The Assessment of the Treatment and Management Landscape of Phenylketonuria Survey Study: Findings from 19 Clinics in the United States

P045

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Background

- Phenylketonuria (PKU) is an autosomal recessive disorder of amino acid metabolism characterized by chronic elevations of blood phenylalanine (Phe) that can lead to neuropsychological and cognitive impairment[1,2]
- Lifelong management with medical nutrition therapy (MNT) or pharmacological treatments is needed to maintain recommended blood Phe levels and to manage PKU-associated symptoms
- In 2015, a survey of medical professionals from PKU clinics in the US was conducted to assess management practices, including metrics of blood Phe levels and testing frequency, patient adherence to clinic recommendations, and clinic staffing[3]
  - Since the 2015 survey, the US Food & Drug Administration approved pegvaliase as an additional pharmacological treatment option for adults with PKU with blood Phe >600 µmol/L (May 2018)[4]
- To date, it is unclear how the treatment landscape has evolved since the introduction of pegvaliase, and an updated assessment of current management practices is needed
- The objective of the Assessment of the Treatment and management LAndScape of phenylketonuria (ATLAS) survey study was to evaluate contemporary PKU treatment and management practices, including:
  - Healthcare professional (HCP) experience of patient adherence to PKU treatment management plans
  - Use of quality of life (QoL) questionnaires and neurocognitive assessments for management of patients with PKU

Methods

- **Study design:** A global web-based survey of HCPs who treat patients with PKU was conducted in 8 countries between December 2022 and July 2024; results from the US are presented here
- **Site eligibility:** Eligible clinics were those managing at least 10 active patients with PKU; patients were defined as active if they were seen by the clinic virtually or in person at least once in the past 3 years
  - Eligible sites were approached for participation in the survey, and 1 HCP from each site was invited to participate
- **HCP eligibility:** Eligible HCPs were those who managed patients with PKU at eligible clinics, had access to the clinic's patient database or medical charts, and provided informed consent to participate in the survey
- **Data collection:**
  - A web-enabled survey captured data on current PKU treatment and management practices at each site
  - To complete the survey, HCPs were instructed to collate information from the clinic's patient database or medical charts and operating procedures/clinical guidelines, and to consult with clinic members to provide accurate answers
  - Patient information was summarized in aggregate to respond to questions, where applicable; therefore, no individual patient-level data were collected
  - Each site was asked to complete the survey within 4 weeks after receipt of all required local approvals

Results

Clinic characteristics

- 19 clinics in the US participated in the ATLAS survey; median length of experience managing patients with PKU at participating clinics was 40 years
- Clinics had a median of 2 full-time equivalent (FTE) physicians, 1.5 FTE dietitians, 1 FTE nurse/nurse practitioner, 1 FTE genetic counselor, and <1 FTE social worker
- The median number of patients with PKU being managed per clinic was 86

	Participating clinics (N=19)
Years managing patients with PKU	
Mean (SD)	37.6 (14.3)
Median (min, max)	40 (10, 60)
Clinic location (US region), n (%)	
Northeast	4 (21.1)
North Central	4 (21.1)
South	5 (26.3)
West	6 (31.6)
Provider FTE per clinic, median (min, max)	
Physician	2 (0.0, 4.3)
Dietitian	1.5 (0.0, 6.0)
Social worker	0.2 (0.0, 1.0)
Psychologist/neuropsychologist/psychiatrist	0 (0.0, 1.0)
Nurse/nurse practitioner	1 (0.0, 2.5)
Genetic counselor	1 (0.0, 6.0)
Number of patients with PKU per clinic	
Mean (SD)	141.1 (96.1)
Median (min, max)	86 (45, 339)
Number of actively managed patients with PKU per clinic*	
Mean (SD)	125.7 (78.6)
Median (min, max)	86 (41, 280)

*Defined as patients seen by the clinic (in person or virtually) at least once within the past 3 years
FTE, full-time equivalent; max, maximum; min, minimum; PKU, phenylketonuria; SD, standard deviation

QoL and neurocognitive testing

- 2 of 19 clinics (10.5%) routinely administer QoL questionnaires to support management of patients
  - Questionnaires administered included the PKU-QoL, which was reportedly administered once a year or less than once a year by each clinic
- 3 of 19 clinics (15.8%) routinely administered neurocognitive assessments to support management of PKU patients
  - Questionnaires administered included: Attention Deficit Hyperactivity Disorder Rating Scale-IV (ADHD RS-IV), Behavior Rating Inventory of Executive Function (BRIEF), and Conners' Adult ADHD Rating Scales (CAARS)
  - 2 of 3 clinics reported administering these questionnaires once a year

