# Baseline characteristics by age of a global cohort of patients diagnosed with pyruvate kinase deficiency – a descriptive analysis from the Peak Registry

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Paola Bianchi, BSc, PhD,[1] Eduard J. van Beers, MD,[2] Joan-Lluis Vives Corrons, MD,[3] Bertil Glader, MD, PhD,[4] Andreas Glenthøj, MD,[5] Hitoshi Kanno, MD, PhD,[6] Kevin H. M. Kuo, MD,[7] Carl Lander, RN,[8] D. Mark Layton, MB, BS,[9] Dagmar Pospíšilová, MD,[10] Vip Viprakasit, MD, DPhil,[11] Jean Williams, MPH,[12] Yan Yan, MS,[12] Bryan McGee, PharmD,[12] Rachael F. Grace, MD,[13]

[1]UOC Ematologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Van Creveldkliniek, Department of Internal Medicine, University Medical Center Utrecht, Utrecht, Netherlands; [3]Institute for Leukaemia Research Josep Carreras ENERCA Coordinator, University of Barcelona, Barcelona, Spain; [4]Stanford University School of Medicine, Palo Alto, CA, USA; [5]Department of Hematology, Rigshospitalet, Copenhagen, Denmark; [6]Department of Transfusion Medicine and Cell Processing, Tokyo Women's Medical University, Tokyo, Japan; [7]Division of Hematology, University of Toronto, Toronto, Canada; [8]Metabolic Support UK, Wrexham, Wales; [9]Department of Haematology, Hammersmith Hospital, Imperial College Healthcare NHS Foundation Trust, London, UK; [10]Deparment of Pediatrics, Palacky University and University Hospital, Olomouc, Czech Republic; [11]Siriraj Hospital, Mahidol University, Bangkok, Thailand; [12]Agios Pharmaceuticals, Inc., Cambridge, MA, USA; [13]Dana-Farber/Boston Children's Cancer and Blood Disorder Center, Boston, MA, USA

## BACKGROUND

- Pyruvate kinase (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 adenosine triphosphate (ATP) generation[1]
- Despite current supportive interventions, patients may develop serious complications, such as iron overload, regardless of their age or transfusion history
- Longitudinal data describing the real-world burden of disease among the pediatric population is limited
- 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 between 2018 and 2024

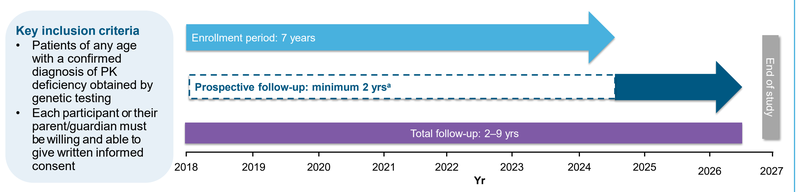
## OBJECTIVE

- This analysis aimed to describe the clinical characteristics and disease management strategies for pediatric (<18 years) and adult (≥18 years) patients with PK deficiency enrolled in the Peak Registry as of March 24, 2020

## METHODS

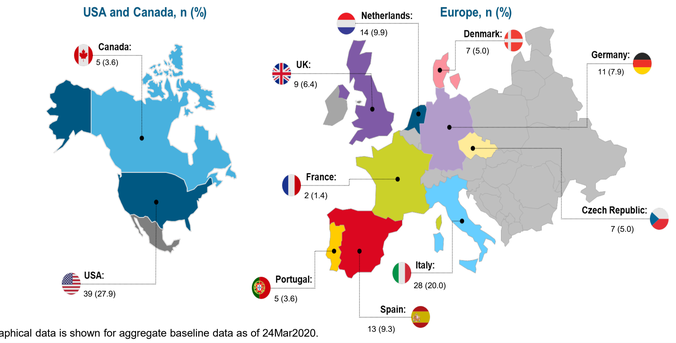
- The Peak Registry is an ongoing, global retrospective and prospective cohort study of adult and pediatric patients diagnosed with PK deficiency
- The study duration and population distribution are shown in **Figures 1 and 2**

### Figure 1. Study duration




[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; Yrs = years.

