

Understanding Meaningful Changes in Autism Spectrum Disorder Clinical Trial Outcomes Using an Exit Interview Methodology

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Disclosures

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Objective

- Exit interviews are being conducted in clinical trials evaluating balovaptan to improve understanding of the perception of meaningful change in core characteristics of Autism Spectrum Disorder (ASD) captured by the Vineland™ Adaptive Behavior Scales, Second Edition (Vineland™-II), and also in health-related quality of life (HRQoL)
- This poster outlines the methodology used to conduct these exit interviews

Conclusions

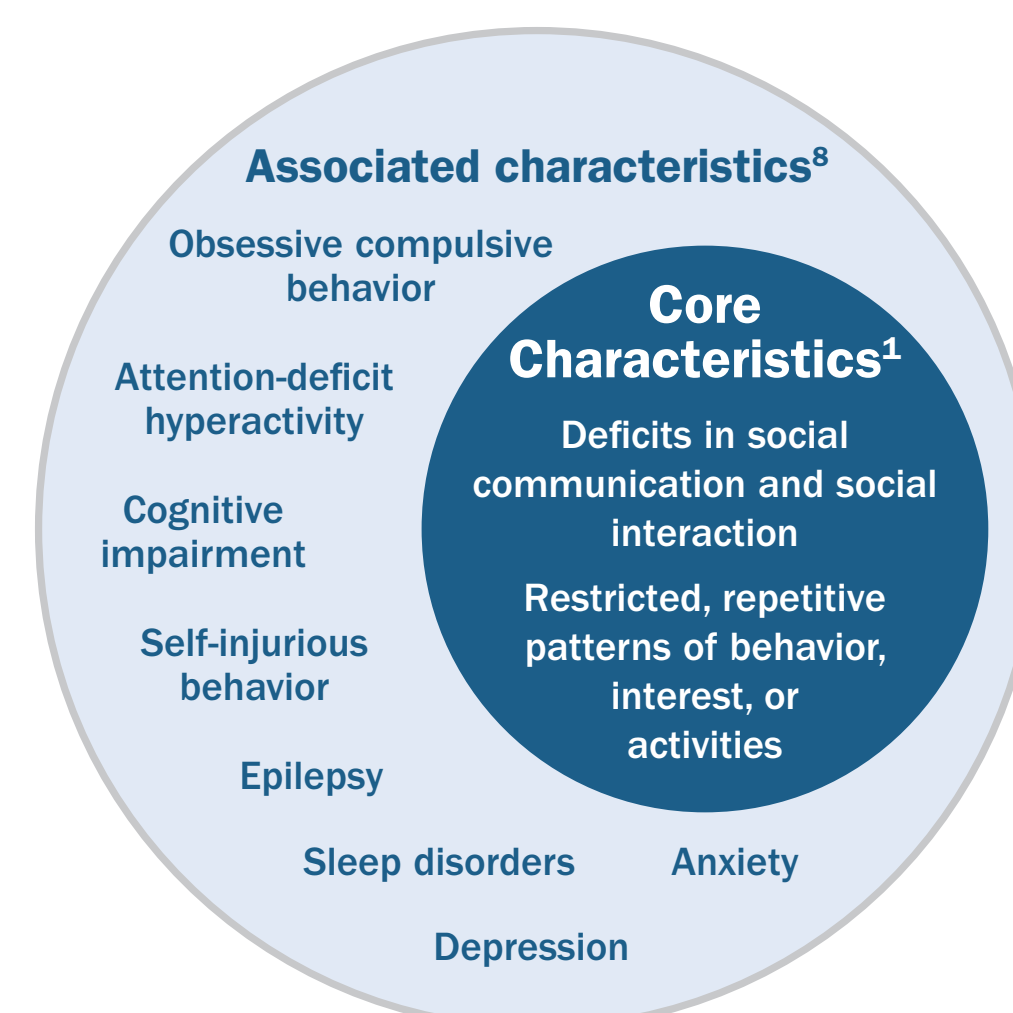
- Exit interviews conducted after completion of clinical trials will provide a rich source of both qualitative and quantitative data, which will inform a detailed understanding of what constitutes a meaningful change in ASD outcomes
- This methodology will provide a valuable way to interpret the clinical meaningfulness of changes both in Vineland™-II and additional outcome measures in future ASD trials, thus enabling the communication of the value of interventions in development

