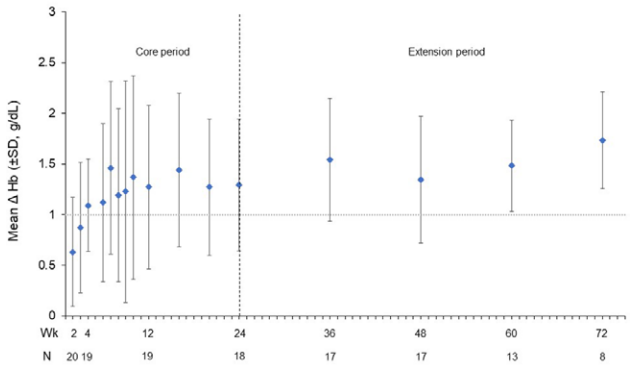
discontinued (pt decision). Median duration of treatment for pts in the LTE was 70.9 wks (range 54.7, 105.6), with 8 pts receiving ≥72 wks of treatment as of data cutoff. Median pt age in the LTE was 44 yrs (range 29, 67). Mean BL (SD) Hb, total bilirubin and lactate dehydrogenase (LDH) was 8.1 (1.2) g/dL, 40.1 (26.2) µmol/L and 272.4 (121.7) U/L, respectively. Median BL erythropoietin (EPO) was 70.5 (range 15, 11191) IU/L. Hb improvements achieved in the core period were sustained in the LTE (Figure). Mean Hb (SD) increase from BL to Wk 60 (α-thalassemia, n=4; β-thalassemia, n=9) and Wk 72 (β-thalassemia, n=8) were 1.5 (0.4) and 1.7 (0.5) g/dL, respectively. Improvements in markers of hemolysis and ineffective erythropoiesis observed in the core period were maintained in the LTE up to Wk 72 (mean [SD] bilirubin and LDH, –15.8 [16.6] µmol/L and –63.6 [216.0] U/L, respectively; median [range] EPO, –33.0 [–72.0, –16.0] IU/L). The safety profile was consistent with that observed in the core period. AEs in ≥15% of pts were headache (5/17) and back pain (3/17), none were grade ≥3. No trends for decreases in bone mineral density were observed. No treatment-related serious AEs occurred.

Conclusions: A favorable efficacy-safety profile was observed with long-term mitapivat in pts with α- or β-thalassemia. Data show sustained improvements in Hb, hemolysis and ineffective erythropoiesis despite globin genotypic heterogeneity, and no new safety findings. Mitapivat, through its unique mechanism of action, may represent a novel therapeutic approach for this condition. Two ph 3 trials of mitapivat in α- and β-thalassemia, (NTD and transfusion-dependent pts), are enrolling.

Figure. Mean Hb change from baseline over the core and extension periods



Hb = hemoglobin; SD = standard deviation; Wk = week.

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S117 LONG-TERM FOLLOW UP OF DUTCH PATIENTS WITH SCD DIAGNOSED BY NEONATAL SCREENING -- EFFECT ON THE MORBIDITY AND MORTALITY IN THE NETHERLANDS.

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Background: Newborn screening for sickle cell disease (SCD) has been introduced in January 2007 in the Netherlands. The objective of this study is to assess the effect of this neonatal screening for SCD by describing the residual risks of death and major disease-related events during the first fourteen years of life in children diagnosed with SCD at birth in the Netherlands.

Aims: The objective of this study is to assess the effect of this neonatal screening for SCD by describing the residual risks of death and major disease-related events during the first fourteen years of life in children diagnosed with SCD at birth in the Netherlands.

Methods: Here we report the first data of one center (Amsterdam UMC) of this prospective, national multicenter study. Following informed consent data were collected from medical files of all children born after 1 January 2007, diagnosed by neonatal screening. Descriptive data on SCD genotype, occurrence of major disease-related events (hospitalization for vaso-occlusive crisis (VOC), acute chest syndrome/pneumonia, severe infections and neurological complications) are presented. Overall survival and survival without specific SCD-related complications were analyzed by Kaplan-Meier curves.

Results: Up until now, 98 (56%) out of 174 eligible subjects from this institution were included, with a total follow-up of 805 patient-years. This concerns approximately 35% of the national number. The majority (55%) had the severe genotype (HbSS/ beta0-thalassemia), the remainder had the milder genotype (HbSC or HbS/beta+-thalassemia). Survival by the age of 14 was 98.9%, with 1 death at the age of 1 years due to sepsis. Seven patients (7.1%) had a severe infection (meningitis, sepsis, osteomyelitis) caused by Streptococcus Pneumoniae in 3/7 cases. Two patients experienced a symptomatic cerebral infarction at the age of 11 months and 1.5 years. At the age of 10 years the survival without hospitalization for vaso-occlusive crisis was 27% (95% CI: 12.7 – 43.14%) and 51% (25.3 – 72.0%) for the SS/Sβ0 and SC/Sβ+ genotype respectively.

Conclusion: In this cohort of neonatally screened patients with SCD, the SCD-related mortality and morbidity is still impressive with 1% mortality, 3 severe infections caused by Streptococcus Pneumoniae, and 2 patients with neurological complications. A final analysis of the effect of neonatal screening for SCD will follow after completion of data collection in all participating centers in the Netherlands.

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S118 LONG-TERM SAFETY AND EFFICACY OF VOXELOTOR FOR PATIENTS WITH SICKLE CELL DISEASE: RESULTS FROM AN OPEN-LABEL EXTENSION OF THE PHASE 3 HOPE TRIAL

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Background: Sickle cell disease (SCD), a lifelong, inherited blood disorder, leads to sickle hemoglobin (HbS) formation. HbS polymerization causes red blood cell sickling, leading to hemolysis, chronic anemia, and vaso-occlusive crises (VOCs). Patients with SCD are at higher risk of end-organ damage, increased morbidity, and early mortality due to low hemoglobin (Hb) and increased hemolysis.[1]

Voxelotor, a HbS polymerization inhibitor, is approved in the US for SCD treatment in adults and adolescent patients aged ≥12 years.[2] The randomized, placebo-controlled HOPE trial showed that significantly more patients on voxelotor 1500 mg had a >1 g/dL Hb increase than those on placebo at any time to week 72. These Hb increases were associated with reduced hemolysis markers.[3] Here we report an interim analysis of an ongoing open-label extension (OLE) of the

Methods: Patients who completed the phase 3 HOPE trial were eligible to enroll in the multicenter OLE study and receive treatment as long as they continued to receive clinical benefit and/or until they had access to voxelotor through commercialization or a managed access program. All patients received voxelotor 1500 mg as ongoing treatment. Adverse event data were collected from the date of informed consent through 28 days after voxelotor discontinuation. Measurements of Hb and clinical markers of hemolysis are ongoing and summarized here for 48 weeks of the OLE. Data presented are based on an interim data cut (December 31, 2020).

Results: Of the 199 patients who completed the HOPE trial, 178 (89.4%) were enrolled and dosed in the OLE. Median age at enrollment was 25 years (15.7% adolescents, 84.3% adults). At the cutoff date, the median voxelotor exposure duration in the OLE was 69.9 weeks (range: