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3 Things to Do

1. Actively participate in the meeting by **responding to ARS** and/or **asking the faculty questions**

   (It's ok if you miss answering a question or get them wrong, you can still claim MOC)

2. Complete the evaluation form found on your tables

   (For live stream participants, follow the credit claim link)

3. Be sure to fill in your **ABIM ID number** and **DOB** (MM/DD) on the evaluation, so we can submit your credit to ABIM.

Getting Ahead of Migraine

INTEGRATING PREVENTIVE STRATEGIES INTO MIGRAINE CARE

APRIL 18, 2018
6:30 PM – 8:00 PM

Dinner begins at 6:00 PM
Program begins at 6:30 PM

New Orleans Marriott Downtown
Blaine Kern Ballroom

www.CMEOutfitters.com/MigraineCare

This event is not a part of the official Internal Medicine Meeting 2018 Education Program.

Provided by:
CME Outfitters

Commercial Support

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

This activity is supported by an educational grant from Teva Pharmaceuticals.

Andrew C. Charles, MD

Professor of Neurology
Meyer and Renee Luskin Chair in Migraine and Headache Studies
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#MigraineCare

Grace Forde, MD

Director of Neurological Services
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#MigraineCare

Learning Objective 1

Apply knowledge of clinical features, symptoms, and key diagnostic criteria in the differential diagnosis of migraine.

Learning Objective 2

Assess safety and efficacy data supporting the role of agents that target CGRP in the prevention and management of migraine.

Learning Objective 3

Employ a patient-centered approach to the care of patients with migraine in order to improve outcomes, patient satisfaction, and treatment adherence.

Patient-Guided Content

- Developed following a telephone survey that highlighted patient's needs, concerns, and experiences with migraine
- Leveraged social media to express the "patients voice" in health care
- Represents feedback from a social media community of thousands of people with migraine

Speaking as a patient or on behalf of your patient community, in what ways have your migraines impacted your ability to function both personally and professionally?

"They affect my quality of life each day, because some days leading up to and after a migraine, I'm pretty much out of commission. And the day of a migraine, I definitely can't do that much, so sometimes I have to cancel work, meetings or social engagements."

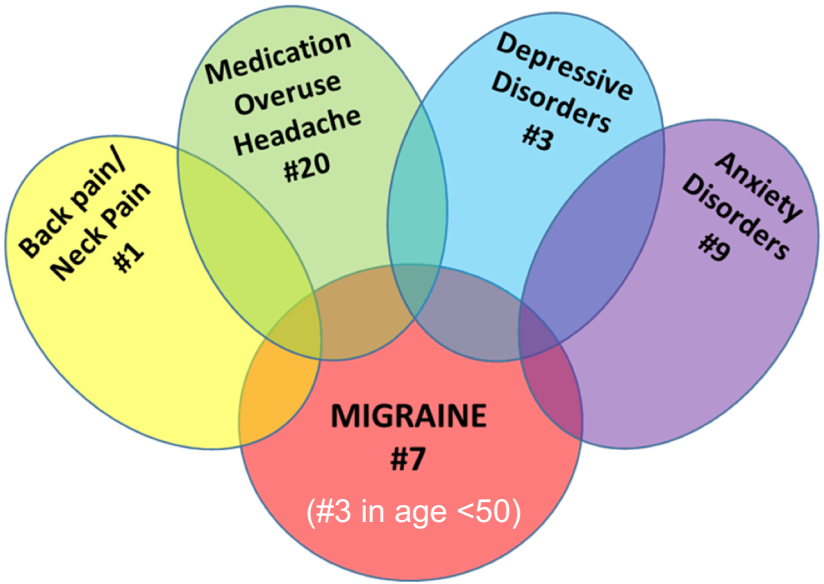
"I have been completely sidelined from by career due to chronic migraines. I was once working more than full-time while raising two young children. My episodic migraines have turned chronic and I had to seek disability."

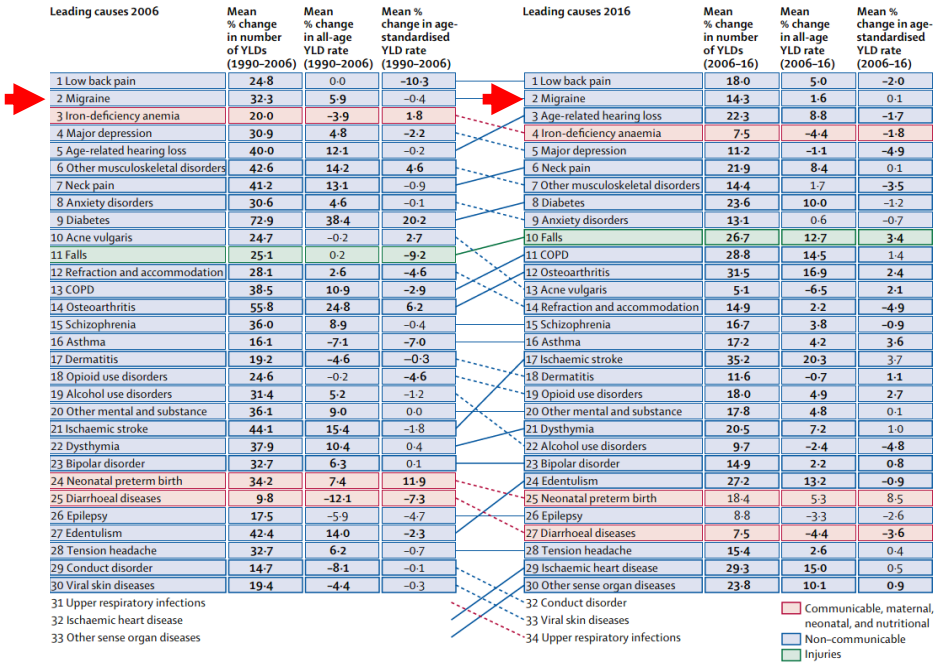
Migraine: Highly Prevalent, but Receives Little Attention as a Public Health Issue

- May begin in childhood but increases at 10-14 years of age, continuing to increase until 35-39 years of age
- 2-3 times more prevalent in women
  - Prevalence at its peak in women is > 25%
- As many as 1 in 25 women may have chronic migraine with headache more than 15 day/month

Charles A. *N Engl J Med*. 2017;377(6):553-561.

