Baseline characteristics of patients in Peak: A global, longitudinal registry of patients with pyruvate kinase deficiency

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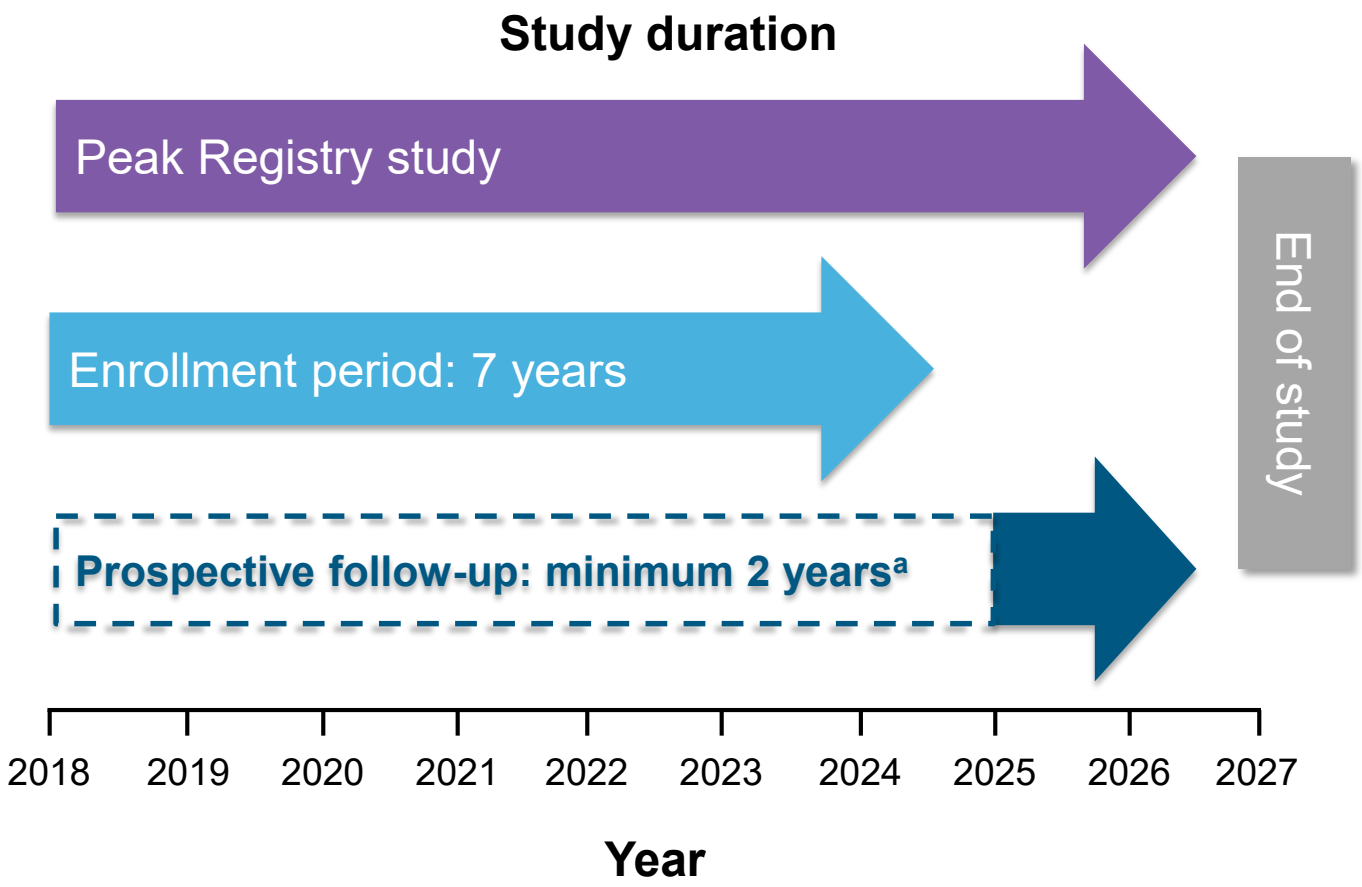
Background and objective

