Prevalence & Burden of Migraine

- 13% prevalence in US in any given year
- 18% women; 6-7% men
- One of leading causes of disability world-wide
- High socio-economic burden
- Most common neurologic disease seen in primary care
- Migraine most common type of primary headache seen in a primary care office
- Not enough neurologists or headache specialists to see the 38 million Americans with migraine

Diagnosis of Migraine

At least 5 attacks lasting 4-72 hours with at least 2 of the following:

1. Unilateral location
2. Pulsating quality
3. Moderate to severe pain
4. Aggravation or avoidance of physical activity

During the headache at least one of the following:

1. Nausea and/or vomiting
2. Photophobia & phonophobia
3. Not better accounted for by another ICHD-3 diagnosis

ID Migraine

During the last 3 months, did you have the following with your headaches?

1. You felt nauseated or sick to your stomach
   Yes ___   No ___

2. Light bothered you (a lot more than when you don’t have headaches)
   Yes ___   No ___

3. Your headaches limited your ability to work, study, or do what you needed to do?
   Yes ___   No ___


Classification of Migraine

• Episodic - less than 15 days per month of headache
• Infrequent Episodic < 4 headache days/month
• Frequent Episodic 4 or more days/month
• Chronic - 15 or more days per month of headache for at least 3 months
• Migraine may or may not be associated with medication overuse
Meet Nancy

- 38-year-old school teacher with 20 year history of migraine without aura
- Takes oral Sumatriptan 100 mg for acute treatment
- Does not work well if nauseated or if wakes up with severe headache as is typical when on her menses
- Tried Sumatriptan 6 mg injection but caused flushing, chest tightness, and headache seemed to get worse before it got better
- Would like other options for acute treatment
- Has no medication allergies
- No cardiac disease

Nancy’s Journey

- Migraine attacks are now 1-2 times per week
- Missing 1 day of work per month due to migraine
- Topiramate caused cognitive impairment & fatigue
- Amitriptyline caused dry mouth, constipation, and weight gain
- Anti-hypertensives not ideal due to low blood pressure
- Has 2 children ages 8 and 10
- Husband had vasectomy
- Asks “What is new for acute & preventive treatment”
- She states “I want my life back”
Evolution of Chronic Migraine (CM) from Episodic Migraine (EM)

- Patients may transition among these 3 migraine states in the direction of increasing and decreasing frequency
- Transitions occur over weeks to months
- CM develops in individuals with EM at the rate of 2.5% per year


Patient Characteristics of EM Versus CM

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>EM</th>
<th>CM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Characteristics</strong></td>
<td></td>
<td></td>
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<tr>
<td>Headache frequency, days/mo</td>
<td>&lt;15</td>
<td>≥15</td>
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<tr>
<td>Report severe headache pain (%)</td>
<td>78.1</td>
<td>92.4*</td>
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<tr>
<td>Duration of headache pain without medication (mean h)</td>
<td>38.8</td>
<td>65.1*</td>
</tr>
<tr>
<td>Duration of headache pain with medication (mean h)</td>
<td>12.8</td>
<td>24.1*</td>
</tr>
<tr>
<td><strong>Sociodemographic Characteristics</strong></td>
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<tr>
<td>Race, % white</td>
<td>87.3</td>
<td>90.7</td>
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<td>Women, %</td>
<td>80.0</td>
<td>78.6</td>
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<tr>
<td>Low household income, % &lt;$22,500/y</td>
<td>24.9</td>
<td>29.9*</td>
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<tr>
<td><strong>Comorbidities</strong></td>
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<tr>
<td>Depression, %</td>
<td>17.2</td>
<td>30.2*</td>
</tr>
<tr>
<td>Anxiety, %</td>
<td>18.8</td>
<td>30.2*</td>
</tr>
<tr>
<td>Obesity, %</td>
<td>21.0</td>
<td>25.5*</td>
</tr>
<tr>
<td>Cutaneous allodynia, %</td>
<td>63.2</td>
<td>68.3*</td>
</tr>
</tbody>
</table>