Years Lived With Disability





Leading causes 2006	Mean % change in number of YLDs (1990–2006)	Mean % change in all-age YLD rate (1990–2006)	Mean % change in age-standardised YLD rate (1990–2006)
1 Low back pain	24·8	0·0	−10·3
2 Migraine	32·3	5·9	−0·4
3 Iron-deficiency anemia	20·0	−3·9	1·8
4 Major depression	30·9	4·8	−2·2
5 Age-related hearing loss	40·0	12·1	−0·2
6 Other musculoskeletal disorders	42·6	14·2	4·6
7 Neck pain	41·2	13·1	−0·9
8 Anxiety disorders	30·6	4·6	−0·1
9 Diabetes	72·9	38·4	20·2
10 Acne vulgaris	24·7	−0·2	2·7
11 Falls	25·1	0·2	−9·2
12 Refraction and accommodation	28·1	2·6	−4·6
13 COPD	38·5	10·9	−2·9
14 Osteoarthritis	55·8	24·8	6·2
15 Schizophrenia	36·0	8·9	−0·4
16 Asthma	16·1	−7·1	−7·0
17 Dermatitis	19·2	−4·6	−0·3
18 Opioid use disorders	24·6	−0·2	−4·6
19 Alcohol use disorders	31·4	5·2	−1·2
20 Other mental and substance	36·1	9·0	0·0
21 Ischaemic stroke	44·1	15·4	−1·8
22 Dysthymia	37·9	10·4	0·4
23 Bipolar disorder	32·7	6·3	0·1
24 Neonatal preterm birth	34·2	7·4	11·9
25 Diarrhoeal diseases	9·8	−12·1	−7·3
26 Epilepsy	17·5	−5·9	−4·7
27 Edentulism	42·4	14·0	−2·3
28 Tension headache	32·7	6·2	−0·7
29 Conduct disorder	14·7	−8·1	−0·1
30 Viral skin diseases	19·4	−4·4	−0·3
31 Upper respiratory infections			
32 Ischaemic heart disease			
33 Other sense organ diseases			

Leading causes 2016	Mean % change in number of YLDs (2006–16)	Mean % change in all-age YLD rate (2006–16)	Mean % change in age-standardised YLD rate (2006–16)
1 Low back pain	18·0	5·0	−2·0
2 Migraine	14·3	1·6	0·1
3 Age-related hearing loss	22·3	8·8	−1·7
4 Iron-deficiency anaemia	7·5	−4·4	−1·8
5 Major depression	11·2	−1·1	−4·9
6 Neck pain	21·9	8·4	0·1
7 Other musculoskeletal disorders	14·4	1·7	−3·5
8 Diabetes	23·6	10·0	−1·2
9 Anxiety disorders	13·1	0·6	−0·7
10 Falls	26·7	12·7	3·4
11 COPD	28·8	14·5	1·4
12 Osteoarthritis	31·5	16·9	2·4
13 Acne vulgaris	5·1	−6·5	2·1
14 Refraction and accommodation	14·9	2·2	−4·9
15 Schizophrenia	16·7	3·8	−0·9
16 Asthma	17·2	4·2	3·6
17 Ischaemic stroke	35·2	20·3	3·7
18 Dermatitis	11·6	−0·7	1·1
19 Opioid use disorders	18·0	4·9	2·7
20 Other mental and substance	17·8	4·8	0·1
21 Dysthymia	20·5	7·2	1·0
22 Alcohol use disorders	9·7	−2·4	−4·8
23 Bipolar disorder	14·9	2·2	0·8
24 Edentulism	27·2	13·2	−0·9
25 Neonatal preterm birth	18·4	5·3	8·5
26 Epilepsy	8·8	−3·3	−2·6
27 Diarrhoeal diseases	7·5	−4·4	−3·6
28 Tension headache	15·4	2·6	0·4
29 Ischaemic heart disease	29·3	15·0	0·5
30 Other sense organ diseases	23·8	10·1	0·9
32 Conduct disorder			
33 Viral skin diseases			
34 Upper respiratory infections			

Communicable, maternal, neonatal, and nutritional
Non-communicable
Injuries

Global, regional and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015.[1]

Global, regional and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries , 1990-2015: a systematic analysis for the Global Burden of Disease Study 2016.[2]

1. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. *Lancet*. 2016;388(10053):1545-1602.
2. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. *Lancet*. 2017;390(10100):1211-1259.

Diagnosing Migraine

Andrew Charles, MD

Case Presentation: Julie

- Julie is a 32 yo mother of 2 young children (15 mons and 3 yrs), working full-time as an accountant presents with complaint of headache
- Pain is bilateral and maxillary in location, constant, not throbbing, often extending down the back of her neck
- Wonders if it might be weather or sinus related, “I’ve always been able to tell when the barometric pressure changes and a storm is coming”
- The past 2-3 times, she has had to leave work not only because of headache and often nausea, but she just can’t concentrate and focus on her work and has made some mistakes she would rarely make

Case Presentation: Julie

- She has managed with OTC naproxen sodium, but lately hasn't been as effective, and she's concerned about "taking too much and getting an ulcer"
- She made an appointment with her ophthalmologist because of some blurriness that she has experienced
- With 2 small children and working full-time, she's already not sleeping much and fatigued. Adding in the headaches really has her down and she confesses she's not a great to be around some days. She shares that she experienced depressive episodes and is currently taking 100mg of sertraline daily.
- BMI of 32

Test Your Knowledge: Round 1

What is the best option to take as part of the examination?

