Cost-Effectiveness Analysis of Ofatumumab for Relapsing Remitting Multiple Sclerosis Treatment in Italy

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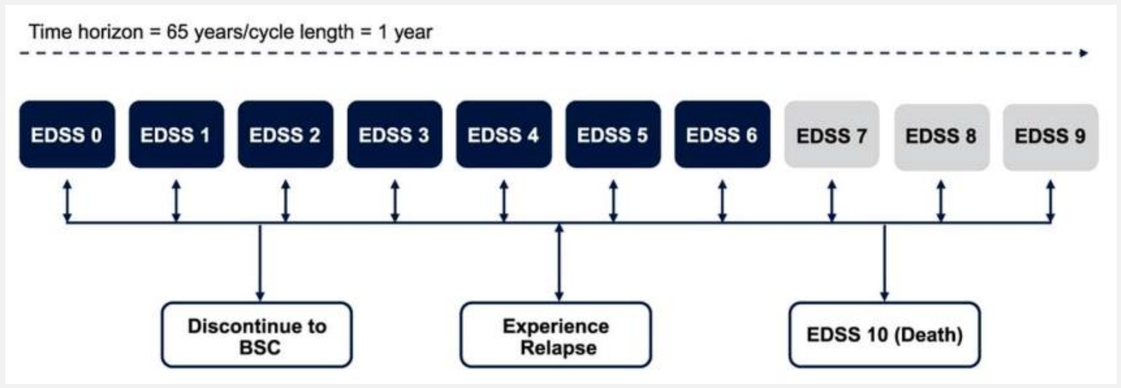
BACKGROUND & AIMS

- Multiple sclerosis (MS) is the most prevalent chronic inflammatory disease of the central nervous system, affecting more than 2 million people worldwide [1] and remains the major cause of neurological disability in young adults [1-3]. MS is associated to a high economic burden, characterized by high direct costs associated to the health care resources consumption, but also high indirect costs associated to informal care, services and loss of productivity [4]. Management of Relapsing Remitting MS (RRMS) involves disease-modifying therapies (DMTs), which aim to reduce relapse frequency and severity, and prevent or decrease disability. However, there is an important unmet need for an easy-to-administer DMT with high efficacy and a favorable beneft–risk profle that can be used early in the treatment pathway. Ofatumumab, the first fully human monoclonal antiCD20 antibody, is approved in Italy for second-line therapy in the treatment of adult patients with RRMS with active disease. Ofatumumab is among the most efficacious DMTs with respect to disease progression and reduction in relapse rates [5], with a subcutaneous injection that can be self-administered at home. However no economic evaluation are avilavble I Italy to define the value of Ofatumamab.
- This study aimed at evaluating the cost-effectiveness of ofatumumab compared with ocrelizumab in patients with RRMS by the Italian National Healthcare System (NHS) perspective.

METHODS

- A cohort multi-state Markov transition model was developed in Microsoft® Excel® to predict the costs and effectiveness of ofatumumab an ocrelizumab treatments in adults with RRMS. In the model (Figure 1), patients can progress through a series of disability states, which are based on the Expanded Disability Status Scale (EDSS) score. At the beginning of observation, patients have RRMS and a disability status (EDSS level) between 0 and 6.5. Over time, patients may progress to EDSS states of greater or lesser disability based on data from British Columbia Database [6], may maintain the same initial level of disability, may discontinue treatment due to the occurrence of adverse reactions or loss of efficacy and move to best supportive care (BSC), or may go on to death. In this model, it was assumed that: EDSS is the main determinant for assessing costs and clinical ouctome, subjects may discontinue a treatment over time, and treatment with the DMTs under study is discontinued when patients reach an EDSS level of 7 or higher. In addition, the mortality rates applied in the model depend on age, sex, and EDSS score. No direct effect of treatments on mortality was simulated, which instead possess an indirect effect by reducing progression to states with higher EDSS levels with which higher mortalities are associated.



