

8.4 Fremanezumab to prevent migraine headaches

Dr. David Dodick (whose conflict of interest disclosures for this paper run 4.75 column inches in JAMA) and colleagues recently reported results of a randomized, double-blind trial of fremanezumab, a new monoclonal antibody¹ used to prevent migraine headache (1) The investigators compared monthly and quarterly doses of fremanezumab with placebo; for simplicity we will focus only on comparisons of the (more effective) monthly dosing with placebo.

- a.) The proportion of patients who achieved at least a 50% reduction in the number of headache days per month was 47.7% in the monthly fremanezumab group compared with 27.9% in the placebo group. What was the number needed to treat with fremanezumab to get one additional patient with a $\geq 50\%$ reduction in headache days?

- b.) Fremanezumab costs about \$600/monthly dose.² It was well tolerated in the trial. If we ignore possible late adverse effects and focus only on the medication cost, what is the approximate cost per month per patient who achieved a 50% reduction in headache days?

- c.) Per the abstract, "From baseline to 12 weeks, mean migraine days per month decreased from 8.9 days to 4.9 days in the fremanezumab monthly dosing group, and from 9.1 days to 6.5 days in the placebo group. This resulted in a difference with monthly dosing vs placebo of -1.5 days/month (95% CI, -2.01 to -0.93 days; $P < .001$)."
If we consider a migraine day a bad outcome, what would be the CBOP, i.e., the approximate cost to prevent one migraine day?

- d.) Let's suppose that this medication only works for true migraines and that everyone in the trial was sufficiently screened that all of them had true migraines. But out in the "real world" we are considering treating someone with headaches that we think might be migraines, but we are unsure. If we believe it is worth \$500 to prevent one headache day, and if there were no other therapeutic options available, at what probability of migraine would the headache reduction benefit of fremanezumab justify the cost?

¹ It targets calcitonin gene-related peptide.

² Price for Ajovy® 225mg/1.5 ml injection with a free coupon at www.GoodRx.com, accessed 10/24/18.

e.) The investigators excluded patients who had previously failed 2 classes of migraine-preventive medicine from the study and compared fremanezumab with placebo. What effect do these study design decisions have on the clinical usefulness of the study results?

1. Dodick DW, Silberstein SD, Bigal ME, Yeung PP, Goadsby PJ, Blankenbiller T, et al. Effect of Fremanezumab Compared With Placebo for Prevention of Episodic Migraine: A Randomized Clinical Trial. *JAMA*. 2018;319(19):1999-2008.