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POSTER ABSTRACTS

904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Experience with Accelerometer Physical Activity Tracking in Adults and Adolescents with Hemophilia A: Tool Validation Using Results from the XTEND-1 Efanesoctocog Alfa Phase 3 Trial

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Introduction

Wearable physical activity trackers have become increasingly common within clinical studies, patient monitoring, and health assessments. Physical activity is a key endpoint of interest when evaluating treatments for hemophilia. The objective of this analysis was to describe the psychometric properties of five outcome measures of physical activity from the accelerometer activity monitor used in the XTEND-1 study.

Methods

XTEND-1 (NCT04161495) was a Phase 3, open-label, multicenter study of the efficacy, safety, and pharmacokinetics of efanesoctocog alfa in previously treated adults and adolescents aged ≥ 12 years with severe hemophilia A. Patients receiving prior standard-of-care prophylaxis factor VIII (FVIII) received once-weekly (qw) prophylactic efanesoctocog alfa for 52 weeks (Arm A); patients on prior on-demand FVIII treatment received efanesoctocog alfa on-demand for 26 weeks, then prophylactic efanesoctocog alfa qw for 26 weeks (Arm B). Patients wore a triaxial medical grade accelerometer activity monitor device for continuous monitoring during pre-specified intervals 8 consecutive days after (or before) scheduled visits (to collect data for a full 7-day week + 1 additional day): after the screening, baseline, Week 4, 13, 26, 39 visits, and before the Week 52 visit. Compliance was assessed based on number of monitoring intervals and number of days wearing the device, and number of minutes spent wearing the device within those days. Five outcomes were assessed: light physical activity (LPA), moderate-to-vigorous activity, sedentary behavior (minutes/day spent in these individual outcomes out of total number minutes wearing device while awake), steps (number of steps taken per day), and metabolic equivalent of a task (MET; total estimated metabolic rate per day). Psychometric analyses of these outcomes using data from Arm A were conducted to evaluate test-retest reliability (TRTR), concurrent validity, known-groups validity, ability to detect change, and meaningful within-patient change (MWPC) of physical activity measurements (**Table 1**). An analysis to detect potential influential outlier patients for each outcome that could potentially bias results, was conducted.

Results

In total, 132 out of 133 patients in Arm A and 26 out of 26 patients in Arm B, distributed in 19 countries, had accelerometer data. Compliance was defined post-hoc as ≥ 12 consecutive wear hours/day and results are presented for days achieving this threshold; no meaningful differences in results were found when incorporating number of monitoring intervals or number of days within the interval in the compliance definition.

Most patients maintained or improved physical activity as measured by the activity monitors, with an overall increase in mean (SD) minutes during each monitoring period for LPA (baseline: 636 [234]; Week 52: 653 [237]), though there were variable changes throughout the study period. Measurements of LPA demonstrated acceptable TRTR, concurrent validity with three validation criteria, and ability to detect change with all or most of the anchor variables, while demonstrating good separation for improvement and deterioration thresholds to provide for MWPC (**Table 1**). Two patients were identified as influential outliers for LPA. For moderate-to-vigorous activity, the concurrent validity showed that two validators met the criteria, and for steps, four validators met the criteria. Sedentary behavior and MET did not meet criterion with any of the validators (**Table 1**). Out of the outcomes assessed, LPA showed the best psychometric properties within the study.

Conclusion

These analyses show how physical activity tracking through wearables was used to assess outcomes in patients with severe hemophilia A, who switched to a FVIII replacement therapy that provided normal to near-normal FVIII activity for most of the

weekly dosing interval, resulting in reduced pain and improved physical functioning as assessed by patient-reported outcome measures. Analyses of these results revealed limitations in the psychometric properties of the assessed outcomes. To further understand the personal motivation and barriers for improving physical activity, addition of goal-setting could be considered in future clinical studies.

Disclosures Wilson: *Sanofi*: Current Employment, Current equity holder in publicly-traded company. **Msihid:** *Sanofi*: Current Employment, Current equity holder in publicly-traded company. **Ayasse:** *OPEN Health*: Ended employment in the past 24 months. **Dumont:** *Sanofi*: Current Employment, Current equity holder in publicly-traded company. **Willemze:** *Sanofi*: Current Employment, Current equity holder in publicly-traded company.

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Table 1. Summary of psychometric validation and outlier analysis of the five outcome measurements of physical activity from the accelerometer activity monitor

Analysis	Moderate-to-Vigorous Physical Activity	Light Physical Activity	Sedentary Behavior	Steps	Metabolic Equivalent of a Task
Test-Retest Reliability	Not acceptable	Acceptable	Not acceptable	Not acceptable	Not acceptable
Concurrent Validity	2/10 validators met criterion	3/10 validators met criterion	No validators met criterion	4/10 validators met criterion	No validators met criterion
Known-Groups Validity	No known-groups met criterion	2/2 known-groups met criterion	No known-groups met criterion	1/2 known-groups met criterion	1/2 known-groups met criterion
Ability to Detect Change	2/3 anchors met criterion	3/3 anchors met criterion	3/3 anchors met criterion	No anchors met criterion	1/3 anchors met criterion
Meaningful Within-Patient Change	Thresholds not interpretable	Good separation for improvement & deterioration thresholds	Good separation for improvement & deterioration thresholds	Thresholds not interpretable	Thresholds not interpretable
Outlier Detection Analysis	3 outlier subjects	2 outlier subjects	5 outlier subjects	7 outlier subjects	1 outlier subject

Test-retest reliability was measured by the two-way random intra-class correlation coefficient between baseline and Week 26 anchored to no change defined on three anchors: Patient Global Impression of Change (PGIC), Patient Global Impression of Severity (PGIS) Joint, PGIS Activity. Concurrent validity was measured by baseline correlations with validators. Known-groups validity was measured by estimated baseline activity monitor physical activity score differences across groups produced by different responses to PGIS Joint and PGIS Activity. Ability to detect change was measured by whether differences in ActiGraph physical activity change scores between baseline and Week 52 were predicted by change measured by PGIC, PGIS Joint, and PGIS Activity between Baseline and Week 52. Meaningful within-patient change was measured as mean ActiGraph physical activity change score estimates between baseline and Cycle 6 Day 1 stratified on anchor groups defined based on PGIC, PGIS Joint, and PGIS Activity (improvement, no change, deterioration) and empirical cumulative distribution functions and empirical probability density functions). Analysis was also conducted to detect potential patients acting as influential outliers for each of the five ActiGraph physical activity outcomes by estimation of Cook's Distance for each patient for each outcome.

Figure 1