Estimating the Long-Term Clinical and Societal Outcomes of Ofatumumab Compared with Teriflunomide and Evaluating the Impact of Immediate vs Delayed High Efficacy Therapy in Treating Patients with Relapsing Multiple Sclerosis in Spain

P913

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Background

- Multiple sclerosis (MS) is a debilitating, neurological disease that typically affects people during their prime working years.[1] The economic burden of MS in Spain is substantial, with estimates suggesting an annual cost burden of €1,395 million in 2016.[2]
- Ofatumumab (Kesimpta®) is a fully human anti–CD20 monoclonal antibody approved in March 2021 in Europe for the treatment of adults with relapsing multiple sclerosis (RMS).[3] The efficacy and safety of ofatumumab vs teriflunomide has been demonstrated in two pivotal clinical trials (ASCLEPIOS I and II).[4] However, the long-term cost and productivity outcomes of ofatumumab compared to teriflunomide in patients with RMS remains unexplored.

Objective

- To assess the economic and clinical/societal consequences of delaying high efficacy treatment (HET) with ofatumumab in RMS patients compared with early ofatumumab initiation through cost consequence analysis from a Spanish societal perspective.

Methods

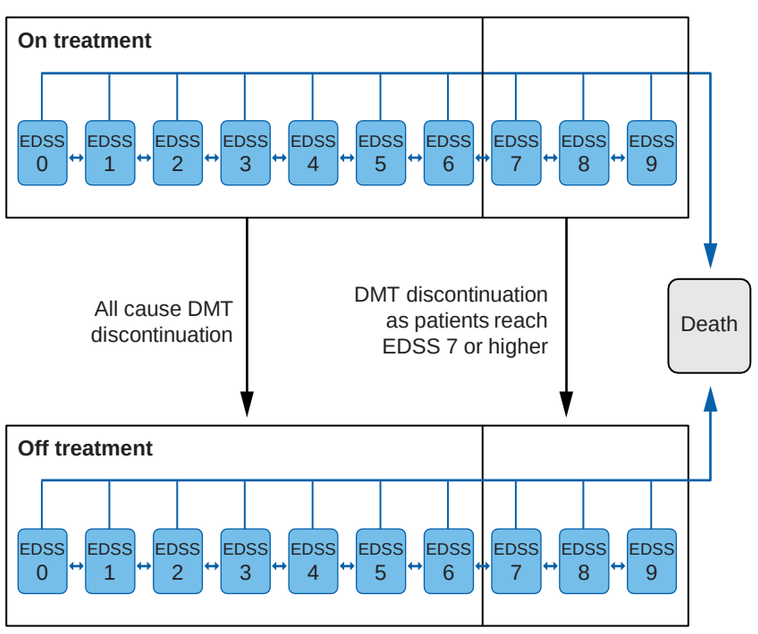
Study population

- The patient population considered in this model was aligned to the population included in the ASCLEPIOS I & II trials.[4] The mean age of the cohort was 38.2 years (standard error: 0.005), 32.4% were male, and had a baseline expanded disability status scale (EDSS) scores between 0–5.5.[4] The interventions considered were ofatumumab 20 mg administered subcutaneously once every month and teriflunomide 14 mg administered orally once daily.[3,5]

Model structure and inputs

- A discrete time Markov model based on EDSS health states (EDSS 0=neurologically normal; EDSS 10= death) was developed in Microsoft Excel® to simulate the natural history of disease progression in RMS patients.
- During each cycle of the model, patients could remain at the same EDSS state or move to a higher/lower EDSS state or dead, as well as experience a relapse **(Figure 1)**.
- The analysis was conducted using a hypothetical cohort of RMS patients with cycle length of 1–year and time horizon of 10 years.

Figure 1. Model structure



DMT, disease modifying therapy; EDSS, expanded disability status scale.

- The transition probabilities between EDSS states of the untreated model were based on the British Colombia natural history dataset.[6] The annual relapse rate (ARR) by EDSS during the untreated course of the disease were based on a study of British MS patients and a prospective long–term study natural history data.[7,8]
- For the treatment–adjusted model, the hazards ratio (HR) for time to 6–month confirmed disability progression (CDP), rate ratio (RR) for ARR, were sourced from a network meta-analysis.[9] The annual discontinuation probabilities for ofatumumab and teriflunomide were sourced from ASCLEPIOS trials and a network meta–analysis.[4,9]
- Mortality rates for the general population were derived from the age–and gender specific mortality rates for Spain,[10] adjusted for the MS population using the mortality multipliers reported in the literature.[11]
- Productivity loss data (% employed, working full time, informal care), disability weights of health states, and disease–related costs were retrieved from published literature.[12-15] Additionally, relapse management costs were applied according to the severity of relapse (mild, moderate, and severe) and were derived from Hawton et al.[16] The costs were inflated to the year 2020 using the consumer price index.
- Three scenarios were simulated. The two base scenarios evaluated ofatumumab (i.e., 10 years on ofatumumab) versus teriflunomide (i.e., 10 years on teriflunomide). The third scenario simulated a 3–year delay in ofatumumab treatment (i.e., 3–year treatment with teriflunomide followed by 7–year ofatumumab treatment).

