

Effects of mitapivat on iron burden and spleen size in patients with erythrocyte membranopathies and congenital dyserythropoietic anemia type II

56-Week follow-up results from the SATISFY study

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Disclosures

No conflicts of interest

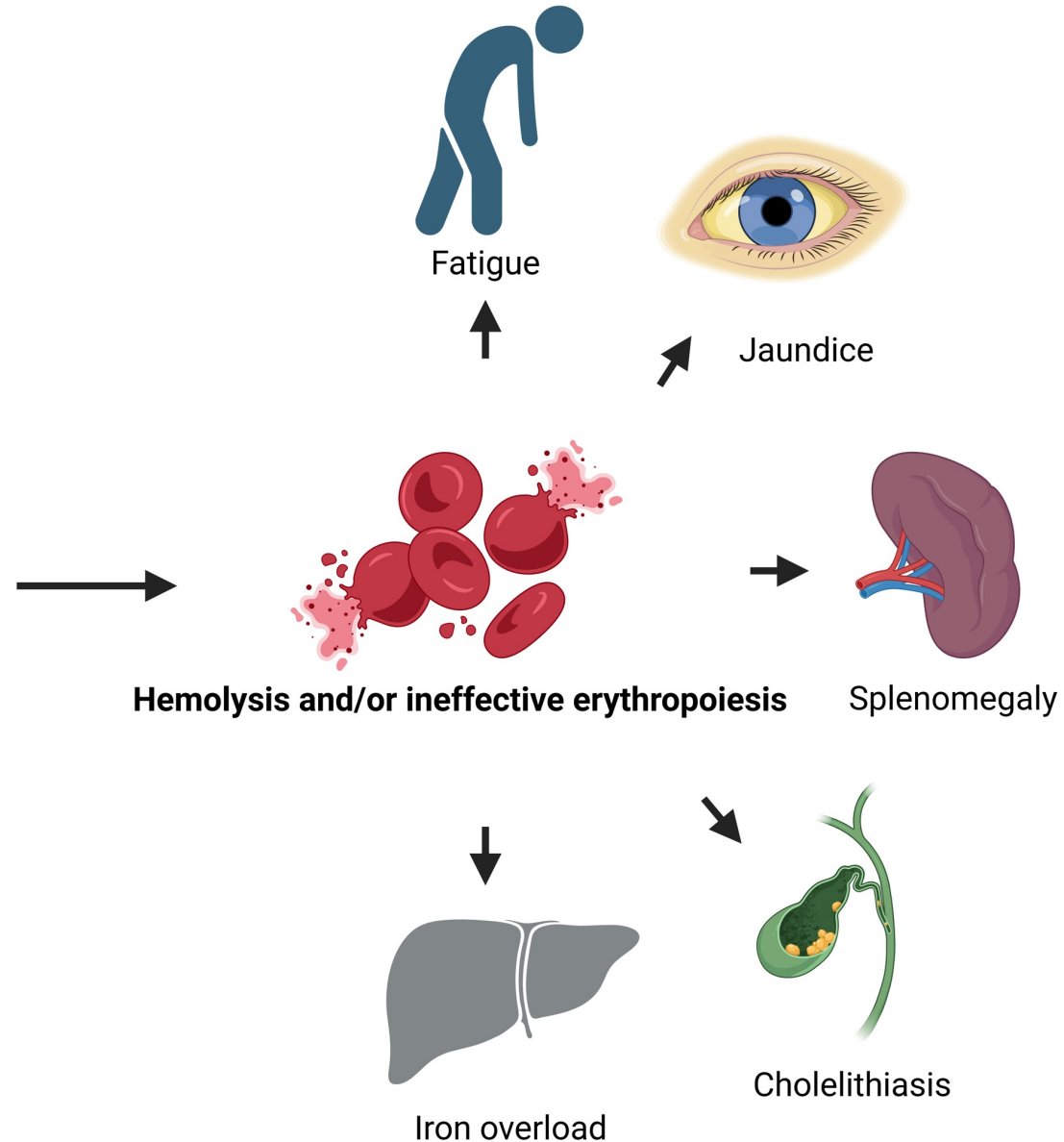
Erythrocyte membranopathies and CDA II

Hereditary anemias

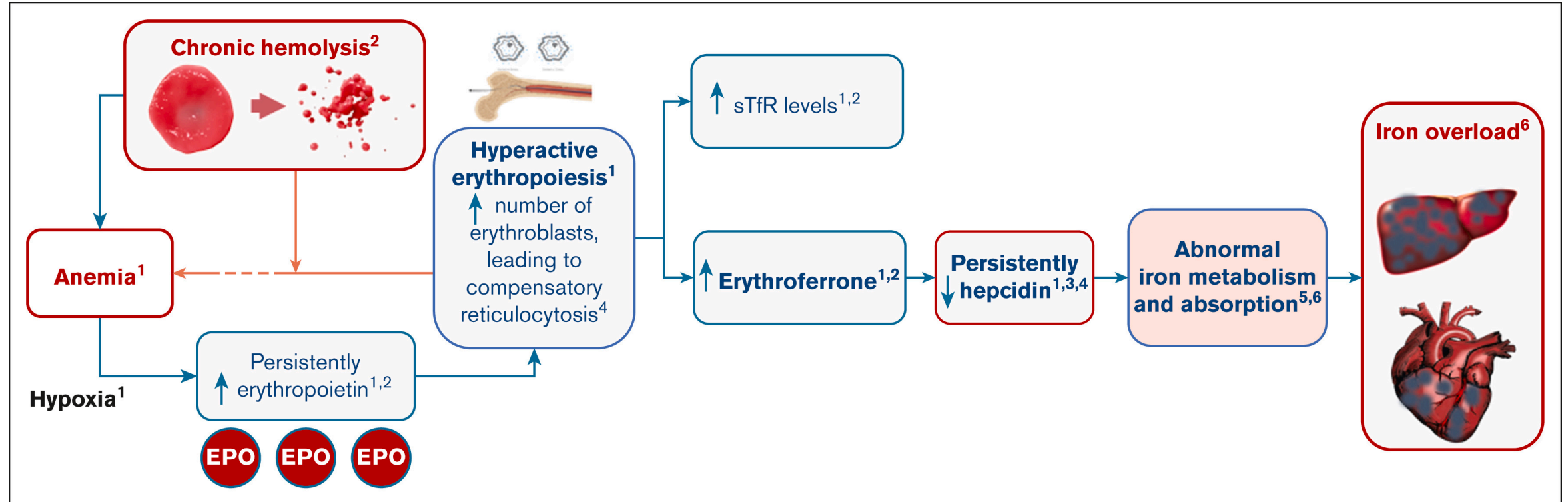
Hereditary spherocytosis

Hereditary xerocytosis

