

Cost-Utility Analysis of Ocrelizumab for Treating Relapsing Multiple Sclerosis in Austria

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Objectives

Multiple Sclerosis (MS), a disease that predominantly affects young, working-age adults, is a chronic, immune-mediated disorder of the central nervous system. Globally, approximately 2.9 million individuals are currently affected by MS, with a rising prevalence among children and adolescents [1]. In Austria, the disease impacts 14,470 individuals (prevalence: 159/100,000; 68.48% relapsing-remitting MS [RRMS]) [2].

Ocrelizumab is approved for the treatment of RMS and PPMS and has a well-established efficacy and safety profile [3, 4, 5]. According to current European and international treatment guidelines, disease-modifying therapies (DMTs) for RRMS can be categorized as moderate-efficacy agents (e.g., interferons, glatiramer acetate, dimethyl fumarate, teriflunomide) and high-efficacy therapies (e.g., ocrelizumab, natalizumab, alemtuzumab, cladribine, ofatumumab), with growing evidence supporting early use of high-efficacy treatment to delay disability progression. [6, 7]

This study aims to assess the cost-utility of ocrelizumab versus alternative RRMS therapies under different treatment algorithms and to highlight the broader value of this highly effective therapy.

Methods

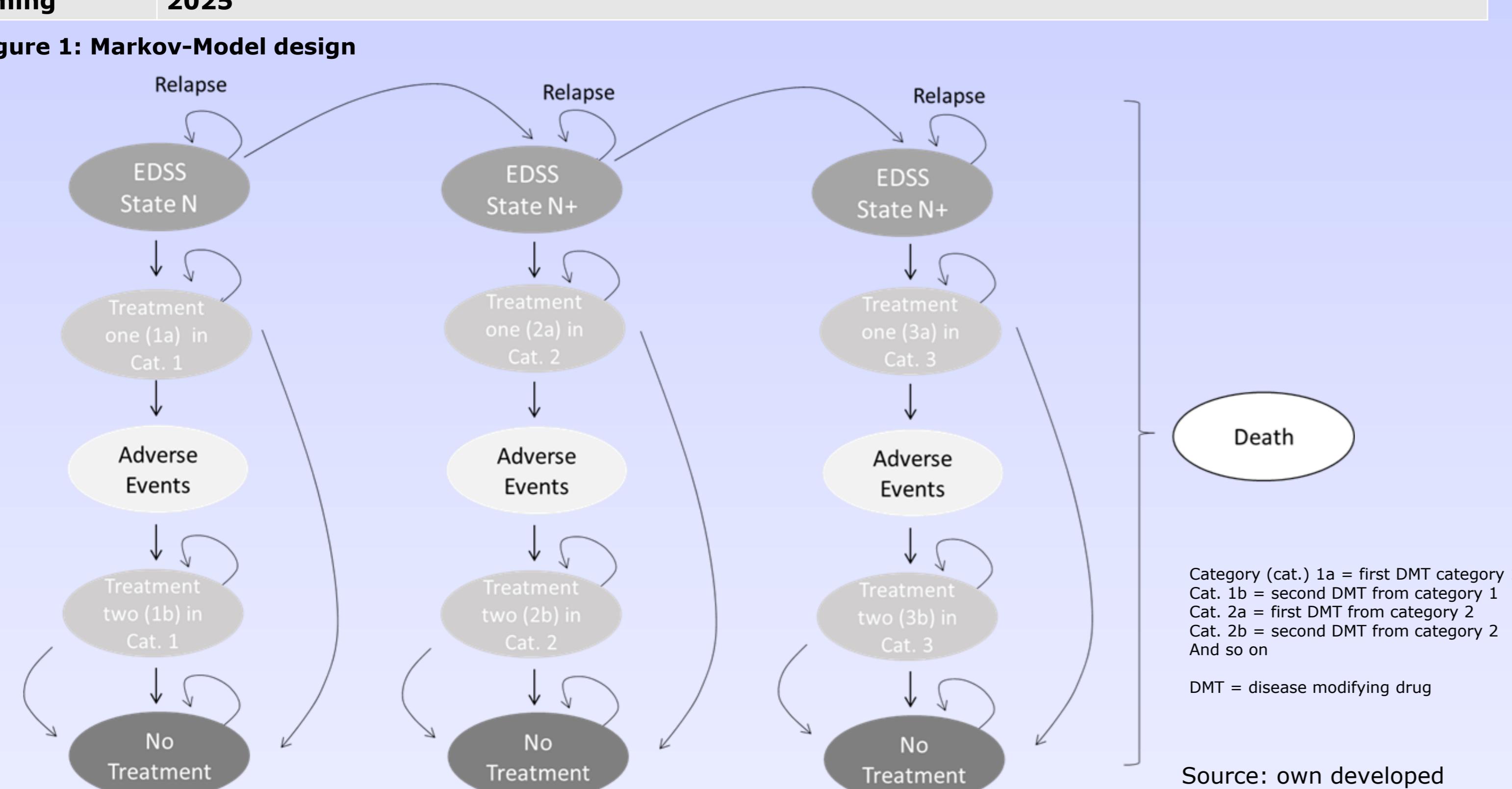
The following methods were adopted:

