Characterization of the gait in patients with relapsing–remitting multiple sclerosis and secondary progressive multiple sclerosis measured by FeetMe® integrated sensor insole system: Results of the interim analysis

P222

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Introduction

- **Multiple sclerosis** (MS) is a **chronic inflammatory disease** of the central nervous system that causes severe physical limitations and lack of autonomy.
- **Gait disorder** causes **disability** and **decrease quality of life** in multiple sclerosis (MS) patients. For this reason, **gait analysis** contributes significantly to **monitor disease progression**.
- **FeetMe®** was the **first validated medical** device allowing a **portable monitoring of the gait of MS patients** which objectively assess and monitor gait disorder in MS patients.

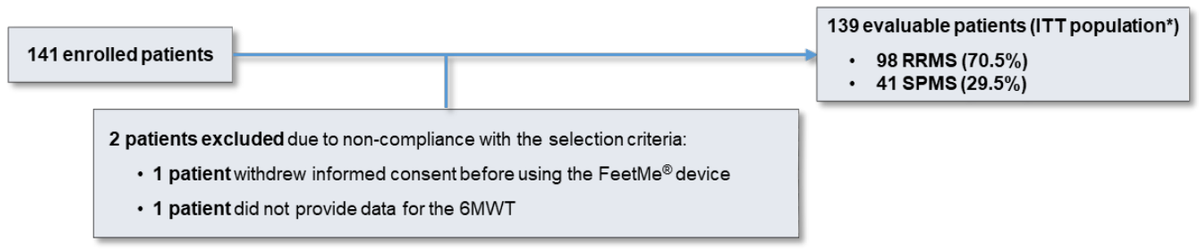
Objective

- To **characterize** and **compare gait pattern** in relapsing-remitting MS (**RRMS**) and secondary-progressive MS (**SPMS**) patients (**physicians' criteria**) **measured by FeetMe®** and collected with **different tests**.

Methods

- **MsFeet PRO** (CBAF312AES03) is an **observational**, **non-interventional**, **cross-sectional** and **multicenter** study carried out at a national level with **patients diagnosed with MS** recruited consecutively by **neurologists**, **30 public and private hospitals in Spain**.
- **Inclusion criteria**: patients 18-65 years old, diagnosed with MS (McDonald 2010/2017 criteria), with EDSS between 2.5-6.5, and relapse free within 30 days from recovery prior to the study initiation.
- Patients were classified as **SPMS or RRMS** according to **two perspectives**:
  - **Objective criteria**: RRMS according to McDonald 2010/2017 criteria, and SPMS according to physicians' criteria plus patients with RRMS who met Lorscheider et al (2016) criteria.
  - **Subjective criteria**: according to physicians' criteria.
- All patients performed **three tests with FeetMe®** device:
  - **6-minute walk test** (6MWT): which measured the distance (meters) a patient could walk quickly on a flat surface for six minutes with or without resting.
  - **2-minute walk test** (2MWT): which measured the distance (meters) a patient could walk quickly on a flat surface for two minutes with or without resting. The 2MWT was derived from the 6MWT, selecting the first 120 seconds after the beginning of the 6MWT.
  - **Timed 25-foot walk test** (T25FWT): measured the time (seconds) needed to walk 25 feet, as fast as possible and safely.
- **Primary endpoint** was the **gait pattern measured by FeetMe®** and collected in the 2MWT.
- Main gait parameters analyzed were:
  - **Distance** obtained in **6MWT** (meters).
  - **Distance** obtained in **2MWT** (meters).
  - **Velocity** (cm/s): obtained as the ratio between walked distance and ambulation time.
  - **Cadence** (steps/min): number of steps taken in one minute.
  - **Ambulation time** (seconds): time taken to perform the test.
  - **Stride length** (cm): measured on the progression line between two consecutive heel centers of the same foot.
  - **Stride time** (seconds): time between the initial contact instants of two consecutive steps on the same foot.
  - **Double support** (gate cycle; %): the two periods when both feet were in contact with the ground are called initial double support and final double support.
- Interim results from **139 patients** from the intention-to-treat (ITT) population are presented here (**Figure 1**).

