

INTRODUCTION

- While anti-C5 therapies effectively control IVH, real-world data show 31.7% of Chinese PNH patients remain transfusion-dependent, and the majority remain anemic due to C3-mediated extravascular hemolysis (EVH).
- Ciprocopan is a novel, oral, once-daily factor B inhibitor. In complement inhibitor-naïve PNH patients (Phase 2), it demonstrated robust efficacy (95.7% transfusion avoidance; +50.7 g/L Hb increase) and favorable safety.

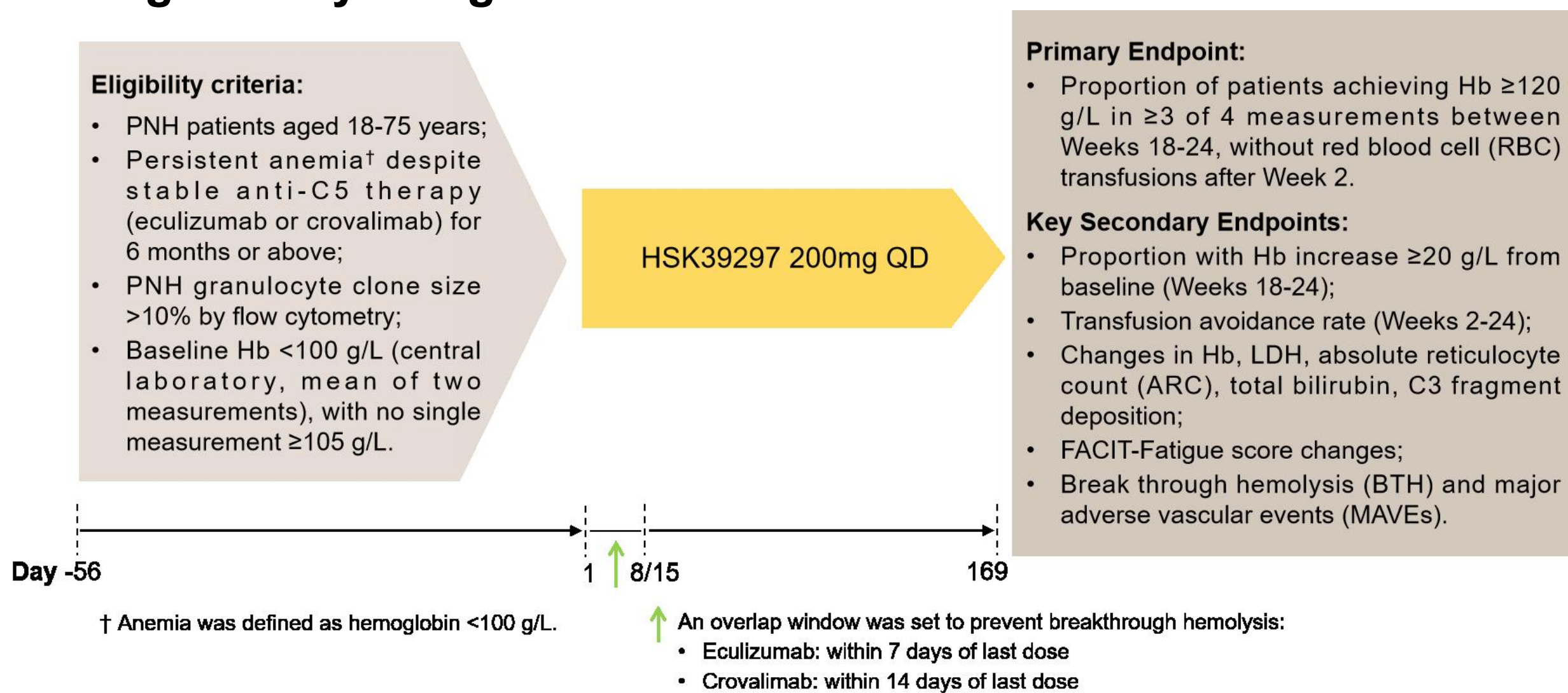
AIM

To evaluate the efficacy and safety of switching from anti-C5 therapy to oral ciprocopan monotherapy (200 mg once daily) in PNH patients with persistent anemia (Hb <100 g/L) despite stable anti-C5 treatment.

