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

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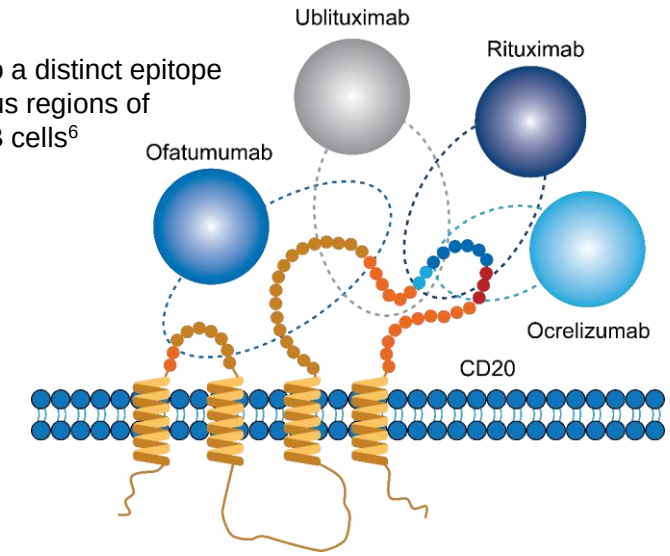
Background and objective

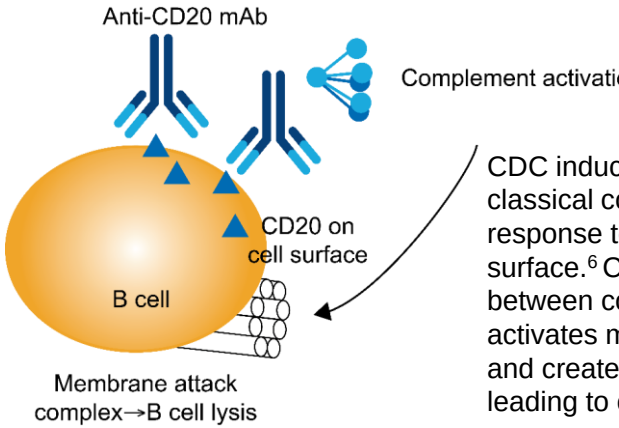
- Depletion of B cells with anti-CD20 mAbs has been shown to limit disease activity in patients with RMS[1-3]
  - Treatment reduces ARR, Gd+ T1 and new/enlarging T2 lesions, and delays time to CDW[1-3]
- Ofatumumab is a fully human anti-CD20 mAb that induces B-cell lysis[4]
  - Administered as monthly subcutaneous 20 mg dose by patients via autoinjector pen
- 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

Ofatumumab binds to a distinct epitope on two non-continuous regions of CD20 on surface of B cells[6]



