Diagnosing and Managing Primary Headache Disorders in the Primary Care Setting: Challenges and Opportunities

TUESDAY, OCTOBER 13, 2020

This event is not a part of the official AAFP FMX.
PROGRAM OVERVIEW
This case-based live virtual activity will cover the treatment and management of patients with headache disorders, including migraine and cluster headache.

TARGET AUDIENCE
This activity is intended for primary care providers, including family practice physicians, physician assistants, and nurse practitioners who are involved in the care of patients with headache disorders, including migraine and cluster headache.

Learning Objectives
- Implement best practices for the timely and accurate diagnosis of primary headache disorders in primary care settings and for referral to specialists when necessary
- Identify the mechanisms of action and clinical profiles of new and emerging therapeutic options for the acute and preventative treatment of patients with primary headache disorders
- Design individualized evidence-based treatment plans for patients with primary headache disorders, with focus on cluster headache, in the primary care setting
- Utilize patient-specific factors to select therapies for patients with primary headache disorders, including quality-of-life assessment and goal setting
- Implement strategies to effectively communicate with patients and educate them in order to establish treatment plans and encourage adherence

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Purpose: This program would be beneficial for nurses involved in the long-term treatment and management of patients with headache disorders, including migraine and cluster headache. CNE Credits: 1.5 ANCC Contact Hours.
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2. Participate in the live streamed activity; and
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This activity is supported by an educational grant from Lilly.

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AGENDA

- **Overview of Primary Headache Disorders**
  - Epidemiology, impact on disability and quality of life, societal impact, economical burden
  - Headache screening and useful questions to ask
  - Diagnosis: differentiating between types of headache
  - Types of primary headache disorders (e.g., CM, EM, CCH, ECH)
  - Excluding secondary causes

- **Initial Treatment Considerations**
  - Case study
  - The headache treatment map
    - Lifestyle, biobehavioral, pharmacologic, neuromodulation, complementary/integrative
  - When to refer
  - Improving communication

- **Q/A**

- **A New Era in Targeting the Underlying Pathology of Migraine and Cluster Headache**
  - Types of treatment/prevention
  - Guidelines
  - Traditional therapies
  - Role of CGRP and the 5HT1F serotonin receptor in the pathophysiology of primary headache disorders (e.g., migraine and CH)
  - Clinical profiles of CGRP mAbs and 5HT1F serotonin receptor agonists headache management
  - Ongoing clinical trials

- **Conclusions and Q/A**
Diagnosing and Managing Primary Headache Disorders in the Primary Care Setting: Challenges and Opportunities

Dawn C. Buse, PhD
Clinical Professor, Department of Neurology
Albert Einstein College of Medicine of Yeshiva University
Assistant Professor, Clinical Health Psychology Doctoral Program
Ferkauf Graduate School of Psychology of Yeshiva University
Board Member at Large, American Headache Society

Andrew Charles, MD
Professor of Neurology
Director, UCLA Goldberg Migraine Program
Meyer and Renee Luskin Chair in Migraine and Headache Studies
David Geffen School of Medicine
University of California Los Angeles
Los Angeles, CA
President-Elect, American Headache Society

Disclosures

• Dr. Buse is a consultant for Allergan, Amgen, Biohaven, Dr. Reddy’s/Promeius, Lilly, and Teva.

• Dr. Charles is a consultant for Alder, Amgen, Biohaven, Eli Lilly, and eNeura. He has conducted research for Takeda Pharmaceuticals.