METHOD

HSK39297-302 was a Phase 3, open-label, single-arm, multicenter study conducted at 9 centers in China (NCT07052838).

Fig 1. Study design



REFERENCES

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ACKNOWLEDGEMENT

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KEY FINDINGS

- Sustained Hb improvement and near-complete elimination of transfusions, mean Hb increased from 81.04 g/L to 123.58 g/L by Week 24 (LSM change: +42.08 g/L, [95% CI: 37.21, 46.94]).**
- Rapid control of hemolysis: Marked reductions in reticulocytes and total bilirubin, with near-complete suppression of C3-mediated extravascular hemolysis (C3d+ RBC decreased from 9.31% to 0.19%).**
- Meaningful fatigue improvement: FACIT-Fatigue LSM change +9.6 points (95% CI: 8.4, 10.9).**
- Favorable safety: most TEAEs were CTCAE Grade 1–2; no TEAEs led to treatment discontinuation or death.**
- Ciprocopan represents a promising once-daily oral treatment option for PNH patients with persistent anemia despite anti-C5 therapy.**

RESULTS

A total of 53 patients were screened, and 36 (67.9%) were enrolled. All 36 patients completed the 24-week treatment period.

Table 1. Demographics and Baseline Characteristics

Characteristic	Ciprocopan (N=36) n(%)
Age, Mean± SD -- years	41.4 ± 12.5
Female	22 (61.1)
PNH disease duration (Min,Max) --years	9.44 (0.7-45.3)
Prior anti-C5 therapy, n%	
Eculizumab	26 (72.2)
Crovalimab	10 (27.8)
Duration of prior C5 therapy -- years	1.72 ± 1.13
≥1 year, n%	26 (72.2)
Hemoglobin, Mean± SD -- g/L	81.04 ± 12.32
LDH ≤ 1.5 ULN, n%	33(91.7)
Transfusion history (prior 6 months), n%	10 (27.8)
MAVE history (prior 12 months), n%	2 (5.6)

Efficacy

□ Hematologic Response

- Primary Endpoint (Hb ≥120 g/L) *: 52.8% (19/36) (95%CI: 35.5, 69.6), met the protocol-specified efficacy threshold.
- Hb increase ≥20 g/L *: 91.7% (33/36) (95% CI: 77.5, 98.2).
- Transfusion avoidance†: 97.2% (35/36) (95% CI: 85.5, 99.9).
- Least Squares Mean (LSM) change in Hb from baseline, g/L (Weeks 18–24): +42.08 g/L (95% CI: 37.21, 46.94).

*Achieved in ≥3 of 4 measurements between Weeks 18 and 24, in the absence of RBC transfusions after Week 2.

† Defined as no RBC transfusions received between Weeks 2 and 24.

