Don't Give Yourself a Headache:

Summary of New Migraine Treatments

A presentation for HealthTrust Members

February 8, 2023

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Speaker Disclosures

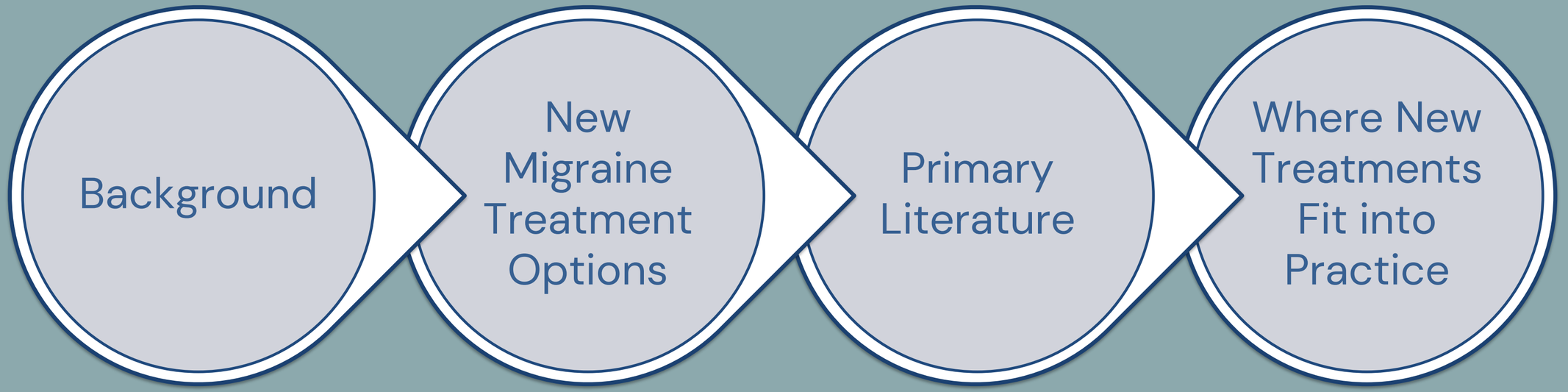
- The presenter and their preceptor have no financial relationships with any commercial interests pertinent to this presentation.

- This program may contain the mention of drugs, brands or suppliers presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any particular drug, brand or supplier.

Objectives

- Recall new pharmacologic treatment options for migraines
- Recognize primary literature surrounding the safety and efficacy of new migraine treatment options
- Identify where the new migraine treatment options fit into current standards of practice

Overview


Background
New Migraine Treatment Options
Primary Literature
Where New Treatments Fit into Practice