### Figure 2. Peak Baseline geographic distribution[a]




[a]Geographical data is shown for aggregate baseline data as of 24Mar2020.

- Demographic, medical history, laboratory, and treatment 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 March 24, 2020
- All analyses reported here are descriptive and based on non-missing data as of the time of enrollment in the Peak Registry
  - Continuous variables are summarized by the number of non-missing observations, mean, standard deviation, median, and range
  - Categorical variables are summarized as counts and percentages

## RESULTS

- A total of 140 patients (56 pediatric and 84 adult) were included in this analysis (**Table 1**)
  - 50 (35.7%) of the patients had previously participated in the NHS; the remainder were newly identified for participation in the Peak Registry
- The mean age of participants at enrollment was 7.8 years (SD: 4.6) for the pediatric cohort and 37.4 years (15.5) for adults

### Table 1. Peak Registry baseline demographics

| Characteristic | Overall population: Adult, ≥18 yrs (N = 84) | Overall population: Pediatric, <18 yrs (N = 56) | Pediatric subgroups: 0–5 yrs (N = 19) | Pediatric subgroups: 6–11 yrs (N = 24) | Pediatric subgroups: 12–17 yrs (N = 13) |
|---|---|---|---|---|---|
| **Age at enrollment, N'** | 84 | 56 | 19 | 24 | 13 |
| Mean (SD), yrs | 37.4 (15.5) | 7.8 (4.6) | 2.6 (1.3) | 8.4 (2.1) | 14.0 (1.6) |
| **Female, n/N' (%)** | 48/84 (57.1) | 30/56 (53.6) | 11/19 (57.9) | 11/24 (45.8) | 8/13 (61.5) |
| **Race, N'** | 66 | 46 | 15 | 22 | 9 |
| White, n (%) | 62 (93.9) | 38 (82.6) | 12 (80.0) | 18 (81.8) | 8 (88.9) |
| Black or African American, n (%) | 2 (3.0) | 1 (2.2) | 0 (0) | 1 (4.5) | 0 (0) |
| Asian, n (%) | 2 (3.0) | 5 (10.9) | 2 (13.3) | 2 (9.1) | 1 (11.1) |
| Other[a], n (%) | 0 (0) | 2 (4.3) | 1 (6.7) | 1 (4.5) | 0 (0) |
| **Ethnicity, Hispanic or Latino, n/N (%)** | 9/71 (12.7) | 11/46 (23.9) | 2/15 (13.3) | 4/21 (19.0) | 5/10 (50.0) |

N' represents number of patients with data available.
[a]Other includes patients with mixed races.
SD = standard deviation; Yrs = years.

- In pediatric patients, the higher frequency of splenectomy history with increasing age (0–5 years: 0%; 6–11 years: 52.2%; 12–17 years: 61.5%) coincides with a decrease in the percentage of patients who were regularly transfused (defined as ≥ 6 transfusions within 1 year prior to enrollment): 0–5 years: 46.7%; 6–11 years: 14.3%; 12–17 years: 10.0% (**Table 2**)
- The 6–17 years cohort and the adult cohort had similar frequencies of splenectomy history (55.6% and 51.3%) and regular transfusions (12.9% and 9.4%, **Table 2**)

