NEXT GENERATION
MIGRAINE THERAPIES
AMERICAN HEADACHE SOCIETY

Next Generation Acute and Preventive Treatment

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AMERICAN HEADACHE SOCIETY
www.AmericanHeadacheSociety.org

Disclosure: Cynthia E. Armand, MD

Received Honoria for advisory board services from *Biohaven Pharmaceutical* company

Upon completion of this section of the program, participants will be better able to:

Review current patterns of use of preventive medications

Discuss the role of new drug targets in preventive therapy

Explain evidence-based behavioral interventions

Discuss current acute migraine therapies

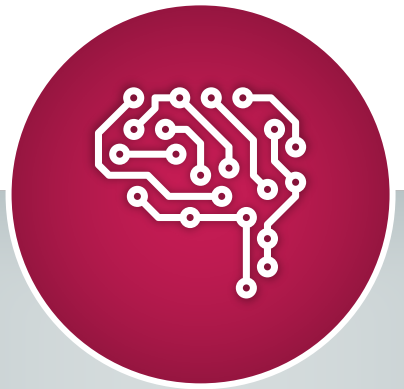
Recognize the risk of cardiovascular disease in migraine patients

Migraine acute treatment modalities

Patient coping strategies

- Relax in a dark, quiet room
- Sleep
- Temperature therapy
- Caffeinated beverage

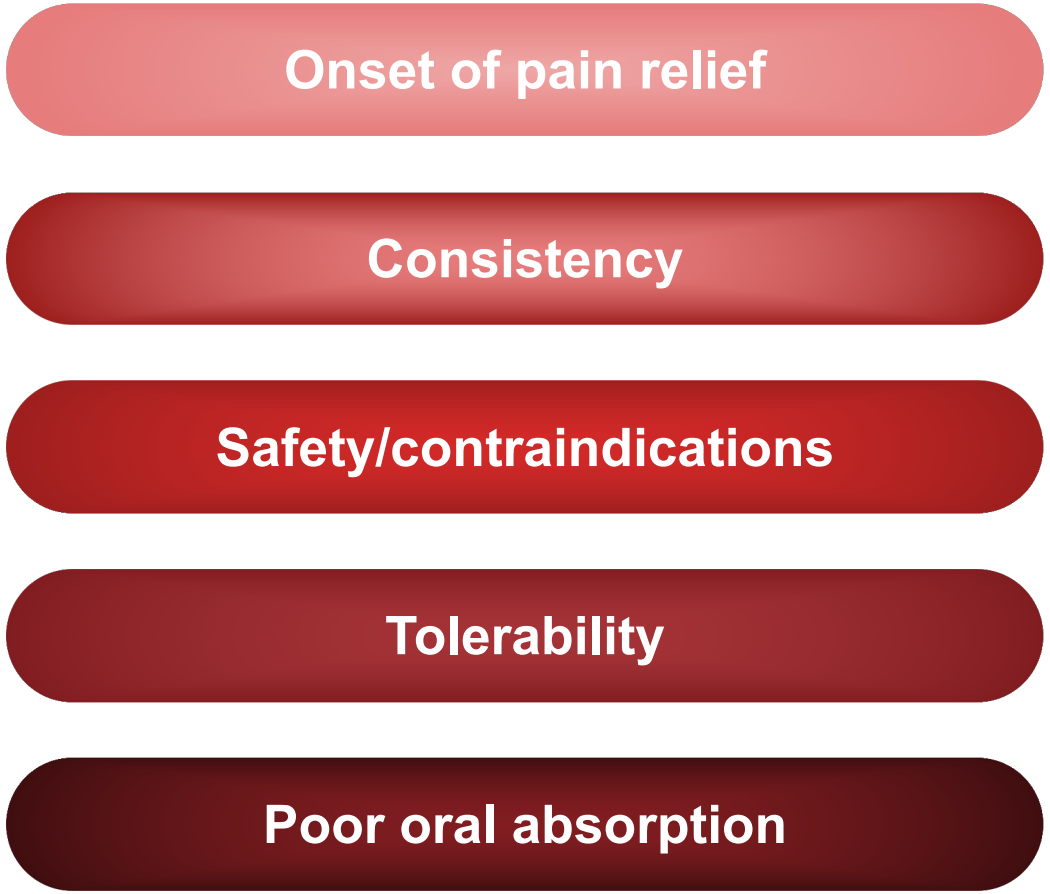
Pharmacotherapy



Neuromodulation

Stay tuned for the next session!