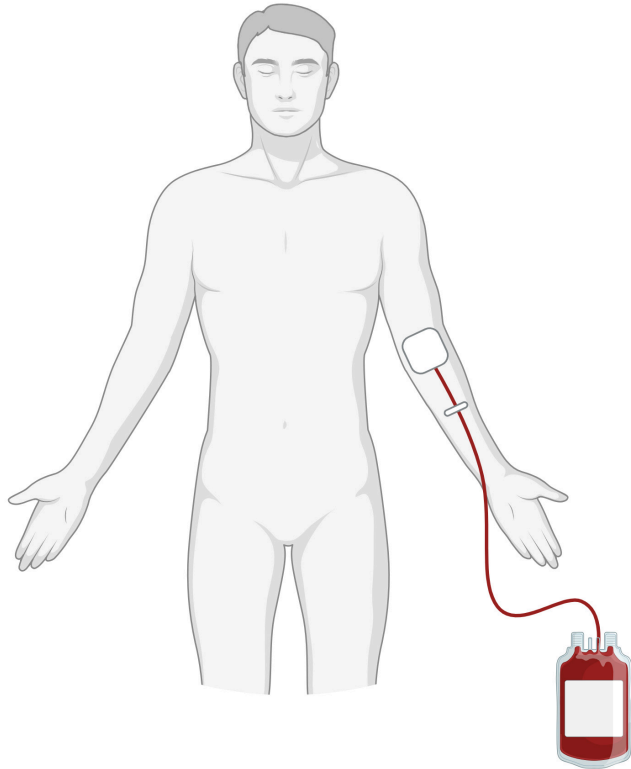
Congenital dyserythropoietic anemia type II



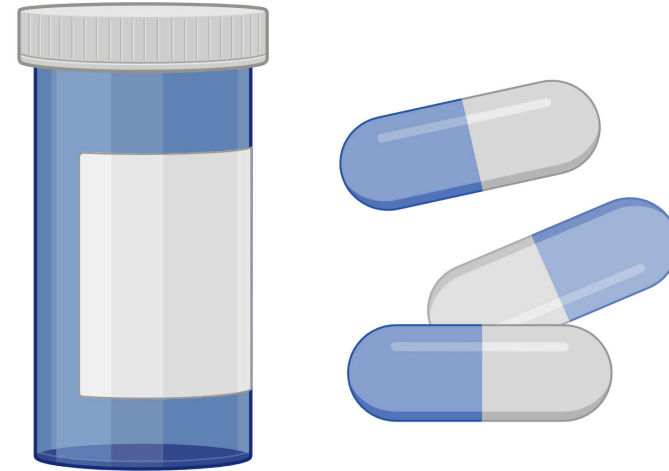
Iron overload is a frequent complication and is associated with increased morbidity



Treatment options for iron overload are limited



Phlebotomy



Iron chelation

Objectives of this follow-up analysis

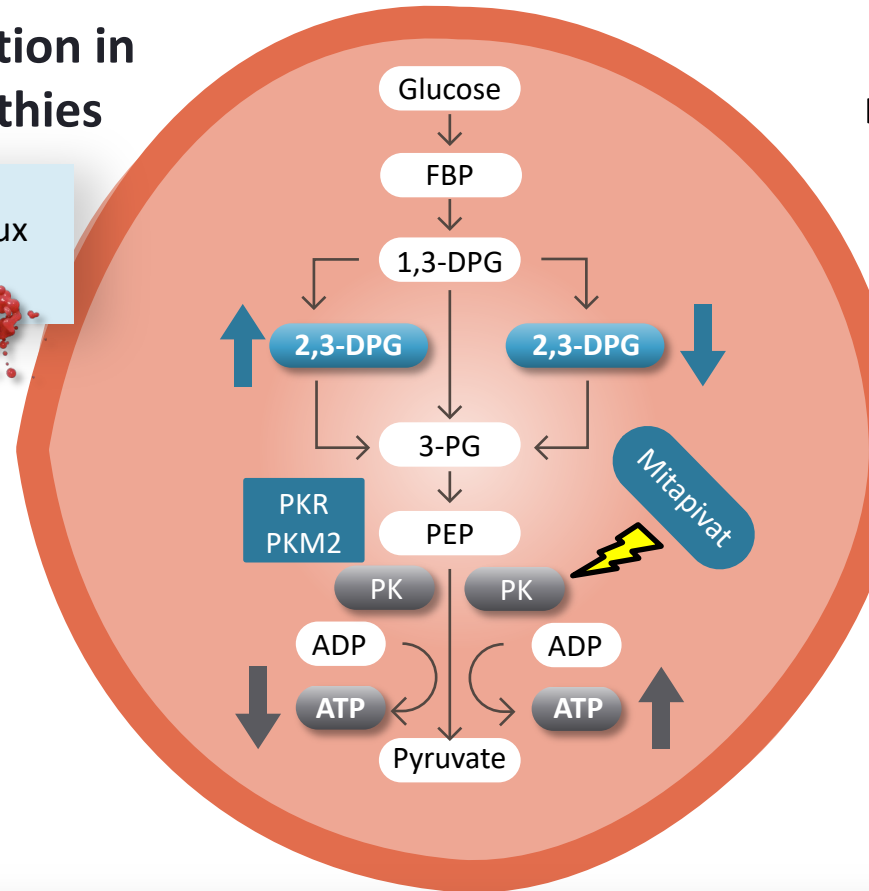
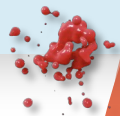
This analysis aims to evaluate the (long-term) effects of mitapivat on

