Impact of Protocol-Mandated Dose Holds on Platelet Response Durability in Pediatric ITP Patients Treated With Avatrombopag: AVA-PED-301 Post Hoc Analysis

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Oral Presentation

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NIH, National Institutes of Health.

Protocol-mandated dose holds may have influenced durability outcomes in AVA-PED-301

Platelet response[1]:
81.5% (AVA) vs 0% (PBO); p<0.0001

Durable platelet response[1]:
27.8% (AVA) vs 0% (PBO); p=0.0077

The study protocol mandated dose hold for platelet counts **>250×10^9/L**[1], a threshold lower than the **>400×10^9/L** threshold referenced in the avatrombopag prescribing information[2]

This post hoc analysis evaluated the incidence, characteristics, and clinical impact of protocol-mandated dose holds during AVA treatment in pediatric ITP

AVA, avatrombopag; ITP, immune thrombocytopenia; PBO, placebo.
1. Grace RF, et al. Lancet Haematol 2025;12:e494–e504. 2. Doptelet [US prescribing information]. Durham, NC: AkaRx,Inc; 2025.

Phase 3 trial AVA-PED-301 (NCT04516967)[1-3]

Children | **Phase 3 (301)**

Multicenter, randomized, double-blind, placebo-controlled, parallel-group trial with an open-label extension phase

Objective

To evaluate efficacy, safety, tolerability and PK/PD profile of AVA for children and adolescents with a diagnosis of primary ITP of ≥6 months in duration and an insufficient response to previous treatments

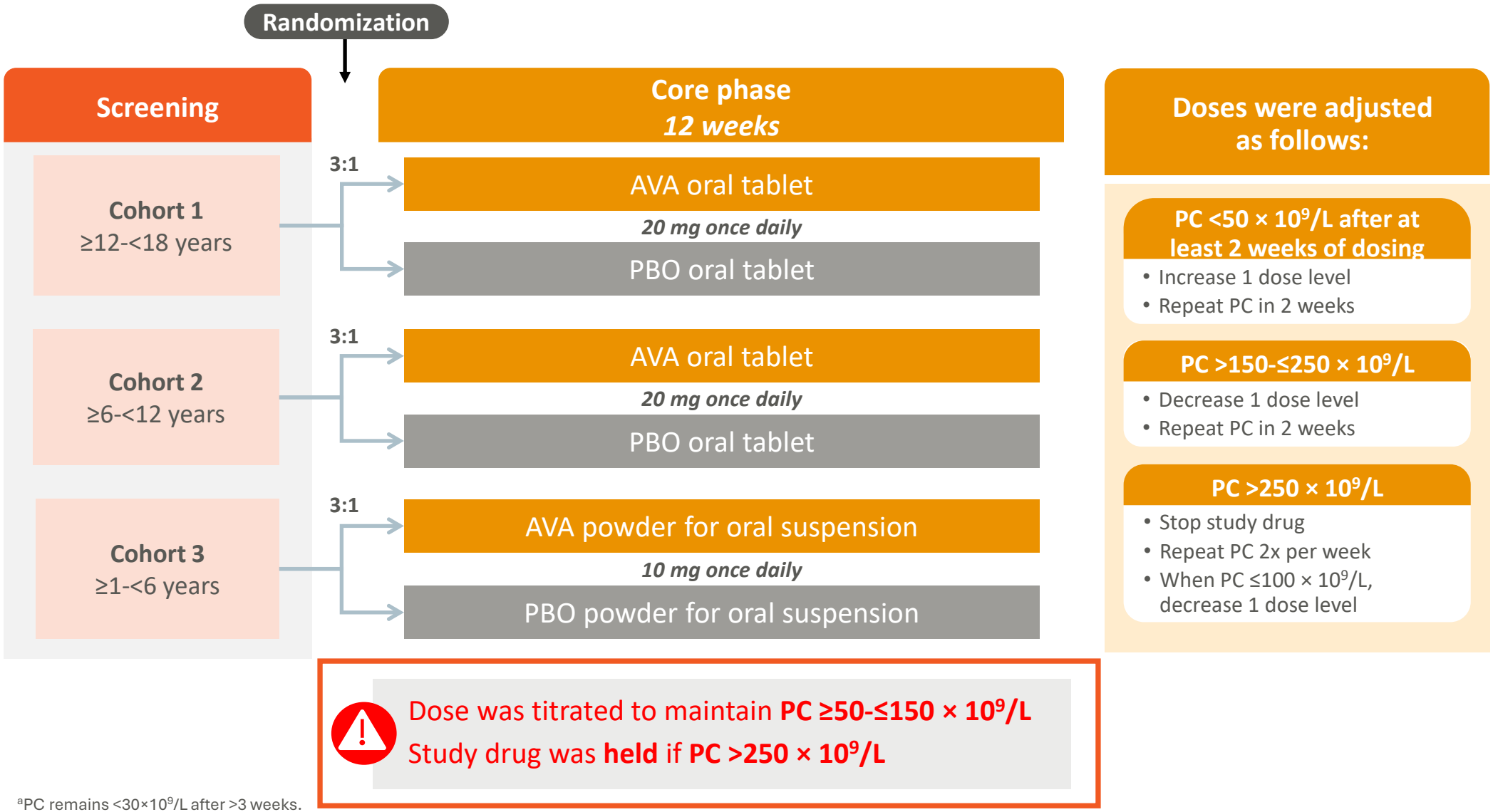
34 sites[a], 12-week (core phase) and 2-year open-label extension phase

