

EPTINEZUMAB

YAN CUI MAGRAM, MD

EASTERN PAIN ASSOCIATION

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MIGRAINES

- Migraines have been shown to afflict up to 15% of the population, and is a leading cause of disability worldwide.¹
- Some factors affecting patient adherence to treatment include intolerable side effects or ineffectiveness found in many classes of medications.



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CALCITONIN RECEPTOR-LIKE RECEPTOR PEPTIDE

- CGRP has long been theorized to be involved in the onset of migraines.
- Synthesized in perivascular nerve cells in the brain and spinal cord, the neuropeptide CGRP functions as a vasodilator, relaxing blood vessels.²
- Role in regulating vascular resistance and end organ blood flow.²
- Targeted therapy: mAbs to CGRP to have a preventative effect on migraines.³

• Imaging credit: www.guidetopharmacology.com

CGRP IN MIGRAINES

- Proposed mechanism of action is CGRP → ↑ production of nitric oxide (NO) → NO diffuses into smooth muscle cells → activates guanylate cyclase → ↑ cGMP and relaxation of the vessels.
- Measured CGRP concentrations from EJ rise during migraine attacks and decrease with triptans.⁴
- Serum CGRP levels are elevated in migrainers.⁴
- IV infusion of CGRP triggers migraines in migrainers.⁴

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- Newest of the group of CGRP antibody drugs for migraine treatment
- Other CGRP antibody drugs include erenumab, fremanezumab, and galcanezumab.
- PROMISE 1 trial: phase 3 study for frequent episodic migraines. monthly migraine days lowered by 4.3 days (baseline 8.0) after first infusion with 300mg vs placebo reduction of 3.2 days. 31% had 100% reduction of migraine days vs. 21% of placebo group.⁵
- PROMISE 2 trial: phase 3 study for chronic migraines. Primary endpoint met with reduction of 8.2 monthly migraine days vs. reduction of 5.6 days for placebo. 61% achieved 50% reduction in migraine days, 33% reached 75% reduction, and 15% saw 100% reduction in migraine days.⁶

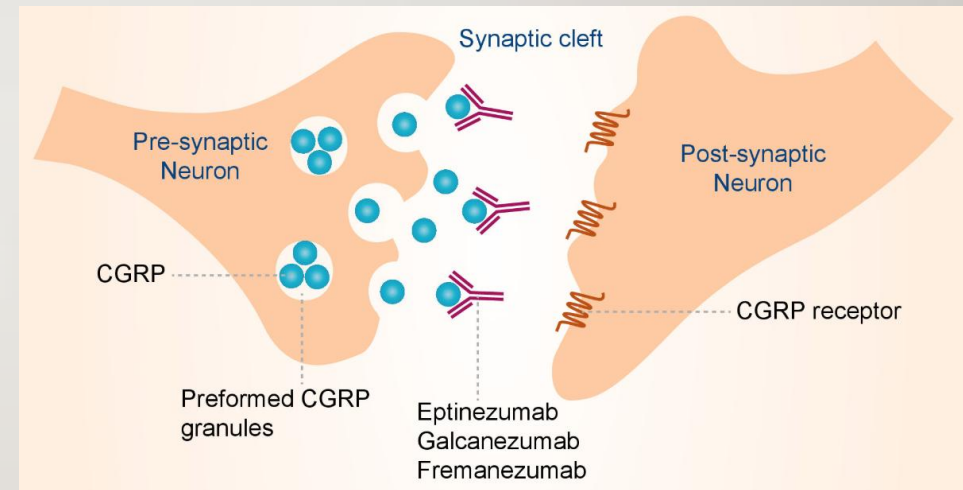


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[Creativebiolabs.net/eptinezumab-overview.htm](https://creativebiolabs.net/eptinezumab-overview.htm)

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PROMISE I trial 12 month data: 70.7% had 50% or greater reduction of migraine days vs. 58.7% for placebo. This is a 8.9% improvement over the first two quarters.⁵



>50% achieved a 75% reduction of monthly migraine days vs. 38.7% of placebo group, an additional improvement of 12.8% from the first two quarters.⁵



Open label safety trial is ongoing.

FUTURE OF EPTINEZUMAB

Safety profile showing very low adverse events at 2%.

FDA Biologics License Application accepted April 2019.

Projected Drug User Fee Act target action date of February 2020.

ADVANTAGES OF EPTINEZUMAB

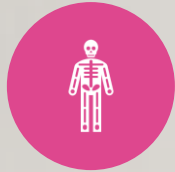


IV infusion and 100% bioavailability may mean immediate effect.



Long half time: No need for daily medications, can be infused on a quarterly basis

DISADVANTAGES TO EPTINEZUMAB



Because CGRP also plays a role in regulation of cardiovascular smooth muscles cells, there is some concern for CV side effects of eptinezumab.



CV: Some reports of Raynaud's like phenomenon.⁸



Theoretical interference in wound healing.



Theoretical contribution to inflammatory bowel disease due to blocking CGRP in the GI tract.⁷



Physicians would need access to infusion center/infusion infrastructure vs. at home administration of a subcutaneous medication.



No long-term studies yet.

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