Background

ALD403 is a humanized, IgG, and anti-CGRP antibody being developed for the prevention of migraine.

Methods

This study was performed in compliance with ICH guidelines for clinical trials, was approved by an institutional Review Board and written informed consent prior to enrollment. The trial was registered prior to enrollment (Clinicaltrials.gov identifier: NCT01772524). The study was conducted at 28 clinical research centers in the United States of America.

Results - Disposition

Adverse events were experienced by 31.4% and 31.9% of subjects in the placebo and ALD403 group respectively. The most frequent adverse events in the placebo and ALD403 group were: upper respiratory tract infection (7.3% vs 8.6%), urinary tract infection (4.9% vs 6.0%), and nasal congestion (4.6% vs 6.0%). Adverse events were experienced by 52.4% and 56.8% of subjects in the placebo and ALD403 group respectively. In the placebo and ALD403 group, respectively, 32.1% and 33.7% had 

Conclusion

ALD403 was safe and well tolerated and 46.9% of ALD403 patients experienced a 50% or greater reduction in migraine days compared to placebo. ALD403 appears to be effective in preventing migraine with frequent episodic migraine. This study supports further phase II studies of ALD403 in the prevention of migraine.

Results - Safety

Adverse events were experienced by 5.2% and 5.6% of subjects in the placebo and ALD403 group respectively. The most frequent adverse events in the placebo and ALD403 group were: upper respiratory tract infection (7.3% vs 8.6%), urinary tract infection (4.9% vs 6.0%), and nasal congestion (4.6% vs 6.0%). Adverse events were experienced by 52.4% and 56.8% of subjects in the placebo and ALD403 group respectively. In the placebo and ALD403 group, respectively, 32.1% and 33.7% had

Conclusions

ALD403 appears to be effective in preventing migraine in subjects with frequent episodic migraine. There appears to be a substantial subgroup of patients who are responders to CGRP blockade.

This study supports further phase II studies of ALD403 in the prevention of migraine.

Results - Efficacy

More patients on ALD403 than on placebo achieved a 50%, 75%, and 100% reduction in migraine days with the entire 12 weeks (1-12) of the study. Between 20.5% and 41.1% of the patients on ALD403 experienced no migraines during any four-week period (table below).

Baseline Patient Demographics

ALD403 patients maintained a high degree of response for the entire 24 weeks of the study (Figure 5).

Results - Baseline

The treatment difference for the primary endpoint was tested with an extended Cochran-Mantel-Haenszel test stratified by baseline migraine days (5-12 vs 0-4 weeks). Those who received 1-2 and 5-12 migraine days endpoint analysis was also performed. Testing was not performed for the other responder rate and not an outcome measure in migraine prevention trials, a responder endpoint that evaluated overall responder status overall from weeks 1-12 was also performed. This endpoint classifies a subject as a responder from weeks 1-12 if they were a responder for each of the 4 post-dose intervals (week 1-4, 5-8, 9-12, and 12, 24 post-dose. The pre-specified primary analysis of safety and tolerability of a single intravenous (i.v.) infusion of ALD403 was conducted at 26 clinical research centers in the United States of America.

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Main reasons for exclusion before randomization were too many (>14) or too few (<5) migraine days per month during eDiary run-in and lack of compliance with the eDiary run-in.

There were no significant differences in vital signs or laboratory safety data between subjects treated with ALD403 or placebo at any time during the hospitalization. One subject on ALD403 experienced an episode of chest pain during the hospitalization. One subject on ALD403 experienced pyelonephritis that required hospitalization. One subject on ALD403 experienced an episode of chest pain during the hospitalization. One subject on ALD403 experienced pyelonephritis that required hospitalization.

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