• During the course of this lecture, the faculty will mention the use of medications for both FDA-approved and non-approved indications

This activity is supported by an educational grant from Lilly.
Learning Objectives

• Discuss best practices for timely and accurate diagnosis of primary headache disorders
• Identify the mechanisms of action and clinical profiles of new and emerging agents
• Design evidence-based treatment plans for patients with primary headache disorders
• Use patient-specific factors to select therapies for primary headache disorders
• Improve communication with patients for better outcomes

Headache Impact

Dawn C. Buse, PhD
**Migraine Prevalence**

*One in five US adults has migraine*

### Sex
- 9.7% of males
- 20.7% of females

### Race
- American Indian or Alaska Native: 18.4%
- Black or African American: 16.2%
- White: 15.4%
- Asian: 11.3%

### Risk Factors for Migraine
- People who are unemployed: 21.4%
- Annual family income < $35,000: 19.9%
- Ages 18-44: 17.9%
- Elderly or disabled: 16.4%

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**Migraine Impact and Disability**

Migraine is the 2nd leading cause of years lived with disability (YLD) worldwide*:
- Across all ages and sexes
- #1 cause of YLDs in people aged 15-49

Migraine can negatively impact virtually all important aspects of life:*
- Work, school, family, financial, personal, identify, social, etc
- Patient, family, community, colleagues, employers and society

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*YLD represents number of years of healthy life lost as a result of disability caused by the non-fatal experience of disease or injury in a population.

Diagnosis

Headache

• Can be primary headache, such as migraine

• Can be secondary headache, that is due to a different cause:
  – Head injury
  – SAH
  – Brain tumor

SAH = subarachnoid hemorrhage.
ICHD-3 Classification: Migraine vs Tension-type HA

**Migraine**
- ≥5 attacks lasting 4–72 hours
- ≥2 of the following:
  - Unilateral
  - Pulsating
  - Moderate or severe intensity
  - Aggravation by routine physical activity
- ≥1 of the following
  - Nausea and/or vomiting
  - Photophobia and phonophobia
- Not attributable to another disorder

**Tension-type**
- ≥10 attacks lasting 30 min–7 days
- ≥2 of the following:
  - Bilateral
  - Not pulsating
  - Mild or moderate intensity
  - Not aggravated by routine physical activity
- No nausea or vomiting
- One or neither photophobia or phonophobia
- Not attributable to another disorder

HA = headache.


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**Cluster Headache Diagnostic Criteria**

At least 5 attacks fulfilling these criteria:

- **Severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15–180 min** (when untreated)
- Either 1 or both of the following:
  1. **At least 1 of the following symptoms or signs, ipsilateral to the headache:**
     a) conjunctival injection and/or lacrimation
     b) nasal congestion and/or rhinorrhea
     c) eyelid edema
     d) forehead and facial sweating
     e) forehead and facial flushing
     f) sensation of fullness in the ear
     g) miosis and/or ptosis
  2. **Sense of restlessness or agitation**
- Attacks have frequency between 1 every other day to 8 per day for more than half of the time when the disorder is active
- Not better accounted for by another ICHD-3 diagnosis

Simplified Diagnostic Criteria: ID Migraine

• Symptoms in the last 3 months:
  – Light sensitivity
  – Nausea with headache
  – Decreased ability to function with headache

• Any 2 or 3 of above symptoms = migraine


Chronic Migraine

ICHD-3 criteria

• Headache on ≥15 days/month
  ≥3 months with ≥5 prior migraine attacks
• On ≥8 days/month, headache fulfills criteria for migraine
• Not attributed to another causative disorder
• Medication-overuse headache (MOH) is classified separately as a secondary chronic daily headache

FDA-approved simplified diagnosis for chronic migraine (phenotype approach)

• Headache ≥15 days/month
  AND
• Duration of ≥4 hours/day

Migraine With Aura

Headache preceded by ≥1 neurologic symptom

Visual
- Flashing lights

Sensory
- Numbness
- Paresthesia

Other
- Weakness (hemiplegic migraine)
- Aphasia

Menstrual-Related Migraine

Patients with headache (%)

Day of menstrual cycle

Chronic Migraine

- Episodic migraine (EM) occurs in 12% of the population, CM in 1%\(^1,2\)
- CM evolves as a complication of EM (2.5%/year) and is much more disabling\(^1,3\)
- Risk factors for development of CM include:\(^4\)
  - Headache features (attack frequency, cutaneous allodynia)
  - Headache-related disability
  - Comorbidities (anxiety, depression, obesity)
  - Iatrogenic factors (medication type and frequency of use)


Headache Tool 1
(Patient Symptoms)

Note: a link to the following tool is located in the interactive resources folder so you can explore further.
The tool below will help guide you through a series of questions to determine the type of headache your patient may have.