- For patients receiving ofatumumab and ocrelizumab, natural history data were adjusted by a treatment effect derived from a NMA by Samjoo et al. [5], which estimated the comparative efficacy of DMTs for 6-month confirmed disability progression (CDP-6) and ARR. (Table 1)
- **Table 1.** Clinical data [5]

Treatments	Annualized relapse rate - RR (95% CI)	Confirmed disability progression at 24 weeks – HR (95%CI)
Ofatumumba	0.30 (0.22-0.40)€	0,43 (0,25-0,72)
Ocrelizumab	0.33 (0,25-0.44)	0,47 (0,25-0,88)

- Cost data for each EDSS level was retrieved by a cost of illness study conducted in Italy on a clinical registry combine with an administrative databased and updated based on the monetary revaluation indexes at October 2021 price. [7] (Table 2) The treatments costs were estimated based on posology reported in RCP and ex-factory price reported by the Italian Medicines Agency (ofatumumab € 1,233.21 per 20 mg and ocrelizumab €5,640.63 per 300 mg). The monitoring and administration costs were estimated based on the literature and expert opinion [8] and set to € 1.115 (first year) and € 340 (following year) for ofatumumba and € 1.150 (first year) and € 363 (following year) for ocrelizumab. Utility data for each EDSS levele was retrived by the cost of illness study conducted in Italy by Battaglia et al. [9] (Table 2) A disutility of 0,18 was applied to each relapse event.
- **Table 2**. Cost and utility data for EDSS level

EDSS	0	1	2	3	4	5	6	7	8	9
Utility – Mean (SE)	0,923 (0,045)	0,882 (0,048)	0,836 (0,048)	0,777 (0,052)	0,783 (0,048)	0,755 (0,047)	0,718 (0,047)	0,579 (0,049)	0,310 (0,050)	0,040 (0,074)
Mean yearly cost	€2,081	€2,081	€2,081	€2,081	€4,349	€4,349	€4,349	€10,339	€10,339	€10,339

- The model estimated the costs (€), the life years and the QALYs gained for each treatment included in the analysis. The cost-effectiveness results were reported as incremental cost-effectiveness ratio (ICER) per QALY gained. An ICER under the willingness-to-pay threshold of 40,000€ per QALY gained was considered cost-effective. A one-way sensitivity analysis and a probabilistic sensitivity analysis was performed to assess the reliability of base case analysis results.

RESULTS

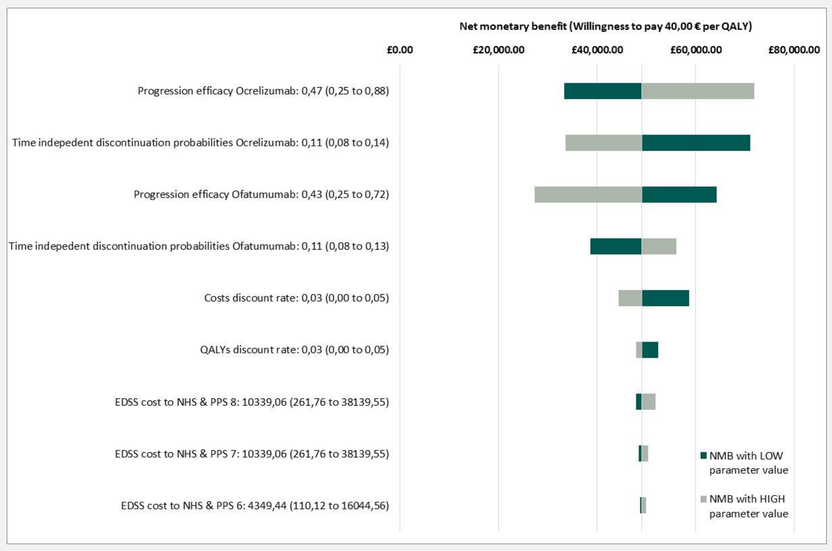
- In the base-case scenario, ofatumumab was more effective than ocrelizuamb. (Table 3). The QALYs estimated for a patient treated with ofatumumab was 15.68 compared to 15.81 in patients treated with ocrelizumab.
- Ofatumumab was also less expensive than ocrelizumab with a cost per patient of €214.114 compare to € 259.245. The cost difference was mainly due to a lower treatment and monitoring/administration cost of ofatumumab (€ 103,913 per patient) compare to ocrelizumab (€147,037 per patient)
- Ofatumumba treatment produced a cost saving of € 41.153 and a QALY gained of 0.13.
- Based on the higher efficacy and the lower cost, ofatumumab was a cost-saving option compared with ocrelizumab.

