Orexin receptor 2 agonist improves sleepiness in narcolepsy

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For patients with narcolepsy type 1, an orexin receptor 2 agonist,
TAK-994, improves measures of sleepiness and cataplexy over eight weeks compared with placebo but is associated with hepatotoxic adverse events, according to a study published in the July 27 issue of the New England Journal of Medicine.

Yves Dauvilliers, M.D., from Gui de Chauliac Hospital and the University of Montpellier in France, and colleagues conducted a phase 2 randomized, placebo-controlled trial of TAK-994 in patients with narcolepsy type 1. Seventy-three patients were randomly assigned to receive twice-daily oral TAK-994 (30 mg [17 patients], 90 mg [20 patients], and 180 mg [19 patients]) or placebo (17 patients).

Owing to hepatotoxic adverse events, the phase 2 trial and extension trial were terminated early. Primary end point data were available for 41 patients. The researchers found that the least-squares mean changes to week 8 in average sleep latency on the Maintenance of Wakefulness Test were 23.9, 27.4, 32.6, and −2.5 minutes in the 30-, 90-, and 180-mg groups and placebo group, respectively. The corresponding least-squares mean changes to week 8 in the Epworth Sleepiness Scale were −12.2, −13.5, −15.1, and −2.1, respectively. The corresponding weekly incidences of cataplexy at week 8 were 0.27, 1.14, 0.88, and 5.83 (rate ratios versus placebo, 0.05, 0.20, and 0.015, respectively).

"The outcomes described in the current report may be seen as a backward step because of the decision to terminate the trial," write the authors of an accompanying editorial. "However, the impressive efficacy is a major step forward in helping patients with narcolepsy type 1."

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