**Is your patient’s headache:**

**PLEASE CLICK ON ONE OF THE FOLLOWING:**

- **Primary**
  - **Primary:** headaches that are not the result of another medical condition

- **Secondary**
  - **Secondary:** headaches due to an underlying medical condition such as neck injury or sinus infection
Headache Type: Decision Tool Part 1

- Number and duration of attacks per month:
  - ≥5 lasting 4-72 hrs
  - ≥10 lasting 30 min – 7 days
  - Other

- Symptoms:
  - Unilateral or Bilateral
  - Pulsating or Not pulsating
  - Moderate to Severe or Mild to Moderate
  - Aggravation by routine physical activity or Not aggravated by routine physical activity

- Other Symptoms:
  - Nausea/Vomiting or Photophobia
  - Phonophobia or Other symptoms not listed here

- Attributable to any other disorder?
  - No or Yes

Please click to return to primary/secondary back or click here to reset or submit.
## Headache Type: Decision Tool Part 1

### Symptoms:
- **Unilateral** or **Bilateral**
- **Pulsating** or **Not pulsating**
- **Moderate to Severe** or **Mild to Moderate**
- **Aggravation by routine physical activity** or **Not aggravated by routine physical activity**

### Other Symptoms:
- **Nausea/Vomiting**
- **Photophobia**
- **Phonophobia**
- **Other symptoms not listed here**

### Attributable to any other disorder?
- **No**
- **Yes**

### Number and duration of attacks per month:
- ≥ 5 lasting 4-72 hrs
- ≥ 10 lasting 30 min – 7 days
- Other

### Instructions:
- **Please click all of the symptoms that apply.**
- **Please click one of the following.**
- **Click to return to primary/secondary.**
- **Click to return to primary/secondary.**
- **Click here to reset.**
- **Click here to submit.**

---

### Headache Type: Decision Tool Part 1

### Symptoms:
- **Unilateral** or **Bilateral**
- **Pulsating** or **Not pulsating**
- **Moderate to Severe** or **Mild to Moderate**
- **Aggravation by routine physical activity** or **Not aggravated by routine physical activity**

### Other Symptoms:
- **Nausea/Vomiting**
- **Photophobia**
- **Phonophobia**
- **Other symptoms not listed here**

### Attributable to any other disorder?
- **No**
- **Yes**

### Number and duration of attacks per month:
- ≥ 5 lasting 4-72 hrs
- ≥ 10 lasting 30 min – 7 days
- Other

### Instructions:
- **Please click all of the symptoms that apply.**
- **Please click one of the following.**
- **Click to return to primary/secondary.**
- **Click to return to primary/secondary.**
- **Click here to reset.**
- **Click here to submit.**
Based on your choices your patient’s headache could be a **migraine**

- ≥5 attacks lasting 4-72 hrs
- ≥2 of the following features:
  - Unilateral
  - Pulsating
  - Moderate or severe intensity
  - Aggravation by routine physical activity
- ≥1 of the following symptoms:
  - Nausea and/or vomiting
  - Photophobia and Phonophobia
- Not attributable to another disorder

CLICK HERE FOR MORE INFORMATION ON Migraine

OR CLICK THE BACK BUTTON TO EXPLORE MORE OPTIONS

---

**Initial Treatment Considerations**
Headache Tool 2
(Patient Case)

Note: a link to the following tool is located in the interactive resources folder so you can explore further.