- PK deficiency is a rare, inherited hemolytic anemia caused by autosomal recessive mutations in the *PKLR* gene, whereby a glycolytic defect causes a reduction in ATP generation[1]
- To better understand the natural history, treatment patterns, and burden of disease, the observational PK Deficiency Natural History Study (NHS; NCT02053480) enrolled 254 adult and pediatric patients with PK deficiency at 30 sites across 6 countries between 2014 and 2017, and followed patients for 2 years[2,3]
- The Peak Registry (NCT03481738) was developed as a retrospective and prospective registry to continue and expand on the NHS by enrolling approximately 500 adult and pediatric patients at ~ 60 sites across up to 20 countries
- This analysis aimed to characterize the baseline demographics and clinical characteristics of patients with PK deficiency enrolled in the Peak Registry as of 24March2020

ATP = adenosine triphosphate; NHS = Natural History Study; PK = pyruvate kinase.

1. Tanaka KR et al. *Blood* 1962;19:267–95. 2. Grace RF et al. *Blood* 2018;131:2183–92. 3. van Beers EJ et al. *Haematologica* 2019;104:e51–e53.

Peak study duration and participants



Peak Inclusion Criteria

- Patients of any age with a confirmed diagnosis of PK deficiency obtained by genetic testing
- Each participant or their parent/ guardian must be willing and able to give written informed consent

[a]Participants in the Peak Registry who were originally included in the NHS and for whom data are integrated within the Peak Registry may have a cumulative follow-up exceeding 11 years.
NHS = Natural History Study; PK = pyruvate kinase.

Methods

- Demographic, diagnostic, medical history, laboratory, treatment, and other relevant data were collected from participating clinicians via electronic case report forms
- Patients were eligible for inclusion in this analysis if they had available demographic information as of the data cut-off date of 24March2020
- All analyses reported here are descriptive and based on data as of the date of enrollment in the Peak Registry
  - Continuous variables are summarized by the number of non-missing observations, mean, standard deviation, and range
  - Categorical variables are summarized as counts and percentages

Peak Registry baseline demographics [1/2]

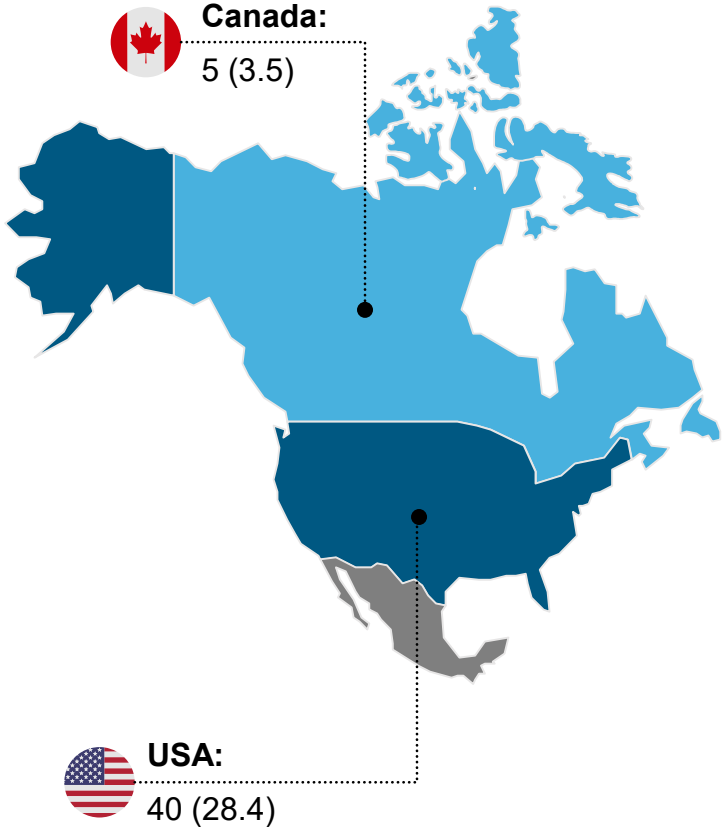
Characteristic	n (%)[a]
Age at enrollment, n	140
y, mean (SD)	25.5 (19.1)
Age group, n	140
≤ 5 y	19 (13.6)
6–11 y	24 (17.1)
12–17 y	13 (9.3)
≥ 18 y	84 (60.0)
Female	78/141 (55.3)
Race, n	113
White	101 (89.4)
Black or African American	3 (2.7)
Asian	7 (6.2)
Other[b]	2 (1.8)
Ethnicity, n	118
Hispanic or Latino	20 (16.9)
Amish	0/106 (0)