Table 1: Cost-effectiveness analysis - Base case results

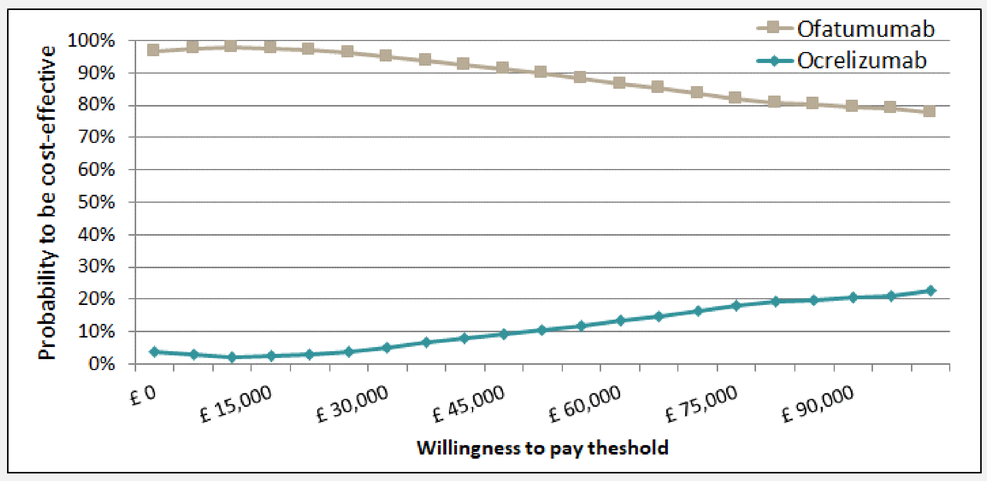
Treatments	Total costs (€)*	Δ Total costs(€)*	QALYs*	Δ QALYs*	ICER
Ocrelizuamb	€ 259,245	-	15,68	-	-
Ofatumumab	€ 214.114	-45.131	15,81	+0.13	Ofatumumab dominant

* discounted costs and outcomes at 3.0%

- All parameter values changes in the line way sensitivity analysis reported ofatumumba as the cost saving option compare to ocrelizumab, with .efficacy data reporting the highest impact on the results (Figure 2) Due to the dominant profile o ofatumumab compare to ocrelizuamb, the results of one-way sensitivity analysis was reported as Net monetary benefit (NMB) using a willingness to pay of €40,000 per QALY gained.
- **Figure 2**. One way sensitivity analysis.



- The PSA analysis showed that ofatumumab had a 92% probability to be cost-effective compared to ocrelizumab, considering a WTP threshold of 40,000€/QALY gained.
- **Figure 2**. Probabilistic sensitivity analysisi: cost-effectiveness accepatbility curves



CONCLUSIONS

- In the base case scenario, ofatumumba (fully human monoclonal antiCD20 antibody administrated with a subcutaneous injection) was dominant compare to ocrelizumab (humanized anti-CD20 monoclonal antibody administered intravenously). An improvement of 0.13 QALY per patient using ofatumumba is associated to a cost reduction of € 45,131. Results were confirmed by sensitivity analyses.
- Ofatumumab is administrated with a subcutaneous injection that can be self-administered at home, allowing greater patient independence, reduced healthcare resource utilization, and treatment access in areas outside of infusion facilities.
- Additional studies are required to confirm the favorable economic profile of ofatumumab compare to the other second line DMTs available in Italy.

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The study was funded by Novartis Farma Italy.

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