Economic Evaluation of disease modifying treatments in patients with relapsing remitting Multiple Sclerosis in Germany: long term analysis and cost effectiveness of Natalizumab, interferon-beta and glatiramer acetate

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Background

- Multiple sclerosis (MS) affects approximately 120 000 patients in Germany[1].
- Within the last decades different disease modifying therapies (DMT) have proven their benefits for patients with rapid remitting multiple sclerosis (RRMS)[2-4] but these DMTs come at high costs[7].

Objective

- To conduct a health economic evaluation of Natalizumab (Nb) compared to other disease modifying drugs (DMD) in RRMS patients based on literature and German real-life treatment data.

Method

Decision-analytic model:

- A Microsoft Excel™-based Markov model was constructed to compare the costs and outcomes of Natalizumab (Nb), Interferon-beta (INF-b), glatiramer acetate (GA) and best supportive care (BSC).

Model Framework & Patient cohort	
Model Type	Markov, stage-transition model
Time horizon	30 years
Cycle length	3 months
Perspective	Societal perspective
Patient starting age	35 years
Gender distribution	72.50% females, 27.50% males
Annual discount rate	3%

- Clinical Trials and published literature were used to derived the model parameter:
  - Efficacy and withdrawal rates were derived from trials[4] (Nb) or published meta analysis[2,3,5,6] (IFN-b and GA).
  - Costs and utilities were taken from a published retrospective analysis of cost associated with MS in Germany[7].
  - Side effects inclusive progressive multifocal leukoencephalopathy (PML) are reflected in costs and utilities.
- An univariate sensitivity analysis of multiple model parameters was performed

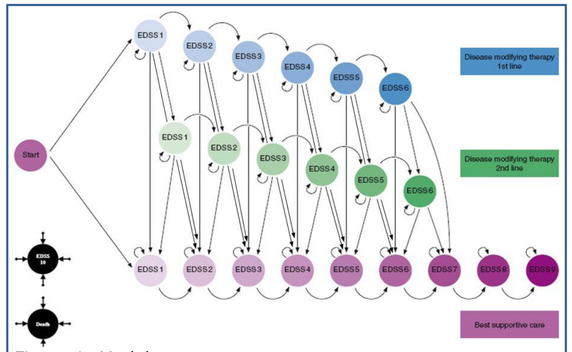

Figure 1: Model structure

Method *(cont.)*

- The mutually exclusive Markov states are defined by the Expended Disability Status Scale (EDSS) stages and the course of treatment (Figure 1).
- The model transitions are defined by disease progression. Patients can switch medication or withdraw from treatment at all within each cycle.
- Cost-effectiveness was measured as incremental cost per relapse avoided and per quality-adjusted life-year (QALYs) gained.

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.
- Relapse: Only one per cycle; constant risk for relapse in EDSS state 1 to 6; no relapses in EDSS 7 to 9.

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 patients treated with DMTs for RRMS within the last 2 years were collected retrospectively.
- Data sources: Universitätsklinikum Essen, Neurologische Klinik Köln, Kantonsspital St. Gallen and NeuroTransData (one large network of office based neurologists).

Method *(cont.)*

Inclusion criteria	
Age	> 18
Diagnosis	RRMS
EDSS Score	< 6
Course of treatment	Nb, INF-b or GA
Treatment switches	< 2 treatment switches
Treatment history	At least treated for 2 years in one center

Results of real life data collection

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

DMT *[95% CI]*	N	Initial EDSS	Relapse rate
Nb	153	3.46 *[3.21-3.72]*	0.23 *[0.14-0.33]*
INF-b	196	1.32 *[1.21-1.51]*	0.44 *[0.33-0.56]*
GA	205	1.73 *[1.53-1.93]*	0.46 *[0.34-0.57]*
Total	554	2.12 *[1.97 -2.27]*	0.39 *[0.33–0.45]*

All values reported as mean [95% CI]

Results of model

- Model results indicate that patients managed by best supportive care experience an average 15 relapses within 30 years.

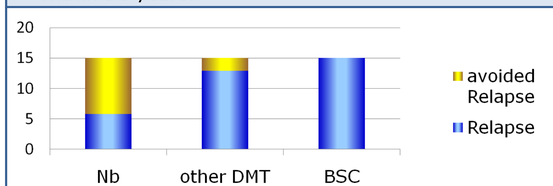

Figure 2: Avoided relapses per patient

Results of model *(cont.)*

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		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 DMT.

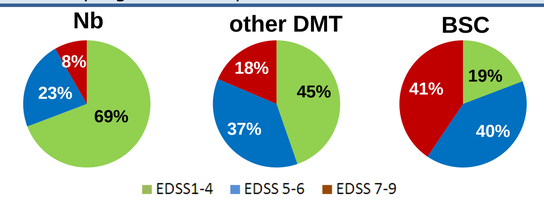

Figure 3: Patient distribution after 30 years

- According to the sensitivity analysis the model is most sensitive to parameter related to the progression.
- The ICER of Nb is € 33,664 per QALY using real life data as an alternative setting.

Conclusion

- Treatment with DMT improves the situation of patients, with Nb showing the highest efficacy and best cost-effectiveness ratio.
- The ICER suggests that the additional cost per QALY are in an acceptable range with € 37,552.

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Disclosure of conflict of interests:
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