Patient characteristics

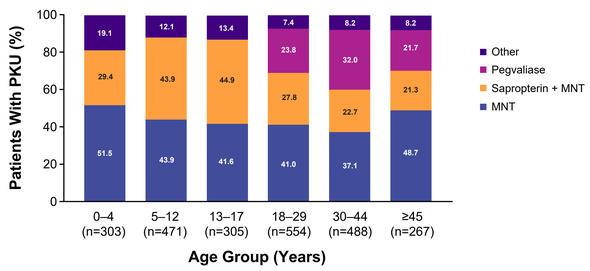
- 89.1% of patients with PKU at participating study sites were actively managed
- Just over half of actively managed patients were female (52.1%) and were adults aged ≥18 years (54.8%)

	Patients
Patients with PKU	2681
Actively managed patients with PKU, n (%)	2388 (89.1)
Sex, n (%)*	
Female	1245 (52.1)
Male	1143 (47.9)
Age categories, n (%)*	
0–4 years	303 (12.7)
5–12 years	471 (19.7)
13–17 years	305 (12.8)
18–29 years	554 (23.2)
30–44 years	488 (20.4)
≥45 years	267 (11.2)

*Percentage of actively managed patients. Actively managed patients were defined as patients seen by the clinic (in person or virtually) at least once within the past 3 years
PKU, phenylketonuria

PKU treatment by age

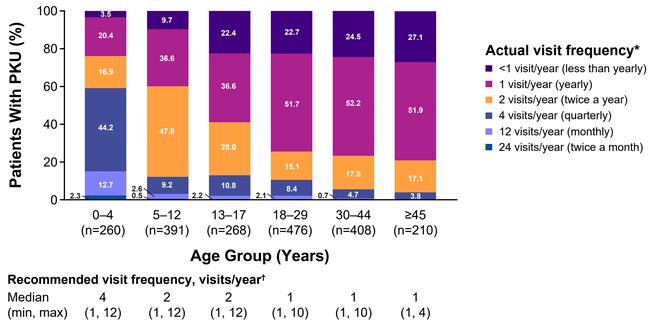
- Overall, 986 actively managed patients (41.3%) were treated with MNT alone, 781 (32.7%) with sapropterin (+ MNT), and 372 (15.6%) with pegvaliase
- The age group with the highest proportion of patients treated with pegvaliase was 30–44 years (32.0%)



Notes: Nearly all participating PKU clinics (94.7%, or 18 of 19 sites) prescribed pegvaliase. Figure shows data for actively managed patients (N=2388)
MNT, medical nutrition therapy; PKU, phenylketonuria

Frequency of clinic visits

- 17 of 19 clinics (89.5%) had a recommendation for the number of clinic visits per year for patients with PKU
- The distribution of actual patient visit frequencies by age group is shown
- Visit frequency was highest in younger ages (monthly or quarterly) and decreased with increasing age (≤1 per year for adults)
- The majority of patients (for all age groups) attended clinic at a frequency in accordance with recommendations



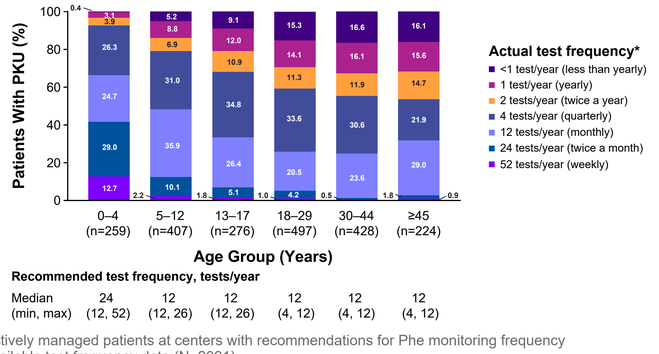
Recommended visit frequency, visits/year†

	0–4 (n=260)	5–12 (n=391)	13–17 (n=268)	18–29 (n=476)	30–44 (n=408)	≥45 (n=210)
Median (min, max)	4 (1, 12)	2 (1, 12)	2 (1, 12)	1 (1, 10)	1 (1, 10)	1 (1, 4)

*For actively managed patients at centers with recommendations for visit frequency with available visit frequency data (N=2064); †At centers with recommendations for visit frequency (n=17)
max, maximum; min, minimum; PKU, phenylketonuria

