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Roche

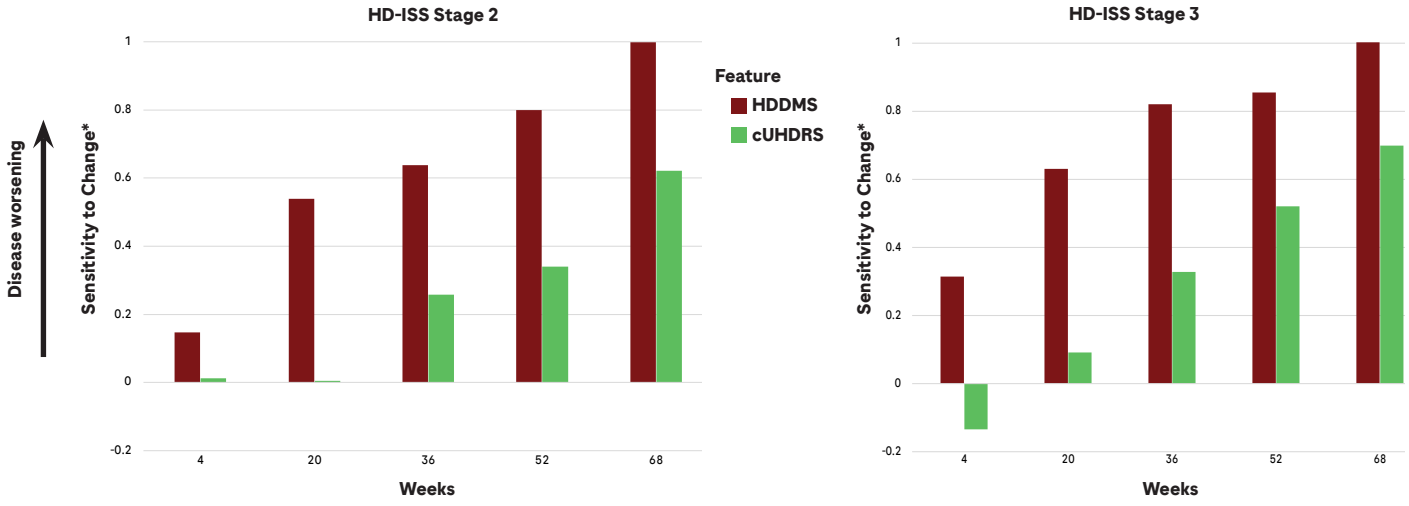
Digital Biomarkers Solution may enable smaller and faster clinical trials

Huntington's disease (HD) clinical trial sponsors may gain an earlier indication of progress using digital biomarkers.[1]

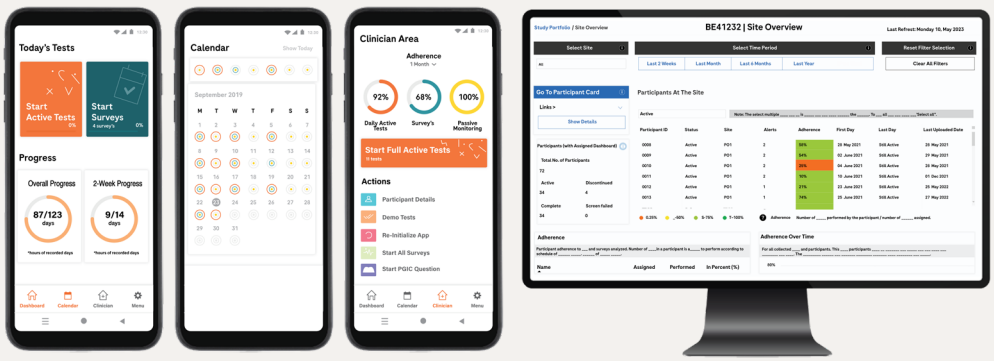
With the growing number of therapies being developed for Huntington's Disease, sensitive measures for disease progression are becoming increasingly important to enable Ph1/2 trials of recruitable size. The Roche HD digital biomarker solution has been used across multiple studies, collecting a dataset comprising more than 1000 individuals with HD. Roche has developed a digital motor score based on data from three trials, and validated it on data of a fourth. Analysis of data showed that the HD Digital Motor Score (HDDMS) has a **higher sensitivity than the composite Unified HD Rating Scale (cUHDRS) in ISS Stage 2 & 3**. Furthermore, if a study is powered using the digital motor score, one can achieve **a sample size reduction of 75%**.