### Table 2. Peak Registry medical history

| Characteristic | Overall population: Adult, ≥18 yrs (N = 84) | Overall population: Pediatric, <18 yrs (N = 56) | Pediatric subgroups: 0–5 yrs (N = 19) | Pediatric subgroups: 6–11 yrs (N = 24) | Pediatric subgroups: 12–17 yrs (N = 13) |
|---|---|---|---|---|---|
| **Age at diagnosis, N'** | 76 | 51 | 18 | 22 | 11 |
| Median (range), yrs[a] | 16 (0–68) | 1 (-1–11) | 0 (-1–2) | 1.0 (-1–11) | 4 (-1–11) |
| **Genotype, N'** | 65 | 27 | 8 | 11 | 8 |
| Missense/Missense, n (%) | 41 (63.1) | 11 (40.7) | 2 (25.0) | 5 (45.5) | 4 (50.0) |
| Missense/Non-missense, n (%) | 21 (32.3) | 11 (40.7) | 5 (62.5) | 4 (36.4) | 2 (25.0) |
| Non-missense/Non-missense, n (%) | 3 (4.6) | 5 (18.5) | 1 (12.5) | 2 (18.2) | 2 (25.0) |
| **Ever had splenectomy, n/N' (%)** | 41/80 (51.3) | 20/54 (37.0) | 0/18 (0) | 12/23 (52.2) | 8/13 (61.5) |
| **Age at splenectomy, N'** | 38 | 19 | 0 | 12 | 7 |
| Median (range), years | 6 (1–27) | 5 (2–12) | NA | 5 (2–10) | 6 (4–12) |
| **Ever had chelation therapy, n/N' (%)** | 22/72 (30.6) | 28/51 (54.9) | 9/18 (50.0) | 12/22 (54.5) | 7/11 (63.6) |
| **Ever transfused, n/N' (%)** | 48/76 (63.2) | 50/54 (92.6) | 17/18 (94.4) | 22/23 (95.7) | 11/13 (84.6) |
| **Transfusion history over the 12 months prior to enrollment, N'** | 64 | 46 | 15 | 21 | 10 |
| Regularly transfused (≥ 6 transfusions), n (%) | 6 (9.4) | 11 (23.9) | 7 (46.7) | 3 (14.3) | 1 (10.0) |
| # of transfusions, mean (SD) | 9.2 (2.8) | 9.5 (3.1) | 10.0 (3.6) | 8.7 (3.1) | 9.0 (NA) |
| Non-regularly transfused (0–5 transfusions), n (%) | 58 (90.6) | 35 (76.1) | 8 (53.3) | 18 (85.7) | 9 (90.0) |
| # of transfusions, mean (SD) | 0.4 (1.1) | 0.9 (1.5) | 1.1 (1.9) | 1.0 (1.5) | 0.7 (1.3) |

N' represents number of patients with data available.
[a]-1 age at diagnosis denotes 'presumably diagnosed *in utero*'.
NA = non-applicable; SD = standard deviation' Yrs = years.

- The median hemoglobin levels at enrollment were 8.4 g/dL (range: 5.8–12.3 ) in the pediatric cohort and 9.5 g/dL (6.7–12.9) in adults (**Table 3**)
- The median ferritin levels in the pediatric cohort were 772 ng/mL (78–2499) and 404 ng/mL (19–2263) in adults

### Table 3. Peak Registry baseline hematologic and iron markers

| Characteristic | Overall population: Adult, ≥18 yrs (N = 84) | Overall population: Pediatric, <18 yrs (N = 56) | Pediatric subgroups: 0–5 yrs (N = 19) | Pediatric subgroups: 6–11 yrs (N = 24) | Pediatric subgroups: 12–17 yrs (N = 13) |
|---|---|---|---|---|---|
| **Hemoglobin, N'** | 38 | 36 | 12 | 16 | 8 |
| Median (range), g/dL | 9.5 (6.7–12.9) | 8.4 (5.8–12.3) | 8.6 (5.8–12.3) | 8.3 (7.1–10.9) | 8.2 (6.8–11.4) |
| **Percent reticulocyte count, N'** | 17 | 13 | 5 | 6 | 2 |
| Median (range), % | 5.3 (2.6–40.7) | 9.3 (2.2–42.5) | 3.4 (2.2–29.1) | 25.3 (3.6–42.5) | 24.1 (13.4–34.8) |
| **Indirect bilirubin, N'** | 25 | 18 | 6 | 9 | 3 |
| Median (range), mg/dL | 3.3 (0.8–23.1) | 3.1 (1.4–12.0) | 3.4 (1.4–3.9) | 2.9 (1.5–12.0) | 3.9 (2.9–6.2) |
| **Lactate dehydrogenase, N'** | 22 | 12 | 3 | 5 | 4 |
| Median (range), IU/L | 225 (133–849) | 654 (135–2949) | 710 (552–2949) | 568 (206–1551) | 677 (135–1798) |
| **Ferritin, N'[a]** | 26 | 16 | 6 | 6 | 4 |
| Median (range), ng/mL | 404 (19–2263) | 772 (78–2499) | 847 (123–2000) | 430 (78–925) | 1474 (264–2499) |