- These data could also help to identify important trial experiences that may enable the development of more patient-centric clinical trials, e.g. with novel measurement strategies evaluating meaningful changes in ASD outcomes

Background

Reliable, Valid, and Sensitive Measures of Social Communication Challenges That Reflect Meaningful Change Are Essential For Assessing the Efficacy of New Interventions

- Core characteristics of ASD include social communication and interaction difficulties and restricted, repetitive patterns of behavior, interests, or activities¹
- The selection of appropriate outcome measures for assessing meaningful changes in these core characteristics of ASD in a clinical trial setting can be challenging²⁻⁵
- Recent Food and Drug Administration (FDA) guidelines highlight the importance of patient-focused drug development and continue to request meaningful change threshold estimates (informed by qualitative data) for clinical outcome assessments
 - The FDA reviews all clinical outcome assessments for reliability, validity, ability to detect change, and interpretability^{6,7}

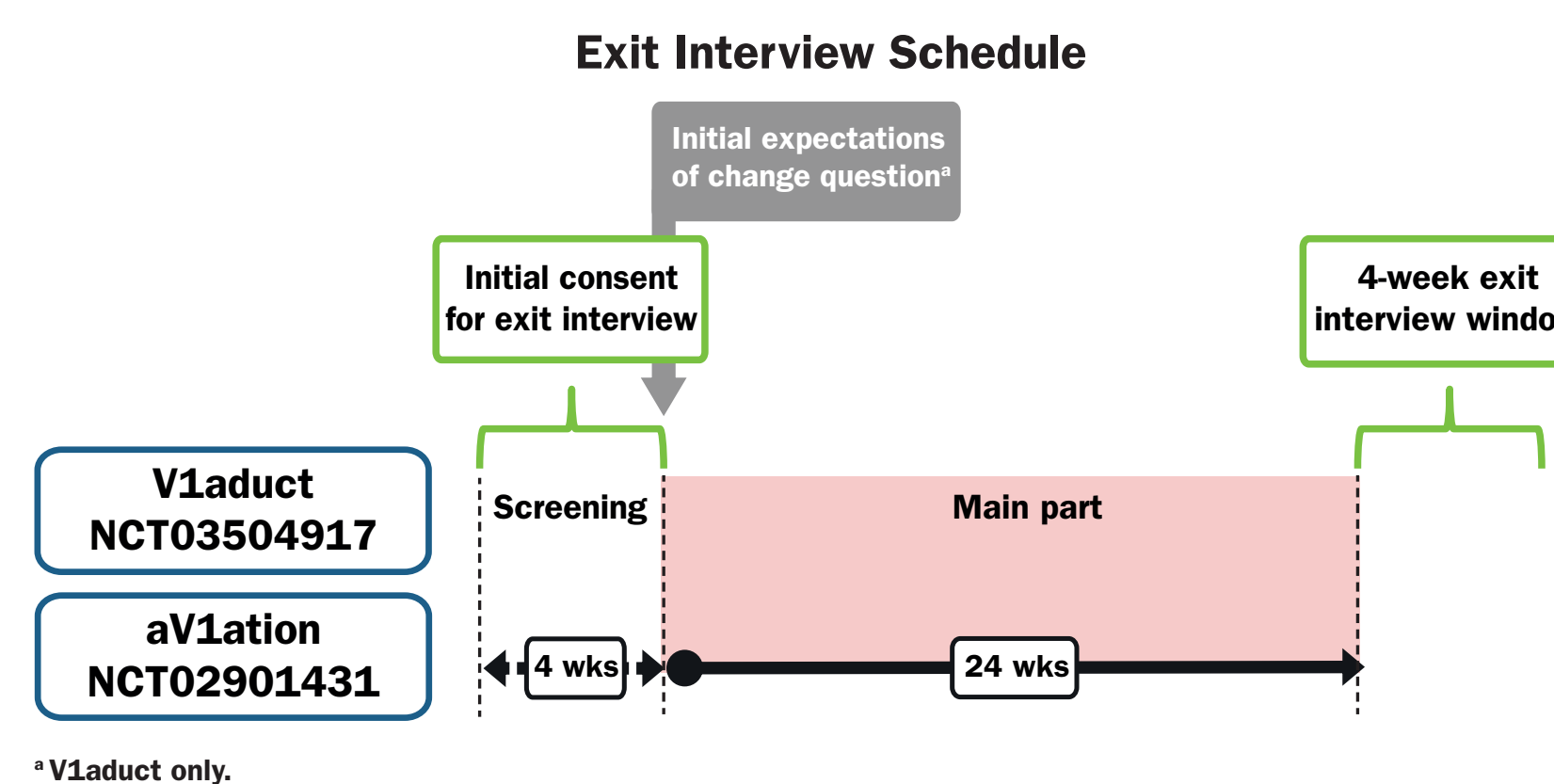


There is a pressing need to identify reliable and valid measures of social communication that also reflect meaningful changes in a real-world setting

Methods

Exit Interviews Are Being Conducted With Study Partners of Participants of the aV1ation and V1aduct Trials

- Study partners will take part in an in-depth, telephone-based, 60-minute conversation in the subject's native language as soon as possible, but no later than 4 weeks after the end of the double-blind period of the aV1ation and V1aduct trials