*Indicates statistical significance (P<0.05) between EM and CM

Pathophysiology of Migraine

Migraine - An Inflammatory Event

- Activation of the trigeminovascular (TG) system occurs during migraine
- Neuropeptides include CGRP, Substance P, Bradykinin & PACAP38 (released from neurons and glial cells)
- Neurotransmitters include Glutamate, GABA & dopamine and may be involved in migraine and inflammation
- Prostaglandin, especially PGE, is elevated during migraine and contributes to vasodilatation & hyperalgesia
Key Steps in Migraine Evolution

- Trigeminovascular system gets activated
- Trigeminal nerves release neurotransmitters and neuropeptides such as CGRP
- Nociceptive (painful) signals can be transmitted through this pathway during a migraine
- Primary afferents of the trigeminal ganglion innervate the dura and dura vasculature and synapse onto the trigeminocervical complex in brainstem (2nd order neurons)
- Transmission of pain can travel up to thalamus and cortex

What is CGRP?

- Calcitonin gene-related peptide - a 37 amino acid polypeptide in neurons & glial cells ( Universally present)
- Receptors to CGRP are located throughout the trigeminal system and multiple brain regions
- CGRP is a vasodilator and causes neurogenic inflammation
- CGRP modulates pain signaling
CGRP & Migraine: Where is the evidence?

- CGRP levels elevated during migraine attack (measured external jugular vein)\(^1\)
- Infusion of CGRP in migraine patients can cause migraine\(^2\)
- Infusion of CGRP blocking medication can resolve a migraine attack in a migraine individual\(^3\)
- Development of new targeted CGRP blocking molecules show promise in migraine treatment (including large monoclonal antibodies and small molecule oral medications called “gepants”)


Acute Migraine Treatment Goals

- Rapid relief of headache pain
- Relief of “most bothersome symptoms” (MBS) including nausea, photophobia, and phonophobia
- Sustained pain freedom
- No need to rescue or take a 2\(^{nd}\) dose
- Return to full function
- Little to no side-effects from acute medication
### Current, New & Emerging Acute Migraine Treatment Options

- Triptans
- Ergots/Dihydroergotamine
- NSAIDS
- Non-specific Options (Analgesics, Butalbital, Narcotics)
- SpringTMS
- GammaCore
- Cefaly Device
- Oral CGRP antagonists in clinical development
- Lasmiditan in clinical development

### Safety Concerns of Acute Migraine Prescription Treatment Options

- Triptans and Ergots/Dihydroergotamine are all contraindicated in patients with coronary artery disease, peripheral vascular disease, uncontrolled high blood pressure & those at high risk of cardiac disease
- Triptans and Ergots/Dihydroergotamine should not be taken in the same 24 hour period due to risk of vasoconstriction
- Risk of medication overuse with triptans
- Narcotics and Butalbital are non-specific in treatment of acute migraine, can lead to medication overuse, overdose, sedation, abuse, and can cause preventives to be less effective
- NSAIDs contraindicated in many patients due to GI issues or those at risk for GI bleeding and those with certain kidney conditions

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Triptans - What Is New?

- Seven triptans (Sumatriptan, Rizatriptan, Zolmitriptan, Almotriptan, Eletriptan, Naratriptan, Frovatriptan)
- Sumatriptan has oral, injectable, nasal, breath-powered formulations
- New: 3 mg injectable Sumatriptan in auto-injector (Zembrace)  
  Key feature: tolerability and ease of use, dose is 3 mg subcutaneous injection may repeat 1 hour, max is 12 mg in 24 hours
- New: breath-powered nasal delivery of Sumatriptan powder to posterior nasal cavity - Onzetra Xsail 1 nosepiece each nostril 11 mg per nosepiece, total dosage 22 mg; may repeat 2 hours; max 44 mg in 24 hours