A. Recommend that she begin to take butalbital complex (fiorinal, fioricet)
B. Order CT scan to investigate neck pain
C. Order CT or MRI to investigate headache, vision, and cognitive complaints
D. Palpate head, arteries, and check balance
E. Conduct a funduscopic exam

How confident are you in your answer?

A. Not confident
B. Somewhat confident
C. Confident
D. Very confident

Diagnostic Challenges

- Traditional focus on severity and quality of pain as primary diagnostic criteria
- Perception that if pain is not one-sided, it is not migraine
  - Although pain is characteristically severe, unilateral, and throbbing, it can also be moderate, bilateral and constant in quality
- Belief that migraine is related to sinus disease
  - Majority of patients who receive a diagnosis of sinus headache have migraine

Charles A. *N Engl J Med*. 2017;377(6):553-561.

Diagnostic Challenge: Symptom Overlap

- Many patients who believe they have tension-type headaches (TTH) or sinus headaches report a range of symptoms and experiences that fit the definition of migraine
- Heterogeneity of migraine—can change over a series of attacks
- Shared risk factors and triggers
  - Menstrual period, skipped meals, irregular sleep
- Comorbid conditions can complicate diagnosis

Cady R, et al. *J Pharm Pract.* 2015;28(4):413-418.

Medications That May Make Migraines Worse

- Opioids
- Oral contraceptives
- Hormone replacement therapy
- SSRI antidepressants
- Decongestants
- Proton pump inhibitors?
- Bone density medications?

Differentiating Headaches: Tension Headache vs. Sinus Headache

Tension headache

- Pericranial tenderness is commonly detected and recorded by manual palpation
- Mild or moderate intensity
- Pain does not worsen with routine physical activity
- Is not associated with nausea
- Photophobia or phonophobia may be present

Sinus headache

- Headache caused by chronic infectious or inflammatory disorder of the paranasal sinuses and associated with other symptoms and/or clinical signs of the disorder
- Developed in temporal relation to onset of chronic rhinosinusitis
- Waxes and wanes in parallel with sinus congestion
- Is exacerbated by pressure over paranasal sinuses

The International Classification of Headache Disorders, 3rd Edition. *Cephalalgia*. 2018;38(1):1-211.

Timeline of a Migraine Attack

4-72 hours

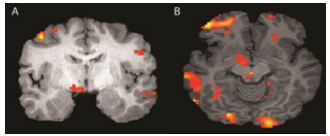
Premonitory | Aura | Headache | Postdrome

Symptoms

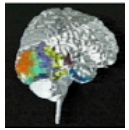
- Yawning, Polyuria
- Neck Pain, Fatigue, Mood change
  Light sensitivity, Sound sensitivity
- Nausea
- Visual changes
  Numbness/tingling
  Language dysfunction
  Cognitive dysfunction
  Brainstem symptoms
- Headache
- Cutaneous allodynia

Predisposing Factors
Genes
Hormones
Metabolism
Environment
Medications

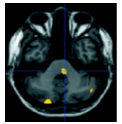
Brain Activation



Hypothalamus, Brainstem
Cortex

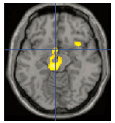


Cortex

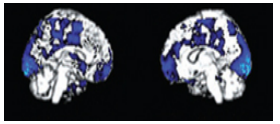


Brainstem

Thalamus



Hypothalamus



Cortex Thalamus
Hypothalamus

Neurophysiology Thalamocortical circuit changes — Pain/emotion network changes

Neurochemistry Dopamine? Glutamate? CGRP, PACAP Release
Hypothalamic peptides?

CGRP = Calcitonin gene-related peptide; PACAP = Pituitary adenylate cyclase-activating polypeptide
Adapted from Charles A. *N Engl J Med*. 2017;377(6):553-561.

Chronic Migraine

- Headache occurring on 15 or more days/month for more than 3 months, which on at least 8 days/month, has the features of migraine headache
  - Generally requires a headache diary to record information on pain and symptoms day by day for at least 1 month
  - Most common cause of symptoms suggestive of chronic migraine is medication overuse
    - ~ 50% revert to episodic upon withdrawal

The International Classification of Headache Disorders, 3rd Edition. *Cephalalgia*. 2018;38(1):1-211.

Migraine with Aura: ICHD-3 Diagnostic Criteria

A. At least 2 attacks fulfilling criteria B and C

B. One or more of the following fully reversible aura symptoms
   1. Visual
   2. Sensory
   3. Speech and/or language
   4. Motor
   5. Brainstem
   6. Retinal

C. At least 3 of the following 6 characteristics
   1. At least 1 aura symptom spreads gradually over ≥ 5 min
   2. 2 or more aura symptoms occur in succession
   3. Each individual aura symptom is unilateral
   4. At least 1 aura symptom is positive
   5. Aura is accompanied or following within 60 min by headache

D. Not better accounted for by another ICHD-3 diagnosis

The International Classification of Headache Disorders, 3rd Edition. *Cephalalgia*. 2018;38(1):1-211.

Migraine without Aura: ICHD-3 Diagnostic Criteria

A. At least 5 attacks fulfilling criteria B-D

B. Headache attacks lasting 4-72 hrs (when untreated or unsuccessfully treated)

C. Headache has at least 2 of the following characteristics
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

D. During headache at least one of the following
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

The International Classification of Headache Disorders, 3rd Edition. *Cephalalgia*. 2018;38(1):1-211.