- 141 eligible patients enrolled in the Registry as of 24March2020
- 50 patients (35.5%) had completed 2 years of follow-up in the NHS and then moved to the Peak Registry
- 91 patients (64.5%) were newly recruited to the Peak Registry

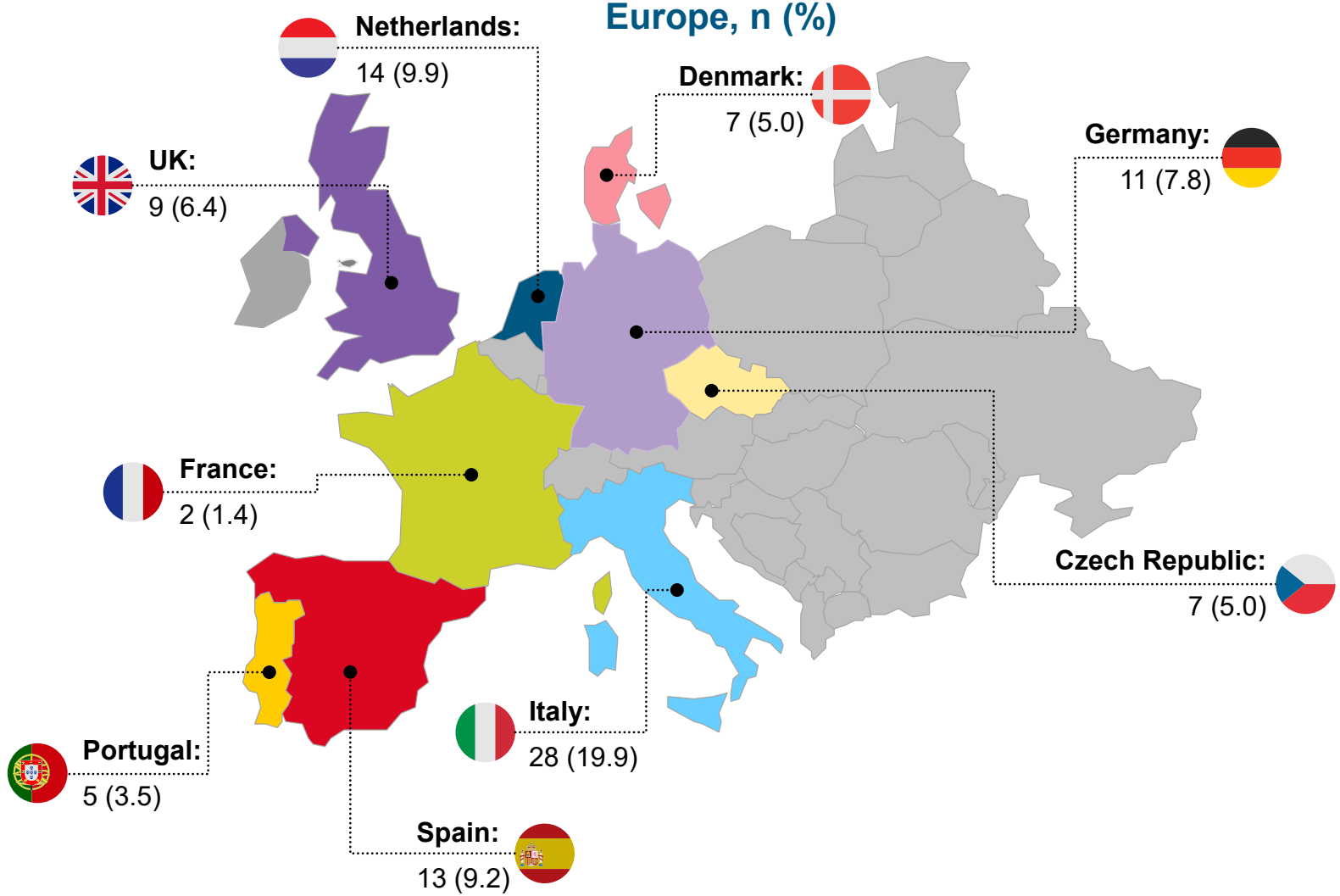
[a]A total of 141 eligible patients were enrolled in the Peak Registry as of 24March2020, however, denominators for some analyses may be smaller due to unknown or incomplete data. [b]One patient was two or more races (unknown); the other was mixed white/Iranian.
NHS = Natural History Study; y = year.