Oral tablet (20 mg, ages 6-<18 years) or pediatric formulation (10 mg, ages 1-<6 years) once daily

Avatrombopag is administered orally with food and without food type restrictions, has no significant hepatotoxicity, and a low immunogenicity risk (as compared with parenterally administered agents)[4,5]

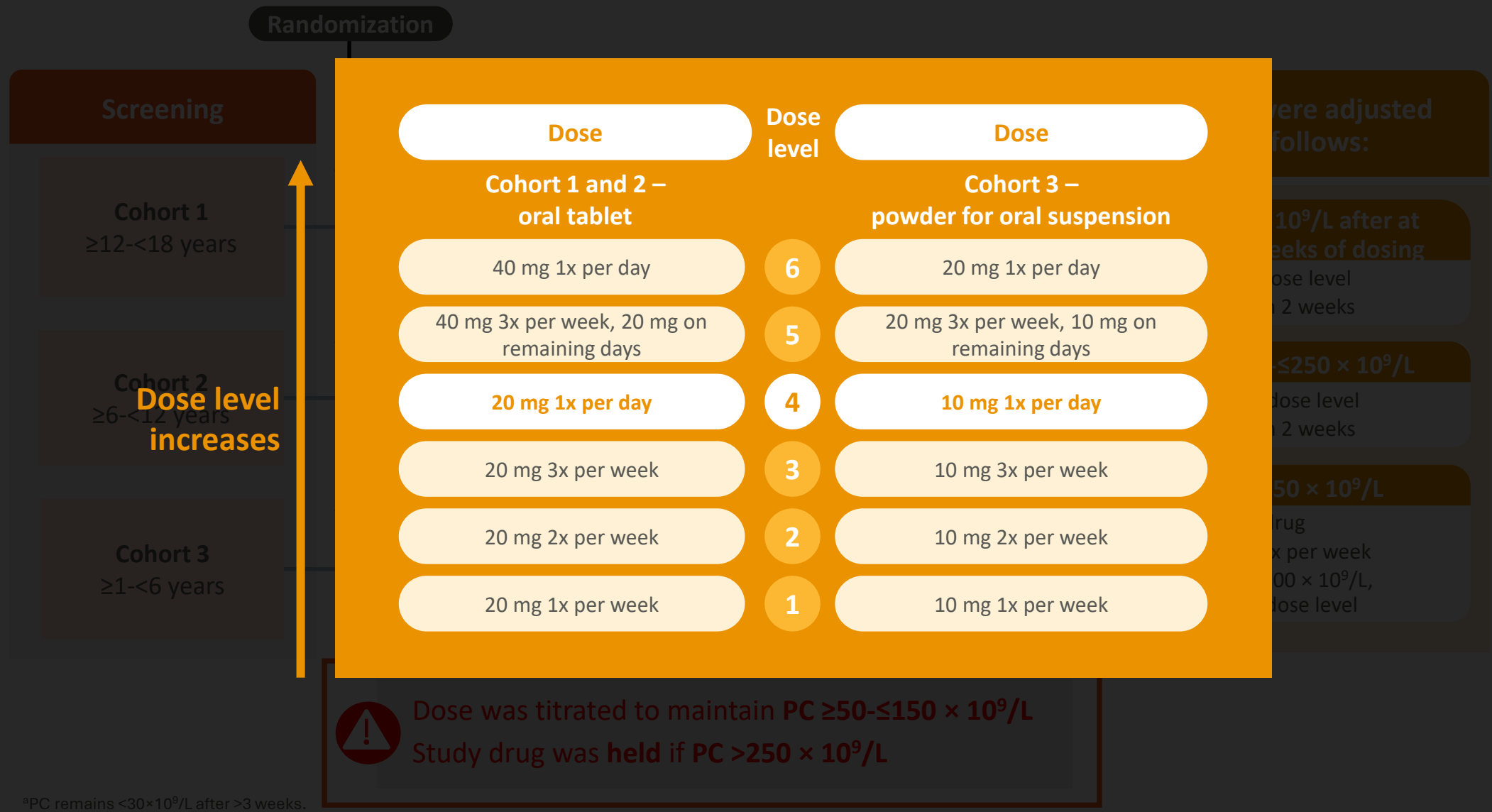
[a]Initiated at 62 sites, of which 34 enrolled patients.
AVA, avatrombopag; ITP, immune thrombocytopenia; PD, pharmacodynamic; PK, pharmacokinetic.
1. ClinicalTrials.gov. NCT04516967. 2. Grace et al. *Blood* 2021. 3. Grace et al. *Lancet Haematol* 2025;12:e494-504. 4. Doptelet [US prescribing information]. Durham, NC: AkaRx,Inc; 2025. 5. Jurczak W, et al. *Br J Haematol*. 2018;183:479–490.

