Introduction to Odyssey: Real-world rare disease data collection program from digitized health records for patients with long-chain fatty acid oxidation disorders (LC-FAOD) in the United States

Eliza Kruger, MEdCon1; Eray Yang, MS2; Bridget Reinkeing, MS, RD1; Nina Thomas, MPH2
Kieran Mace, PhD2; Megan Tierney, PhD, RN2; Emily Cibelli, PhD1; Dan Drozd, MD, MS1; Nathan Ross3; Amy Kritzer, MD4
1Ultragenyx Pharmaceutical Inc, Novato, CA, USA; 2PlainsHealth, San Francisco, CA, USA; 3Division of Genetics and Genomics, Boston Children’s Hospital, Boston, MA, USA

BACKGROUND

Introduction

- LC-FAOD are a group of rare genetic disorders stemming from inborn errors of metabolism.
- These chronic diseases present across a broad clinical spectrum, punctuated by episodes of acute, life-threatening metabolic decompensation.
- Data are limited for real-world LC-FAOD management and outcomes.

The LC-FAOD Odyssey Program is a central IRB-approved research study from Ultragenyx Pharmaceutical and PlainsHealth, a digital health company, to better understand LC-FAOD.

Odyssey uses a novel patient-centered design to collect prospective and retrospective data on the real-world impact of LC-FAOD, and prospective data of patient- and caregiver-reported outcomes (PROs).

Study Eligibility

- Patients must have an LC-FAOD diagnosis, living in the U.S., and who remained care in the U.S. in the past 7 years is eligible to join this study.
- Caregivers can enroll those under the age of 15 years.
- Additional assess is required for participants 7 to 17 years old.

All types of LC-FAOD are eligible, including:
- CPT II (carnitine palmitoyltransferase II)
- CACT (carnitine-acylcarnitine translocase)
- LCHAD (long-chain 3-hydroxyacyl-CoA dehydrogenase)
- VLCAD (very long-chain acyl-CoA dehydrogenase)
- MCT (medium-chain triglyceride)
- CPT I (carnitine palmitoyltransferase I)
- TIPPC (familial tyrosinemia)
- LHAD (long-chain 3-hydroxyacyl-CoA dehydrogenase)

Study population:
- 33 patients with LC-FAOD enrolled from August 2020 – August 2021.
- Initial retrospective medical records are available for 13 patients (Table 1).
- All types of LC-FAOD are eligible, including:
- CPT II (carnitine palmitoyltransferase II)
- CACT (carnitine-acylcarnitine translocase)
- LCHAD (long-chain 3-hydroxyacyl-CoA dehydrogenase)
- VLCAD (very long-chain acyl-CoA dehydrogenase)
- MCT (medium-chain triglyceride)
- CPT I (carnitine palmitoyltransferase I)
- TIPPC (familial tyrosinemia)
- LHAD (long-chain 3-hydroxyacyl-CoA dehydrogenase)

Table 1: Retrospective Records Patient Characteristics (N = 13)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>5 (38%)</td>
</tr>
<tr>
<td>Male</td>
<td>8 (62%)</td>
</tr>
<tr>
<td>Age at Onboarding</td>
<td>16 (12.5)</td>
</tr>
<tr>
<td>Years of Data</td>
<td>7.8 (2.2, 12.4)</td>
</tr>
<tr>
<td>Number of Providers</td>
<td>12 (9.2)</td>
</tr>
<tr>
<td>Number of Care Sites</td>
<td>6.0 (3.0, 9.0)</td>
</tr>
<tr>
<td>Number of Visits</td>
<td>28 (16, 96)</td>
</tr>
<tr>
<td>Number of Outpatient Visits</td>
<td>25 (15, 74)</td>
</tr>
<tr>
<td>Number of ER Visits</td>
<td>1.0 (0.0, 6.0)</td>
</tr>
<tr>
<td>Number of Hospitalizations</td>
<td>3.1 (1.1)</td>
</tr>
<tr>
<td>Total Hospital Days</td>
<td>8.1 (1.15)</td>
</tr>
<tr>
<td>Hospitalizations/Year</td>
<td>0.9 (0.0, 1.07)</td>
</tr>
<tr>
<td>Hospitalization Days/Year</td>
<td>0.7 (0.2, 1.85)</td>
</tr>
</tbody>
</table>

LC-FAOD Management

- Of 18 patients with PROs, 8 take triheptanoin and 7 take MCT currently (Figure 3).

RESULTS

Dosing and Fasting

- 10 patients reported their MCT and triheptanoin doses (actual and prescribed doses), which was converted to percentage DCI to enable comparison across ages and treatment modalities.
- Average prescribed percentage DCI for MCT patients (n = 4) was 20.5% (range: 8.6%–43.3%) and actual consumption was 17.6% (Range: 8.6%–38.5%).
- Triheptanoin patients (n = 8) reported average prescribed and average actual percentage DCI of 27.2% (range: 8.3%–36.4%) and 23.9% (range: 3.8%–30.3%), respectively.

Fasting Intervals

- A total of 10 patients (4 adults) reported their fasting intervals.
- Most patients (80%) reported a fasting interval of 8 hours.
- The weighted average for all patient’s fasting interval was 7.75 hours.
- 8.25 hours for pediatrics (median: 8; range: 4–10) and 7 hours for adults (median: 8; range: 4–10).
- Average fasting interval for triheptanoin treated patients (n = 4) and MCT patients (n = 4) were both 7.5 hours (median: 8; range: 4–10).

CONCLUSIONS

- Preliminary results from Odyssey demonstrate the utility of linking patients’ longitudinal medical records and patient reported outcomes:
  - Data can be extracted across U.S. care providers to derive meaningful data.
  - LC-FAOD care is complex, with multiple procedures, care sites, and management strategies.
  - Future real-world LC-FAOD research will investigate outcomes of diagnostic, burden of illness, disease course and progression, treatment effectiveness, disease management, and unmet patient needs.
  - Additional enrollment will provide a larger real-world dataset for LC-FAOD researchers to use in understanding treatment patterns, their effectiveness, and understanding differences in outcomes.

- Greater sample size may enable comparison between types of LC-FAOD.
- Researchers will be able to access anonymized data from LC-FAOD Odyssey through PicnicHealth to further research efforts.
- Published results will be shared directly with patients enrolled in the study.

As data continue to mature, Odyssey will advance LC-FAOD research in a multi-phased approach over the next two years.

Future analyses (pending sample size): Clinical manifestations by type, outcomes by treatment status

REFERENCES

10. Published results will be shared directly with patients enrolled in the study.