1. Hemoglobin levels and hemolytic markers
2. Iron overload (iron markers and liver iron concentration)
3. Spleen size and spleen volume

Mitapivat – an allosteric pyruvate kinase activator

Glycolytic pathway dysfunction in erythrocyte membranopathies

Decreased PK activity and glycolytic flux



Mitapivat enhances PK activity and restores glycolytic flux, resulting in:

Increase in ATP levels

Improved RBC hydration
Reduced membrane vesiculation
Improved osmotic fragility

Decrease in 2,3-DPG levels
Increase in Hb-oxygen affinity

Decrease in iron overload

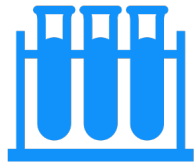
Decrease in spleen size



Primary results of the 32-week core period

Mitapivat demonstrated a favorable safety profile, with improvements in hemoglobin levels, hemolytic markers, and patient-reported outcomes, particularly pronounced in HS.

Study design



Setup

Investigator initiated,
multicenter, single-arm
phase 2 trial.



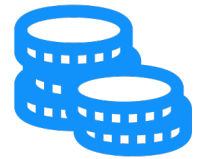
Locations

Denmark
The Netherlands
Sibling study in Canada



Sponsor

EuroBloodNet Association
(Non-profit)



Funding

Agios Pharmaceuticals

Key eligibility criteria

Key Inclusion Criteria



Membranopathy or
CDAII



Genetically confirmed
ACMG class 3, 4, or 5



Age ≥ 18 years



Hb concentration:
<13.0 g/dL for males
<11.0 g/dL for females



Adequate organ function

Key Exclusion Criteria

PKLR

Pyruvate kinase deficiency
diagnosed with decreased PK activity
or two pathogenic PKLR alleles



