Quality of life in adolescent and adult individuals with Angelman syndrome: baseline results from the Phase 2 STARS study

Raquel Cabo1, Nasreen Khan2, Rebecca D. Burdine3, Christopher Keary4

1Ovid Therapeutics Inc., New York, NY, USA; 2Real World Economics & Consultancy, LLC, Mendham, NJ, USA; 3Department of Molecular Biology, Princeton University, Princeton, NJ, USA; 4Massachusetts General Hospital for Children, Boston, MA, USA

Disclosures: Raquel Cabo is an employee and stakeholder of Ovid Therapeutics Inc. Dr. Khan has received personal compensation for consulting, serving on a scientific advisory board, speaking, or other activities with Ovid Therapeutics Inc. Dr. Burdine has received personal compensation for consulting, serving on a scientific advisory board, speaking, or other activities with National Center for Faculty Development and Diversity, and Ovid Therapeutics. Dr. Burdine has received compensation for serving on the Board of Directors of Perlara Inc. Dr. Keary has received personal compensation for consulting, serving on a scientific advisory board, speaking, or other activities with Ovid Therapeutics Inc. Dr. Keary has received research support from Ovid Therapeutics Inc.

Acknowledgments: The authors would like to thank RTI for assistance with statistical analyses. Writing and editorial support, funded by Ovid Therapeutics Inc. (New York, NY, USA), was provided by Gian Greenberg, PhD, Anne Cooper, MA, and Joshua Safran of Ashfield Healthcare Communications (Middletown, CT, USA).

Funding: The study has been funded by Ovid Therapeutics Inc.
INTRODUCTION: Background of Angelman Syndrome

Background

• Angelman syndrome (AS) is a rare, genetic neurodevelopmental condition characterized by severe impairments in behavior, motor function, communication, and sleep as well as intellectual disability, seizures, and ataxia, which cause significant challenges for these individuals and their families.  

• AS is a severe condition with heterogeneous clinical manifestations. There are no approved treatments for AS that target its neuropathophysiology.

• The current clinical practice is management of the comorbidities and symptoms associated with the condition. Most individuals with AS take several medications to help manage the multiple symptoms.

• To the best of our knowledge, no published study has reported the health-related quality of life (HRQoL) and utility scores of individuals with AS.

Objective

• The objective of this analysis is to report the HRQoL and utility scores of adolescents and adults with AS using the baseline data available from participants in a clinical trial of gaboxadol in AS.

**STARS Study Design**

- The STARS study (ClinicalTrials.gov ID: NCT02996305) was a randomized, double-blind, placebo-controlled trial of OV101 (gaboxadol) in adolescents and adults with AS (Figure 1)
  - HRQoL and utility scores were derived using the EuroQol-5 Dimension-5 Level (EQ-5D-5L) health questionnaire proxy version 1
  - The EQ-5D-5L proxy questionnaire, which was completed by caregivers due to participants’ limited expressive language abilities, measured caregivers’ perceptions of participants’ HRQoL at baseline

**Figure 1. Overall Design of STARS Trial**

- **Screening**
- **Baseline and randomize**
- **Assessment point (weeks)**
  - 0: Placebo (placebo morning, placebo night)
  - 6: Gaboxadol QD (placebo morning, 15 mg night)
  - 12: Gaboxadol BID (10 mg morning, 15 mg night)

BID, twice daily; QD, once daily.

Data on file, Ovid Therapeutics Inc.
METHODS: The EQ-5D-5L Health Questionnaire Was Utilized to Assess Quality of Life

**EQ-5D-5L**

- The EQ-5D-5L is a standardized generic measure of HRQoL developed by the EuroQol Group.\(^1\) It is commonly used in clinical and economic appraisal to calculate quality-adjusted life-years
  - It has a single descriptive system comprised of 5 dimensions—mobility, self-care, usual activities, pain/discomfort, and anxiety/depression—each of which is given 1 of 5 grades: no problems, slight problems, moderate problems, severe problems, and extreme problems (Figure 2)
  - The questionnaire also includes a visual analogue scale (VAS) ranging from 0 (the worst imaginable health state) to 100 (the best imaginable health state)\(^2\)
  - The 3,125 possible health states defined by the EQ-5D-5L descriptive system were converted into a single index value (or utility score) using US general population specific value sets, which reflect societal valuation of health states\(^3\)
    - The index value could range from less than 0 (where 0 represents the equivalent of being dead) to 1 (perfect health)

**Statistics**

- Descriptive statistics presented include mean, median, and standard deviation for continuous variables and frequency distributions for categorical variables

---

## RESULTS: Baseline Characteristics

- Baseline EQ-5D-5L data were available for 87 participants (Table 1)
  - The mean age was 23±6.9 years
  - Participants were mostly white and non-Hispanic, and the majority were male

