Treatment, utilisation and safety of medicines for Multiple Sclerosis (TELEMUS)

Telemus is Eurymus’ son, a prophet and a master at reading signs

nicole.pratt@unisa.edu.au
Multiple Sclerosis

- Multiple Sclerosis (MS) is an immune mediated demyelinating and degenerative central nervous system disease, which results in multifocal disability that can include limb weakness, visual impairment, sensory loss, gait ataxia, incontinence and cognitive dysfunction
  - >2.8 million people worldwide are estimated to be living with MS
  - Age at diagnosis is commonly between 20 and 40 years
  - MS affects three times more women than men
- The majority of people living with MS will have disease free periods punctuated with periods of relapse (relapsing-remitting multiple sclerosis, RRMS), which often leads to residual deficits after each relapse
- RRMS is managed by using disease modifying treatments (DMTs) to induce apparent remission (i.e., no evidence of disease activity or a state of clinical and MRI stability) and delay progression of disease
1. What is the prevalence of multiple sclerosis across the APAC region?

Conclusions

The global prevalence of MS has risen since 2013, but good surveillance data is not universal. Action is needed by multiple stakeholders to close knowledge gaps.
Phenotype Phebruary!


1. There is no specific test for MS. Doctors use a medical history, physical exam, neurological exam, MRI, and other tests to diagnose.

2. Given that MS is a disease with a natural tendency to remit spontaneously it is important to define what kind of MS patients we want to model?
   a. Patients with a new and first ever onset of MS
   b. Patients with relapsing MS
   c. **Patients with evidence of MS regardless of the stage or the status of their disease**
<table>
<thead>
<tr>
<th>Cohort</th>
<th>Logic (entry event, inclusion criteria)</th>
<th>Exit criteria</th>
<th>Cohort in atlas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earliest occurrence of Multiple sclerosis</td>
<td>Earliest occurrence of MS diagnosis, requiring 1 hospitalization with MS or 5+ occurrence of MS diagnosis in 2 year</td>
<td>End of observation period</td>
<td>ATLAS 2</td>
</tr>
<tr>
<td>Widdifield</td>
<td>Earliest occurrence of MS diagnosis, requiring ≥3 MS-related occurrences of any combination of inpatient or outpatient diagnosis, or S-specific disease-modifying therapies (DMT) within a 1-year time period;</td>
<td>End of observation period</td>
<td>ATLAS 1</td>
</tr>
<tr>
<td>Culpepper 3x</td>
<td>Earliest occurrence of MS diagnosis, requiring ≥3 MS-related occurrences of any combination of inpatient or outpatient diagnosis, or S-specific disease-modifying therapies (DMT) within a 1-year time period;</td>
<td>End of observation period</td>
<td>ATLAS 6</td>
</tr>
</tbody>
</table>
The more specific algorithms (Widdifield and Culpepper) showed higher PPV than the sensitive 1X code algorithm. The interesting thing that I saw was that if there was a choice between Widdifield and Culpepper it seems that Culpepper wins. In 2 of the 3 databases it had higher PPV as well as higher sensitivity in 2 of the 3. It had both higher PPV and sensitivity in Medicaid. That said, the performance on sensitivity and PPV were actually quite similar with the exception of a large sensitivity gain with Culpepper in CCAE, people of working age and their dependents. Widdifield requires a hospitalization (early in the disease possibly so may not need hospitalization) or 5 codes (early in the disease so may not need clinical care as frequently as those farther along with the condition) which may be less likely in younger subjects.
2. What is the utilisation of multiple sclerosis treatments across the APAC region?

<table>
<thead>
<tr>
<th>Early aggressive/highly effective</th>
<th>Medicine</th>
<th>Concept_ID</th>
<th>Traditional/escalation</th>
<th>Medicine</th>
<th>Concept_ID</th>
<th>Other FDA approved</th>
<th>Medicine</th>
<th>Concept_ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>natalizumab</td>
<td>735843</td>
<td></td>
<td>peginterferon beta-1a</td>
<td>45775146</td>
<td></td>
<td>Daclizumab</td>
<td>19036892</td>
<td></td>
</tr>
<tr>
<td>alemtuzumab</td>
<td>1312706</td>
<td></td>
<td>Glatiramer</td>
<td>751889</td>
<td></td>
<td>Mitoxantrone</td>
<td>1309188</td>
<td></td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>1593457</td>
<td></td>
<td>teriflunomide</td>
<td>42900584</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rituximab</td>
<td>1314273</td>
<td></td>
<td>diroximel fumarate</td>
<td>37497593</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ofatumumab</td>
<td>40167582</td>
<td></td>
<td>dimethyl fumarate</td>
<td>43526424</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cladribine</td>
<td>19054825</td>
<td></td>
<td>fingolimod</td>
<td>40226579</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>siponimod</td>
<td>1510913</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ozanimod</td>
<td>37499437</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Interferon beta-1a</td>
<td>722424</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Interferon beta-1b</td>
<td>713196</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. What is the utilisation of multiple sclerosis treatments across the APAC region?

It’s a dynamic market!

Early aggressive/highly effective
2. What are the treatment pathways of multiple sclerosis medicines across the APAC region?

Has there been a change overtime in the use of High Efficacy treatments earlier in the treatment pathway?
3. Real world safety and effectiveness of treatments for MS?

Recent findings

- **Natalizumab** promising efficacy in RCTs and observational studies when compared with placebo, the injectable DMTs, and fingolimod.

- The anti-CD20 B cell depleting therapies (**rituximab, ocrelizumab, and ofatumumab**) demonstrated superiority in RCTs compared to their comparator group (placebo, interferon, and teriflunomide, respectively) and

- **Rituximab** has shown in observational studies to be more effective than older injectable therapies and some of the oral therapies.

- **Alemtuzumab** has shown good efficacy in RCTs and observational studies yet has several potentially severe side effects limiting its use.

Has the increased use of High Efficacy treatments earlier in the treatment pathway led to better outcomes for patients diagnosed with MS?
RCTs that are investigating the effectiveness of traditional MS treatments with HET strategies

• The ‘Determining the Effectiveness of early Intensive Versus Escalation Approaches for the treatment of Relapsing-remitting MS’ (DELIVER-MS) (NCT03535298) trial will directly compare traditional MS with HET strategies and their impact on clinical and radiologic outcomes.

• The ‘TRaditional versus Early Aggressive Therapy for MS’ (TREAT-MS) (NCT03500328) trial aims to 1) evaluate, jointly and independently among patients deemed at higher risk vs. lower risk for disability accumulation, whether an "early aggressive" therapy approach, versus starting with a traditional, first-line therapy, influences the intermediate-term risk of disability, and 2) to evaluate if, among patients deemed at lower risk for disability who start on first-line MS therapies but experience breakthrough disease, those who switch to a higher-efficacy versus a new first-line therapy have different intermediate-term risk of disability.”

• The DELIVER-MS study is due for completion in 2025 while the TREAT-MS study is due for completion in 2024.
Thank you!

- **Next steps**
  - Finalise MS Phenotype
  - Finalise MS medicines list

- **Developing Protocol**

- **Fortnightly meetings at 11am Korean Time on Wednesday**