A CME-certified Grand Rounds Activity

Jointly provided by the Potomac Center for Medical Education and Rockpointe

This activity is supported by an educational grant from Lilly. For further information concerning Lilly grant funding visit www.lillygrantoffice.com.

Educational Objectives

At the conclusion of this activity, participants should be able to:

- Examine the epidemiology, differential diagnosis, and impact of migraine within the primary-care patient population
- Describe the pathophysiology of migraine, including the role of calcitonin gene-related peptide (CGRP)
- Delineate current standards of pharmacologic and nonpharmacologic management for the preventive and acute management of migraine
- Assess clinical safety and efficacy data for emerging therapeutic agents for the prevention and treatment of migraine

Several Types of Headaches (HAs)

Primary Examples

- Migraine
- Tension type
- Cluster

Our focus today will be migraines

Secondary Examples

- Infectious (Meningitis, Sinusitis)
- Space occupying lesion (abscess, mass)
- Bleeding (SAH)
- Vascular (cerebral venous thrombosis, cervical artery dissection)
- Rheumatologic (GCA)
- Ophthalmological (angle-closure glaucoma, optic neuritis)
- Neurological (trigeminal neuralgia, post-herpetic neuralgia)
- Idiopathic intracranial hypertension
- Others (acute hypertension, CO poisoning)

Migraine Impact and Epidemiology

- One in five US adults has migraine[1]
  - 28 million persons have migraine each year in the US
- Prevalence
  - Women 25% (lifetime)
  - Men 8% (lifetime)
  - ~ 70% of migraineurs have positive family history in first-degree relative
- 5–9 million PCP office visits per year in US due to migraines[3]
- 5 million headache annual visits to US EDs[2]
  - Ranks #5 for annual emergency department visits[1]
- Associated with ~ $17 billion/year in direct and indirect healthcare costs[1]

1. Sinclair AJ et al. *Pract Neurol*. 2015; 15:411-423. 2. Becker WJ et al. *Can Fam Physician*. 2015;61:670-679.
3. Minen MT et al. *Cephalgia*. 2015;36:358-370.

Lizzy, a 31-year-old Mother

- Asks you for help with her sinus headaches. She has been getting them for several years but they are occurring almost daily now.
- Predominantly frontal and maxillary in location; not throbbing.
- Takes acetaminophen almost daily, along with pseudoephedrine preparations and occasional loratadine when she has watery eyes and nasal congestion.
- *What else do you need to know to help Lizzy?*
- *What treatments could be offered?*

Differentiating Migraine from Other Types of Headache

Basics of the History and Physical Exam
Headache Screening

- Inquire about
  - Timing/frequency
  - Exacerbating factors/triggers
    - What meds have been tried
    - Use/overuse of meds
  - Location
  - Intensity
  - Nature of pain
  - Associated symptoms
    - Visual, motor, sensory, GI
- Evaluate
  - Patient walking, body language
  - Assess symmetry of CN, motor, sensory, coordination, DTRs
  - Palpate head, arteries, trigger points
  - Examine neck for stiffness and ROM
  - Perform fundoscopic exam
  - Examine oral cavity/TMJ

Diagnosis and Treatment of Headache. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI); 2009.

Episodic Migraine (EM) Recognition by ICHD Criteria

Migraine without Aura (1.1)

At Least FIVE Attacks with:

- At least 2 of the following
  - Unilateral
  - Pulsating
  - Moderate to severe pain
  - Aggravated by or avoidance of routine physical activity
- At least 1 of the following
  - Nausea and/or vomiting
  - Photo and phonophobia
- No organic disease

Migraine with Aura (1.2.1-6)

At Least TWO Attacks with:

- At least 1 fully reversible symptom without motor
  - Visual + and/or -
  - Sensory + and/or -
  - Dysphasic speech
- At least 2 of the following
  - At least one aura symptom develops gradually over ≥5 min or different symptoms occur in succession over ≥5 min
  - Each symptom lasts ≥5 and ≤60 min
- 1.1 begins with aura or in ≤60 min
- No organic disease

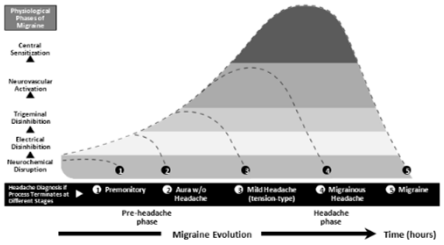
ICHD = International Classification of Headache Disorders. International Headache Society. *Cephalalgia.* 2013;33:629-808.

