Evaluating the long-term clinical, societal, and economic outcomes of ofatumumab vs teriflunomide / interferon β-1a and the impact of early vs delayed ofatumumab initiation in relapsing multiple sclerosis patients in Greece

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Background

- Multiple sclerosis (MS) is a debilitating, neurological disease that typically affects people during their prime working years.[1] According to a previous Greek study, the mean annual cost per patient was estimated at €26,118, with higher costs among those with severe (€45,442) compared with mild and moderate (€32,126), and mild MS (€20,702).[2]
- Ofatumumab (Kesimpta®; OMB) 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 OMB has been demonstrated in two pivotal clinical trials (ASCLEPIOS I & II).[4] However, the cost and consequences of OMB compared to teriflunomide (TERI) or interferon β-1a (IFN-β-1a) in patients with RMS remains unexplored in Greece.

Objective

- To estimate the long-term clinical, societal, and economic outcomes of OMB vs TERI or IFN-β-1a and evaluate the impact of early (at first-line) vs delayed (3-year / 5-year delay) OMB initiation in RMS patients from a Greek societal perspective.

Methods

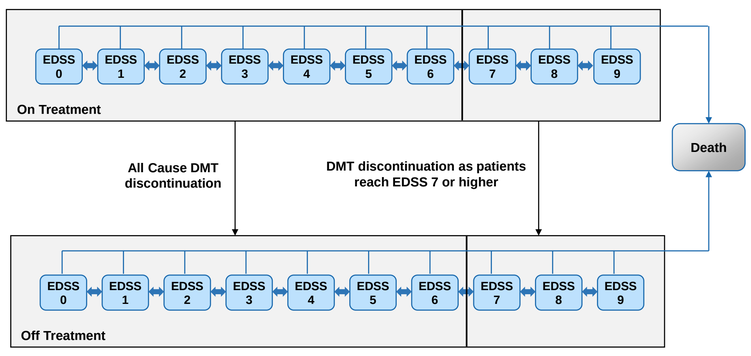
Study Population and Intervention

- 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 (with an average EDSS score of 2.9).[4]
- The interventions considered were OMB 20 mg administered subcutaneously once every month, comparators considered were TERI 14 mg administered orally once daily and IFN β-1a 44 μg/0.5ml (equivalent to 12 million international units [MIU]) administered subcutaneously three times per week.[3,5,6]

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.[7] 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.[8,9]
- For the treatment-adjusted model, the hazard 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 rates for OMB, TERI and IFN-β-1a were sourced from ASCLEPIOS trials and a network meta-analysis.[4,10]
- Mortality rates for the general population were derived from the age- and gender specific mortality rates for Greece,[11] adjusted for the MS population using the mortality multipliers reported in the literature.[12]
- Productivity loss data (% retired early, informal care), disability weights of health states, and disease-related costs were retrieved from published literature and the official price list.[2,13,14] Additionally, relapse management costs were applied according to the severity of relapse (mild, moderate, and severe).[15]
- Four scenarios with a time horizon of 10 years were simulated.
  - The two base scenarios evaluated OMB (i.e., 10 years on OMB) versus TERI (i.e., 10 years on TERI) or IFN-β-1a (i.e., 10 years on IFN-β-1a) without any treatment switches.
  - The third scenario simulated a 3-year delay in OMB treatment (i.e., 3-year treatment with TERI or IFN-β-1a followed by 7-year OMB treatment)
  - The fourth scenario simulated a 5-year delay in OMB treatment (i.e., 5-year treatment with TERI or IFN-β-1a followed by 5-year OMB 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]

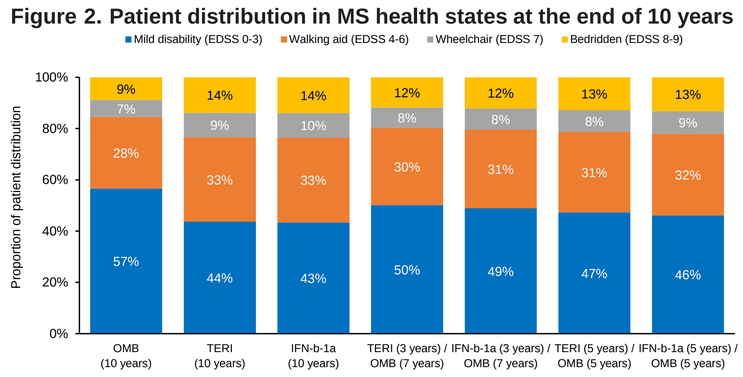
Model Outcomes

- Clinical outcomes included the distribution of patients in the different EDSS states, the time spent in different health states, the proportion of patients with increased disability (EDSS ≥7), number of relapses suffered, 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 (drug cost, disease management, drug administration and monitoring, adverse event management and non-medical). Relapse costs were those associated with the management of relapse events. Indirect costs were costs associated with MS-related productivity loss (% early retired). All costs are expressed in 2021 Euros.

Results

- At the end of 10 years, the proportion of patients in the mild disability state (EDSS 0-3) was projected to be higher in the OMB cohort (57%) vs TERI (44%) or IFN-β-1a (43%) cohorts (**Figure 2**). Moreover, patients in OMB cohort stayed longer in mild disability state as compared those in the TERI or IFN-β-1a cohort.

