Earlier Ofatumumab Treatment may Reduce Disease Progression and Relapses for Patients with Relapsing-Remitting Multiple Sclerosis: Results from a Cost-Consequence Model

P00275

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Introduction

- Relapsing-remitting multiple sclerosis (RRMS) is typified by the occurrence of relapses, followed by complete or partial recovery and separated by periods of remission.[1] Increased disease progression becomes evident over time and is associated with a higher number of relapses.[2]
- Oral disease-modifying therapies (DMTs), such as dimethyl fumarate (DMF), are among the most common treatments prescribed for RRMS in the National Health Service (NHS) and are often used as first-line treatments.[3] Monoclonal antibody DMTs are less frequently used in the first instance.
- Ofatumumab, an anti-CD20 monoclonal antibody which is intended to be self-administered subcutaneously, is superior at reducing relapses and slowing disease progression compared with oral teriflunomide, as demonstrated in the ASCLEPIOS trials.[4] During the NICE appraisal, clinical experts noted that ofatumumab could be used as a first-line treatment for RRMS in adults with active disease, defined by clinical or imaging features.

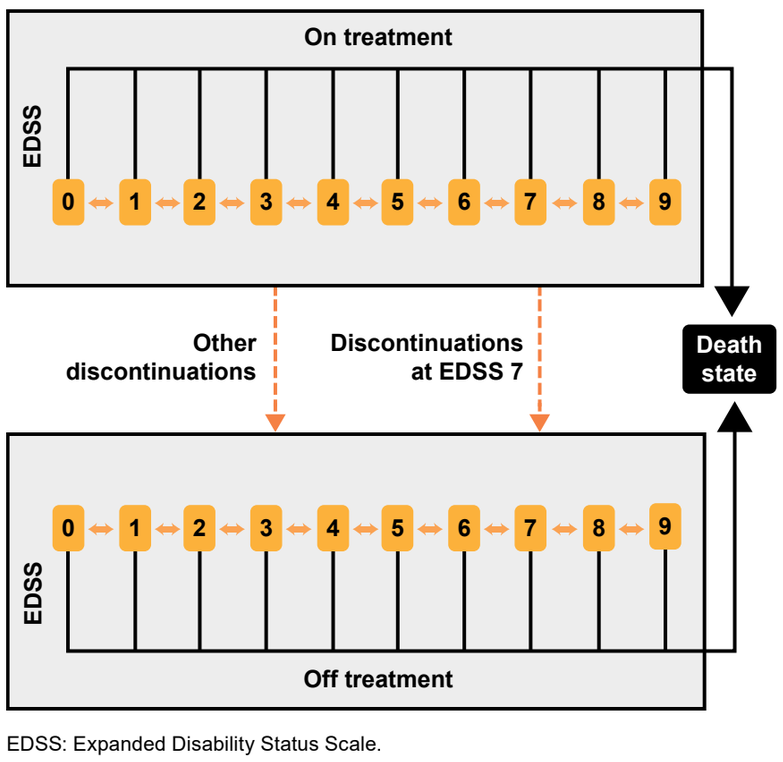
Objective

- To compare disease progression and number of relapses in patients with RRMS treated with first-line ofatumumab versus those receiving second-line ofatumumab after initial DMF use.

