MRI Activity versus Relapses as Markers of Disease Activity in SPMS: Data from Real World and Pivotal Clinical Studies

P001

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Introduction

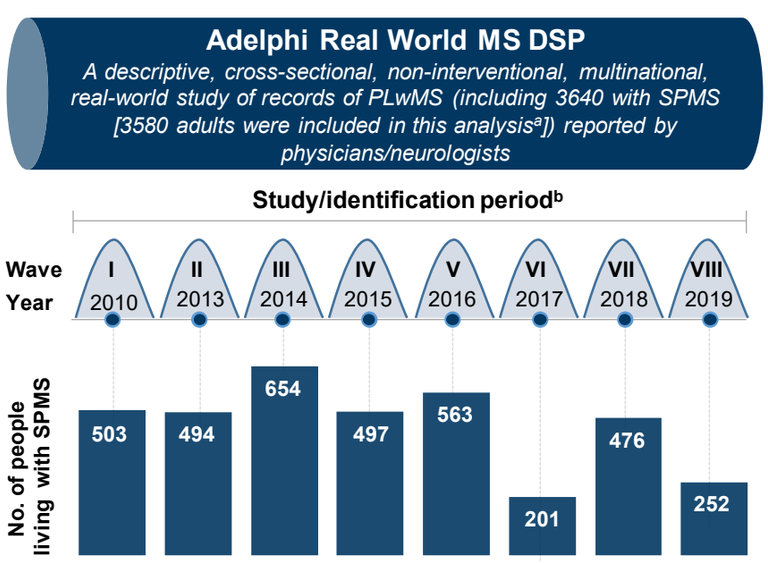
- Multiple sclerosis (MS), considered a disease continuum, may progress from a relapsing-remitting to a secondary progressive course[1]
- People living with secondary progressive MS (SPMS) are often categorised as active (aSPMS) or non-active (naSPMS) based on the evidence of their disease activity;[1] however, the relative contribution of magnetic resonance imaging (MRI) activity and/or relapses in defining disease activity in both the real world and clinical trial settings is not well understood

Objectives

- To evaluate:
  - Adelphi Real World MS Disease Specific Programme (DSP): The real-world differences between aSPMS and naSPMS groups
  - The contribution of MRI activity and relapses in defining disease activity in people living with SPMS in real world (Adelphi Real World MS DSP) and clinical settings (EXPAND)
  - EXPAND Phase 3 trial: Whether participants in the placebo group categorised as naSPMS at baseline remain in the same category or can revert to aSPMS

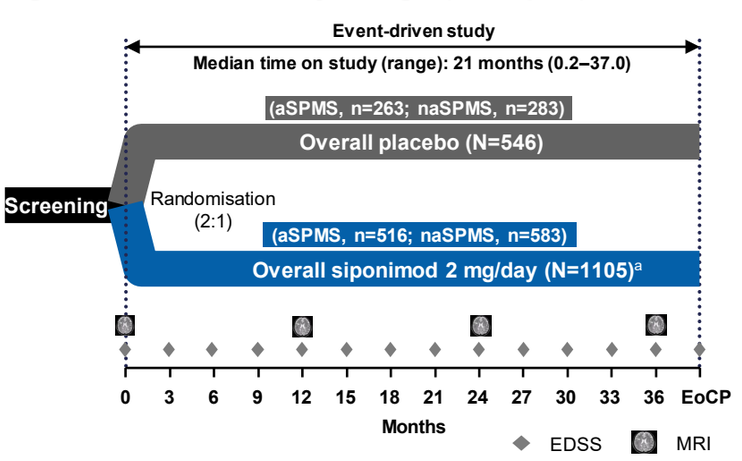
Methods

Figure 1. Adelphi Real World MS DSP study design



DSP, Disease Specific Programme; DMT, disease-modifying therapy; MS, multiple sclerosis; PLwMS, people living with MS; SPMS, secondary progressive MS.
[a]Adults with only one reported DMT per regimen (Age ≥18 years at index [the day of physician visit]). [b]Data were retrospectively collected in annual waves during the period of 1 January 2011 to 31 December 2019 and included in this study. In each wave the next 10 PLwMS visiting their physician were included in this study. All associated dates relate to the day of survey completion. Data were not collected between 2011 and 2012.