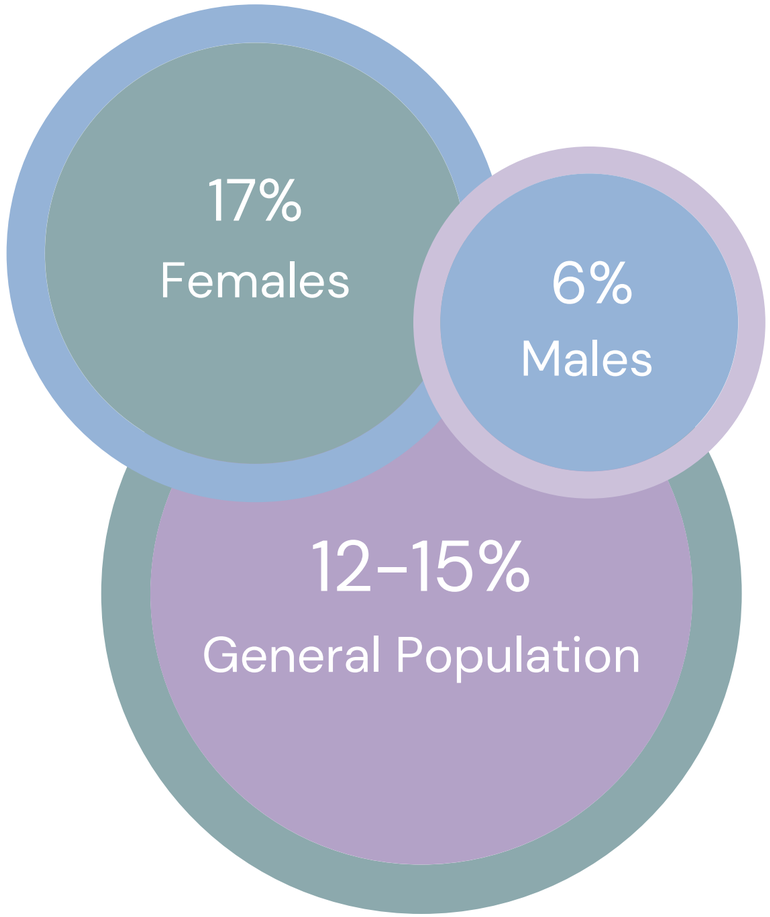
Background

Migraines

- Episodic disorder
- Severe headache
- Nausea
- Light and sound sensitivity

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.

Epidemiology



- Most common in those aged 30 to 39
- Genetic
- Major cause of disability

Source: Ailani J, et al. *Headache.* 2021;61(7):1021-1039.

Clinical Features

Prodrome

- 77% patients
- Several hours to days
- Yawning, euphoria, depression, irritability, food cravings, constipation, neck stiffness

Aura

- 25% patients
- Gradual development & duration <1 hour
- Positive & negative features
- Complete reversibility

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.

Clinical Features

Headache

- Unilateral & throbbing or pulsatile quality
- Nausea/vomiting
- Photophobia or phonophobia
- 4 hours to several days

Postdrome

- Sudden head movement causes pain
- Fatigue or mild euphoria

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.

Exacerbating Factors

Emotional stress	Hormones in females	Not eating	Weather	Sleep disturbances
Odors	Neck pain	Light	Alcohol	Smoke
Sleeping late	Heat	Food	Exercise	Sexual activity

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.

Goals of Treatment

- Rapid and consistent freedom from pain and associated symptoms
- Restored ability to function
- Minimal need for repeat dosing or rescue medications
- Optimal self-care and reduced subsequent use of resources
- Minimal or no adverse events
- Cost considerations

Source: Mayans L, et al. *Am Fam Physician*. 2018;97(4):243-251.

Acute Migraine Treatments

Acute Migraine Treatments

First-line

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Example: Ibuprofen 400mg-600mg orally x 1
- Acetaminophen 1000mg orally x 1

Second-line

- Triptans
  - Example: Sumatriptan 50-100mg orally x 1
- Triptans + NSAIDs
  - Example: Sumatriptan/naproxen 85mg/500mg orally x 1

Nausea & Vomiting

- Antiemetics
  - Example: Metoclopramide 10mg intravenously x 1

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.
Source: Acute treatment of migraines in adults. UpToDate

New Acute Migraine Treatments

Novel Drug Classes

Calcitonin gene-related peptide (CGRP) receptor antagonist

Serotonin $(5\text{-}HT)_{1F}$ receptor agonist

CGRP Receptor Antagonist

Rimegepant
(Nurtec® ODT)

Ubrogepant
(Ubrelvy™)