Peak Registry baseline demographics [2/2]

USA and Canada, n (%)



Europe, n (%)



Peak Registry medical history

Parameter	n (%)[a]
Age at first symptoms, n	97
y, mean (SD)	5.8 (13.2)
Age at diagnosis, n	128
y, mean (SD)	11.7 (16.0)
Genotype[b], n	93
Missense/Missense	53 (57.0)
Missense/Non-missense	32 (34.4)
Non-missense/Non-missense	8 (8.6)
History of splenectomy,	61/135 (45.2)
Age at splenectomy, n	57
y, mean (SD)	7.2 (5.2)
History of cholecystectomy	55/133 (41.4)
Ever had chelation therapy	50/124 (40.3)
Ever transfused	99/131 (75.6)
Received any transfusions in 12 months prior to enrollment	45/77 (58.4)
No. of transfusions, mean (SD)	5.1 (4.3)
Received ≥ 6 transfusions[c]	18/45 (40.0)

- Almost half of patients had a splenectomy
- Approximately ¾ of patients had received transfusions in their lifetime
  - Among patients who received ≥ 1 transfusion in the 12 months prior to enrollment, 40% received ≥ 6 transfusions
- Approximately 40% of patients received chelation therapy

[a]A total of 141 eligible patients were enrolled in the Peak Registry as of 24March2020, however, denominators for some analyses may be smaller due to unknown or incomplete data. [b]Genotype classification was determined by expert review. [c]Among patients with ≥1 transfusion during that period.
y = year.

Peak Registry baseline hematological and iron markers

Variable[a]	n[b]	Mean (SD)	Range
Hemoglobin (g/dL)	55	8.9 (1.7)	5.8–12.9
Mean corpuscular volume (fL)	36	103.8 (14.7)	60.0–131.0
Reticulocyte count (%)	18	19.8 (15.5)	2.2–42.4
Indirect bilirubin (mg/dL)	32	4.3 (4.0)	0.8–23.1
Lactate dehydrogenase (IU/L)	16	381.7 (232.1)	135.0–849.0
Ferritin (ng/mL)	27	867.9 (673.1)	78.1–2499.0

- Hemoglobin values varied widely from 5.8–12.9 g/dL
- Of the 27 patients with available ferritin data, 18 patients (66.7%) had elevated levels (> 500 ng/mL) that warranted monitoring for iron overload

[a]All laboratory values represent results at or closest to enrollment date.
[b]A total of 141 eligible patients were enrolled in the Peak Registry as of 24March2020, however, denominators for some analyses may be smaller due to unknown or incomplete data.

Summary

- The Peak Registry population is demographically heterogenous and represents a broad geography
- Patients have a wide range of hemoglobin levels, and iron overload is common
- The substantial rates of splenectomy, cholecystectomy, transfusions, and chelation use are indicative of a high disease and treatment burden in patients with PK deficiency

Data emerging from the Peak Registry will provide rich insight into the patient characteristics, treatment patterns, and burden of disease associated with PK deficiency

PK = pyruvate kinase.

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