Risk Perception in Multiple Sclerosis: Reasons for Switching Treatment Between High Efficacy and Non-high Efficacy Disease-modifying Therapies

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Disclosures

James Pike and Eddie Jones are employees of Adelphi Real World.
Gustavo Seifer, Patricia Domínguez-Castro, Rainel Sanchez-de la Rosa and Simone Hiltl are employees of Novartis.

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Background

• Multiple sclerosis is a complex chronic disease of the CNS characterized by inflammation and neurodegeneration; it is the most common autoimmune disorder among young adults.

• DMTs approved for the treatment of MS include various Non-HETs and HETs, and have variable benefit-risk profiles that need to be suitable for each patient's disease severity and personal preference.

• Decision to initiate a DMT can be strongly influenced by an individual's risk perception.

• Risk perception is dynamic and influenced by personal, emotional, social, and experiential factors of both the patient and the neurologist and might differ from one region to another.

• HETs are potentially perceived by physicians as having greater safety concerns than Non-HETs and are generally reserved for patients with high disease activity or in cases of suboptimal response.

CNS, central nervous system; DMT, disease-modifying therapy; HET, high efficacy treatment

To investigate the influence of risk perception on switching treatment decisions that are made by physicians when prescribing Non-HETs and HETs

**Primary endpoint**
- The proportion of patients who were switched based on risk perception (infections, malignancies, others) in patients previously treated with Non-HET versus HET

**Secondary endpoints**
- Reasons for switching treatment in the previous Non-HET and HET groups
- Proportion of patients who switched due to lack of efficacy or due to new or enlarging lesions on MRI, increase in the frequency and/or severity of the relapses, progression in physical disability measured by EDSS or patient compliance issues between the groups
- Proportion of patients who changed treatment group versus patients who continued in the same treatment group

EDSS, Expanded Disability Status Scale; HET, high efficacy treatment; MRI, magnetic resonance imaging
Methods

- Data were drawn from the Adelphi Real-World MS DSP, a retrospective non-interventional cross-sectional, multi-cohort study\(^1\); the patient selection flow chart is presented in figure.
- Descriptive statistics (n, %) and Fisher’s Exact test were used to compare risk perception (malignancies/infections), and other reasons for influencing treatment switches.

Patient selection flow chart

RMS (RRMS and SPMS) patients aged ≥18 years identified between Q1 2017–Q2 2021, with both current and previous treatment and whose physician decided to switch their treatment.

Patient population

- Patients with current and previous DMT data (N=4361)
- Physician provided reason for switching from the previous DMT (N=4129)
- Non-HET group included patients on previous Non-HET\(^2\); N=3538 (interferons, glatiramer acetate, dimethyl fumarate and teriflunomide)
- HET group included patients on previous HET\(^2\); N=591 (alemtuzumab, ofatumumab, ocrelizumab, natalizumab, cladribine, fingolimod)
- Risk perception that triggers the switch

^The classification of HET and Non-HET is based on Samjoo IA, et al. publication cited below.

• Of 4361 patients with data available for current and previous DMT, the reason for switching from previous DMT was provided by physicians for 4129 (Non-HET, N=3538; HETs, N=591) patients

• Patients in the previous HET group had longer time since initial MS diagnosis (9.5 vs 7.9 years), higher current EDSS score (mean: 3.5 vs 2.7), lower proportion of patients with RRMS (72.0% vs 86.1%) and higher proportion of patients with rapid deterioration (3.9% vs. 1.5%) versus Non-HET group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (N=4361)</th>
<th>Previous Non-HET (N=3768)</th>
<th>Previous HET (N=593)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>42.1 (11)</td>
<td>42.0 (11.1)</td>
<td>42.5 (10.4)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>65.5</td>
<td>64.8</td>
<td>69.8</td>
</tr>
<tr>
<td>Time since initial MS diagnosis (years), mean (SD)</td>
<td>8.1 (6.1)</td>
<td>7.9 (6.0)</td>
<td>9.5 (6.4)</td>
</tr>
<tr>
<td>Current diagnosis: RRMS (%)</td>
<td>84.2</td>
<td>86.1</td>
<td>72.0</td>
</tr>
<tr>
<td>Current diagnosis: SPMS (%)</td>
<td>15.8</td>
<td>13.9</td>
<td>28.0</td>
</tr>
<tr>
<td>Current EDSS, mean (SD)</td>
<td>2.8 (1.8)</td>
<td>2.7 (1.7)</td>
<td>3.5 (1.9)</td>
</tr>
<tr>
<td>Working full time (%)</td>
<td>47.7</td>
<td>49.0</td>
<td>39.4</td>
</tr>
<tr>
<td>Unemployed (%)</td>
<td>8.3</td>
<td>7.9</td>
<td>10.9</td>
</tr>
<tr>
<td>Patients improving (%)</td>
<td>6.9</td>
<td>7.1</td>
<td>5.1</td>
</tr>
<tr>
<td>Patients deteriorating rapidly (%)</td>
<td>1.8</td>
<td>1.5</td>
<td>3.9</td>
</tr>
<tr>
<td>Duration of previous treatment (years), mean (SD)</td>
<td>3.3 (3.2)</td>
<td>3.3 (3.3)</td>
<td>3.0 (2.4)</td>
</tr>
</tbody>
</table>

DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HET, high efficacy treatment; MS, multiple sclerosis; RRMS, relapsing remitting MS; SD, standard deviation; SPMS, secondary progressive MS
Results: Common current DMTs switched to from previous DMT

Switch from previous Non-HET to HET

Switch from previous HET to Non-HET

The most common current DMTs (HET/Non-HET) switched to from previous DMT are presented in figure.

DMT, disease-modifying therapy; HET, high efficacy treatment
• Switch due to any risk of infections or malignancies was rare irrespective of switching from HET or Non-HET
• Although the overall combined perceived risk of malignancy/infection was significantly higher in the previous HET versus previous Non-HET, very few patients switched treatment for risk of malignancies/infections versus those switched for no risk of malignancies/infections (0.9% vs 99.1%)
• Risk perception of infection was low and not significantly higher in patients with previous HET versus previous Non-HET

**Physicians’ risk perception of malignancies and infections as a reason for switching therapies**

<table>
<thead>
<tr>
<th>Reason for switch from previous regimen</th>
<th>Overall N=4129a</th>
<th>Previous Non-HET N=3538</th>
<th>Previous HET N=591</th>
<th>p-valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>No switch due to risk of malignancies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switch due to risk of malignancies</td>
<td>0.3</td>
<td>0.1</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>No switch due to risk of infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switch due to risk of infection</td>
<td>0.6</td>
<td>0.5</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>No switch due to risk of infection/ malignancies</td>
<td>0.9</td>
<td>0.6</td>
<td>2.4</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients (%)</th>
</tr>
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<tbody>
<tr>
<td>0 - 20</td>
</tr>
<tr>
<td>20 - 40</td>
</tr>
<tr>
<td>40 - 60</td>
</tr>
<tr>
<td>60 - 80</td>
</tr>
<tr>
<td>80 - 100</td>
</tr>
<tr>
<td>100 - 120</td>
</tr>
</tbody>
</table>

Results: Physicians’ risk perception of malignancies/infections

- Risk of malignancies: p<0.0001
- Risk of infection: p=0.0851
- Risk of malignancies/infections: p=0.0002

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4129 patients for whom the reason for switch from previous DMT was provided by the physician were included for the analysis; of those, 3538 switched from Non-HET and 591 from HETs

bDerived from Fisher’s exact test

DMT, disease-modifying therapy; HET, high efficacy treatment
Results: Reasons for switching the treatment

- The top 3 reasons for switching the treatment in the overall group were lack of efficacy (50.8%), relapse frequency (25.1%) and increased number of lesions (19.1%)
  - Non-HET group: Lack of efficacy (53.3%), relapse frequency (26.8%), and patient request (20.6%)
  - HET group: Lack of efficacy (35.9%), risk of PML* (23.9%), and new T2 or Gd+ T1 lesion (17.9%)

Most common (>10% in any group) reasons for switching treatment

*Largely contributed by Natalizumab
EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; HET, high efficacy treatment; PML, progressive multifocal leukoencephalopathy

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*Overall N=4129
Previous Non-HET N=3538
Previous HET N=591
Lack of efficacy, relapse frequency and increased number of lesions are the main factors influencing treatment switching, especially in the case of previous Non-HETs.

Patients switching treatment due to lack of efficacy, relapse frequency and increased lesions:

- **Lack of efficacy**: 53.3% (p<0.0001) Previous Non-HET, 35.9% (p<0.0001) Previous HET
- **Relapse frequency**: 26.8% (p<0.0001) Previous Non-HET, 15.2% (p<0.0001) Previous HET
- **Increased number of lesions**: 20.3% (p<0.0001) Previous Non-HET, 12.4% (p<0.0001) Previous HET
Conclusions

• Physicians’ risk perception of malignancies and infection is not a leading factor when switching from high efficacy treatments (HETs) or Non-HETs

• Lack of efficacy, including relapse frequency, increased lesions and relapse severity are the main factors influencing treatment switching, especially in Non-HETs

• Patients in the previous HET group already had more progressive disease prior to initiation of the HETs which might be indicative of a widespread escalation approach

• Our findings suggest early initiation of HET in treating MS and underscore the need for evaluation of the current approach of escalation therapy

• The choice of treatment should be made based on the benefit-risk profile of the specific treatment