Headache Types

Chronic Migraine (CM)	Medication Overuse Headache (MOH)
• Headache ≥15 days/month AND duration ≥4 hours/day x > 3 mo • Not just "more" episodic migraine! • Evolves as complication of EM (2.5%/year) • More disabling with higher costs • Risk factors include: – Comorbidities (anxiety, depression, obesity) – Iatrogenic factors (medication type and frequency of use) • Can be reversed; goal is revert back to episodic migraine	• Pharmacologically maintained HA • >15 d/mo with HA • Regular acute drug use >10 d/mo (>15 d for simple analgesics) for >3 mo HA worsens over time of overuse • HA resolves or reverts to previous pattern within 2 mo of overuse elimination • ANY abortive medication can cause medication overuse headache!!

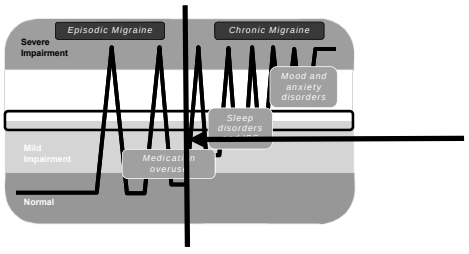
Natoli JL et al. *Cephalalgia.* 2010;30:599-609; CDCP. Census projections request (http://wonder.cdc.gov/population-projections.html). Accessed 10/9/17; Buse DC et al. *J Neurol Neurosurg Psychiatry.* 2010;81:428-432; Blumenfeld AM et al. *Cephalalgia.* 2011;31:301-315;. American Headache Society. http://www.americanheadachesociety.org/assets/1/7/Stephen_Silberstein_-_Medication_Overuse_Headache.pdf.

Understanding the Chronology of Migraine



Cady RK et al. *Headache.* 2002;42:204-216.

Migraine Evolution
From Episodic Attacks to Chronic Disease



Cady R et al. *Curr Pain Headache Rep.* 2005;9:47-52.

ID Migraine™ – A Validated Screener
Closing the HA Diagnosis Gap

Choose Yes or No

- When you have a HA, do you feel nauseated or sick to your stomach?
- When you have a HA, does light bother you (a lot more than when you don't have a HA)?
- During the last 3 months, have your HAs limited your ability to work, study, or do what you needed to do?

2/3 Yes for migraine:
- Sensitivity: 0.81
- Specificity: 0.75

= Positive predictive value of 93% in primary care setting

Lipton RB, et al. *Neurology.* 2003;61:375-382.

Indications for Diagnostic Testing

Red Flags
- Systemic symptoms: fever, weight loss
- Secondary risk factors: HIV, cancer
- Neurologic symptoms or signs
- Onset: new, sudden, abrupt, or split-second
- Older: especially >50 years
- Pattern change

Diagnostic testing indicated if ANY red flags are present

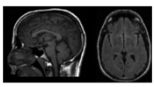
Green Flags
- Stable pattern >6 months
- Long-standing HA history
- Family history of similar HA
- Normal exams
- Consistently triggered by
  - Hormonal cycle
  - Specific sensory input
  - Weather changes

Diagnostic testing NOT indicated if only green flags present

Dodick D. *Adv Stud Med*. 2003;3:87-92.

If Indicated, Which Diagnostic Test?

- CT or MRI? With or without contrast?
  - Yield minimal without neurologic signs: <1% identify cause for HA
  - MRI: greater detail, more false positives
  - MRI for posterior fossa disease
  - MRI + MRA for suspected aneurysm/other vascular lesions
  - CT without contrast to R/O subarachnoid hemorrhage



- Weigh radiation exposure with CT, renal contrast concerns with CT and MRI vs potential yield of study
- CHOOSING WISELY: Don't perform neuroimaging studies in patients with stable headaches that meet criteria for migraine

Ropper A, Brown R, eds. *Adams and Victor's Principles of Neurology*. Eighth ed. New York, NY: McGraw-Hill; 2005:16-21; Avitzur O. *Neurology Today*. 2013;13:22-24; American Headache Society. http://www.choosingwisely.org/as-part-of-choosing-wisely-campaign-american-headache-society-releases-list-of-commonly-used-tests-and-treatments-to-question.