AVA-PED-301: Study Design



[a]PC remains <30×10^9/L after >3 weeks.
AVA, avatrombopag; PBO, placebo; PC, platelet count.
Grace et al. 2024 (Submitted).

AVA-PED-301: Study Design



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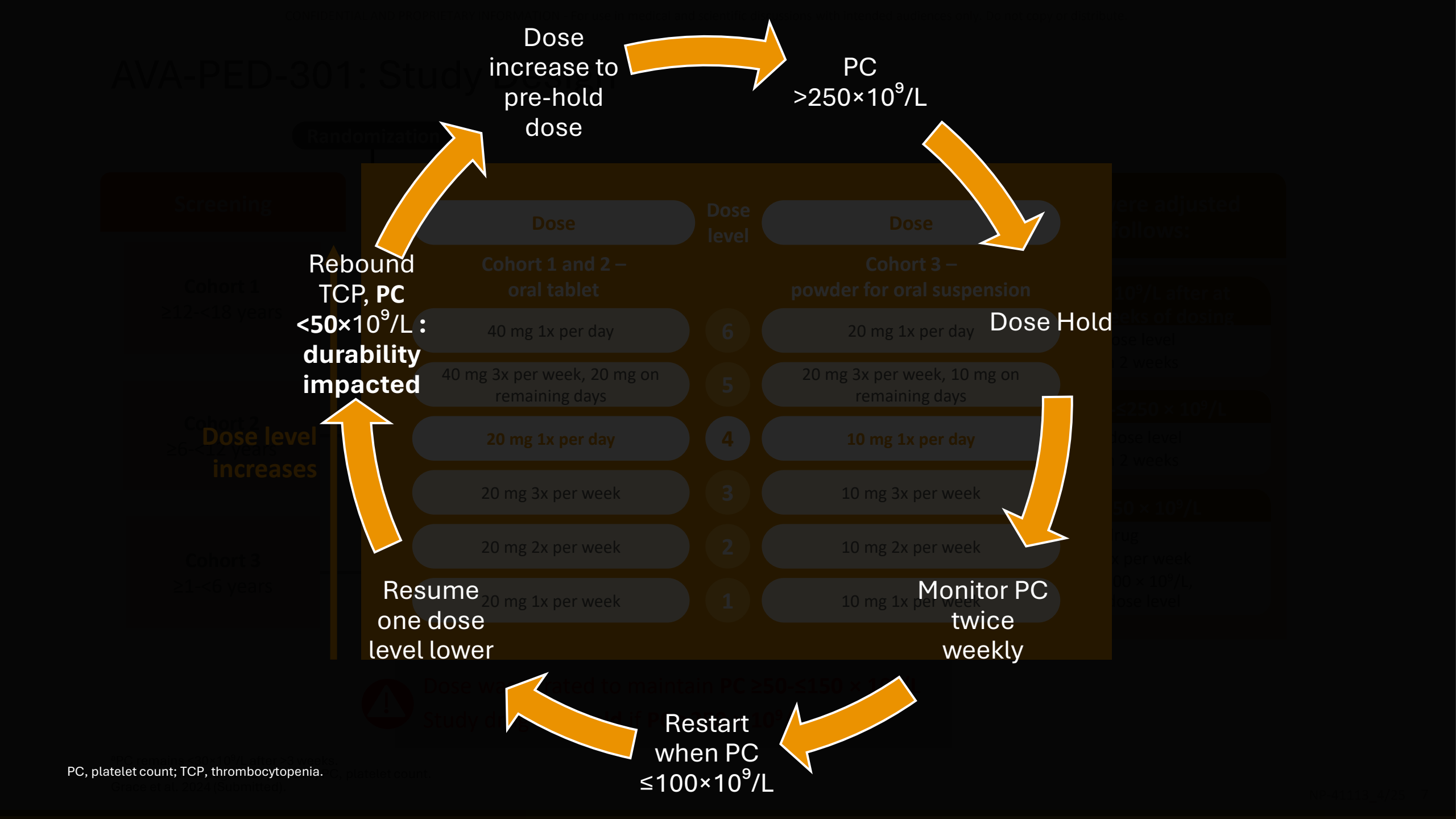
