**Introduction**

- The current safety concerns and shortened duration of clinical trials of novel medications in Multiple Sclerosis (MS) has driven the need for enhanced risk management.
- The Gilena® Risk and Support Management Program (GRASP) was developed by the Eastern Health MS Service to ensure appropriate monitoring and risk minimisation in Gilena® therapy.
- The safety risks of Gilena® risks are classified as unavoidable risks, however early intervention and detection generally result in better patient outcomes.
- Unforeseeable risks are managed through systematic processes for pharmacovigilance and reporting of adverse events.
- Non-adherence to the monitoring regimen and the medications itself was also identified as a possible risk.

**Cardiac Abnormalities at First Dose Administration**

Cardiac screening and electrocardiograms (ECG’S) are performed at all sites before therapy initiation. Patients are admitted to hospital for first dose monitoring at all 3 sites.

<table>
<thead>
<tr>
<th>Cardiac Event</th>
<th>Monitoring</th>
<th>Observations (n = 410)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic bradycardia with arrhythmia</td>
<td>Extended</td>
<td>0</td>
</tr>
<tr>
<td>Asymptomatic sinus bradycardia</td>
<td>Extended</td>
<td>5</td>
</tr>
<tr>
<td>Asymptomatic bradycardia with arrhythmia</td>
<td>Nil</td>
<td>2</td>
</tr>
<tr>
<td>Symptomatic sinus bradycardia</td>
<td>Extended</td>
<td>3</td>
</tr>
<tr>
<td>Symptomatic sinus bradycardia</td>
<td>Extended</td>
<td>3</td>
</tr>
<tr>
<td>Symptomatic sinus bradycardia</td>
<td>Extended</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>11</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Abnormal Liver Function**

Liver function abnormalities are reported as non-symptomatic abnormal liver function reports. No symptomatic liver function abnormalities were reported.

- X10 (ULN) IN LIVER TRANSAMINASES
- X5 (ULN) IN LIVER TRANSAMINASES

**Adherence to Follow Up Protocol**

Patients commencing therapy were informed and given details of the follow safety requirements. If the test had not been performed within 2-4 weeks of being due, a reminder letter was sent.

**Key Features of GRASP**

- Risk screen checklist
- MS Nurse education session
- Letter to patient outlining GRASP requirements and first dose administration details

**FIRST DOSE ADMINISTRATION**

- Policy and protocol for first dose administration
- Appropriate facilities, staff and resources established with medical support
- Capacity for extended monitoring
- Education and support session on the day

**FOLLOW UP PROGRAM**

- Database to track patients key safety screening tests
- Detailed correspondence documentation local health care providers sent before or same day as first dose administration
- Handout information for patients about follow up requirements
- One month review at MS nurse clinic
- Text and email reminder system for patients (implemented only recently)

**REVISIONS**

Since the introduction of the program in April 2011 many changes have been made to accommodate recognised deficits in the program and in response to new safety information and Therapeutic Goods Australia (TGA) requirements.

**Data Collection**

The data was collected from 3 major MS services in Melbourne, Australia.

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk Man. Program</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Health MS Service</td>
<td>GRASP</td>
<td>149</td>
</tr>
<tr>
<td>Royal Melbourne Hospital</td>
<td>Other</td>
<td>189</td>
</tr>
<tr>
<td>St Vincent's Public Hospital Melbourne</td>
<td>Other</td>
<td>72</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>410</strong></td>
</tr>
</tbody>
</table>

Note: Data collection at site B was limited as many patients were followed up by other services. Data collection was limited at site C due to staff changes during the data collection period. This is noted where applicable throughout the results.

**Discontinuations**

- Site A: 8 (6%) Fructose Intolerance, X1
- Site B: 8 (4%) Worsening MS X2, Macular Oedema, Visual changes X2, Side effects X1, LFT Abnormalities X1, Unrelated Cancer X1
- Site C: Unknown

**Adherence to Medication**

Three measures used to record compliance including script compliance, lymphopenia on full blood examination and patient reported compliance. A total of 58 compliant patients.

- Lymphopenic & script & patient reported compliance requested
- Lymphopenic, reported compliance, unconfirmed script source
- Lost to Follow Up
- Not Lymphopenic with a script, reported compliant

**Macular Oedema**

2 incidences of macular oedema were found across sites A and B (N = 207)

**Discussion**

- To date, there have been no unexpected safety concerns within this cohort of patients.
- We acknowledge that the therapy time duration limits this data significantly with no patient receiving Gilena® for more than 9 months.
- Importantly, this data demonstrated that patients have poor compliance with follow up.
- Recently, we have initiated a text and email reminder system for patients and look forward to evaluating the usefulness of this system.
- We aim to continue to collect and analyse data according to patient non-compliance characteristics to aid us in identify patients who may be non-compliant.
- The GRASP program has assisted us in evaluating our approaches to other MS therapies and creating appropriate risk management plans. The MS Nurse Consultant has the primary responsibility of developing and implementing the risk management programs. Adherence to therapy and monitoring will continue to be an important aspect of the MS nurse’s role.