**Mitapivat (AG-348) long-term safety and efficacy in pyruvate kinase deficiency: 3-year results of the DRIVE-PK study**

Rachael F Grace1, D Mark Layton2, Frédéric Galactéros3, Wilma Barcellini4, Eduard J van Beers5, Hassan M Yaish6, Yaddanapudi Ravindranath7, Kevin HM Kuo8, Sujit Sheth9, Janet L Kwiatkowski10, Lei Hua11, Peter F Hawkins11, Chris Mix11, Bertil Glader12

1. Dana Farber Cancer Institute and Brigham and Women’s Hospital, Boston, MA, USA; 2. University of Wisconsin, Madison, WI, USA; 3. University of California, San Diego, CA, USA; 4. Università degli Studi di Torino, Torino, Italy; 5. Universiteit Maastricht, Maastricht, NL, The Netherlands; 6. Qatar National Research Fund, Doha, Qatar; 7. Ospedale San Giovanni, Rieti, Italy; 8. National Taiwan University Hospital, Taipei, Taiwan; 9. Stanford University, Stanford, CA, USA; 10. Istituto Superiore di Sanità, Rome, Italy; 11. Agios Pharmaceuticals, Cambridge, MA, USA; 12. Karolinska Institutet, Stockholm, Sweden.

**BACKGROUND**

Pyruvate kinase (PK) deficiency is an under-recognized autosomal recessive disease caused by mutations in the PKLR gene.

**METHODS**

**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 NCT02479761).

**RESULTS**

- **Characteristics Total Continued**
  - **Male, n (%)**
    - Total: 35 (67.3)
    - Continued: 25 (52.1)
  - **Age at screening (median, range), years**
    - Total: 34 (18-61)
    - Continued: 33 (19-61)
  - **White, n (%)**
    - Total: 43 (81.5)
    - Continued: 37 (74.5)
  - **Hb baseline, median (range), g/dL**
    - Total: 8.9 (6.5-12.3)
    - Continued: 9.7 (7.9-12.0)
  - **Splenectomy, n (%)**
    - Total: 43 (82.7)
    - Continued: 11 (22.2)
  - **Hypertriglyceridemia, n (%)**
    - Total: 1 (5.6)
    - Continued: 3 (16.7)
  - **Hypertriglyceridemia, n (%)**
    - Total: 1 (5.6)
    - Continued: 3 (16.7)
  - **Iron chelation prior to enrollment, n (%)**
    - Total: 25 (48.1)
    - Continued: 5 (27.8)
  - **Osteoporosis, n (%)**
    - Total: 8 (15.4)
    - Continued: 2 (11.1)
  - **Cholecystectomy, n (%)**
    - Total: 38 (73.1)
    - Continued: 14 (77.8)

- **SAFETY**

  - **Four patients had a grade 3 or 4 adverse event during the extension period**
    - **General adverse events**
      - Nausea: 6 (33.3) vs 2 (11.1)
      - Fatigue: 4 (22.2) vs 5 (27.8)
      - Headache: 10 (55.6) vs 7 (38.9)
      - Arthralgia: 4 (22.2) vs 2 (11.1)
      - Hot flush: 1 (5.6) vs 0 (0.0)
      - Arthritis: 4 (22.2) vs 2 (11.1)
      - Fatigue: 4 (22.2) vs 5 (27.8)
      - Hypertriglyceridemia: 1 (5.6) vs 0 (0.0)
      - Nausea: 6 (33.3) vs 2 (11.1)

**CONCLUSIONS**

- Mitapivat is a novel, first-in-class, PKR 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 hemolysis markers were sustained at optimized individual doses during the extension period (Table 1).
- Chronic daily dosing with mitapivat for a median of 3 years and up to 42 months was well tolerated.
- Consistent safety profile over the duration of treatment and no new safety signals observed.

Table 1. Demographic characteristics of all patients and those who continued in the extension period

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 Oppositions management: Mitapivat is only for those patients enrolled at baseline. This study was funded by Agios Pharmaceuticals. Inc. These data were previously presented in Grace RF et al. Ash Annual Meeting. December 7-10, 2019. Chicago, IL. 12th Poster 2022 RXP Agios – consultant, advisory committee member, research funding; Nicosia – investigator; Nicosia – research funding; Ospedale San Giovanni – investigator; Beijing, China – advisory committee member; Kung C – investigator; Agios Pharmaceuticals, Cambridge, MA – research funding. Purdue Pharma LP, Cambridge, MA, USA – research funding; Novartis Pharma, South Korea – research funding. Research sponsored by project title. MPF, South Korea, China, Canada, and Europe.

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