Mechanism of Action

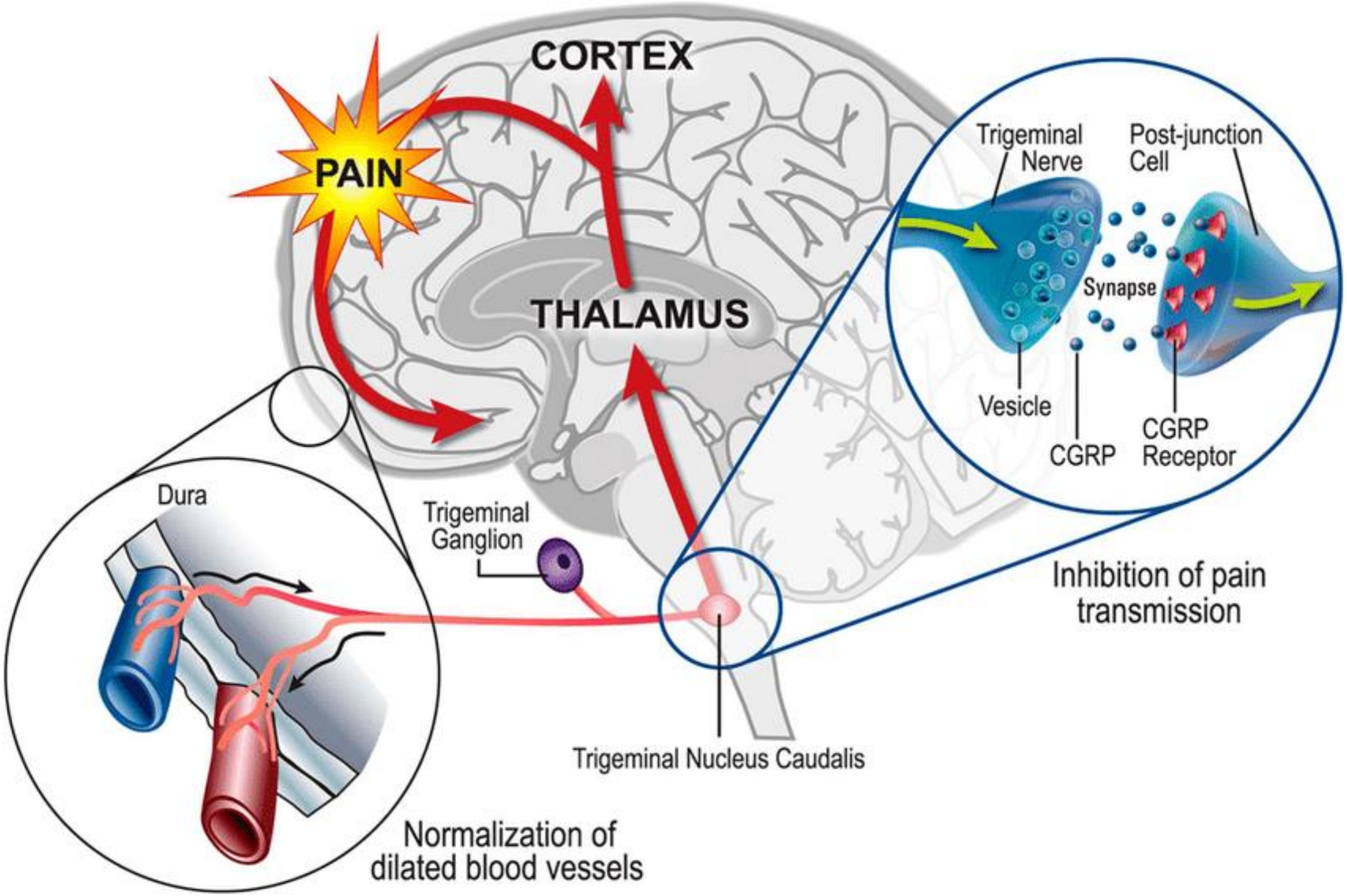


Image from researchgate.net

JAMA | Original Investigation

Effect of Ubrogepant vs Placebo on Pain and the Most Bothersome Associated Symptom in the Acute Treatment of Migraine

The ACHIEVE II Randomized Clinical Trial

Study Design

Purpose

- Evaluate the efficacy and tolerability of ubrogepant 25mg and 50mg for the acute treatment of migraine.

Methods

- Randomized 1:1:1 to placebo, 25mg of ubrogepant, or 50mg of ubrogepant

Outcomes

- Pain freedom and absence of most bothersome migraine-associated symptoms at 2 hrs

Source: Lipton RB, et al. *JAMA.* 2019;322(19):1887–1898.

