Smartphone-Based Assessment of Gait with Floodlight in Multiple Sclerosis Shows Sensitivity to Change Over a Follow-Up Period of 3 Years

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Sensitivity to Longitudinal Change
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OBJECTIVE

To assess sensitivity to change in gait outcome measures provided by remote smartphone-based Floodlight 2MWTs in PwPMS treated with ocrelizumab in the ongoing Phase IIIb CONSONANCE study (NCT03523858)

KEY TAKEAWAYS

The Floodlight 2MWT shows sensitivity to change over time and ability to discriminate between groups of patients with EDSS progression events and patients without EDSS progression events that are comparable to that of the in-clinic T25FW

Unlike the in-clinic T25FW, the Floodlight 2MWT can remotely track changes in ambulation due to MS disease progression beyond gait speed, which may be of clinical value

- Floodlight gait characteristics capture change earlier than the in-clinic T25FW
- Floodlight gait characteristics may be sensitive to change in PwPMS considered to be stable according to their EDSS score

BACKGROUND

- Smartphone-based tests have the potential to enable shorter clinical trials with reduced sample size[1]
- For such tests to have value in advancing MS clinical trials, their analytical validity, cross-sectional clinical validity and sensitivity to longitudinal change must be established
- In separate analyses presented at ECTRIMS 2024, we show that the Floodlight 2MWT has analytical and cross-sectional clinical validity[2,3]
- Here, we evaluate the Floodlight 2MWT's sensitivity to longitudinal change and its ability to discriminate between groups of patients with EDSS progression events and patients without EDSS progression events

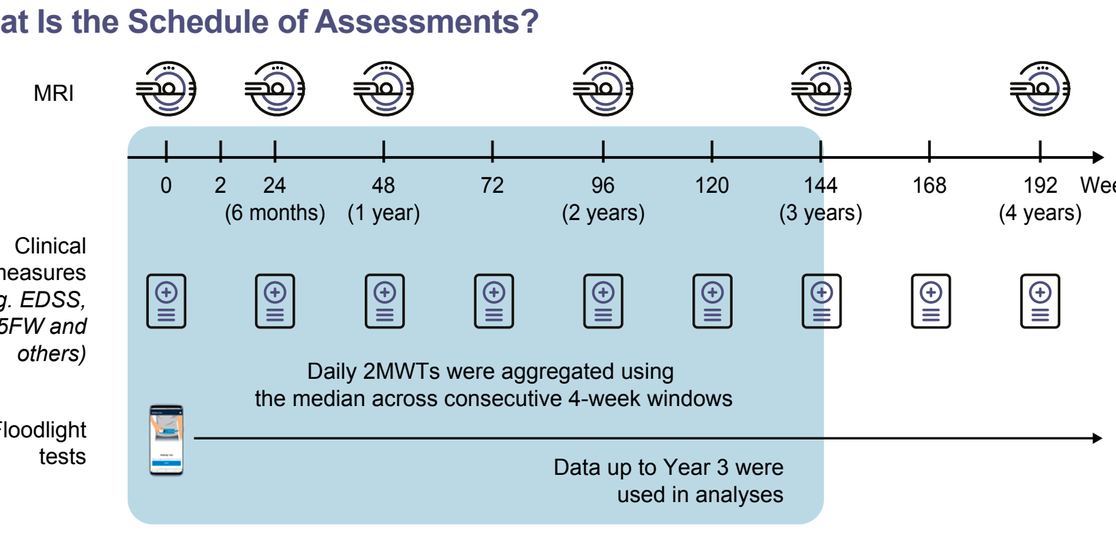
METHODS

How Are the Clinical Associations of the Floodlight 2MWT Evaluated Across a Wide Range of MS-Related Disability and Gait Impairment Levels?

