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Dexpramipexole versus placebo for patients with amyotrophic lateral sclerosis (EMPOWER): a randomised, double-blind, phase 3 trial.

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Collaborators (81)

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Erratum in
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Abstract

BACKGROUND: In a phase 2 study, dexpramipexole (25-150 mg twice daily) was well tolerated for up to 9 months and showed a significant benefit at the high dose in a combined assessment of function and mortality in patients with amyotrophic lateral sclerosis. We aimed to assess efficacy and safety of dexpramipexole in a phase 3 trial of patients with familial or sporadic disease.

METHODS: In our randomised, double-blind, placebo-controlled phase 3 trial (EMPOWER), we enrolled participants aged 18-80 years (with first amyotrophic lateral sclerosis symptom onset 24 months or less before baseline) at 81 academic medical centres in 11 countries. We randomly allocated eligible participants (1:1) with a centralised voice-interactive online system to twice-daily dexpramipexole 150 mg or matched placebo for 12-18 months, stratified by trial site, area of disease onset (bulbar vs other areas), and previous use of riluzole. The primary endpoint was the combined assessment of function and survival (CAFS) score, based on changes in amyotrophic lateral sclerosis functional rating scale-revised (ALSFRS-R) total scores and time to death up to 12 months. We assessed the primary endpoint in all participants who received at least one dose and had at least one post-dose ALSFRS-R measurement or died. We monitored adverse events in all participants. This study is registered with ClinicalTrials.gov, number NCT01281189.

FINDINGS: Between March 28, 2011, and Sept 30, 2011, we enrolled 943 participants (474 randomly allocated dexpramipexole, 468 randomly allocated placebo, and one withdrew). Least-square mean CAFS scores at 12 months did not differ between participants in the dexpramipexole group (score 441·76, 95% CI 415·43-468·08) and those in the placebo group (438·84, 412·81-464·88; p=0·86). At 12 months, we noted no

differences in mean change from baseline in ALSFRS-R total score (-13·34 in the dexpramipexole group vs -13·42 in the placebo group; p=0·90) or time to death (74 [16%] vs 79 [17%]; hazard ratio 1·03 [0·75-1·43]; p=0·84). 37 (8%) participants in the dexpramipexole group developed neutropenia compared with eight (2%) participants in the placebo group, and incidence of other adverse events was similar between groups.

INTERPRETATION: Dexpramipexole was generally well tolerated but did not differ from placebo on any prespecified efficacy endpoint measurement. Our trial can inform the design of future clinical research strategies in amyotrophic lateral sclerosis.

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Comment in

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