Emerging Triptan Treatment

- DFN-02 (Nasal Sumatriptan 10 mg combined with an absorption enhancement agent to increase bioavailability)¹
- Key features - quick onset of action, well-tolerated, and good sustained pain-free results in clinical studies
- Not yet FDA approved

NSAIDS & Migraine

- **Diclofenac 50 mg powder** FDA approved for acute treatment of migraine (Cambia). Dosage is 1 packet (50 mg) in a 24 hour period. Most common adverse effects in clinical trials greater than placebo were nausea and dizziness.

- **Naproxen 500 mg combined with Sumatriptan 85 mg** (Treximet) FDA approved for acute treatment of migraine.

- **Emerging**: oral form of Celecoxib under development for acute migraine. In a placebo-controlled, double-blind, cross-over study, 63 patients treated 3 moderate to severe migraine headaches. In the 120 mg Celecoxib group, 2-hour pain freedom occurred in 29.1% of patients, 26.1% in the 240 mg Celecoxib group, and 17.6% in placebo group. Most common side-effects in active group dysgeusia (11.8%) and nausea (5.9%). The 120 mg dose is being evaluated in follow-up clinical trials.

- **Black box warning** for all NSAIDs includes increased risk of cardiovascular thrombotic events and increased risk for GI adverse events.


Neurostimulators & Migraine
SpringTMS device

- Non-invasive neurostimulator (transcranial magnetic stimulation)
- Referred to as the sTMS mini (newer smaller version)
- FDA approved for acute & preventive treatment of migraine with and without aura
- Efficacious & safe in clinical studies\(^1\)
- Dose is 2-4 pulses, wait 15 minutes, may repeat for acute
- Dose is 4 pulses twice a day for prevention
- Requires a prescription ($750 for 90 days) and is a rental unit\(^2\)
- $450 for first 90 days with refund if less than 30% reduction in headache days based on diary collection for minimum of 21 days each month for first 3 months
- Proposed mechanism of action (MOA) is inhibition of cortical spreading depression

2. www.eneura.com accessed 9/09/18

Cefaly Device

- Supraorbital (1\(^{st}\) branch of trigeminal nerve) non-invasive neurostimulator
- FDA approved for acute & prevention of migraine
- Showed efficacy & safety for acute migraine\(^1\)
- Dose is 60 minutes for acute migraine at high intensity
- Dose is 20 minutes daily for migraine prevention
- Requires a prescription in the US $349 for acute or prevention unit; $499 for the dual unit; 60 day money back guarantee\(^2\)
- Small on-going cost for electrodes once purchased

2. www.cefaly.us Accessed 9/09/18
GammaCore Device

- Non-invasive vagal nerve stimulator
- MOA inhibition of glutamate, decreased cortical spreading depression
- FDA approved for acute treatment of cluster and migraine headache\(^1\)
- Dose for cluster: 3 pulses (2 minutes each) wait 3 minutes may repeat x3 pulses
- Dose for migraine: 2 pulses x2 wait 20 minutes may repeat
- Rental unit, available as a prescription
- 31 day free trial available

MOA = mechanism of action


CGRP Oral Antagonists - Emerging Acute Treatment Ubrogepant

- Limitations of current acute migraine treatment include those who can’t take triptans due to contraindications or side-effects or ineffectiveness
- CGRP oral medications appear to be free of vasoconstriction and have similar efficacy to triptans for acute migraine. None currently available - all in clinical development
- Ubrogepant 5-7 hour half-life; T max is 1.5 hours
- Two pivotal phase 3 clinical trials with Ubrogepant now completed.
  - ACHIEVE I study enrolled 1,327 adults and was a single migraine attack treatment for moderate to severe migraine looking at 50 and 100 mg dose Ubrogepant vs placebo. Statistically significant difference in pain-freedom vs placebo as well as absence of most bothersome symptom (MBS) and most common MBS photophobia.
  - ACHIEVE II enrolled 1,686 patients ages 18-75 and looked at 25 and 50 mg dose Ubrogepant vs placebo. Both doses superior to placebo for pain-freedom. The 50 mg dose superior in relief of MBS vs placebo.
- Most common side-effects were nausea and dizziness in less than 2.5% of patients enrolled in the clinical trials. Four causes of liver enzymes reported but none felt to be related to the study drug.

