FULL-LENGTH ARTICLE NPub.org/a9cium

Randomized trial of daily high-dose vitamin D_3 in patients with RRMS receiving subcutaneous interferon β-1a

Raymond Hupperts, PhD, Joost Smolders, MD, PhD, Reinhold Vieth, PhD, et al., on behalf of the SOLAR Study Group

Correspondence
Dr. Hupperts
r.hupperts@zuyderland.nl

Cite as: *Neurology*® 2019;93:e1906-e1916. doi:10.1212/WNL.0000000000008445

Study objective and summary result

This study assessed the efficacy of high-dose vitamin D_3 supplementation in patients with relapsing-remitting multiple sclerosis (RRMS) who were already taking interferon β-1a, and it found that high-dose vitamin D_3 supplementation does not counter disease activity in such patients.

Classification of evidence

Class II.

What is known and what this paper adds

Past investigations into the potential benefits of vitamin D supplementation for patients with MS have reported inconsistent results. This investigation provides evidence against a clear benefit on absence of disease activity.

Participants and setting

The investigators recruited 229 patients with RRMS through 40 centers in 11 European countries between February 2011 and May 2015. At recruitment, the patients had been receiving subcutaneous interferon β-1a (thrice-weekly 44-μg doses) for 3–18 months and had serum 25-hydroxyvitamin D levels <150 nmol/L.

Design, size, and duration

In this double-blind trial, the participants were randomized 1:1 to groups receiving oral vitamin D_3 supplementation at 14,007 IU/d (n = 113) or placebo supplementation (n = 116). Randomization was achieved with an interactive voice recognition system and involved stratification by body mass index, sex, and relapse frequency. The participants underwent assessments over 96 weeks. Participants with no relapses, no disability progression, and no new lesions in gadolinium-enhanced MRI scans or new or enlarged lesions in T2-weighted MRI scans were regarded as having no evidence of disease activity (NEDA-3).

Primary outcome measures

The primary outcome was NEDA-3 status at 48 weeks.

Table Selected outcomes at 48 weeks

Outcome	OR[a] or incidence rate ratio[b] (95% CI) for outcome in intervention group vs placebo group
NEDA-3 status[a]	0.93 (0.53–1.63)
Annualized relapse rate[b]	0.69 (0.41–1.16)
Number of combined unique active MRI lesions[b]	0.68 (0.52–0.89)

Main results and the role of chance

The placebo and intervention groups had similar NEDA-3 status prevalences at 48 weeks ($p = 0.8$).

Harms

The placebo and intervention groups had similar adverse event rates.

Bias, confounding, and other reasons for caution

Studies with longer follow-up durations may identify clinical benefits from vitamin D_3 supplementation.

Generalizability to other populations

The present study's focus on patients with early-stage RRMS may limit the generalizability of the results to patients with advanced disease.

Study funding/potential competing interests

This study was funded by Merck. Some authors report receiving lecture honoraria, consulting fees, committee appointments, travel expenses, and funding from healthcare companies, including Merck; receiving patent royalties; receiving funding from the Norwegian government; and being current or former Merck employees. Dr. Barkhof is the Director of IAC, which was contracted by Merck to perform blinded MRI analyses. Go to Neurology.org/N for full disclosures.

Trial registration number

NCT01285401 on ClinicalTrials.gov.

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

