Modafinil Dose Higher in Narcolepsy Than Apnea

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PHILADELPHIA — The median dose of modafinil was 300 mg for patients with obstructive sleep apnea and 400 mg for patients with narcolepsy in long-term open-label extensions of placebo-controlled trials, Jonathan Schwartz, M.D., said at the annual meeting of the Associated Professional Sleep Societies.

The labeling for modafinil (Provigil) calls for a dosage of 200 mg/day to improve wakefulness in patients with excessive sleepiness associated with either condition.

"Modafinil dosing was flexible—between 200 and 400 mg/day—based on the investigators' impressions of clinical efficacy and tolerability [during the open-label extensions]. The dose was slightly higher in patients with narcolepsy, which may be attributable to the underlying differences in severity of excessive sleepiness between the two conditions," said Dr. Schwartz, a pulmonologist in Oklahoma City.

Narcolepsy and obstructive sleep apnea are both tied to excessive sleepiness, but narcoleptics are usually sleepier than nCPAP-treated patients with OSA.

The open-label extensions involved two double-blind, placebo-controlled trials of modafinil in patients with narcolepsy and one in patients with nasal continuous positive airway pressure (nCPAP)–treated obstructive sleep apnea (OSA).

In the narcolepsy studies, 84% of 478 patients were titrated to a modafinil dose greater than 200 mg, with 50% at 400 mg, 34% at 300 mg, and 16% at 200 mg. In the OSA study, 76% of the 266 patients were titrated to a modafinil dose greater than 200 mg, with 43% at 300 mg, 33% at 400 mg, and 24% at 200 mg.

Modafinil was well tolerated in both populations at all doses, Dr. Schwartz said. Adverse events were similar in the two patient populations.

Treatment duration was 40 weeks for both narcolepsy studies and 12 months for the OSA study.

Baseline excessive sleepiness was assessed by mean score on the Epworth Sleepiness Scale (ESS); the score was significantly higher in the narcolepsy patients than in the OSA population (17.4 vs. 14.5, respectively; $P < .001$).

"Narcolepsy and obstructive sleep apnea are both frequently associated with excessive sleepiness, but patients with narcolepsy are usually sleepier than nCPAP-treated patients with OSA," said Dr. Schwartz.

In OSA, modafinil is indicated as an adjunct to standard treatments for the underlying obstruction in patients who continue to experience residual excessive sleepiness, despite treatment of the underlying obstruction, he added.

At least 20% of OSA patients are still sleepy despite nCPAP therapy, he said.

The mean change in ESS scores from baseline to final clinic visit in the study populations was virtually identical—about 4.25 points—for the narcolepsy and OSA patients, said Dr. Schwartz. In other words, there was a similar efficacy (mean reduction in sleepiness), despite the difference in the mean dose.

The mean body mass index was significantly lower in the narcolepsy group (28.8 kg/m^2) than in the OSA patients (36.2 kg/m^2). Despite having significantly lower body mass indexes than OSA patients, patients with narcolepsy were titrated to higher modafinil doses to achieve clinical improvement, Dr. Schwartz observed.

The mean age for the narcolepsy patients was 42 years; the OSA patients' mean age was 50 years. Of the narcolepsy patients, 46% were male, as were 77% of the OSA patients.

Overall, 84% of patients in the studies completed the specified treatment period, but completion rates were higher in the 40-week narcolepsy studies (95%) than in the single 12-month OSA study (66%).

Clinic visits for both narcolepsy studies were scheduled at baseline and after 1, 2, 6, 8, 16, 24, and 40 weeks.

Clinic visits for the OSA study were scheduled at baseline and at 3, 6, 9, and 12 months.

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