ID Migraine Screener

Patients answering “yes” to at least two of these questions probably have migraine	Yes or No
Over the last 3 months, have you limited your activities on at least 1 day because of your headaches?	
Do lights bother you when you have a headache?	
Do you get sick to your stomach or nauseated with your headache?	

Strategies for Migraine Prevention

Grace Forde, MD

Case Presentation: Julie

- Julie was prescribed a triptan to manage her acute migraine attacks and it was effective for two years
- Julie is here today because for the past 6 months, her migraines have gotten more frequent, more severe and lasting longer, sometimes up to 2 days
- She is using her triptan often “3-4 times per week”, but admits that sometimes she tries to hold off, hoping it will pass
- Her visual disturbances are getting more pronounced
- Migraines have interrupted her exercise routine and she has gained 10 lbs., admitting she is not eating as healthy as she should

Test Your Knowledge: Round 2

What would *not* be your next course of action be with Julie?

A. Stop her triptan because it is contraindicated when using sertraline
B. Consider having her add a behavioral management strategy to her regiment such as relaxation techniques, cognitive behavioral therapy (CBT), or EMG biofeedback
C. Consider discontinuing her sertraline
D. Ask her to revisit her headache diary for the next month to see what triggers may be contributing to her headache

How confident are you in your answer?

A. Not confident
B. Somewhat confident
C. Confident
D. Very confident

Test Your Knowledge: Round 3

Julie works on identifying triggers and implements behavioral management, but does not find relief. What is your best next step?

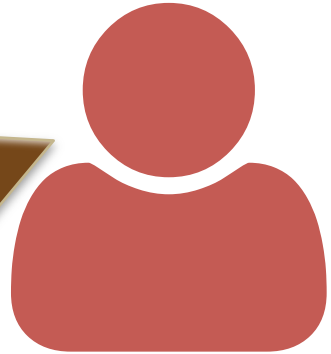
A. Switch her medication
B. EMG biofeedback
C. Initiate a preventive strategy
D. Recommend that she try acupuncture
E. Recommend that she supplement with an opioid

How confident are you in your answer?

A. Not confident
B. Somewhat confident
C. Confident
D. Very confident

Speaking as a patient or on behalf of your patient community, what information have you received from your HCP about the pros and cons of prophylaxis or preventive measures for migraine?

"I think providers will talk about pros and cons. So pros, you have less migraine days, less frequency, that also the intensity is less. They tell you it is a better life quality when you have these treatments that work, the preventive treatments. And obviously that is extremely appealing. When they talk about cons, obviously they talk about side effects, they talk about long-term effects and especially about tolerance build up..."



When to Consider Preventive Therapy for Migraine

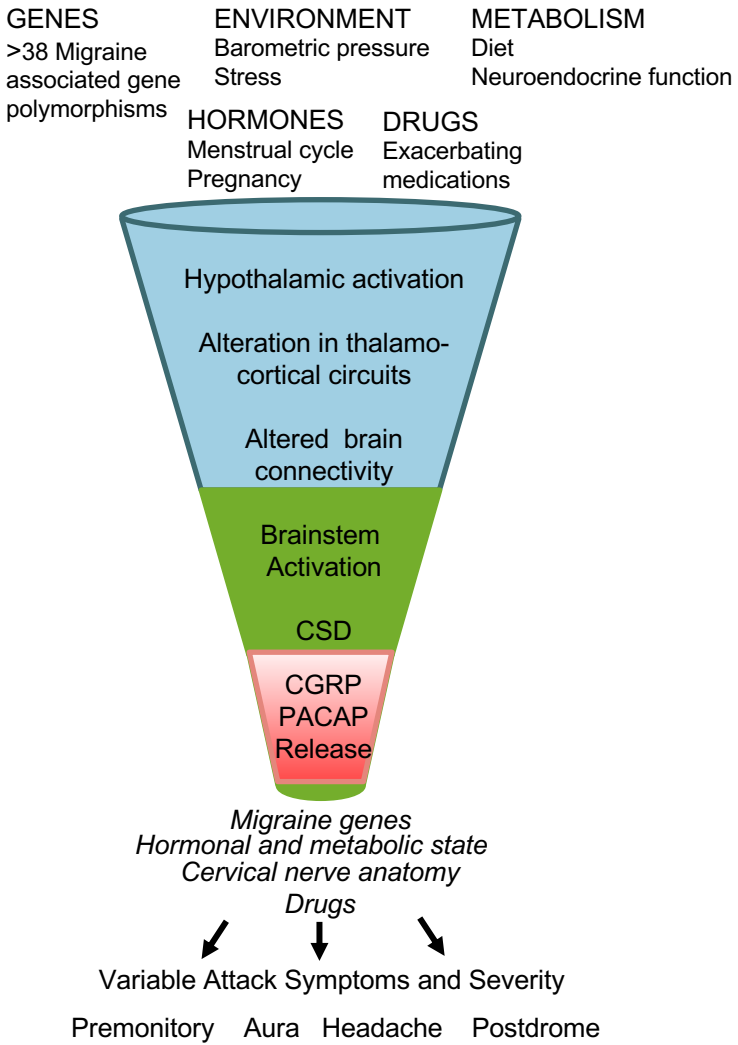
- Decision to initiate preventive strategies should be based on:
  - Attack frequency: Migraine occurs >1/week or on 4 or more days per month
  - Responsiveness to medication for acute migraine
  - Coexisting conditions

Charles A. *N Engl J Med*. 2017;377(6):553-561.

