Dokumenttyp: journal article

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Titel des Beitrags: Duloxetine and pregabalin: high-dose monotherapy or their combination? The “COMBO-DN study” - a multinational, randomized, double-blind, parallel-group study in patients with diabetic peripheral neuropathic pain.

Abstract: This multicentre, double-blind, parallel-group study in diabetic peripheral neuropathic pain addressed whether, in patients not responding to standard doses of duloxetine or pregabalin, combining both medications is superior to increasing each drug to its maximum recommended dose. For initial 8-week therapy, either 60 mg/day duloxetine (groups 1, 2) or 300 mg/day pregabalin (groups 3, 4) was given. Thereafter, in the 8-week combination/high-dose therapy period, only nonresponders received 120 mg/day duloxetine (group 1), a combination of 60 mg/day duloxetine and 300 mg/day pregabalin (groups 2, 3), or 600 mg/day pregabalin (group 4). Primary outcome (Brief Pain Inventory Modified Short Form [BPI-MSF] 24-hour average pain change after combination/high-dose therapy) was analyzed comparing combination (groups 2, 3 pooled) with high-dose monotherapy (groups 1, 4 pooled). Secondary end points included response rates, BPI-MSF severity items, and comparison of duloxetine and pregabalin in BPI-MSF average pain. Eight hundred four patients were evaluated for initial therapy and 339 for combination/high-dose therapy. There
were no significant differences between combination and high-dose monotherapy regarding BPI-MSF average pain (mean change: combination: -2.35; high-dose monotherapy: -2.16; $P = 0.370$) and most secondary end points, which, however, consistently favoured combination therapy. Fifty-percent response rates were 52.1% for combination and 39.3% for high-dose monotherapy ($P = 0.068$). In exploratory analyses of the initial 8-week therapy uncorrected for multiple comparisons, 60 mg/day duloxetine was found superior to 300 mg/day pregabalin ($P < 0.001$). Both drugs and their combination were well tolerated. Although not significantly superior to high-dose monotherapy, combination therapy was considered to be effective, safe, and well tolerated.