Blood transfusion within
last 3 months or
>5 units the last year

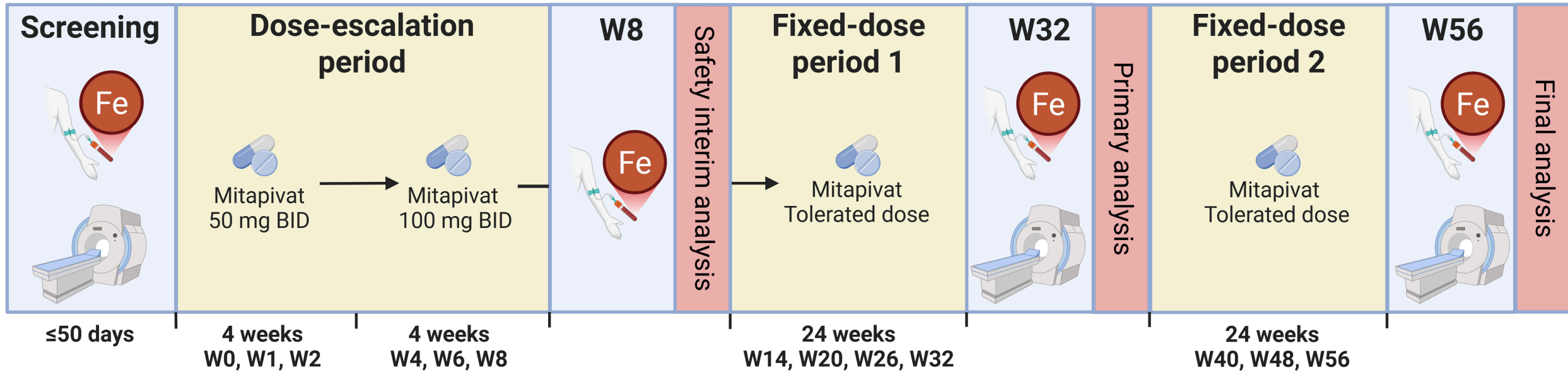


Significant medical
comorbidity

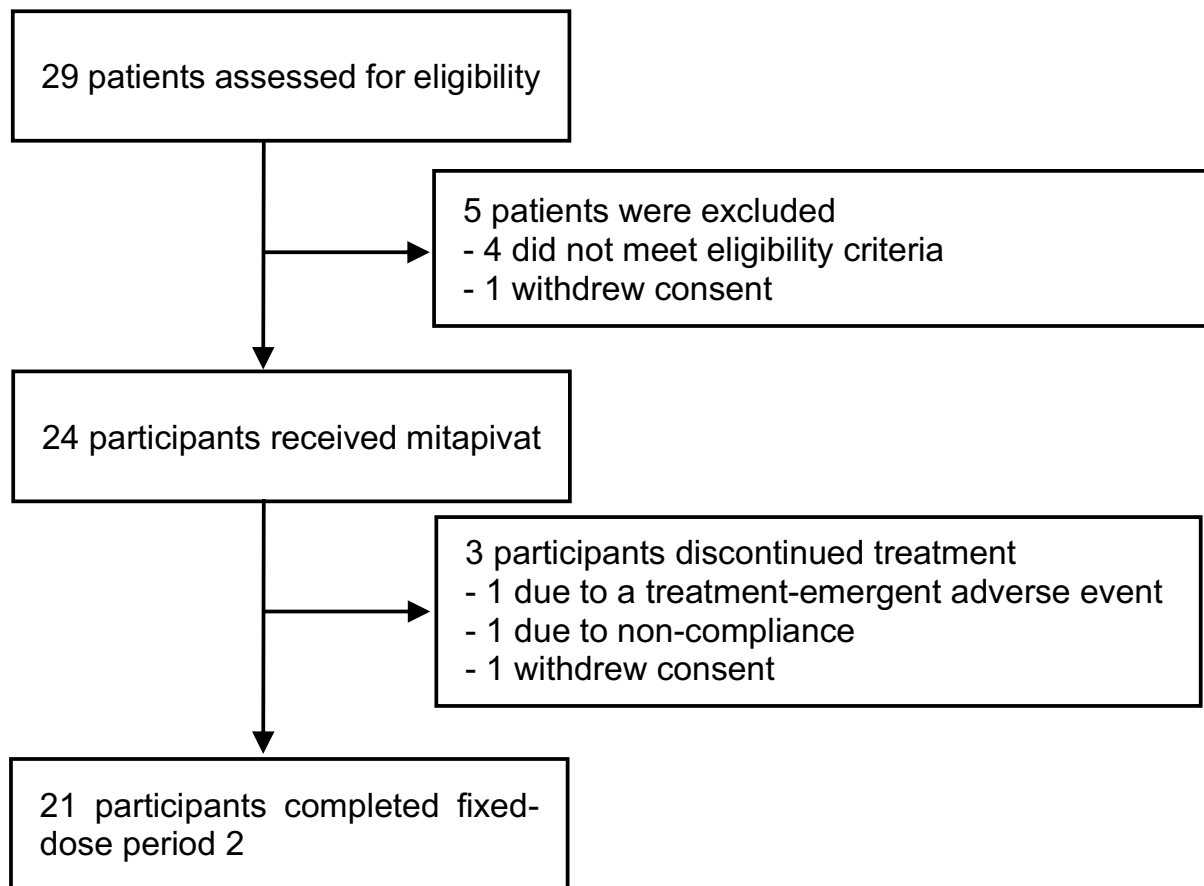


Receiving
hematopoietic
stimulating agents

Study scheme

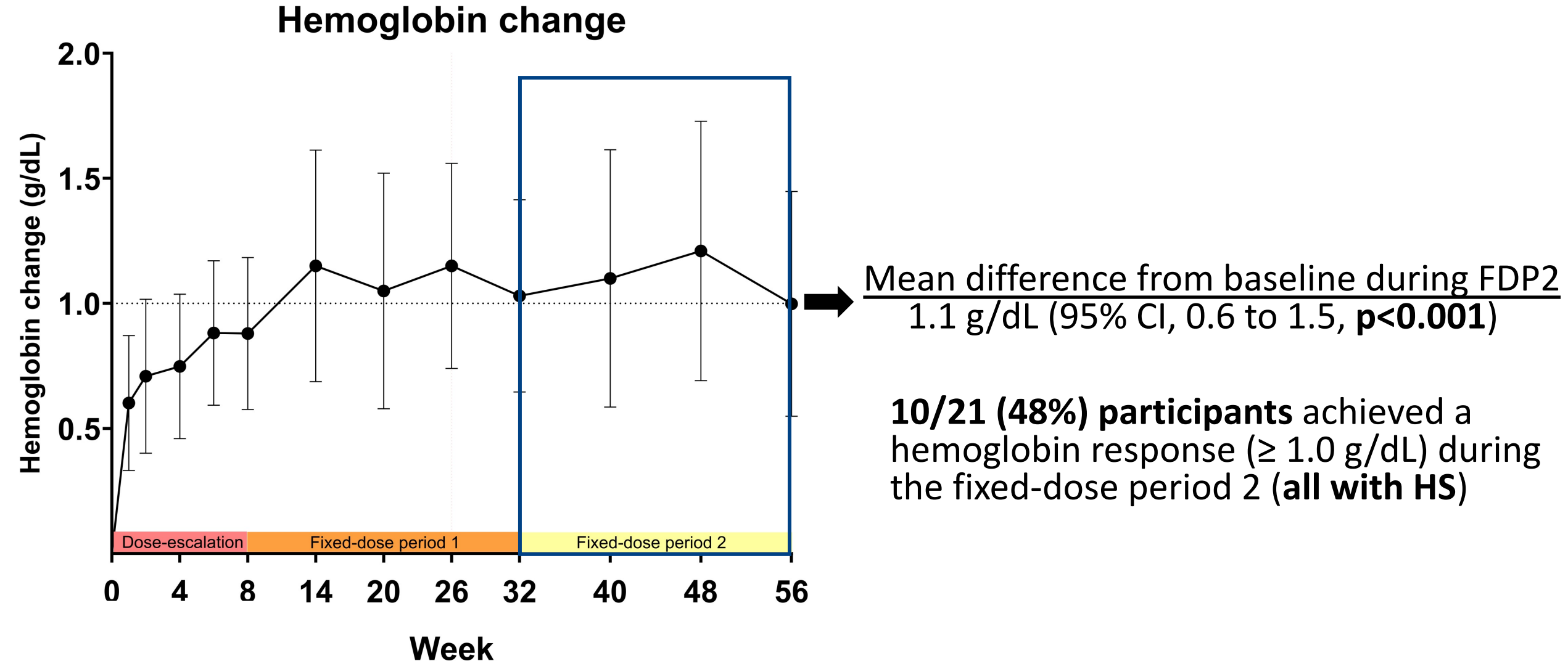


Results



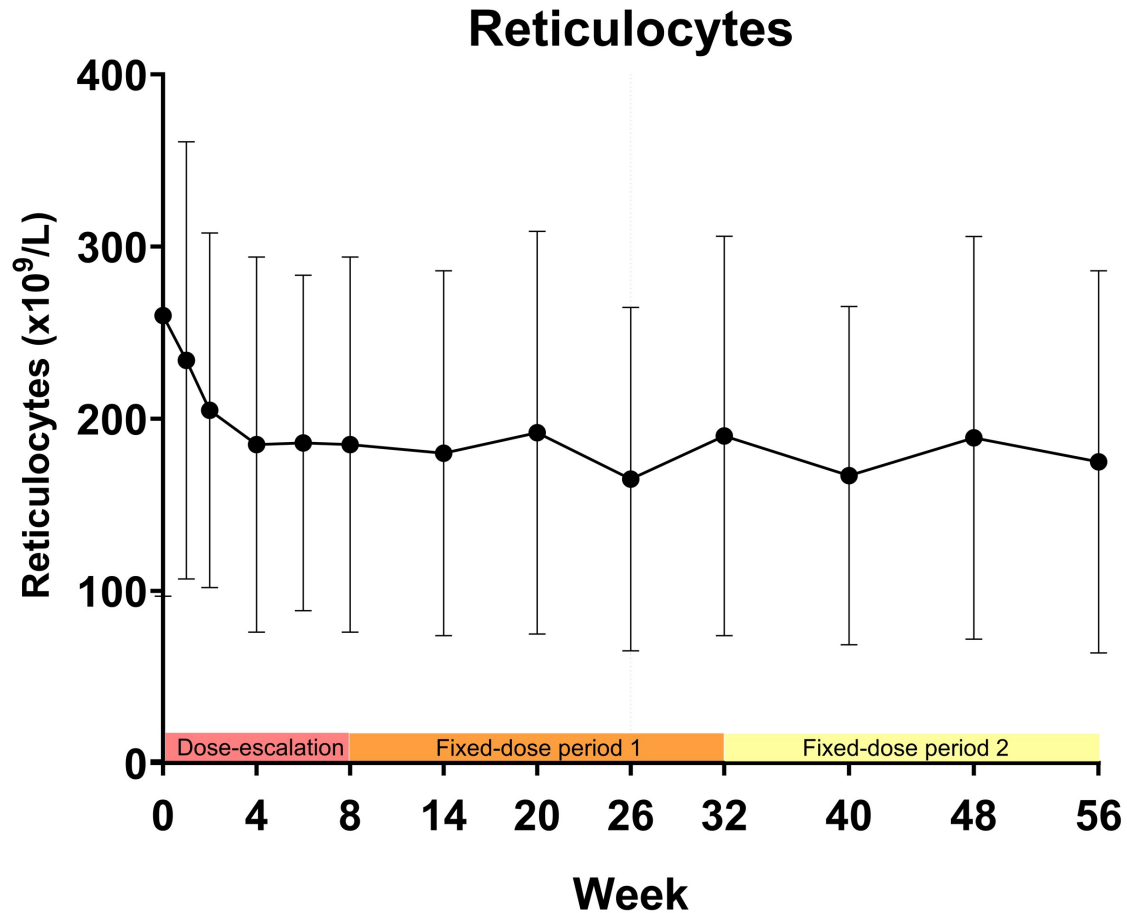
	W56 analysis set (n=21)
Age, median (range)	44 (24-67)
Female sex, n (%)	10 (48)