Case 1: Sally
Continue →
Sally

Age: 27

- History of migraine with aura from age 8 to 13
- "They went away when I started my cycle"
- Family history of migraine in mother and sister
- Now complains of recurrent sinus headache
- Complains that sinus headaches are getting more severe and frequent
- Engaged, wants to start a family

CONTINUE TO TREATMENT HISTORY

Sally

- Takes oral contraceptive
- No other current medications

CONTINUE TO CURRENT VISIT
- Current headaches start about the brow; described as “pressing”
- When severe, loses appetite
- Prefers to lie down, uses ice and naproxen as needed
- Clear drainage at times, no fever
- Exam is normal except mildly sensitive across temples, suboccipital area

CONTINUE TO QUESTION 1

---

**Question 1**

What is the first step in diagnosing Sally's condition?

**PLEASE SELECT ONE ANSWER**

A. Brain magnetic resonance imaging (MRI) scan

B. Headache diary

C. Headache history

D. Response to a trial of medication

Submit
19

Based on presentation and history, the diagnosis here may be migraine, though more complete history and description of headache is needed to confirm.

Thank you for your answer

Question 2

Sally is eventually diagnosed with migraine, and is interested in exploring non-medication options first.

PLEASE SELECT ONE ANSWER

A Non pharmacological treatment?

B Behavioral strategies?

Submit
Question 2

Sally is eventually diagnosed with migraine, and is interested in exploring non-medication options first.

PLEASE SELECT ONE ANSWER

A  Non pharmacological treatment?

B  Behavioral strategies?

Thank you for your answer

The Headache Treatment Map

Education & Lifestyle

Behavioral

Pharmacologic

Neuromodulation

Complementary & Integrative
Lifestyle (Headache Hygiene) & Education

- SLEEP
- EXERCISE
- EATING
- HYDRATION
- STRESS MANAGEMENT
- SOCIAL SUPPORT
- EDUCATION

Biobehavioral Therapies

- Grade A Evidence
  - Cognitive Behavioral Therapy
  - Relaxation Training
  - Biofeedback

- Emerging Techniques
  - Mindfulness Based Therapies (MBCT, MBSR)
  - Acceptance & Commitment Therapy (ACT)

MBCT: Mindfulness-based cognitive therapy; MBSR: Mindfulness-based stress reduction
Pharmacologic Treatments

<table>
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<th>Acute</th>
<th>Preventive</th>
<th>Interventional</th>
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<td>NSAIDs</td>
<td>CGRP-targeted mAbs</td>
<td>Trigger points</td>
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<td>Beta-blockers</td>
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<td></td>
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</table>

Acute Preventive Interventional

NSAID = nonsteroidal antiinflammatory drug; CGRP = calcitonin gene-related peptide; mAb = monoclonal antibody.

Neuromodulation

- **sTMS mini™**
- **gammaCore®**
- **Relivion®**
  - Approved in Europe
- **Nerivio™**
- **Cefaly®**
Complementary and Integrative Medicine

- Acupuncture
- Nutritional Supplements
- Yoga
- Light Therapy
  - Therapeutic glasses
  - Green Light

Improving Communication

- Patient education is KEY:
- What to do at headache onset
- What to do for prevention
- What to do if treatment is not helping, ie, what is the rescue plan?
- Awareness of side effects of any existing/new medications
- What is a red flag or emergency? What to do.
- Special instructions: travel; stressful events; pregnancy

When to Refer to a Specialist?

- When diagnosis is uncertain
- When patient does not respond to usual acute or preventive treatment
- When the patient has new neurologic signs
- When the patient is getting progressively worse

Questions and Answers
Headache Treatment

Andrew Charles, MD

Headache Treatment

• **Education!**

• **Acute (abortive)**
  – Taken after attack has begun to relieve pain and disability and stop progression

• **Preventive**
  – Taken to reduce attack frequency, severity, and duration of attacks

• Some newer therapies have overlapping acute and preventive properties
Headache Treatment (continued)

• Effective management depends on:
  – Making an accurate diagnosis
  – Addressing headache impact
  – Engaging patients in their therapy

• Ultimate goals of treatment:
  – Identify and remove exacerbating factors (including medications)
  – For acute treatment: rapid and sustained relief from pain and other symptoms (acute treatment)
  – For preventive treatment: reduced frequency, severity, and duration of migraine attacks and associated disability
  – For both types of treatment: minimal adverse effects, eg, dizziness, cognitive dysfunction, weight change, etc.