Dataset	• **CONSONANCE (NCT03523858)[4]**
Study design	• Multinational, single-arm Phase IIIb study of ocrelizumab in progressive MS
Key inclusion criteria	• Have a definite diagnosis of PMS (as per the revised McDonald 2010 criteria for PPMS or Lublin *et al*. 2014 for PMS)[5,6] • EDSS score ≤6.5 at screening • Disability progression independent of relapse activity at any point in time over the 2 years prior to screening
Smartphone-based tests included in the analysis	• The Floodlight 2MWT was performed daily for up to 3 years in a remote setting[a] and onsite during clinic visits – In the remote setting, the Floodlight 2MWT was made available once a day, and the PwPMS could complete the test at a time of day most convenient to them – Individual 2MWTs were aggregated using the median across consecutive 4-week windows – Smartphone was carried in a waist-worn belt bag
Cohorts	• The **matched population at baseline** included all PwPMS who had both Floodlight 2MWT and in-clinic T25FW data at baseline, i.e.: – At least one available Floodlight 2MWT during the first 4-week window AND – In-clinic T25FW data available for the baseline visit • The **matched population at each clinic visit after the baseline visit** included all PwPMS who were included in the matched population at baseline and additionally had: – At least one available Floodlight 2MWT during the week of the study visit and the preceding 3 weeks AND – T25FW data collected at the clinic visits (imputed T25FW data were permissible)[a]
Statistical analysis	• **Longitudinal change analysis** compares the percent change from baseline on the Floodlight 2MWT with the percent change from baseline on the T25FW • **The 'progressor' versus 'non-progressor' analysis** compares retrospectively the ability of the Floodlight 2MWT and the in-clinic T25FW to qualitatively discriminate between groups of patients with EDSS progression events and patients without EDSS progression events[b] – PwPMS with a recorded EDSS progression event up to Year 3 were considered as progressors, and those without as non-progressors

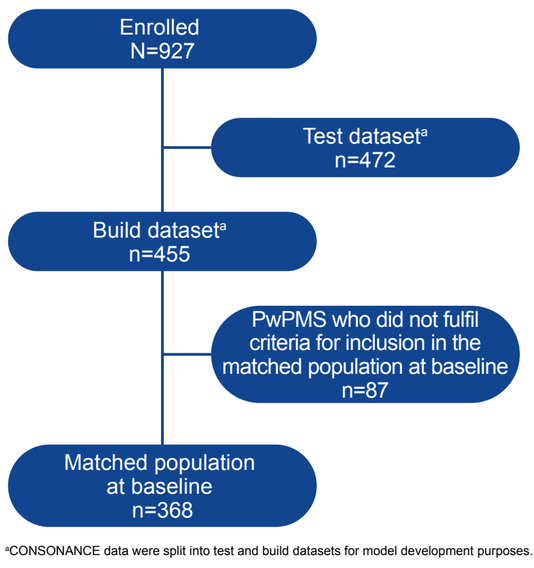
[a]T25FW data collected during clinic visits other than the baseline visit were imputed with 180 s for PwPMS who were not able to complete the test due to their MS; [b]An EDSS progression event was defined as a 1.0-point increase from a baseline score of 5.5 or a 0.5-point increase from a baseline score of 6.0, confirmed 24 weeks apart.[7]

What Is the Schedule of Assessments?