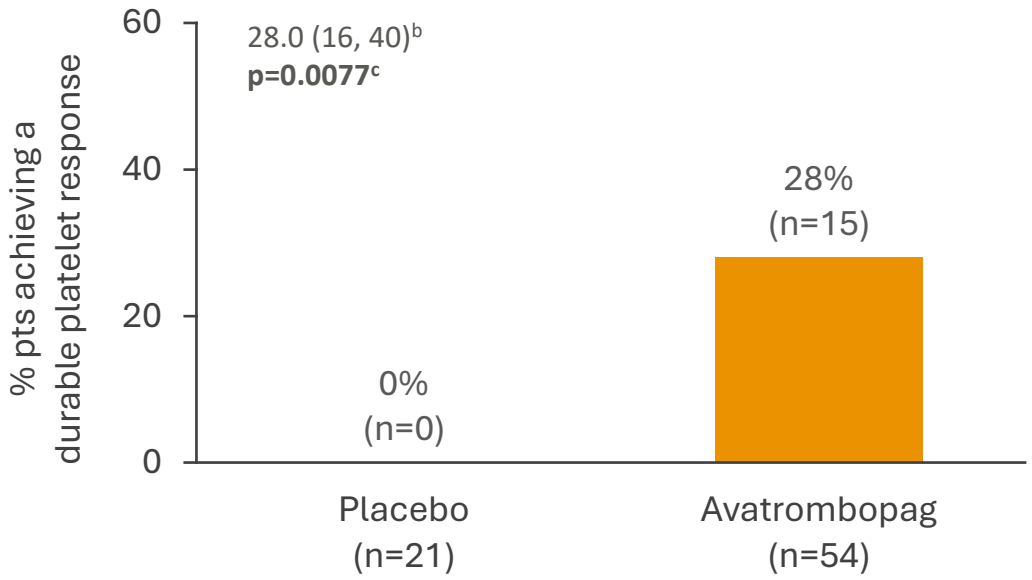


PC, platelet count; TCP, thrombocytopenia.

Avatrombopag improved platelet response, but durability was assessed under strict protocol hold rules

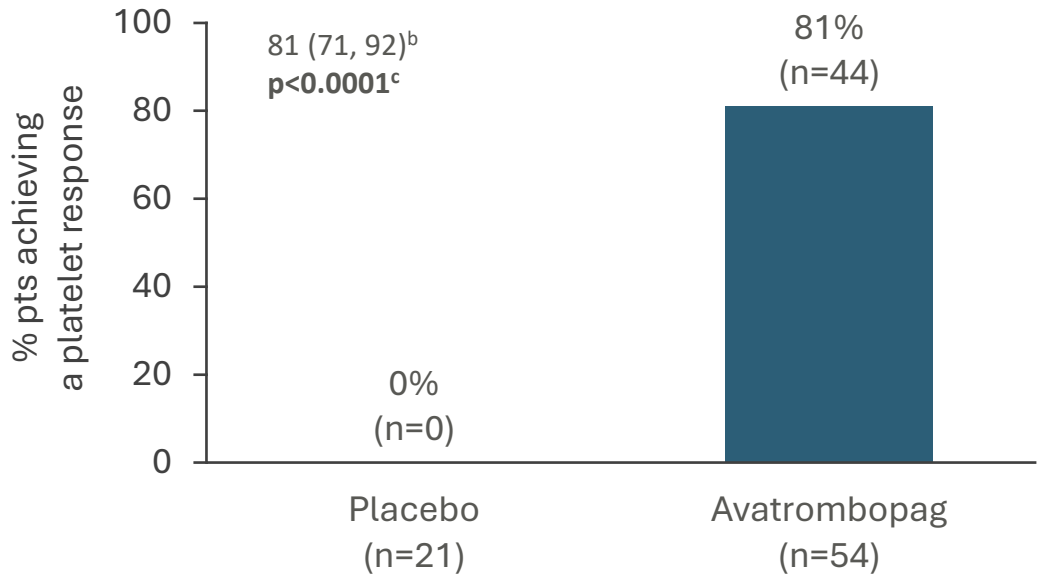
Primary endpoint[1]