Study Results

Results

Pain freedom at 2 hrs	• 50mg: 21.8%; P=0.01 • 25mg: 20.7%; P=0.03 • Placebo: 14.3%
Absence most bothersome migraine-associated symptoms at 2 hrs	• 50mg: 38.9%; P=0.01 • 25mg: 34.1%; P=0.07 • Placebo: 27.4%

Conclusion

- Ubrogepant 25mg showed greater rates of pain freedom than placebo
- Ubrogepant 50mg showed greater rates of pain freedom and freedom from bothersome symptoms than placebo

Source: Lipton RB, et al. *JAMA.* 2019;322(19):1887–1898.

Clinical Pearls

Rimegepant	Ubrogepant	Considerations
• Acute & preventative • 75mg orally as needed (MAX 75mg/24hrs)* • Avoid in severe hepatic impairment	• Acute • 50mg or 100mg orally as needed • 2nd dose > 2 hrs after initial (MAX 200mg/24hrs) • Severe hepatic and renal impairment: 50mg	• Nausea, somnolence • Use with strong CYP3A4 inhibitors • No pregnancy data

Source: Ubrelvy. Package Inset. 2021.
Source: Nurtec. Package Insert. 2022.

Serotonin $(5\text{-HT})_{1F}$ Receptor Agonist

Lasmiditan
(Reyvow®)