Model assumptions

- Treatment effects were applied in the model in the form of delaying disability progression and reducing the number of relapses.
- Patients were assumed to discontinue treatment and move to best supportive care either when they reach EDSS 7 or higher or all cause discontinuation in line with ASCLEPIOS trials.[4]

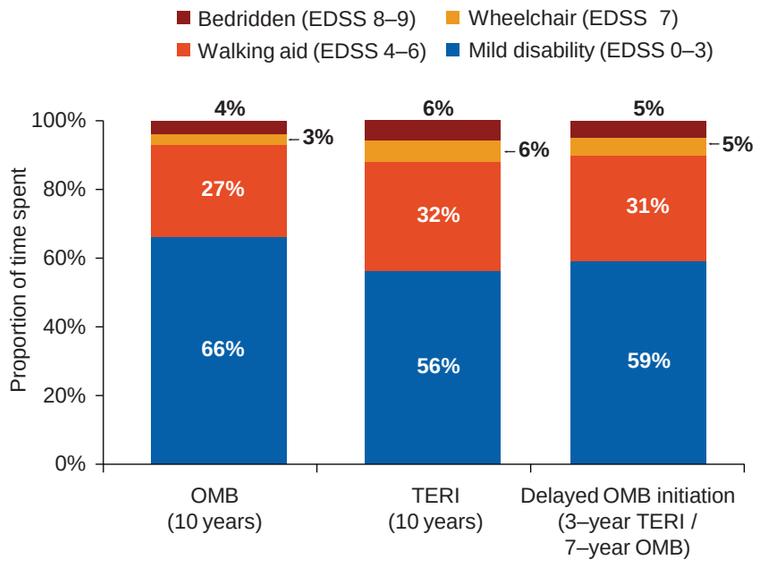
Model outcomes

- Clinical outcomes included the distribution of patients in the different EDSS states, the time spent in different health states, the proportion of wheelchair patients (EDSS ≥7), number of relapses, and productivity measures (% employed and % early retired). Additionally, the number of disability–adjusted life years (DALYs) was calculated as the sum of the years of life lost (YLL) due to premature mortality and years lived with disability (YLD).[13]
- Economic outcomes included direct, relapse, and indirect costs. Direct costs comprised healthcare costs (disease management, drug administration and monitoring, adverse event management, relapse and non–medical), and excluded DMT acquisition costs. Relapse costs were those associated with the management of relapse events. Indirect costs were costs associated with MS–related productivity loss (% employed and % early retired) and caregiver costs. All costs are expressed in 2020 Euros.

Results

- At the end of 10 years, the proportion of patients in the mild disability state (EDSS 0–3) were projected to be higher in the ofatumumab cohort compared to teriflunomide cohort (57% vs 44%). Moreover, patients in ofatumumab cohort stayed longer in mild disability state as compared those in the teriflunomide cohort **(Figure 2)**.

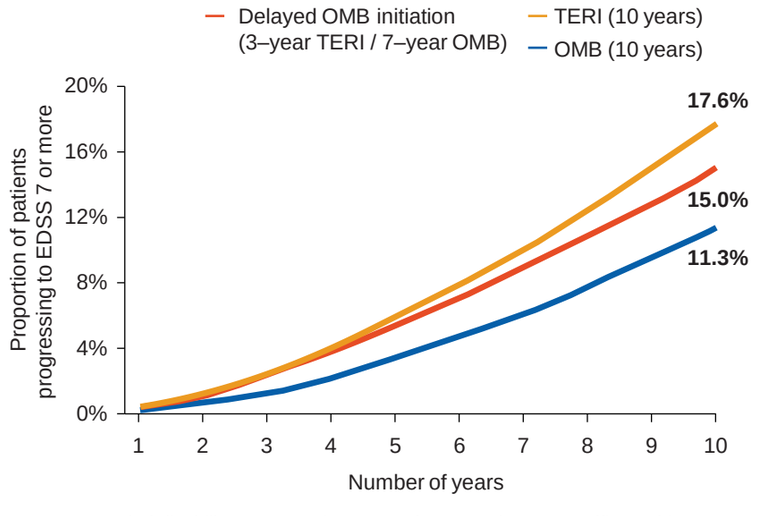
Figure 2. Time spent in MS health states over 10 years



EDSS, expanded disability status scale; OMB, ofatumumab;TERI, teriflunomide; MS, multiple sclerosis