- The primary outcome was the modelled incremental cost-effectiveness ratio (ICER; €/quality-adjusted life-year [QALY] gained, threshold 25,000 €, discount rate 3%) over 10 years from the societal perspective.
- A Markov model with 3 month cycles captured patient transitions between Expanded Disability Status Scale (EDSS) states, conversion to secondary progressive MS, relapses, adverse events, and death (Figure 1).
- Natural history and transition probabilities were derived from a published network meta-analysis.[8]
- Treatment switching of immunotherapies by disease activity (Table 2) and discontinuation were considered; i.e., treatment sequences were compared for pre-treated and treatment-naïve patients (Table 1).
- Resource utilization and costs reflected Austrian clinical practice and local tariffs.
- Utility inputs were drawn from literature.[9]
- Alternative treatment strategies were modelled in pre-treated and naïve cohorts with baseline characteristics based on registry data. [9,10]

Tab. 1: Overview of methods applied

| Methods | |
|---------------|--|
| Type of study | Cost-utility analysis (CUA) |
| Model type | Markov cohort model |
| Perspective | Austrian societal perspective (direct and indirect costs) |
| Time horizon | 10 years, with a cycle length of 3 months |
| Discount rate | 3% for costs & 3% for outcomes |
| Population | Eligible patients: reflected the OPERA I/II trial cohorts, representing typical RRMS patients with a mean age of 37 years. The current model analyzed two cohorts of patients with RRMS: treatment-naïve patients starting treatment. |
| Intervention | The treatment sequences for the pre-treated patient: DMTs from category 1 > Ocrelizumab > other than Ocrelizumab from category 3 The treatment sequences for the treatment-naïve patient: Ocrelizumab > other than Ocrelizumab from category 3 |
| Comparator | The treatment sequences for the pre-treated patient: DMTs from category 1 > DMTs from category 2 > DMTs from category 3 (other than Ocrelizumab) > DMTs from category 3 The treatment sequences for the treatment-naïve patient: DMTs from category 3 (other than Ocrelizumab) > DMTs from category 3 > DMTs from category 3 (other than Ocrelizumab) |
| Costs | Direct costs: Medication costs, Monitoring costs, Relapse costs, EDSS stage costs and AE costs Indirect costs: short-term and long-term absence from workplace |
| Outcomes | Quality-adjusted life-years (QALYs); Utility weights for different EDSS states were derived from an Austrian source by Berger et al (2017). Disutilities associated with MS relapse and adverse events derived by a literature search. |
| Results | Incremental cost utility ratio (ICUR) |
| Timing | 2025 |

Figure 1: Markov-Model design



The model assumes the following disease dynamics and treatment pathways:

- Disease progression is represented by Expanded Disability Status Scale (EDSS) health states, comprising 11 levels (EDSS 0-9, including 6.5)
- Relapses are associated with additional costs and a temporary reduction in quality of life (disutility) at onset. They initiate treatment in the naïve cohort and prompt a switch to the next treatment category in the pre-treated cohort.
- Adverse events lead to switches within treatment categories, whereas some patients discontinue therapy without transition to another treatment.
- Relapsing-remitting multiple sclerosis (RRMS) may evolve into secondary progressive multiple sclerosis (SPMS).
- Mortality may occur from any health state.