Unmet needs in migraine therapy



Lipton RB, et al. *Headache*. 2019;Sep 22. doi: 10.1111/head.13642 [Epub ahead of print].

AHS recommendations for acute migraine pharmacotherapy

Mild-to-moderate attacks

Non-opioid analgesics
- Acetaminophen
- NSAIDs

Caffeinated analgesic combinations
- eg, aspirin + APAP + caffeine

Moderate or severe attacks and mild-to-moderate attacks that respond poorly to NSAIDs or caffeinated combinations

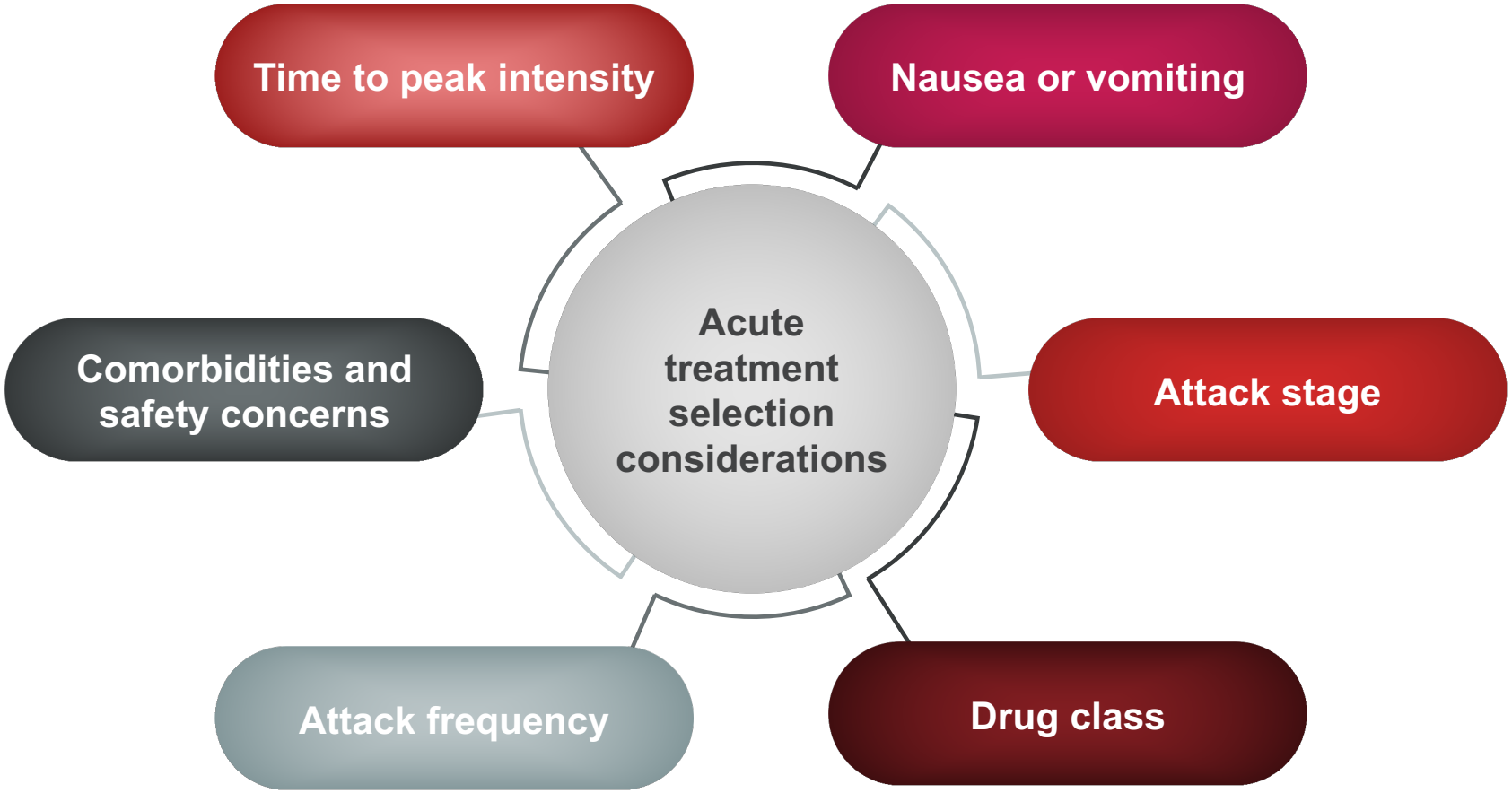
Triptans

DHE

DHE, dihydroergotamine; NSAID, non-steroidal anti-inflammatory drug.

