Developing Angelman Syndrome-Specific Clinician-Reported and Caregiver-Reported Measures to Support Holistic, Patient-Centered Drug Development

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Background and Objective

- Disease-specific clinical outcome assessment measures for Angelman syndrome (AS) symptoms and impairments are needed for clinical trials2
- Food and Drug Administration (FDA) guidelines highlight the importance of patient-centered drug development and outline a standard process to ensure clinical outcome assessments used in clinical trials are underpinned by an understanding of the most relevant disease symptoms, plus are valid, reliable, and able to detect change3

AS is a complex, heterogeneous neurodevelopmental disorder with several features that could benefit from treatment3
- Despite considerable impact on individuals, caregivers, and no-disease-modifying therapies are currently available for AS
- This poster describes the development of AS-specific measures, following FDA guidance, for use in clinical trials

Best practice FDA guidance was followed to develop AS-specific measures for use in clinical trials

- Robust qualitative methods were employed to elicit input from expert clinicians, patient advocates, and caregivers at multiple timepoints

Clinicians and caregivers identified the most important AS symptoms and impairments

- A patient-centered conceptual model of AS symptoms and impacts was developed to inform the content of these measures

- A stepwise approach was used, in line with FDA guidance3 and with input from clinicians, patient advocates, and members of the Angelman Syndrome & Outcomes Measures Alliance

The draft measures were discussed with clinicians and caregivers during cognitive debriefing interviews

- Five experienced, practicing AS clinicians and five patient advocates reviewed the draft clinician-reported measures
- Most important focus areas
- Measured in SAS-CGI – Severity
- Most frequently reported symptoms
- Measured in CASS – Impact

The final conceptual model of AS was defined by concepts, individual and caregiver impact concepts, and modifiers4

Conclusions

- Unique Symptoms of Angelman Syndrome – Clinical Global Impression (SAS-CGI) and Caregiver-reported Angelman Syndrome Scale (CASS) measures were designed to capture the most challenging AS symptoms needing treatment
- Measures were developed following FDA guidelines, collaborating with AS caregivers, advocates, and clinicians, and resulted in content-valid, robust measures
- These have been incorporated into AS clinical studies, which will allow evaluation of their psychometric properties and determine whether further refinements are needed

AS-specific clinician and caregiver measures capture the most salient symptoms needing treatment

- SAS-CGI
- CASS
- Overall AS symptoms
- Perceived meaningfulness of any change

Development of AS conceptual model

- Close collaboration with clinicians and patient advocates
- Draft conceptual model development
- Clinicians & patient advocates interviewed to elicit symptoms and measures
- Caregivers interviewed to elicit symptoms and measures
- Clinicians & patient advocates interviewed to elicit symptoms and measures
- Caregivers interviewed to elicit symptoms and measures
- Clinical & patient advocate interview to elicit clinical definitions for all AS symptoms

A detailed manual accompanies the SAS-CGI describing the aspects of each symptom or impairment to be considered

If an individual has an AS symptom or impairment that is consistent with peers of the same age with no developmental impairments needing treatment, then ‘none’ (SAS-CGI – Severity) or ‘not at all’ (CASS – Impact) is selected for that item

The measures’ instructions, items, and response options were refined based on feedback from these interviews, along with input from clinical experts at Roche and external measurement experts

The final measures are being evaluated in clinical studies to determine if further refinements are needed

Some days or some nights he does wake up from like 1 o’clock in the morning to 4

Seizures

I think honestly they [the measures] hit the majority of all kinds of the symptoms that you and I had discussed before we ever went into life.”

Skin

Parent of 4-year-old

Some individuals have an AS symptom or impairment that is consistent with peers of the same age with no developmental impairments

The draft measures were discussed with clinicians and caregivers during cognitive debriefing interviews

- Five experienced, practicing AS clinicians and five patient advocates reviewed the draft clinician-reported measures
- After these revisions, the measures were again cognitively debriefed with the same clinicians and patient advocates
- The draft caregiver-reported measures were also reviewed by 15 caregivers

SAS-CGI

Clinician-reported Angelman Syndrome Scale (CASS)

Based on observations over the past 7 days

Time to complete

10–15 minutes

Yes; plus free text description

SAS-CGI

CASS

- Overall AS symptoms
- Perceived meaningfulness of any change

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Disclosures

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