Methods

- A discrete-time cohort Markov model based on disease progression through Expanded Disability Status Scale (EDSS) health states with annual cycles and 10-year time horizon was employed using a UK NHS perspective (**Figure 1**). Outcomes relating to relapses and disease progression are reported. During each cycle, patients' EDSS health state could increase, decrease, or remain the same.
- Patient baseline characteristics were aligned with those of the ASCLEPIOS trials of ofatumumab (N=1882).[4] The mean age was 38.2 years (SD: 9.1), 32.4% were male and EDSS scores were between 0 and 5.5.
- Natural history (NH) transition probabilities for EDSS health state scores were obtained from the British Columbia database.[5] The NH annualised relapse rate (ARR), dependent on EDSS health state, was calculated using data obtained from the UK MS survey, combined with a prospective study of NH data.[6,7]
- The effect of treatment on disease progression and number of relapses was modelled by applying a hazard ratio (HR) for 6-month confirmed disease progression (6M-CDP) to the NH transition probabilities and a rate ratio (RR) to the NH ARRs. The HRs for 6M-CDP (ofatumumab: 0.43; DMF: 0.68) and ARR RRs (ofatumumab: 0.30; DMF: 0.50) were obtained from a network meta-analysis.[8]
- In line with NHS guidelines, treatment was modelled to discontinue when patients reached EDSS ≥7.[9] All-cause discontinuation for ofatumumab was taken from the ASCLEPIOS trials and for DMF was obtained from the literature.[4,8]
- General population mortality rates were obtained from National Life Tables for England and Wales (2018–2020).[10] MS mortality multipliers from the literature were applied.[11]
- Three treatment scenarios were explored: ofatumumab only; delayed ofatumumab (DMF for 3 years before patients remaining on treatment were modelled to switch to ofatumumab for 7 years); DMF only.

Figure 1. Structure of the discrete-time cohort Markov model employed

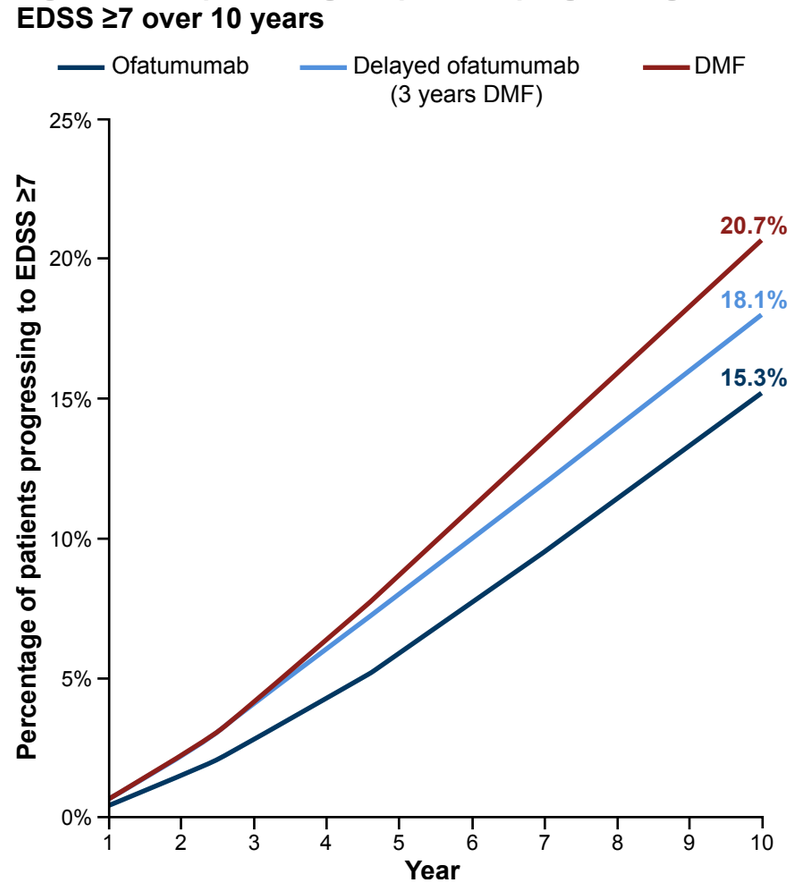


EDSS: Expanded Disability Status Scale.