Diagnosis, n	
HS	15
HX	2
CDA II	4
Baseline hemoglobin, g/dL, mean (SD)	10.3 (1.5)
Baseline liver iron concentration, mg/g dry weight, mean (SD)	4.4 (3.3)

Mitapivat treatment resulted in rapid and sustained hemoglobin improvements

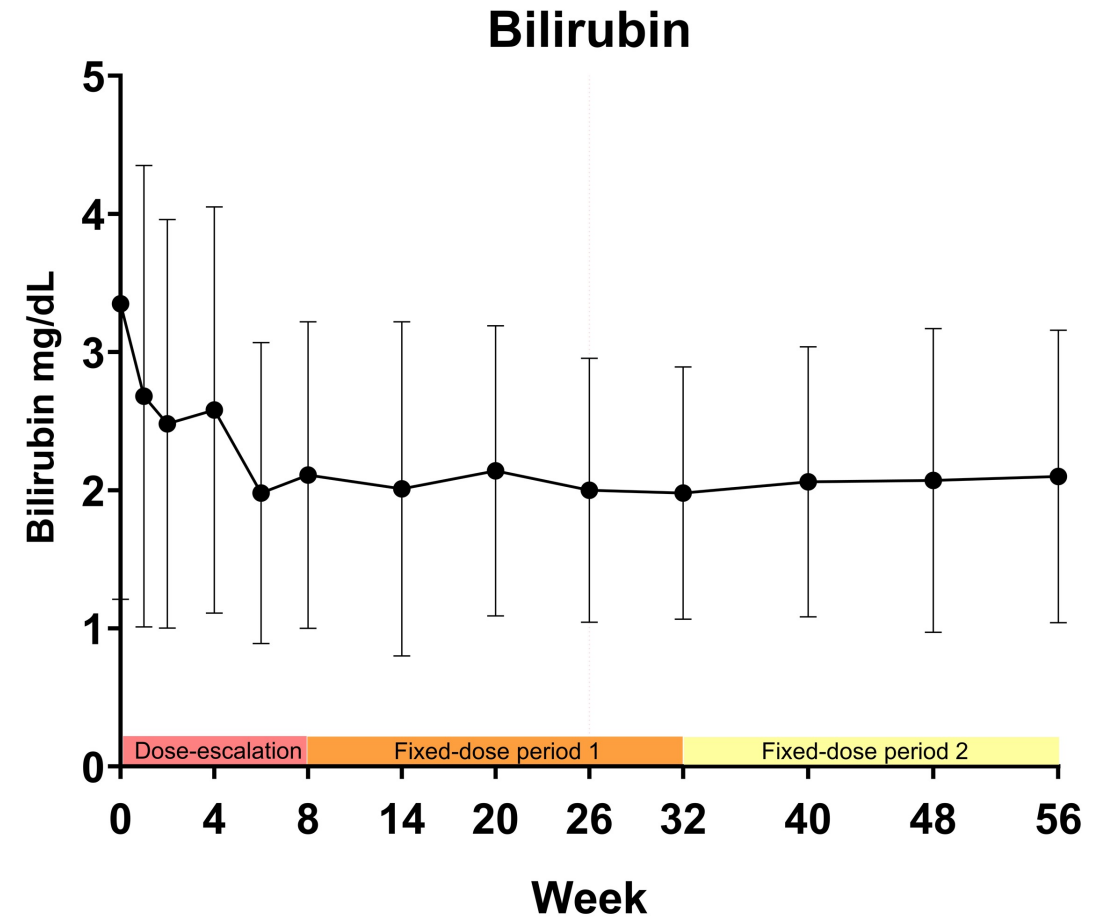


*Error bars represent 95% confidence interval

Mitapivat treatment resulted in rapid and sustained improvements in reticulocytes and bilirubin

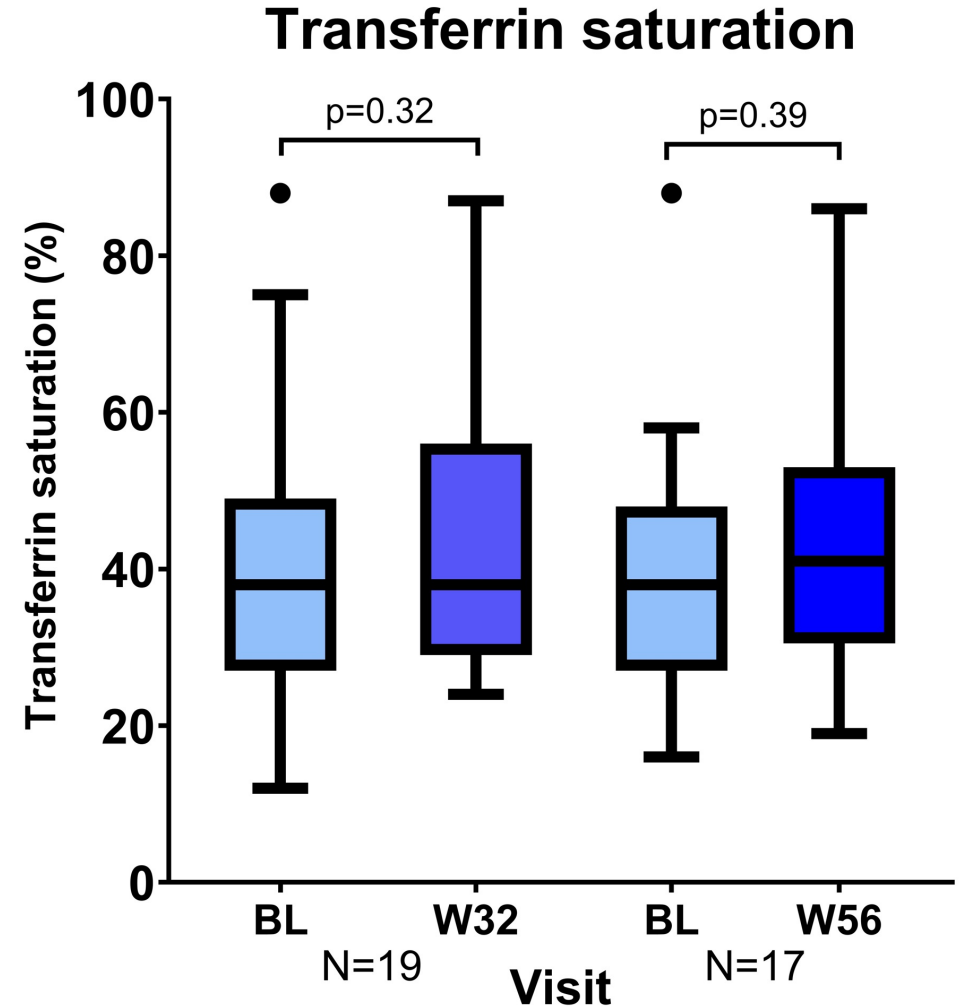
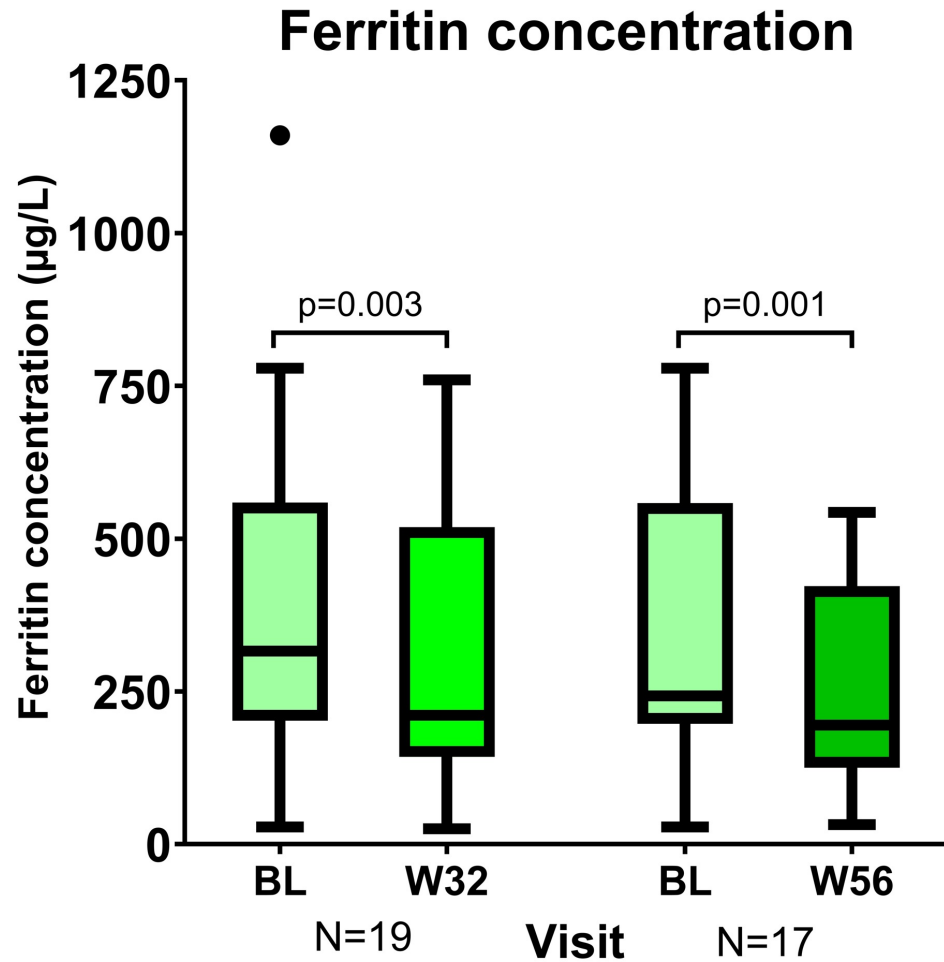