 - aV1ation trial population:** children and adolescents aged 5–17 years with moderate-to-severe ASD (IQ \geq 70, Clinical Global Impression - Severity scale \geq 4, Social Responsiveness Scale 2 \geq 66)
 - V1aduct trial population:** adults aged \geq 18 years with moderate-to-severe ASD (IQ \geq 70, Social Responsiveness Scale 2 \geq 66)
- Entry questions were also conducted at the start of the V1aduct trial to understand the improvement expectations for study partners during the trial
- The interviews consist of participant-led, open-ended discussions to gain insights into the impact of ASD on the lives of individuals and their families followed by focused discussion on the meaning of changes experienced over the course of the trial
 - Closed-ended questions are included that elicit data that can be used as anchors



Both Quantitative and Qualitative Data Are Obtained From the Exit Interviews

Thematic analysis

- All interview data are audio-recorded, transcribed, and analyzed using thematic analysis
- Key areas of change, and common themes relating to the real-world impact of the changes that are most important to study participants, are identified

Quantitative data

- Quantitative ratings of change from baseline, overall and per domain (based on 7-point scales) are obtained from interviews and clinical trial assessments
- Experienced, independent clinician reviewers rate the changes using the same rating scales, for a number of transcripts (n = 20)

Mixed-methods approach

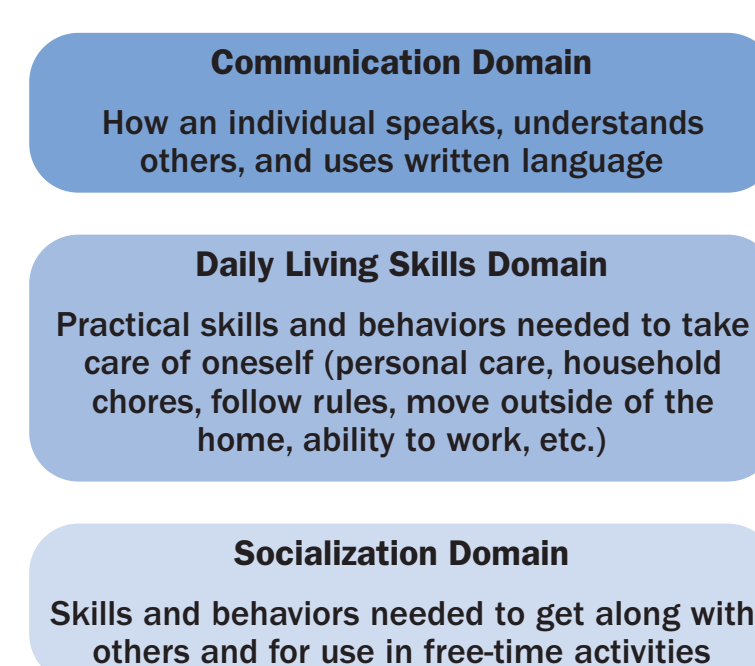
- Quantitative and descriptive data will be cross-walked to clinical trial outcome variables using a mixed-methods approach
- Results will inform anchor-based analyses exploring the interpretation of meaningful change on Vineland™-II