Durable platelet response (% pts achieving at least 6 out of 8 weekly PCs ≥50 × 10^9/L during the last 8 weeks of the core phase, in the absence of rescue therapy)



Alternative primary endpoint[1]

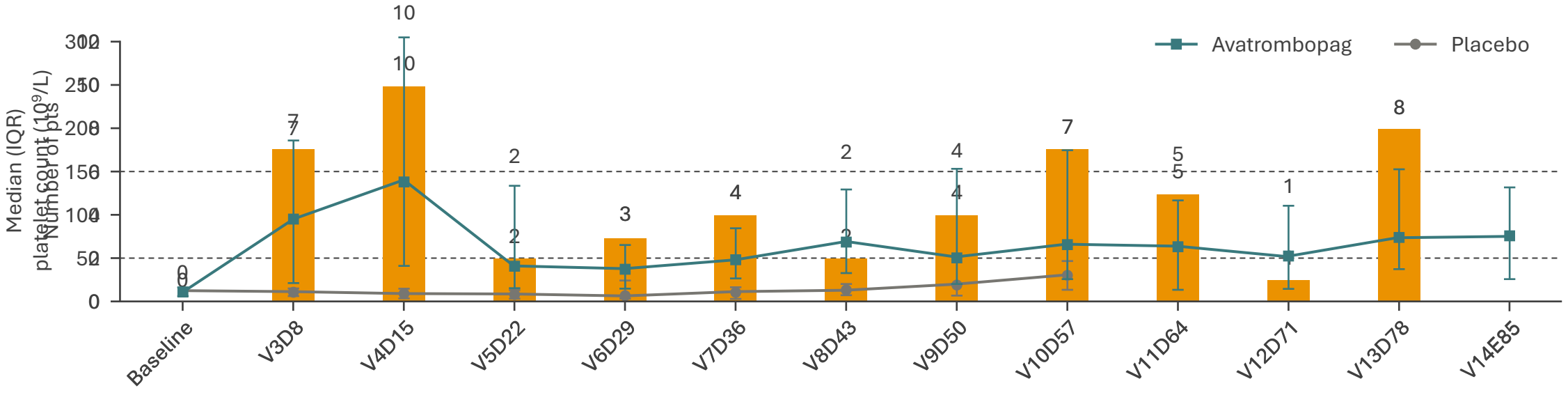
Platelet response (% pts with at least 2 consecutive PCs ≥50 × 10^9/L over the core phase, in the absence of rescue therapy)



[a]Full analysis set. [b]Difference in proportion for PBO vs AVA (95% CI). [c]Fisher's Exact Test.
AVA, avatrombopag; CI, confidence interval; PBO, placebo; PC, platelet count; pts, patients.
1. Grace et al. *Lancet Haematol* 2025;12:e494-504

Protocol-mandated dose holds occurred in a majority of AVA treated patients[1]

Dose holds[a] per study visit, overall



	Baseline	V3D8	V4D15	V5D22	V6D29	V7D36	V8D43	V9D50	V10D57	V11D64	V12D71	V13D78	V14E85
Avatrombopag	54	51	51	49	49	49	48	47	47	47	46	44	44
Placebo	21	18	17	15	13	11	8	3	2				

Number of pts who experienced a dose hold: **33 (61.1%)** pts in the **AVA group**
1 (4.8%) pt in the **PBO group**

