ISCTM
International Society for CNS Clinical Trials and Methodology

How can we use digital technology to augment conventional cognitive assessments?

Kristin Hannesdottir and Gül Erdemli

ISCTM Boston September 2022

NOVARTIS | Reimagining Medicine

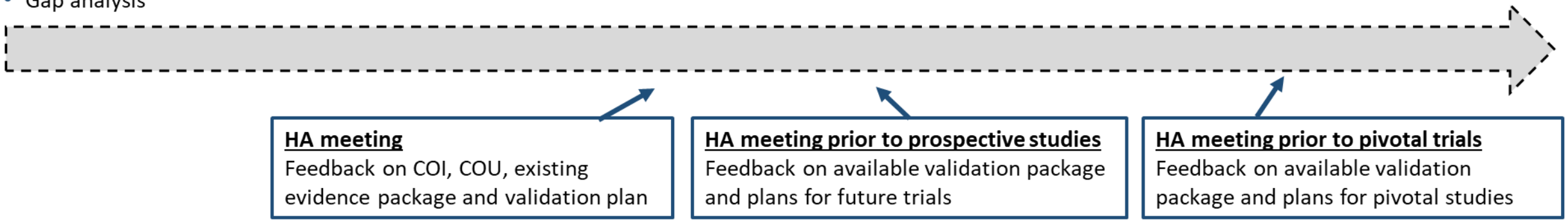
Disclosure

- Kristin Hannesdottir and Gül Erdemli are employees of Novartis and hold Novartis shares

Validation for regulatory acceptance

- Lengthy process requiring step wise approach – can only be achieved if started early in development
- Early Health Authority (HA) interactions are essential to understand gaps and address them in timely manner

Early activities	Cross-sectional non-interventional study	Qualitative study (Patient insight)	Longitudinal non-interventional study	Phase 2a Randomized controlled trial	Future Phase 2b & pivotal trials in AD
Continuously monitor scientific literature, therapeutic and regulatory landscape					
• Establishment of Concept of Interest (CoI) and Context of Use (CoU) • Selection of tool/technology • Gap analysis	• Start establishing COA is fit-for-purpose • Patient insight	• Clinical validation in early AD patients • Further patient insight • Sensitivity to change	• Prospective design • Clinically meaningful change	• Method finalization • Deployment in pivotal studies to support label claims	



Context of Use and Concept of Interest

An electronic performance outcome assessment (ePerfO) for cognition in the regulatory evaluation of new drugs for the treatment of early AD

CoU - In early AD (i.e., mild cognitive impairment due to AD and mild AD), ePerfO will be considered as a secondary or primary efficacy endpoint of interventional randomized controlled trials to confirm that new drugs results in attenuation of cognitive impairment relative to placebo.

Initial focus would be validation for a specific agent but broader validation for all AD treatments will also be explored with HAs. Progress will be reviewed in a data driven fashion.

End point positioning:

- For a co-primary endpoint, as a component of a comprehensive cognitive test battery in addition to scales for functional assessment (e.g., ECog or ADCS-iADL)
  - **Concept of interest**: cognitive function (comprehensive)
- For a secondary endpoint, as a standalone test
  - **Concept of interest**: specific cognitive domains assessed by the ePerfO

Expected project outcomes

- A validated digital endpoint to use in early AD trials across drug development phases
- Extensive data and operational know-how to allow use in additional indications
- Validation know-how to advance additional digital endpoints across drug development phases

Key activities prior to pivotal studies

- Definition of patient population
- Establishing clinically important difference for protective study design
- HA feedback on the existing validation package

Conclusion: value of novel endpoints

Augment existing endpoints for improved accuracy → **reduce failed trials**

Greater understanding of the impact of disease on patient's lives → **clinical meaningfulness**

Reduce endpoint variability and increase effect size → **smaller, more efficient trials**

Briefer, at home assessments → **lower burden** to sites and trial participants

Augmented endpoints hold promise to

1. Streamline and increase accuracy of early clinical trials → de-risking late-stage development
2. Increase understanding of disease

➢ *Ultimately* ***delivering better medicines to patients faster***

Acknowledgements

Novartis Translational Medicine

- **Kristin Hannesdottir (medical lead)**
- Jang-Ho Cha

Novartis Drug Regulatory Affairs

- **Gul Erdemli (regulatory lead)**

Novartis Operations

- **Vanessa Vallejo (study lead)**
- Mateusz Piksa
- Mark Deurinck
- Huld Sveinbjoernsdottir
- Brynja Einarsdottir
- Steinthora Thorisdottir

Novartis Data Analytics

- **Jelena Curcic (digital lead)**
- Jennifer Sorinas
- Evan Remington

Novartis Biostatistics

- **Alex Sverdlov**
- Jens Praestgaard
- Shivam Gupta

Landspítali University Hospital

Memory clinic, Landakot

- **Jón Snædal (Principal Investigator)**
- Helena Eydal
- Guðbjörg Jóhannsdóttir

Thank you

NOVARTIS