Back to Lizzy

- Further history: she used to have more common migraine headaches as a teen; these changed over time to less intense, daily "sinus" type headaches
  - In 2 studies, 86-88% of patients self diagnosed as sinus headaches actually met ICHD criteria as migraine or probable migraine[1,2]
- Based on diary review, 94% of headaches that prompt a visit to the PCP are migraine type headaches[3]
- You diagnose Lizzy with migraines; the appropriate treatments you provide help reduce her headaches by >50% over next couple of months

International Conference Headache Disorders/International Headache Classification from International Headache Society (ICS)[4]

1. Schreiber CP et al. *Arch Intern Med*. 2004;164:1769-1772.
2. Eross E et al. *Headache*. 2007;47:213-224.
3. Tepper SJ et al. *Headache*. 2004;44:856-864.
4. International Headache Society. IHS Classification ICHD-3. https://www.ichd-3.org/.

Key Takeaways

- If a patient self diagnoses their headache, don't assume they're right!!
- Migraine is the most common cause of headache that brings a patient to the doctor
- Recurring moderate to severe headache is migraine until proven otherwise
- Migraine patients can experience many different types of HAs from the same underlying mechanism
- Prompt treatment may restore normal neurologic function and prevent the evolution of EM to CM

The Many Manifestations of Migraine
And Current Approaches to Management

Ricky, a 31-year-old CPA

- Has history of very occasional migraines since his early 20s. Naproxen and/or a triptan usually provided relief
- Started new job 6 months ago, requiring him to work long hours
- Headaches have increased and now occur several days a week, especially on most weekend days for the last few months
- He is now taking an abortive medication most days a week

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
- Non-pharmacologic (behavioral, neuromodulation, complementary/alternative)

Principles of Management for the Patient

- Establish realistic expectations
  - ≈50% reduction with prevention
  - ≥70% relief with acute treatment
  - There is no cure!
- Encourage patients to participate in their care
  - Keep a headache diary, identify triggers
  - Accept that some Rx side effects are inevitable
  - Optimize behavioral management
  - Acute: administer treatment early; do not use more than 2-3x/week or 9 days/month
  - Prevention: follow guidelines for drug/complementary/alternative treatments
  - Regular patient follow-up with dose/drug/combination changes as needed

Behavioral Strategies

1. Sleep – 6 to 8 hours, consistent within 1 hour to bed/rise (even weekends!)
2. Exercise – Any better than none; aerobic >> nonaerobic
3. Stress management – Biofeedback/relaxation, cognitive-behavioral, time management
4. ↓Substance use – Taper caffeine to maximum 1-6 oz cup – Eliminate artificial sweeteners, decongestants, smoking
5. Eat – Fresh, non-processed, small, frequent healthy meals/snacks

Keeping a headache diary can help identify possible triggers

Acute (Abortive) Migraine Medications

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

Specific
- Triptans
- Ergotamine/DHE

CHOOSING WISELY
Don't recommend prolonged or frequent use of OTC pain meds for headache

New Formulations (FDA-approved)
- Breath-powered intranasal sumatriptan dry powder[1]
- New sumatriptan autoinjectors[2]

New Formulations (In development)
- Microneedle array skin patches (zolmitriptan, sumatriptan)
- Orally inhaled (zolmitriptan, DHE)
- New intranasal delivery: dry powder, enhanced permeation
- Sumatriptan liquid spray
- Gepants
- 5-HT1F receptor agonist (lasmiditan)[3]

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

Silberstein S. *Expert Opin Pharmacother.* 2012;13:1961-1968. 1. Tepper SJ *Headache.*2016;56:817; 2. Munjal S et al. *J Headache Pain.* 2017;18:17; 3. Tepper SJ et al. *Headache.* 2015;55:621-635.