Mechanism of Action

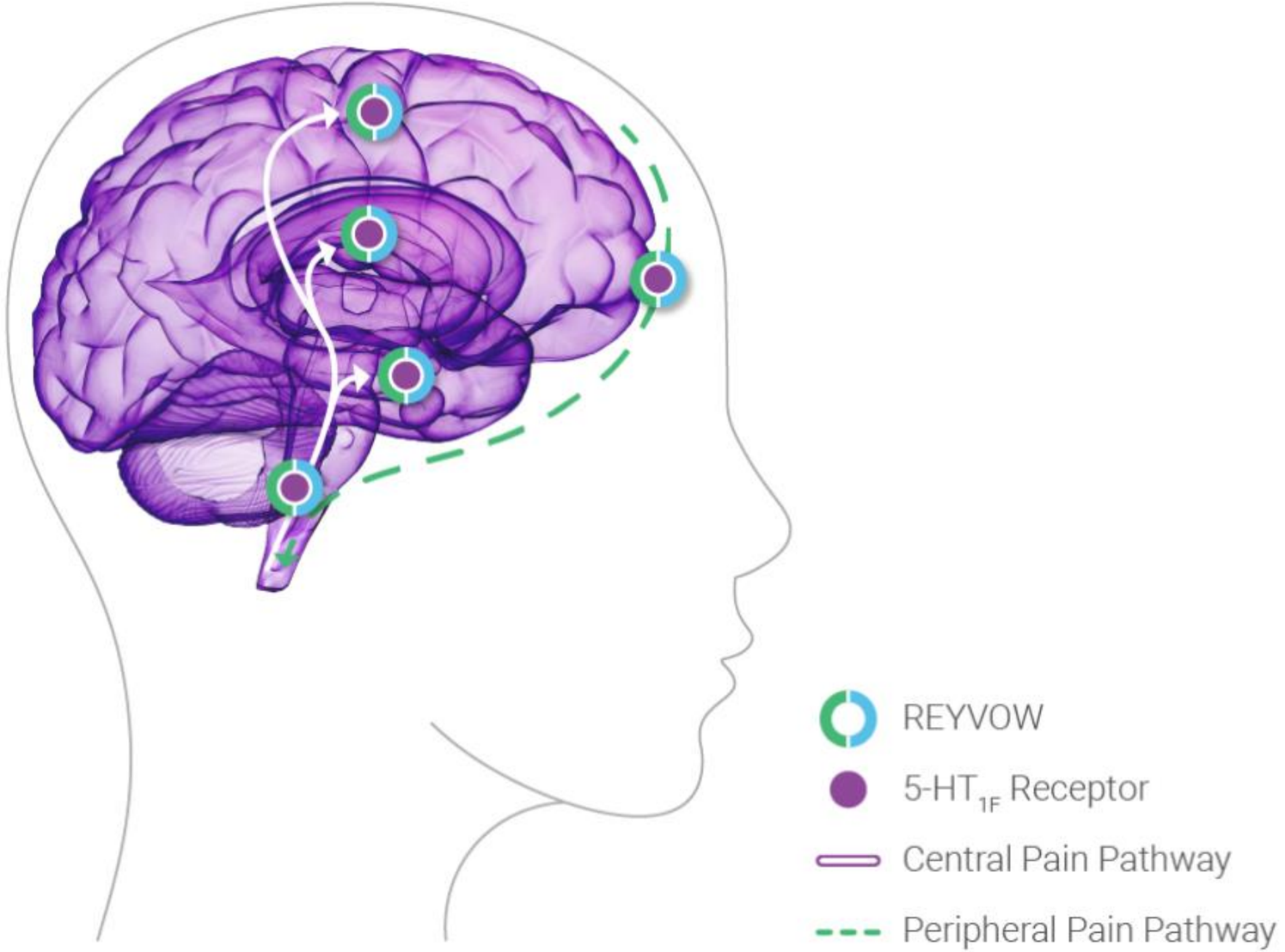


Image from: www.reyvow.com

BRAIN
A JOURNAL OF NEUROLOGY

CLINICAL TRIAL

Phase 3 randomized, placebo-controlled, double-blind study of lasmiditan for acute treatment of migraine

Study Design

Purpose

- Confirm the efficacy and safety of three doses of oral lasmiditan versus placebo for the acute treatment of a single migraine attack in patients with migraine

Methods

- Randomized 1:1:1:1 to lasmiditan 200mg, 100mg, 50mg, or placebo

Primary Objective

- Efficacy of lasmiditan at 2hr compared to placebo on the proportion of patients achieving headache-pain freedom and freedom from the most bothersome symptoms (MBS)

Source: Goadsby PJ, et al. *Brain*. 2019;142(7):1894-1904.

Study Results

Results

Headache pain-free at 2hr	• 200mg: P<0.001 • 100mg: P<0.001 • 50mg: P=0.003
MBS free at 2hr	• 200mg: P<0.001 • 100mg: P<0.001 • 50mg: P=0.009

Conclusion

- Lasmiditan > Placebo

Source: Goadsby PJ, et al. *Brain*. 2019;142(7):1894-1904.

Clinical Pearls

Acute treatment of migraine with or without aura in adults

Schedule V

Dose: 50mg, 100mg, or 200mg orally as needed (MAX 1 dose/24hrs)

Contraindications: None

Adverse reactions: Dizziness, fatigue, paresthesia, sedation

Precautions:

- Driving
- Central nervous system depression
- Serotonin syndrome
- Cardiovascular disease

No dose adjustment for mild-moderate hepatic impairment

Source: Reyvow. Package Insert. 2020.

Assessment Question 1:

Which of the following is not a new migraine treatment class?

1. Serotonin $(5\text{-HT})_{1F}$ receptor agonists
2. CGRP receptor antagonists
3. CGRP antagonists
4. Selective serotonin receptor agonists

Assessment Question : Correct Response

Which of the following is not a new migraine treatment class?

1. Serotonin $(5\text{-HT})_{1F}$ receptor agonists
2. CGRP receptor antagonists
3. CGRP antagonists
4. Selective serotonin receptor agonists

Preventative Migraine Treatments

Preventative Migraine Treatments

Optimized acute therapy

- Discussed previously

First-line

- Beta-blockers
  - Example: Propranolol 20mg orally twice daily
- Topiramate titrated to 100mg orally daily
- Candesartan 16mg orally daily

Second-line

- Tricyclic antidepressants
  - Example: Amitriptyline 20-50mg orally at bedtime
- Valproate sodium/Divalproex sodium 500-1000mg orally daily

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.
Source: Preventive treatment of episodic migraines in adults. UpToDate.