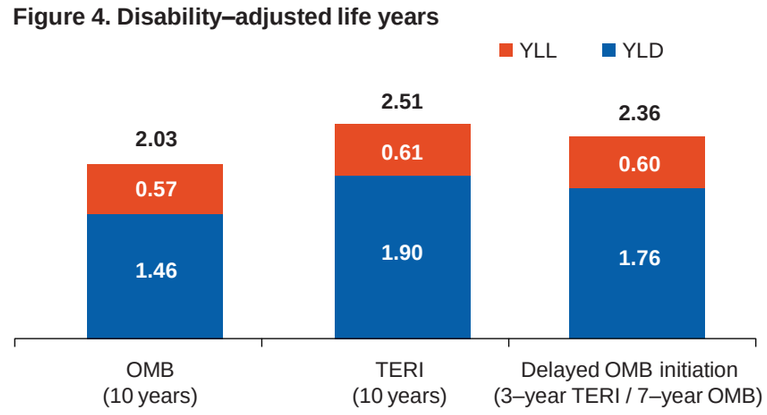
- Overall, in the ofatumumab cohort, 35.6% less patients in the would progress to EDSS ≥7 **(Figure 3)** and experience 27.8% less relapses (3.8 vs 5.3) compared with the teriflunomide cohort.
- At the end of 10 years, the proportion of patients employed was higher (40.0% vs 35.2%) and the percentage of patients who retired early was relatively lower (13.0% vs 15.4%) in the ofatumumab cohort compared with the teriflunomide cohort. Additionally, patients in the ofatumumab cohort would require 7.3% less informal care time (1,542 vs 1,664 days) and experience 19% reduction in DALYs (2.03 vs 2.51) compared with the teriflunomide cohort **(Figure 4)**.
- A 3–year delay in the initiation of ofatumumab treatment was estimated to result in 32.2% more patients progressing to EDSS ≥7 **(Figure 3)**, 20.2% more relapses (4.6 vs 3.8), 5.4% increased informal care time (1,625 vs 1,542 days), and 16.6% more DALYs compared with early initiation of ofatumumab treatment **(Figure 4)**. Furthermore, productivity was lower (i.e., 6% less employed; 9.1% retired early) in patients with delayed vs early ofatumumab initiation.

Figure 3. Proportion of MS patients progressing to EDSS ≥7



EDSS, expanded disability status scale; OMB, ofatumumab; TERI, teriflunomide; MS, multiple sclerosis.

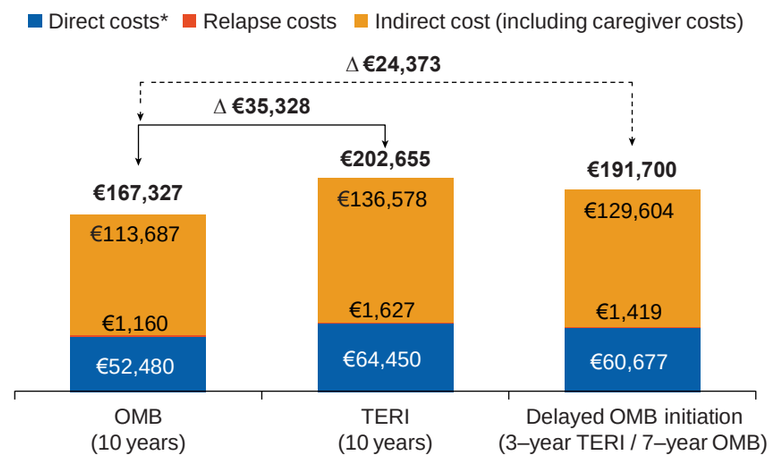
Figure 4. Disability–adjusted life years



EDSS, expanded disability status scale; OMB, ofatumumab; TERI, teriflunomide; YLD, years lived with disability; YLL, years of life lost.

- In addition to the clinical benefits, patients receiving ofatumumab were estimated to incur 17.4% lower costs compared with teriflunomide (€167,327 vs €202,655 per patient). Additionally, a 3–year delay in ofatumumab initiation was projected to result in 14.6% more costs compared to those with early ofatumumab initiation (€191,700 vs €167,327 per patient) **(Figure 5)**.

Figure 5. Total annual cost (per patient) at the end of 10 years



OMB, ofatumumab; TERI, teriflunomide.

Note: *Includes costs for disease management, drug administration and monitoring, adverse event management, and direct non-medical. Excludes DMT acquisition costs

Conclusions

- At the end of 10 years, patients receiving ofatumumab are projected to experience comparatively better outcomes (clinical and economic) than those receiving teriflunomide. The proportion of patients progressing to EDSS ≥7 (i.e., requiring a wheelchair or bedridden) was lower in ofatumumab cohort than teriflunomide cohort.
- Furthermore, a strategy of early use of a HET such as ofatumumab versus its delayed use, has the potential to further improve the outcomes compared to an escalation strategy in RMS patients having characteristics similar to those in ASCLEPIOS trials.

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Disclosures

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