Figure 1. Included patients



*ITT population included all patients enrolled in the study who fulfilled all selection criteria in which any of the gait parameters had been obtained using FeetMe® device (2MWT, 6MWT or T25FWT). Patients who withdrew informed consent were not included in this population.
2MWT, 2-minute walk test; 6MWT, 6-minute walk test; ITT, intention-to-treat; T25FWT, timed 25-foot walk test

Results

Baseline sociodemographic and clinical characteristics

- **98 patients with RRMS** (70.5% of the total ITT population) and **41 patients with SPMS** (29.5%) were included (**Table 1**).

Table 1. Baseline sociodemographic and clinical characteristics

Characteristic	RRMS (N=98)	SPMS (N=41)	Total (N=139)
Age, years, mean (SD)	45.6 (8.7)	51.1 (7.5)	47.2 (8.7)
Sex, female, n (%)	71 (72.4%)	25 (61.0%)	96 (69.1%)
Education level, n (%)			
Primary education	5 (5.2%)	5 (12.5%)	10 (7.3%)
Secondary education	23 (23.7%)	11 (27.5%)	34 (24.8%)
Higher education	69 (71.1%)	24 (60.0%)	93 (67.9%)
Current employment status, n (%)			
Non-active	55 (56.1%)	31 (77.5%)	86 (62.3%)
Active	43 (43.9%)	9 (22.5%)	52 (37.7%)
Years since first symptoms, mean (SD)	15.5 (8.9)	21.3 (8.8)	17.2 (9.2)
Years since MS diagnosis, mean (SD)	12.9 (8.0)	18.5 (8.7)	14.5 (8.6)
EDSS score, mean (SD)	4.0 (1.3)	5.2 (1.2)	4.4 (1.4)
Number of relapses in the last year, n (%)			
None	75 (76.5%)	40 (97.6%)	115 (82.7%)
1 or more relapses	23 (23.5%)	1 (2.4%)	24 (17.3%)
Months since last relapse, mean (SD)	7.3 (4.1)	6.5 (0.0)	7.2 (4.0)

EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis

Gait parameters obtained in the 2MWT measured by FeetMe®

- **Table 2** shows the **main gait parameters assessed in the 2MWT**, comparing between RRMS and SPMS patients (physicians' criteria).

Table 2. Main gait parameters obtained in the 2MWT for RRMS and SPMS patients

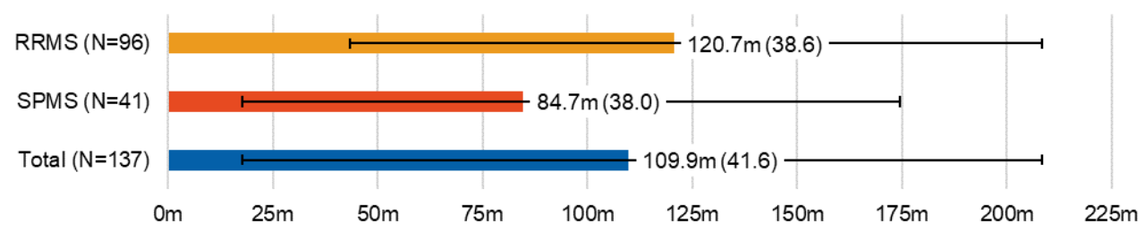
Gait parameters	RRMS (N=98)	SPMS (N=41)	p-value
Step count, mean (SD)	203.3 (38.8)	172.5 (44.3)	**<0.0001**
Velocity, cm/second, mean (SD)	100.3 (30.9)	72.6 (30.3)	**<0.0001**
Cadence, steps/minute, mean (SD)	102.1 (17.6)	88.5 (18.9)	**<0.0001**
Ambulation time, seconds, mean (SD)	121.5 (2.1)	121.6 (0.3)	0.7283
Stride length, cm, mean (SD)	115.3 (21.0)	94.9 (26.6)	**<0.0001**
Stride time, seconds, mean (SD)	1.2 (0.3)	1.4 (0.4)	**0.0006**
Double support, % gate cycle, mean (SD)	33.1 (4.1)	35.0 (7.4)	**0.0495**

