AAV8-mediated Liver-directed Gene Therapy as a Potential Therapeutic Option in Adults with Glycogen Storage Disease Type Ia: Interim Results From a Phase 1/2 Clinical Trial

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BACKGROUND

Glycogen Storage Disease Ia (GSDIa) – A metabolic disorder caused by a deficiency of the enzyme glucose-6-phosphatase (G6Pase), which catalyzes the hydrolysis of glucose 6-phosphate (G6P) to glucose and inorganic phosphate, leading to hyperglycemia during fasting. The primary treatment is a severe restriction of cornstarch intake and the use of corticosteroids.

RESULTS – COHORTS 1, 2, AND 3

Cohort 1: 15.1 x 1012 GC/kg (Nov 2018; prophylactic steroids)
Cohort 2: 6.0 x 1012 GC/kg (Jan 2019)
Cohort 3: 6.0 x 1012 GC/kg (Feb 2019; optimized reactive treatment with prednisone)
Cohort 4: 6.0 x 1012 GC/kg (Nov 2020; prophylactic steroids)

METHODS

A Phase 1/2 Global, Open-label, Dose Escalation Trial of DTX401 in Adult GSDIa Patients

Figure 4. All Patients Reduced Cornstarch Therapy While Maintaining or Improving Time in Euglycemia

Impact on Quality of Life

Patients reported through Week 52 exit interviews:
- Improved energy and stamina
- Better mental clarity
- Improved mood
- Increased ability to participate in social events

Figure 3. Day +4 After DTX401 Dose in Patient 9

Baseline Demographics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender</th>
<th>Genotype</th>
<th>BMI</th>
<th>Cornstarch Intake</th>
<th>Time to Hypoglycemia</th>
<th>Mean Cornstarch</th>
<th>Time in Euglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>Male</td>
<td>c.79del</td>
<td>25</td>
<td>720 gm</td>
<td>120 min</td>
<td>220 gm</td>
<td>10 h</td>
</tr>
<tr>
<td>35</td>
<td>Female</td>
<td>c.1039C&gt;T</td>
<td>24</td>
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<td>90 min</td>
<td>180 gm</td>
<td>8 h</td>
</tr>
<tr>
<td>40</td>
<td>Male</td>
<td>c.379_380dup</td>
<td>28</td>
<td>500 gm</td>
<td>60 min</td>
<td>150 gm</td>
<td>6 h</td>
</tr>
</tbody>
</table>

ADVERSE EVENTS

All Adverse Events Were Grade 1 (Mild) or Grade 2 (Moderate)

- No serious or life-threatening adverse events were reported
- No drug-related serious adverse events were reported
- No deaths were reported

CONCLUSIONS

A reduction of 75% in cornstarch intake resulted in Patient 3 requiring only one box of cornstarch on a 10-day trip rather than a suitcase full of cornstarch.

The average adult requires 300 to 350 grams of cornstarch per day to maintain euglycemia.

All patients showed decreased cornstarch needs: at Week 52, overall mean cornstarch reduction was 77% compared with baseline (p<0.0001).

- Patients in Cohort 2 had significant reductions in total daily cornstarch intake and euglycemia increased.

All adverse events were grade 1 or 2.

All adverse events were grade 1 or 2.

- No serious or life-threatening adverse events were reported
- No deaths were reported

REFERENCES


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Study Coordinators / Research Team

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All authors listed themselves as authors and made substantive contributions.

DISCLOSURES

- All authors listed themselves as authors and made substantive contributions.
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