Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis
The VELOCe study

Amit Bar-Or, MD, FRCPC, Jonathan C. Calkwood, MD, Cathy Chognot, PhD, et al.


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 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.

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

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.

Copyright © 2020 American Academy of Neurology
Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis: The VELOCE study
Amit Bar-Or, Jonathan C. Calkwood, Cathy Chognot, et al.
Neurology 2020;95:e1999-e2008 Published Online before print July 29, 2020
DOI 10.1212/WNL.0000000000010380

This information is current as of July 29, 2020

Updated Information & Services
including high resolution figures, can be found at:
http://n.neurology.org/content/95/14/e1999.full

References
This article cites 21 articles, 5 of which you can access for free at:
http://n.neurology.org/content/95/14/e1999.full#ref-list-1

Citations
This article has been cited by 3 HighWire-hosted articles:
http://n.neurology.org/content/95/14/e1999.full##otherarticles

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
All Immunology
http://n.neurology.org/cgi/collection/all_immunology
All Infections
http://n.neurology.org/cgi/collection/all_infections
Class II
http://n.neurology.org/cgi/collection/class_ii
Clinical trials Randomized controlled (CONSORT agreement)
http://n.neurology.org/cgi/collection/clinical_trials_randomized_controlled_consort_agreement
Multiple sclerosis
http://n.neurology.org/cgi/collection/multiple_sclerosis

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.neurology.org/about/about_the_journal#permissions

Reprints
Information about ordering reprints can be found online:
http://n.neurology.org/subscribers/advertise

Neurology ® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2020 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.