cm, centimeter; MS, multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis

Distance walked and collected with FeetMe® in different tests

- **2-minute walk test:**

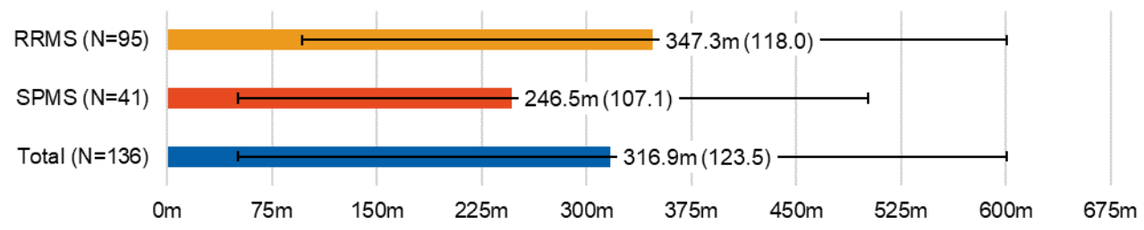
Figure 2. Performance (distance in meters) on the 2MWT for RRMS and SPMS patients



The coloured bars represent the mean distance walked in meters. Standard deviation shown inside brackets.The thinner black bars represent the minimum and maximum distance walked in meters.
RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis

- **6-minute walk test:**

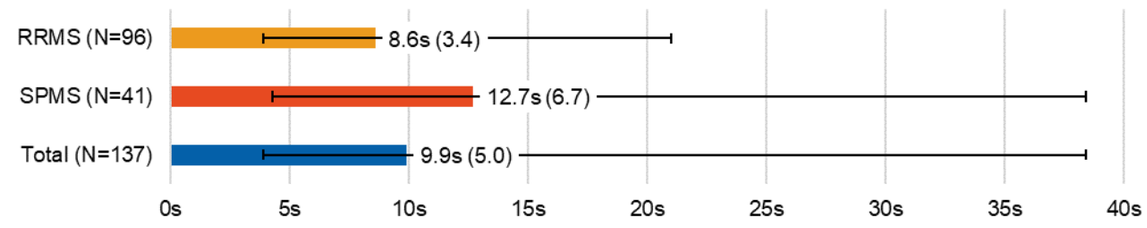
Figure 3. Performance (distance in meters) on the 6MWT for RRMS and SPMS patients



The coloured bars represent the mean distance walked in meters. Standard deviation shown inside brackets. The thinner black bars represent the minimum and maximum distance walked in meters.
RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis

- **Timed 25-foot walk test:**

Figure 4. Performance (time in seconds) on the T25FWT for RRMS and SPSMS patients



The coloured bars represent the mean time to complete the test in seconds. Standard deviation shown inside brackets. The thinner black bars represent the minimum and maximum time to complete the test in seconds.
RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis

Conclusions

- **SPMS patients walked** a significantly **shorter distance** at a **lower speed, cadence, and stride length** than RRMS patients in 2MWT.
- In addition, **SPMS patients** showed a significant **increase in stride time and double support** gait cycle than RRMS patients.
- Overall, **SPMS patients performed worse than RRMS patients** in 2MWT, 6MWT and T25FWT **measured by FeetMe®**.

