of acute migraine in adults. This study investigated the efficacy and safety of ZNS in the acute treatment of migraine headache in adolescents.
METHODS: The study was a global, multicenter, randomized, double-blind, parallel-group study of ZNS compared with placebo (NCT01211145). Adolescents (12-17 years old) with an established diagnosis of migraine with or without aura were enrolled. All enrolled patients completed a 30-day placebo challenge run-in period, where at least 1 migraine attack was treated with placebo. Patients who did not respond during the placebo run-in period were randomized to treat a single migraine attack with ZNS or placebo within 10 weeks of the randomization visit. Patients were randomized to ZNS 5 mg, 2.5 mg, 0.5 mg, or placebo in a 5:3:3:5 ratio. After treatment of migraine, patients completed a headache diary for 24 hours. The primary outcome was pain-free status at 2 hours post-treatment; secondary outcomes included pain-free status at other time points, headache response, ability to perform normal activities, and use of rescue medication within 24 hours of treatment. Adverse events (AEs) were recorded during treatment. Safety was assessed in all patients who received study treatment. An interim futility analysis was conducted in order to discontinue ZNS doses unlikely to be more effective than placebo on the primary efficacy variable.
RESULTS: A total of 1653 patients were enrolled and 798 were randomized (mean [SD] age: 14.4 [1.69]; 61.8% female). Most patients (58.8%) reported a history of migraine without aura. Of those patients randomized, 90.4% completed the study; no patients discontinued due to AEs. The percentage of patients who were pain-free at 2 hours was significantly greater in the 5 mg ZNS group (29.7%) compared to placebo (16.6%, $p < 0.001$). The 2.5 mg and 0.5 mg doses were discontinued at the interim analysis because they met the pre-set futility criteria. At the end of the study, these doses were not significantly different from placebo for the primary endpoint. The 5 mg ZNS group also significantly improved pain-free status at 3 and 4 hours post-dosing compared to placebo (both $p < 0.001$). Headache response rates at 2 hours for ZNS 5 mg and 2.5 mg (50.7% and 53.1%) were significantly higher (p=0.010 and p=0.021) than for placebo (39.1%). From hours 3-24, the 5 mg and 2.5 mg ZNS groups had significantly higher percentage of patients who were able to perform normal activities compared to placebo ($p < 0.05$ for all time points). The percentage of patients using rescue medication within 24 hours after treatment was significantly lower in the 5 mg ZNS group (20.3%) compared to placebo (31.6%, p=0.004). Incidence of AEs increased with dose of ZNS with 9.9%, 15.2%, 11.1%, and 25.5% of patients reporting at least 1 AE in the placebo, 0.5 mg, 2.5 mg, and 5 mg groups, respectively. Dysgeusia was the most commonly reported AE in ZNS groups, reported in 6.5%, 6.2%, and 12.6% of patients in 0.5 mg, 2.5 mg, and 5 mg groups, respectively, vs 1.2% for placebo.
CONCLUSION: ZNS 5 mg significantly improves pain-free status compared to placebo, suggesting utility in the treatment of adolescent migraines. Reported AEs were consistent with the known AE profile of the drug in adult and adolescent populations.

LBP06

Results of the Open-Label Extension of a Phase 2, Randomized, Double-Blind, Placebo-Controlled, Study to Evaluate the Efficacy and Safety of AMG 334 for the Prevention of Episodic Migraine

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BACKGROUND: Migraine is a prevalent, disabling primary headache disorder. Calcitonin gene–related peptide (CGRP) is involved in migraine pathophysiology. AMG 334 is a human monoclonal antibody against the CGRP receptor. We report here interim results of the open-label extension (OLE) phase of a randomized, double-blind (DB), placebo-controlled, phase 2 trial, which evaluates the maintenance of efficacy and the long term safety/tolerability of AMG 334 (ClinicalTrials.gov identifier: NCT01952574).

