Real-world Outcomes of Nusinersen or Onasemnogene Apeparovac Monotherapy, or Switching to Nusinersen from Onasemnogene in SMA Patients Aged 26 Months

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Introduction

- SMA is a rare, genetic neuromuscular disease caused by a deletion or mutation of the SMN1 gene associated with loss of voluntary motor function and bulbar function, which are essential for breathing and swallowing3
- DMTs have substantially improved the prognosis of SMA with US FDA approval of targeted gene replacement therapy
  - Nusinersen, a SMN2 splicing modifier, is a antisense oligonucleotide that delivers a fully functional copy of the SMN2 gene into target motor neurons via intrathecal injection every 4 months after a series of loading doses
- Almost all patients in clinical trials of nusinersen were <6 months of age and none had prior DMT2
- In real-world practice however, patients 30 months of age may be treated, and patients may receive other DMTs before switching to nusinersen

Methods

- Real-world data on treatment outcomes and HCRU associated with FDA-approved SMA therapies are limited, particularly for patients who have received more than one treatment or for patients who were excluded from interventional clinical trials (e.g., patients 26 months of age at treatment initiation)

Objective

- We aimed to describe real-world outcomes and HCRU for patients in the United States with SMA who received nusinersen or onasemnogene abeparvovec monotherapy, or switched to nusinersen from onasemnogene abeparvovec from 26 months of age

Results

Patients

- This chart review included 55 patients (19 nusinersen monotherapy, 21 onasemnogene abeparvovec monotherapy, 15 nusinersen switching to onasemnogene abeparvovec) (Table 1)
- On the index date, most patients (64.2% treated with nusinersen monotherapy, 61.5% treated with onasemnogene abeparvovec monotherapy, and 60.0% patients switching from nusinersen to onasemnogene abeparvovec from nusinersen) weighed ≥8.5 kg (n=35, 63.2% treated with onasemnogene abeparvovec monotherapy, n=21, 60.0% treated with nusinersen monotherapy, n=12, 66.7% switched to onasemnogene abeparvovec from nusinersen) (Figure 1)
- Most patients were not smokers for SMA as新征程

Table 1. Demographics and baseline clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nusinersen</th>
<th>Onasemnogene</th>
<th>Switching from Nusinersen to Onasemnogene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at SMA diagnosis, months</td>
<td>Median: 12.0, IQR: 13.0</td>
<td>Median: 13.0, IQR: 12.2</td>
<td>Median: 13.0, IQR: 12.3</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>Male: 11 (57.9), Female: 8 (42.1)</td>
<td>Male: 11 (52.4), Female: 10 (47.6)</td>
<td>Male: 9 (60.0), Female: 6 (40.0)</td>
</tr>
<tr>
<td>≥8.5 kg, n (%)</td>
<td>61.9%</td>
<td>65.2%</td>
<td>60.0%</td>
</tr>
<tr>
<td>Bulbar function measures (crying, speaking, eating)</td>
<td>Median: 31 (15.3), IQR: 47 (17.7)</td>
<td>Median: 15 (6.5), IQR: 47 (17.7)</td>
<td>Median: 47 (17.7), IQR: 47 (17.7)</td>
</tr>
<tr>
<td>Range</td>
<td>0, 87.0</td>
<td>0, 70.0</td>
<td>0, 78.0</td>
</tr>
<tr>
<td>Weight at nusinersen initiation or onasemnogene abeparvovec administration, kg</td>
<td>Median: 11.9, IQR: 14.9</td>
<td>Median: 13.8, IQR: 14.9</td>
<td>Median: 13.8, IQR: 14.9</td>
</tr>
<tr>
<td>Weight at onasemnogene abeparvovec initiation, kg</td>
<td>Median: 13.8, IQR: 16.7</td>
<td>Median: 15.0, IQR: 16.7</td>
<td>Median: 15.0, IQR: 16.7</td>
</tr>
<tr>
<td>Rate PPY</td>
<td>0.74</td>
<td>0.54</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Motor milestones and motor function assessments

- Improvement of motor milestones from index was achieved by 63.3% (n=12/19) of patients who received nusinersen abeparvovec monotherapy, 56.0% (n=7/13) of patients who switched to onasemnogene abeparvovec from nusinersen, and 42.1% (n=8/19) of patients who received nusinersen monotherapy

Figure 4. SMA-related inpatient admission and emergency room visit rates at baseline vs. follow-up

Limitations

- Small number of patients per treatment group
- Limited number of data points across chart
- Results are descriptive and do not account for differences in patient characteristics or other potential confounders
- Duration of baseline and follow-up periods was variable across patients; however, rates were standardized to PPY to account for this variation

Conclusions

- Patients with SMA improved or maintained function across multiple outcomes after receiving nusinersen abeparvovec at 26 months of age, regardless of prior nusinersen therapy
- Time to improvement in developmental milestones was the shortest for patients who received nusinersen abeparvovec monotherapy (within 2 months after treatment initiation)
- A greater percentage of patients who received nusinersen abeparvovec monotherapy achieved improved/maintained normal cry and speech function and improved/maintained any eating function compared with patients who received nusinersen monotherapy or who switched to onasemnogene abeparvovec from nusinersen
- Inpatient admissions in the post-treatment follow-up period were reduced compared with baseline, with no admissions reported after onasemnogene abeparvovec from nusinersen
- Rates of emergency room visits during follow-up were lower for patients who received nusinersen abeparvovec monotherapy, rates were comparable to nusinersen from nusinersen to onasemnogene abeparvovec

Disclosures

- The authors have no relevant financial relationships to disclose

References


Bulbar function

- At the end of the follow-up period, a greater percentage of patients who received nusinersen abeparvovec monotherapy achieved/maintained normal cry and speech function and improved/maintained any eating function (e.g., thin liquids by mouth, some food consistency by mouth) in 100% (n=7), compared with patients who received nusinersen monotherapy or who switched from nusinersen to onasemnogene abeparvovec from nusinersen

Figure 3. Patients achieving/maintaining bulbar function at end of follow-up period

Health care resource utilization

- HCRU, as measured by inpatient admission rates and emergency room visits, was generally reduced in the post-treatment follow-up period versus baseline period for patients in each treatment group (Figure 4)

Figure 4. SMA-related inpatient admission and emergency room visit rates at baseline vs. follow-up

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