

Safety, Patient-Reported Outcomes, and Clinical Assessment of Walking Ability for Prolonged-Release Fampridine Treatment in Routine Clinical Practice: Results of the LIBERATE Study

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Introduction

- Impaired walking is common in multiple sclerosis (MS), and negatively impacts patients lives¹⁻³
- Prolonged-release fampridine (PR-FAM; dalfampridine extended-release tablets in the US) is the only treatment approved for the improvement of walking ability in adults with MS with walking disability (EDSS 4–7)⁴⁻⁶
- As of 31 December 2019, there were > 373,000 patients treated with PR-FAM worldwide, representing > 514,000 patient-years of exposure
- LIBERATE is a long-term, multicenter, observational postauthorization safety study of PR-FAM in patients with MS in clinical practice

Methods

LIBERATE recruited patients with MS newly prescribed PR-FAM (10 mg tablets, twice daily) at 201 sites in 13 countries^a

Data Acquisition

- At enrollment visit and during follow-up visits up to 12 months
- Safety data collected from first dose of PR-FAM until study completion or early discontinuation

Data Assessment

- MSIS-29 for physical (PHYS) and psychological (PSYCH) health
 - Negative change indicates an improvement
- CGI-I assessment of walking ability
 - Rates the patient's overall walking ability relative to baseline ranging from 1 (very much improved) to 7 (very much worse)

The primary objective of the study was to collect additional safety data, including the incidence rate of seizures and other specific adverse events of special interest, from patients taking PR-FAM in routine clinical practice

Patient Demographics for the Total Population and Both European and Non-European Populations

	European Countries n = 4439	Non-European Countries n = 207	Total N = 4646
Age at enrollment, y			
Mean (SD)	52.6 (10.5)	51.0 (11.2)	52.5 (10.5)
< 65, n (%)	3873 (87.2)	184 (88.9)	4057 (87.3)
Sex			
Female, n (%)	2913 (65.6)	138 (66.7)	3051 (65.7)
Race			
Black, n (%)	0 (0)	1 (0.5)	1 (< 0.1)
Asian, n (%)	0 (0)	2 (1.0)	2 (< 0.1)
White, n (%)	0 (0)	198 (95.7)	198 (4.3)
Not reported, ^a n (%)	4439 (100.0)	2 (1.0)	4441 (95.6)
Other, n (%)	0 (0)	4 (1.9)	4 (< 0.1)
EDSS ^b			
Mean (SD)	5.2 (1.1)	5.0 (1.1)	5.2 (1.1)
Time from diagnosis, ^c y			
Mean (SD)	13.6 (9.5)	12.2 (8.6)	13.6 (9.4)
MS type ^d			
RRMS, n (%)	1730 (39.0)	123 (59.4)	1853 (40.0)

EDSS = Expanded Disability Status Scale; MS = multiple sclerosis; N = number of patients overall; n = number of patients in a category; RRMS = relapsing-remitting multiple sclerosis
Data cutoff date: 21 June 2019. Percentages calculated using the total number of patients (N) as the denominator.

^aNot reported due to confidentiality regulations. ^bEuropean, n = 3967; non-European, n = 191; total, n = 4158. ^cTime from diagnosis = (enrollment date – imputed diagnosis date + 1)/365.25, where partial diagnosis date is imputed with the first day of the month if day is missing and with 1 January if month and day are missing; European, n = 4372; non-European, n = 207; total, n = 4579. ^dEuropean, n = 4431; non-European, n = 207; total, n = 4638.

Patient Disposition for the Total Population and Both Subgroup Populations

	Safety^a n = 4646	Not in Safety^b n = 91	Total N = 4737
Number of patients, n (%)			
Enrolled	4646 (100.0)	91 (100.0)	4737 (100.0)
Completed	3251 (70.0)	5 (5.5)	3256 (68.7)
Discontinued treatment, n (%)			
Lack of efficacy	1158 (24.9)	0 (0)	1158 (24.4)
Adverse events	753 (16.2)	0 (0)	753 (15.9)
Other	369 (7.9)	0 (0)	369 (7.8)
Loss to follow-up	123 (2.6)	0 (0)	123 (2.6)
Withdrawal of consent	44 (0.9)	0 (0)	44 (0.9)
Investigator decision	25 (0.5)	0 (0)	25 (0.5)
Death	2 (< 0.1)	0 (0)	2 (< 0.1)
Pregnancy	1 (< 0.1)	0 (0)	1 (< 0.1)

N = number of patients overall; n = number of patients in a category; PR-FAM = prolonged-release fampridine
Data cutoff date: 21 June 2019. Percentages calculated using the total number of patients (N) as the denominator.

