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

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TW and JS are full-time employees of F. Hoffmann-La Roche Ltd CB is an employee of Clinical Outcomes Solutions Ltd, which received funding from F. Hoffmann-La Roche Ltd for the conduct of this research Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance for this poster was provided by Anna Bacon of Articulate Science, UK.

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 healthrelated 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

■ Quantitative data

Ouantitative

from baseline,

overall and per

domain (based

from interviews

and clinical trial

assessments

Experienced,

independent

clinician reviewers

rate the changes

using the same

for a number of

transcripts (n = 20)

rating scales,

are obtained

on 7-point scales)

ratings of change

Both Quantitative and Qualitative Data Are Obtained From the Exit Interviews

Quantitative and

descriptive data will

clinical trial outcome

be cross-walked to

variables using a

Results will inform

analyses exploring

the interpretation of

meaningful change

on Vineland™-II

mixed-methods

anchor-based

approach

Mixed-methods approach

Improved

understanding

of meaningfu

changes

in ASD

This novel approach will

substantiate and contextualize

change in individuals with ASD

by quantitative estimates of

Vineland[™]-II

approach

the understanding of meaningful

in a real-world setting, supported

meaningful change captured by

Initial data from the aV1ation

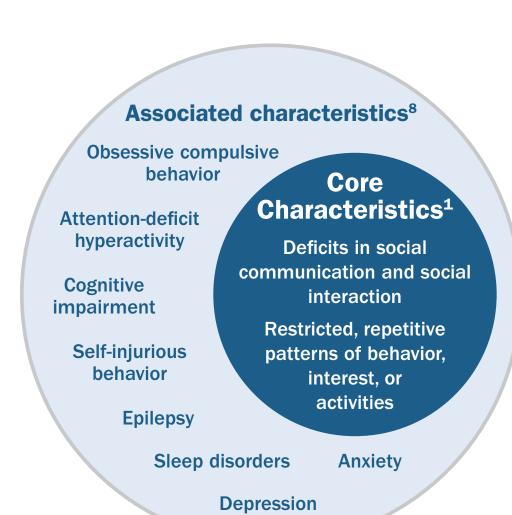
and V1aduct trials support this

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 challenging^{2–5}
- 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}

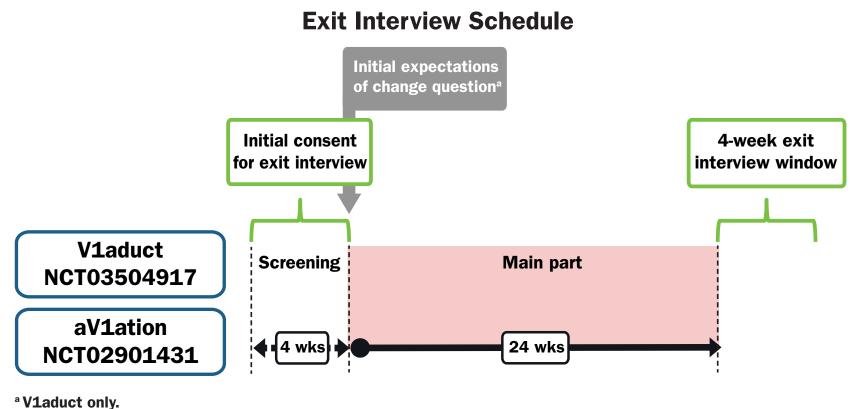
There is a pressing need to identify reliable and valid measures of social communication that also reflect meaningful changes in a real-world setting



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 moderateto-severe ASD (IQ ≥70, **Clinical Global Impression** - Severity scale ≥4, Social Responsiveness Scale 2 ≥66)
- V1aduct trial population: adults aged ≥18 years with moderate-to-severe ASD (IQ ≥70, Social Responsiveness Scale 2 ≥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

Results

Thematic analysis

All interview data

transcribed, and

analyzed using

Key areas of

change, and

thematic analysis

common themes

relating to the real

world impact of the

changes that are

most important to

study participants,

are identified

are audio-recorded

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)

"He's much more compliant... It's a huge reduction of anxiety. I feel like we're able to focus on more enjoyable activities, and not focus so much on managing behaviors." - Child caregiver

"She used to be one of the kids that would kind of float around the outskirts and would not engage in play or try to join into play without an explicit invitation... Now, I'm starting to see her finding little groups and approaching them and participating more openly." - Child caregiver

"Every time he's able to do something, I can see the pride in him and how happy he is and how excited he is that he's able to do something and he takes ownership in that. So I know it's a big deal for him." - Child caregiver

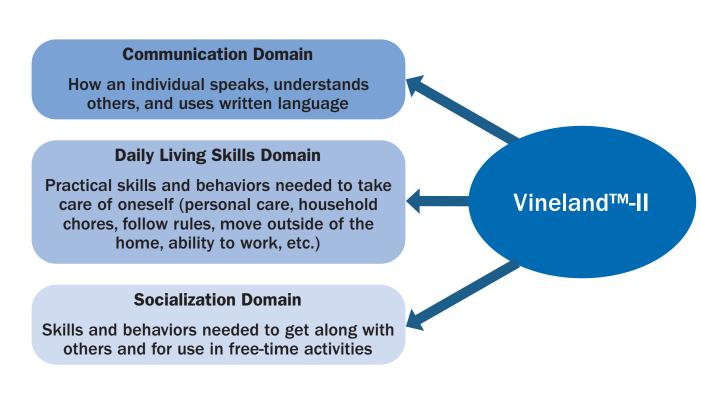
"Well, when he can express himself without getting angry, then we are able to find what, you know, what his needs and meet his needs a little bit more than when

"He's opening up to different ideas. He's not just focused on one specific thing. He can branch out into different areas." - Adult study partner

"I think that it's a sense of accomplishment that she is able to, um, go out and do things and go to classes even if she may be a little bit afraid. [...] So it is, it's a big sense of accomplishment to her." - Adult study partner

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
- VinelandTM-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

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 A discussion guide is used to focus the interview, with key questions about each area, examples on the right:

What can you tell me about how [study subject's name]'s autism is now, compared with before they started the study? Compared with how [trial subject] was before the study started, how would you rate their [domain/concept] on the following scale? very much worse; much worse; minimally worse; no change; minimally improved; much improved; or very much improved Would you consider this to be a meaningful change? (yes, no, or N/A if they reported no change in this area to the previous question) What does this change mean to [study subject's name]/you/others close to [study subject's name]? Geeping in mind all the things we've been talking about so far, what is the most important change that you have noticed in [domain] since the study started? Why is [change] the most important change?

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