Guidelines for Initiating Migraine Prevention Therapy

- Goals: reduce disability and medication overuse
- Many migraineurs qualify for prevention, few are offered it
- Institute preventive strategies if:
  - 2 attacks/mo with disability totaling >3 d/mo
    Recurring HA significantly interfering with patient's daily routine despite acute Rx
  - Presence of uncommon migraine conditions: hemiplegic migraine, prolonged aura, migrainous infarction
  - Patient preference, cost considerations, med intolerance
  - Acute medications overused >2 d/wk, ineffective, intolerable side effects, or contraindicated

Migraine Preventive Therapies
US Classification/Level of Evidence

Level of Evidence/Efficacy	Drug Class/Agent	
Level A Established Efficacy	Antiepileptic drugs: Divalproex sodium, sodium valproate, topiramate Beta blockers: Metoprolol, propranolol, timolol Triptans: Frovatriptan (for menstrual-related migraine) Angiotensin receptor blockers: Candesartan (studies now suggest level A efficacy)**	
Level B Probably Effective	Antidepressants/SSRI/SSNRI/TCA: Amitriptyline, venlafaxine Beta blockers: Atenolol, nadolol Triptans: Naratriptan, zolmitriptan (for menstrual-related migraine)	
Level C Possibly Effective	ACE inhibitors: Lisinopril Beta blockers: Nebivolol, pindolol Alpha agonists: Clonidine, guanfacine	Antiepileptic drugs: Carbamazepine Antihistamines: Cyproheptadine

Start low and go slow. Allow 2-3 months for full effect

*In ≥2 Class I Trials; †In 1 Class I or 2 Class II studies; ‡In 1 Class II Study
Silberstein SD et al. *Neurology* 2012;78;1337-1345. ** Not in original paper *Not approved for migraine prevention*

Treatment for Chronic Migraine
Institute Behavioral Strategies and Prevention Medications

- Specific FDA-approved medication: OnabotulinumtoxinA
  - Approved for prophylaxis of chronic migraine (≥15 headache days/month)
  - 8-9 fewer HA compared to 6-7 with placebo
  - 31 injection sites into head/neck Q 3 mo
  - Boxed warning re: possibility for spread causing weakness in distant area(s)
- OnabotulinumtoxinA blocks the presynaptic release of neurotransmitters, as an endopeptidase that interrupts the vesicle docking process

Linsenmeyer TA. *J Spinal Cord Med*. 2013;36:402-419.

Key Takeaways

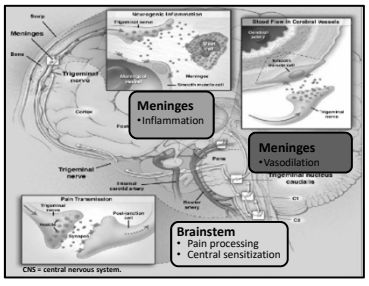
- Successful treatment of migraines includes a comprehensive approach of patient education, behavioral strategies, pharmacologic therapies and non-pharmacologic interventions
- Consider preventive medications for prolonged, severe or complicated HAs, or if abortive therapies are required more than 2x/week

Insights into Migraine Pathophysiology

Maria, a 38-year-old Female

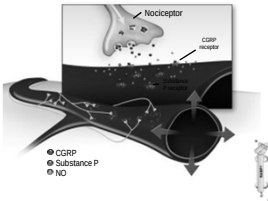
- Migraines began when she was 14
- Currently compliant with topiramate 50 mg BID; uses a triptan as needed
- In the last 3 months, her headaches have increased from 1x/wk to 3-4 days/wk despite optimal lifestyle management and trigger avoidance; they are not always relieved despite prompt triptan use

Migraine Pathogenesis

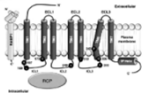


Adapted from Durham PL. *N Engl J Med*. 2004;350:1073-1075.

Calcitonin Gene Related Protein (CGRP) First Identified as a Potential Mediator of Trigeminal Inflammation



- 1st discovered as a potent vasodilator
- Initially considered important in migraine because of its potential *peripheral* actions
  - Vasodilation
  - Neuroinflammation
- Belongs to calcitonin family (calcitonin, amylin, adrenomedullin, intermedin) In humans, α-CGRP and β-CGRP isoforms



Brain et al. *Nature*. 1985;313:354; Edvinsson L, Uddman R. *Brain Res Brain Res Rev*. 2005;48:438-456; McCulloch J et al. *Proc Natl Acad Sci USA*.1986;83:5731-5735; Moskowitz MA. *Neurol Clin*. 1990;8:801-815.

