Primary results from the **SATISFY** study: A EuroBloodNet, Multicenter, Single-Arm, Phase 2 Study

Safety and Efficacy of Mitapivat in Erythrocyte Membranopathies and Congenital Dyserythropoietic Anemia Type II

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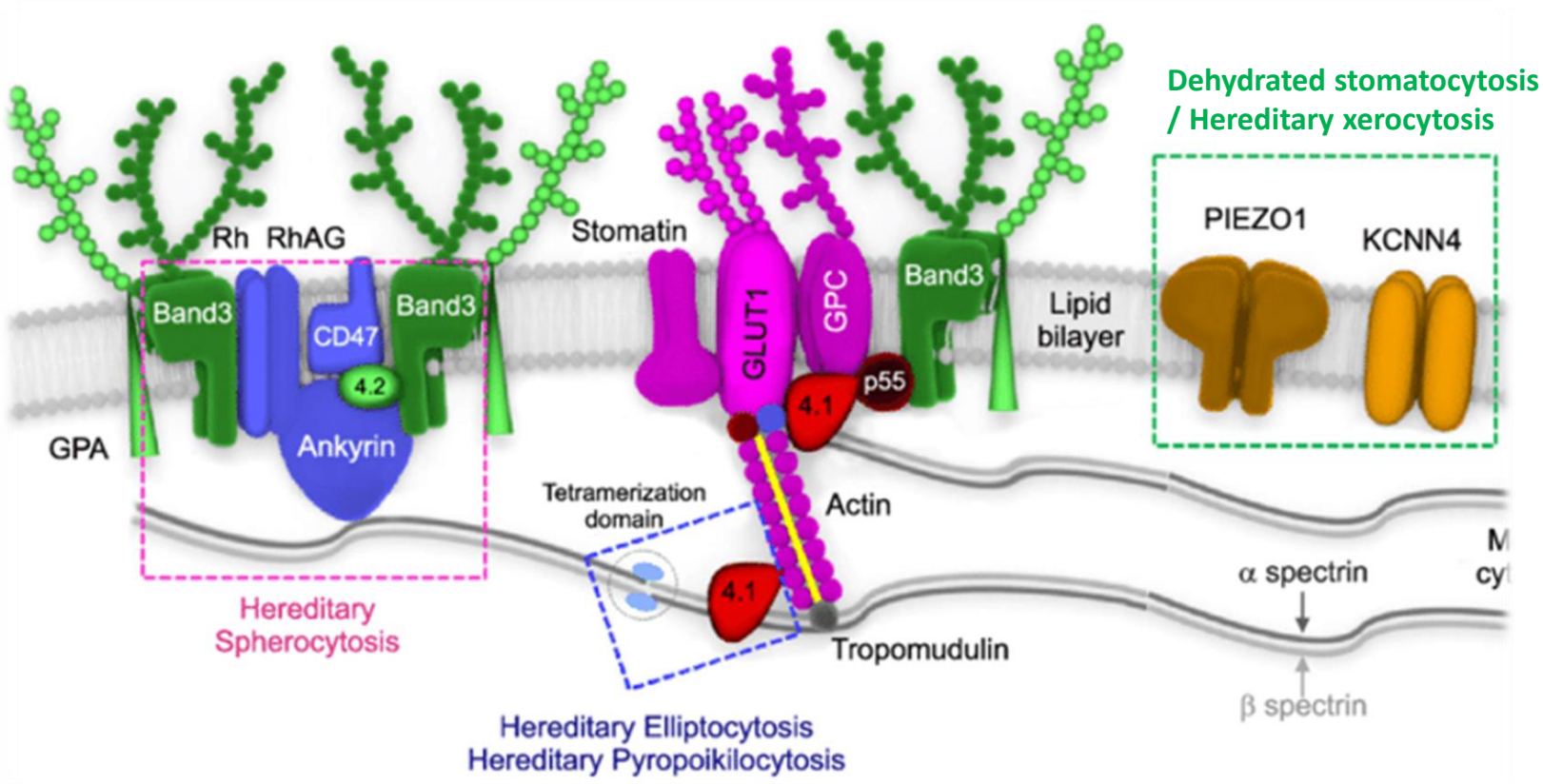
Disclosures

No conflicts of interest

Erythrocyte membranopathies

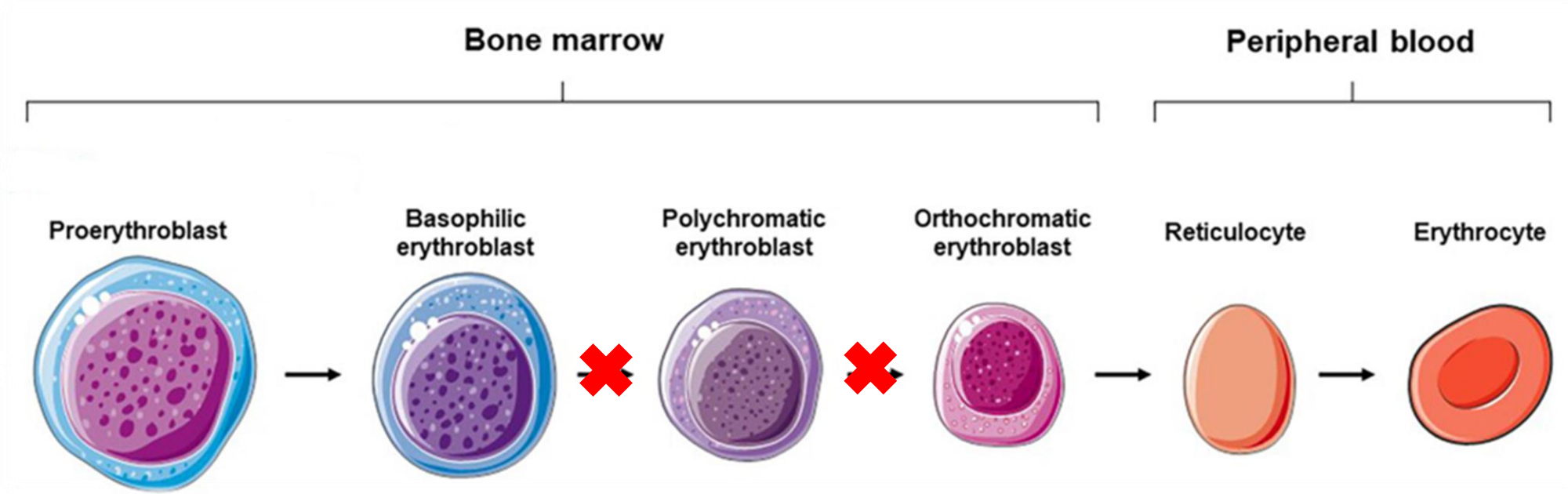
Genetic defects in cytoskeletal, (trans)membrane or ion-channel proteins