This promising outcome indicates the potential to enable smaller and faster early-stage trials for a rare disease with a limited pool of participants.

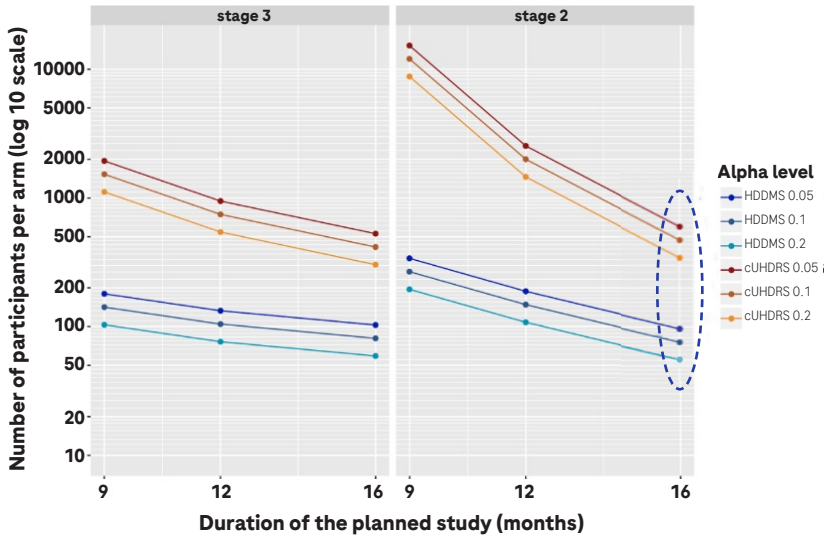
HDDMS showed a higher Sensitivity to Change vs. cUHDRS



*Sensitivity to change is the change from baseline divided by the variability in this change



Reduced sample sizes and trial durations possible with HDDMS



Results:

At 16 months and alpha=0.2, a study in ISS stage 2 powered for HDDMS requires **>75% fewer patients per arm than if powered for cUHDRS (56 vs 342)**
Potential impact: Reducing the number patient required in the study, leading to cost savings and attainable recruitment targets.

Data source: Generation HD1*. ISS stage 2 patients are DCL 4

Assumptions:

- Minimal detectable difference (MDD) = 40%
- Type I error = 0.2
- 1:1:.. randomization (numbers for one arm)

*Generation HD1 PBO data used in the calculation is biased toward lower disease progression, and may not be fully representative of the Generation HD1 study population.

Roche Digital Biomarkers Solution for Clinical Trials

Elevate comprehensive decision-making in Huntington's disease drug development

- Validation based on large digital data set of HD individuals
- Potential to reduce future trial sizes[1]
- Used in clinical trials[1,3]

Expertise Across Roche Portfolios

Credibility with regulatory bodies and research community

- Endpoint development effort in close consultation with regulatory bodies
- Embedded in the research community

Global clinical trial operationalization experience

- Proven ability to deploy in Ph I-IV global multi-center trials across 100+ sites and 40+ countries[4]

Reliable partner

- Extensive experience in developing Digital Biomarkers in 10+ indications
- Leading Diagnostics organization championing biomarkers for support in clinical trials
- Built-in data security and patient privacy practices
- Backed by Roche with 125 years of financial strength

Disclaimer:
The Roche Digital Biomarkers Solution is intended to collect, store and process digital clinical data to support exploratory research in clinical trials. This solution is not meant to be used for diagnosis and treatment decision making for individual patients.

1. Giboin, L.S.,et al. A digital motor score for sensitive detection of disease progression in early manifest Huntington's disease. CHDI 2023
2. Tabrizi et al., (2022): A biological classification of Huntington's disease: the Integrated Staging System. Lancet Neurology 21(7):632-644
3. Lipsmeier F. et al. A remote digital monitoring platform to assess cognitive and motor symptoms in HD: cross-sectional validation study. J Med Internet Res 2022;24(6):e32997
4. Data on file with Roche