METHODS: Following completion of the DB phase at week 12, patients were eligible to receive AMG 334 70 mg during the OLE phase for up to 256 weeks. During the OLE phase, patients continued to complete the daily diary until week 64. For this interim analysis, patients received AMG 334 70 mg up to week 76 as of January 30, 2015. Safety and tolerability were evaluated monthly. Efficacy endpoints were analyzed in two groups up to week 64: Group 1: patients who transitioned to AMG 334 70 mg after receiving placebo, AMG 334 7 mg, or AMG 334 21 mg during the DB phase (ie, DB ineffective doses); Group 2: patients who continued to receive AMG 334 70 mg during the OLE phase (ie, DB effective dose). The efficacy endpoints included: change from baseline in monthly migraine days (included migraine and probable migraine), 50% responder rate, monthly migraine attacks, monthly migraine-specific medication use days (ie, triptans, ergots), and monthly headache days.
RESULTS: Overall, 383 of 395 (97%) patients who were eligible to enter the OLE, received open-label AMG 334 70 mg. As of January 30, 2015, the median duration of exposure to AMG 334 70 mg in the OLE phase was 239 days (34.1 weeks), with a total exposure of 263.7 patient-years. Compared with week 12 of the DB phase (primary endpoint), a further reduction from baseline in mean monthly migraine days was observed during the OLE phase (week 16 to 64) regardless of the DB treatment received (Group 1: −2.4 days at week 12 vs −4.0 days at week 16; Group 2: −3.5 days at week 12 vs −3.9 days at week 16). The treatment effect was sustained during the OLE phase with the reduction from baseline in mean monthly migraine days ranging from −4.0 to −6.2 days and −3.7 to −4.9 days for Group 1 and 2, respectively. Similar results were observed for the 50% responder rate, monthly migraine attacks, monthly headache days, and migraine-specific medication use. Adverse events (AEs) were reported for 243 of 383 (63%) patients. The most common AEs (≥ 3%) were nasopharyngitis, upper respiratory tract infection, arthralgia, influenza, back pain, and sinusitis. Most AEs were CTCAE Grade 1 or 2. Serious AEs were reported in 13 patients (3%), of which 1 (< 1%) was deemed treatment related (per investigator). Eleven patients (3%) discontinued due to AEs. There were no clinically significant findings on vital signs or laboratory tests (including liver function tests).
CONCLUSION: Patients who entered the OLE phase and received AMG 334 70 mg showed a clinically meaningful and sustained reduction in migraine days. Safety and tolerability were consistent with that observed in the DB phase, with no new safety signals observed.

LBP07
Efficacy and Safety Outcomes of the Non-invasive Vagus Nerve Stimulation for the Acute Treatment (ACT1) of Cluster Headache Study
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BACKGROUND: To report primary and secondary efficacy outcomes and safety findings from the ACT1 study.
METHODS: ACT1 was a large multicenter, double-blind, randomized, sham-controlled study that investigated non-invasive vagus nerve stimulation (nVNS) for the acute treatment of episodic and chronic cluster headache (CH). A 1-month randomized phase, where subjects were treated with nVNS or an active sham device, was followed by a 3-month open-label phase where all subjects received nVNS. Treatment comprised 3 consecutive 120-second stimulations applied to the right side of the neck at the onset of CH pain. The primary efficacy end point was response rate, defined as the proportion of subjects who had a headache intensity of 0 or 1 on the pain intensity scale (0, *no pain*; 4, *very severe pain*) 15 minutes after treatment initiation for the first CH attack. The primary safety end point was the incidence of serious adverse device effects (SADEs). Secondary efficacy end points were sustained treatment response (ie, response at 15 minutes and 1 hour after treatment initiation) and mean pain intensity of all (up to 5) CH attacks in the randomized phase 15 minutes after treatment initiation.
RESULTS: Of the 150 enrolled subjects, 73 received nVNS and 77 received the sham device; most were male (84%) and had been diagnosed with episodic CH (67.3%). During the randomized phase, no significant difference in response rates between nVNS (26.7%) and sham (19.7%) arms (P=0.35) was noted in the overall