Results

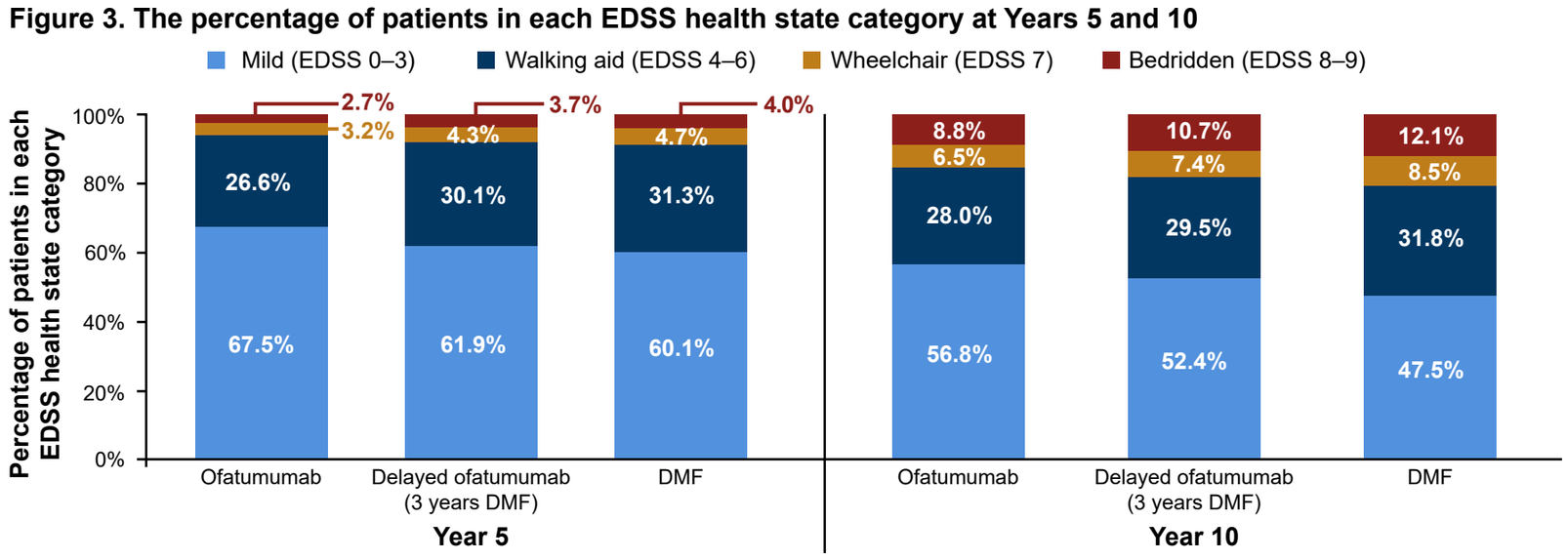
- Over 10 years, a patient treated with early ofatumumab from Year 0 was predicted to have fewer relapses (3.78) than one treated with DMF for 3 years (4.23) before switching to delayed ofatumumab, or treated with DMF only (4.67).
- First-line treatment with ofatumumab was predicted to be more effective at reducing the percentage of patients progressing to EDSS ≥7 than delayed ofatumumab or DMF only (**Figure 2**).
  - After 5 years, 2.1% fewer patients receiving early ofatumumab from Year 0 progressed to EDSS ≥7 than those who received delayed ofatumumab (3 years on initial DMF treatment). After 10 years, this difference increased to 2.8%.
  - Compared with DMF only, 2.8% fewer patients treated with ofatumumab only progressed to EDSS ≥7 at Year 5. At Year 10, the difference was predicted to be 5.4%.
- Earlier ofatumumab treatment resulted in a higher proportion of patients with mild disease (**Figure 3**). The difference between early ofatumumab and delayed ofatumumab at Years 5 and 10 was 5.6% and 4.4%, respectively. The difference between patients treated with ofatumumab only and DMF-treated patients at Years 5 and 10 was 7.4% and 9.3%, respectively.
  - A lower percentage of patients treated only with ofatumumab had EDSS ≥7 at Years 5 and 10 compared with those receiving delayed ofatumumab (Year 5: 5.9% versus 8.0%; Year 10: 15.3% versus 18.1%).
- Over 10 years, earlier ofatumumab treatment was also associated with a higher percentage of time spent in lower EDSS health states compared with delayed ofatumumab (**Figure 4**).