Emerging Therapies for Migraine

Andrew Charles, MD

The Pathophysiology of Migraine: Implications for Clinical Management



CSD = Cortical spreading depolarization
CGRP = Calcitonin gene-related peptide
PACAP = Pituitary adenylate cyclase-activating polypeptide

Charles A. *Lancet Neurol.* 2018;17(2):174-182.

Evidence of a Key Role for CGRP in Migraine

CGRP is Released During a Migraine Attack

CGRP Levels are Elevated in Chronic Migraine

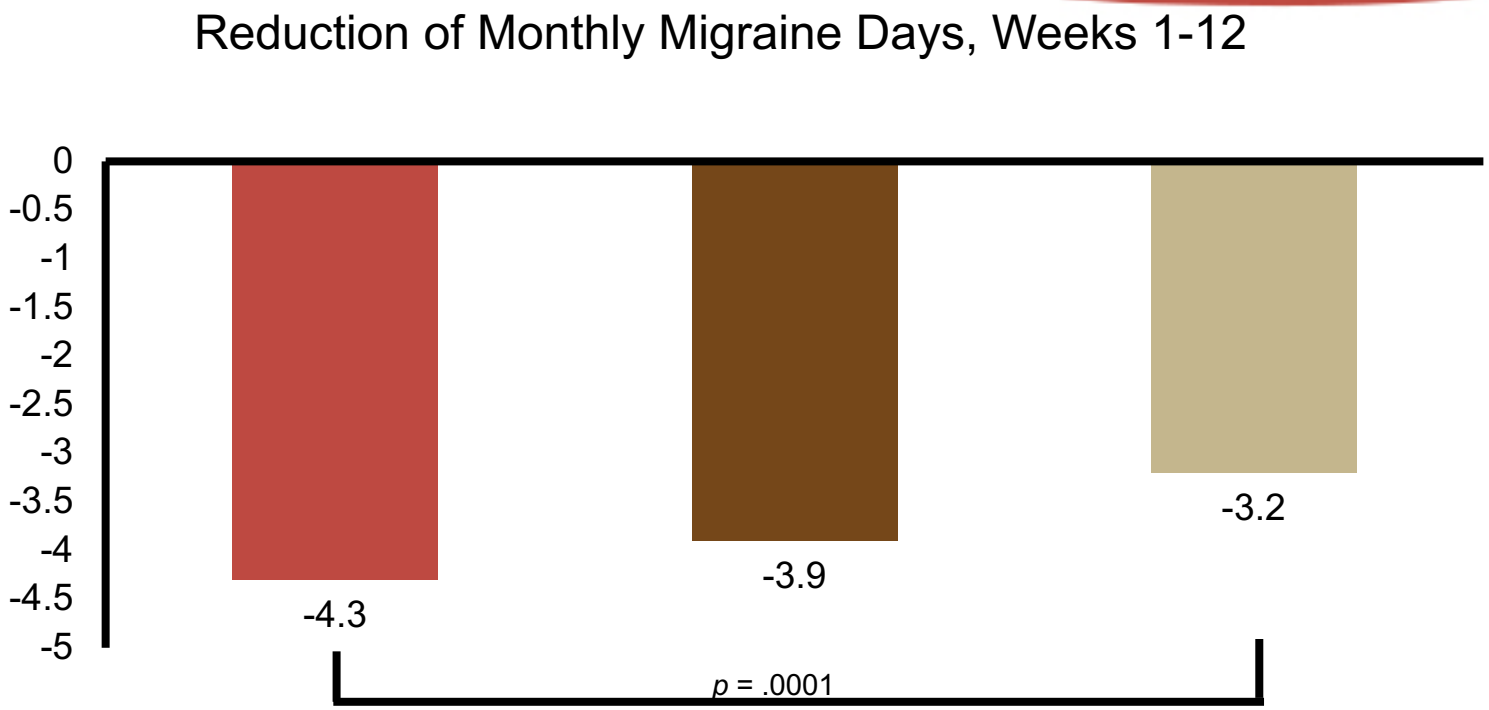
CGRP Administration Triggers Migraine

Small Molecule CGRP Antagonists Abort Migraine

Antibodies to CGRP or its Receptor Prevent Migraine

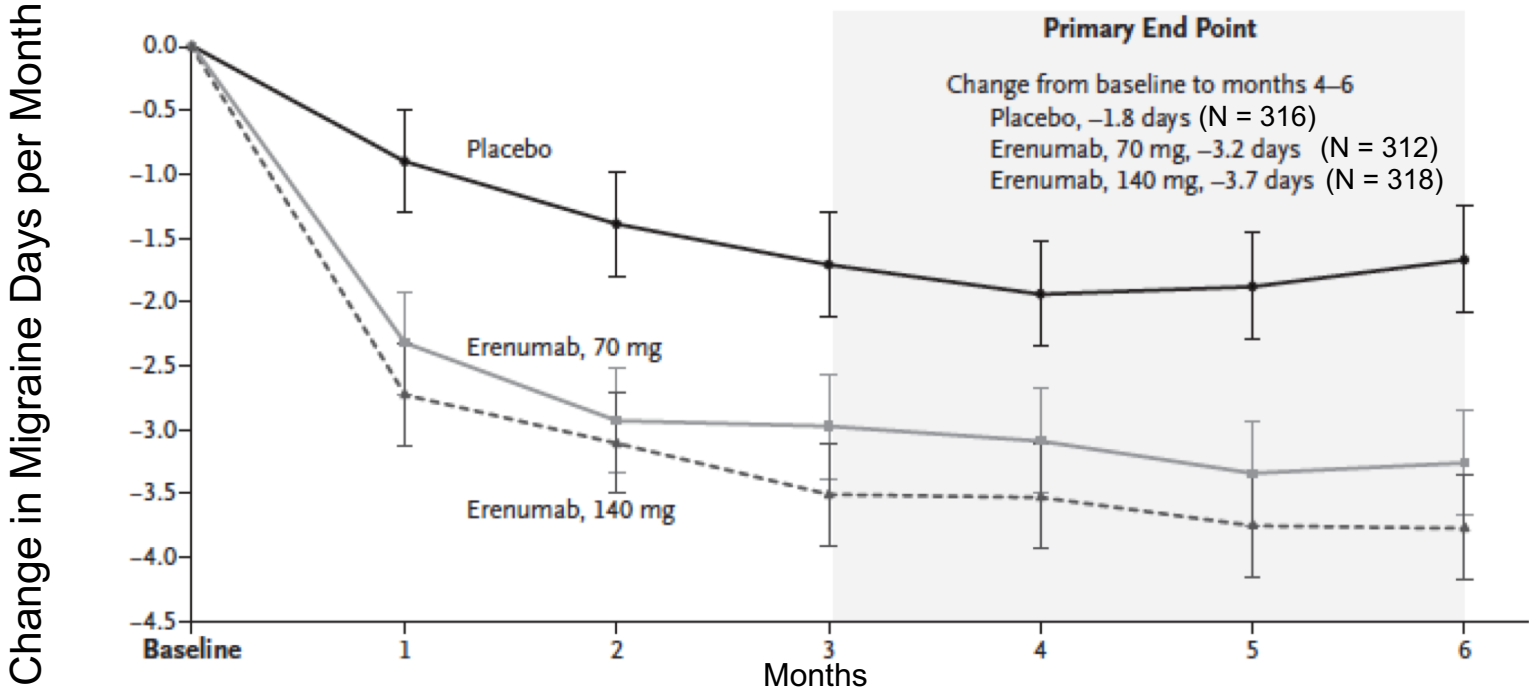