Traditional Acute Migraine Treatments

**Non-specific**
• NSAIDs
• Combination analgesics
• Neuroleptics/antiemetics
• Corticosteroids

**Specific**
• Ergotamine/DHE
• Triptans

**New formulations**
• FDA-approved
  – Breath-powered intranasal sumatriptan dry powder
  – New sumatriptan autoinjectors

• In development
  – Microneedle-array skin patches (zolmitriptan, sumatriptan)
  – Orally inhaled (zolmitriptan, DHE)
  – New intranasal delivery
    • Sumatriptan liquid spray with enhanced permeation

NSAID = non-steroidal antiinflammatory drug; DHE = dihydroergotamine.

Consider Prevention When...

- Migraine significantly interferes with patients’ daily routine despite acute treatment
- Frequent attacks (>1 day/week) with risk of CM or MOH
- Acute medications are ineffective, contraindicated, have troublesome AEs, or are overused
- Patient preference
- Special circumstances such as:
  - Hemiplegic migraine
  - Migraine with brainstem aura (basilar migraine)
  - Migraine with prolonged aura
  - Migrainous infarction

AE = adverse effect/event.

AAN Preventive Guidelines

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<th>Level A: Effective</th>
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<th>Level C: Possibly effective</th>
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<td>Anticoagulants</td>
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<td>Cyproheptadine</td>
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<td>Protriptyline</td>
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*Studies now suggest Level A evidence
AAN = American Academy of Neurology; AED = antiepileptic drug; ARB = angiotensin-receptor blocker; ACE = angiotensin-converting enzyme; Ca = calcium.
Recently Approved Acute Therapies

• NEW TRIPTAN FORMULATIONS
  – Breath powered intranasal sumatriptan powder
  – Sumatriptan liquid spray with enhanced permeation

• NEUROMODULATION
  – Transcranial magnetic stimulation (sTMS mini®)
  – Transcutaneous supraorbital nerve stimulation (Cephaly®)
  – Transcutaneous vagus nerve stimulation (Gammacore®)

• LASMIDITAN
• UBROGEPANT
• RIMAGEPANT

Lasmiditan
SAMURAI and SPARTAN Phase 3 Studies

Primary endpoint: proportion of patients free from pain at 2 hours post-dose

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• Selective 5HT1F receptor agonist
• Unlike triptans, no effects on vasculature

Lasmiditan: Pain-Free and MBS-Free at 2 Hours

Pain-free at 2 hours

MBS-free at 2 hours

*P <.05; †P <.001 compared to placebo; ‡Number of patients reporting MBS-free outcomes was lower than for pain-free outcome because not all patients reported a most bothersome symptom at baseline.

MBS = most bothersome symptom.


Lasmiditan in Acute Treatment of Migraine

SPARTAN Results—Safety and Tolerability

Treatment-emergent adverse events

- Serious AEs: 5, with 2 considered treatment related (dystonic reaction and presyncope)
- Discontinuation on treatment: 1 on lasmiditan 200 mg (fatigue and dizziness)
- Tests: no laboratory or electrocardiogram differences

CGRP in Migraine

- CGRP immunoreactive nerves innervate human cerebral arteries
- CGRP is a potent vasodilator of human cerebral arteries
- CGRP is released into jugular venous system during migraine
- Serum CGRP levels are elevated in chronic migraine
- CGRP infusion evokes migraine
- Small-molecule CGRP-receptor antagonists (ie, gepants) effectively abort migraine attacks
- Anti-CGRP and anti-CGRP-receptor monoclonal antibodies prevent episodic migraine and chronic migraine

Small-Molecule CGRP Receptor Antagonists: Gepants

**Acute treatment of migraine**
- Olcegepant (IV) worked; comparable to triptans: proof of concept\(^1\)
- BI 44370 TA (oral): effective vs placebo in phase 2\(^2\)
- Telcagepant showed promise and efficacy comparable with triptans, but development stopped due to liver toxicity in phase 3\(^3\)
- MK3207: effective and well tolerated in phase 2 but liver toxic
- Rimegepant: FDA approved for acute treatment of migraine
- Ubrogepant: FDA approved for acute treatment of migraine