New, Emerging and Alternative Approaches to Treating Migraine Headaches

CGRP in Migraine

- Potent vasodilator of cerebral arteries
- Released into jugular venous system during migraine
- Serum CGRP levels elevated in CM
- CGRP infusion evokes migraine
- Small-molecule CGRP-receptor antagonists (gepants) effectively abort migraine attacks
- Large molecule anti-CGRP and anti-CGRP-receptor monoclonal antibodies (mAbs) prevent EM and CM
  - *Because of large size, potential to cross blood brain barrier limited*
  - *mAb activity likely peripheral*

Adapted from AHS CMEP. Edvinsson L et al. *Neurosci Lett.* 1985;58:213-217; McCulloch J et al. *Proc Natl Acad Sci USA.* 1986;83:5731-5735; Edvinsson L et al. *Ann Neurol.* 1987;21:431-437; Lassen LH et al. *Cephalalgia.* 2002;22:54-61; Goadsby PJ, Edvinsson L. *Brain.* 1994;117:427-434; Olesen J et al. *N Engl J Med.* 2004;350:1104-1110; Ho TW et al. *Neurology.* 2008;70:1304-1312; Voss T et al. *Cephalalgia.* 2016;36:887-898.

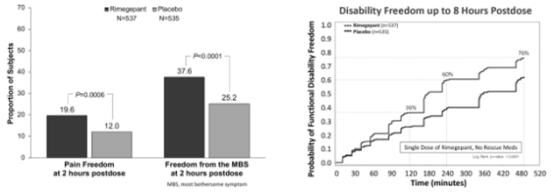
Small Molecule Approach

CGRP-Receptor Antagonists: The Gepants

- Development of older gepants stopped because of liver toxicity
- Newer, safer gepants in development:
  - For acute treatment of episodic migraine
    - BI 44370 TA (oral): effective vs placebo in phase II
    - Rimegepant: effective vs placebo in phase III
    - Ubrogepant: effective vs placebo in phase II; 5 phase III ongoing
  - For preventive treatment of episodic migraine
    - Atogepant vs placebo underway in phase II for migraine prevention
    - Rimegepant: phase 2 in progress
  - Gepants have NEVER failed on EFFICACY

Olesen J et al. *N Engl J Med.* 2004;350:1104-1110; Diener HC et al. *Cephalalgia.* 2011;31:573-584; Ho TW et al. *Lancet.* 2008;372:2115-2123; Marcus R et al. *Cephalalgia.* 2014;34:114-125; Voss T et al. *Cephalalgia.* 2016;36:887-898.

Rimegepant – Phase III Trial for Abortive Use



Safety and tolerability comparable to placebo, including LFTs

Lipton et al, presented at AHS June 2018.

Large Molecule Approach

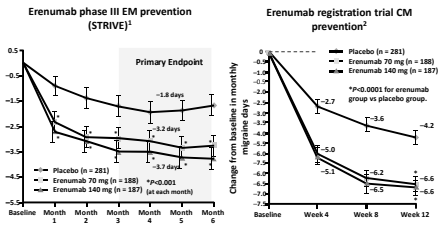
Four Monoclonal Antibodies to CGRP or Its Receptor Approved or in Development

	Erenumab	Eptinezumab	Galcanezumab	Fremanezumab
Studied for	EM, CM	EM, CM	EM, CM, eCH, cCH	EM, CM, eCH, cCH
Dosing	Monthly SC	Q3 month IV	Monthly SC	Monthly or Q3 month SC
	Fully human	Humanized	Humanized	Humanized
Target	CGRP receptor	CGRP peptide or ligand	CGRP peptide or ligand	CGRP peptide or ligand
Regulatory status	Approved	EM,CM Phase III announced (+)	Approved	Approved

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

Erenumab (FDA Approved): Phase III Studies

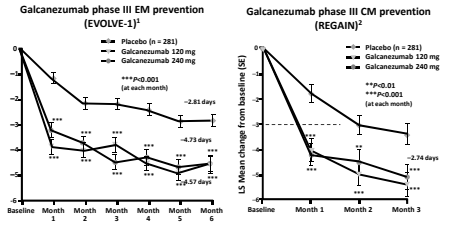
Migraine Day Reduction vs Placebo



1. Goadsby PJ et al. *Headache.* 2017;57(suppl 3):128-129 (abstract IOR04). 2. Tepper S et al. *Lancet Neurol.* 2017;16:425-434.

