Biologics for episodic and chronic migraines

Sandra Trkulja Pharmd Trudy Huyghebaert Pharmd Joey Ton Pharmd Clark Svrcek MD CCFP

Clinical question

What is the efficacy of calcitonin gene-related peptide (CGRP) inhibitors in migraine prophylaxis?

Bottom line

Treating 5 to 8 patients with CGRP inhibitors will lead to 1 patient having at least a 50% reduction in monthly migraine days (MMD) compared with placebo. From baseline, a decrease of 1 to 2 MMD may be seen. Cost may limit use.

Evidence

Results are statistically significant unless noted.

- A systematic review (5 RCTs, 2928 patients, about 9 to 18 MMD, 84% female) of patients treated with either 70 mg or 140 mg of subcutaneous erenumab monthly for 12 weeks: more patients in the 70-mg dose group achieved at least a 50% reduction in MMD compared with the placebo group (42% vs 27%; number needed to treat [NNT]=7). Similar results were found in the 140mg dose group versus the placebo group (40% vs 21%; NNT=5). A reduction of 1.5 to 2.0 MMD was found.
- A systematic review (3 RCTs, 2886 patients, about 9 to 19 MMD, 85% female)² of patients treated with 120 mg or 240 mg of subcutaneous galcanezumab monthly for 12 to 24 weeks: about 41% of patients in both the 120-mg and 240-mg dose groups achieved at least a 50% reduction in MMD compared with 26% in the placebo group (NNT=7). A reduction of 1.9 MMD was found.
- In 5 RCTs (3379 patients, about 16 MMD)³ of patients treated with 675 mg of subcutaneous fremanezumab every 3 months: more patients in the treatment group achieved at least a 50% reduction in MMD compared with the placebo group (41% vs 19%; NNT=5). A reduction of 2.2 MMD was found.
- Another systematic review had similar findings.⁴
- Adverse events: There was no difference except for injection site pain (11% vs 8% with placebo).^{1,2,4}
- Limitations: These were industry-sponsored studies of short duration (12 to 24 weeks); long-term efficacy and safety are unknown. Trials often excluded patients for whom more than 2 to 3 medication groups failed.

Context

• Other medications achieving more than a 50% reduction in MMD include propranolol (NNT=4)⁵ and tricyclic

- antidepressants (NNT=5).6 Candesartan (about 1.5 days) and topiramate (about 1.0 day) have shown headache frequency reduction versus placebo.^{5,7}
- In Canada, CGRP inhibitors cost about \$7000 per year.⁸
- Guidelines⁹ recommend a trial of at least 2 oral agents before prescribing CGRP inhibitors.

Implementation

Clinicians may start prophylactic medications if acute treatments are ineffective, or if headache frequency is more than 8 days per month despite use of acute treatments.10 Guidelines have recommended that oral prophylactic medication such as propranolol, amitriptyline, and nortriptyline are generally trialed before other interventions (eg, onabotulinumtoxinA injections). 10 Migraine triggers can include alcohol, caffeine overuse, diet, smoking, and vasodilating antihypertensives. 11 Tools to track and monitor migraines include the Canadian Migraine Tracker and the Migraine Buddy app. 12,13 #

Dr Sandra Trkulia is a complex care pharmacist at Alberta's Children Hospital in Calgary, Dr Trudy Huvghebaert is a pharmacist at the South Health Campus Family Medicine Teaching Centre in Calgary, Dr Joey Ton is Clinical Evidence Expert for the CFPC. Dr Clark Svrcek is a family physician in the Department of Family Medicine at the University of Calgary in Alberta.

None declared

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

References

- Zhu C, Guan J, Xiao H, Luo W, Tong R. Erenumab safety and efficacy in migraine: a systematic review and meta-analysis of randomized clinical trials. Medicine (Baltimore) 2019;98(52):e18483.
- Förderreuther S, Zhang Q, Stauffer VL, Aurora SK, L\u00e4inez MJA. Preventive effects of galcan-ezumab in adult patients with episodic or chronic migraine are persistent: data from the phase 3, randomized, double-blind, placebo-controlled EVOLVE-1, EVOLVE-2, and REGAIN studies. J Headache Pain 2018;19(1):121.
- Gao B, Sun N, Yang Y, Sun Y, Chen M, Chen Z, et al. Safety and efficacy of fremanezumab for the
- prevention of migraine: a meta-analysis from randomized controlled trials. Front Neurol 2020;11:435. Deng H, Li GG, Nie H, Feng YY, Guo GY, Guo WL, et al. Efficacy and safety of calcitonin-generelated peptide binding monoclonal antibodies for the preventive treatment of episodic migraine—an updated systematic review and meta-analysis. *BMC Neurol* 2020;20(1):57.
- Kapusta MJ, Allan GM. Are antihypertensive medications effective for migraine prophylaxis? Tools for Practice #52. Edmonton, AB: Alberta College of Family Physicians; 2015.
 Allan GM, Levy M. Antidepressants for preventing headaches: which work and how well? Tools for
- Practice #51. Edmonton, AB: Alberta College of Family Physicians; 2015.
 Linde M, Mulleners WM, Chronicle EP, McCrory DC. Topiramate for the prophylaxis of episodic
- Linde M, Mulleners WM, Cironice EP, McCrory DC. Topiramate for the prophylaxis of episodic migraine in adults. Cochrane Database Syst Rev 2013;(6):E0016010.

 Pharmacoeconomic review report: Erenumab (Aimovig): (Novartis Pharmaceuticals Canada Inc.): indication: for prevention of migraine in adults who have had at least four migraine days monthly. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health; 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK566785/. Accessed 2021 Nov 16.
- American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. Headache 2019;59(1):1-18. Epub 2018 Dec 10. Er-
- ratum in: Headache 2019;59(4):650-1. Epub 2019 Apr 1.

 10. Becker WJ, Findlay T, Moga C, Scott NA, Harstall C, Taenzer P. Guideline for primary care management of headache in adults. Can Fam Physician 2015;61:670-9 (Eng), e353-54 (Fr).
- Sacco S, Braschinsky M, Ducros A, Lampl C, Little P, van den Brink AM, et al. European headache federation consensus on the definition of resistant and refractory migraine; developed with the
- endorsement of the European Migraine & Headache Alliance (EMHA). J Headache Pain 2020;21(1):76. 12. Leroux E. The Canadian Migraine Tracker: a keep it simple approach to the headache diary. Calgary, AB: Canadian Headache Society; 2019. Available from: https://headachesociety.ca/news/the-canadian-migraine-tracker/. Accessed 2021 Sep 28.
- 13. Migraine Buddy [website]. Migraine Buddy; 2021. Available from: https://migrainebuddy.com/. Accessed 2021 Sep 28.

Can Fam Physician 2021;67:911. DOI: 10.46747/cfp.6712911

Tools for Practice articles in Canadian Family Physician are adapted from peer-reviewed articles at www.toolsforpractice.ca and summarize practice-changing medical evidence for primary care. Coordinated by Dr. G. Michael Allan and Dr Adrienne J. Lindblad, articles are developed by the Patients, Experience, Evidence, Research (PEER) team and supported by the College of Family Physicians of Canada and its Alberta, Ontario, and Saskatchewan Chapters. Feedback is welcome and can be sent to toolsforpractice@cfpc.ca.