Improved understanding of meaningful changes in ASD

This novel approach will substantiate and contextualize the understanding of meaningful change in individuals with ASD in a real-world setting, supported by quantitative estimates of meaningful change captured by Vineland™-II
– Initial data from the aV1ation and V1aduct trials support this approach

Vineland™-II Has Been Used in Multiple Clinical Trials, Including Those Evaluating Balovaptan

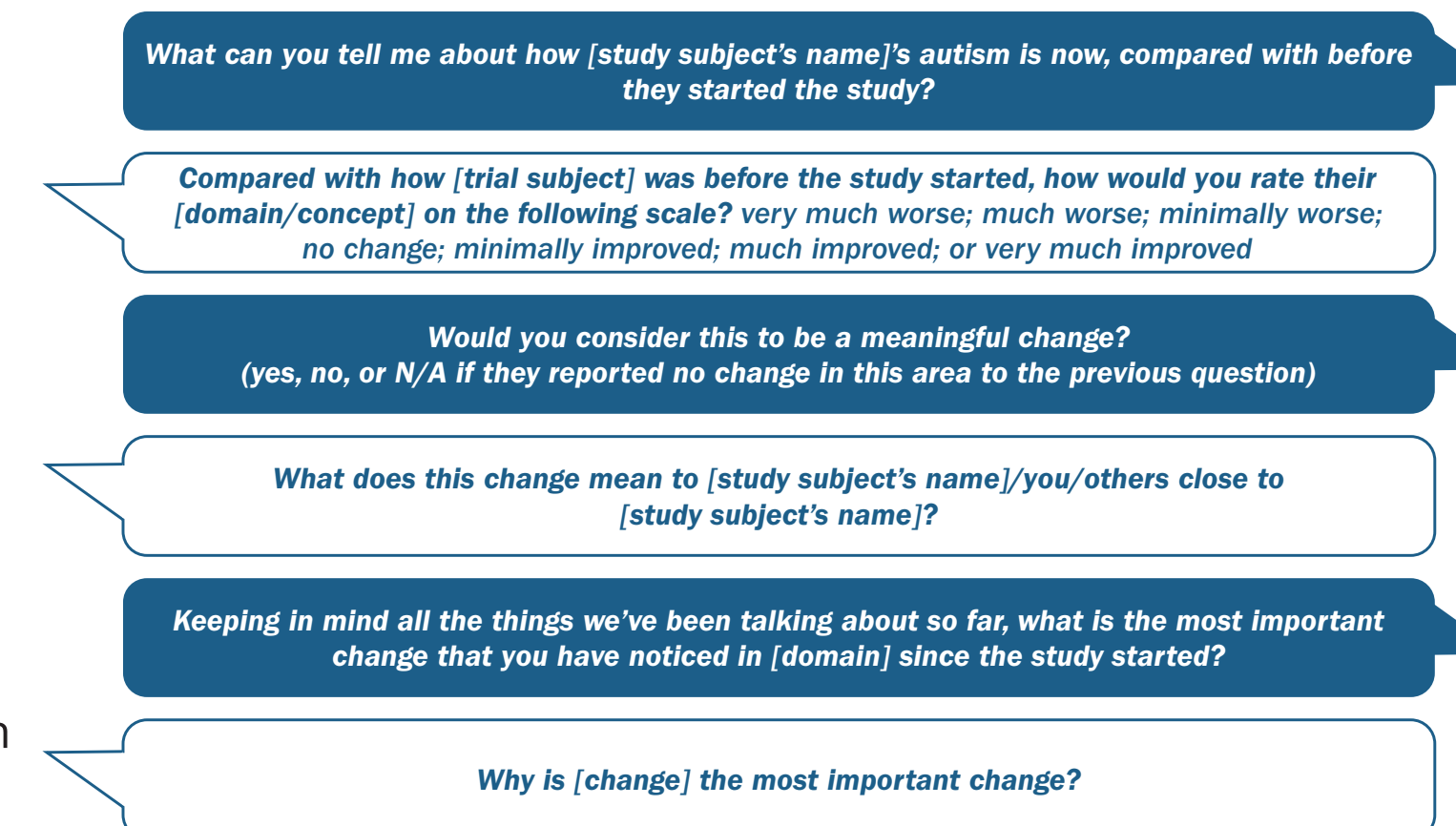
Core Vineland™-II Domains



- The Vineland™-II is a measure of adaptive behavior abilities and is one of six measures of social communication recommended (with some limitations) by a panel of experts who reviewed and assessed existing measures to determine suitability for use in clinical trials in ASD⁹
- Vineland™-II has been used in multiple clinical trials, including those evaluating balovaptan (VANILLA [NCT01793441]¹⁰, aV1ation [NCT02901431]¹¹, V1aduct [NCT03504917]¹²)