Fig 2. Mean (±SD) Hemoglobin Concentration Over Time

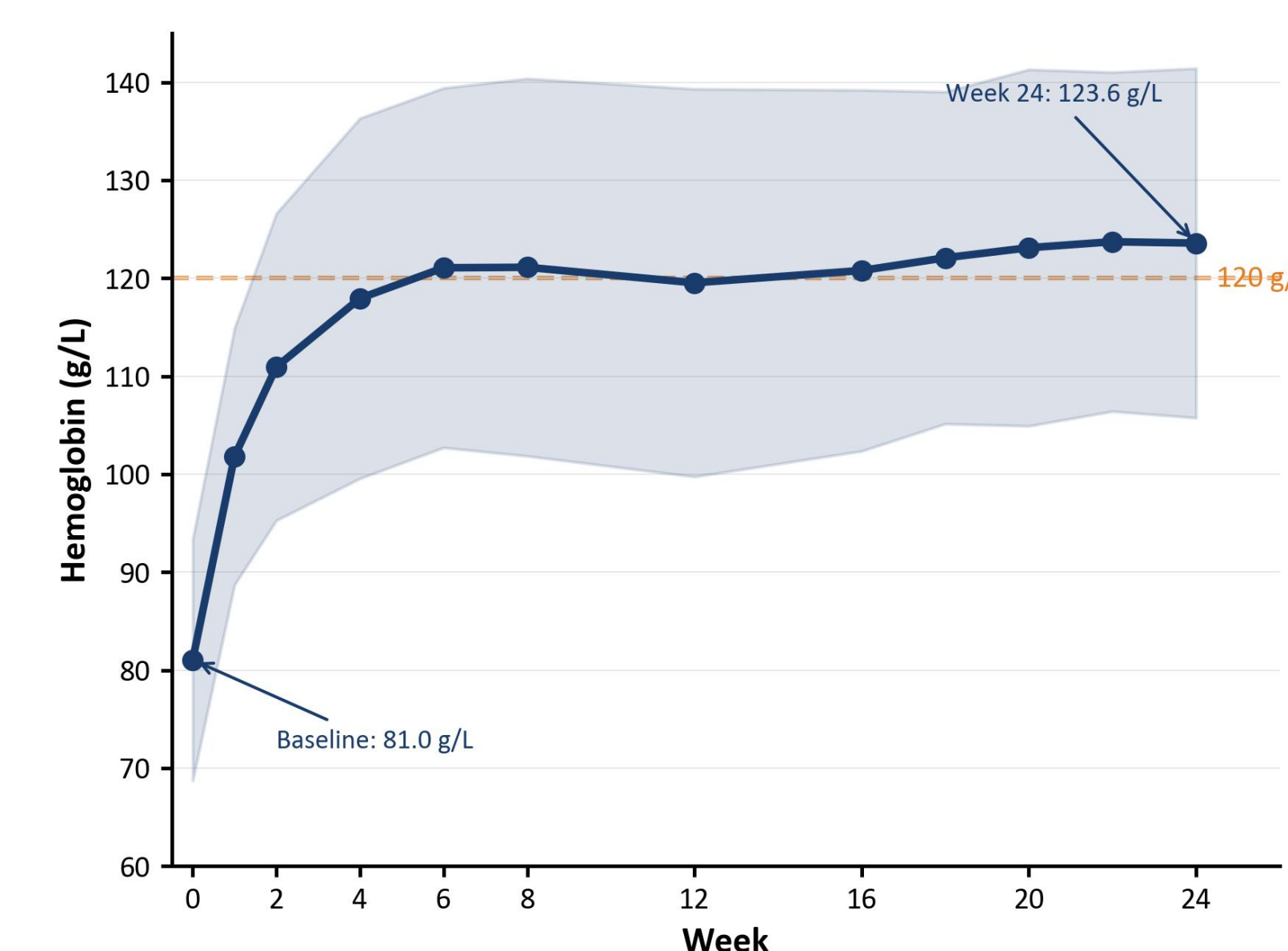