Figure 2. EXPAND study design (Core part)



aSPMS, active SPMS; EDSS, Expanded Disability Status Scale; EoCP, end of Core part; MRI, magnetic resonance imaging; naSPMS, non-active SPMS; SPMS, secondary progressive multiple sclerosis.
[a]Five participants did not receive the study drug. One participant was excluded from all safety and efficacy analyses (no signed consent form was supplied at study start).

- In Adelphi Real World MS DSP (**Figure 1**):
  - People living with SPMS (n=3580) were grouped into aSPMS (≥1 new lesion on the most recent MRI and/or ≥1 relapse in the past 12 months; n=1889) and naSPMS (no new lesion and no relapse in the past 12 months; n=665) cohorts
  - MRI activity, relapse status, disease characteristics and treatment were analysed descriptively
- In EXPAND (Phase 3 clinical trial in SPMS; **Figure 2**):
  - Participants (N=1651) with ≥1 relapse in the 2 years prior to screening and/or ≥1 gadolinium-enhancing (Gd+) T1 lesion at baseline on MRI were categorised as aSPMS (n=779); and those with no relapse in prior 2 years and with no Gd+ lesion on MRI at baseline were categorised as naSPMS (n=866)
  - At baseline, participants in the placebo group (N=546) were categorised as aSPMS (n=263) or naSPMS (n=283). During the study, evidence of disease activity was assessed either by MRI (examined yearly) or relapses (examined whenever relapses occur at or outside visits). Here, we present the on-study data for confirmed relapses and MRI activity for naSPMS participants in the placebo group from EXPAND (Core part)
- No direct comparisons were made among groups from Adelphi Real World MS DSP and the EXPAND trial (Core part)

Results

Adelphi Real World MS DSP

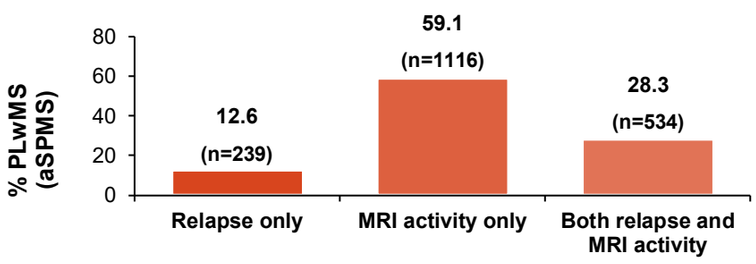
- In the past 12 months, PLwMS categorised as naSPMS (vs aSPMS) had a higher mean Expanded Disability Status Scale (EDSS) score and were less frequently monitored with MRI (lower proportion had undergone MRI, and less MRI scans were done per person; **Table 1**)
- Higher proportions of PLwMS categorised as naSPMS (vs aSPMS) had moderate-to-severe disease (based on their physician's perception) and were not on any disease-modifying therapy (DMT; **Table 1**)
- Of PLwMS categorised as aSPMS, activity was most commonly detected via MRI than relapse in the real world (**Figure 3**)

Table 1. Characteristics of PLwMS and MRI utilisation (Adelphi Real World MS DSP)

Characteristics	aSPMS (N=1889)	naSPMS (N=665)
EDSS score in the past 12 months, mean (SD)	n=1463 4.6 (1.72)	n=606 5.2 (1.76)
Change in EDSS score in the past 12 months, mean (SD)	0.43 (0.56)	0.20 (0.49)
Proportion of PLwMS having moderate-to-severe disease based on the physician's perception (%)[a]	73.5	87.8
Number of PLwMS with MRI conducted in the past 12 months (% non-missing)	1657 (87.7)	390 (58.7)
Number of MRIs conducted in the past 12 months	1848	576
Number of MRI scans conducted per person in the past 12 months, mean (SD)	1.24 (0.77)	0.87 (0.78)
Proportion of PLwMS not on any DMT (%)	23.4	45.1

aSPMS, active SPMS; DMT, disease-modifying therapy; DSP, Disease Specific Programme; EDSS, Expanded Disability Status Scale; MRI, magnetic resonance imaging; MS, multiple sclerosis; naSPMS, non-active SPMS; PLwMS, people living with MS; SD, standard deviation; SPMS, secondary progressive MS.
[a]All data related to disease severity or level of activity contained within the Adelphi Real World MS DSP have no clinical thresholds or requirements but are based entirely on each physician's interpretation.