Kim et al. (2017) – Blood research

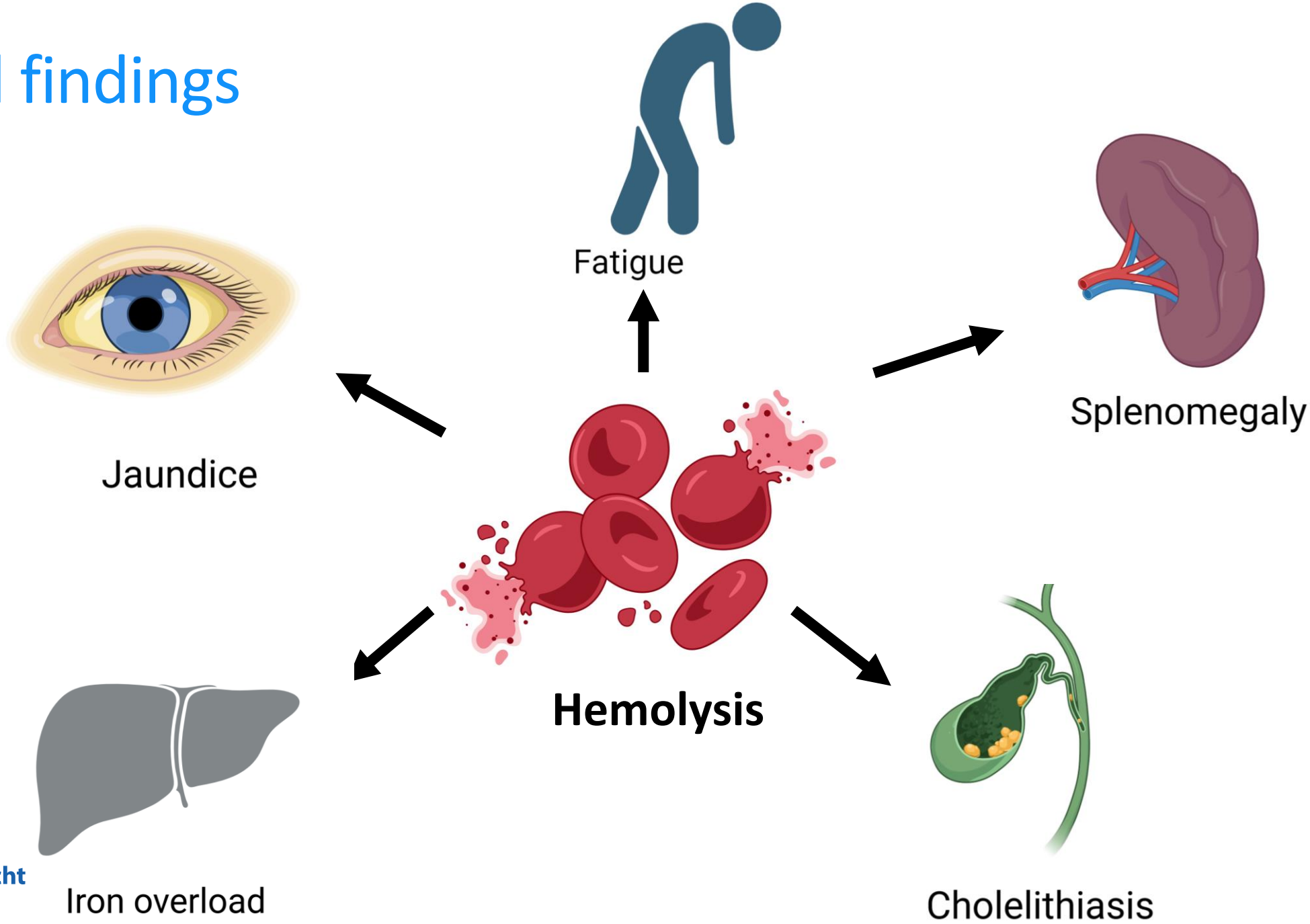
Congenital Dyserythropoietic Anemia Type II (CDA II)

Genetic defects in *SEC23B*



Kim et al. (2017) – Blood research

Clinical findings



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There is a significant unmet need in the current treatment

Current treatment is primarily supportive

Transfusions

Folic acid

Iron management

A splenectomy is the only therapeutic option

- No indication in **mild-moderate disease**
- Increased infection susceptibility and thrombosis risk
- Contra-indicated in **hereditary xerocytosis (HX)** and limited effect in **CDA II**

