 (4.3%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other/Unknown	4 (10.5%)	2 (8.7%)	2 (13.3%)	4 (9.8%)	2 (10.5%)	2 (9.1%)
Clinical Characteristics						
ITP disease duration at index, Median [IQR] years	2.6 [0.5, 8.1]	2.3 [0.5, 3.6]	6.4 [0.4, 14.0]	3.1 [0.8, 7.1]	4.5 [1.3, 8.4]	2.2 [0.5, 6.2]
Number of ITP treatments ever used prior to AVA initiation, Mean ± SD	3.1 ± 1.4	3.2 ± 1.4	2.9 ± 1.6	4.0 ± 1.4	4.4 ± 1.6	3.7 ± 1.2
Duration of prior ELT/ROMI, Median [IQR] months	2.9 [1.2, 5.3]	2.9 [1.3, 5.3]	2.9 [1.1, 6.4]	9.7 [3.1, 23.8]	9.1 [5.8, 23.1]	10.0 [3.0, 29.7]
Baseline PC[2], Median [IQR] k/μL	48.0 [34.0, 82.0]	46.3 [32.3, 53.8]	52.0 [38.0, 114.5]	80.0 [41.0, 120.0]	57.0 [20.5, 82.5]	91.0 [69.5, 219.0]
AVA Treatment Characteristics During Follow-up						
Duration of follow-up, Median [IQR] months	21.7 [14.8- 34.5]	21.9 [12.3-33.3]	20.8 [17.4-42.8]	22.5 [10.6-37.8]	29.8 [9.3-44.4]	18.7 [12.9-34.5]
Duration of AVA treatment, Median [IQR] months	14.7 [3.7-22.6]	13.1 [3.7-22.8]	18.4 [5.9-22.5]	9.2 [5.0-21.3]	8.9 [4.6-29.5]	11.9 [6.2-19.0]

Notes:
[1] Categories are not mutually exclusive.
[2] Baseline PC was defined as the median PC value among the three PC observations closest to the index date and within 3 months prior to the index date. PCs obtained during or immediately after rescue therapy use were not considered in the baseline PC assessment.

Figure 1. Primary reason for AVA initiation by most recent TPO-RA prior to AVA initiation



PC Response to AVA (Figure 2; Figure 3)

- A PC threshold of ≥30k/μL was achieved or maintained by 89.5% of patients who switched from ELT to AVA and 87.8% of patients who switched from ROMI to AVA. The reason for switching did not have a substantive impact on achieving a PC response.
- Similarly, the proportion of patients who achieved or maintained a PC response ≥50k/μL in the Prior ELT cohort was 87.0% among patients who switched due to lack of efficacy and 86.7% among patients who switched for other reasons. In the Prior ROMI cohort, these values were 73.7% and 95.5% respectively (**Figure 2**).
- The proportion of patients who achieved or maintained a PC response ≥100k/μL ranged from 52.6% to 90.9%, depending on the prior treatment and the reason for initiating AVA
- The median durability of response to AVA at 30k/μL, 50k/μL, and 100k/μL was 94%, 92%, and 72%, respectively, among patients that switched to AVA from ELT and 97%, 93%, and 79%, respectively, among patients that switched to AVA from ROMI (**Figure 3**).

Figure 2. AVA response rates by most recent TPO-RA and reason for switch across response thresholds

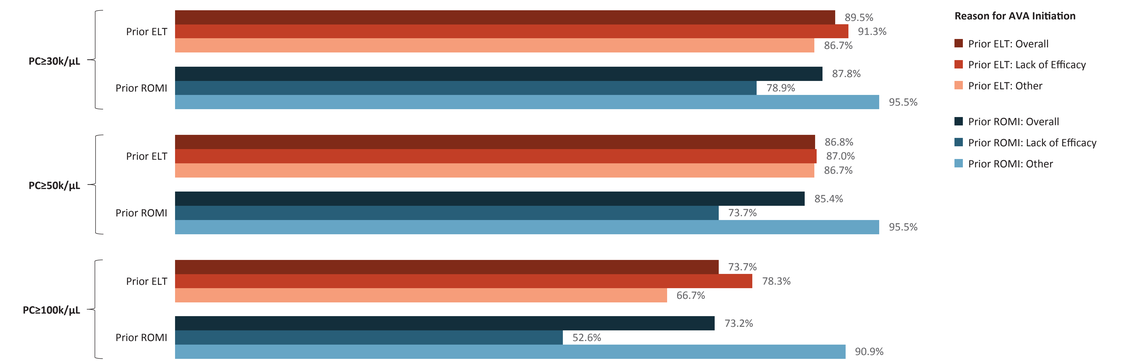
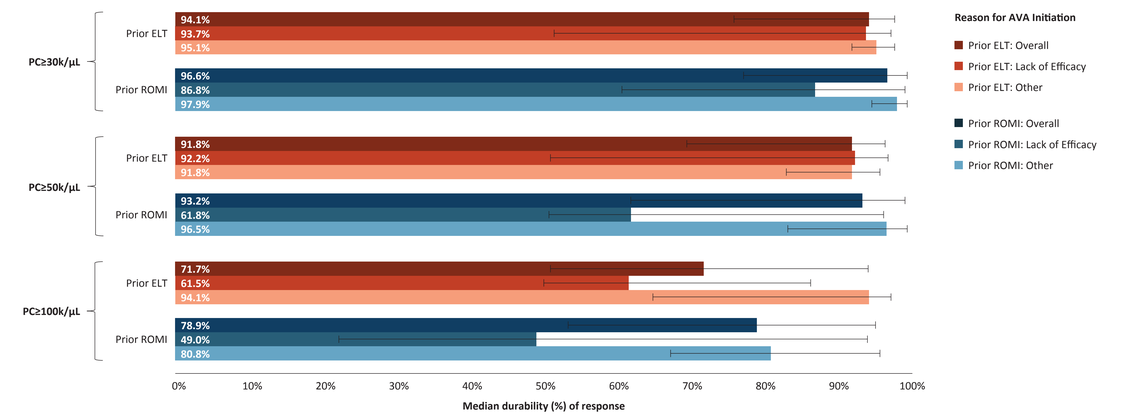


Figure 3. Durability of response to AVA by most recent TPO-RA and reason for switch across response thresholds



Note: The error bars represent the IQR of durability.

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ABBREVIATIONS

AE, adverse events; AVA, avatrombopag; CI, confidence interval; ELT, eltrombopag; IQR, interquartile range; ITP, immune thrombocytopenia; IVIG, intravenous immunoglobulin; k/μL, thousand per microliter; PC, platelet count; ROMI, romiplostim; SD, standard deviation; TPO-RA, thrombopoietin receptor agonists.

DISCLOSURES

Authors SN, ML, SC, ES, DG, AG, LO, and SS are consultants of Sobi, Inc. Authors SK, AO, CB, and MV are employees of Sobi, Inc.

LIMITATIONS

- This study used real-world data from multiple clinical centers. Data on PCs may not have been uniformly available for all patients.
- Patients needed at least 6 months of follow-up after starting AVA for inclusion in the study, unless deceased. Patients lost to follow-up after treatment initiation may differ from the study patients.
- The sample included a roughly equal number of males and females, which may not reflect the broader U.S. ITP population, where females are more commonly affected.
- Despite standardized training across centers, data entry errors may still have occurred during abstraction.

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