RESULTS

Baseline Demographics and Disease Characteristics

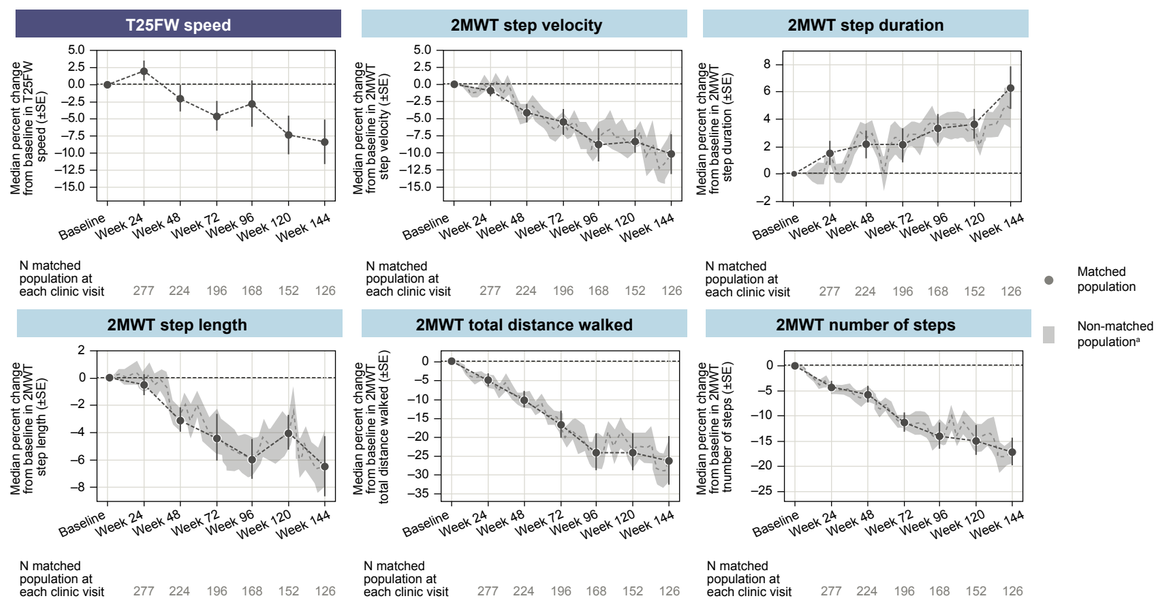


	Matched population at baseline n=368
Female, n (%)	193 (52)
Age, mean (SD), years	48.5 (9.5)
Diagnosis, n (%)	
PPMS	175 (48)
SPMS	193 (52)
EDSS score, mean (SD)	5.0 (1.3)
MSWS-12 transformed total score, mean (SD)	62.7 (25.2)
T25FW time, mean (SD), s	14.5 (16.3)

[a]CONSONANCE data were split into test and build datasets for model development purposes. Blinding procedures were applied to the test dataset.

How Does the Sensitivity to Longitudinal Change on the Floodlight 2MWT Compare with That on the In-Clinic T25FW?

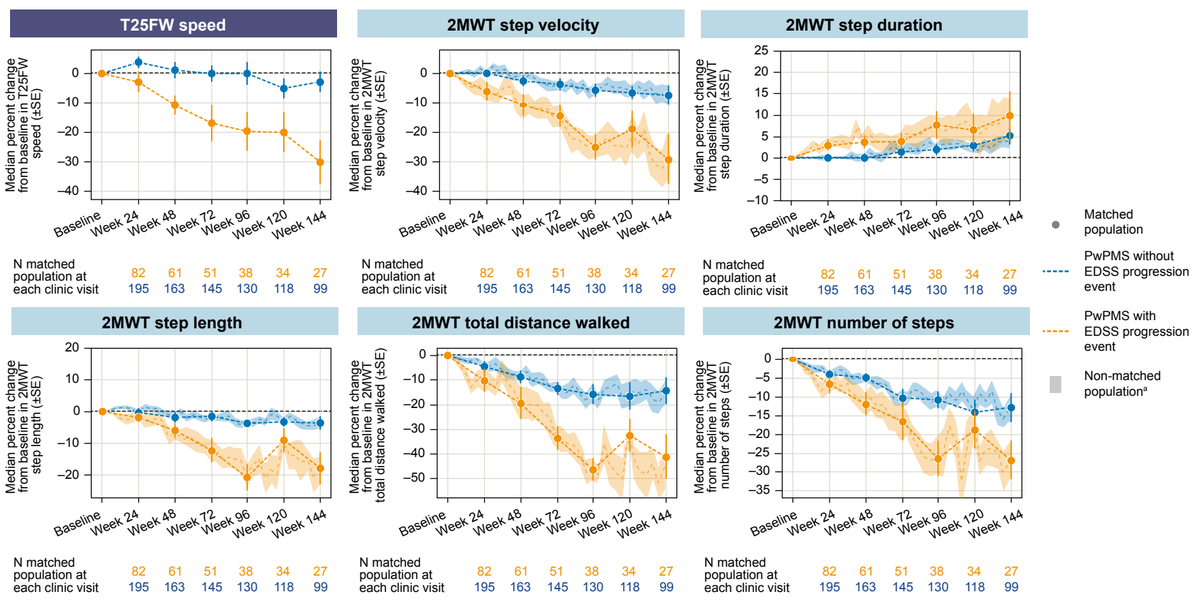
- 2MWT step velocity shows comparable percent change from baseline at Year 3 to that of T25FW speed (–10% vs –8%)
- Consistent with previous findings,[8] total distance walked and number of steps on the 2MWT show the largest worsening as well as a change as early as Weeks 5–8 (see grey-shaded areas that do not overlap with zero)



[a]The non-matched population includes all PwPMS for whom 2MWT data at baseline period and at the respective clinic visit period are available, regardless whether or not T25FW data are available.