**Preventive treatment of migraine**
- Telcagepant studied in 2 incomplete studies, with one terminated early due to hepatotoxicity and the other for evaluation of liver in MRM mini-prevention
- Rimegepant phase 3 study demonstrated efficacy in migraine prevention with every-other-day dosing
- Atogepant vs placebo underway in phase 2 for migraine prevention


**ACHIEVE I: Ubrogepant**
Freedom from Headache Pain

Includes data collected after the use of optional second dose of study medication (placebo or ubrogepant) or rescue medication

\(^{2}\) PBO = placebo.

**Increasing Benefit in Pain Freedom Over Time After Single Dose of Rimegepant 75 mg ODT**

Pain freedom 2–8 hours after single-dose rimegepant 75 mg

Estimates computed using the modified intention-to-treat (mITT) population and Cochran-Mantel-Haenszel (CMH) methods. Subjects using rescue medications at or before the assessment and those not providing data, are classified as failures.

**Rimegepant Met Primary Endpoint of Reduction in Monthly Migraine Days**

Mean change from baseline in monthly migraine days at 3 months

**Small Molecules (Gepants) vs Large Molecules (Monoclonal Antibodies)**

<table>
<thead>
<tr>
<th>Small molecules</th>
<th>Monoclonal antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target specificity lower</td>
<td>Target specificity high</td>
</tr>
<tr>
<td>Clearance (liver, kidney)</td>
<td>Clearance RES</td>
</tr>
<tr>
<td>Size &lt;1 kD</td>
<td>Size ~150 kD</td>
</tr>
<tr>
<td>Oral</td>
<td>Parenteral</td>
</tr>
<tr>
<td>Can cross BBB</td>
<td>Do not cross BBB</td>
</tr>
<tr>
<td>Half-life = minutes to hours</td>
<td>Half-life = 3–6 weeks</td>
</tr>
<tr>
<td>Immunogenicity (no)</td>
<td>Immunogenicity (yes)</td>
</tr>
</tbody>
</table>

RES = reticuloendothelial system; BBB = blood-brain barrier.


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**Naming Conventions For Therapeutic mAbs**

<table>
<thead>
<tr>
<th>Source (% human protein)</th>
<th>Mouse (0% human)</th>
<th>Chimeric (65% human)</th>
<th>Humanized (&gt; 90% human)</th>
<th>Human (100% human)</th>
</tr>
</thead>
</table>

**Generic suffix:** -omab, -ximab, -zumab, -umab

**Immunogenicity potential**

High

Low

Four Injectable Monoclonal Antibodies to CGRP or Its Receptor

<table>
<thead>
<tr>
<th></th>
<th>Erenumab</th>
<th>Fremanezumab</th>
<th>Galcanezumab</th>
<th>Eptinezumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Studied for</strong></td>
<td>EM, CM</td>
<td>EM, CM, eCH, cCH</td>
<td>EM, CM, eCH, cCH</td>
<td>EM, CM</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>Monthly SC</td>
<td>Monthly or Q3 month SC; IV load for CH</td>
<td>Monthly SC</td>
<td>Q3 month IV</td>
</tr>
<tr>
<td><strong>AB Type</strong></td>
<td>Fully human</td>
<td>Humanized</td>
<td>Humanized</td>
<td>Humanized</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>CGRP receptor</td>
<td>CGRP peptide or ligand</td>
<td>CGRP peptide or ligand</td>
<td>CGRP peptide or ligand</td>
</tr>
<tr>
<td><strong>Indication(s)</strong></td>
<td>Migraine prevention</td>
<td>Migraine prevention</td>
<td>Migraine prevention, Cluster headache</td>
<td>Migraine prevention</td>
</tr>
</tbody>
</table>

eCH = episodic cluster headache; eCH = chronic cluster headache.