1. Goadsby PJ, et al. *Ann Neurol* 1990;28:183-187.; 2. Goadsby PJ, Edvinsson L. *Brain*. 1994;117(Pt 3):427-434.; 3. Hansen JM, et al. *Cephalalgia.* 2010;30(10):1179-1186.; 4. Cernuda-Morollon E, et al. *Neurology* 2013;81(14):1191-1196.; 5. Olesen J, et al. *N Engl J Med*. 2004;350:1104-1110.; 6. Ho TW, et al. *Neurology*. 2008;70:1304-1312

Eptinezumab: Phase III Data



Poster (PO-01-194) presented at the 18th Congress of the International Headache Society. September 7-10, 2017 Vancouver, Canada.

Erenumab: Phase III Data

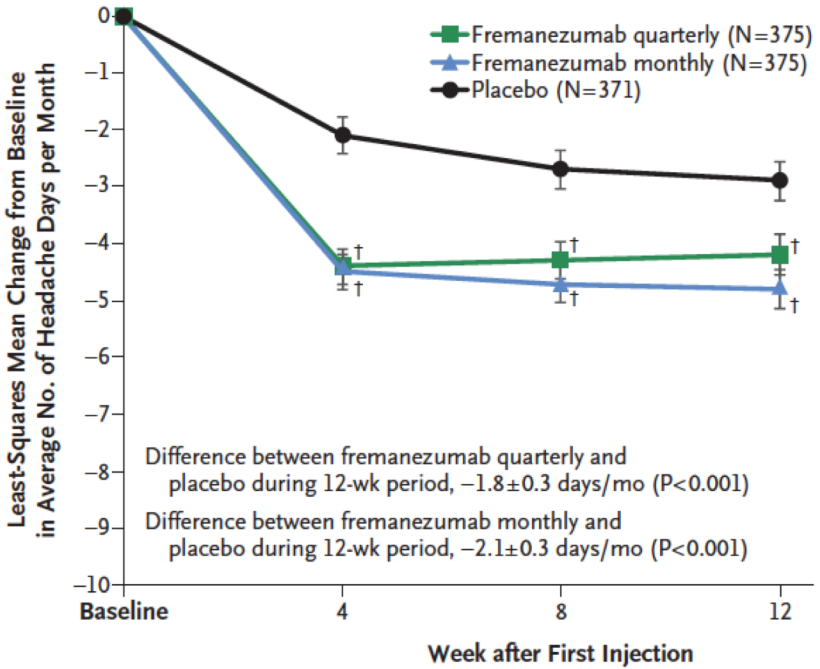


p < .001 for months 4, 5, 6 for each dose of erenumab compared to placebo.

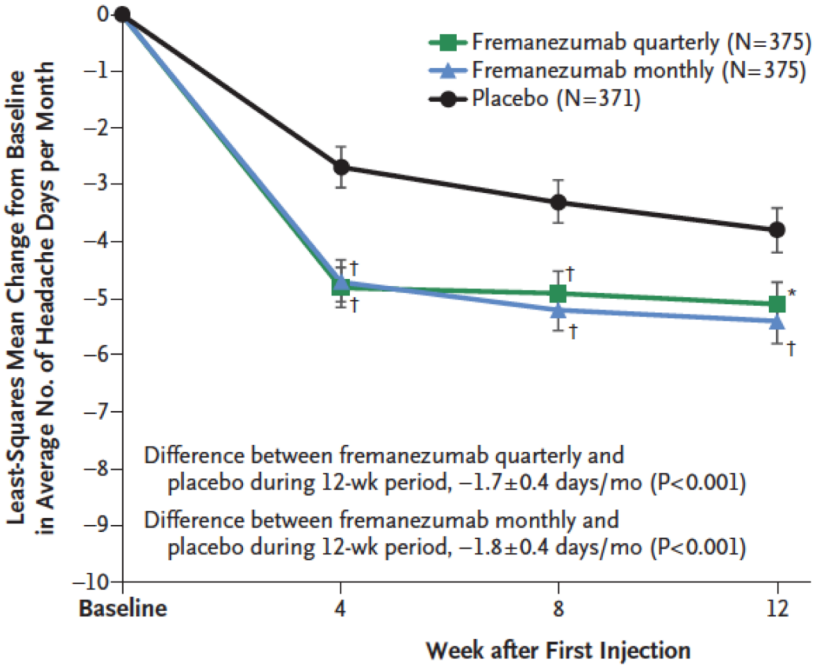
Goadsby P, et al. *N Engl J Med*. 2017;377:2123-32.