Galcanezumab (FDA Approved): Phase III Studies

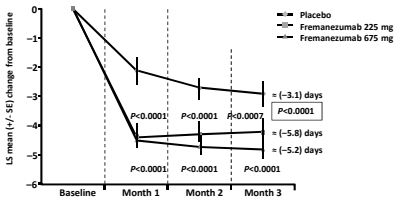
Migraine Day Reduction vs Placebo at 3 Months



1. Stauffer V et al. *Headache*. 2017;57(suppl 3):190 (abstract PS18). 2. Detke HC et al. AHS meeting, June 8-11 2017 (late-breaking abstract PS-89LB).

Fremanezumab (FDA Approved): Phase III Studies (HALO)

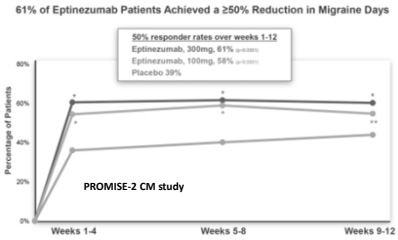
Change from Baseline in Headache Days of at Least Moderate Severity (Migraine Days) at 3 Months



Aycardi E et al. *Headache*. 2017;57(suppl 3):129-130 (abstract IOR05).

Eptinezumab Phase III CM Prevention

Primary Endpoint: Reduction of Monthly Migraine Days, Weeks 1–12



Winner PK et al. American Headache Society 2018. Abstract IOR03.

New Abortives in Development: "ditans" – Serotonin$_{1F}$ Receptor Agonists

- Lasmiditan, positive in Phase III (Samurai and Spartan) studies as abortive
- Oral tablet 50-400 mg
- AEs: dizziness, drowsiness, paresthesias
- Does not constrict vessels

PRIMARY ENDPOINT	100 mg (n=503)	200 mg (n=518)	Placebo (n=524)
% of Subjects Pain-free[1] at 2h	28.2%	32.2% {38.8%}	15.3% {21.3%}
Odds ratio (95% CI)	2.2 (1.6 – 3.0)	2.6 (2.0 – 3.6)	
p value	< 0.001	< 0.001	

KEY SECONDARY ENDPOINT	100 mg (n=469)	200 mg (n=481)	Placebo (n=488)
% of Subjects MBS[2] Free at 2h	40.9%	40.7%	29.5%
Odds ratio (95% CI)	1.7 (1.3 – 2.2)	1.6 (1.3 – 2.1)	
p value	p < 0.001	p < 0.001	

[1] Headache pain-free is as a reduction in headache severity from mild (1), moderate (2), or severe (3) at baseline to none (0) at the indicated assessment time

[2] Most Bothersome Symptom (MBS) of either nausea, phonophobia or photophobia

Neurology; April 9, 2018

Key Takeaways

- New agents in development target molecules involved in migraine pathogenesis
- One such target is CGRP, a potent vasodilator of peripheral and cerebral arteries
- CGRP receptor antagonists include
  - Small molecules: gepants, taken orally for acute treatment
  - Large molecules: monoclonal antibodies (mAbs) injected monthly or quarterly for preventive treatment
- All mAbs display positive results, have quick onset, are well tolerated with low discontinuation rates
- Another class in development includes the "ditans," serotonin$_{1F}$ receptor agonists
- None of the newer agents is associated with vasoconstriction
- As with all new agents, close vigilance is warranted

Sophie, a 55-year-old Female

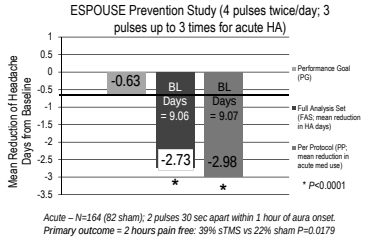
- Diagnosed with episodic migraines over 20 years ago. Now has history of CAD and decided to embrace a "clean" life style. She no longer wants to use naproxen and a triptan. She has begun an aerobic exercise regimen and her sleeping schedule has improved; however, she continues to experience headaches 5 times a month.
- She is asking you if there are any non-pharmacologic therapies that she could use to reduce her migraines?

