An ongoing, global, longitudinal, observational study of patients with pyruvate kinase deficiency: The Peak Registry

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BACKGROUND AND OBJECTIVES

Pyruvate kinase (PK) deficiency: disease overview

- Under-recognized hereditary disease
- Heterogeneous disease with variable severity among all ages
- Often presents in childhood
- Caused by mutations in the PKLR gene
- Reduced PK-R enzyme activity leads to defective glycolysis and decreased red blood cell lifespan

Eligibility

- Lifelong hemolytic anemia
- Iron overload and jaundice
- Infection risk post splenectomy
- Signs and symptoms negatively affect health-related quality of life

Diagnosis and treatment

- PK-R enzyme activity and genetic testing
- Supportive treatment: transfusions, splenectomy, iron chelation

Rationale for development of a global registry

- The PK Deficiency Natural History Study (ClinicalTrials.gov NCT02053480) is an observational patient registry assessing the range of disease burdens among all ages
- The registry is governed by a steering committee, which comprises representatives from different geographic areas, and clinicians and diagnosticians treating adult or pediatric patients

REGISTRY DESIGN

- The Peak Registry is a global, longitudinal, observational study for adult and pediatric patients with PK deficiency.
- The registry is summarized in Figure 1

- To report the design elements of the Peak Registry and progress to date, and to provide information on the integration of data from the Natural History Study into the Peak Registry

Study duration

- Enroll approximately 500 eligible patients
- Study duration: 7 years
- Prospective follow-up: minimum 2 years

HARMONIZING PK DEFICIENCY NATURAL HISTORY STUDY AND PEAK REGISTRY DATA

- Digital harmonization of the data collected during the Natural History Study and the Peak Registry aims to maximize the amount of longitudinal data available (Figure 2)
- A digital platform (N of 1) is being developed to allow participating physicians to view their patients’ aggregated clinical data
- The portal will also allow migration of Natural History Study data to enable combined views of both Peak Registry and Natural History Study datasets

Participants

- Inclusion criteria: Patients with a confirmed diagnosis of PK deficiency obtained by genetic testing
- Each participant or their parent/guardian must be able to give written informed consent/assent

EXCLUSION CRITERIA

- Patients who are actively enrolled in any Agios-sponsored clinical trial involving treatment with a PK activator are not eligible to enroll

Data to be collected

- Medical history and physical findings, with particular interest in:
  - Translation history
  - Splenectomy/hematopoietic
  - Hepatic and cardiac iron load
  - Thrombosis
  - Bone imaging
  - Stains self transplant
  - Phor and current medications, including iron chelation therapy

Summary

- The Peak Registry is a global, longitudinal, observational study for adult and pediatric patients with PK deficiency that aims to extend the scope of the Natural History Study with additional patients from an expanded geographical distribution and longer follow-up.
- Site and patient recruitment are ongoing, with startup of registry sites in Thailand and feasibility assessment of sites in Japan and South Korea ongoing, and plans to activate sites in Switzerland, Sweden, and Turkey by year end.
- A portal has been developed to allow combined analyses of Peak Registry and Natural History Study datasets, and will be available to Peak Registry physician participants in 2020.
- Further information is available at https://peakregistry.com and www.clinicaltrials.gov.

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Disclosures

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References


Figure 1. Peak Registry design.

Figure 2. Data harmonization between the Natural History Study and the Peak Registry.

Figure 3. Enrollment status by month.

Figure 4. Peak Registry activity as of November 2019.

Figure 5. Data cutoff timeline.