

Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis

The VELOCE study

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Study question

Are tetanus toxoid (TT)-containing vaccine, Pneumovax (23-PPV), and keyhole limpet hemocyanin (KLH) vaccine, effective in patients with relapsing multiple sclerosis (MS) treated with ocrelizumab (OCR)?

What is known and what this paper adds

OCR depletes CD20-expressing B cells. This trial's results show that OCR attenuates humoral responses to tested vaccines.

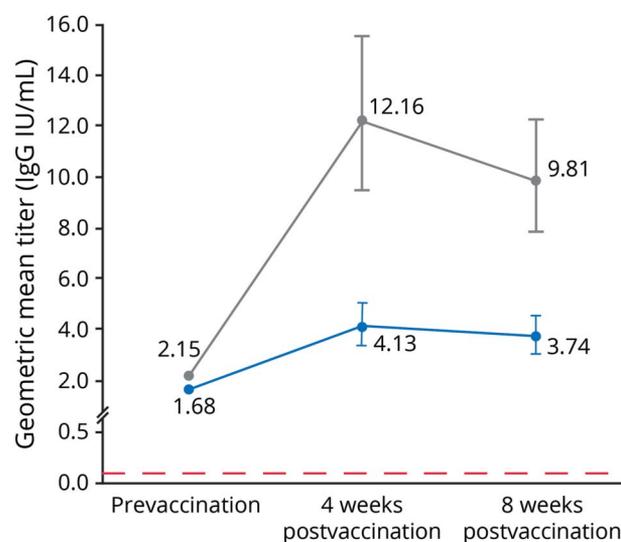
Methods

Recruitment for this phase 3b clinical trial occurred through 21 US and Canadian centers between October 2015 and August 2016. The investigators recruited 102 adults with relapsing MS who had received no tetanus toxin (TT)-containing vaccine in the 2 years prior to screening. The investigators used an interactive response system to randomize the patients to a 600-mg OCR group (n = 68) or a control group (n = 34) that received interferon β therapy or no disease-modifying treatment. The OCR group members received several vaccines including a TT-containing vaccine, Pneumovax and keyhole limpet hemocyanin starting 12 weeks after OCR initiation, and the control group members received them immediately. The participants received a TT-containing booster vaccine at 8 weeks. The primary outcome measure was the response to the TT-containing vaccine, with a positive response defined as anti-TT immunoglobulin G (IgG) antibody titers ≥ 0.2 IU/mL in patients with prevaccination titers < 0.1 IU/mL or ≥ 4 -fold antibody titer increases in patients with prevaccination antibody titers ≥ 0.1 IU/mL.

Results and study limitations

Positive responses 8 weeks after vaccination were less common in the OCR group than in the control group (23.9% vs 54.5%; treatment difference, -30.7% ; 95% confidence interval, -10.8 to -50.5%). This is Class II evidence of

Figure Anti-TT IgG antibody titers in the OCR (blue) and control (gray) groups at various timepoints



attenuated humoral responses to the vaccine in OCR-treat patients. Cellular immune responses to the vaccines were not measured, so the overall vaccine response may have been under-estimated. The question of response durability remains unaddressed. This trial's results may not generalize across the age-span including to patients with primary progressive MS who are older on average.

Registration, study funding, and competing interests

This study was funded by Hoffmann-La Roche and registered at ClinicalTrials.gov (NCT02545868). Some authors report additional competing interests. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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