Neuromodulation/Complementary and Alternative Treatments

Single-Pulse Transcranial Magnetic Stimulation (sTMS)

Approved for Acute and Preventive Treatment

Rental – $150/month for first 3 months; $200/month for the first year thereafter



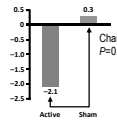
Acute – N=164 (82 sham); 2 pulses 30 sec apart within 1 hour of aura onset.
***Primary outcome** = 2 hours pain free: 39% sTMS vs 22% sham P=0.0179*

BL=baseline

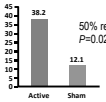
Lipton RB et al. *Lancet Neurol.* 2010;9:373-380.; Holland P et al. *Cephalalgia.* 2009;29(Suppl 1):22; Starling AJ et al. *Cephalalgia.* 2018;38:1038-1048

Transcutaneous Supraorbital Neurostimulator (tSNS)

- Device covers the supratrochlear and supraorbital nerves
- FDA approved: for acute[1] and preventive[2] migraine treatment
- 67-patient RCT; turn it on and wear it 20 minutes/day



Change in HA days (NS)
P=0.054



50% responder rates
P=0.023

- Cost: $400 to buy, can return for money back within 60 days, $25 q2-3 mos. for replacement electrodes

1.www.prnewswire.com/news-releases/fda-releases-cefaly-for-acute-treatment-of-migraine-attacks-300523385.html.
2. https://migraine.com/pro/fda-approves-cefaly.

Schoenen J et al. *Neurology.* 2013;80;697-704. Tepper D. *Headache.* 2014;54:1415-1416.

Non-invasive Vagal Nerve Stimulator

(nVNS)

- Handheld, patient-controlled device that:
  - Preferentially activates vagal afferents, not vagal efferent pathways that cause bradycardia and bronchoconstriction[1,2]
  - Inhibits rat CSD,[3] central trigeminovascular, and thalamocortical pathways[4-6]
- Approved in US for acute treatment of migraine as well as episodic cluster headache
- No serious AEs, minimal-risk device

CSD = cortical spreading depression.

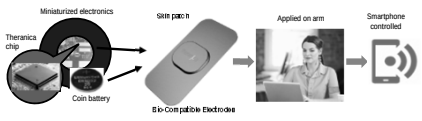
1. Schoenen J et al. AAN, 2016; abstract I3.006. 2. Mourdoukoutas et al. AAN 2016. 3. Chen SP et al. *Pain.* 2016;157:797-805.
4. Hawkins et al. AAN, 2016. 5. Akerman et al. AAN, 2016. 6. Nonis R et al. AAN, 2016.

Investigational Device

Nerivio Migra

- Proven high efficacy, rapid pain relief
- 100% safe, no side effects, no limitations on use
- No significant AEs
- Modulates Descending Tracts in the brain
- Small, affordable
- Simple, intimate, comfortable

Allows patient to carry on with daily routine even on migraine days



Complementary and Alternative Considerations

- Riboflavin
- Magnesium
- Acupuncture
- Spinal/osteopathic manipulation
- Physical therapy
- Exercise
- Yoga
- Tai Chi
- Melatonin
- Hypnotherapy
- Cold therapy
- Massage
- Homeopathy
- Coenzyme Q10

Key Migraine Takeaways

- Recurring HA with disability is migraine until proven otherwise
- Patients should institute acute therapies as soon a possible after headache onset
- Use of acute meds >9 days/month can lead to medication overuse or transformation to chronic migraine
- Preventive treatment should be offered early to reduce adverse outcomes
- Newer modalities such as CGRP antagonists, neuromodulators and complementary options may supplement the therapeutic benefits offered by traditional therapies

Residency Connect

- In development
- Site to extend educational experience for Residents/Fellows
  - Online webcourses
  - Clinical tools and apps
  - Patient resources
- Place to make connections with colleagues
- Sign-up to be notified of the launch at: http://residencyconnect.rockpointe.com/

CME Credit

- Post-activity Survey and CME Evaluation
  - If you're seeking CME credit, ***please take a moment*** to answer the Post-activity Survey questions on your form
  - Your answers are important and will help us identify remaining educational gaps and shape future CME activities
  - After the post-activity survey, please ***complete*** the rest of the Evaluation form and ***ensure*** you fill in your name and demographic information after the questions
  - Return all forms to on-site CME staff

Thank you for joining us today!