Fig 3. Mean (±SD) Total Bilirubin Over Time

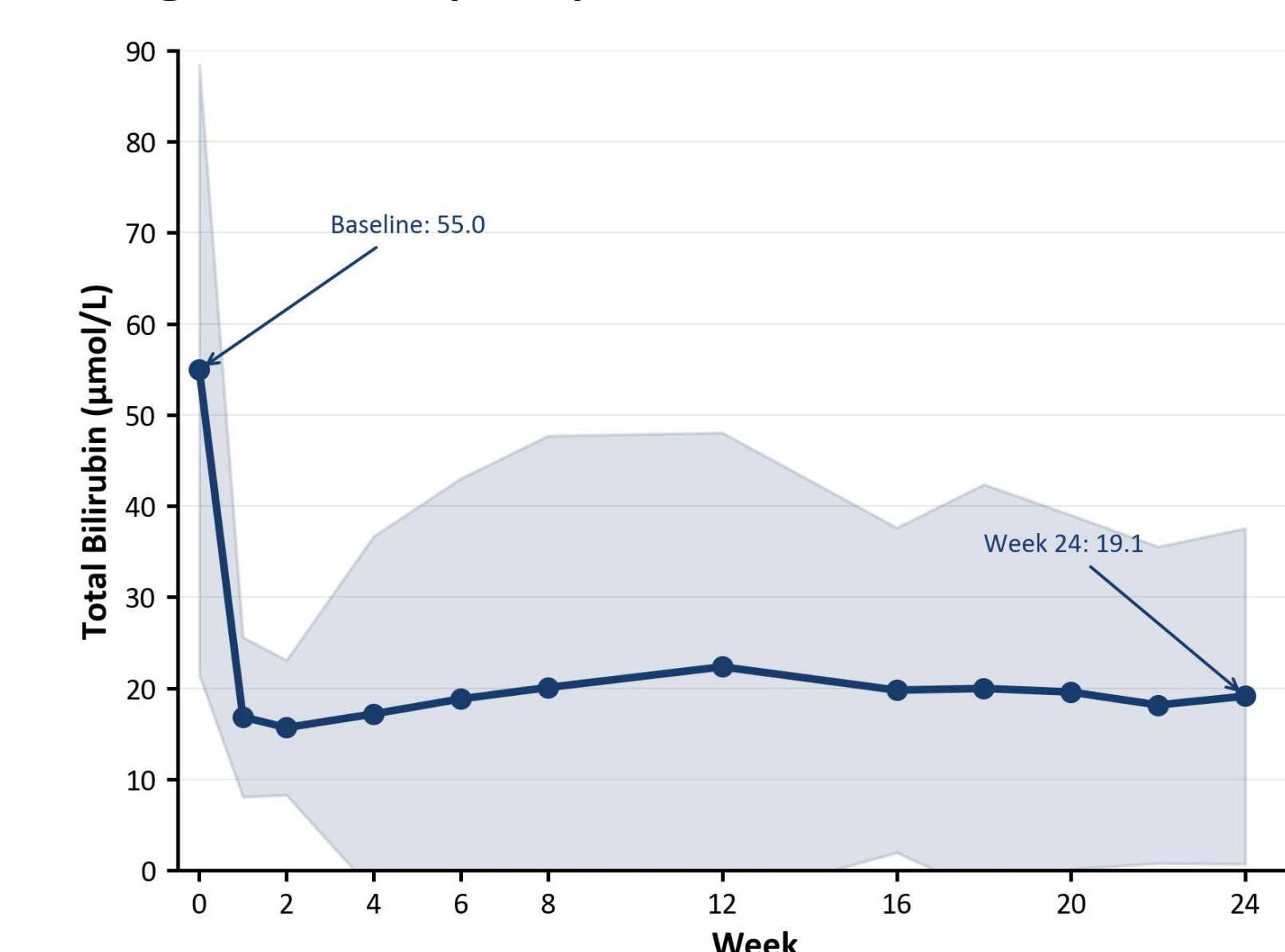


Fig 4. Mean (±SD) C3d+ RBC Over Time

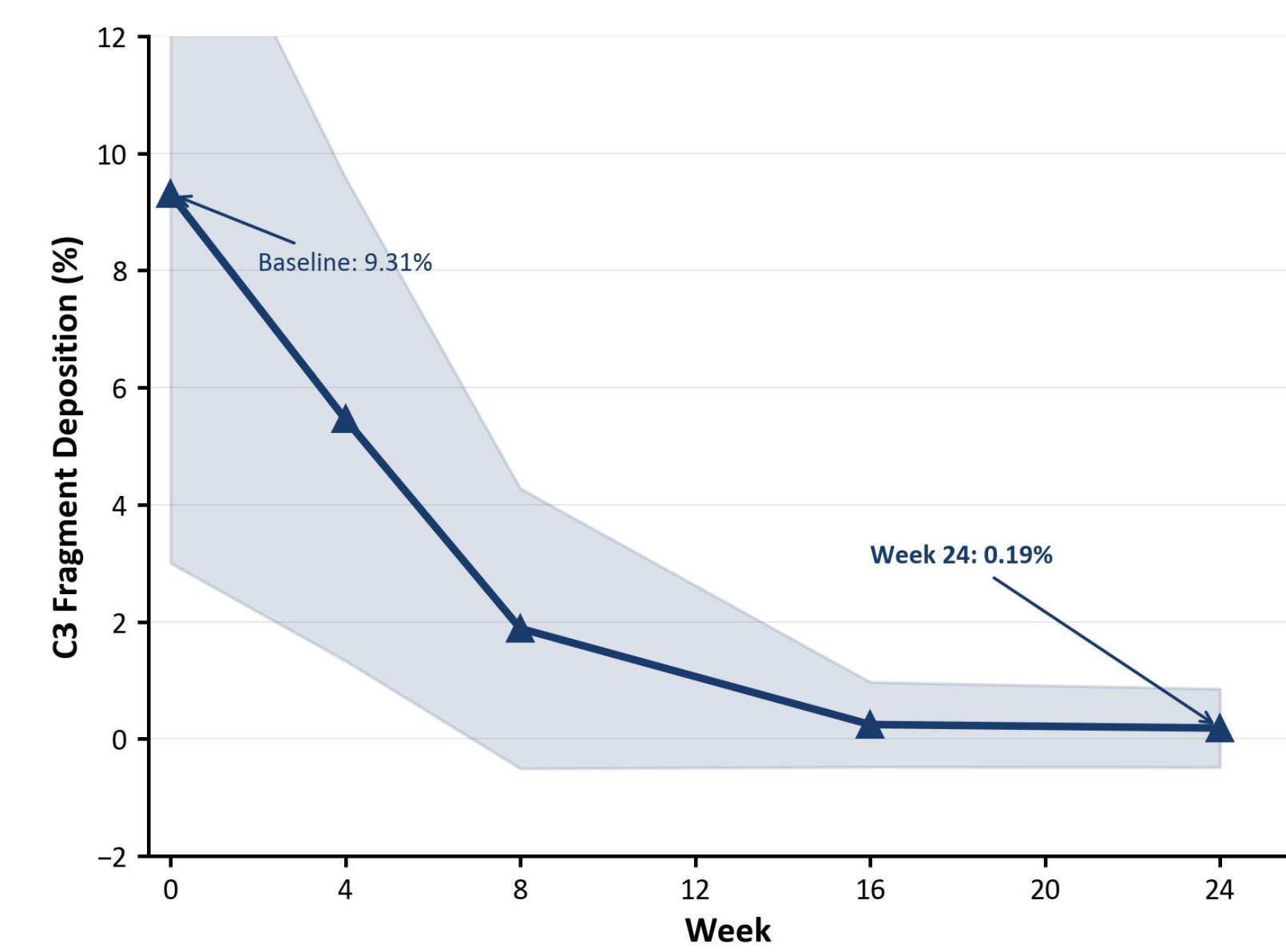
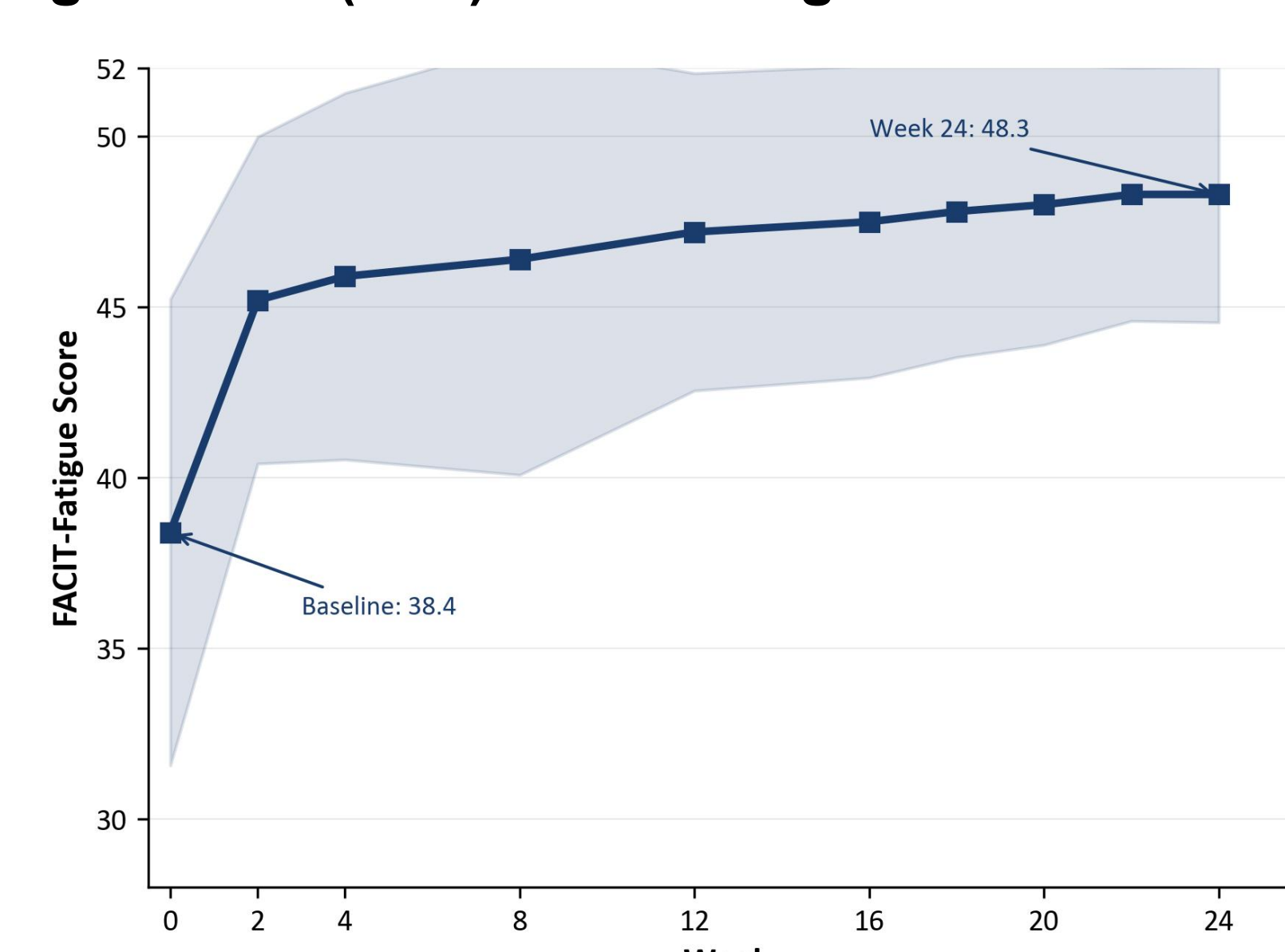