[a]Study drug was held if PC >250 × 10^9/L. [b]Dose was titrated to maintain PC ≥50-≤150 × 10^9/L during the 12-week core phase; dashed lines represent the limits of the optimal PC range.
AVA, avatrombopag; D, day; E, extension; IQR, interquartile range; PBO, placebo; PC, platelet count; pts, patients; V, visit.
1. Grace et al. *Lancet Haematol* 2025;12:e494-504

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Non-durable responders experienced more dose holds

	AVA Durable responders n=10	AVA Non-durable responders n=23
Dose holds in Core Phase, n	13	40
Per patient, n	1.3	1.7
Dose holds in final 10 weeks	8	36
Per patient, n	0.8	1.6
Patients with multiple dose holds in Core Phase, n (%)	3 (30.0)	13 (56.5)
Patients with **multiple dose holds** in final 10 weeks, n (%)	0	12 (52.2)

AVA, avatrombopag; n, number.

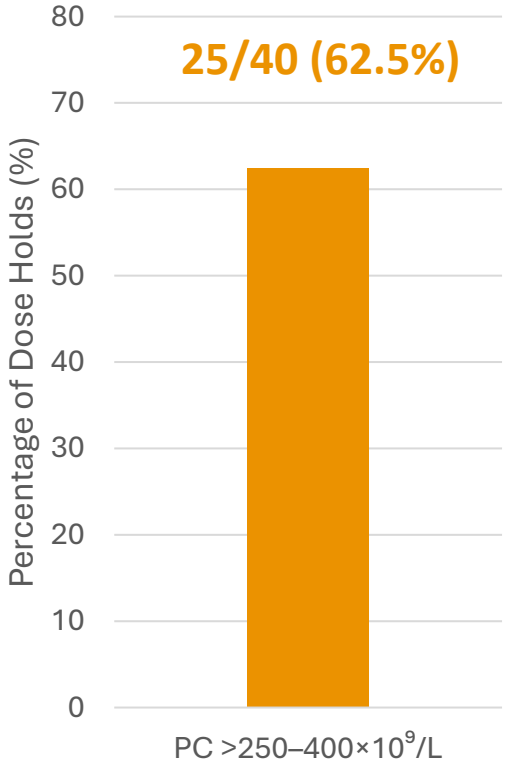
Dose holds were frequently followed by platelet counts below response threshold

	AVA Durable Responders (n=10)	AVA Non-durable Responders (n=23)
Patients with post-dose hold PC <50×10^9/L for ≥15 days, n (%)		
Last 10 weeks of the core phase	4 (40.0)	11 (47.8)
Time spent with post-dose hold PC <50×10^9/L in Last 10 weeks of Core Phase		
Median (Q1, Q3), days	19.5 (18.0, 21.3)	25.0 (21.0, 38.0)
Mean (SD), days	19.8 (2.1)	29.0 (9.9)
Post-dose hold nadir PC, × 10^9/L		
Median (Q1, Q3)	20.0 (14.0, 25.0)	11.5 (5.0, 23.5)

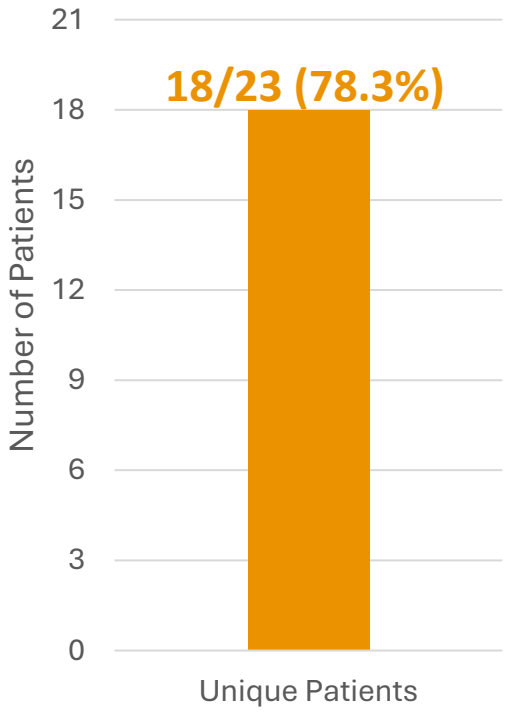
AVA, avatrombopag; PC, platelet count; Q1, first quartile; Q3, third quartile; SD, standard deviation.