CGRP Oral Antagonists - Emerging Acute Treatment
Rimegepant

- Rimegepant is an oral CGRP antagonist in development
- Half-life is 10 hours
- Dosage in phase 3 trials is 75 mg
- Two pivotal trials: Study 301 & 302 met primary end-points of pain-freedom and relief of MBS. In Study 301, 1,084 adults. 19.2% pain-free at 2 hours vs 14.2% placebo, 36.6% relief of MBS vs 27.7% placebo. Study 302 had 1,072 patients, 19.6% pain-free at 2 hours vs 12.0% placebo, 37.6% relief of MBS vs 25.2% placebo. At 2-24 hours sustained pain relief 38.9% vs 27.9% placebo. Study 301 and Study 302 the 2-24 hour sustained pain relief was 42.6% active drug vs 26.5% placebo
- Well-tolerated with 1.4% nausea compared to 1.1% placebo. No “triptan” like side-effects
- An open label trial with daily Rimegepant underway


Lasmiditan

- Oral serotonin receptor agonist that targets 5-HT 1F receptor (unlike triptans which target 5-HT 1B/1D receptors)
- No vasoconstrictive effects
- Could be useful for patients with cardiovascular disease for whom triptans contraindicated
- At 2 hours, 60-65% had pain relief with Lasmiditan 200 mg compared to 40% with placebo
- Some CNS side-effects including dizziness, paresthesia, somnolence, and fatigue
- Chest tightness (common side-effect of triptans) did not occur
- Not yet FDA approved

Positive Pivotal Trials. Family Practice News. August 2018; Vol 48 (12); 1,4,6.
New & Emerging Preventive Migraine Treatments

Current Preventive Landscape

- Anti-depressants
- Anti-epileptics
- Anti-hypertensives
- Onabotulinum Toxin A
- Non-invasive neurostimulators
- Herbal Preventives
- Hormonal Approaches
### FDA Approved Oral Medications for Prevention of Episodic Migraine

- Divalproex sodium
- Topiramate
- Timolol
- Propanolol

Note: others commonly used but not FDA approved include Amitriptyline, Venlafaxine, Metoprolol, Naldolol, Atenolol, Nortriptyline, Duloxetine, Verapamil, Gabapentin, Candesartan, Fluoxetine, Escitalopram, Cyproheptadine.

Short-term prevention menstrual migraine: Frovatriptan, Naratriptan, Sumatriptan, Zolmitriptan, Rizatriptan. All have shown efficacy in clinical trials but not FDA approved for prevention.

### Onabotulinum Toxin A (Botox)

- FDA approved for chronic migraine only (not EM)
- Approved protocol is 155 units injected in 31 individual sites every 12 weeks
- Sites include procerus, corrugators, frontalis, temporalis, occipitalis, upper paracervicals, and upper trapezius
- FDA approved for chronic migraine in 2010
- MOA includes inhibition of release of neuropeptides including CGRP from peripheral nervous system
CGRP Monoclonal Antibodies

Specifically designed to target migraine prevention

New: CGRP Monoclonal Antibodies for Migraine Prevention

• Target specific preventive treatment to block the activity of CGRP either by binding directly to the CGRP ligand or by blocking the CGRP receptor in the peripheral nervous system
• Net effect is to block CGRP activity, lessen the migraine cascade of inflammatory activity, and prevent transmission of pain signals to travel to higher order neurons
• All CGRP monoclonal antibodies (CGRP mAB) work on the peripheral nervous system (PNS) and do not work directly on the central nervous system (CNS)
• CGRP mAB are large monoclonal antibodies and cannot cross the blood-brain barrier to any significant degree
Key Features CGRP mAB’s