Clinical Data

The model assumes that MS patients in both comparison groups receive SoC therapy.

- The SoC therapy, including disease modifying treatments (DMTs) according to the recommendations outlined in the guidelines of the German Society of Neurology (2023) (ref. Table 2).
- Treatment decisions are differentiated based on the severity of the condition, categorized as mild/moderate or (highly) active forms of MS, for which various treatment options are available.

Tab. 2: Overview of immunotherapies clustered by efficacy according to German treatment guidelines

| Category 1 (moderate efficacy) | Category 2 (intermediate efficacy) | Category 3 (high efficacy) |
|--------------------------------|------------------------------------|----------------------------|
| Dimethylfumarate | Cladribin | Alemtuzumab |
| Glatiramerazetat | Fingolimod | Natalizumab |
| Interferon beta | Ozanimod | Ocrelizumab |
| Teriflunomid | Ponesimod | Ofatumumab |

Source: German Society of Neurology (2023).

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Costs

Direct costs

The cost assessment relied on attributing costs to various health states.

- Costs associated with each health state were determined based on the utilization of resources linked to that state.
- This resource usage, encompassing the type and frequency of medical goods and services provided to the patient, along with their monetary value (comprising prices, tariffs, and/or opportunity costs per unit of medical goods and services), was employed to compute the total direct costs within the Austrian context.

Indirect Costs

- Indirect costs were based on Berger et al. (2017), incorporating Austrian data on productivity losses due to both short-term sick leave and long-term work absence related to multiple sclerosis. All cost inputs were indexed to 2025 values using national inflation rates and stratified by EDSS level to reflect disability-dependent variations in economic burden [9].