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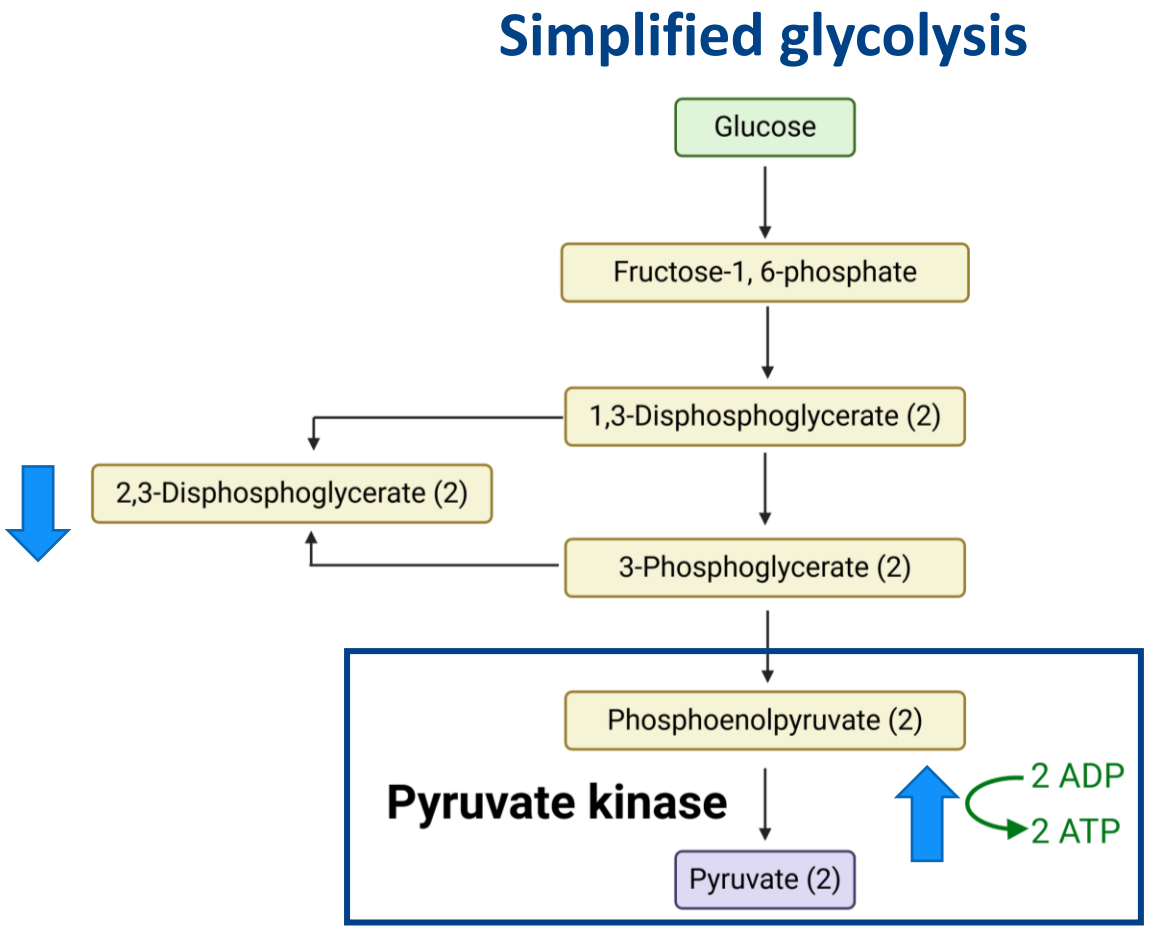
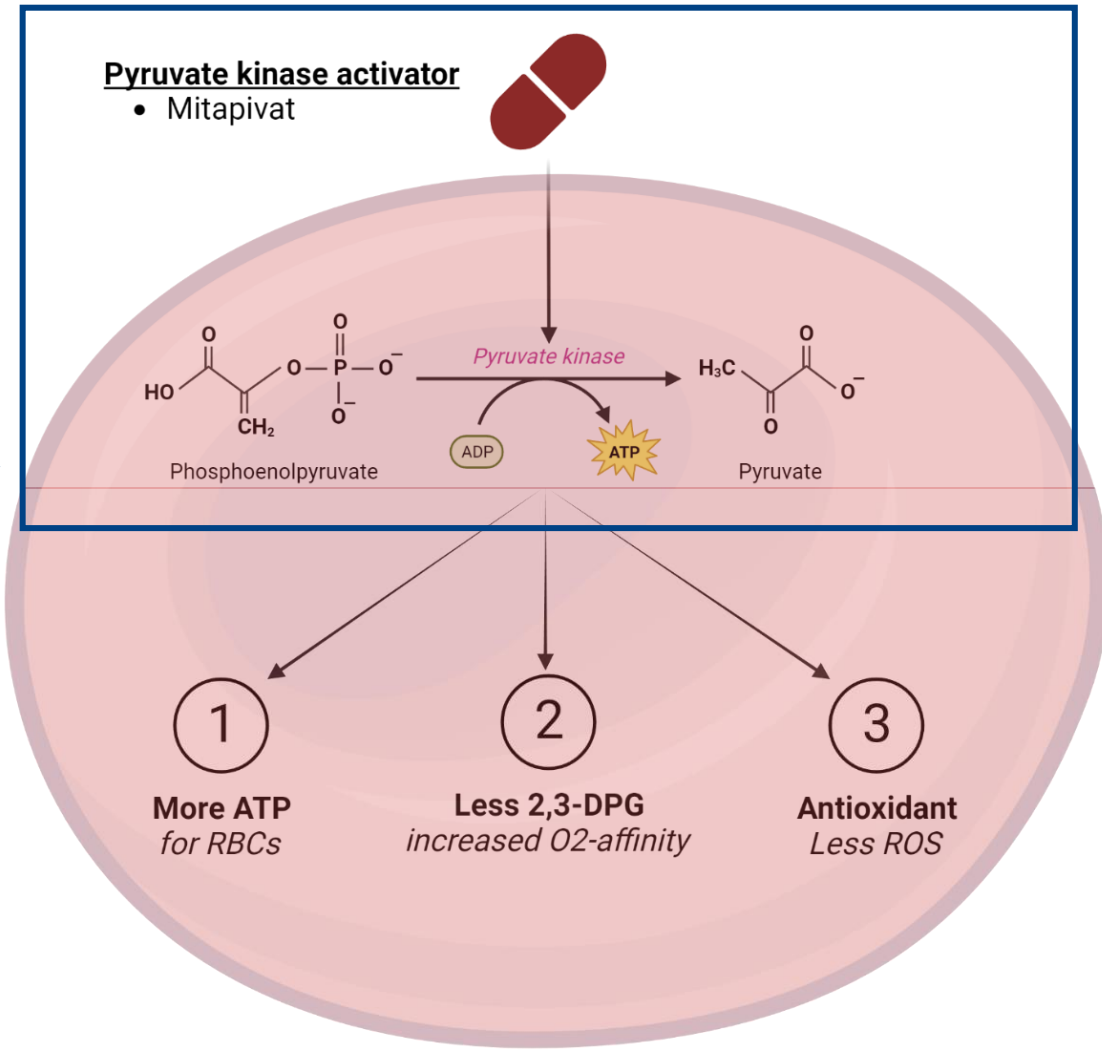
Mitapivat – an allosteric pyruvate kinase activator





