**BACKGROUND**
- Pyruvate kinase (PK) deficiency is an under-recognized autosomal recessive disease caused by mutations in the PKLR gene.
- Pathogenic mutations lead to reduced activity of PK-R, the red blood cell-specific PK enzyme, which results in lifelong hemolymia anemia.1,2
- Acute and chronic complications of supportive care (e.g., transfusions, splenectomy, or iron chelation) can additionally burden patients with PK deficiency.

**METHODS**
- DRIVE PK is a phase 2, randomized, open-label, dose-ranging study of mitapivat in adults with PK deficiency who were not regularly receiving red blood cell transfusions. Results from the first 6 months of the study showed:
  - A rapid increase from baseline of >1.0 g/dL in hemoglobin (Hb) levels in 50% of patients.
  - An acceptable safety profile.3
- DRIVE PK is a global study, with patients enrolled at 14 centers in the US, Canada, Europe, and China.
- Patients with PK deficiency have been treated with mitapivat for a median of 3 years and up to 8 years.

**OBJECTIVE**
- To report long-term safety and efficacy of mitapivat in patients with PK deficiency continuing in the extension period of DRIVE PK (ClinicalTrials.gov NCT02476916).

**RESULTS**
- **Treatment**: Of the 18 patients continuing in the extension period, last-post-taper mitapivat dose was:
  - ≤25 mg BID (excluding missed doses; n=12)
  - >25 mg BID (n=6)
  - 200 mg BID (n=1)
- **Baseline characteristics**: No differences in age, race, or sex were observed between patients who continued in the extension period and those in the total cohort (Table 1).
- **Safety**
  - Mitapivat was generally well tolerated; the majority of AEs were grade 1–2.
  - No new safety signals observed.

**DISPOSITION**
- Of the 52 patients enrolled in the study, 43 completed the core period (24 weeks) and 18 remained in the study as of March 27, 2019 (Figure 2).

**Efficacy**
- **Improvements in hemoglobin and other markers of hemolysis, including reticulocytes, indirect bilirubin, and haptoglobin, achieved during the core period were sustained during the extension period (up to 42 months)** (Figure 3).

**CONCLUSIONS**
- Mitapivat is a novel, first-in-class, PK-R activator in clinical testing as a potential disease-altering therapy for patients with PK deficiency.
- Patients who responded to mitapivat had long-term durable responses:
  - Improvements in hemoglobin and other hemoglobin markers sustained at optimized individual doses during the extension period.
  - Chronic daily dosing with mitapivat for a median of 3 years and up to 42 months was well tolerated:
    - No new safety signals observed.
  - Two phase 3 trials are ongoing to further study the efficacy of mitapivat in patients with PK deficiency.

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