Mean difference W56
-81 x10⁹/L (95% CI, -115 to -47, **p<0.001**)



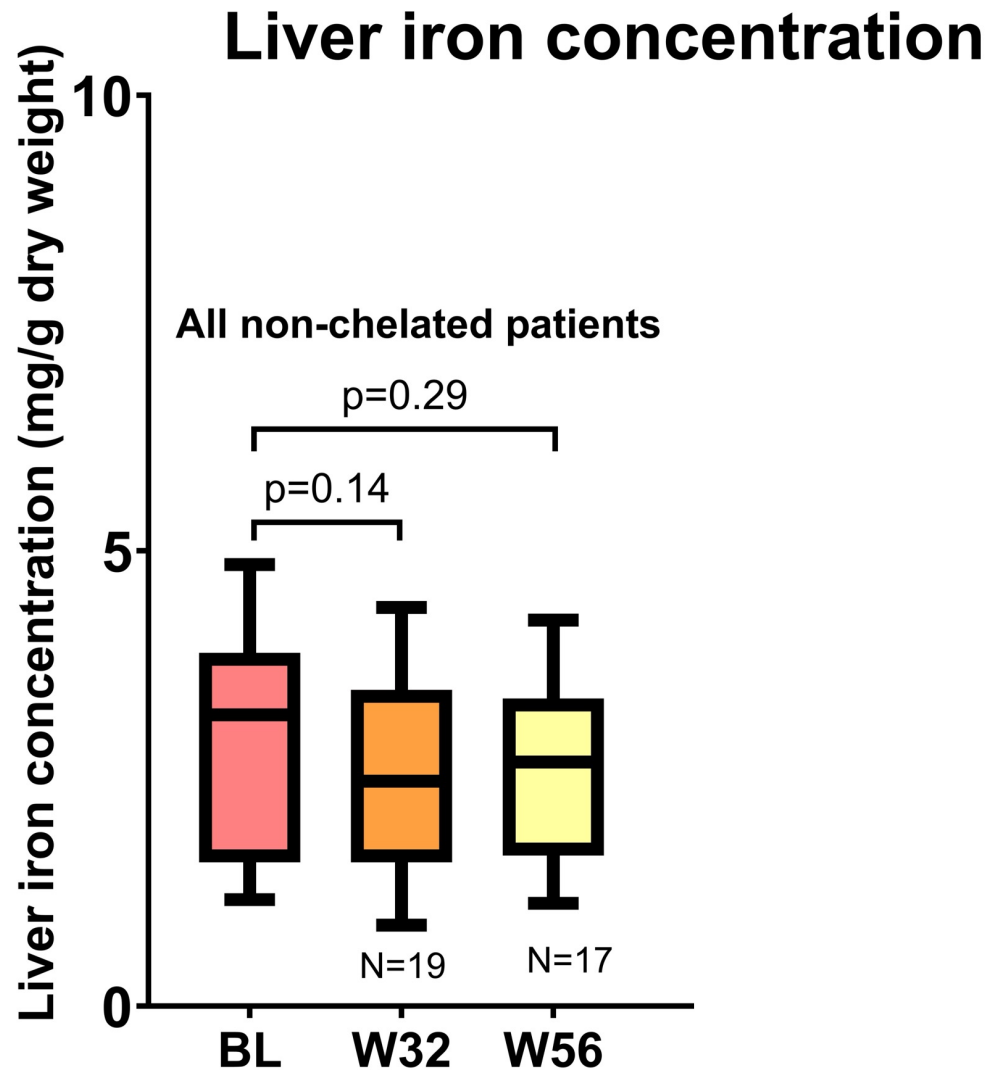
Mean difference W56
-1.4 mg/dL (95% CI, -2.1 to -0.8, **p<0.001**)

