treated (compassionate use program [n=16], another pitolisant trial [n=13]). Mean age was 36 years; 44.1% were male. At baseline, mean ESS was 17.1 ± 3.1; 73.5% of patients had cataplexy. Sixty-eight patients completed ≥12 months of treatment. Mean pitolisant exposure was 260 and 548 days for de novo and previously treated patients, respectively; 72% of patients received pitolisant 36 mg/d. During this 12-month period, 56.9% of patients reported adverse events: headaches (11.8%), insomnia (8.8%), weight gain (7.8%), anxiety (6.9%), depression (4.9%), and nausea (9%). Mean ESS reduction was 4.3 points overall; 4.9 (P<0.01) in de novo patients and 4.2 in previously treated patients. Overall, 63.2% (43/68) of patients were responders (ESS final ≤10 and/or ESS baseline - ESS final ≥3) and 36.8% (25/68) were normalized (ESS final ≤10); mean ESS decreased from 15.3 to 6.6 in normalized patients. Partial and total cataplexy attacks were reduced (-64% and -75%, respectively), as were hypnagogic hallucinations (-54%) and sleep paralysis (-63%).

Conclusion: This 1-year analysis of a long-term, open-label study supported the safety and efficacy of pitolisant for the treatment of EDS in narcolepsy and cataplexy in narcolepsy.

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0624 ANTICATAPLECTIC EFFICACY OF PITOLISANT; THE FIRST POTENT AND HIGHLY SELECTIVE HISTAMINE H3-RECEPTOR ANTAGONIST/INVERSE AGONIST
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Introduction: Pitolisant, the first potent and highly selective histamine H3-receptor antagonist/inverse agonist, has demonstrated efficacy in reducing excessive daytime sleepiness (EDS) in narcolepsy and cataplexy in narcolepsy. In this report, the anticitaplectic efficacy results of pitolisant are summarized from five phase 2 and 3 studies.

Methods: Weekly Rate of Cataplexy (WRC) attacks was estimated based on daily diary reporting by adults with narcolepsy treated with pitolisant once daily (dose up to 36 mg). WRC was the primary endpoint in phase 3 (HARMONY-CTP, HARMONY II) studies and a secondary endpoint in phase 3 (HARMONY I and III) and phase 2 (P6-06) studies. In some studies, selective serotonin reuptake inhibitors and sodium oxybate were permitted.

Results: In a 7-week, placebo-controlled, phase 3 study (n=105), pitolisant reduced WRC by 75%, from 9.15 to 2.27 (P=0.0001 vs placebo). Significant reduction of WRC was confirmed in the subgroup of patients presenting with WRC >15 (P=0.0001 vs placebo). In an 8-week, placebo- and active-controlled, phase 3 study (n=76), pitolisant reduced WRC by 62% (P=0.034 vs placebo). In a long-term, open-label, phase 3 study (n=104), pitolisant reduced total and partial WRC by 76% and 64%, respectively, after 12 months of treatment. In an open-label, phase 2 study (n=27), pitolisant reduced WRC by 40% (P=0.024) after 1 month. In an 8-week, phase 3 study (n=15), WRC was reduced by 56% in the pitolisant-only subgroup and by 71% in the pitolisant + modafinil subgroup.

Conclusion: Pitolisant demonstrated a potent anticitaplectic effect (reduction by 60%-75% in placebo-controlled studies), which was consistent across all clinical studies and was maintained for ≥12 months. The anticitaplectic effect of pitolisant, in combination with its efficacy in reducing EDS and favorable safety profile, indicates that pitolisant may be a new therapeutic option for patients with type 1 narcolepsy.

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