- Work on peripheral nervous system (PNS)
- No central nervous system side-effects (CNS)
- No effect on liver or kidney
- No significant drug to drug interactions
- Degraded by enzymatic proteolysis
- Favorable side-effect profile in clinical trials
- Approved for migraine prevention in adults
- No data in pregnancy & breast-feeding
- Not available in oral tablet
- Expensive to make (grown in cell cultures)

Erenumbab-aooe

- FDA approved May 2018 for the preventive treatment of migraine in adults
- Fully humanized immunoglobulin (IgG2) selectively targets and blocks the CGRP receptor
- Competes with the binding of CGRP & inhibits its function at the CGRP receptor site
- Half-life is 28 days
- Dose is 70 or 140 mg monthly subcutaneous injection into upper arm, abdomen or thigh with auto-injector
- Brand name Aimovig (Amgen/Novartis)
Clinical Study Highlights

- STRIVE - multi-center, PB, DB, 24-week study Aimovig vs placebo in EM
- Mean Migraine Frequency Baseline 8 MMD; 3.7 reduction in 140 mg-arm Aimovig, 3.2 reduction in 70-mg arm; 1.8 reduction in placebo arm; statistically significant (months 4-6 compared to baseline)
- Exploratory analysis 22% in 140 mg-arm, 20.8% in 70 mg-arm, and 7.9% in placebo arm 75% or greater reduction MMD
- CM study multi-center, PB, DB, 12-week study in CM reduction in MMD by 6.6 compared to 4.2 placebo group
- Post-hoc analysis 21% (140 mg-arm), 17% (70 mg-arm), 8% (placebo arm) 75% or greater reduction in MMD

MMD = monthly migraine days

Aimovig (erenumab-aooe) prescribing information. 2018. Amgen Inc.

Safety Concerns

- Erenumab has been evaluated in 2,537 patients with migraine who received at least 1 dose of Erenumab. Among this population, 2,057 were exposed to Erenumab (70 or 140 mg monthly) for 6 or more months
- The most common adverse reactions (incidence ≥3%) were injection site reactions and constipation. Injection site reactions were 3% in the placebo group, 6% in the 70 mg group, 5% in the 140 mg group. Constipation occurred in 1% of the placebo group, 1% in the 70 mg group, 3% in the 140 mg group
- Potential for immunogenicity. In studies with Erenumab, 6.2% of patients receiving 70 mg monthly developed anti-erenumab antibodies, 2.6% of patients receiving 140 mg monthly developed anti-erenumab antibodies. No impact on efficacy or safety was noted in these patients but data too limited to make a definitive conclusion

Fremanezumab-vfrm

- FDA approved 9/14/18 for the prevention of migraine in adults
- Fully humanized immunoglobulin (IgG2a) binds to the CGRP ligand
- Half-life is 31 days
- Dose is 225 mg monthly or three 225 mg subcutaneous injections quarterly
- Available in a pre-filled syringe (1.5 ml)
- May be injected in upper arm, abdomen, or thigh
- Brand name Ajovy (Teva)

Ajovy (Fremanezumab-vfrm) prescribing information. 2018. Teva.