Mitapivat treatment resulted in a decrease in serum ferritin concentration



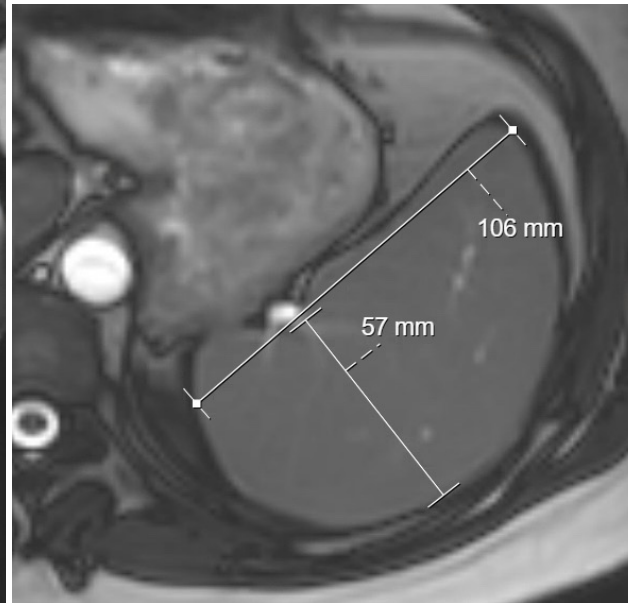
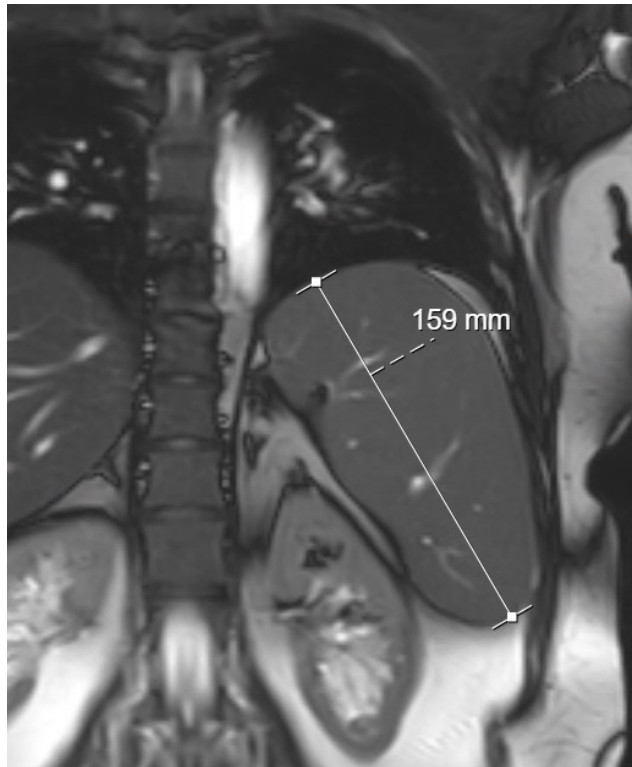
Mean difference W56:
-92 µg/L (95% CI, -133 to -51. p=0.001)

Mitapivat improved liver iron concentration in hemoglobin responders

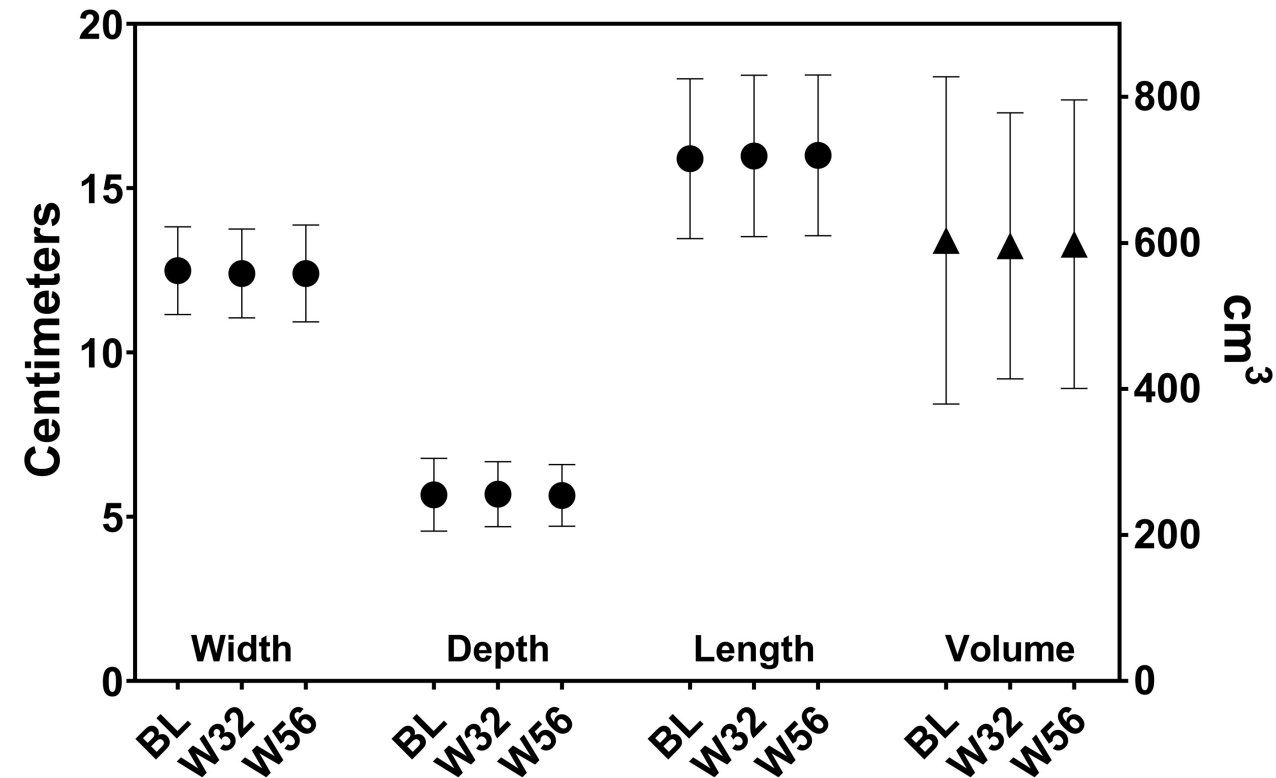


Mean difference
-0.44 mg/g dw (95% CI, -0.73 to -0.16, **p=0.009**)

No changes in spleen size and volume were observed



Splenic measurements



Summary

- In this follow-up analysis, mitapivat treatment resulted in **sustained improvements in hemoglobin concentrations and hemolytic markers, most pronounced in patients with HS**
- Mitapivat led to a **decrease in ferritin concentrations**, and among patients with a hemoglobin response, a **reduction of liver iron concentration**
- **No changes in spleen size and spleen volume** were observed
- Further investigation in populations with higher iron burden and extended follow-up is warranted.
- Analyses focusing on markers of iron homeostasis are currently ongoing

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