Fig 5. Mean (±SD) FACIT-Fatigue Score Over Time



□ Comprehensive Hemolysis Control

- ARC: Rapid decrease from 295.9 to 131.8 × 10⁹/L at Weeks 18-24 (LSM change: -166.3 × 10⁹/L [95% CI: -179.5, -153.1]).
- Total Bilirubin: Rapid reduction observed by Week 24 LSM change: -35.8 μmol/L [95% CI: -40.6, -31.0]).
- LDH: Maintained baseline levels (mean: 278.71 U/L) during Weeks 18-24 (geometric mean ratio: 0.92 [95% CI: 0.81, 1.05]).
- C3d+ RBC: Near-complete elimination observed at Week 24, dropping from 9.31% to 0.19% (LSM change: -9.08% [95% CI: -9.36%, -8.80%]).

□ Patient-Reported Outcomes (FACIT-Fatigue)

Baseline mean was 38.4, with an LSM increase of 9.6 (95% CI: 8.4, 10.9) at Weeks 18-24.

□ BTH and MAVE

Only 1 patient (2.8%) experienced breakthrough hemolysis (triggered by a urinary tract infection), and 0 major adverse vascular events (MAVEs) occurred.

Safety

- Tolerability: Most TEAEs were CTCAE Grade 1-2. None led to dose reduction, discontinuation.
- Serious TEAEs (TESAEs): Occurred in 8.3% (3/36) patients (foot fracture, anal abscess, mesangioproliferative glomerulonephritis), none were related to ciprocopan. No deaths occurred.

Table 2. Most Frequent AEs During treatment (Reported in ≥10% of Patients)

Preferred Term	Incidence (N=36) n (%)
Numbers of subjects with at least one AE	29 (80.6)
Platelet count decreased	8 (22.2)
Neutrophil count decreased	6 (16.7)
Hypertriglyceridaemia	6 (16.7)
Urinary tract infection	5 (13.9)
Upper respiratory tract infection	4 (11.1)
Alanine aminotransferase increased	4 (11.1)

CONCLUSIONS

- Switching to oral ciprocopan monotherapy demonstrated rapid, sustained Hb improvement and near-complete transfusion independence, driven by comprehensive resolution of both EVH and IVH.
- Ciprocopan significantly reduced fatigue and maintained a favorable safety profile, establishing it as a highly promising once-daily oral treatment option for PNH patients with persistent anemia on anti-C5 therapies.

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