Starting the conversation on gene therapy for phenylketonuria: Current perspectives of patients, caregivers, and advocates

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Background

- Phenylketonuria (PKU) is a rare genetic disorder characterized by inborn error(s) in the gene encoding phenylalanine hydroxylase (PAH) resulting in phenylalanine (Phe) accumulation in the blood and brain, leading to progressive neurocognitive impairment.
- Conventional treatment of PKU requires a strict, lifelong regimen of dietary therapy and medical supplements to minimize Phe intake, impeding a lifelong burden of management on patients and caregivers.
- Novel investigational therapies aiming to address the underlying cause of PKU are in clinical development, among which are gene therapy technologies.
- Despite investigation into its use as a treatment modality in PKU, perceptions of gene therapy have not been assessed in the PKU community.
- This study aimed to qualitatively evaluate existing knowledge and perceptions of gene therapy in members of the PKU community in Europe and the US, and to identify educational gaps on the topic for this audience.

Methods

- Patients, caregivers, and patient advocates were recruited for interviews in the US, Ireland, Germany, and Spain (Figure 1).
- Interviews were conducted via telephone, and followed a discussion guide which aimed to assess participants’ perceptions of living with PKU, as well as their knowledge and perception of gene therapy for PKU before and after provision of an educational primer consisting of a short document covering information about gene therapy.

Figure 1. Screening for patient, caregiver, and advocate participants

RESULTS

- A total of 33 participants were recruited to the study (Table 1).
- The patient group (n=24) was well balanced between male and female caregivers and younger and older age groups (age 18-29 years and 30-55 years, respectively).
- 50% of patients (n=12) reported experience with prescription medications, most of whom were based in the US (n=10/12).

Table 1. Participant baseline characteristics

<table>
<thead>
<tr>
<th>Age group, n (%)</th>
<th>Patients (n=24)</th>
<th>Caregivers (n=9)</th>
<th>Patient advocates (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-29</td>
<td>12 (50)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>30-55</td>
<td>12 (50)</td>
<td>2 (40)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>55+</td>
<td>0 (0)</td>
<td>2 (40)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Not stated</td>
<td>0 (0)</td>
<td>1 (20)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>Male</td>
<td>11 (46)</td>
<td>3 (60)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>13 (54)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Not stated</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Geography, n (%)</td>
<td>US</td>
<td>12 (50)</td>
<td>2 (40)</td>
</tr>
<tr>
<td></td>
<td>EU</td>
<td>12 (50)</td>
<td>3 (60)</td>
</tr>
</tbody>
</table>

- Participants had PKU (i.e., a phenotype or patients whose caregivers provided care but were not themselves to be assessed managing their condition) if they reported using prescription PKU medications, dietary therapy or special supplements, and/or regularly testing serum Phe levels.

Living with PKU

- Patients and caregivers reported predominantly negative perceptions of living with PKU (Figure 2), but with some positive emotions linked to sense of personal responsibility and strength and hope for future treatments.

Figure 2. Word cloud of patient and caregiver responses to “What are 3 words that describe how living living for someone with PKU makes you feel emotionally?” and supporting quotes

- “A feeling of difference or being out of the odd one out”
- “Frustrated because it requires that extra level of thought and it can’t be ‘normal’ and just go out with my friends”

Conclusions

- The burden of managing and living with PKU among patients and caregivers was consistent with previous reports in the literature, including frustrations with current treatments.
- The majority of participants in this study showed moderate or high knowledge of gene therapy, but educational gaps and trends in perception of gene therapy demonstrate the need for education around the theoretical risk/benefit profile of gene therapy.
- Despite current unknowns around gene therapy, this study demonstrates the important role of health care professionals as educators who can use available data to provide balanced information to patients and caregivers using patient-friendly language.

Disclosures

- Hilf has acted as a paid consultant for Sobi AB pharmaceutical companies. Hilf, Nisula, and Sloboda have received speaker fees from Biogen, Genzyme, and Sobi. Nisula has received speaker fees from Biogen, Genzyme, and Sobi. Sloboda has received speaker fees from Biogen. The other authors declare no competing interests.

Acknowledgments

The authors thank the participants of the study. Study interviews were conducted by the PHENOMA research group (Philadelphia, USA; London, UK). Editorial assistance in the development of the paper was provided by Adelphi Communications USA, LLC, sponsored by Biogen.

Funding

- Sobi AB pharmaceutical companies provided funding for the study, data analysis, writing, editing, and poster production.

References


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Background

- Phenylketonuria (PKU) is a rare genetic disorder characterized by inborn error(s) in the gene encoding phenylalanine hydroxylase (PAH) resulting in phenylalanine (Phe) accumulation in the blood and brain, leading to progressive neurocognitive impairment.

- Conventional management of PKU requires a strict lifelong regimen of dietary therapy and medical supplements to minimize Phe intake, imparting a lifelong burden of management on patients and caregivers.

- Novel investigational therapeutics aiming to address the underlying cause of PKU are in clinical development, among which are gene therapy technologies.

- Despite investigation into its use as a treatment modality in PKU, perceptions of gene therapy have not been assessed within the PKU community.

- This study aimed to qualitatively evaluate existing knowledge and perceptions of gene therapy in members of the PKU community in Europe and the US, and to identify educational gaps on the topic for this audience.