Phase 3 Trials: 6-Month EM Prevention

Erenumab (EREN) and Galcanezumab (GAL) Efficacy

Primary endpoint: monthly migraine day (MMD) reduction vs placebo

**Erenumab STRIVE**

- BL = baseline; LS = least squares; SE = standard error.
Phase 3 Trials: 3-Month EM Prevention

Erenumab, Fremanezumab (FREM), and Eptinezumab (EPT) Efficacy

Primary endpoint: reduction of MMDs


Pivotal or Phase 3 CM Trials

Erenumab, Galcanezumab, and Fremanezumab Efficacy

Primary endpoint: reduction in MMDs

Eptinezumab Phase 2 CM Prevention

*P < .05; †P < .005 vs placebo (one-sided, not corrected for multiplicity)


Trial of Galcanezumab in Prevention of Episodic Cluster Headache

<table>
<thead>
<tr>
<th>End Point</th>
<th>Placebo (N=57)</th>
<th>Galcanezumab (N=49)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in Weekly Frequency of Cluster Headache (least-squares mean; wks 1-3)</td>
<td>-5.2 ± 1.4</td>
<td>-8.7 ± 1.4</td>
<td>0.04</td>
</tr>
<tr>
<td>% Response at Wk 3</td>
<td>53%</td>
<td>71%</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Safety and Tolerability of mABs

• In phase 2 and 3 trials of mABs, discontinuation rate due to AEs was 0–3.7% vs 8–27% for placebo; this discontinuation for mABs is much lower than occurred in studies and occurs clinically with currently approved oral preventive drugs

• The tolerability of the mABs is excellent, and injection-site reactions are the only AEs seen a bit more often than with placebo in the 3 subcutaneous mABs

• Safety also has been excellent, with no safety signals and no plan for requiring blood monitoring or other monitoring

Clinical Utility of the 4 mAbs

• For example, with erenumab in CM prevention, a 6.7-day reduction in MMDs was found in the pivotal trial, which would represent 79 fewer migraine days per year\textsuperscript{1}

• In galcanezumab EM registration studies\textsuperscript{2,3} and eptinezumab phase 2 CM studies,\textsuperscript{4} ≥75% responder rates were ≥33%

• All 4 mAbs work in CM prevention with medication overuse and without (pre-specified secondary analyses)\textsuperscript{4-7}

• Erenumab (140 mg) worked better in patients who had failed ≥2 preventive meds vs none, odds ratio 4.2 vs 1.3 (pre-specified secondary analysis)\textsuperscript{8}

Conclusions:
Reasons for Optimism

• Better recognition of individual patient characteristics
• New routes of administration of existing therapies
• New acute medications in development
• New preventive treatments in development
• Better understanding of migraine physiology
Diagnosing and Managing Primary Headache Disorders in the Primary Care Setting: Challenges and Opportunities

Extra Resources

- Click here for the Interactive Decision Tree
- Click here for the Interactive Headache Cases
- Click here for the Migraine Advances Website

This activity is supported by an educational grant from Lilly.
Diagnosing and Managing Primary Headache Disorders in the Primary Care Setting: Challenges and Opportunities

Please visit HTTPS://MIGRAINE.POSTERPROGRAM.COM/
Additional Reading

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## Resources and Societies

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<td>American Migraine Foundation</td>
<td><a href="https://americanmigrainefoundation.org/">https://americanmigrainefoundation.org/</a></td>
</tr>
<tr>
<td>International Headache Society Classification; ICHD-3</td>
<td><a href="https://ichd-3.org/">https://ichd-3.org/</a></td>
</tr>
<tr>
<td>International Headache Society</td>
<td><a href="https://www.ihs-headache.org/">https://www.ihs-headache.org/</a></td>
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<tr>
<td>National Institute of Neurological Disorders and Stroke</td>
<td><a href="https://www.ninds.nih.gov/Disorders/All-Disorders/Headache-Information-Page">https://www.ninds.nih.gov/Disorders/All-Disorders/Headache-Information-Page</a></td>
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