^aSafety population: patients who enrolled in the study and received ≥ 1 dose of PR-FAM. ^bNot in the safety population: patients who enrolled in the study but did not receive PR-FAM treatment.

Overall Adverse Events and Adverse Events of Special Interest

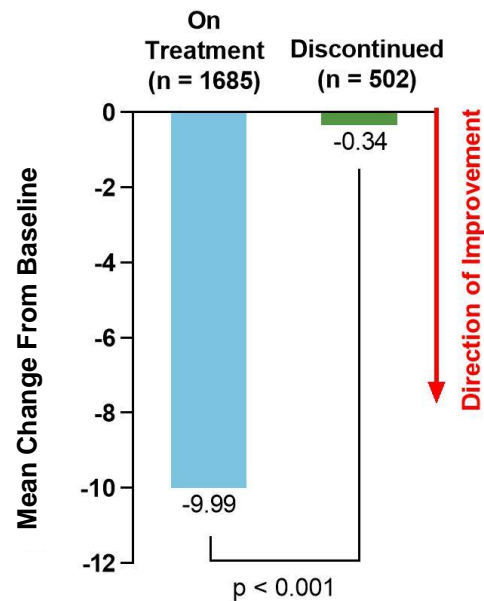
Preferred Term	European Countries n = 4439	Non-European Countries n = 207	Total N = 4646
Any TEAE, n (%)	2407 (54.2)	41 (19.8)	2448 (52.7)
Serious TEAEs, n (%)	277 (6.2)	2 (1.0)	279 (6.0)
TEAEs of special interest, n (%)	1767 (39.8)	32 (15.5)	1799 (38.7)
Serious TEAEs of special interest, n (%)	127 (2.9)	1 (0.5)	128 (2.8)
Seizure TEAEs, n (%)	17 (0.4)	0 (0)	17 (0.4)
Incidence rate/100 person-years (95% CI)	0.5 (0.3–0.8)	0 (0)	0.5 (0.3–0.8)
Serious hypersensitivity-related TEAEs, n (%)	1 (< 0.1)	0 (0)	1 (< 0.1)
Incidence rate/100 person-years (95% CI)	< 0.1 (0–0.2)	0 (0)	< 0.1 (0–0.2)
UTI-related TEAEs, n (%)	399 (9.0)	7 (3.4)	406 (8.7)
Incidence rate/100 person-years (95% CI)	14.9 (13.6–16.3)	5.5 (2.4–10.8)	14.5 (13.3–15.8)
Severe infections other than UTI-related TEAEs, n (%)	148 (3.3)	0 (0)	148 (3.2)
Incidence rate/100 person-years (95% CI)	5.1 (4.4–6.0)	0 (0)	4.9 (4.2–5.7)

Overall Adverse Events and Adverse Events of Special Interest (cont.)

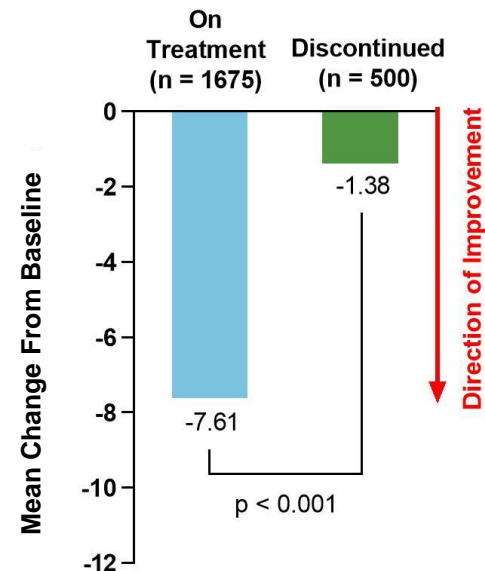
Preferred Term	European Countries n = 4439	Non-European Countries n = 207	Total N = 4646
Depression- and suicide-related TEAEs, n (%)	59 (1.3)	0 (0)	59 (1.3)
Incidence rate/100 person-years (95% CI)	1.8 (1.4–2.3)	0 (0)	1.7 (1.3–2.2)
Anxiety-related TEAEs, n (%)	68 (1.5)	1 (0.5)	69 (1.5)
Incidence rate/100 person-years (95% CI)	2.1 (1.6–2.6)	0.7 (0–3.8)	2.0 (1.6–2.5)
TEAEs suggestive of central nervous system stimulation, n (%)	1382 (31.1)	26 (12.6)	1408 (30.3)
Incidence rate/100 person-years (95% CI)	58.3 (55.7–60.9)	20.6 (13.9–29.4)	56.7 (54.3–59.3)
Cardiovascular-related TEAEs, n (%)	80 (1.8)	1 (0.5)	81 (1.7)
Incidence rate/100 person-years (95% CI)	2.5 (2.0–3.1)	0.7 (0–3.8)	2.5 (2.0–3.0)
Clinically significant hematological abnormality–related TEAEs, n (%)	26 (0.6)	0 (0)	26 (0.6)
Incidence rate/100 person-years (95% CI)	1.1 (0.7–1.5)	0 (0)	1.0 (0.7–1.4)