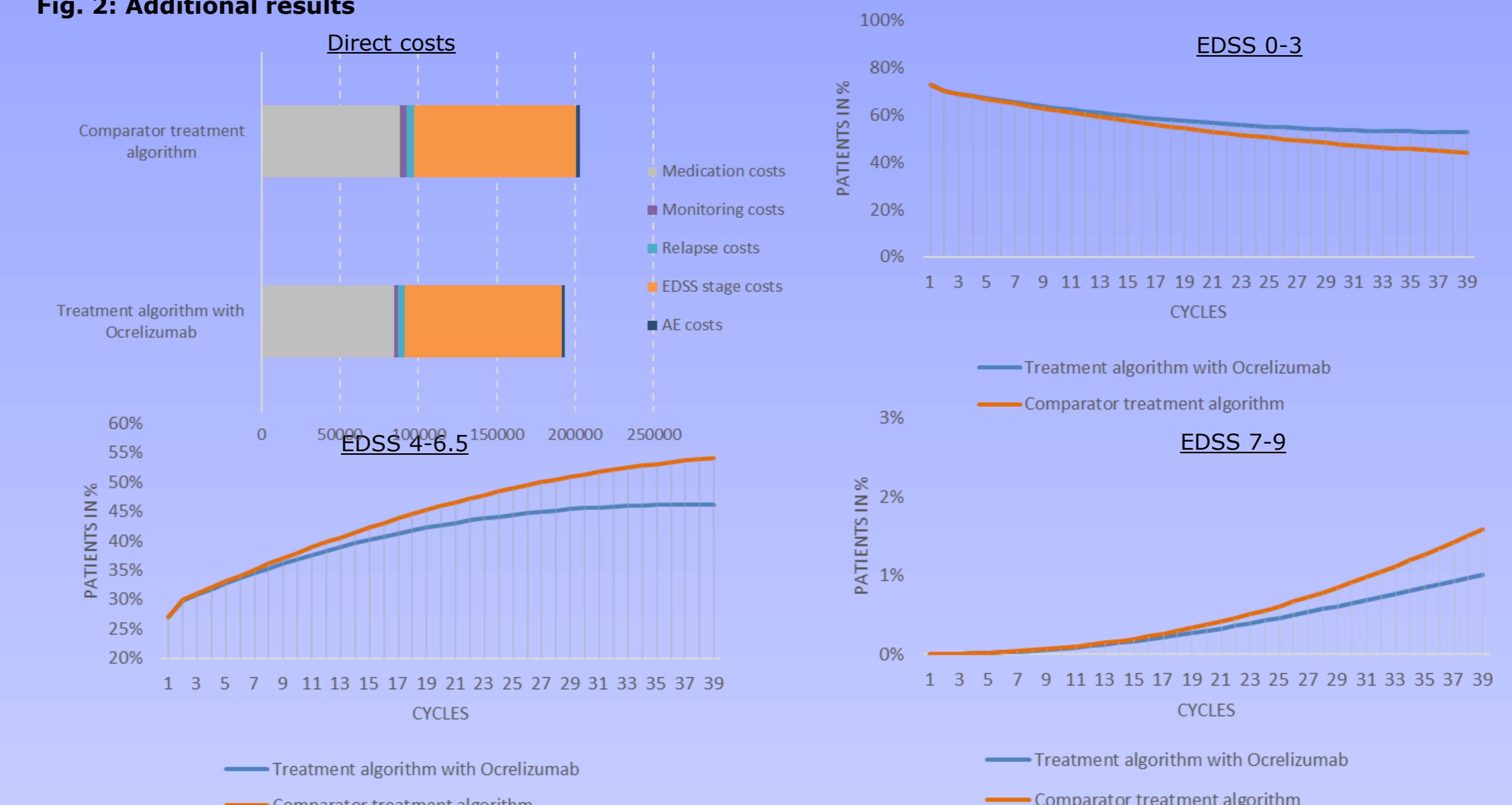
Results

For pre-treated patients, initiating ocrelizumab one line earlier reduced total costs by 24,594 € (9,532 € direct; 15,062 € indirect) compared to less effective therapies. This strategy yielded a dominant ICER, providing 279,934 € in total savings per QALY gained, with higher QALY (+0.09) and a lower EDSS score (-0.34) (Table 3). First-line ocrelizumab use resulted in even greater cost savings, totaling 46,871 € compared to other first-line comparators (Table 4).

Tab. 3: Results for pre-treated patients

| Costs | Treatment algorithm with Ocrelizumab | Comparator treatment algorithm | Incremental |
|-------------------------------------|--------------------------------------|--------------------------------|------------------------------|
| Direct costs | 193,636 € | 203,167 € | -9,532 € |
| Indirect costs | 123,466 € | 127,147 € | -15,062 € |
| Total costs | 317,102 € | 341,696 € | -24,594 € |
| Outcomes | | | |
| QALYs | 5.86 | 5.77 | 0.09 |
| ICUR Incremental cost-utility ratio | | | Dominant [-279,934 €] |

Fig. 2: Additional results



Source: own calculations

Among pre-treated patients, earlier initiation of ocrelizumab was associated with improved clinical outcomes compared to later-line use. The baseline mean EDSS was 2.4, increasing to 3.3 at the end of the modeled period for ocrelizumab-treated patients versus 3.64 for comparator therapies. The number of relapses was also slightly lower with ocrelizumab (3.16 vs. 3.22), reflecting reduced disease activity and slower disability progression.