Preclinical and mouse model results provide a rationale for the use of mitapivat in membranopathies

Matte et al. (2023) – JCI insight
Andres et al. (2019) - BJH
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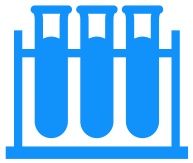
Study design

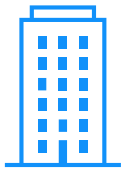


Setup

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

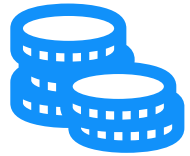
Locations

Denmark
The Netherlands
Sibling study in Canada



Sponsor

EuroBloodNet Association (Non-profit)



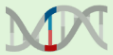
Funding

Agios Pharmaceuticals

Key eligibility criteria

Key Inclusion Criteria

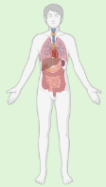
Membranopathy or CDAII



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

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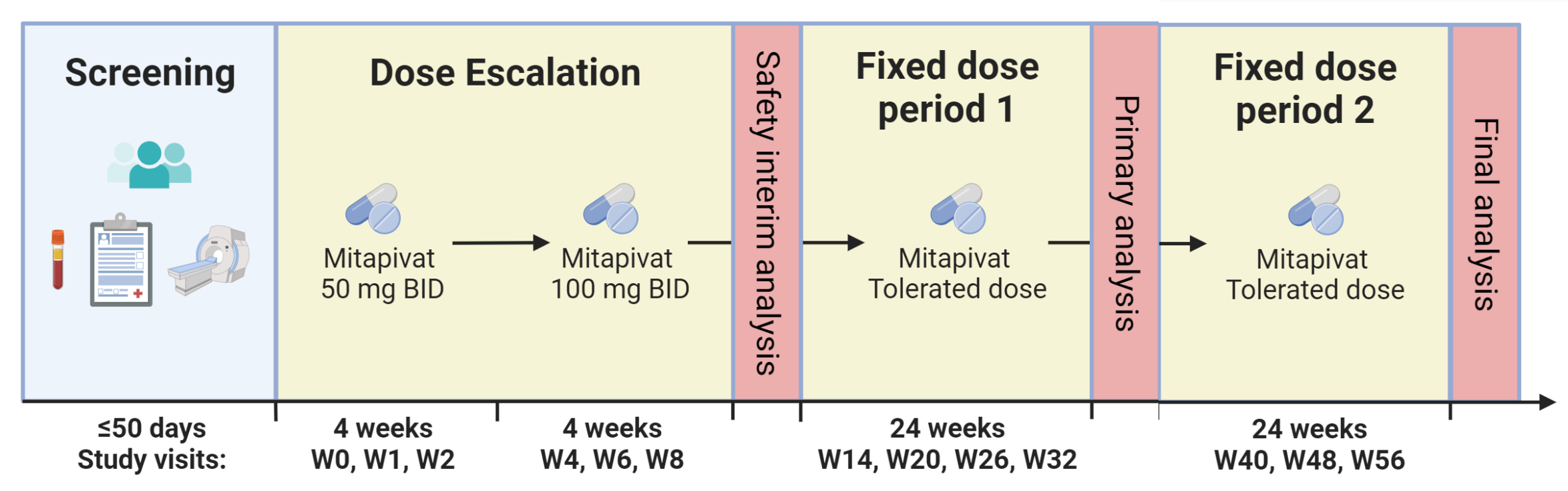
Study scheme



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Endpoints

Primary endpoint

Safety - Incidence of treatment-emergent adverse events (TEAEs)

Key secondary endpoint

Efficacy - Hemoglobin response, defined as ≥1.0 g/dL increase in Hb concentration from baseline (sustained at two scheduled visits in the fixed dose period)

Other secondary endpoints

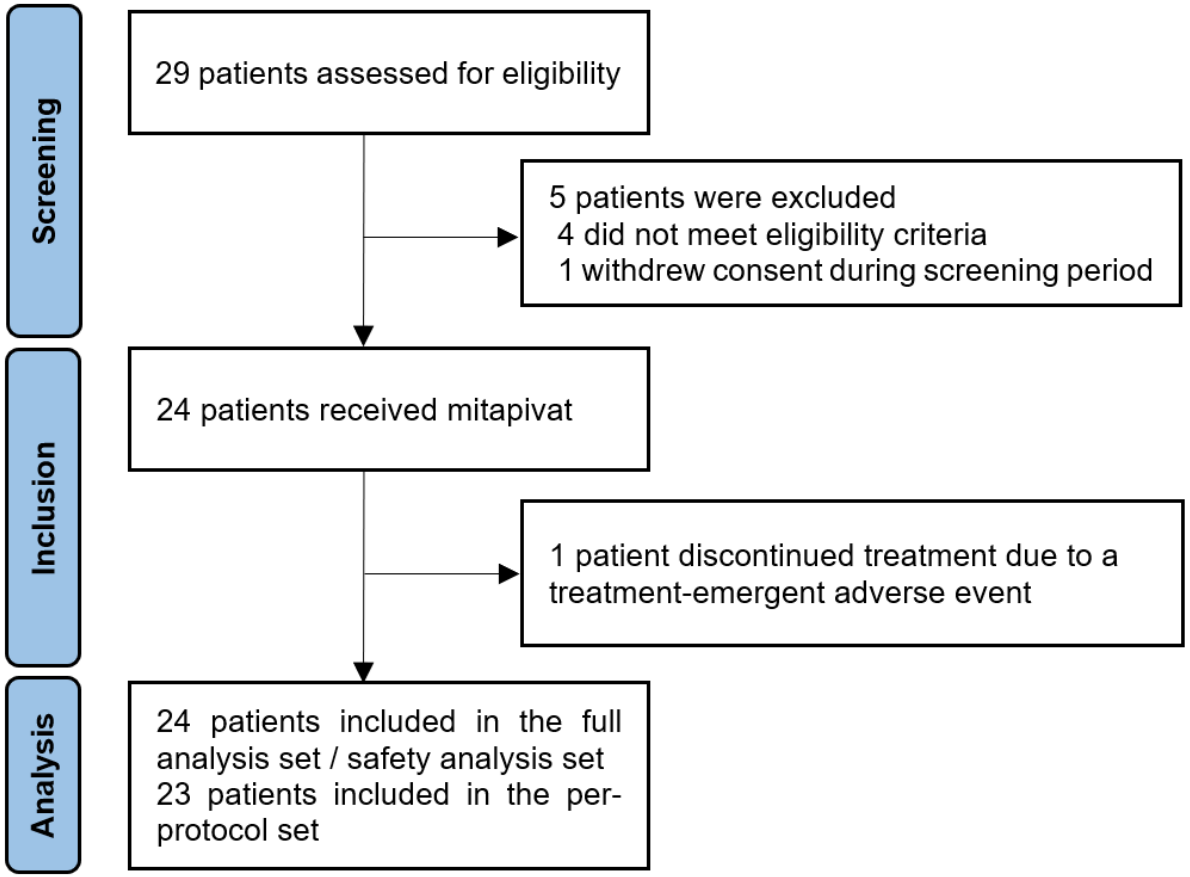
Change from baseline in **hemolytic markers**