American Headache Society. *Headache.* 2019;59:1–18.

Factors influencing selection of acute therapy



Attributes of acute migraine medications important to patients

Patients want consistent, effective acute pain medication[1]

- Most patients (58%) desire pain freedom at 1 hour[2]
  - Current acute therapies take >1 hour for meaningful relief
- <50% of patients have consistent response across attacks

Acute migraine therapy clinical trial endpoints now typically include most bothersome non-headache symptom[3]

Patients most often identify photophobia as the most bothersome symptom (49%)[4]

Patients who had treated at least one migraine with a triptan in the past 12 months (n=206).

1. Lipton RB, et al. *J Headache Pain*. 2004;5:123–130. 2. Ferrari MD, et al. *Lancet*. 2001;358:1668–1675. 3. U.S. FDA Center for Drug Evaluation and Research. Migraine: Developing Drugs for Acute Treatment. Guidance for Industry. https://www.fda.gov/media/89829/download [accessed Oct 1, 2019]. 4. Munjal S, et al. *Headache*. 2019;59(Suppl. 1):65–66.

Oral delivery of migraine treatments may be suboptimal for some patients with migraine

Migraine is associated with gastric stasis and may lead to delayed absorption of oral medication

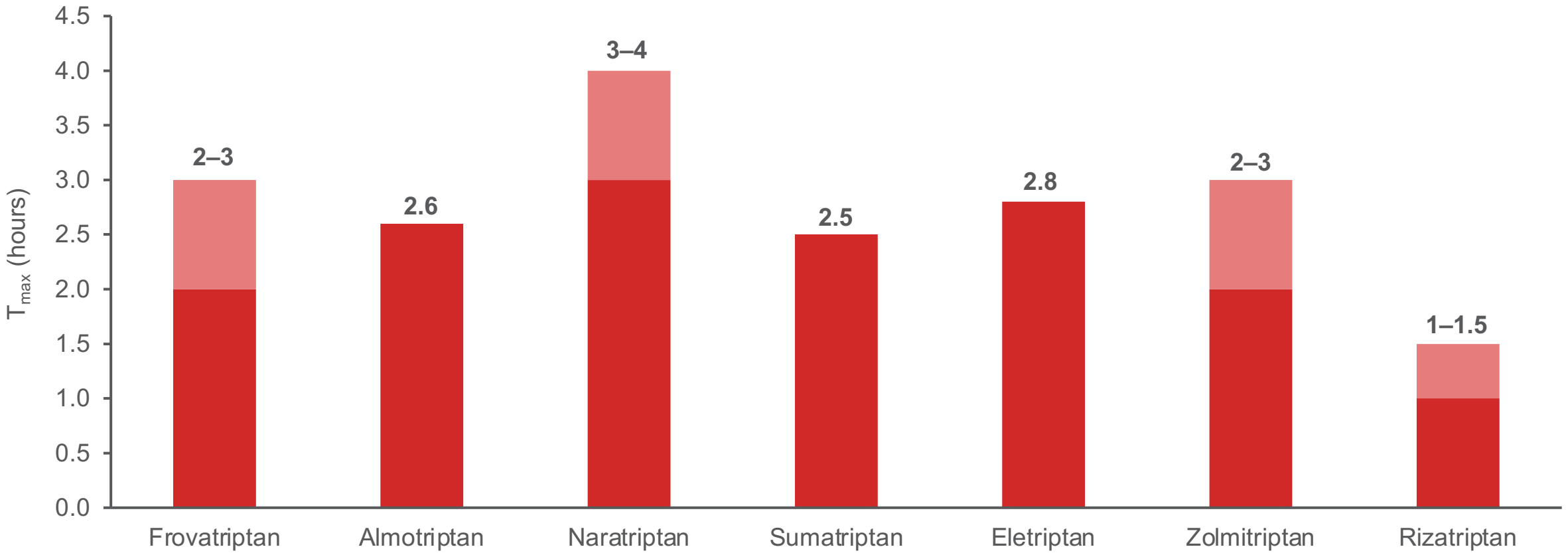
Use of some oral migraine medications can induce or exacerbate nausea or vomiting