Methods

- Patients, caregivers, and patient advocates were recruited for interviews in the US, Ireland, Germany, and Spain (Figure 1).

- Interviews were conducted via telephone, and followed a discussion guide which aimed to assess participants’ perceptions of living with PKU, as well as their knowledge and perception of gene therapy for PKU before and after provision of an educational primer consisting of a short document covering information about gene therapy.

Figure 1. Screening for patient, caregiver, and advocate participants.

RESULTS 2/3

Knowledge of gene therapy in PKU

- Most participants reported moderate-to-high baseline knowledge of gene therapy in PKU (Table 2).

Table 2. Participant characteristics by interviewer-assessed baseline level of gene therapy knowledge

<table>
<thead>
<tr>
<th>Level* (n=5)</th>
<th>Low+ (n=10)</th>
<th>Moderate (n=16)</th>
<th>High* (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identity, n (%)</td>
<td>Patient</td>
<td>5 (100)</td>
<td>10 (56)</td>
</tr>
<tr>
<td></td>
<td>Caregiver</td>
<td>0 (0)</td>
<td>5 (28)</td>
</tr>
<tr>
<td></td>
<td>Patient advocate</td>
<td>0 (0)</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Age group, n (%)</td>
<td>18–29</td>
<td>3 (60)</td>
<td>4 (22)</td>
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<tr>
<td></td>
<td>30–55</td>
<td>2 (40)</td>
<td>8 (44)</td>
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<tr>
<td></td>
<td>55+</td>
<td>0 (0)</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Not stated</td>
<td>0 (0)</td>
<td>4 (22)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>Male</td>
<td>2 (40)</td>
<td>7 (39)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>3 (60)</td>
<td>9 (51)</td>
</tr>
<tr>
<td>Not stated</td>
<td>0 (0)</td>
<td>2 (11)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Geography, n (%)</td>
<td>US</td>
<td>1 (20)</td>
<td>10 (56)</td>
</tr>
<tr>
<td></td>
<td>EU*</td>
<td>4 (80)</td>
<td>8 (44)</td>
</tr>
</tbody>
</table>

*Notified as knowledgeable or with knowledge of gene therapy.
+Notified as unaware of gene therapy or as uncertain and did not have a regular regimen for PKU.
+Notified as existing knowledge of gene therapy exclusively via seeking, gene editing, or CureMP3.

Both positive and negative perceptions of gene therapy were expressed at baseline (Figure 3), which tended to group according to level of knowledge.

Figure 3. Participant quotes expressing perceptions of gene therapy for PKU at baseline

Conclusions

- The burden of managing and living with PKU among patients and caregivers was consistent with previous reports in the literature, including frustrations with current treatments.

- The majority of participants in this study showed moderate or high knowledge of gene therapy, but educational gaps and trends in perception of gene therapy demonstrate the need for education around the theoretical risk/benefit profile of gene therapy.

- Despite current unknowns around gene therapy, this study demonstrates the important role of health care professionals as educators who can use available data to provide balanced information to patients and caregivers using patient-friendly language.

Disclosures

- All authors acted as a paid consultant for BiogeniX Pharmaceuticals Inc., Horizon, Kuliak, and Uhtioke, and have received speaker fees from BiogeniX, Cominco Therapeutics, Uhtioke, and Waltho International Ltd.

Acknowledgments

- The authors thank the participants of the study. Study interviews were conducted by THE PLANNING SHOP or Adhikari group company (Philadelphia, US, London, UK). Editorial assistance in the development of the paper was provided by Adhikari Communications Ltd, UK, sponsored by BiogeniX.

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- BiogeniX Pharmaceuticals Inc. provided funding for the study, data analysis, writing, editing, and paper production.

References


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• Conventional management of PKU requires a strict, lifelong regimen of dietary therapy and medical supplements to minimize Phe intake, imparting a lifelong burden of management on patients and caregivers6–9
• Novel investigational therapies aiming to address the underlying cause of PKU are in clinical development, among which are gene therapy technologies10
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Figure 1. Screening for patient, caregiver, and advocate participants

RESULTS 3/3

Knowledge of gene therapy in PKU

• Participants with low baseline knowledge were more likely to express low levels of concern and predominantly positive perceptions of gene therapy, whereas those with high knowledge were more likely to express higher levels of concern and negative perceptions (Figure 4)
• After reading the educational primer, greater levels of concern or mixed emotions were observed

Figure 4. Participants’ level of concern and perceptions on gene therapy for PKU by baseline level of gene therapy knowledge

Insights into educational gaps around gene therapy in PKU

• Participants’ experiences and feedback on the gene therapy educational primer indicated some key knowledge gaps and potential learnings that could inform future education on this topic (Figure 5)

Figure 5. Educational gaps and learnings for medical education around gene therapy in PKU: Themes and illustrative patient quotes

Conclusions

• The burden of managing and living with PKU among patients and caregivers was consistent with previous reports in the literature, including frustrations with current treatments
• The majority of participants in this study showed moderate or high knowledge of gene therapy, but educational gaps and trends in perception of gene therapy demonstrate the need for education around the theoretical risk/benefit profile of gene therapy
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Disclosures

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References


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