Patient-reported outcome measures

- **SF-36:** Short form-36 (health-related quality of life)

- **PKDIA:** Pyruvate Kinase Deficiency Impact Assessment (impact of hemolysis on daily living)

Patient selection and baseline characteristics



24 participants (EU)

- 16 Hereditary spherocytosis (HS)
- 4 Hereditary xerocytosis (HX)
- 4 CDA II

Median (range) age 43 (24-79) years

Female sex 13/24 (54%)

Prior splenectomy 1/24 (4%)

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Safety analysis

TEAEs were mostly (96%) **mild events** (grade 1-2)

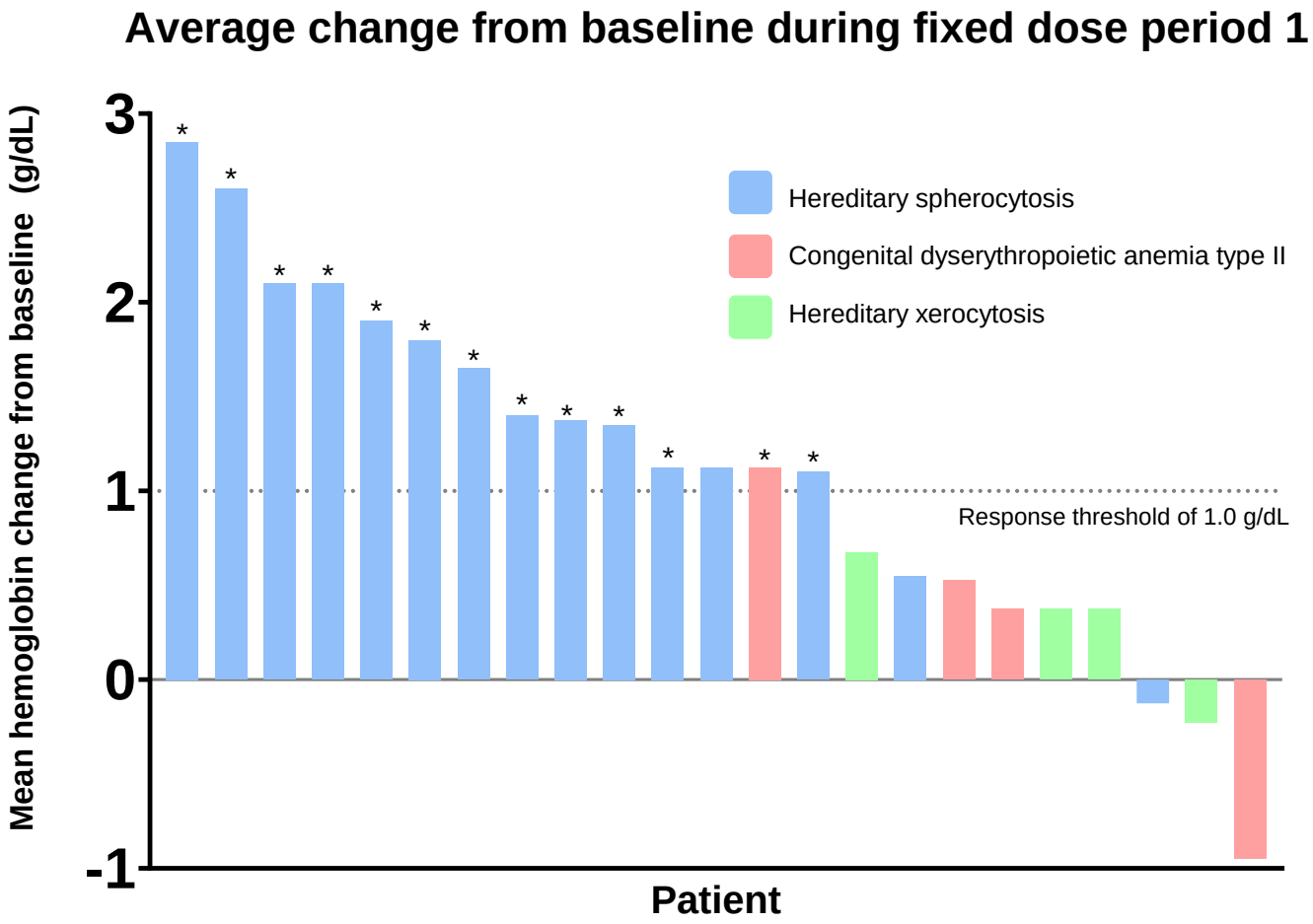
Most frequent reported (mild) events

- Headache 12/24 (50%)
- Upper respiratory infection 11/24 (46%)
- Insomnia 8/24 (33%)