New Preventative Migraine Treatments

Assessment Question 2:

True or False. Lasmiditan was shown to decrease headache pain at 2 hours better than placebo:

1. True
2. False

Assessment Question 2 : Correct Response

True or False. Lasmiditan was shown to decrease headache pain at 2 hours better than placebo:

1. True
2. False

Novel Drug Classes

Calcitonin gene-related peptide (CGRP) receptor antagonist

Calcitonin-gene related peptide antagonist

CGRP Receptor Antagonist

Rimegepant
(Nurtec® ODT)

Atogepant
(Qulipta™)

Clinical Pearls

Rimegepant*

- Acute & preventative
- 75mg orally every other day **

*Clinical pearls discussed previously
**The safety of using > 18 doses in 30-day period is undefined

Atogepant

- Preventative
- 10mg, 30mg, or 60mg orally once daily
- Severe renal impairment: 10mg

Adverse events: Nausea, constipation, and fatigue

Drug Interactions: CYP3A4 inhibitor, strong and moderate CYP3A4 inducers, and OATP inhibitors

Pregnancy: May cause harm

Source: Nurtec. Package Insert. 2022.
Source: Qulipta. Package Insert. 2021.

Calcitonin-gene Related Peptide Antagonist

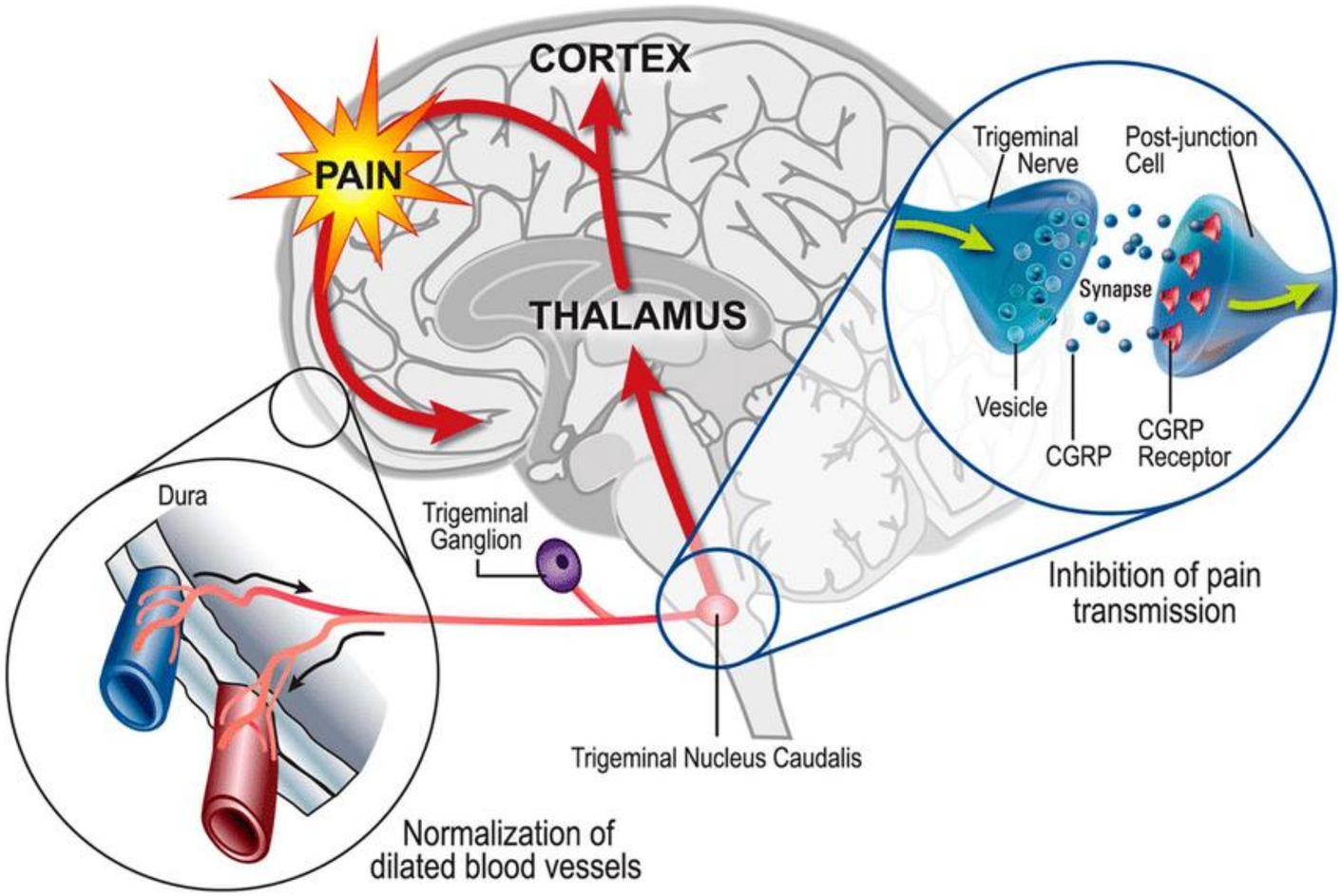
Eptinezumab (Vyepti®)