- Clinical Outcomes Solutions is collaborating with Roche to conduct exit interviews with the study partners of subjects from the aV1ation and V1aduct trials to explore meaningful changes in Vineland™-II scores

Open-ended Questions Are Used to Gain Insights Into How ASD Affects the Individual

- Interview questions consider changes in HRQoL and key aspects of ASD, with a focus on three key domains that are captured on the Vineland™-II:
 - Socialization
 - Communication
 - Daily living skills
- A discussion guide is used to focus the interview, with key questions about each area, examples on the right:

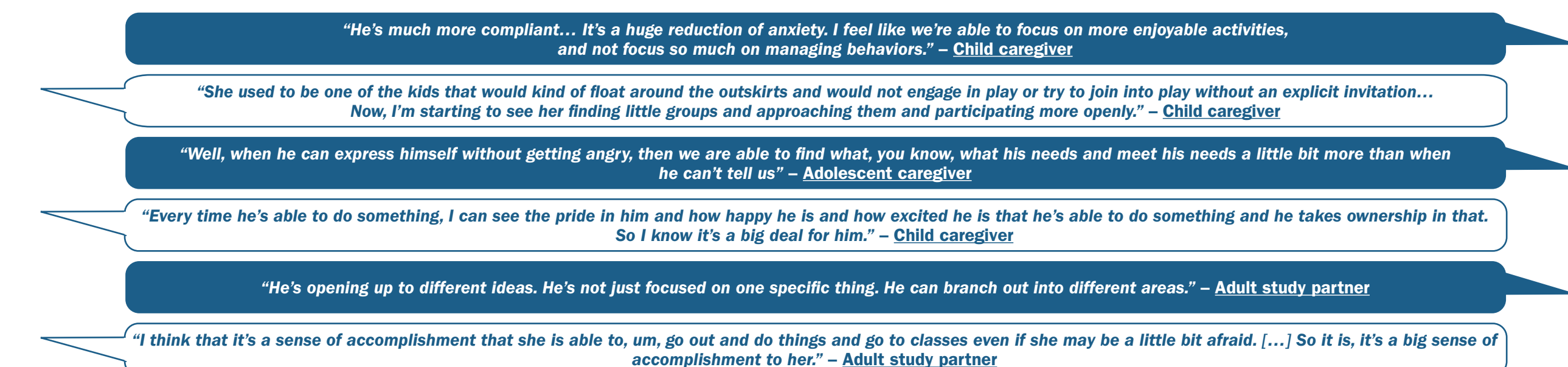


Results

Preliminary Insights From the Thematic Analysis Phase

- The rich, qualitative accounts of observed changes and their real-world impact provide meaningful evidence to support the relevance of numerical changes observed on Vineland™-II

Quotes from study partners/caregivers of participants in either trial arm (balovaptan or placebo)



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