Clinical Study Highlights

- In the Halo-EM Phase 3 Trial, 875 patients randomized to 225 mg monthly dose of Fremanezumab, a single dose of 675 mg followed by placebo, or placebo for 12 weeks. Mean monthly migraine days (MMD) decreased from 8.9 to 4.9 in monthly dosing group, decreased from 9.2 to 5.3 in the single-higher dose group, and 9.1 to 6.5 in placebo group. Statistically significant 1.3-1.5 reduction in mean MMD compared to placebo.
- In the Halo-CM Phase 3 Trial, 1,130 patients randomized to Fremanezumab quarterly dosing, monthly dosing, or placebo in a 23 week study. Primary endpoint was mean change in number of headache days from baseline. Reduction was 4.3 in quarterly dosing group, 4.6 with monthly dosing group, and 2.5 with placebo group. Patients with at least 50% reduction in headache days per month was 38% in quarterly group, 41% in monthly group, and 18% in placebo group. 20-22% of patients continued on current preventive medication but had to be off Onabotulinum Toxin A for at least 4 months before screening.

**Safety Concerns**

- Fremanezumab was studied in 2,512 patients who received at least one dose of Fremanezumab. Most common adverse reactions seen in the clinical trials (incidence at least 5% & greater than placebo) were injection site reactions including injection site pain, induration, and erythema. Injection site reactions occurred in 43% of the 225 mg monthly dose group, 45% of the 675 mg quarterly group, and 38% in placebo group. Total of 1% discontinued in the clinical trial.

- Fremanezumab contraindicated in patients with serious hypersensitivity to Fremanezumab or to any of the excipients (EDTA, L-histidine, polysorbate, sucrose).

- Hypersensitivity reactions (rash, pruritus, urticaria) were mild to moderate in most cases and were reported from hours to 1 month after administration in the clinical trials. A few cases required corticosteroid treatment. No cases of anaphylaxis were reported.

- Potential for immunogenicity. In 3-month placebo-controlled studies, development of anti-fremanezumab antibodies as observed in .4% of treated patients. No conclusions can be made on any impact of ADA on safety of efficacy.

ADA = anti-drug antibodies

Fremanezumab-vfrm prescribing information. 2018. Teva Pharmaceuticals USA.

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**Galcanezumab-gnIm**

- FDA approval 9/27/18 for the prevention of migraine in adults
- Fully humanized immunoglobulin (IgG4) binds to the CGRP ligand
- IgG4 less innate immune response compared to IgG2
- Half-life is 27 days
- Two cases urticaria (not anaphylaxis) in clinical trials seen – was not immediate nor after 1st injection
- Approved dose is loading dose of 240 mg subcutaneous injection (given as two 120 mg auto-injectors) followed by monthly 120 mg injection
- Brand name Emgality (Lilly)

Clinical Study Highlights

- Galcanezumab was studied for EM in EVOLVE-1 and EVOLVE-2 DB, PC, 6-month clinical trials with 120 mg dose vs placebo. Primary objective was change in monthly migraine days. Reduction of 4.7 MMD vs 2.8 placebo in EVOLVE-1 trial and reduction of 4.3 vs 2.3 placebo in EVOLVE-2. Baseline was 9 MMD in these EM trials. 59-62% at least 50% reduction vs 36-39% placebo. 34-39% at least 75% reduction vs 18-19% placebo.

- REGAIN was a 3 month DB, PC, 3 month study. Propanolol or Topiramate was continued in 15% of study participants. The 240 mg dose was not superior to the 120 mg in this study. Baseline MMHD was 20. In the active group 4.3 fewer MMHD vs 2.7 reduction in placebo group.

- Open label-extension study with 240 mg loading dose Galcanezumab followed by 120 mg monthly injection (80% EM, 20% CM) demonstrated 6.4 fewer MMHD from baseline of 10 at 12 months.


Safety Concerns

- Galcanezumab has been studied in over 2,500 patients in clinical trials. Most common adverse reaction greater than placebo was injection site reactions seen in 18% of patients receiving Galcanezumab compared to 13% in placebo group. Rash, urticaria and dyspnea were reported.

- Galcanezumab is contraindicated in patients with hypersensitivity to Galcanezumab or any of its excipients (L-histidine, polysorbate).

- Hypersensitivity reactions occurred in the clinical trials.