Pretreatment nausea predicts a poor response to oral triptans

Patients with nausea may delay or avoid taking oral medications

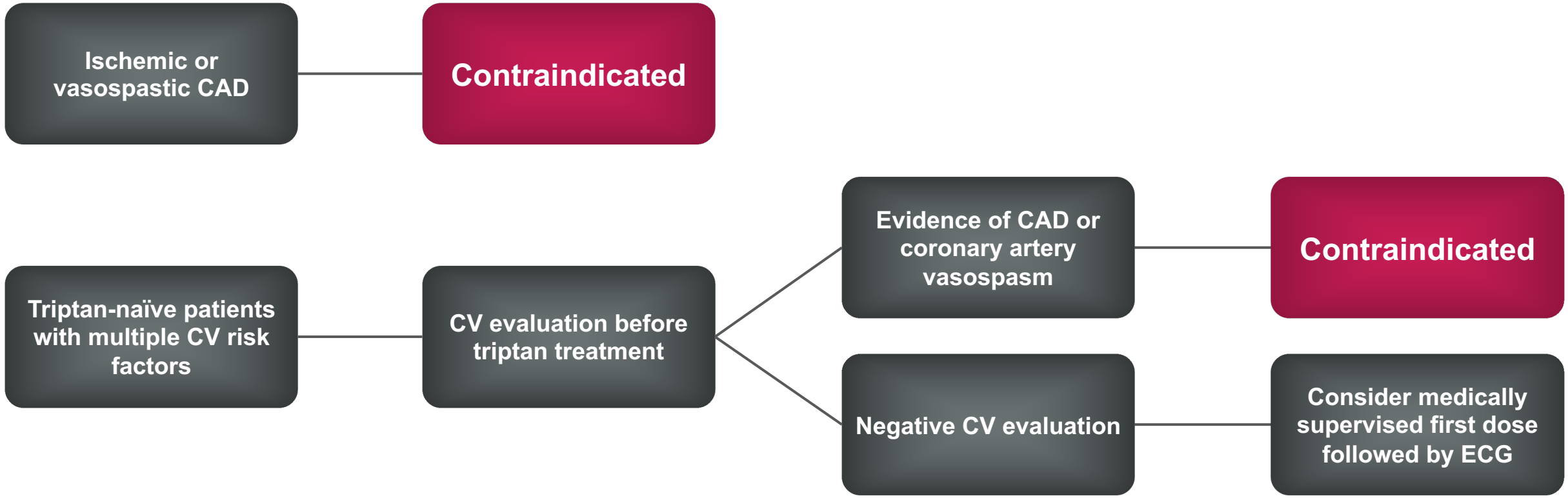
Pierce M. *Headache*. 2013;53:S17–S20. Ho TW, et al. *Headache*. 2009;49:395–403.

Oral triptan treatments may be suboptimal because of T_{max}



T_{max}, time to maximum concentration.
Marcus D. *Arch Neurol*. 2001;58:1056–1058.

Triptan use in patients at risk for CVD



CAD, coronary artery disease; ECG, electrocardiogram.

Data source: US prescribing information.

CVD implications for clinical practice

- Risk factors for CVD: migraine with aura, smoking, hypertension, hormonal contraception, obesity, diabetes, family history of CVD
- Patient's CV history and risk factors
  - Should be evaluated before making treatment decisions
  - Need to be reconsidered over time, as new diagnoses and age-related CV risk factors emerge
- Be vigilant for evidence of CV risk and/or disease in women
  - Although men are at higher CV risk, the majority of patients with migraine who have CVD are women

Buse DC, et al. *Headache*. 2017;57:31–44.