N' represents number of patients with data available.
[a]Ferritin incudes subject w/o chelation.
Yrs = years.

## RESULTS (CONTINUED)

- Patients aged 12–17 years resemble adult patients with regard to transfusion history and hemoglobin levels when viewed by splenectomy history (**Table 4 and Table 5**)

### Table 4. Peak Registry transfusion history by age and splenectomy status

| Characteristic | Overall population: Adult, ≥18 yrs (N = 84) Splenectomy Yes | Overall population: Adult, ≥18 yrs (N = 84) Splenectomy No | Overall population: Pediatric, <18 yrs (N = 56) Splenectomy Yes | Overall population: Pediatric, <18 yrs (N = 56) Splenectomy No | Pediatric subgroups: 0–5 yrs (N = 19) Splenectomy Yes | Pediatric subgroups: 0–5 yrs (N = 19) Splenectomy No | Pediatric subgroups: 6–11 yrs (N = 24) Splenectomy Yes | Pediatric subgroups: 6–11 yrs (N = 24) Splenectomy No | Pediatric subgroups: 12–17 yrs (N = 13) Splenectomy Yes | Pediatric subgroups: 12–17 yrs (N = 13) Splenectomy No |
|---|---|---|---|---|---|---|---|---|---|---|
| **Available transfusion history 12 months prior to enrollment and known splenectomy history, N'** | 32 | 32 | 17 | 29 | 0 | 15 | 11 | 10 | 6 | 4 |
| Regularly transfused (≥ 6 transfusions), n (%) | 6 (18.8) | 0 | 1 (5.9) | 10 (34.5) | NA | 7 (46.7) | 0 | 3 (30.0) | 1 (16.7) | 0 |
| # of transfusions, mean (SD) | 9.2 (2.8) | NA | 9.0 (NA) | 9.6 (3.3) | NA | 10.0 (3.6) | NA | 8.7 (3.1) | 9.0 (NA) | NA |
| Non-regularly transfused (0–5 transfusions), n (%) | 26 (81.2) | 32 (100) | 16 (94.1) | 19 (65.5) | NA | 8 (53.3) | 11 (100) | 7 (70.0) | 5 (83.3) | 4 (100) |
| # of transfusions, mean (SD) | 0.9 (1.5) | 0.0 (0.2) | 0.9 (1.4) | 0.9 (1.7) | NA | 1.1 (1.9) | 1.2 (1.6) | 0.7 (1.5) | 0.4 (0.6) | 1.0 (2.0) |

N' represents number of patients with data available.
NA = non-applicable; SD = standard deviation' Yrs = years.

