Abstract 1656
Efficacy and safety of ofatumumab versus placebo in relapsing multiple sclerosis patients in Japan and Russia: Results from the Phase 2 APOLITOS study

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Background
Ofatumumab, a fully human anti-CD20 monoclonal antibody, demonstrated superior efficacy versus teriflunomide with a favorable safety profile in the Phase 3 ASCLEPIOS I/II trials in relapsing multiple sclerosis (RMS) patients (Global, Ex-Japan). APOLITOS was designed to support ofatumumab registration for RMS treatment in Japan in conjunction with ASCLEPIOS.

Objectives
To evaluate the efficacy and safety of ofatumumab versus placebo in RMS patients and assess consistency of effect in Japanese and non-Japanese patients.

Methods
APOLITOS was a 24-week, double-blind, placebo-controlled study followed by an open-label extension up to week 48. Patients aged 18–55 years with confirmed MS diagnosis (2010 revised McDonald criteria), prior evidence of disease activity (≥1 relapse in the last 2 years AND MRI activity in the last year), and an EDSS score of 0–5.5 were randomized (2:1) to subcutaneous ofatumumab 20 mg or matching placebo (initial doses: Days 1, 7, 14, week 4; subsequent doses: every 4 weeks). Randomization was stratified by region (Japan or ex-Japan) and baseline gadolinium-enhancing (Gd+) T1 lesions (0 or ≥1). The primary endpoint was a reduction in cumulative number of Gd+ T1 lesions across weeks 12, 16, 20, and 24. Secondary outcomes included consistency in reduction of Gd+ T1 lesions across regions, annualized relapse rate (ARR), and safety.

Results
In total, 64 patients were randomized (32 each from Japan and Russia; by treatment: ofatumumab, N=43; placebo, N=21), and 59 completed the double-blind phase. The majority of patients had high baseline disease activity ([mean] 1.5 relapses in the last year, 1.2 Gd+ T1 lesions) and 69% received prior disease-modifying therapies. At week 24, ofatumumab significantly reduced Gd+ T1 lesions versus placebo by 93.6% (p<0.001); the results were consistently in favor of ofatumumab across regions. Ofatumumab reduced the ARR versus placebo by 58.0% (p=0.119). Adverse events occurred in 69.8% of patients with ofatumumab and 81.0% with placebo; injection-related reactions were the most common (20.9% and 19.0%, respectively). One ofatumumab-treated patient was diagnosed with serious chronic inflammatory demyelinating polyradiculoneuropathy after completing the study. No deaths, opportunistic infections, or malignancies occurred during the study.

Conclusions
Ofatumumab demonstrated superior efficacy versus placebo in a RMS population with recent disease activity in Japanese and non-Japanese patients. No new safety signals were observed and the results were consistent with the Phase 3 ASCLEPIOS I/II trials.