Beyond Triptans: A Review of New Migraine Medications in Clinical Trials

Christopher Nakagawa[1], Garret Hino Jr[1], Sheri Tokumaru, PharmD[1], Nicole Young, PharmD[1]

1. The Daniel K. Inouye College of Pharmacy, University of Hawaii, Hilo, HI

Background

- Migraines are a very common and debilitating headache disorder characterized by moderate to severe throbbing headache pain, which can be associated with nausea, vomiting, sensitivity to light and sensitivity to sound.
- Migraines are also a huge economic and social burden, causing many people to miss productive days at work and school.[1]
- Acute migraine attacks cause about 1.2 million visits to the emergency department a year![2]
- There are many different options for treatment of acute migraine, one of the most effective classes being the triptans, which were first developed in the early 1990's.
- Despite having many different classes of drugs for treating migraine, many people who suffer from migraines still are not able to fully control their migraine attacks.
- There have not been any new effective treatment for migraines since the development of triptans, and the research question is then, "Are there any new drugs in development for treatment of migraines and if so, what are they?"

Methods

- This study is a literature review of recent and ongoing clinical trials for new classes of pharmacologic treatments for acute migraine
- Key words "migraine", "novel drugs", and "treatment" were searched in PubMed and ClinicalTrials.gov

Results

Targeting Calcitonin Gene-Related Peptide (CGRP) - An inflammatory protein that is shown to be released in the brain during a migraine headache.[4]

CGRP Blocking Drugs - Also called 'gepants', competitively blocks the receptor of CGRP. Gepants were shown to be highly effective in the treatment of migraines in past clinical trials, but a couple agents were associated with liver toxicity. Newer gepants, such as ubroregepant and rimegepant, are currently in phase 3 active clinical trials for long-term safety and efficacy for acute migraine treatment and seem to be more promising[5,6]

CGRP Targeted Monoclonal Antibodies - Blocks the CGRP receptor or CGRP itself. Fremanezumab and erenumab have shown high efficacy with their monthly subcutaneous injections versus placebo in preventing migraines[7,8] Both treatments have had mild adverse effects.

ALLOD-2

ALLOD-2 is a combination of two non-opioid drugs with a dual mechanism of action that blocks the process of inflammation and production of pain molecules[8,9] This drug is currently recruiting for a phase 2 clinical trial to compare with sumatriptan and placebo for acute treatment of migraine (expected completion date: October 2018)

Serotonin 5HT1F Receptor Blockers

Lasmiditan (COL-144) is the first drug of its kind to block the specific serotonin receptor, 5HT1F, which is thought to play a role in migraine pathways in the brain[11]

Recent completed studies reported that oral and intravenous lasmiditan are well tolerated.

A phase 3 clinical study is currently recruiting patients with migraines to evaluate the safety, tolerability, and efficacy of long-term intermittent use for treatment of acute migraine attacks.

Discussion

There are typically four phases of clinical trials, phase 0 – III prior to FDA approval. Phase 0 trials are exploratory studies. Phase 1 trials look at safety of a new drug. Once a new drug is deemed safe, it is able to start small scale studies to look for efficacy in Phase 2 trials. Phase 3 trials would test for efficacy on a larger scale, usually comparing the new drug to the current standard treatment. Thus, these CGRP targeting drugs, ALLOD-2, and serotonin 5HT1F blocking drugs, all in phase II-III trials, have shown adequate safety and are undergoing studies for efficacy. There are many other classes of drugs that have also been in recent clinical trials and have been discontinued for unknown reasons. The few classes of drugs mentioned here are what seemed to be the most promising.

Conclusion

Many drugs are being studied for the treatment and prevention of migraine, but nothing since the triptan class has made a breakthrough as of yet. CGRP targeted drugs, ALLOD-2, and serotonin 5HT1F blockers new drugs for migraine treatment showing promise in clinical trials.

Disclosures

The authors of this presentation have nothing to disclose.

References

1. Headache Disorders. World Health Organization. http://www.who.int/mediacentre/factsheets/fs277/en/. Accessed March 9, 2018.
2. Cephalalgia 2015;35(4):301-309.
3. FDA Approved Drugs by Medical Condition. *Center Watch.* Accessed March 9, 2018.
4. *Genome Med*. 2018;10(1).
5. An Extension Study to Evaluate the Long-Term Safety and Tolerability of Ubrogepant in the Treatment of Migraine. *ClinicalTrials.gov.* Accessed March 3, 2018.
6. Safety and Efficacy in Adult Subjects With Acute Migraines. *ClinicalTrials.gov*. Accessed March 3, 2018.
7. *N Engl J Med*. 2017;377(22):2113-2122.
8. *N Engl J Med*. 2017;377(22):2123-2132..
9. Oral ALLOD-2 vs. Oral Sumatriptan and vs. Placebo in the Acute Treatment of Migraine With Associated Nausea (ANODYNE-2). *ClinicalTrials.gov*. Accessed March 10, 2018.
10. Product Pipeline. *Allodyne Therapeutics*. Accessed March 10, 2018.
11. *Neurotherapeutics*, Feb 2018, E-pub ahead of print. doi:10.1007/s13311-018-0615-6.