SATISFY: A EuroBloodNet Multicenter, Single-Arm Phase 2 Trial of Mitapivat in Adult Patients with Erythrocyte Membranopathies and Congenital Dyserythropoietic Anemia Type II – Results from the 8-Week Dose-Escalation Period

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Background

- Erythrocyte membranopathies are a group of hemolytic disorders arising from defects in cytoskeletal or ion-channel proteins
- Congenital dyserythropoietic anemia type II (CDA II) is a disorder affecting erythropoiesis with phenotypic similarities to membranopathies
- Current treatment options are mainly supportive
- Mitapivat increases ATP within the red blood cell by activating pyruvate kinase (PK)
- Clinical trials evaluating mitapivat in several hemolytic anemias, as well as in an HS mouse model, have demonstrated its efficacy in increasing hemoglobin (Hb) levels[1]

Objectives – Dose escalation period

Primary endpoint: Safety
- Incidence of treatment-emergent adverse events (TEAEs)

Secondary endpoint: Efficacy
- Hemoglobin response (≥1 g/dL increase from baseline)
- Change in hemolytic and erythropoietic markers

Methods

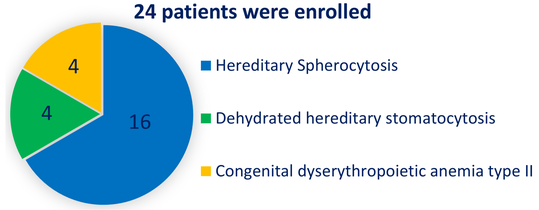
Study design
- Investigator-initiated, prospective, multicenter, single-arm phase 2 trial
- Conducted in Denmark and the Netherlands
- Sibling study in Canada

Study cohort
- Inclusion criteria: Membranopathy or CDA II, ≥ 18 years, Hb concentration < 13.0 g/dL for males and < 11.0 g/L for females, adequate organ function
- Exclusion criteria: PK deficiency, recent or regularly scheduled blood transfusions, significant comorbidity, receiving hematopoietic stimulating agents

Intervention
- During the 8-week dose escalation period, participants received mitapivat 50 mg twice daily (BID). After 4 weeks, dose will be increased to 100 mg BID
- Participants will continue in two consecutive 24-week fixed dose periods

Results – Baseline characteristics

24 patients were enrolled



Mean (SD) age 46 (16) years

13/24 participants were female

1/24 participants had prior splenectomy

Safety analysis – occurrence of TEAEs

- 23/24 patients completed the dose-escalation period (one participant dropped out due to an allergic reaction to mitapivat)
- One non-study treatment-related serious adverse event occurred

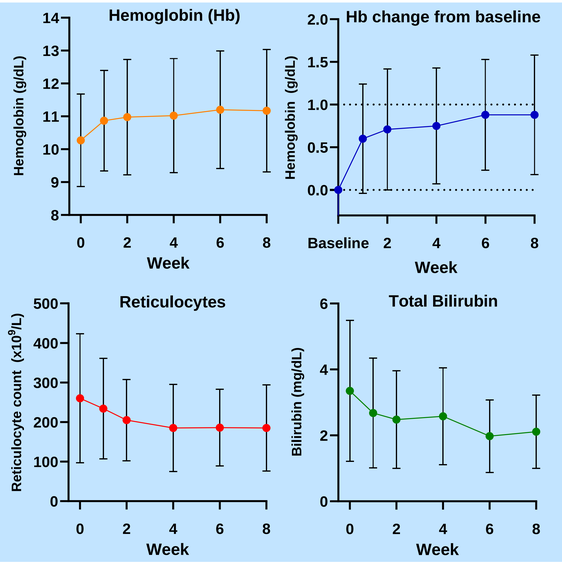
Total	Grade 1 n= 27	Grade 2 n= 17	Grade 3 n= 1
Headache	9 (38%)	2 (8%)	
Insomnia	7 (29%)	1 (4%)	
Upper respiratory infection		5 (21%)	
Fatigue	3 (13%)		
Flu-like symptoms	3 (13%)		
Abdominal pain	1 (4%)	1 (4%)	
Non-cardiac chest pain	1 (4%)	1 (4%)	
Pain in extremity	2 (8%)		
Skin infection			1 (4%)
Dry eye		1 (4%)	
Mucosal infection		1 (4%)	
Nausea	1 (4%)	1 (4%)	
Neck pain		1 (4%)	
Phlebitis		1 (4%)	
Urticaria		1 (4%)	
Urinary tract infection		1 (4%)	

Data is presented as n (%). Grade 1 adverse events occurring in only 1 participant were arthritis, diarrhea, dry mouth, dysgeusia, limb edema, hordeolum, hot flashes, hyperhidrosis, infective arthritis, irritability, decreased libido, decreased appetite, palpitations

Efficacy analyses – Change in hemoglobin, hemolytic and erythropoietic markers

Full study cohort

- 13/23 (56%) patients who completed the dose-escalation period reached the efficacy endpoint of ≥1 g/dL Hb increase from baseline

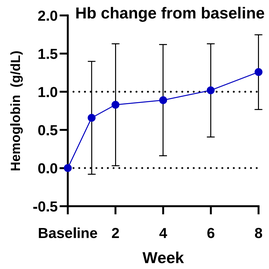


	Baseline (n = 24)[1]	Week 8 (n = 23)[1]	Mean difference[2]	P-value[3]
Hemoglobin (g/dL)	10.3 (1.4)	11.2 (1.9)	0.9 (0.6 to 1.2)	<0.001
Reticulocytes (x 10^9/L)	260 (163)	185 (109)	-72 (-103 to -41)	<0.001
Bilirubin (mg/dL)	3.4 (2.1)	2.1 (1.1)	-1.3 (-2.0 to -0.6)	0.001
LDH (U/L)	218 (58)	222 (58)	6 (-6 to 16)	0.307

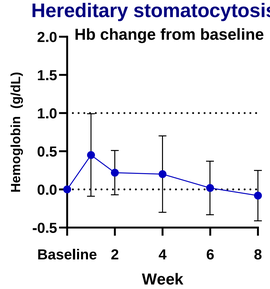
[1] Mean (SD) [2] Mean difference (95% CI) [3]P-values calculated using paired sample t test

Subgroup analysis according to diagnosis

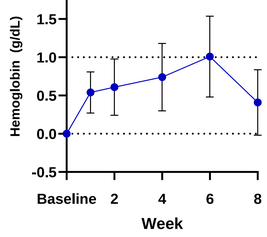
Hereditary spherocytosis



Hereditary stomatocytosis



CDA II



Summary of findings from the dose-escalation period

Safety profile: Consistent with previous mitapivat clinical trials
Laboratory: Improvements in hemoglobin and hemolytic markers
Long-term: Core-period results expected in 2025

Acknowledgments

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References

[1]van Dijk MJ, Rab MAE, van Oirschot BA, Bos J, Derichs C, Rijneveld AW, et al. One-year safety and efficacy of mitapivat in sickle cell disease: follow-up results of a phase 2, open-label study. Blood Adv. 2023 Dec 26;7(24):7539–50.

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