### Table 1. Descriptive Characteristics by Age at Baseline

<table>
<thead>
<tr>
<th>Descriptive Characteristics*</th>
<th>Age 13–17 (n=21)</th>
<th>Age 18–43 (n=66)</th>
<th>All participants (N=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at informed consent, mean±SD, years</td>
<td>15±1.3</td>
<td>25±6.2</td>
<td>23±6.9</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (52)</td>
<td>42 (64)</td>
<td>53 (61)</td>
</tr>
<tr>
<td>Female</td>
<td>10 (48)</td>
<td>24 (36)</td>
<td>34 (39)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>18 (86)</td>
<td>62 (94)</td>
<td>80 (92)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Multiple</td>
<td>3 (14)</td>
<td>3 (5)</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>3 (15)</td>
<td>11 (17)</td>
<td>14 (16)</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>17 (85)</td>
<td>55 (83)</td>
<td>72 (84)</td>
</tr>
</tbody>
</table>

*All values presented as n (%) unless otherwise noted.
SD, standard deviation.
RESULTS: Severity Level of Problems in EQ-5D-5L Domains

- The domains in which caregivers reported participants’ problems to be most severe were self-care, usual activities, and mobility (Figure 3)
  - All adolescents and 93% of adults had at least moderate problems in self-care activities, such as washing or dressing themselves
  - More than half of adolescents and adults had at least moderate issues with mobility and usual activities
  - About 30% of adolescents and adults had moderate-to-extreme problems with anxiety/depression
  - By contrast, most participants in both age groups had only slight or no pain/discomfort

Figure 3. Severity Level of Problems in EQ-5D-5L Domains by Age Group
RESULTS: EQ-5D-5L Utility Scores

- EQ-5D-5L utility scores were notably low, suggesting that AS is associated with a rather poor quality of life as measured by societal valuation of health states (Figure 4)
  - Utility scores were consistent across age groups

**Figure 4.** Mean EQ-5D-5L Utility Scores by Age Group
RESULTS: EQ-5D-5L VAS Scores

• Mean EQ-5D-5L VAS scores ranged from 82 to 85 (Table 2)

Table 2. EQ-5D-5L VAS Scores by Age Group

<table>
<thead>
<tr>
<th></th>
<th>Age 13–17 (n=21)</th>
<th>Age 18–43 (n=66)</th>
<th>All participants (N=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>82 (16.1)</td>
<td>85 (14.0)</td>
<td>84 (14.5)</td>
</tr>
<tr>
<td>Median</td>
<td>89</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Min</td>
<td>49</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Max</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

EQ-SD-5L, EuroQol-5 Dimension-5 Level health questionnaire proxy version 1; SD, standard deviation; VAS, visual analogue scale.
A limitation of this study is that it measures HRQoL from a caregiver perspective, which may not fully reflect the reality that individuals with AS experience.

- It is challenging to perceive another person’s depressive state or pain, especially if that person has developmental issues and difficulty in communicating.
- Even individuals with AS who could communicate clearly might not be able to put their experience with a depressive state into words.

In addition, some items in the EQ-5D-5L are grouped together (e.g., problems with anxiety and depression are assessed in the same question, which thus cannot measure the separate impact of each disorder).

Further analysis is required to evaluate the suitability and sensitivity of the EQ-5D-5L in the AS population.
CONCLUSIONS: Utility and VAS Score Comparison

- The utility score estimated using the EQ-5D-5L was notably low regardless of participants’ age, indicating poor HRQoL compared with the US general population,\(^1\) which is consistent with the utility scores observed with other rare neurodevelopmental disorders (Table 3).

- By comparison with utility scores, VAS scores were relatively high across age groups. This finding, previously reported in other studies (Table 3), may be explained by the fact that utility scores represent a societal assessment of participants’ health state, whereas VAS scores represent participants’ own assessment (or, in this case, caregivers’ perception of participants’ own assessment) of their health state.

Table 3. EQ-5D-5L Index and VAS Scores for Other Rare Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>EQ-5D-5L utility scores</th>
<th>EQ-5D-5L VAS scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic fibrosis(^2)</td>
<td>Children: 0.783±0.200</td>
<td>Children: 77.12±15.49</td>
</tr>
<tr>
<td></td>
<td>Adults: 0.667±0.251</td>
<td>Adults: 65.56±19.98</td>
</tr>
<tr>
<td></td>
<td>All: 0.730±0.231</td>
<td>All: 71.90±18.53</td>
</tr>
<tr>
<td>Duchenne muscular dystrophy(^3)</td>
<td>0.24</td>
<td>50.5</td>
</tr>
<tr>
<td>Fragile X syndrome(^4)</td>
<td>Children: 0.46±0.23</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Adults: 0.52±0.25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All: 0.49±0.24</td>
<td></td>
</tr>
<tr>
<td>Prader-Willi syndrome(^5)</td>
<td>0.40–0.81</td>
<td>51.3–90.0</td>
</tr>
</tbody>
</table>

EQ-5D-5L, EuroQol-5 Dimension-5 Level health questionnaire proxy version 1; NA, not available; VAS, visual analogue scale.

CONCLUSIONS: Summary

• We believe that this is the first report on HRQoL and utility scores in individuals with AS using the EQ-5D-5L, a validated instrument for measuring generic health status.

• The EQ-5D-5L data suggest that the domain in which symptoms associated with AS have the greatest impact is self-care activities.

• In summary, the data indicate rather poor QoL among individuals with AS across age groups and support the conclusion that there is a high unmet need in this population.