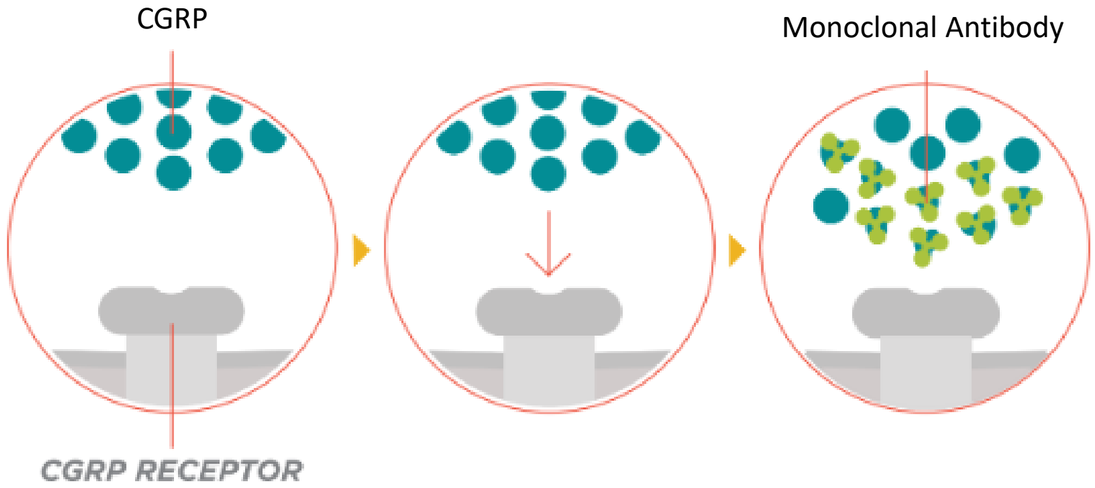
Galcanezumab (Emgality®)

Fremanezumab (Ajovy®)

Erenumab (Aimovig®)

Mechanism of Action





CGRP = calcitonin gene-related peptide.

Images from: researchgate.net and www.emgality.com

Original Article

Cephalalgia
An International Journal of Headache

Erenumab versus topiramate for the prevention of migraine – a randomised, double-blind, active-controlled phase 4 trial

Study Design

Purpose

- Directly compare the tolerability and efficacy of erenumab to topiramate

Methods

- 1:1 randomization to either topiramate group or erenumab group

Endpoints

- Primary Endpoint: proportion of patients who discontinued erenumab or topiramate due to an adverse event
- Secondary Endpoint: proportion of patients in each group that achieved > 50% reduction in monthly migraine days

Source: Reuter U, et al. *Cephalalgia*. 2022;42(2):108-118.

