Narcolepsy Requires Higher Modafinil Dose

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Philadelphia: The median thera-
pic dose of modafinil was 300 mg for
patients with obstructive sleep apnea and narcolepsy in long-term open-label extensions of placebo-controlled trials, Dr. Jonathan Schwartz said at the annual meeting of the Associ-
ated Professional Sleep Societies. The labeling for modafinil (Provigil) calls for a dosage of 200 mg/day to im-
prove wakefulness in patients with exces-
sive sleepiness associated with either con-
dition. "Modafinil dosing was flexible—between 200 and 400 mg/day—based on the investigators' impressions of clinical response and the two placebo-controlled trials. The dose was slightly higher in patients with narcolep-
yxia, which may be attributable to the un-
derlying differences in severity of sleepiness between the two conditions," said Dr. Schwartz, a pulmonologist in Ok-
lahoma City.

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

In the narcolepsy studies, 84% of 478 pa-
tients were titrated to a modafinil dose un-
der 200 mg, with 30% 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 both the narcolep-
yxia and OSA patient populations. Treatment duration was 40 weeks for both narcolepsy studies and 12 months for the OSA study.

Baseline excessive sleepiness was as-
essed by the Epworth Sleepiness Scale (ESS); the score was sig-
nificantly higher in the narcolepsy pa-
tients than in the OSA population (17.4 vs. 14.5, respectively, P < .001).

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

Modafinil is indicated as an ad-
joint to standard treatments for the un-
derlying obstruction in patients who con-
tinue to experience residual excessive sleepiness, de-
spite treatment of the underlying obstruc-
tion, he added.

At least 20% of OSA patients are still sleep 
less, according to the mean score on the nCPAP 
therapy, he said.

The mean change in ESS scores from baseline to final clinical visit in the study popu-
lations was virtually identical—about 4.25 points—for the narcolepsy and OSA pa-
tients, said Dr. Schwartz. In other words, there was no meaningful difference in change (mean reduction in sleepiness), despite the difference in the mean dose.

The mean body mass index was signifi-
cantly lower in the narcolepsy group (28.8 kg/m²) than in the OSA patients (36.2 kg/m²). Despite having significantly low-
er body mass index than OSA patients, pa-
tients with narcolepsy were titrated to higher modafinil doses to achieve clinical improvement, Dr. Schwartz observed.

The mean age for the narcolepsy pa-
tients was 42 years; the OSA patients' mean age was 50 years. Of the narcolep-
yxia 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, 3, 4, and 5 months. Clinic visits for the OSA study were scheduled at baseline and at 3, 6, 9, and 12 months.

The study included patients who with-
drew after two evaluations if their with-
drawal was not due to adverse events. The study was funded by Cephalon Inc., the maker of modafinil.