How Does the Ability of the Floodlight 2MWT to Discriminate Between PwPMS with and Without EDSS Progression Events Compare with That of the In-Clinic T25FW?

- The 2MWT and the T25FW show comparable ability to discriminate between groups of patients with EDSS progression events and patients without EDSS progression events
- On the 2MWT, patients without EDSS progression events show subtle, but stronger and more consistent worsening than the T25FW (median percent change from baseline at Year 3 on 2MWT gait measures: –3% to –13% vs T25FW speed: <5%)
  - This worsening is in line with previously reported findings that showed a change on digital measures of gait in people considered to be clinically stable[8]
  - The 2MWT could be explored in future research as a potential biomarker for screening study participants or as an outcome measure in future Phase II clinical trials of progressive MS



[a]The non-matched population includes all PwPMS for whom 2MWT data at baseline period and at the respective clinic visit period are available, regardless whether or not T25FW data are available.

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ABBREVIATIONS

2MWT, Two-Minute Walk Test; **CDP**, confirmed disability progression; **EDSS**, Expanded Disability Status Scale; **MS**, multiple sclerosis; **MSWS-12**, 12-item Multiple Sclerosis Walking Scale; **PMS**, progressive multiple sclerosis; **PPMS**, primary progressive multiple sclerosis; **PwPMS**, people with progressive multiple sclerosis; **SE**, standard error; **SPMS**, secondary progressive multiple sclerosis; **T25FW**, Timed 25-Foot Walk.

DISCLOSURES

J Rodrigues is a contractor for F. Hoffmann-La Roche Ltd. **G Bogaarts** is an employee of F. Hoffmann-La Roche Ltd. **A Festanti** is a contractor for F. Hoffmann-La Roche Ltd. **C Simillion** is an employee of F. Hoffmann-La Roche Ltd. **S Hubeaux** is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. **VP Illiano** is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. **L Leocani** has received compensation for consulting services from Almirall, EXCEMED, F. Hoffmann-La Roche Ltd, Merck, Novartis, Biogen, Janssen-Cilag and Bristol Myers Squibb. **M McGinley** has served on scientific advisory boards for Genzyme and Genentech; received research support from Novartis, the National Institutes of Health (NIH), Agency for Healthcare Research and Quality (AHRQ), Genentech and Biogen; and is receiving funding from a KL2 (KL2TR002547) grant from Clinical and Translational Science Collaborative of Cleveland, from the National Center for Advancing Translational Sciences component of the National Institutes of Health; and consultancy fees from Genentech and EMD Serono. **MP Sormani** has received personal compensation for serving as a consultant for Biogen, F. Hoffmann-La Roche Ltd, Sanofi, Merck, Celgene, Novartis, GeNeuro and Immunic; and for serving on a scientific advisory or data safety monitoring board for MedDay, Sanofi and F. Hoffmann-La Roche Ltd. **G Comi** has received compensation for consulting services from Almirall, Chugai, EXCEMED, F. Hoffmann-La Roche Ltd, Forward Pharma, Genzyme, Merck, Novartis, Receptos, Sanofi and Teva Pharmaceuticals; and compensation for speaking activities from Almirall, EXCEMED, F. Hoffmann-La Roche Ltd, Genzyme, Merck, Novartis, Receptos, Sanofi and Teva Pharmaceuticals. **A Kazlauskaite** is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. **L Craveiro** is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. **MD Rinderknecht** is a contractor for F. Hoffmann-La Roche Ltd. **M Zanon** is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. **H Butzkueven** is an employee of Monash University and has accepted travel compensation from Merck; his institution receives honoraria for talks, steering committee activities and research grants from Roche, Merck, Biogen, Novartis, UCB Pharma, Medical Research Future Fund Australia, NHMRC Australia, Trish MS Foundation, MS Australia and the Pennycook Foundation. He receives personal compensation for steering group activities for the Brain Health Initiative from Oxford Health Policy Forum and is funded by an NHMRC Australia Investigator Grant.

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