- 4/91 (4%) **grade 3** events occured, whilst **no grade 4-5** events occurred

- Two **serious adverse events** occurred, both unrelated to the study drug

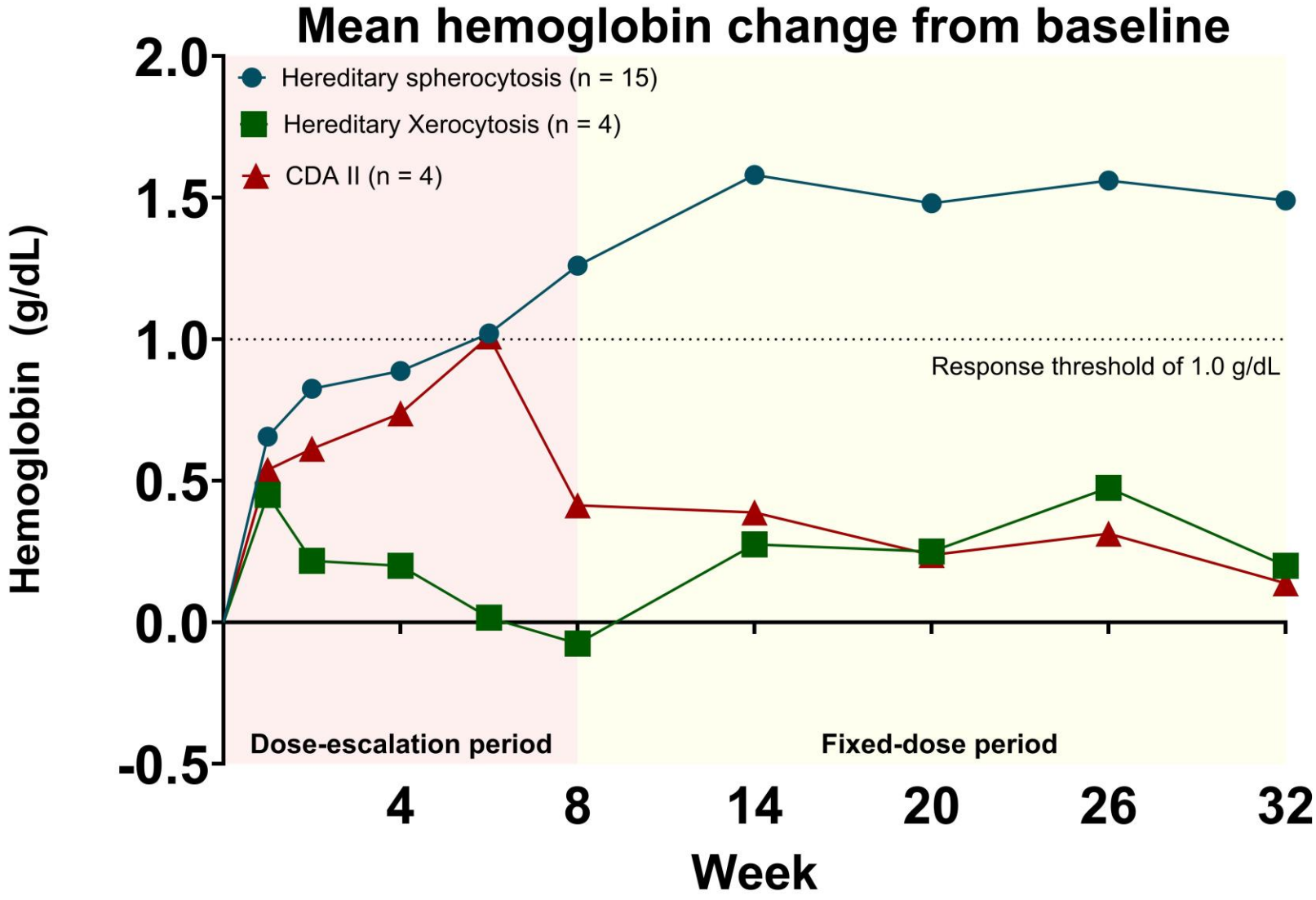
Efficacy analysis – Hemoglobin change from baseline



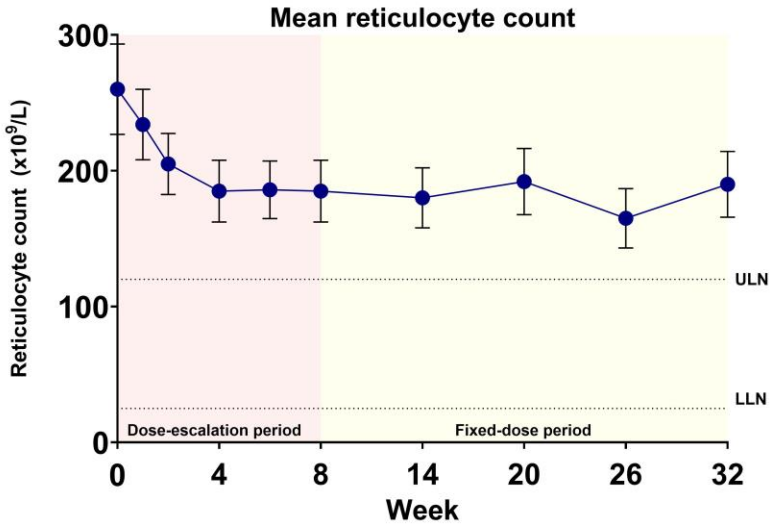
*Participants that reached the key secondary endpoint, defined as a hemoglobin response of ≥1.0 g/dL sustained at two consecutive visits

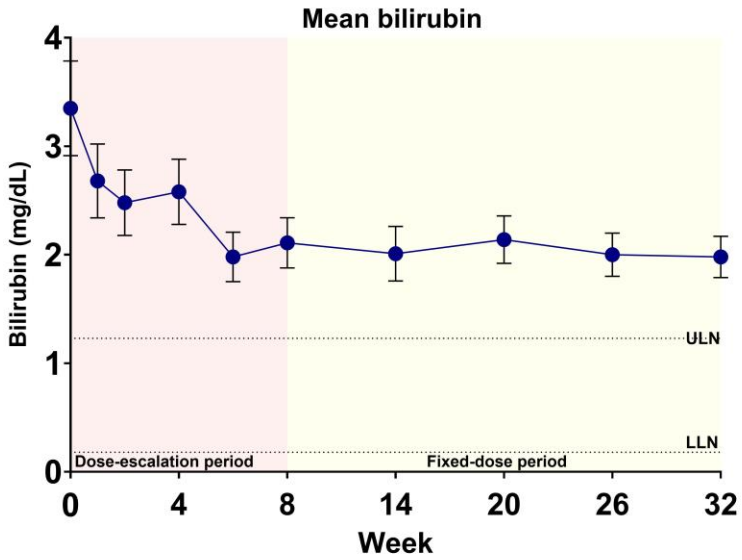
13/23 (57%) participants reached the key secondary endpoint, of which **12/13 (92%) with HS**