- Potential for immunogenicity. In the 3-6 month trials, 4.8% of patients developed antibodies to Galcanezumab. In the 12 month trial, up to 12.5% developed ADA. No affect was seen on pharmacokinetics. No conclusions can be made on any impact of ADA on safety of efficacy.

ADA = anti-drug antibodies

Emgality Prescribing Information. 2018. Data on File Lilly USA.
Eptinezumab

- In clinical development. Promise-2 trial results presented at AAN 2018. 1,072 patients with CM ages 18-65 enrolled and received either 100 or 300 mg Eptinezumab or placebo. Reduction of 7.7 to 8.2 MMDs vs 5.6 in placebo group over week 1-12. About 1/3 of patients achieved 75% or greater reduction in MMDs in week 1-12 vs 15% in placebo group.
- CGRP mAb given intravenously; if approved expected to be q3 months.
- Fully humanized immunoglobulin.
- Features include quick onset of action and high bioavailability. Reduction in migraine seen first 24 hours post-infusion in Promise-2 Study.
- Drawback is the need for access for infusion & added cost of infusion.


Important Points about CGRP mAb’s

- No head to head comparator trials.
- Onabotulinum Toxin A had to be stopped 4 months or more before CGRP trial entry so safety of having patients on both preventives not known.
- Long-term safety not known (could there be a downside of long-term CGRP suppression).
- No data on safety during pregnancy & lactation.
- Only FDA approved for 18 & over in US.
Atogepant

- Oral CGRP Receptor Antagonist in clinical development for prevention of migraine
- Phase 2b/3a study looked at daily dosing ranging from 10 mg daily up to 60 mg bid compared to placebo in 834 subjects. All treatment groups showed statistical significance over placebo in primary efficacy endpoint of reduction from baseline in mean migraine/probable migraine days per month
- Side-effects included nausea, fatigue, constipation, nasopharyngitis, and UTI in a small number of participants. No sign of hepatotoxicity in this 12 week trial
- Has a 10 hour half-life
- Potential option for patients who prefer oral daily preventive for migraine as opposed to injection or IV administration of a CGRP mAB


Back to Nancy

- Acute non-oral options include Sumatriptan 3 and 4 mg injection for potentially less side-effects she had with the 6 mg dose and/or a nasal formulation of a triptan and/or nasal dihydroergotamine (DHE)
- Short-prevention for menstrual migraine with Frovatriptan or Naratriptan & an NSAID
- Prevention with one of the new CGRP Monoclonal Antibodies based on tolerability issues with 2 standard oral preventives tried in the past (Topiramate and Amitriptyline)
- Onabotulinum Toxin A an option if she transforms to CM (her current pattern is 1-2 migraine headache days per week)
- Non-pharmacologic treatment including exercise, healthy eating, adequate sleep, stress-reduction, keeping a headache diary, and close follow-up
Who is a candidate for a CGRP mAB?

- Adults with migraine who have 4 or more monthly migraine headache days
- Migraines are disabling
- Current or past standard preventives have either not been tolerated or have been ineffective (most insurance companies will require trial of 2 preventives prior to approval of CGRP mAB)
- If adult has chronic migraine, insurance company may require failure of 6 month trial with Onabotulinum Toxin A

Summary

- CGRP is a neuropeptide that plays a key role in migraine pathogenesis
- CGRP Monoclonal Antibodies represent a new category for migraine prevention for adults in the US and 3 CGRP mAB’s are now FDA approved
- New & emerging acute migraine treatment options include new formulations for Sumatriptan and in development an oral 5-HT 1F agonist
- Oral CGRP receptor antagonists in clinical development show promise for both acute and preventive treatment of migraine
- Non-invasive neurostimulators for migraine include the Cefaly device, TMS device, and GammaCore. All require a prescription in the US
- Knowledge of how to incorporate new acute and preventive migraine treatments in our migraine patients can reduce the burden of migraine in our patients lives
Suggested Articles


