OLIKOS study design: exploring maintained ofatumumab efficacy in relapsing MS patients who transition from intravenous anti-CD20 therapy

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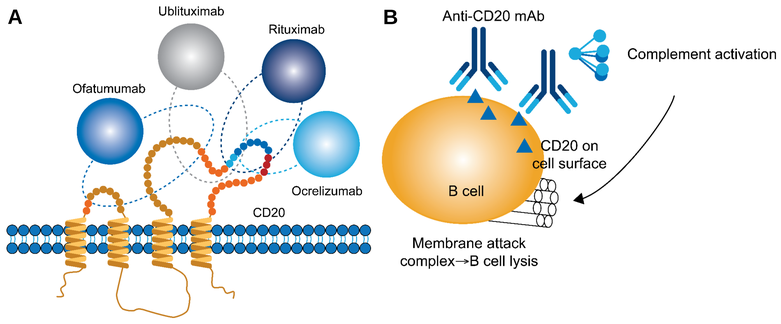
Background

- Depletion of B cells with anti-CD20 mAbs has been shown to limit disease activity in patients with RMS[1-3]
  - Treatment reduces ARR, Gd+ T1 and new/enlarging T2 lesions, and delays time to CDW[1-3]
- Ofatumumab is a fully human anti-CD20 mAb that induces B-cell lysis[4]
  - Administered as monthly subcutaneous 20 mg dose by patients via autoinjector pen
  - Ofatumumab binds to a distinct epitope on two non-continuous regions of CD20 on surface of B cells6 (**Figure 1A**)
  - CDC induced by activation of classical complement pathway in response to mAb binding at cell surface.6 Cascade of interactions between complement components activates membrane attack complex, and creates pore in membrane, leading to cell death (**Figure 1B**)
- In phase 3 ASCLEPIOS I and II studies, ofatumumab significantly reduced ARR, CDW and MRI lesions vs once daily oral teriflunomide[5]
  - ARR relative reductions: 51% and 58% in ASCLEPIOS I and II, respectively (both p<0.001)
  - Relative risk reduction in CDW: 34% (p=0.002) in 3 month CDW and 32% (p=0.01) in 6 month CDW (meta-analysis)
  - MRI lesions relative reductions: Gd+ T1, 97% and 94%; and new or enlarging T2, 82% and 85%, in ASCLEPIOS I and II, respectively (all *p*<0.001)
- No outcome data currently exist relating to patients previously treated with anti-CD20 IV therapies (eg, ocrelizumab or rituximab) transitioning to ofatumumab

Objective

- **OLIKOS study will explore the efficacy of ofatumumab in patients with RMS who transition from IV anti-CD20 mAb therapy**

Figure 1. Depletion of B cells with anti-CD20 mAbs



Study design

- This is a 12-month, single arm, multicenter, prospective study; ~100 participants with RMS enrolled from 20-30 centers in the USA (**Figure 2**):
  - who received at least 2 consecutive IV courses of ocrelizumab or rituximab every 6 months, and
  - for whom last dose was within 4-9 months before OLIKOS baseline/Day 1
- Participants receive open label ofatumumab 20 mg SC once monthly for 12 months following initial loading regimen of 20 mg SC doses on Days 1, 7 and 14
- Inclusion and exclusion criteria are described in **Table 1**
- Study endpoints are summarized in **Figure 3**

Figure 2. Study design

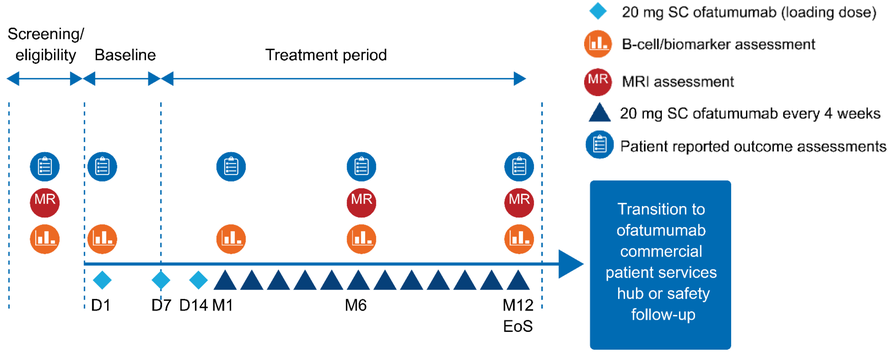
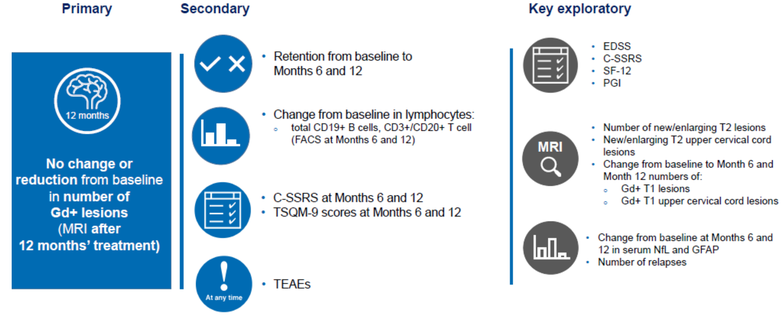


Table 1. Key inclusion and exclusion criteria

Key inclusion criteria
Men or women, aged 18 to 55 years
Diagnosis of RMS (2017 Revised McDonald criteria)
Received 2-5 consecutive IV courses of ocrelizumab or rituximab; last dose 4-9 months before baseline
EDSS score ≤5.5
Neurologically stable for 1 month before first study drug administration

Key exclusion criteria
Suboptimal response to anti-CD20 therapy in prior 6 months • Definition: relapse, ≥2 active Gd+ lesions, new/enlarging T2 lesions or clinical worsening
Discontinued anti-CD20 therapy because of severe infusion-related reactions, recurrent infections or decreased IgG requiring IVIg treatment
Progressive disease
Treated with other anti-CD20 mAbs

Figure 3. Study endpoints



Conclusions

- OLIKOS will be the first prospective study to assess maintained clinical efficacy, participant retention and satisfaction, and safety and tolerability of monthly ofatumumab
  - Administered via auto-injector pen in patients with RMS previously treated with ocrelizumab or rituximab
- OLIKOS will provide relevant clinical information
  - Ability to maintain therapeutic effects for patients transitioning from other anti-CD20 mAbs
  - Efficacy and safety of ofatumumab in RMS patients switching from anti-CD20 mAbs

Abbreviations

ARR, annual relapse rate; CDC, complement-dependent cytotoxicity; CDW, confirmed disability worsening; Gd+, gadolinium-enhancing; IV, intravenous; mAb, monoclonal antibody; MRI, magnetic resonance imaging; RMS, relapsing multiple sclerosis; D, day; EDSS, Expanded Disability Status Scale; EoS, end of study; Gd+, gadolinium-enhancing; IgG, immunoglobulin G; IV, intravenous; IVIg, intravenous immunoglobulin; M, month; mAb, monoclonal antibody; SC, subcutaneous; C-SSRS, Columbia-Suicide Severity Rating Scale; EDSS, Expanded Disability Status Scale; FACS, fluorescence-activated cell sorting; Gd+, gadolinium-enhancing; NfL, neurofilament light chain; PGI, Patient Global Impression; SF-12, short form-12; TSQM-9, Treatment Satisfaction Questionnaire for Medication; TEAEs, treatment-emergent adverse events

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Disclosures

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