Most dose holds in non-durable responders occurred within the 250–400×10^9/L range

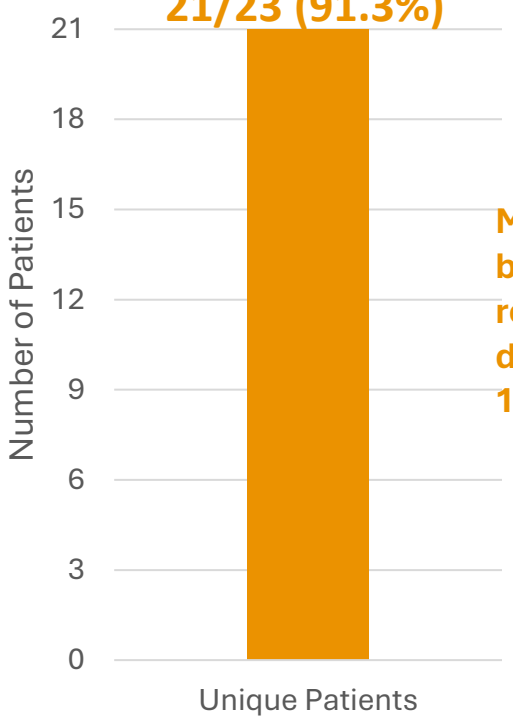
Number of dose holds in PC >250–400×10^9/L range among AVA-non responders



Unique patients with dose holds in 250–400×10^9/L range among AVA-non responders



Total patients with dose cycling following dose hold among AVA-non responders



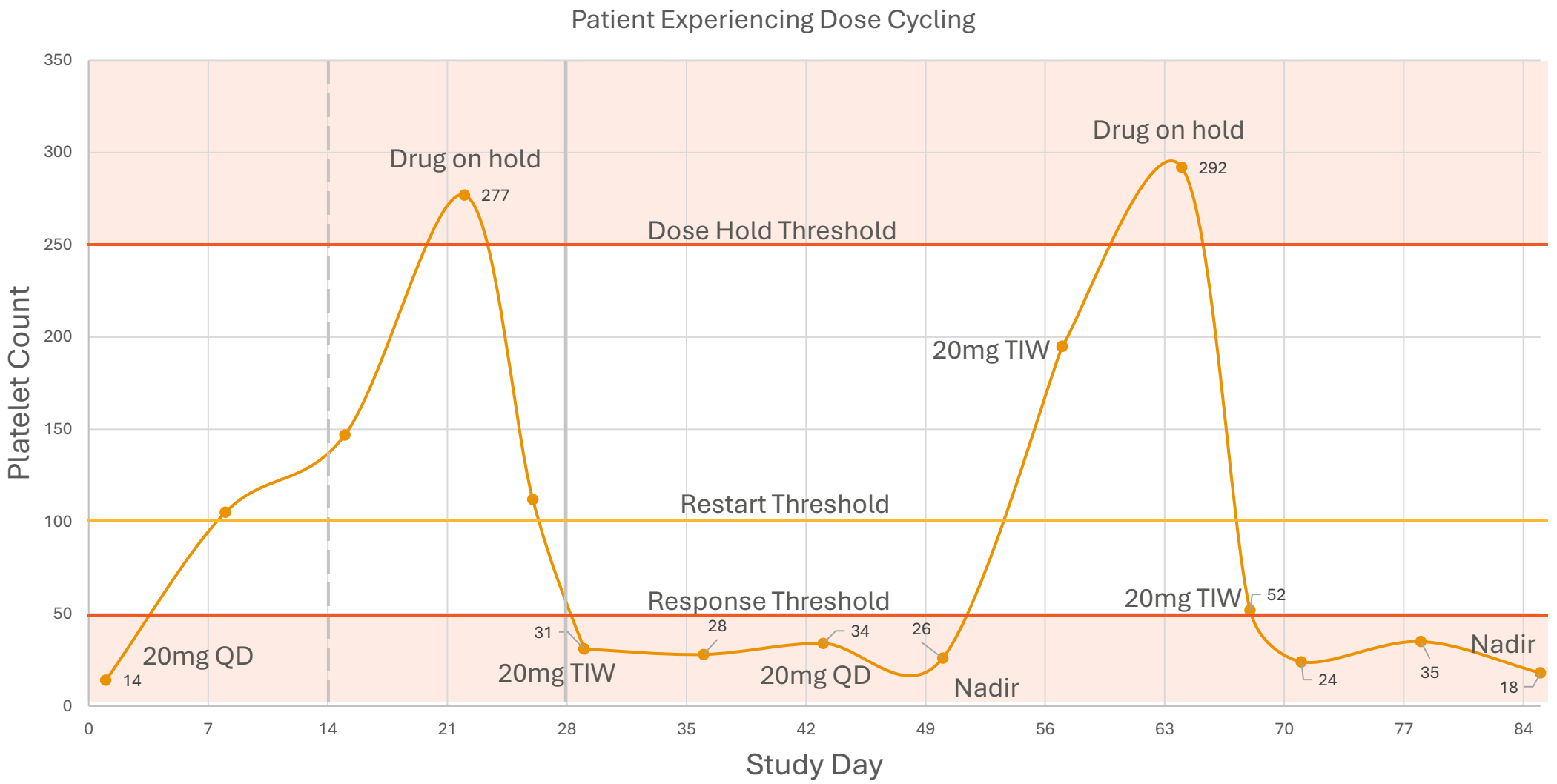
Median days between reinitiation and dose increase: 14 days