Fremanezumab: Phase III Data

Headache Days

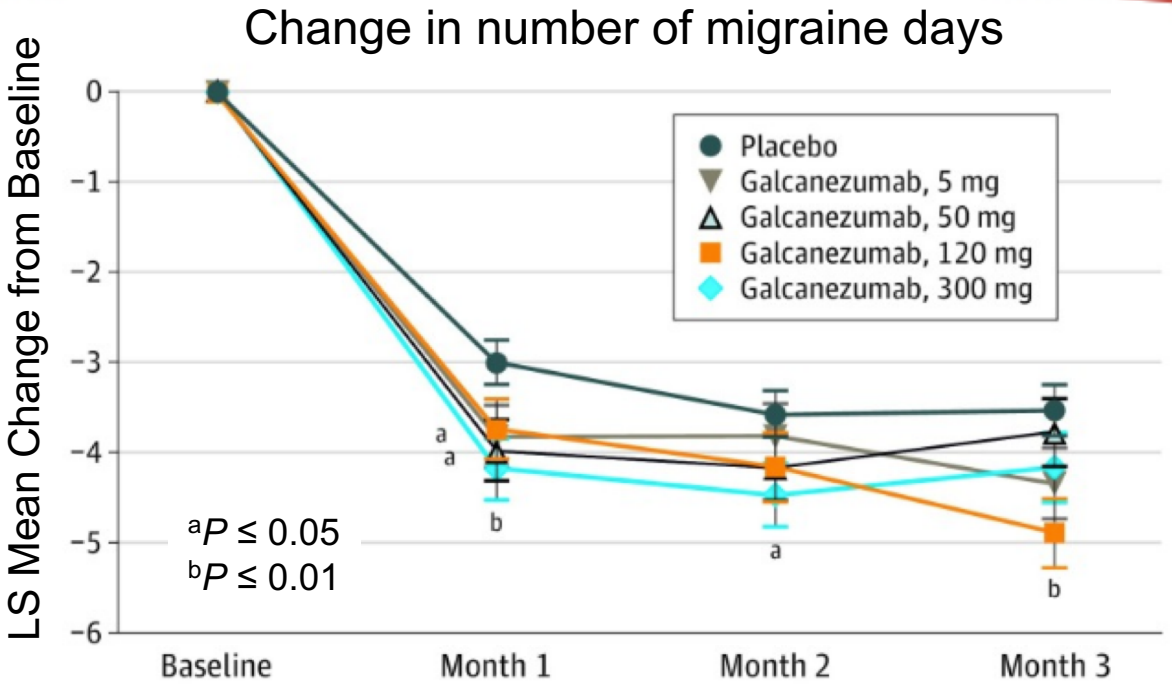


Migraine Days



Silberstein SD, et al. *N Engl J Med*. 2017;277:2113-22.

Galcanezumab: Phase III Data



- Galcanezumab 120 mg significantly reduced the mean number of migraine headache days vs. placebo
- Overall change from baseline in the number of migraine headache days significant for both galcanezumab 120 mg (-4.3) and 300 mg (-4.3) vs placebo (-3.4)
- Functional impact from monthly migraines was significantly improved with galcanezumab 120 mg compared to placebo

Placebo (N = 126), galcanezumab 5 mg (N = 59), galcanezumab 50 mg (N = 66), galcanezumab 120 mg (N = 62), galcanezumab 300 mg (N = 62)

Skljarevski V, et al. *JAMA Neurol*. 2018;75(2):187-193.

CGRP in Migraine: Safety and Tolerability

Drug	Common Adverse Events (Note: Data not reflective of head to head trials)
Eptinezumab	Frequency and severity of adverse events were similar between eptinezumab and placebo. Reports of injection site pain, nasopharyngitis, sinusitis, upper respiratory tract infection[1]
Erenumab	Frequency and severity of adverse events were similar between erenumab and placebo. Reports of injection site pain, nasopharyngitis, upper respiratory tract infection[2]
Fremanezumab	Frequency and severity of adverse events were similar between fremanezumab and placebo. Reports of injection site pain, liver enzyme elevation, but did not lead to discontinuation.[3]
Galcanezumab	Frequency and severity of adverse events were similar between galanezumab and placebo. Reports of injection site pain, back pain, sinusitis, bronchitis, urinary tract infection, influenza, neck pain.[4]

1. Poster (PO-01-194) presented at the 18th Congress of the International Headache Society. September 7-10, 2017 Vancouver, Canada.; 2. Goadsby P, et al. *N Engl J Med*. 2017;377:2123-32.; 3. Silberstein SD, et al. *N Engl J Med*. 2017;277:2113-22.; 4. Skljarevski V, et al. *JAMA Neurol*. 2018;75(2):187-193.

Patient-Centered Approaches to Migraine Management

Grace Forde, MD

Speaking as a patient or on behalf of your patient community, what ideas, concepts, or feelings about migraine would patients most like to discuss with their HCP?