Figure 2. The percentage of patients progressing to EDSS ≥7 over 10 years



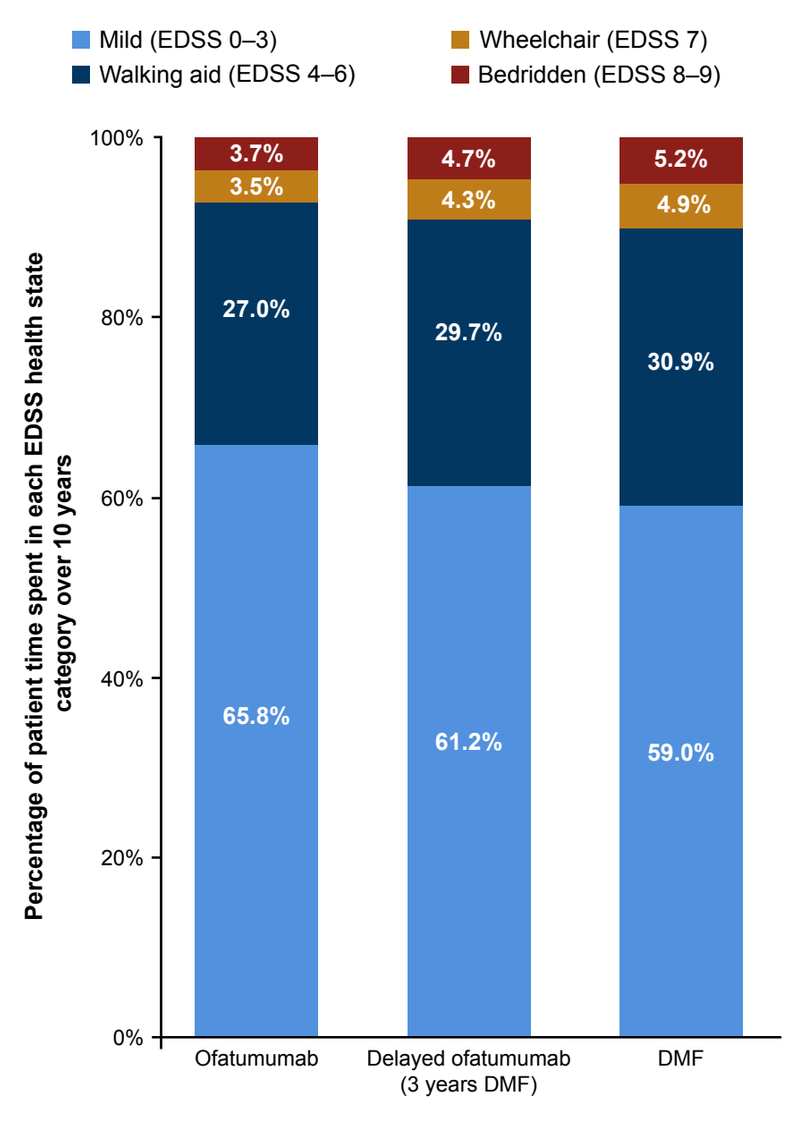
DMF: dimethyl fumarate; EDSS: Expanded Disability Status Scale.

Figure 3. The percentage of patients in each EDSS health state category at Years 5 and 10



DMF: dimethyl fumarate; EDSS: Expanded Disability Status Scale.

Figure 4. The percentage of patient time spent in each EDSS health state category



DMF: dimethyl fumarate; EDSS: Expanded Disability Status Scale.

Conclusions

- Over a modelled time horizon of 10 years, earlier ofatumumab treatment was predicted to reduce relapse events, slow disability progression and increase the time spent in lower EDSS health states compared with delayed ofatumumab (after 3 years of DMF), or DMF only.

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Disclosures

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LG and **SM:** Employees of Costello Medical. **AD:** Employee of Novartis Pharmaceuticals UK Ltd and owner of shares in Novartis at the time of conducting this research; current employee of Vertex Pharmaceuticals. **JL:** Employee of Novartis Pharmaceuticals UK Ltd and owner of shares in Novartis.

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