Note: This 250–400×10^9/L range would not have warranted a dose hold under avatrombopag prescribing guidance (US), but rather dose reduction[1]

DH, dose hold; PC, platelet count; US, United States.

1. Doptelet [US prescribing information]. Durham, NC: AkaRx,Inc; 2025

AVA-PED-301 Patient Experiencing Multiple Dose Holds



Note: This 250–400×10^9/L range would not have warranted a dose hold under avatrombopag prescribing guidance (US), but rather dose reduction

PC, platelet count; QD, once daily; TIW, 3 times weekly; US, United States.

Summary

- Avatrombopag produced high platelet response rates in a heavily pretreated pediatric ITP population[1]
- Protocol-mandated holds at PC >250×10^9/L were common and frequently occurred during the durability assessment window[1]
- Dose holds were followed by platelet declines, rebound thrombocytopenia, and eventual dose cycling
- Many holds occurred at platelet counts of 250–400×10^9/L, a range that would generally prompt dose reduction rather than interruption in real-world practice
- These findings suggest AVA-PED-301 may have underestimated the durability of platelet response achievable with avatrombopag under approved dosing recommendations

AVA, avatrombopag; ITP, immune thrombocytopenia; PBO, placebo; PC, platelet count; PK, pharmacokinetic; TPO-RA, thrombopoietin receptor agonist.

1. Grace et al. *Lancet Haematol* 2025;12:e494-504.

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Sobi rewiewed the presentation and provided feedback.
The authors had full editorial control of the presentation and provided their final approval of all content.

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BACKUP

Avatrombopag-treated patients had advanced, heavily pretreated ITP at baseline

	Placebo (n=21)	Avatrombopag (n=54)
Age, years (mean ± SD)	9.9 ± 4.1	8.9 ± 4.4
Sex, female, n (%)	12 (57.1)	24 (44.4)
Baseline PC, n (%)		
≤15 × 10^9/L	17 (81.0)	45 (83.3)
Baseline PC, mean ± SD (median)	11.2 ± 6.6 (11.5)	12.0 ± 6.8 (10.4)
Disease duration, n (%)		
Persistent ITP (6-12 months[b])	3 (14.3)	13 (24.1)
Chronic ITP (>12 months)	18 (85.7)	41 (75.9)
≥3 previous ITP medications received since diagnosis, n (%)[b]	14 (66.7)	37 (68.5)
Previous TPO-RA use, n (%)	15 (71.4)	40 (74.1)
Eltrombopag[c]	15 (100)	38 (95.0)
Romiplostim[c]	6 (40.0)	24 (60.0)

- **Most avatrombopag-treated patients had chronic ITP: 41/54, 75.9%; persistent ITP was present in 13/54, 24.1%**
- **Baseline platelet counts were low, with 83.3% of avatrombopag-treated patients having platelet counts ≤15×10^9/L**
- **Prior TPO-RA exposure was common: 40/54, 74.1% of avatrombopag-treated patients had previous TPO-RA use**
- Among avatrombopag-treated patients with prior TPO-RA exposure, 23/40, 57.5% had non-response to prior TPO-RA treatment

[a]Full analysis set. [b]Although persistent ITP is defined as an ITP duration of 3-12 months per current guidelines[2], patients were required to have had a confirmed diagnosis of primary ITP for ≥6 months to be eligible for inclusion in the study.
AVA, avatrombopag; ITP, immune thrombocytopenia; PBO, placebo; PC, platelet count; pts, patients; SD, standard deviation.
Grace et al. . *Lancet Haematol* 2025;12:e494-504.