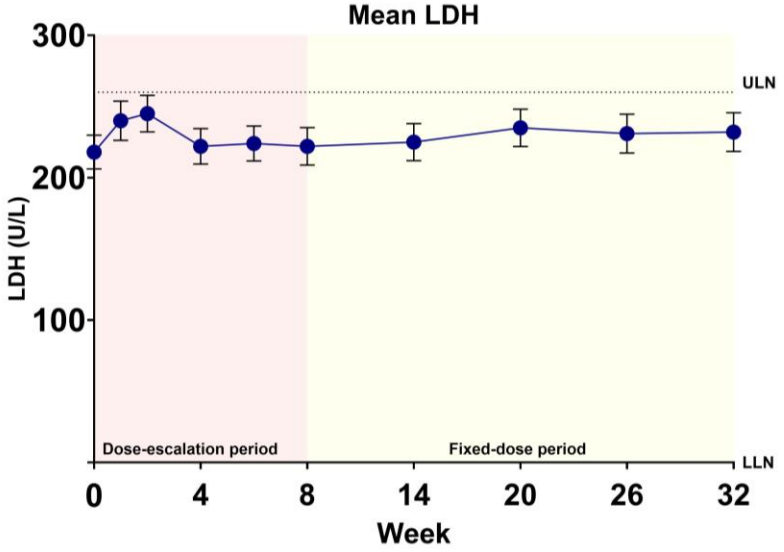
An early and sustained hemoglobin response was observed in HS

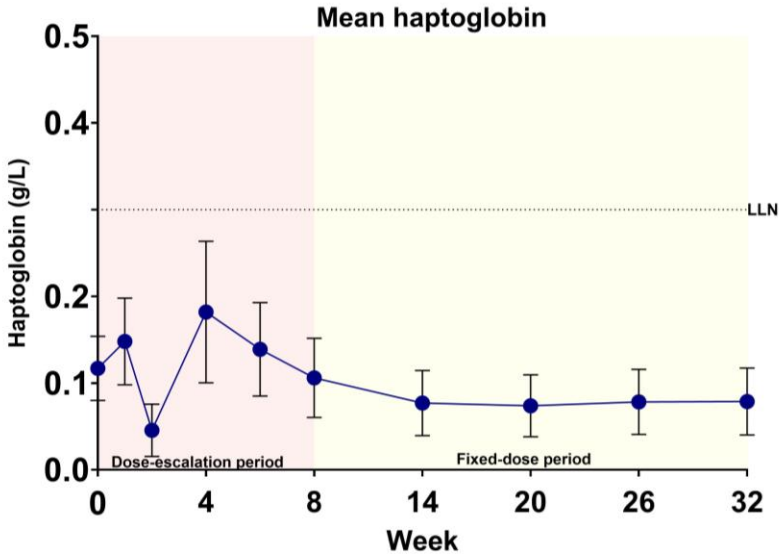


Concomitant decrease in reticulocyte count and bilirubin was observed









Mean reticulocytes count

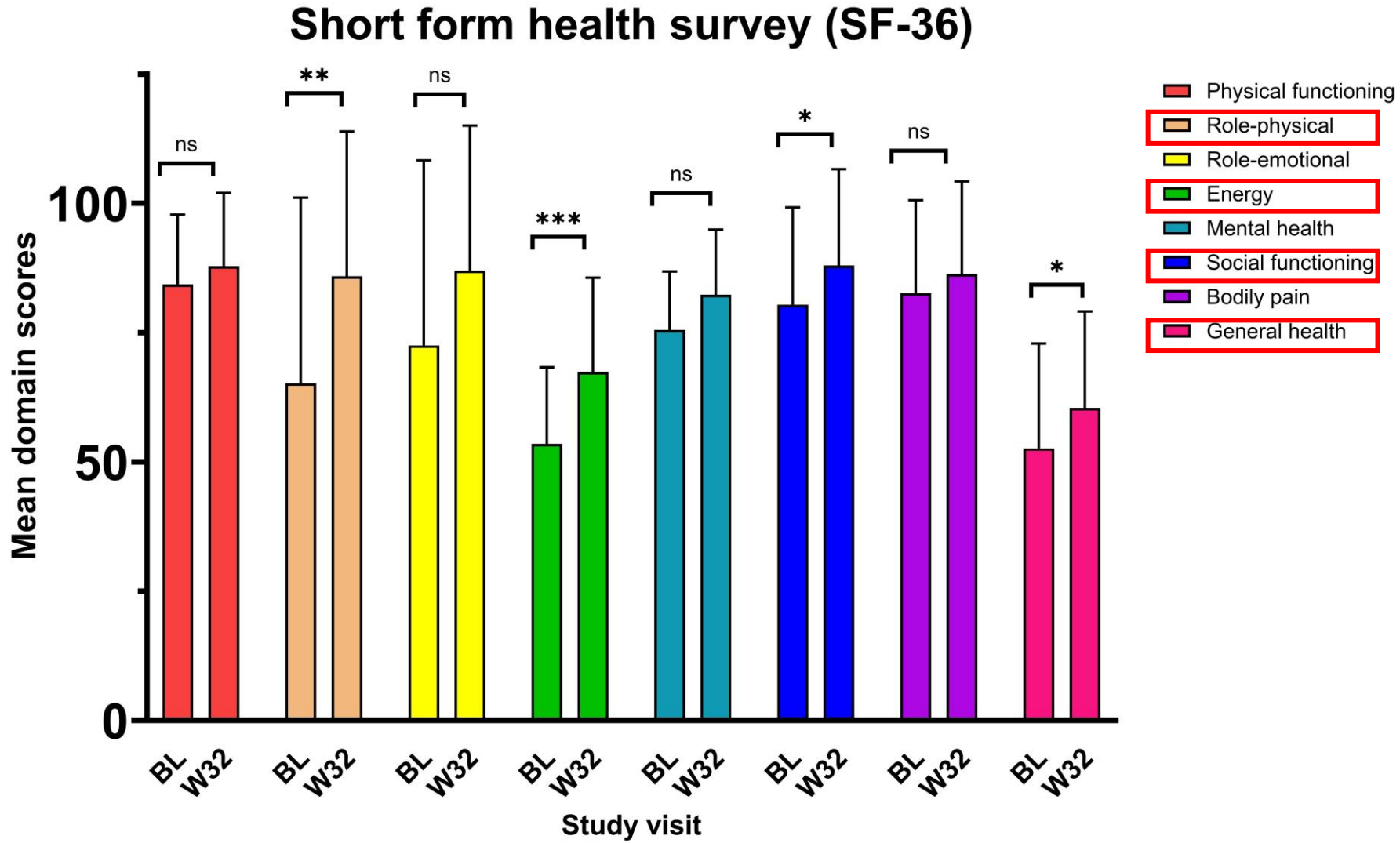
Baseline	257 ± 166
W32	190 ± 116
P	**< 0.001**

