Introduction

- Multiple sclerosis (MS), considered a disease continuum, may progress from a relapsing-remitting to a secondary progressive course.
- 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, 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 determining 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

Figure 2. EXPAND study design (Core part)

• 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 no Gd+ lesion on MRI at baseline were categorised as naSPMS (n=886)
  - 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 (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 relapse than in the real world (Figure 3)

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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>aSPMS (N=1889)</th>
<th>naSPMS (N=665)</th>
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<tbody>
<tr>
<td>EDSS score in the past 12 months, mean (SD)</td>
<td>4.6 (1.72)</td>
<td>5.2 (1.76)</td>
</tr>
<tr>
<td>Number of MRI scans conducted per person in the past 12 months, mean (SD)</td>
<td>1.24 (0.77)</td>
<td>0.87 (0.78)</td>
</tr>
<tr>
<td>Proportion of PLwMS having moderate-to-severe disease based on physician’s perception (%)</td>
<td>72.5</td>
<td>42.5</td>
</tr>
<tr>
<td>Proportion of PLwMS with MRI conducted in the past 12 months (%)</td>
<td>1607 (87.7)</td>
<td>390 (56.7)</td>
</tr>
<tr>
<td>Number of MRI scans conducted in the past 12 months</td>
<td>1848</td>
<td>576</td>
</tr>
<tr>
<td>Number of MRIs conducted in the past 12 months</td>
<td>1848</td>
<td>576</td>
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</table>

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 MRI 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

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