Frequency of Phe monitoring

- All 19 clinics had a recommendation for blood Phe testing frequency
- Generally, Phe testing frequency was seen to decrease with increasing age
- Approximately one-quarter of adults (aged ≥18 years) were being tested monthly or more often; most patients aged >4 years did not have Phe levels tested at the recommended frequency



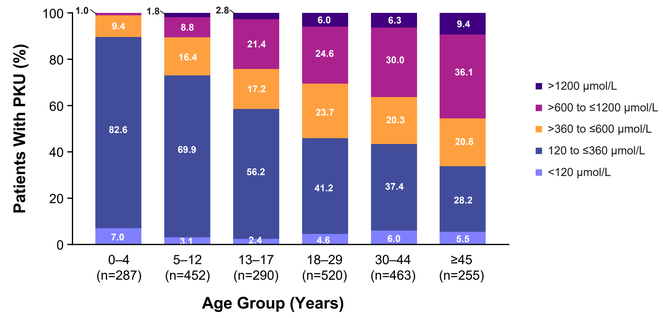
Recommended test frequency, tests/year

	0–4 (n=259)	5–12 (n=407)	13–17 (n=276)	18–29 (n=497)	30–44 (n=428)	≥45 (n=224)
Median (min, max)	24 (12, 52)	12 (12, 26)	12 (12, 26)	12 (4, 12)	12 (4, 12)	12 (4, 12)

*For actively managed patients at centers with recommendations for Phe monitoring frequency with available test frequency data (N=2091)
max, maximum; min, minimum; Phe, phenylalanine; PKU, phenylketonuria

Blood Phe levels

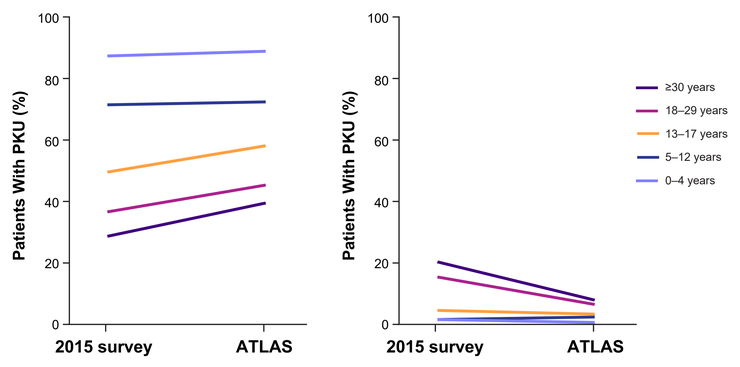
- As recommended by the American College of Medical Genetics and Genomics, the target for blood Phe levels during the study period was 120–360 µmol/L, recently updated to ≤360 µmol/L[5]
- Among actively managed patients with available blood Phe data:
  - Achievement of blood Phe levels ≤360 µmol/L was highest in those aged 0–4 years (89.5%) and declined with increasing age to only 33.7% in those aged ≥45 years
  - The percentage of patients with Phe levels >1200 µmol/L was 0% for those aged 0–4 years and increased with age to 9.4% for those aged ≥45 years



Note: Figure shows data for actively managed patients with available blood Phe data (N=2267)
Phe, phenylalanine; PKU, phenylketonuria

Comparisons of ATLAS survey with 2015 survey[3]

- The ATLAS study results reflect clinical practice over the period 2022–2024
- Comparisons between the 2 studies show:
  - Blood Phe levels remained similar in patients aged ≤12 years from 2015 (pre-pegvaliase introduction) to 2022–2024 (post-pegvaliase introduction)
  - The proportion of patients aged >12 years achieving blood Phe levels ≤360 µmol/L has increased since 2015, while the proportion of adult patients with blood Phe levels >1200 µmol/L has declined



ATLAS, Assessment of the Treatment and management LAndScape; Phe, phenylalanine; PKU, phenylketonuria

Conclusions

- The ATLAS study shows a shift in the treatment landscape and patient achievement of target blood Phe levels in a sample of 19 US PKU clinics
- Few clinics administered QoL and neurocognitive assessments, which may reflect the limited availability of support to clinics by social workers, psychologists, and psychiatrists
- Frequency of clinic attendance and blood Phe monitoring was highest in younger ages and decreased with increasing age; similarly, achievement of recommended blood Phe targets was highest in younger ages and decreased with increasing age
- Comparisons between the ATLAS results and the 2015 survey[3] show an increase in the proportion of adults who achieved blood Phe levels ≤360 µmol/L and a decline in the proportion with blood Phe levels >1200 µmol/L
  - Improvements in blood Phe levels may be explained, at least in part, by the availability of pegvaliase as an additional treatment option

References

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