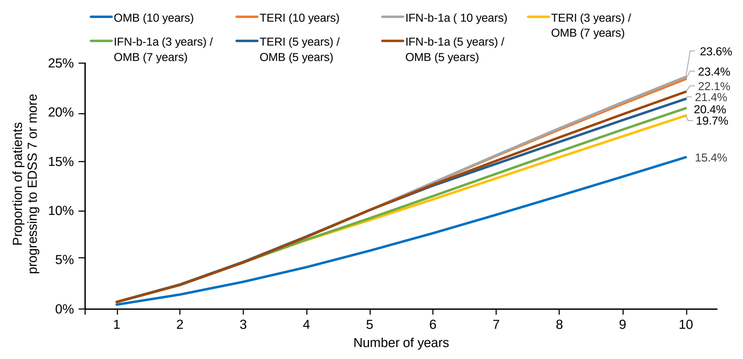
Figure 2. Patient distribution in MS health states at the end of 10 years



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

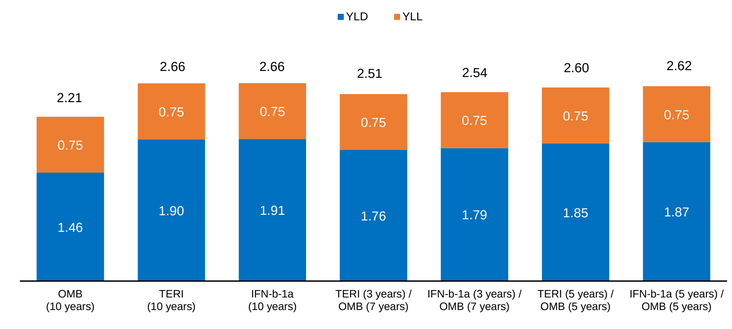
- At the end of 10 years, the proportion of patients progressing to EDSS ≥7 was projected to be lower in OMB cohort (15.4%) compared to TERI (23.4%) or IFN-β-1a (23.6%) (**Figure 3**). Furthermore, patients initiating OMB at the first line were projected to experience fewer relapses (3.79) compared with the TERI (5.26) or IFN-β-1a (5.32) cohorts.
- At the end of 10 years, the percentage of patients who retired early was relatively lower (35% vs 39% & 39%) in the OMB cohort compared with the TERI or IFN-β-1a cohort. Additionally, patients in the OMB cohort required 23% less informal care (194 vs 239 & 239 days) and experience reduction in DALYs (2.21 vs 2.66 & 2.66) compared with the TERI or IFN-β-1a cohort (**Figure 4**).
- A 3-year delay in the initiation of OMB treatment was estimated to result in increased proportion (19.7% [TERI] or 20.4% [IFN-β-1a] vs 15.44% [OMB]) of patients progressing to EDSS ≥7 (**Figure 3**), more relapses (4.56 [TERI] or 4.72 [IFN-β-1a] vs 3.79 [OMB]), increased informal care time (225 [TERI] or 227 [IFN-β-1a] vs 194 days [OMB]), and more DALYs compared with early initiation of OMB treatment (**Figure 4**). Furthermore, productivity was lower (i.e., 37% [TERI] or 38% [IFN-β-1a] vs 35% [OMB] less employed) in patients with delayed vs early OMB initiation.

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



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

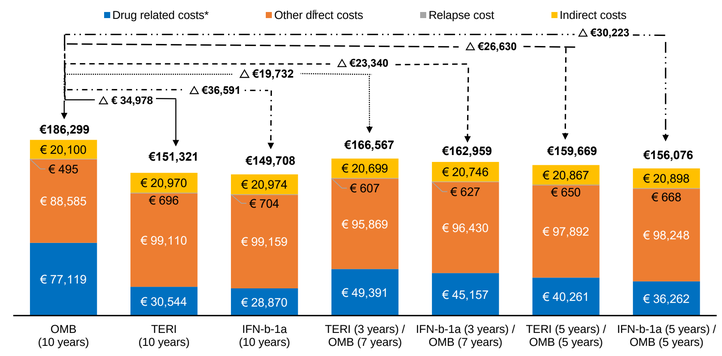
Figure 4. Disability-adjusted life years



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

- Even though early OMB initiation was projected to result in an increase in the drug costs (€77,026) vs TERI (€29,698) or IFN-β-1a (€28,578), it eventually gets partially offset by other direct costs (i.e., inpatient care, outpatient care, consultations, investigations, MS-related comorbidities, over-the-counter drugs, informal care, MS-related investments, and professional assistance), and indirect cost savings.
- In addition to the clinical benefits, patients receiving OMB were estimated to incur 11% lower costs (including other direct costs, relapse cost and indirect cost) compared with TERI or IFN-β-1a cohorts (€109,180 vs €120,776 or €120,837 per patient).
- Additionally, a 3-year delay in OMB initiation was projected to result in 8% more costs (including other direct costs, relapse cost and indirect cost) compared to those with early OMB initiation (€109,180 per patient) vs TERI (€117,175 per patient) or IFN-β-1a (€117,803 per patient) (**Figure 5**). Similar results were seen when OMB initiation was delayed by 5 years (5-year TERI or IFN-β-1a followed by 5-year OMB) (**Figure 5**).

Figure 5. Total Annual Cost (per patient) at the end of 10 years



OMB, ofatumumab; TERI, teriflunomide.

Note: *Includes drug acquisition, administration & monitoring costs, and adverse event management costs

#Includes inpatient care, outpatient care, consultations, investigations, MS-related comorbidities, over-the-counter drugs, informal care, MS-related investments, and professional assistance

Conclusions

- At the end of 10 years, patients receiving OMB are projected to experience comparatively better outcomes (clinical and economic) than those receiving TERI or IFN-β-1a.
- Furthermore, early initiation of high-efficacy therapy such as OMB vs its delayed initiation (3-year/5-year delay) was projected to provide long-term clinical, societal, and economic benefits in RMS patients.

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Disclosures

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