Mitapivat treatment usage, satisfaction, and adherence among adults with pyruvate kinase deficiency in the United States

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BACKGROUND

- Pyruvate kinase (PK) deficiency is a rare, hereditary, autosomal recessive enzyme disorder characterized by chronic hemolytic anemia[1–3]
- Mitapivat is a first-in-class, oral, allosteric activator of pyruvate kinase (PK), including the red cell-specific (PKR) and pyruvate kinase M2 (PKM2) isoforms, approved in the United States (US) for the treatment of hemolytic anemia in adults with PK deficiency, and in the European Union and United Kingdom for the treatment of PK deficiency in adult patients[4–7]
- In the pivotal phase 3 ACTIVATE trial (NCT03548220), ACTIVATE-T (NCT03559699), and their long-term extension study (NCT03853798), treatment with mitapivat led to improvements in hemoglobin, markers of hemolysis, and transfusion burden[8–10]
- Furthermore, mitapivat demonstrated sustained and clinically meaningful improvements on the signs, symptoms, and functional impacts for adult patients with PK deficiency as demonstrated by the PK Deficiency Diary and PK Deficiency Impact Assessment[9,11]
- Data are needed to understand mitapivat usage, satisfaction, and adherence among patients in a real-world setting

OBJECTIVE

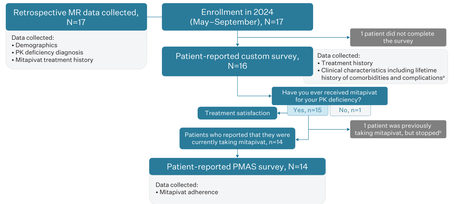
To understand mitapivat usage, satisfaction, and adherence among adults with PK deficiency in the US

METHODS

Study design

- This observational study used data from medical records (MR) and a cross-sectional patient survey of adults (≥18 years) with PK deficiency in the US (**Figure 1**)
- The population was a convenience sample recruited from May to September 2024 via patient outreach channels managed by patient advocacy groups and the Agios patient support program
- Interested individuals were directed to a study website and given the option to enroll
  - Patients were compensated for their participation
  - Patients ever enrolled in a mitapivat clinical trial were excluded

Figure 1. Summary of patient enrollment and data collection



[a]Lifetime history of comorbidities and complications was patient-reported due to incompleteness and limited look-back of the MR data. [b]The patient reported that "not seeing an improvement in labs such as hemoglobin" and "not seeing an improvement in symptoms such as fatigue" were reasons for stopping treatment
MR, medical records; PK, pyruvate kinase; PMAS, PROMIS Medication Adherence Scale; PROMIS, Patient-Reported Outcomes Measurement

Data collection, management and analysis

- This study underwent Institutional Review Board (IRB) approval in March 2024
- The PK deficiency cross-sectional survey included questions addressing clinical characteristics, and mitapivat treatment history, including treatment satisfaction and medication adherence
- Questionnaires and MR collection and abstraction were administered via the PicnicHealth research platform
- MR data collection (including retrospective records when available) began upon patient consent and survey data were collected after consent at a time convenient to the patient
- All data were de-identified and managed in compliance with the HIPAA Privacy Rule
- Data were summarized descriptively

PMAS survey and scoring

- The validated Patient-Reported Outcomes Measurement Information System (PROMIS) Medication Adherence Scale (PMAS) was used to measure medication adherence and only administered to patients who were currently receiving mitapivat
- The PMAS is a nine-item questionnaire focused on different aspects of medication adherence, and contains two subsections: medication beliefs and knowledge and medication-taking behaviors[12,13]
  - For the four items in the medication beliefs and knowledge subsection, response options ranged from "Strongly disagree" (score of 1) to "Strongly agree" (score of 5), with a possible subsection score range from 4 to 20
  - For the five items in the medication-taking behaviors subsection, response options ranged from "Never" (score of 1) to "Always" (score of 5), with a possible subsection score range from 5 to 25
  - The PMAS total score was calculated as the sum of the subsection scores, with a possible range of 9 to 45
  - Additionally, for each item, the frequency and percentage of patients who selected each of the 5 response options was reported
- Mean scores were analyzed for each subsection on medication beliefs and knowledge and medication-taking behaviors, as well as total adherence; a higher score on the PMAS indicates greater medication adherence

RESULTS

- All 17 patients had MR data, and 16 of these patients (94%) completed the survey (**Table 1**)

Table 1. Demographics and study population characteristics

Characteristic	N=17
Sex, n (%)	
Female	12 (71)
Race, n (%)	
White	13 (77)
Black or African American	2 (12)
More than one race	2 (12)
Ethnicity, n (%)	
Hispanic or Latino	1 (6)
Age at enrollment, years	
Median (Q1, Q3)	47.0 (30.0, 59.0)
Min, Max	20.0, 63.0
Age at diagnosis, years	
Median (Q1, Q3)	7.0 (4.0, 20.0)
Min, Max	0.0, 57.0

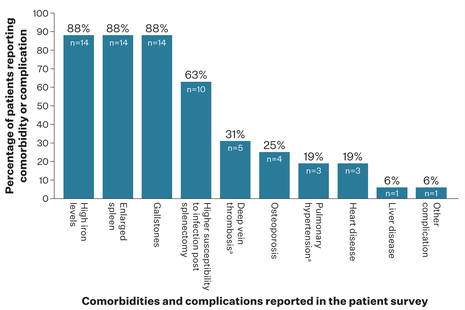
Max, maximum; Min, minimum; Q, quartile

Patient-reported complications[a]