Bilirubin

Baseline	3.4 ± 2.2
W32	2.0 ± 0.9
P	**< 0.001**

LDH and Haptoglobin remained stable

Improvements in quality of life across multiple domains



Error bars represent standard deviation. P-values were calculated using a wilcoxon signed rank test
∗ p<0.05, ∗∗ p<0.01, ∗∗∗ p<0.001

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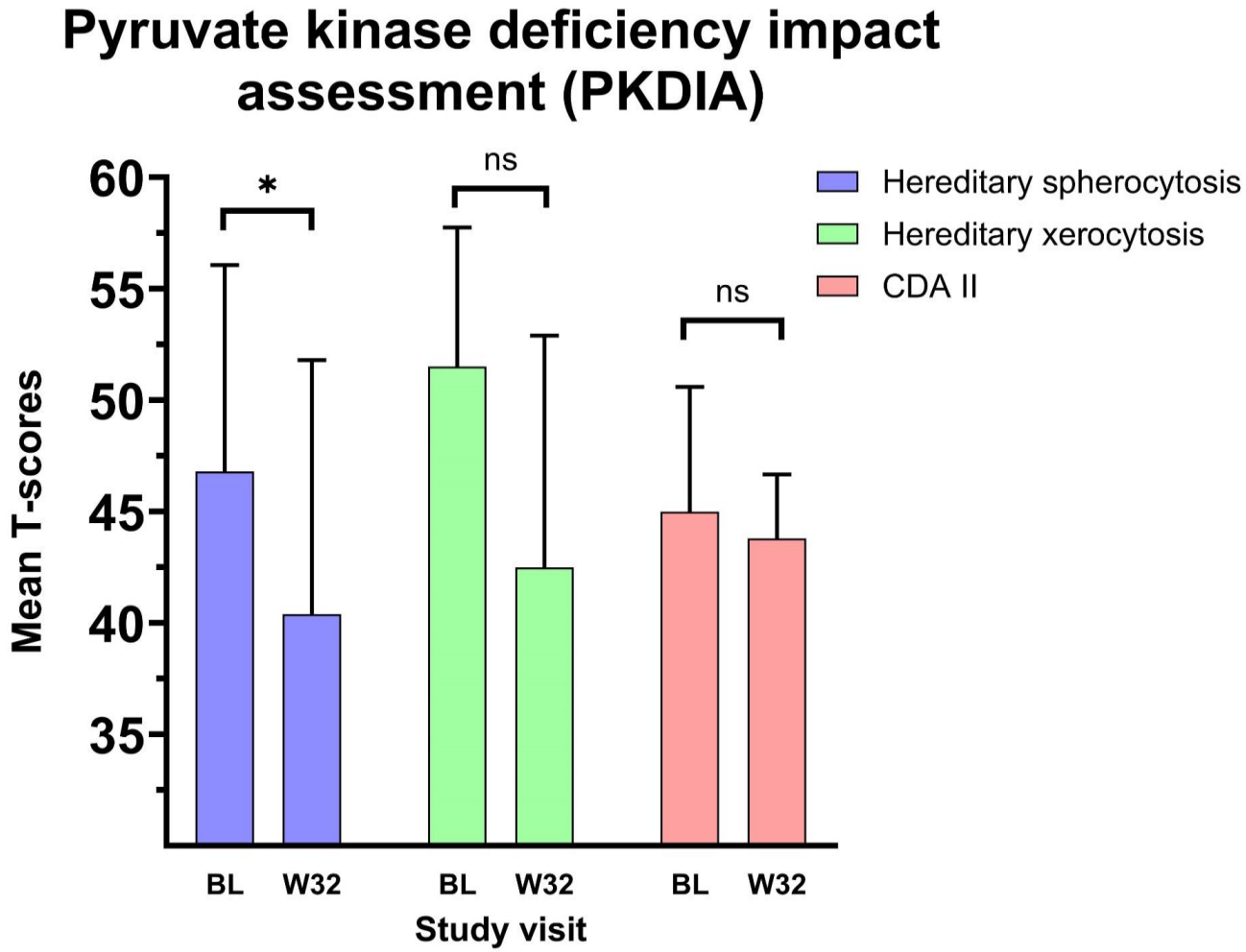
SF-36: Higher scores indicate a better quality of life (range 0-100)

PKDIA scores improved across al disease states with significant improvements in HS



Error bars represent standard deviation. P-values were calculated using a wilcox signed rank test ∗ p<0.05, ∗∗ p<0.01, ∗∗∗ p<0.001

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PKDIA: Higher scores indicate higher disease burden (Range 30-76)

Summary

- **Safety profile** was consistent with that observed in previous mitapivat clinical trials
- Mitapivat demonstrated **sustained improvements** in hemoglobin, hemolytic markers, quality of life and disease burden
- These improvements were particularly pronounced in **hereditary spherocytosis**
- These findings indicate **potential clinical benefit** in this patient population, **supporting continued longer-term evaluation in this trial.**
- A poster (**PS2199)** with the baseline results of the exploratory analysis will be presented at EHA on **Saturday, June 14 (18:30 - 19:30 CEST)**

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