

## **Answers to additional questions posed by the HDTC audience**

There was insufficient time for Peter McColgan and Jonas Dorn to answer all the questions asked after their presentation 'Digital monitoring of cognitive and motor symptoms in Huntington's disease: preliminary longitudinal findings from the GENERATION HD1 study of tominersen'; given the exceptional importance of this trial to the wider HD community, they have kindly provided answers to those unanswered questions here:

### **How did the variance in measures such as SWR that were collected in clinic compare to the variance from more frequent measures from the digital platform?**

We have not systematically compared in-clinic versus at-home tests yet, but we agree that this is an interesting question to look at in the future.

### **Are there plans to look at turning measures in U-turn task more closely to evaluate stride timing, regularity, etc.?**

We have so far focused our analyses on the pre-specified features, i.e., the features that had been selected for analysis before database lock. One of these is the U-turn step frequency variance which does capture the regularity of stride timing, and which does seem to have good measurement properties. We intend to look all the tests, including U-turn, to see whether we may find even more informative features.

### **Study site testing vs at-home testing - can you quantify their correlation?**

We have not looked into this systematically so far.

### **Could differential rates in drop out be used in future trials by independent unblinded data monitoring group to trigger early analyses for safety or efficacy?**

Missing digital data can result for a number of reasons, including technical, motivational, general health-related and specific disease-related factors. As such, it should be interpreted with caution - which we are doing - and would not be appropriate to consider as an indication of safety and efficacy outcomes.

### **Are the smart watches worn on the dominant or non-dominant hand? Can you speculate if this would be an important factor to consider?**

Smartwatches are worn on the non-dominant hand. While one would expect more intentional activity with the dominant hand, wearing the watch on the dominant hand is less convenient for the wearer, as more unintentional (i.e.. chorea) events may be missed, and the data would be less compatible with

passive wrist activity data of other studies, where the standard is to wear devices on the non-dominant hand

**If compliance decreases with disease deterioration, could the higher drop out in the active drug groups be an indication of worsening due to the drug?**

At first glance, drop-outs are similar across treatment arms, but we will investigate this further.

**Interesting data. Did you have a chance to analyse the impact of change of symbol to digital association with each digital expose for impact on practice effects?**

We do see a potential practice effect in SDMT. We plan to analyse this further, and it will be interesting to compare the Roche Natural History Study, where we have weekly digital SDMT, with the placebo arm of GENERATION HD1, where we have monthly digital SDMT.

**In the finger index assessments, are you accounting for differential effect in left-handed subjects?**

In the HD Digital Monitoring platform, participants are asked to perform all upper limb tests with both the left and the right hand, one after the other. In our analyses, tests were regrouped into dominant/non-dominant hand to account for potential differences between dominant and non-dominant hand behavior.

**Likewise, were only right-hand dominant participants included (the instructions all specify to use right hand in the cell phone tasks)?**

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