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

N. Putzki[1,2], D. Eheberg[3], A. Bergmann[4], M. Lang[4], C. Plesnila-Frank[3], V. Limmroth[5], Z. Katsarava[1]

[1] Abteilung für Neurologie, Universitätsklinikum Essen; [2] Klinik für Neurologie, Kantonsspital St. Gallen; [3] IMS HEOR, IMS Health GmbH & Co. OHG, München; [4] NTD-studygroup, NeuroTransData GmbH, Neuburg; [5] Neurologische Klinik, Kliniken 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[7].
- 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 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 month was choosen
- The hypothetical patient cohort had a stating 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 with 3% annually.
- Cost-effectiveness was measured as incremental cost per relapse avoided and per quality-adjusted life-year (QALYs) gained.

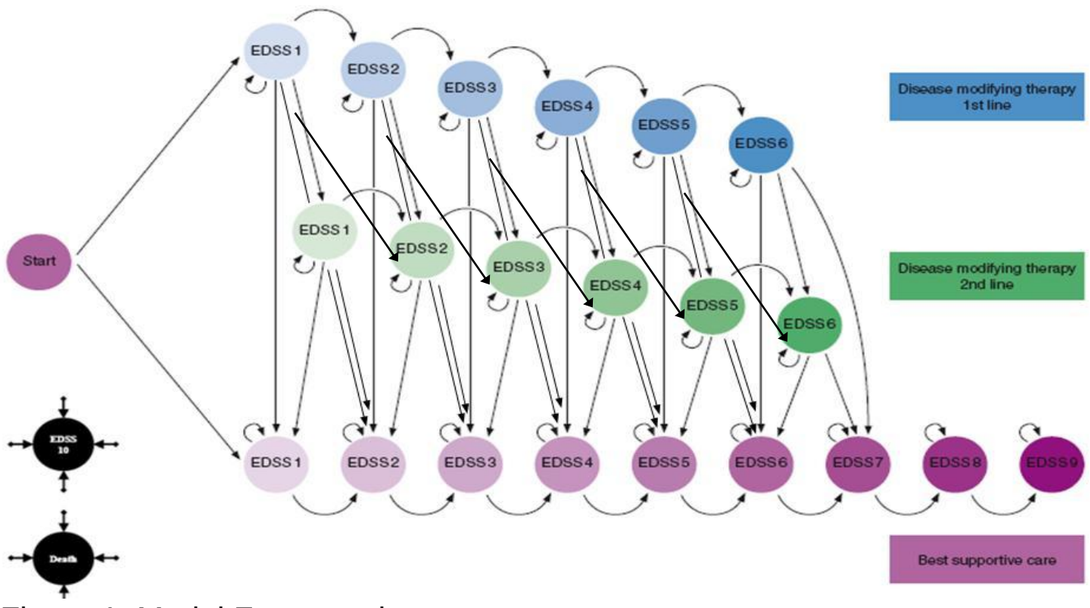

Figure 1: Model Framework

- Parameter were derived from clinical Trials and published literature:
  - Natural disease progression und relapse rates under BSC were modeled according to registry data[5-7].
  - Efficacy and withdrawal rates were derived from trials[4] (Nb) or published meta analysis[2,3,5,8] (IFN-b and GA).
  - Costs and utilities were taken from a published retrospective analysis of cost associated with MS in Germany[9].
  - 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 switches of treatment medication.
- Data sources: Universitätsklinikum 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 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]*

Health economic model:

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

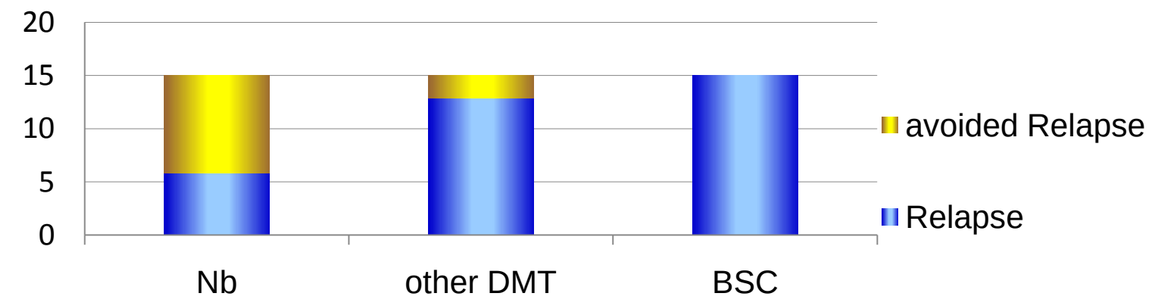

Figure 2: Avoided Relapses within 30 years

- These 15 relapses are reduced to an average of 5.8 relapses under Nb (9.2 avoided relapses) and to 12.9 relapses by 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		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.

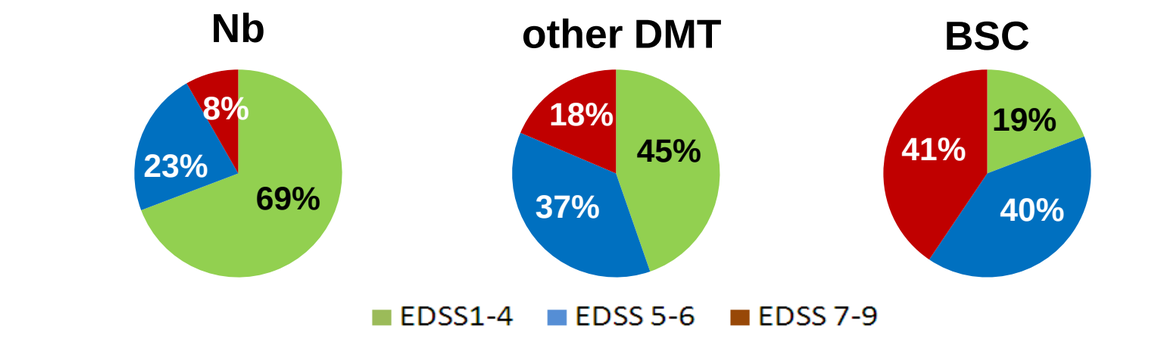

Figure 3: Patient distribution after 30 years

- 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

- 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 are 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

1. Hein T, Hopfenmuller W. Projection of the number of multiple sclerosis patients in Germany. Nervenarzt 2000;71(4):288-294.
2. Cadavid D, Wolansky LJ, Skurnick J et al. Efficacy of treatment of MS with IFNbeta-1b or glatiramer acetate by monthly brain MRI in the BECOME study. Neurology 2009;72(23):1976-1983.
3. O'Connor P, Filippi M, Arnason B et al. 250 mug or 500 mug interferon beta-1b versus 20 mg glatiramer acetate in relapsing-remitting multiple sclerosis: a prospective, randomised, multicentre study. Lancet Neurol 2009;8(10):889-897.
4. Polman CH, O'Connor PW, Havrdova E et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med 2006;354(9):899-910.
5. Confavreux C, Vukusic S, Moreau T, Adeleine P. Relapses and progression of disability in multiple sclerosis. N Engl J Med 2000;343(20):1430-1438.
6. Runmaker & Andersen. Prognostic factors in multiple sclerosis incidence cohort with twenty-five years of follow-up. Brain. 1993; 116: 117-134
7. Weinshenker. The natural history of multiple sclerosis: Update 1998. Sem Neurol. 1998; 18(3): 301-307
8. Rice GP, Incorvaia B, Munari L et al. Interferon in relapsing-remitting multiple sclerosis. Cochrane Database Syst Rev 2001;(4):CD002002.
9. Kobelt G, Berg J, Lindgren P, Fredrikson S, Jonsson B. Costs and quality of life of patients with multiple sclerosis in Europe. J Neurol Neurosurg Psychiatry 2006;77(8):918-926.

Demonstrating the value of medicine

Poster presented at ISPOR, Prague, 6th -9th November 2010
Presentation code: PND19

This study was supported by Biogen Idec GmbH, Munich, Germany