Study Results

Results:

- 777 patients randomized

Primary Endpoint	• Erenumab group 10.6% (41/388) • Topiramate group 38.9% (151/388) • P <0.001
Secondary Endpoint	• Erenumab group 55.4% (215/388) • Topiramate group 31.2% (121/388) • P <0.001

Conclusion

- Erenumab > Topiramate

Source: Reuter U, et al. *Cephalalgia*. 2022;42(2):108-118.

Clinical Pearls

Fremanezumab	• Subcutaneous injection • 225mg monthly or 675mg every 3 months
Galcanezumab	• Subcutaneous injection • 240mg loading dose, then 120mg monthly
Eptinezumab	• Intravenous infusion • 100mg intravenous infusion over 30 minutes every 3 months
Erenumab	• Subcutaneous injection • 70mg once monthly

Source: Ajovy. Package Insert. 2022.
Source: Aimovig. Package Insert. 2022.
Source: Emgality. Package Insert. 2021.
Source: Vyepti. Package Insert. 2022.

Clinical Pearls

Adverse reactions

- Injection site reactions (All but eptinezumab)
- Nasopharyngitis (Eptinezumab)
- Constipation (Erenumab)

Precautions

- Hypersensitivity (All)
- Hypertension (Erenumab)
- Cardiovascular disease (Galcanezumab and fremanezumab)

Pregnancy & Lactation

- No data

Source: Ajovy. Package Insert. 2022.
Source: Aimovig. Package Insert. 2022.
Source: Emgality. Package Insert. 2021.
Source: Vyepti. Package Insert. 2022.

Novel Drug Classes and the Current Standard of Practice

Acute Migraine Treatments

First-line

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Acetaminophen

Second-line

- Triptans
- Triptans + NSAIDs

Third-line

- Rimegepant 75mg orally x 1 or ubrogepant 50-100mg orally x 1
- Lasmiditan 50-100mg orally x 1

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.
Source: Acute treatment of migraines in adults. UpToDate

Preventative Migraine Treatments

Optimized acute therapy

First-line

- Beta-blockers
- Topiramate
- Candesartan

Second-line

- Tricyclic antidepressants
- Valproate sodium/Divalproex sodium

Third-line

- Rimegepant 75mg orally every other day and atogepant 10-60mg orally daily
- CGRP monoclonal antibodies
  - Example: Galcanezumab 120mg subcutaneously monthly

Source: Ailani J, et al. *Headache*. 2021;61(7):1021-1039.
Source: Preventive treatment of episodic migraines in adults. UpToDate.

Assessment Question 3:

Which patient would benefit the most from initiation of lasmiditan?

1. Newly diagnosed acute migraine patient
2. Patient with acute migraines that has had no relief from acetaminophen or triptans
3. Patient who suffers from acute migraines, and recently failed NSAID therapy
4. Pregnant women who suffers from acute migraines and has not had relief from acetaminophen therapy

Assessment Question 3 : Correct Response

Which patient would benefit the most from initiation of lasmiditan?

1. Newly diagnosed acute migraine patient
2. Patient with acute migraines that has had no relief from acetaminophen or triptans
3. Patient who suffers from acute migraines, and recently failed NSAID therapy
4. Pregnant women who suffers from acute migraines and has not had relief from acetaminophen therapy

Let’s Review

New Migraine Treatments:

What to Remember

New migraine therapies have been shown to be efficacious and safe

Recommended to be used as third-line if a patient is not managed on first- or second-line therapies

CGRP receptor antagonists are oral therapies used to **treat (rimegepant and ubrogepant) and prevent migraines (rimegepant and atogepant)**

Lasmiditan is a schedule V medication that can be used to treat **acute migraines**

CGRP monoclonal antibodies (eptinezumab, galcanezumab, fremanezumab, and erenumab) are injection therapies given less often and help to **prevent migraines**

Summary

- Recalled new pharmacologic treatment options for migraines
- Recognized primary literature surrounding the safety and efficacy of new migraine treatment options
- Identified where the new migraine treatment options fit into current standards of practice

References

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THANK YOU

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