Cost-consequence analysis of dimethyl fumarate versus other disease-modifying therapies in Multiple Sclerosis: a French cohort study with SNDS national claims database in France

Pauline Bosco-Lévy1,2, Patrick Biin3, Séverine Lignot-Maleynat, Régis Lassalle, Abdelbail Ahouefauff, Pauline Diez-Andreu4, Marc Debouvierie, Bruno Brochet, Francis Guillemin5, Nicholas Moore6,7, Cecile Droz-Perreault1
1 Bordeaux PharmacoÉpi, Univ Bordeaux, INSERM U1401, Bordeaux, France, 2 Bordeaux Population Health Research Centre, INSERM U1321, Univ Bordeaux, Bordeaux, France, 3 Département de neurologie, CHU Nancy, F-54000 Nancy, France, 4 Université de Lorraine, EA 4166 PERSAM, 56345 Vandoeuvre-lès-Nancy, France, 7 ISCERI, service de Neurologie, CHU de Bordeaux, France, 8 CHU de Nancy, INSERM U14, 1435 Épidémiologie clinique, Nancy, Ostéopathie de Lorraine, EA 4400 APERM, F 54000 Nancy, France, 9 CHU de Bordeaux, Bordeaux, France

Background

- **Multiple sclerosis (MS)**: Incapacitating, progressive, chronic neurological disorder that involves a selective, chronic inflammation and demyelination of the central nervous system.
- **Relapsing-remitting MS form (RRMS)** is the most common, and are characterized by the presence of relapses without disability progression between relapses.
- In France, prevalence in 2015: 135 per 100,000 inhabitants and 87,000 cases in 2017.
- **Current therapeutic strategy of RRMS**:
  - The first line of medications approved were the injectable ImmunoModulators (IMM).
  - Treatment options have broadened to include orally administered dimethylfumarates (DMF), teriflunomide (TERI) and fingolimod (FTY).
- **The cost-consequence of DMF versus other first-line (IMM and TERI) or second-line (FTY) disease-modifying therapies has never been studied in real-world settings using data of a national claims database.**

Objective

- To assess the cost-consequence of DMF versus other disease-modifying therapies indicated in multiple sclerosis (i.e. IMM and two other oral drugs: FTY and teriflunomide TERI) in real-world settings using data of a national claims database.

Methods

**Study Design (Figure 1)**

Cohort study using SNDS (Système National des Données de Santé) national French claims database including all patients with a first reimbursed dispensing of a MS drug from 2015 to 2017, a follow-up from 1 to 3.5 years after initiation (i.e. index date) and at least 4.5-year database history.

**Data**

- **The SNDS database includes individual pseudonymised information from 66 million persons on:**
  - Gender, date of birth, area of residence, date of death;
  - Long-term disease registration with associated ICD codes for full insurance coverage;
  - Outpatient reimbursed healthcare expenditures: visits, medical procedures, lab tests, drugs...;
  - Hospital discharge summaries with ICD-10 codes for diagnosis (primary, linked and associated diagnoses) for all private and public medical, obstetric and surgery hospitalisations, with the date and duration of hospitalisation, medical procedures.

**Outcome**

- The effectiveness was assessed in each treatment group by estimating the Annual Rate of Relapses (ARR), which were identified using a validated algorithm.

**Costs**

- The costs were estimated in euros according to the collective perspective during the first index treatment exposure period.
- Healthcare resources taken into account for the description of the costs of treatment groups:
  - Global healthcare resources use according to the different areas of expenditure: drugs, medical consultations, visits and technical acts, nursing acts, physiotherapy acts, lab tests, products and services; transport; other medical healthcare resources; public hospital external consultations and acts (Medicine, Surgery and Obstetric; MCO); hospitalisations (MCO); sick leaves and daily allowances; assistance, pension and disability allowances; other non-medical healthcare resources.
  - Specific healthcare resources use according to the following specific areas of expenditure:
    - Drugs used specifically in the treatment of MS;
    - MS specific hospitalisations, including related transport;
    - Neurologist medical visits, including related transport;
    -MS specific lab tests, including related transport and related nursing acts plus majorization and travel allowances;
    - MS specific medical devices.

**Data Analyses**

- DMF effectiveness was compared to other treatment groups during the index treatment period after timing and matching on a high-dimensional Propensity Score (hPS). Results were expressed in Relative Risk (RR).
- Annual costs of all reimbursed healthcare expenditures were measured for DMF and the other treatment groups from the collective perspective, overall and by cost components (inpatient, medication and non-medication costs).

Results

- **Annual global cost DMF versus FTY**

<table>
<thead>
<tr>
<th>Resource</th>
<th>No. 1705</th>
<th>No. 1729</th>
<th>No. 1730</th>
<th>No. 1736</th>
<th>No. 1760</th>
<th>No. 1767</th>
<th>No. 1770</th>
<th>No. 1780</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arr. global cost DMF (€)</td>
<td>145316 (±8022)</td>
<td>131976 (±76846)</td>
<td>124773 (±7628)</td>
<td>15976 (±61166)</td>
<td>24206 (±12222) (p&lt;0.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arr. global cost FTY (€)</td>
<td>13222 (1999)</td>
<td>1361 (882)</td>
<td>1761 (138)</td>
<td>1992 (4541)</td>
<td>11478 (6153) (p&lt;0.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Annual specific cost (costs of all healthcare expenditures)**

<table>
<thead>
<tr>
<th>Resource</th>
<th>No. 1705</th>
<th>No. 1729</th>
<th>No. 1730</th>
<th>No. 1736</th>
<th>No. 1760</th>
<th>No. 1767</th>
<th>No. 1770</th>
<th>No. 1780</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arr. specific cost DMF (€)</td>
<td>7832 (3402)</td>
<td>8992 (4541)</td>
<td>1178 (3041)</td>
<td>9672 (4365)</td>
<td>1918 (128)</td>
<td>136 (882)</td>
<td>119 (128)</td>
<td>119 (128)</td>
</tr>
<tr>
<td>Arr. specific cost FTY (€)</td>
<td>76 (563)</td>
<td>80 (563)</td>
<td>76 (563)</td>
<td>11478 (6153) (p&lt;0.001)</td>
<td>136 (882)</td>
<td>119 (128)</td>
<td>119 (128)</td>
<td>119 (128)</td>
</tr>
</tbody>
</table>

**Annual global cost DMF versus FTY**

- **Analysis of the global resource costs during the first index treatment exposure according to the collective perspective in DMF and FTY groups**

<table>
<thead>
<tr>
<th>Resource</th>
<th>No. 1705</th>
<th>No. 1729</th>
<th>No. 1730</th>
<th>No. 1736</th>
<th>No. 1760</th>
<th>No. 1767</th>
<th>No. 1770</th>
<th>No. 1780</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arr. global cost DMF (€)</td>
<td>145316 (±8022)</td>
<td>131976 (±76846)</td>
<td>124773 (±7628)</td>
<td>15976 (±61166)</td>
<td>24206 (±12222) (p&lt;0.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arr. global cost FTY (€)</td>
<td>13222 (1999)</td>
<td>1361 (882)</td>
<td>1761 (138)</td>
<td>1992 (4541)</td>
<td>11478 (6153) (p&lt;0.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion**

- **Compared to TERI and IMM:**
  - DMF is an effective treatment strategy in reducing relapse occurrence in MS patients.
  - DMF entails an additional cost from the collective perspective mostly explained by the price of the drug itself.
- **FTY** involves higher specific medical costs than those of other MS drugs, which may be explained by the more severe clinical profile of MS patients treated with this drug.