



FULL TEXT LINKS



Clinical Trial JAMA. 2015 Sep;314(12):1242-54. doi: 10.1001/jama.2015.10214.

# Effect of Dextromethorphan–Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial

Jeffrey L Cummings<sup>1</sup>, Constantine G Lyketsos<sup>2</sup>, Elaine R Peskind<sup>3</sup>, Anton P Porsteinsson<sup>4</sup>, Jacobo E Mintzer<sup>5</sup>, Douglas W Scharre<sup>6</sup>, Jose E De La Gandara<sup>7</sup>, Marc Agronin<sup>8</sup>, Charles S Davis<sup>9</sup>, Uyen Nguyen<sup>10</sup>, Paul Shin<sup>10</sup>, Pierre N Tariot<sup>11</sup>, João Siffert<sup>10</sup>

Affiliations

PMID: 26393847 DOI: 10.1001/jama.2015.10214

## Abstract

**Importance:** Agitation is common among patients with Alzheimer disease; safe, effective treatments are lacking.

**Objective:** To assess the efficacy, safety, and tolerability of dextromethorphan hydrobromide-quinidine sulfate for Alzheimer disease-related agitation.

**Design, setting, and participants:** Phase 2 randomized, multicenter, double-blind, placebo-controlled trial using a sequential parallel comparison design with 2 consecutive 5-week treatment stages conducted August 2012–August 2014. Patients with probable Alzheimer disease, clinically significant agitation (Clinical Global Impressions–Severity agitation score  $\geq 4$ ), and a Mini-Mental State Examination score of 8 to 28 participated at 42 US study sites. Stable dosages of antidepressants, antipsychotics, hypnotics, and antidementia medications were allowed.

**Interventions:** In stage 1, 220 patients were randomized in a 3:4 ratio to receive dextromethorphan-quinidine (n = 93) or placebo (n = 127). In stage 2, patients receiving dextromethorphan-quinidine continued; those receiving placebo were stratified by response and rerandomized in a 1:1 ratio to dextromethorphan-quinidine (n = 59) or placebo (n = 60).

**Main outcomes and measures:** The primary end point was change from baseline on the Neuropsychiatric inventory (NPI) Agitation/Aggression domain (scale range, 0 [absence of symptoms] to 12 [symptoms occur daily and with marked severity]).

**Results:** A total of 194 patients (88.2%) completed the study. With the sequential parallel comparison design, 152 patients received dextromethorphan-quinidine and 127 received placebo during the study. Analysis combining stages 1 (all patients) and 2 (rerandomized placebo nonresponders) showed significantly reduced NPI Agitation/Aggression scores for dextromethorphan-quinidine vs placebo (ordinary least squares z statistic, -3.95; P < .001). In stage 1, mean NPI Agitation/Aggression scores were reduced from 7.1 to 3.8 with dextromethorphan-quinidine and from 7.0 to 5.3 with placebo. Between-group treatment differences were significant in stage 1 (least squares mean, -1.5; 95% CI, -2.3 to -0.7; P < .001). In stage 2, NPI Agitation/Aggression scores were reduced from 5.8 to 3.8 with dextromethorphan-quinidine and from 6.7 to 5.8 with placebo. Between-group treatment differences were also significant in stage 2 (least squares mean, -1.6; 95% CI, -2.9 to -0.3; P = .02). Adverse events included falls (8.6% for dextromethorphan-quinidine vs 3.9% for placebo), diarrhea (5.9% vs 3.1% respectively), and urinary tract infection (5.3% vs 3.9% respectively). Serious adverse events occurred in 7.9% with dextromethorphan-quinidine vs 4.7% with placebo. Dextromethorphan-

quinidine was not associated with cognitive impairment, sedation, or clinically significant QTc prolongation.

**Conclusions and relevance:** In this preliminary 10-week phase 2 randomized clinical trial of patients with probable Alzheimer disease, combination dextromethorphan-quinidine demonstrated clinically relevant efficacy for agitation and was generally well tolerated.

**Trial registration:** clinicaltrials.gov Identifier: [NCT01584440](https://clinicaltrials.gov/ct2/show/study/NCT01584440).

## Comment in

### [Dextromethorphan and Quinidine for Treating Agitation in Patients With Alzheimer Disease Dementia.](#)

Ballard C, Sharp S, Corbett A.

JAMA. 2015 Sep 22-29;314(12):1233-5. doi: 10.1001/jama.2015.10215.

PMID: 26393843 No abstract available.

### [Combination drug shows promise for treating agitation in patients with Alzheimer's disease.](#)

Wise J.

BMJ. 2015 Sep 22;351:h5015. doi: 10.1136/bmj.h5015.

PMID: 26400972 No abstract available.

### [Dextromethorphan and quinidine are suitable for off-label short-term treatment of agitation in people with Alzheimer's disease following first-line non-drug approaches.](#)

Corbett A, Ballard C.

Evid Based Med. 2016 Feb;21(1):25. doi: 10.1136/ebmed-2015-110324. Epub 2015 Dec 23.

PMID: 26701197 No abstract available.

### [Dextromethorphan-Quinidine for Agitation in Alzheimer Disease.](#)

Newman JC, Steinman MA.

JAMA. 2016 Mar 15;315(11):1166. doi: 10.1001/jama.2015.18286.

PMID: 26978214 [Free PMC article](#). No abstract available.

### [Dextromethorphan-Quinidine for Agitation in Alzheimer Disease--Reply.](#)

Cummings JL, Siffert J.

JAMA. 2016 Mar 15;315(11):1166-7. doi: 10.1001/jama.2015.18289.

PMID: 26978215 No abstract available.

## Related information

[Cited in Books](#)

[MedGen](#)

[PubChem Compound \(MeSH Keyword\)](#)

## LinkOut - more resources

### Full Text Sources

[Ovid Technologies, Inc.](#)

[Silverchair Information Systems](#)

### Other Literature Sources

[The Lens - Patent Citations](#)

### Medical

[ClinicalTrials.gov](#)

[Genetic Alliance](#)

[MedlinePlus Health Information](#)