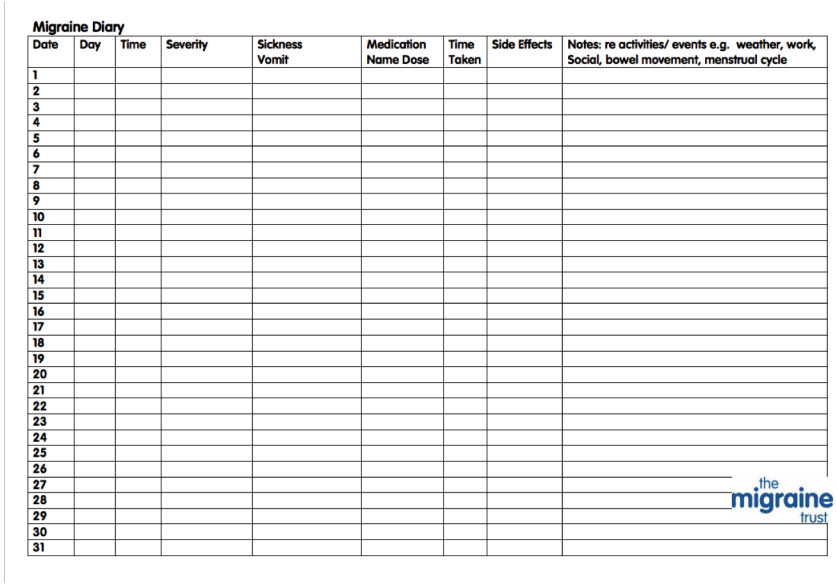
"I think the only things that chronic migraine patients are interested in is, "How can I live my life?" And every treatment option, every conversation needs to be directed around that result of being able to live the life you want to live."

Patient Education

- Open communication with patients is essential to prepare them to take action
  - What to do when migraine occurs
  - Prevention strategies
  - Rescue plans
  - Side effects
  - What is a red flag or emergency?
  - Special instructions: travel, pregnancy, stressful events

Importance of Headache Diaries

- Helps patient recognize migraine attack patterns
  - Warning signs
  - Pain intensity
  - Timing
  - Duration
  - Symptoms
  - Triggers
- Evaluation of medication



Migraine Diary

Date	Day	Time	Severity	Sickness Vomit	Medication Name Dose	Time Taken	Side Effects	Notes: re activities/ events e.g. weather, work, Social, bowel movement, menstrual cycle
1								
2								
3								
4								
5								
6								
7								
8								
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the migraine trust

Knowing the Migraine Triggers

- Stress
- Changes in or irregular sleep schedule
- Hormones
- Caffeine
- Alcohol
- Changes in weather
- Diet
  - Skipped meals
- Dehydration
- Light
- Odors
- Medication overuse

American Migraine Foundation website. https://americanmigrainefoundation.org/understanding-migraine/top-10-migraine-triggers-and-how-to-deal-with-them/. Accessed April 5, 2018.

Lifestyle Changes: Controlling the Controllable

- Migraine hates change: keep things consistent
- Maintain consistent sleep patterns
- If you are going to have caffeine, small amounts on a daily basis
- Don’t skip meals
- Exercise and maintain a healthy weight

American Migraine Foundation website. https://americanmigrainefoundation.org/understanding-migraine/5-migraine-hacks-amf-migraine-community/. Access April 5, 2018

Managing Comorbidities

- Nearly 88% of people with chronic migraine have at least 1 comorbid condition, 39% have 4 or more comorbid conditions
- Estimated cost of chronic migraine is estimated to be $5.4B in the US. Addition of comorbid conditions increases cost to $40B
- 37.2% report comorbid mood and anxiety disorders

Thorpe KE; The Headache and Migraine Policy Forum. Prevalence, health care spending and comorbidities associated with chronic migraine patients. https://www.headachemigraineforum.org/resources/2017/2/10/b00ahzk73jowqoziwanfm5zckmqd7c. Published February 13, 2017. Accessed April 5, 2018.

Patient-Centered Care Coordination

- Communication with the neurologist
  - What to expect
- What can/should be done before the referral?
- Strategies for monitoring: what, how often
- Who ”owns” the patient?

What is your expectation when you refer a patient to the neurologist?

A. Neurologist will assume responsibility for the patient
B. I will receive information related to diagnosis
C. I will receive information about drugs/interventions that have been prescribed
D. Receive a recommendation about what I should be monitoring

Tips and Tricks from the Neurologist

- Create templates in the EHR of simple checklists that can be used with patients
- Tools to use in a time crunch
  - ID Migraine
- Resources to share with patients
  - Handouts
  - Websites
  - Diaries

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Recognize the personal, family, and professional cost of migraine
- Apply ID Migraine to distinguish migraine from tension and sinus headaches
- Use headache diary to tease out frequency and severity of attacks
- Consider preventive therapy when attacks occur >1/wk or 4 or more days per month
- Educate patients to control the controllable by knowing their triggers and keeping open line of communication

Question & Answers

Coming Up Live!

Peeking Beneath the Surface of Atopic Dermatitis: Testing Your Skills from Pathogenesis to Treatment

Thursday, April 19, 2018
Dinner starts at 6:00; Meeting starts at 6:30PM CT
Acadia Ballroom, New Orleans Marriott Downtown
www.cmeoutfitters.com/ADskills

Precision Medicine in Ankylosing Spondylitis: Fine-tuning Diagnosis & Treatment

Friday, April 20, 2018
Dinner starts at 6:00PM – Meeting starts at 6:30PM CT
Blaine Kern Ballroom, New Orleans Marriott Downtown

www.cmeoutfitters.com/ASprecmed

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www.CMEOutfitters.com/MigraineCareResources

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#MigraineCare