FULL-LENGTH ARTICLE NPub.org/jatqks

Increased dose of carbidopa with levodopa and entacapone improves "off" time in a randomized trial

Claudia Trenkwalder, MD, Mikko Kuoppamäki, MD, PhD, Mikko Vahteristo, MSc, et al.

Cite as: *Neurology*® 2019;92:e1487-e1496. doi:10.1212/WNL.0000000000007173

Correspondence
Dr. Trenkwalder
claudia.trenkwalder@med.uni-goettingen.de

Study objective and summary result

This study tested the hypothesis that increasing carbidopa doses to levels exceeding the standard 4:1 levodopa/carbidopa ratio for patients with fluctuating Parkinson disease (PD) who also receive entacapone would improve treatment responses, and it found that increasing the carbidopa doses did improve treatment responses.

Classification of evidence

Class II.

What is known and what this paper adds

The administration of levodopa and carbidopa at a 4:1 dose ratio has been standard practice since the 1980s. However, this study shows that when a catechol-O-methyltransferase inhibitor like entacapone is used, a higher carbidopa dose is appropriate.

Participants and setting

This study included 117 patients with idiopathic PD (44% female; mean age, 67.0 ± 9.6 years) and was conducted through 24 centers in Germany, Finland, Latvia, Lithuania, and Romania. Over 3 consecutive days before randomization, each participant had ≥0.5 hours of OFF time and an average of ≥3 hours of OFF time per day.

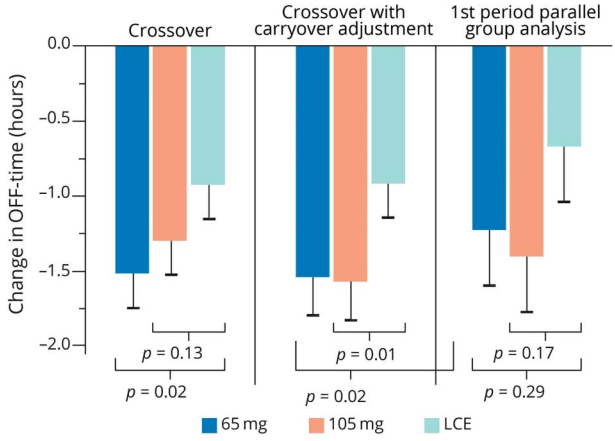
Design, size, and duration

This double-blind, double-dummy, active-controlled, phase 2 trial used an interactive voice response system to randomize participants. This crossover trial included 3 separate 4-week treatment periods in which participants received ODM-101 tablets. The treatment options were a 4:1 levodopa/carbidopa ratio (LCE) and variable levodopa doses with 65 mg/d of carbidopa (ODM-101/65) or 105 mg/d of carbidopa (ODM-101/105). All treatment options included 200 mg/d of entacapone. The participants recorded their daily OFF times in diaries.

Primary outcome measures

For each treatment, the primary outcome was the change in mean daily OFF times from 3 consecutive days at baseline to 3 consecutive days at the period's end.

Figure Changes in mean daily OFF times for the LCE (green), ODM-101/65 (blue), and ODM-101/105 (orange-pink) treatments



Main results and the role of chance

Compared to the LCE treatment, greater mean daily OFF time reductions were achieved with the ODM-101/65 (p = 0.02) and ODM-101/105 (p = 0.01) treatments.

Harms

The treatment groups had comparable adverse event rates.

Bias, confounding, and other reasons for caution

The treatment periods were short.

Generalizability to other populations

This study's reliance on European centers may limit the generalizability of the results.

Study funding/potential competing interests

This study was funded by Orion Pharma. Some authors report being employed by Orion Pharma and receiving honoraria from the European Brain Council and various healthcare companies, including Orion Pharma. Go to Neurology.org/N for full disclosures.

Trial registration number

NCT01766258 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.

Copyright © 2019 American Academy of Neurology

Neurology®

Increased dose of carbidopa with levodopa and entacapone improves "off" time in a randomized trial

Claudia Trenkwalder, Mikko Kuoppamäki, Mikko Vahteristo, et al.

Neurology 2019;92;e1487-e1496 Published Online before print March 1, 2019

DOI 10.1212/WNL.0000000000007173

This information is current as of March 1, 2019

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/92/13/e1487.full
References	This article cites 22 articles, 2 of which you can access for free at: http://n.neurology.org/content/92/13/e1487.full#ref-list-1
Citations	This article has been cited by 1 HighWire-hosted articles: http://n.neurology.org/content/92/13/e1487.full##otherarticles
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): **Clinical trials Randomized controlled (CONSORT agreement)** http://n.neurology.org/cgi/collection/clinical_trials_randomized_controlled_consort_agreement **Parkinson's disease/Parkinsonism** http://n.neurology.org/cgi/collection/parkinsons_disease_parkinsonism
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 Copyright © 2019 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology.. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

AMERICAN ACADEMY OF NEUROLOGY®