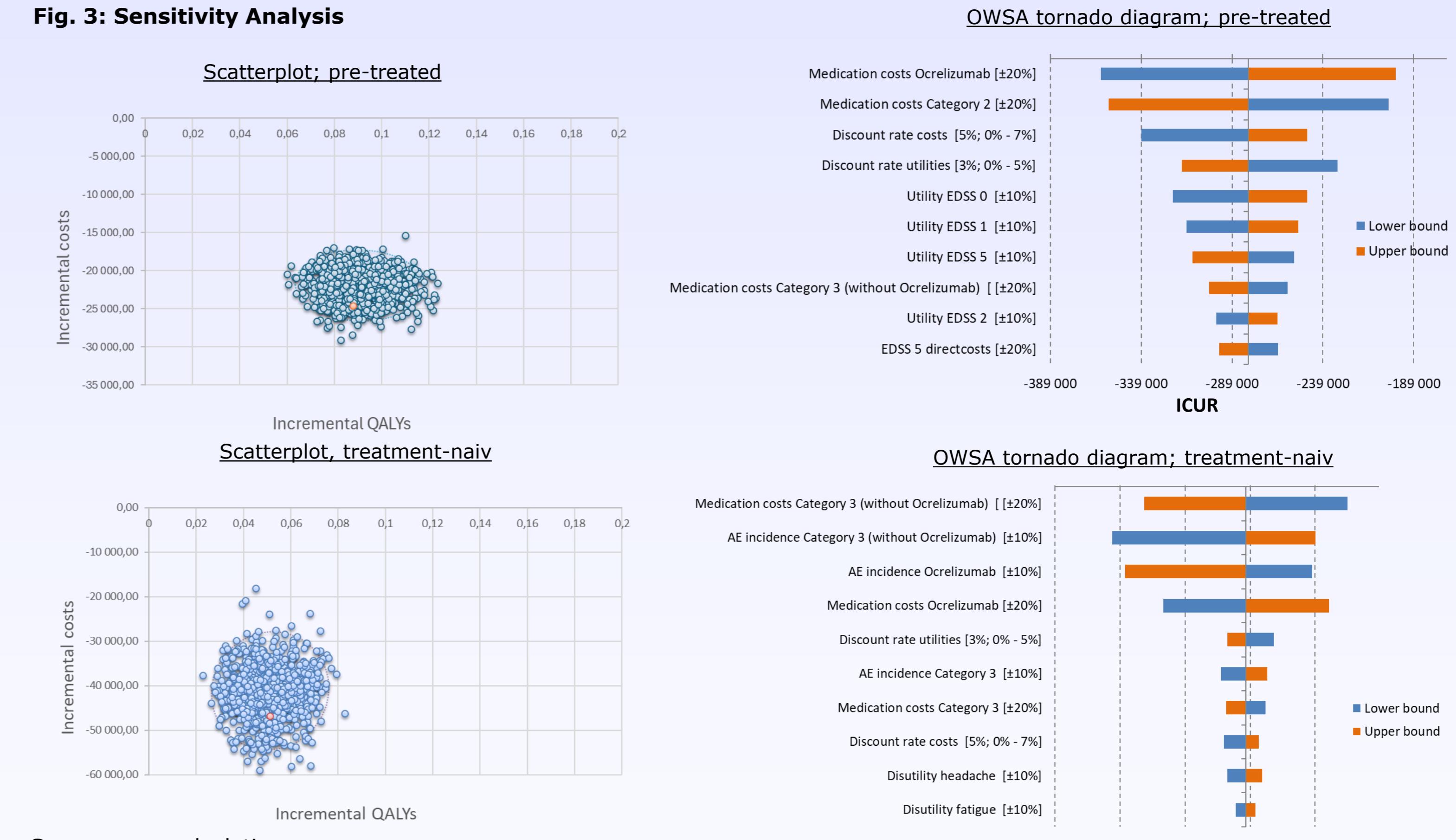
Tab. 4: Results for treatment-naïve patients

| Costs | Treatment algorithm with Ocrelizumab | Comparator treatment algorithm | Incremental |
|-------------------------------------|--------------------------------------|--------------------------------|------------------------------|
| Direct costs | 183,754 € | 220,508 € | -36,754 € |
| Indirect costs | 111,357 € | 121,474 € | -11,314 € |
| Total costs | 295,111 € | 341,982 € | -46,871 € |
| Outcomes | | | |
| QALYs | 6.17 | 6.12 | 0.05 |
| ICUR Incremental cost-utility ratio | | | Dominant [-912,793 €] |

Sensitivity Analysis

Probabilistic sensitivity analysis (PSA) and deterministic one-way sensitivity analysis (OWSA) were carried out to examine the robustness of the model.

Fig. 3: Sensitivity Analysis



Source: own calculations

OWSA confirms probabilistic results. Variations of medication cost of DMTs from category 3 and category 2, the discount rate for costs and utilities and AE of DMTs other than Ocrelizumab represents the greatest influence.

Conclusion

This study demonstrated that early initiation of ocrelizumab is dominant over comparator strategies and associated with lower disability, higher quality-of-life, and lower overall costs. These results support ocrelizumab as dominant from the healthcare-system and societal perspective and as a favorable treatment choice based on its robust safety and efficacy profile.

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Additional literature with the author