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

Benjamin M Greenberg¹, Enrique Alvarez², John Foley³, Roland G Henry⁴, Joel Brown⁵, Elizabeth Camacho⁵, Xiangyi Meng⁵, Marina Ziehn⁶, Brandon Brown⁵, Le H Hua⁷

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¹Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA; ²Department of Neurology, University of Colorado, Aurora, CO, USA; ³Rocky Mountain Multiple Sclerosis Clinic, Salt Lake City, UT, USA; ⁴UCSF Weill Institute for Neurosciences, Department of Neurology, University of California, San Francisco, San Francisco, CA, USA; ⁵Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; ⁶Novartis Pharma AG, Basel, Switzerland; ⁷Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, NV, USA
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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\textsuperscript{1-3}
  o Treatment reduces ARR, Gd+ T1 and new/enlarging T2 lesions, and delays time to CDW\textsuperscript{1-3}
• Ofatumumab is a fully human anti-CD20 mAb that induces B-cell lysis\textsuperscript{4}
  o 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\textsuperscript{5}
  o ARR relative reductions: 51% and 58% in ASCLEPIOS I and II, respectively (both p<0.001)
  o Relative risk reduction in CDW: 34% (p=0.002) in 3 month CDW and 32% (p=0.01) in 6 month CDW (meta-analysis)
  o 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 mechanism of action

- Ofatumumab binds to a distinct epitope on two non-continuous regions of CD20 on surface of B cells\(^1\)

- CDC induced by activation of classical complement pathway in response to mAb binding at cell surface\(^1\)
  - Cascade of interactions between complement components activates membrane attack complex, and creates pore in membrane, leading to cell death

CDC, complement-dependent cytotoxicity; mAb, monoclonal antibody
\(^1\)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:
  - 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
Participants and setting

- Participants enrolled from 10-20 centers in the USA

**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

EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; IgG, immunoglobulin G; IV, intravenous; IVIg, intravenous immunoglobulin; mAb, monoclonal antibody; RMS, relapsing multiple sclerosis
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

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

Secondary

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
  - 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
Thank you