A LONG-TERM COST-EFFECTIVENESS MARKOV MODEL COMPARING DISEASE MODIFYING TREATMENTS IN PATIENTS WITH RELAPSING REMITTING MULTIPLE SCLEROSIS IN GERMANY

N. Putzki1,2, D. Eheberg3, A. Bergmann4, M. Lang4, C. Plesnial-Frank2, V. Limmroth5, Z. Katsarava1

1 Abteilung für Neurologie, Universitätsklinikum Essen; 2 Klinik für Neurologie, Kantonsspital St. Gallen; 3 IMS HEOR, IMS Health GmbH & Co. OHG, München; 4 NTB-studygroup, NeuroTransData GmbH, Neuburg; 5 Neurologische Klinik, Klinikum der Stadt Köln

BACKGROUND

- Multiple sclerosis (MS) is an inflammatory degenerative neurological disease affecting approximately 120,000 patients in Germany.1
- The advanced stages of MS are associated with high costs and severely reduced quality of life.6
- Within the last decades different disease modifying therapies (DMT) have proven their benefit for patients with rapid remitting multiple sclerosis (RRMS)4,4 but these DMTs come at high costs7.

OBJECTIVE

- To conduct a health economic evaluation of Natalizumab (Nb) compared in RRMS from a societal perspective.

METHOD

Decision-analytic model:
- A Microsoft Excel®-based Markov model was constructed to compare the costs and outcomes of Nb, Interferon-beta (INF-b), glatiramer acetate (GA) and best supportive care (BSC).
- A time horizon of 30 years and a cycle length of 3 months was chosen.
- The hypothetical patient cohort had a starting age of 35 years and a gender distribution, which is typical for MS (72.5% female).
- The cost and outcomes are reported from a societal perspective and were discounted at 3% annually.
- Cost-effectiveness was measured as incremental cost per relapse avoided and per quality-adjusted life-year (QALY) gained.

Figure 1: Model Framework

- Parameter were derived from clinical Trials and published literature:
  - Natural disease progression and relapse rates under BSC were modeled according to registry data9.
  - Efficacy and withdrawal rates were derived from trials (Nb) or published meta-analysis10,11,12,13,14,15 (INF-b and GA).
  - Costs and utilities were taken from a published retrospective analysis of costs associated with MS in Germany16.
  - Side effects inclusive progressive multifocal leukoencephalopathy (PML) are reflected in costs and utilities.
  - The mutually exclusive Markov states are defined by the Expended Disability Status Scale (EDSS) stages and the course of treatment.
  - The model transitions are defined by disease progression, switch of treatment medication or withdrawal from DMT. (Figure 1)
- Model assumptions:
  - In each cycle patients can stay at their current EDSS state or move to the next state.
  - Transition between RRMS and secondary progressive MS occurs at state EDSS 7 and treatment with DMTs is stopped.
  - Only one relapse per cycle. A constant risk for relapses in EDSS state 1 to 6 is assumed. No relapses occur in EDSS 7 to 9.
  - An univariate sensitivity analysis of multiple model parameters was performed.

German real-life data collection:
- A real-life data collection was conducted in 2010 to evaluate model parameters and to validate model assumptions.
- Data from 554 adult patients (age > 18) treated with DMTs (Nb, INF-b and GA) for RRMS within the last 2 years were collected retrospectively.
- Further inclusion criteria were an EDSS score of less than 6 and a maximum of two switched of treatment medication.
- Data sources: Universitätshklinikum Essen, Neurologische Klinik Köln, Kantonsspital St. Gallen and NeuroTransData (one large network of office based neurologists).

RESULTS

German real-life data collection
- Overall real-life data supported the model assumptions.
- Risk for relapse were constant for all EDSS stages.
- After 12 months no mean progression could be detected. (0.07; CI -0.13 - 0.01). A proportional increase for the minimal overall improvement is the recovery from prior relapses.

Table: Health economic model:

<table>
<thead>
<tr>
<th>DMT 95% CI</th>
<th>N</th>
<th>Initial EDSS</th>
<th>Relapse rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nb</td>
<td>153</td>
<td>3.46 (2.31-3.72)</td>
<td>0.23 (0.14-0.33)</td>
</tr>
<tr>
<td>INF-b</td>
<td>196</td>
<td>1.32 (1.21-1.51)</td>
<td>0.44 (0.33-0.56)</td>
</tr>
<tr>
<td>GA</td>
<td>205</td>
<td>1.73 (1.53-1.92)</td>
<td>0.46 (0.34-0.57)</td>
</tr>
<tr>
<td>Total</td>
<td>554</td>
<td>2.12 (1.97-2.27)</td>
<td>0.39 (0.33-0.45)</td>
</tr>
</tbody>
</table>

Figure 2: Avoided Relapses within 30 years

- These 15 relapses are reduced to an average of 5.8 relapses under Nb (9.2 avoided relapses) and to 12.9 relapses under other DMTs (2.1 avoided relapses). (Figure 2)

1st line 2nd line Costs [€] QALY Cost per QALY [€]
Nb Other DMT 835,972 14.04 59,532
Other DMT Nb 795,458 12.96 61,361
BSC Nb 581,201 12.20 47,647

The incremental cost-effectiveness (ICER) of Nb versus other DMT is €37,552 per QALY.

The patient distribution after 30 years suggests a slower progression for patients under Nb.

CONCLUSION

- The initial higher treatment costs for Nb result in a higher amount of QALYs and avoided relapses compared to other DMTs.
- The incremental cost-effectiveness suggests that the additional cost per QALY is in an acceptable range with €37,552 for first line and €16,324. However without binding cost-effectiveness thresholds this value has to be discussed.

REFERENCES


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