MSIS-29 PHYS and MSIS-29 PSYCH Scores Improved in Patients Treated With PR-FAM Compared With Patients Off Treatment

Change From Baseline to Month 12 in MSIS-29 PHYS Score



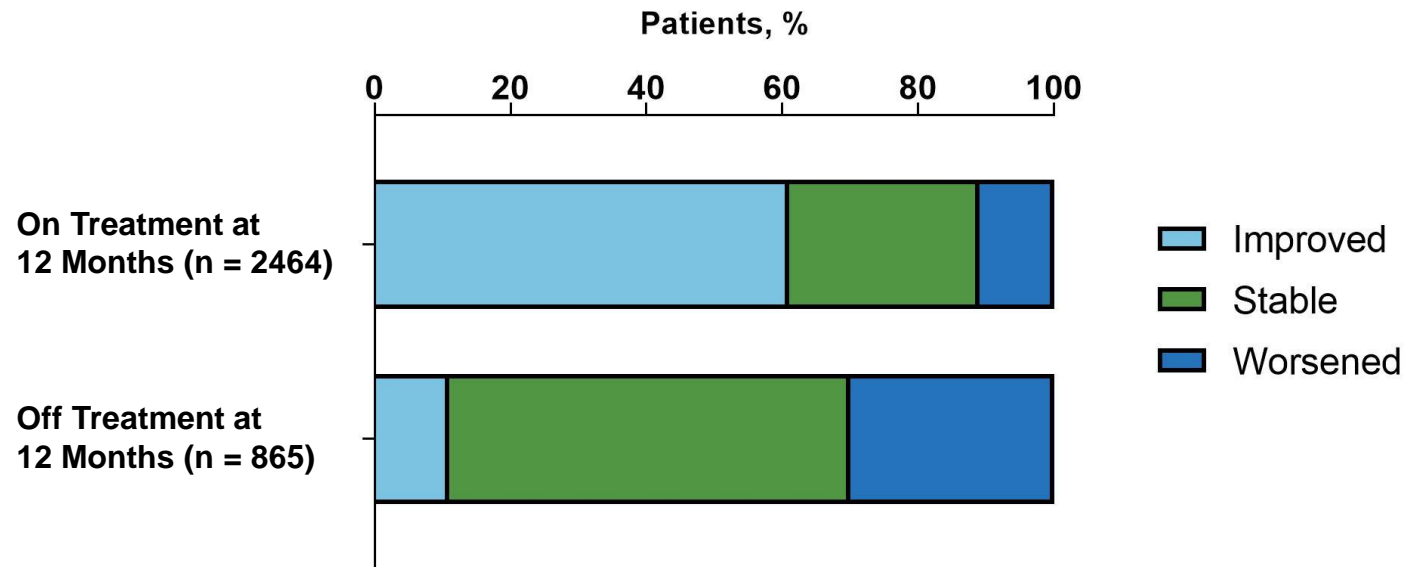
Change From Baseline to Month 12 in MSIS-29 PSYCH Score



Patients on PR-FAM therapy at 12 months had greater mean improvement on the MSIS-29 PHYS and MSIS-29 PSYCH scales than patients who had discontinued treatment

Patients On Treatment With PR-FAM Showed Improved Walking Ability Compared With Patients Off Treatment

Changes From Baseline to Month 12 in CGI-I Score for Walking



At 12 months, 61% of patients on PR-FAM therapy demonstrated improvement in walking ability relative to baseline, measured using the CGI-I, compared with 11% of patients off treatment ($p < 0.001$)

Conclusions



In this analysis of the LIBERATE study:

While some particular adverse events of special interest (e.g., seizures, UTIs) should be monitored, they are well documented in the PR-FAM prescribing information and can be adequately managed by routine risk-minimization activities

There were no unexpected safety concerns from the TEAE analysis



LIBERATE results demonstrate long-term treatment with PR-FAM improves patient-reported well-being and physician-reported walking ability in routine clinical practice in patients with MS