- Per the patient-reported survey, patient lifetime history of PK deficiency complications included high iron levels, enlarged spleen, gallstones (88% for each condition, 14/16), deep vein thrombosis (31%, 5/16), and osteoporosis (25%, 4/16) (**Figure 2**)

[a]Lifetime history of comorbidities and complications was patient-reported due to incompleteness and limited look-back of the MR data

Figure 2. Lifetime history of comorbidities and complications reported by patients with PK deficiency (N=16)



[a]3 patients who experienced pulmonary hypertension were splenectomized, 1 of which also had deep vein thrombosis
PK, pyruvate kinase

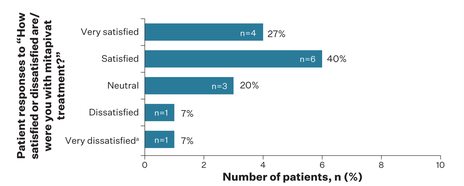
Mitapivat treatment history from MR data

- Mitapivat treatment was documented in 94% (16/17) of patients with MR data
- Median (min, max) treatment duration among the 16 patients was 1.1 (0.2, 2.3) years
- Only one patient had discontinued mitapivat treatment

Mitapivat treatment satisfaction from the patient survey

- Patient-reported outcomes as reported in the patient survey (N=15; one patient from the MR database did not complete the survey)
  - Of the 15 patients who ever took mitapivat, 67% were satisfied/very satisfied with mitapivat, and 20% were neutral (**Figure 3**)

Figure 3. Mitapivat treatment satisfaction among adult patients with PK deficiency (N=15)



[a]The patient who reported that they were "very dissatisfied" with mitapivat treatment was the same patient who discontinued mitapivat per MR
MR, medical records; PK, pyruvate kinase

PMAS survey

- Among the 14 patients currently taking mitapivat, the mean (standard deviation [SD]) PMAS medication beliefs and knowledge subscale score was 19.2 (0.9) out of a maximum possible score of 20, indicating positive beliefs about mitapivat's benefit and a thorough understanding of its use (**Table 2**)
  - All patients (100%) reported that they "strongly agree" with the statement "I know how to take this medicine as recommended"
  - Most patients agreed that mitapivat was working, with 50% reporting "strongly agree", 21% reporting "agree" and 29% reporting "neither agree nor disagree"

Table 2. PMAS survey item responses and total sub-score

PMAS medication-taking behaviors item responses, n (%)[a]	N=14
I took this medicine as recommended	
Sometimes	1 (7)
Almost always	2 (14)
Always	11 (79)
I remembered to take this medicine	
Sometimes	1 (7)
Almost always	7 (50)
Always	6 (43)
I did not take this medicine because of bothersome side effects	
Never	12 (86)
Rarely	2 (14)
I stopped taking this medicine because I thought I did not need it	
Never	14 (100)
I did not take this medicine because of the cost	
Never	14 (100)
Medication-taking behaviors subscale score	
Mean (SD)	23.9 (1.1)
Median (Q1, Q3)	24.0 (24.0, 24.8)
Min, Max	21.0, 25.0
PMAS medication beliefs and knowledge item responses, n (%)	**N=14**
I know how to take this medicine as recommended	
Strongly agree	14 (100)
I understand why I need to take this medicine	
Strongly agree	14 (100)
I believe it is important to take this medicine	
Strongly agree	14 (100)
I believe this medicine is working	
Neither agree nor disagree	4 (29)
Agree	3 (21)
Strongly agree	7 (50)
Medication beliefs and knowledge subscale score	
Mean (SD)	19.2 (0.9)
Median (Q1, Q3)	19.5 (18.3, 20.0)
Min, Max	18.0, 20.0
PMAS survey total score[b]	**N=14**
Mean (SD)	43.1 (1.1)
Median (Q1, Q3)	43.0 (42.3, 44.0)
Min, Max	41.0, 45.0

[a]Item responses for the past seven days prior to the survey; [b]Medication beliefs and knowledge plus medication-taking behaviors
Max, maximum; Min, minimum; PMAS, PROMIS Medication Adherence Scale; PROMIS, Patient-Reported Outcomes Measurement Information System; SD, standard deviation; Q, quartile

- The mean (SD) medication-taking behaviors subscale score was 23.9 (1.1) out of a maximum possible score of 25, indicating high adherence to treatment (**Table 2**)
  - Of the 14 patients currently taking mitapivat, over the seven prior days, 93% almost always or always remembered to take mitapivat and took it as recommended, and no patients stopped taking mitapivat because they thought they did not need it or due to cost
  - All 14 patients currently on mitapivat stated that they rarely (14%) or never (86%) stop taking mitapivat due to bothersome side effects
- The overall mean (SD) PMAS total score was 43.1 (1.1) out of a maximum total score of 45, indicating high overall adherence to mitapivat treatment (**Table 2**)

STUDY LIMITATIONS

- This study has limited generalizability due to the small sample size and geographical recruitment limited to US only
- Recruitment efforts were based on convenience sampling and results may not be generalizable to the entire population of patients with PK deficiency
  - Selection bias may have also contributed to lack of generalizability as recruitment efforts for this study included the Agios patient support program and patient advocacy outreach
- Furthermore, self-reported data may have introduced recall, interpretation, and response bias

CONCLUSIONS

- **In this observational, real-world study of patients with PK deficiency, high rates of adherence and self-reported satisfaction were reported for mitapivat treatment**
- **Mitapivat was a common treatment among this small pool of patients with PK deficiency, with patients reporting positive beliefs about mitapivat and a thorough understanding of its use**

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