Calcitonin Gene-Related Peptide Receptor Antagonists for Migraine Prophylaxis

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Abstract

Migraine is a common disorder affecting 12% of the U.S. population. Prophylaxis is recommended for patients who experience frequent migraines. Because current drugs used for prophylaxis are not 100% effective and cause adverse effects that affect compliance, new strategies have been studied to prevent headaches. One new pharmacologic strategy is to use an inhibitor of the calcitonin gene-related peptide (CGRP). As a class, the CGRP receptor inhibitors have reduced monthly migraine days and are well tolerated. This article will briefly review CGRP inhibitors in development.

Keywords

formulary management/P&T, neurology, investigational drugs, drug information

Epidemiology

Migraine affects 12% of the population and is more prevalent in women than in men, affecting 17% of women and 6% of men. An epidemiology study found that 53.7% of migraine patients have symptoms severe enough to cause activity restriction.¹ The cost to the United States due to management and loss of productivity from migraines is estimated to be as high as \$17 million.²

Current Treatment

Due to the decrease in activity associated with migraines, several drug classes have been used to prevent or reduce the number of headaches. Expert consensus recommended that migraine prophylaxis treatment be offered when patients experience more than 6 headaches per month, 4 headaches per month in patients with some impairment, or 3 headaches per month in patients with severe impairment or a need for bed rest. Prophylaxis can be considered with fewer headaches or less impairment.¹

A trial of lifestyle interventions, such as sticking with a regular schedule for sleeping and eating, exercising and avoiding migraine triggers, is usually tried first. If lifestyle interventions are not effective, pharmacotherapy is initiated. Drug classes with the most evidence for use in preventing migraines include antidepressants, beta-blockers, and anticonvulsants. Current prophylactic drugs decrease headaches by 50% in 50% to 75% of patients.³ As the drugs are not 100% effective and cause adverse effects that

affect compliance, new strategies have been studied to prevent headaches.⁴

New Treatment Options

One pharmacologic strategy is to use an inhibitor of the calcitonin gene-related peptide (CGRP). CGRP is a neuropeptide found in both central and peripheral neurons. CGRP has both cerebral arteriolar dilating and pain modulation properties. An increase in CGRP is thought to decrease inhibitory mechanisms and increase the occurrence of migraine headaches.⁴ As a class, the CGRP receptor inhibitors (Table 1) have reduced monthly migraine days by 50% and eliminated migraines in 10% to 20% of patients.⁵ The onset of prophylaxis appears to be within days instead of months. The drugs also appear to be well tolerated, although no long-term safety and efficacy data are available.⁶

Author's Note

Information is summarized from selected materials, additional information may be available from other sources. Due to the preapproval nature of the information, non-peer-reviewed

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Table 1. CGRP Receptor Antagonists in Development

Generic name	Sponsor	Proposed administration	Comments
Eptinezumab	Alder Biopharmaceuticals	IV infusion every 3 months	Alder announced that in the 888-patient, 56-week, phase 3, PROMISE I trial, eptinezumab reduced monthly migraine days by 1 day compared with placebo.
Erenumab	Amgen, Novartis Pharmaceuticals	Monthly subcutaneous injection	Amgen has filed a BLA with a PDUFA date of 7/17/18. Presentations of data from the 955-patient STRIVE study and the 577-patient ARISE study demonstrated a 1-2 day decrease in monthly migraine-free days compared with placebo.
Fremanezumab	Teva Pharmaceutical Industries, Ltd	Monthly subcutaneous injection	Fremanezumab reduced monthly migraine days in 2 phase 2 trials. Teva announced that in a 1130-patient, 16-week, phase 3 trial (HALO chronic migraine study), fremanezumab reduced monthly migraine days by 2 days with both a 1- and 3-month dosing regimen.
Galcanezumab	Eli Lilly and Co	Monthly subcutaneous injection	Galcanezumab decreased monthly migraine days by 2 days in phase 2 and 3 trials.
Atogepant	Allergan	Oral	A small molecule that potentially may be the first oral CGRP receptor inhibitor.

Note. Information adapted from the Prescribe Right Pharmaceutical Pipeline Tracker database. CGRP = calcitonin gene-related peptide; IV = intravenous; BLA = biologics license application; STRIVE = Study to evaluate the efficacy and safety of erenumab in migraine prevention; ARISE = A phase 3, Randomized, double-blind, placebo-controlled Study to Evaluate the efficacy and safety of erenumab in migraine prevention; HALO = per a letter from Teva Pharmaceutical, HALO has no special meaning; PROMISE = PREvention Of Migraine via Intravenous ALD403 Safety and Efficacy; PDUFA = Prescription Drug User Fee Act.

data may be utilized. The information provided is meant to provide a way to assess the development status of a new drug and should not be used in making patient care decisions.

Declaration of Conflicting Interests

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References

1. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68:343-349.
2. Goldberg LD. The cost of migraine and its treatment. *Am J Manag Care*. 2005;11(2 suppl):S62-S67.
3. Goadsby PJ, Lipton RB, Ferrari MD. Migraine—current understanding and treatment. *N Engl J Med*. 2002;346:257-270.
4. Puledra F, Messina R, Goadsby PJ. An update on migraine: current understanding and future directions [published online ahead of print March 20, 2017]. *J Neurol*. doi:10.1007/s00415-017-8434-y.
5. Adams B. Teva posts positive phase 3 migraine data, plots FDA submission. *FierceBiotech*. <http://www.fiercebiotech.com/biotech/teva-posts-positive-phase-3-migraine-data-plots-fda-submission>. Published May 31, 2017. Accessed July 11, 2017.
6. Silbestein SD, Tepper SJ. Updates in the clinical science of CGRP antagonism for the treatment of migraine. *Medscape*. http://www.medscape.org/viewarticle/867852_transcript. Published 2016. Accessed May 31, 2017.