Disclosures

GIA has received Advisory Board honoraria and research projects from Novartis, Sanofi, Merck Serono, Roche, Actelion, Celgene and Teva. **COG** has received speaker and consultation fees from Biogen Idec, Celgene, Sanofi-Genzyme, Novartis, Roche, Merck, and Teva. **EAR** has received speaker and consultation fees from Merck, Almirall, Bayer Hispania, Biogen and Sanofi-Aventis. **VML** has received consulting or speaking fees from Almirall, Biogen, Genzyme, Merck Serono, Novartis, Roche, Terumo, Sanofi, Teva, Celgene and BMS. **JEML** has received grants and consulting or speaking fees from Almirall, Biogen, Bristol-Meyers-Squibb, Genzyme, Merck, Novartis, Roche and Teva. **LB** has received honoraria, travel expenses, speaker fees and advisory fees from Bayer, Celgene, Biogen, Genzyme, Merck, Novartis, Roche, Almirall and Teva. **RRC** has received compensation for consulting services and speaking honoraria from Biogen Idec, Novartis, Bayer, Merck-Serono, Genzyme, Teva Pharmaceutical Industries Ltd, Almirall, and Roche. **JRA** has received consulting honoraria from Biogen Idec and Novartis, and honoraria for lecturing, travel expenses for attending meetings, or financial support for research from Bayer, Biogen Idec, Merck Serono, Sanofi and Novartis. **MAHP** has received speaker and consulting fees from Bayer HealthCare Pharmaceuticals, Biogen Idec Inc., Genzyme Corporation, Merck Serono, Novartis Sanofi-Aventis, Roche Pharma, Teva Pharmaceuticals. **JDGS** has received consulting, research grant support, or speaker honoraria from Merck, Sanofi-Genzyme, Allergan, Biogen, Roche, UCB and Novartis. **ILD** has received honoraria from Novartis and Sanofi. **MGG** has received speaker honoraria from Novartis, Biogen, Merck Serono, Genzyme, Bristol-Myers, Bial. **AAT** has received speaker honoraria from Biogen, Novartis, Roche, Merck, Genzyme and Almirall. **MLMG** has received compensation for consulting services and speaking fees from Merck, Biogen, Novartis, Sanofi-Genzyme, Almirall, Bayer, BMS, ROCHE and TEVA. **LQG** has received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), GBS-CIDP Foundation International, Novartis Pharma Spain, Roche, UCB and Grifols; provided expert testimony to Grifols, CSL Behring, Novartis, Sanofi-Genzyme, Merck, Annexon, Johnson and Johnson, Alexion, UCB, Takeda and Roche; serves at Clinical Trial Steering Committee for Sanofi Genzyme and is Principal Investigator for UCB's CIDP01 trial. **EM** has received speaker honoraria from Novartis. Merck, Biogen, Sanofi, Roche. **LCFF** has received speaker and consulting honoraria from Almirall, Bayer, Biogen, Biopas, Celgene, Ipsen, Merck, Novartis, Roche, Sanofi-Genzyme and Teva. **RPM** has received speaker honoraria from Almirall, Biogen, Merck, Novartis, Roche and Sanofi-Aventis. **NSV** has received speaking honoraria from Genzyme-Sanofi, Merck-Serono, Almirall and travel reimbursement from Genzyme-Sanofi and Roche for international and national meetings over the last 3 years. **RSM** has received speaker honoraria from Biogen, Roche, Sanofi and Merck. **XM** has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with AbbVie, Actelion, Alexion, Bayer, Biogen, Bristol-Myers Squibb/Celgene, EMD Serono, Genzyme, Hoffmann-La Roche, Immunic, Janssen Pharmaceuticals, Medday, Merck, Mylan, Nervgen, Novartis, Sanofi-Genzyme, Teva Pharmaceutical, TG Therapeutics, Excemed, MSIF and NMSS. **SMY** received honoraria compensation to participate in advisory boards, collaborations as a consultant and scientific communications and received research support, funding for travel and congress expenses from Roche, Biogen Idec, Novartis, TEVA, Merck, Gencyme, Sanofi, Bayer, Almirall and Celgene. **EAM** has received consulting fees from Novartis, BMS, Merck, Roche, Biogen. **EMT** has received honoraria as consultant in advisory boards, and or as chairperson or lecturer in meetings, and has also participated in clinical trials and other research projects promoted by Actelion, Almirall, Bayer, Biogen-Idec, Bristol Myers Squibb, Merck-Serono, Teva, Novartis Roche and Sanofi-Genzyme. **JF** is an employee of Novartis Pharmaceuticals. **RRS** is an employee of Novartis Pharmaceuticals. **BC** have received compensations form Merck, Sanofi-Genzyme, Biogen-Idec, Novartis, and Roche to participate in advisory board. **MBQ, EFD, MMB, MOM** and **RAG** have nothing to disclose.

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