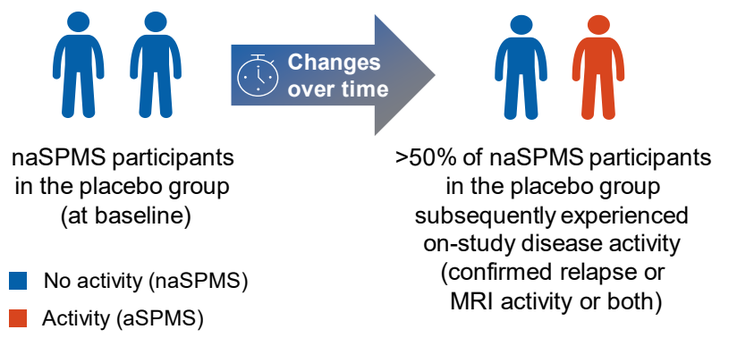
Figure 3. Proportion of PLwMS categorised as aSPMS according to relapse or MRI activity[a] or both (Adelphi Real World MS DSP)



aSPMS, active SPMS; DSP, Disease Specific Programme; MRI, magnetic resonance imaging; MS, multiple sclerosis; PLwMS, people living with MS; SPMS, secondary progressive MS.
[a]T1, T2 and gadolinium-enhancing lesions were assessed.

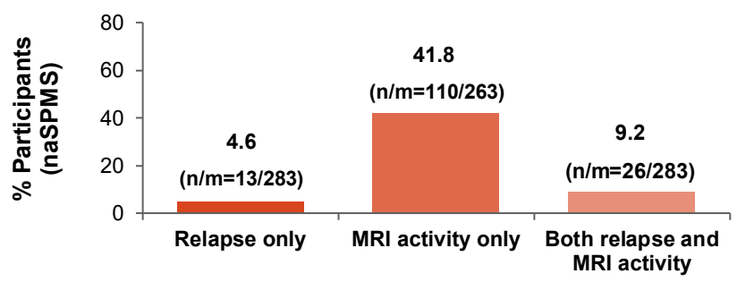
- Disease activity was subsequently identified in >50% of participants categorised as naSPMS at baseline in the placebo group (**Figure 4**), with MRI being a more sensitive detection tool than relapses (**Figure 5**)

Figure 4. Changes in disease activity over time in participants with naSPMS in the placebo group (EXPAND)



aSPMS, active SPMS; MRI, magnetic resonance imaging; naSPMS, non-active SPMS; SPMS, secondary progressive multiple sclerosis.

Figure 5. Proportion of naSPMS participants on placebo with on-study confirmed relapse or MRI activity[a] or both (EXPAND)



Gd+, gadolinium-enhancing; MRI, magnetic resonance imaging; m, number of subjects with result available; n, number of subjects with relapse or MRI activity; naSPMS, non-active secondary progressive multiple sclerosis.
[a]At least 1 Gd+ T1 lesion, or new or enlarging T2 lesion at any post-baseline scan.

Conclusions:

- In both real-world and clinical trial settings, MRI activity appears to be a more sensitive tool to measure disease activity than relapses
- In the Adelphi Real World MS DSP:
  - MRI utilisation was much lower in the naSPMS cohort than in the aSPMS cohort
  - Fewer MRIs in the naSPMS cohort reduced the chance of detecting disease activity
  - Despite higher disease severity, a higher proportion of people living with naSPMS (vs aSPMS) were not on any DMT
- Reduced MRI monitoring in people living with naSPMS in the real-world is a concern, which decreases the chance to detect and treat any new disease activity in this population
- In the EXPAND trial, disease activity was subsequently identified in more than half of the participants categorised as naSPMS at baseline in the placebo group
- These data highlight the difficulties in defining aSPMS and naSPMS reliably, and the potential negative implications of incorrectly defining patients as naSPMS, resulting in suboptimal management of people living with SPMS

Reference

1. Lublin FD, et al. *Neurology*. 2014;83(3):278–286.

Disclosures

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