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

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
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**
- 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

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

**Key exploratory**
- EDSS
- C-SSRS
- SF-12
- PGI
- 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
  o Administered via auto-injector pen in patients with RMS previously treated with ocrelizumab or rituximab

• OLIKOS will provide relevant clinical information
  o Ability to maintain therapeutic effects for patients transitioning from other anti-CD20 mAbs
  o Efficacy and safety of ofatumumab in RMS patients switching from anti-CD20 mAbs

mAbs, monoclonal antibodies; RMS, relapsing multiple sclerosis