BACKGROUND & IMPORTANCE

- Spinal Muscular Atrophy (SMA) is an autosomal recessive neurodegenerative disorder, with an incidence of approximately 1 in 10,000 newborns.
- Depending on the symptoms severity and age of onset, SMA is divided into different phenotypes. SMA I phenotype is one of the most severe, and SMA I infants have a lifespan of <2 years if not treated.
- Zolgensma® is an innovative drug of gene therapy and one strategy for SMA patients. However, there remains considerable uncertainty in the long-term sustainability of Zolgensma® clinical effect.

AIM & OBJECTIVES

- Our study aims to provide a critical review of the literature regarding the clinical outcomes in SMA infants in the real-world setting after the one-time Zolgensma® dosing.

MATERIAL & METHODS

- A review of the literature was constructed, comprising 5 phases: (a) identifying the research question; (b) searching for relevant studies; (c) selecting studies; (d) analyzing data; and (e) presenting results. Data was collected and analyzed until May 2021.

RESULTS

Two real-world studies analyzing Zolgensma® effectiveness were identified:

I. Prospective Long-Term Follow-Up (LT FU) study (13 patients):
- 100% of SMA I infants in the therapeutic-dose cohort were alive and free of permanent ventilation (>5 years after Zolgensma® GRT one-time dosing);
- 20% of SMA I infants achieved the additional milestone of standing with assistance (>5 years after Zolgensma® GRT one-time dosing);
- SMA I infants improved their Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) scores (≥4 points).

II. Retrospective cohort study of SMA I (3 patients) and SMA II infants (4 patients):
- 43% of SMA patients had meaningful increases in the CHOP-INTEND score;
- 57% had increases in the Hammersmith Functional Motor Scale-Expanded (HFMSE) score (Table 1).

CONCLUSIONS & RELEVANCE

- Despite the limited observation period and considering the available data, we conclude that Zolgensma® is effective in SMA I pediatric patients since no clinical regression or waning of effect had been reported.

Table 1: Functional Outcomes and Motor Milestone Acquisition Observed in SMA Infants from the Retrospective Cohort Study.

<table>
<thead>
<tr>
<th>PATIENT</th>
<th>BASELINE CHOP-INTEND (HFMSE)</th>
<th>3 MONTHS CHOP-INTEND (HFMSE)</th>
<th>12 MONTHS CHOP-INTEND (HFMSE)</th>
<th>NEW MOTOR MILESTONES ACHIEVED</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>33</td>
<td>Standing, Crawling, Walking Independently</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>22</td>
<td>Rolling, Standing</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>5</td>
<td>Sitting &gt; 30 seconds, Standing</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>48</td>
<td>6</td>
<td>Sitting &gt; 30 seconds</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>16</td>
<td>Rolling</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>38</td>
<td>-</td>
<td>Sitting &gt; 30 seconds</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>40</td>
<td>58</td>
<td>Sitting &gt; 30 seconds</td>
<td></td>
</tr>
</tbody>
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