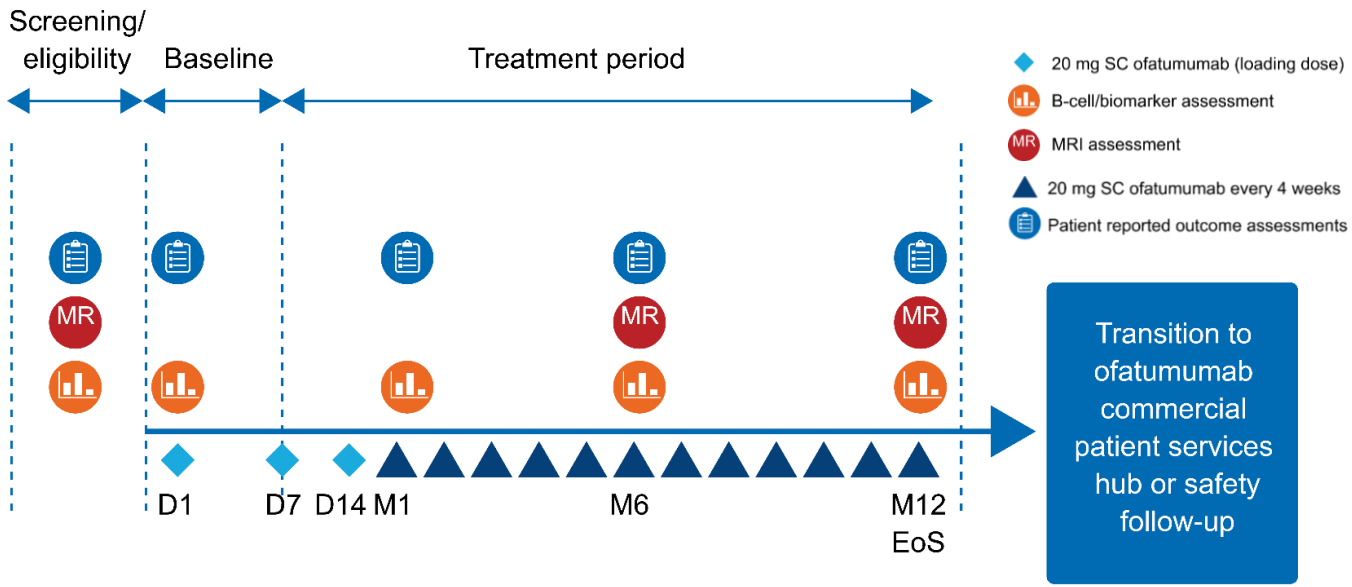


CDC induced by activation of classical complement pathway in response to mAb binding at cell surface.[6] Cascade of interactions between complement components activates membrane attack complex, and creates pore in membrane, leading to cell death

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. 1.Hauser SL, *et al*. *N Engl J Med*. 2008;358(7):676-688; 2. Kappos L, *et al*. *Lancet.* 2011;19:378(9805):1779-1787; 3. Hauser SL, *et al*. *N Engl J Med*. 2017;376:221-234; 4. Teeling JL, *et al*. *J Immunol.* 2006;177:362-371; 5. Hauser S, *et al*. *N Engl J Med.* 2020;383:546-557; 6. Smith P, *et al*. *Mult Scler.* 2016;22(Suppl.3):592

OLIKOS study design

- 12 month, single arm, multicenter, prospective study; ~100 participants with RMS enrolled from 10-20 centers in the USA:
  - who received 2-5 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 every 4 weeks for 12 months following initial loading regimen of 20 mg SC doses on Days 1, 7 and 14



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
Baseline CD19+ B cells depleted to <1%
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

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; MRI, magnetic resonance imaging; RMS, relapsing multiple sclerosis; SC, subcutaneous

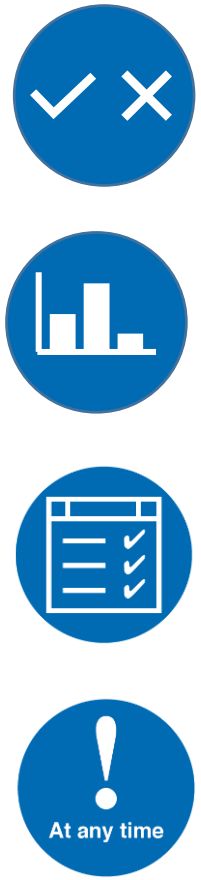
OLIKOS study endpoints

Primary

No change or reduction from baseline in **number of Gd+ lesions** (MRI **after 12 months' treatment)**

Secondary

- Retention from baseline to Months 6 and 12
- Change from baseline in lymphocytes:
  - total CD19+ B cells, CD3+/CD20+ T cell (FACS at Months 6 and 12)
- C-SSRS at Months 6 and 12
- TSQM-9 scores at Months 6 and 12
- TEAEs



Key exploratory

- EDSS
- C-SSRS
- SF-12
- PGI

MRI

- Number of new/enlarging T2 lesions
- New/enlarging T2 upper cervical cord lesions
- Change from baseline to Month 6 and Month 12 numbers of:
  - Gd+ T1 lesions
  - Gd+ T1 upper cervical cord lesions

- Change from baseline at Months 6 and 12 in serum NfL
- Number of relapses

C-SSRS, Columbia-Suicide Severity Rating Scale; EDSS, Expanded Disability Status Scale; FACS, fluorescence-activated cell sorting; Gd+, gadolinium-enhancing; mAb, monoclonal antibody; MRI, magnetic resonance imaging; 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

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**

mAbs, monoclonal antibodies; RMS, relapsing multiple sclerosis