### Table 5. Peak Registry baseline hematologic and iron markers by splenectomy status

| Characteristic | Overall population: Adult, ≥18 yrs (N = 84) Splenectomy Yes | Overall population: Adult, ≥18 yrs (N = 84) Splenectomy No | Overall population: Pediatric, <18 yrs (N = 56) Splenectomy Yes | Overall population: Pediatric, <18 yrs (N = 56) Splenectomy No | Pediatric subgroups: 0–5 yrs (N = 19) Splenectomy Yes | Pediatric subgroups: 0–5 yrs (N = 19) Splenectomy No | Pediatric subgroups: 6–11 yrs (N = 24) Splenectomy Yes | Pediatric subgroups: 6–11 yrs (N = 24) Splenectomy No | Pediatric subgroups: 12–17 yrs (N = 13) Splenectomy Yes | Pediatric subgroups: 12–17 yrs (N = 13) Splenectomy No |
|---|---|---|---|---|---|---|---|---|---|---|
| **Hemoglobin, N'** | 21 | 17 | 12 | 24 | 0 | 12 | 7 | 9 | 5 | 3 |
| Median (range), g/dL | 8.5 (6.7, 12.6) | 10.9 (8.3, 12.9) | 7.9 (6.8, 9.2) | 8.6 (5.8, 12.3) | NA | 8.6 (5.8, 12.3) | 7.7 (7.1, 8.9) | 8.5 (7.7, 10.9) | 8.1 (6.8, 9.2) | 10.0 (7.8, 11.4) |
| **Percent reticulocyte count, N'** | 6 | 11 | 4 | 9 | 0 | 5 | 2 | 4 | 2 | 0 |
| Median (range), % | 32.5 (26.6, 40.7) | 4.1 (2.6, 12.9) | 38.6 (13.4, 42.5) | 5.3 (2.2, 41.4) | NA | 3.4 (2.2, 29.1) | 42.5 (42.4, 42.5) | 7.2 (3.6, 41.4) | 24.1 (13.4, 34.8) | NA |
| **Indirect bilirubin, N'** | 11 | 14 | 5 | 13 | 0 | 6 | 3 | 6 | 2 | 1 |
| Median (range), mg/dL | 4.1 (1.5, 23.1) | 2.4 (0.8, 6.3) | 3.9 (2.4, 6.2) | 3.1 (1.4, 12.0) | NA | 3.4 (1.4, 3.9) | 2.9 (2.4, 4.0) | 2.7 (1.5, 12) | 5.1 (3.9, 6.2) | 2.9 (2.9, 2.9) |
| **Lactate dehydrogenase, N'** | 11 | 11 | 2 | 10 | 0 | 3 | 1 | 4 | 1 | 3 |
| Median (range), IU/L | 228 (153, 478) | 197 (133, 849) | 171 (135, 206) | 719 (347, 2949) | NA | 710 (552, 2949) | 206 (206, 206) | 648 (347, 1551) | 135 (135, 135) | 756 (598, 1798) |
| **Ferritin, N'[a]** | 11 | 15 | 7 | 9 | 0 | 6 | 3 | 3 | 4 | 0 |
| Median (range), ng/mL | 862 (150, 2263) | 304 (19, 706) | 714 (180, 2499) | 829 (78, 2000) | NA | 847 (123, 2000) | 681 (180, 714) | 164 (78, 925) | 1474 (264, 2499) | NA |

N' represents number of patients with data available; [a]Ferritin incudes subject w/o chelation.
NA = not applicable; Yrs = years.

## CONCLUSIONS

- **This analysis provides early insight into the disease and treatment experience for pediatric patients with PK deficiency**
  - **Our data indicate that complications in patients with PK deficiency start early on**
  - **Pediatric patients experience significant anemia, transfusion burden, and chelation before the age of 6 years; the design of the Peak Registry will allow for longitudinal data collection in this young cohort of patients**
- **The decrease in regular transfusions with increasing age in pediatric patients coincides with an increased frequency of splenectomy history, possibly reflecting the impact of splenectomy on partially ameliorating the anemia in PK deficiency**
- **However, despite the high rate of splenectomy in this cohort, many children and adults continue to have substantial anemia and disease burden**

**Data emerging from the Peak Registry will continue to inform our understanding of PK deficiency, and the differences in disease characteristics and treatment patterns by age groups over time**

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