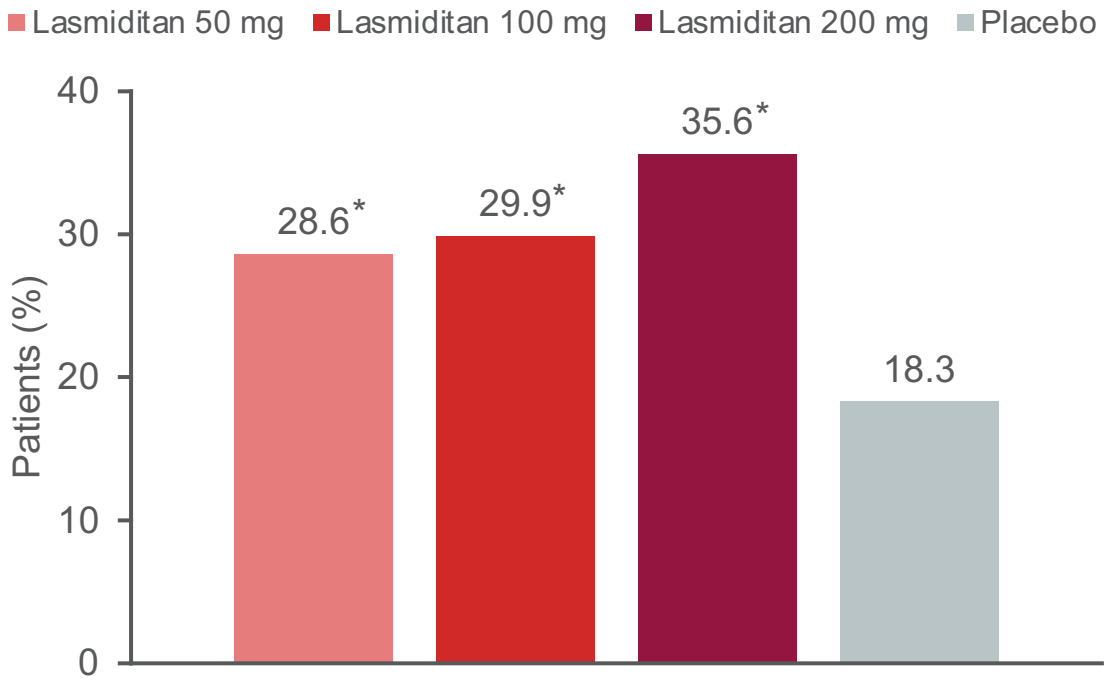
Development of acute migraine drugs designed to be free of CVD risk

- 5-HT_{1F} agonists (ditans)
- Small-molecule CGRP antagonists (gepants)

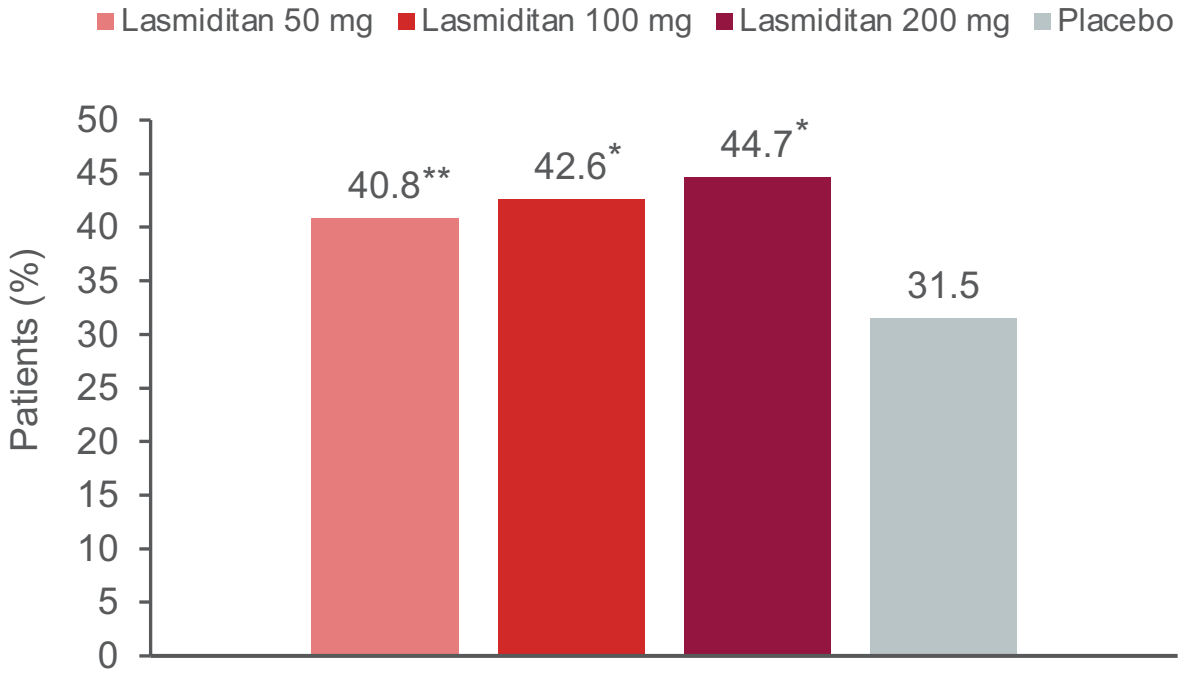
CGRP, calcitonin gene-related peptide; HT, 5-hydroxytryptamine (serotonin).

Lasmiditan integrated phase 3 studies: efficacy results

Pain-free 2h post-dose[1]



Free from most bothersome symptom 2h post-dose[1]



Integrated analysis of data from 5236 patients randomized to treat a single migraine attack within 4 hours of onset with lasmiditan 50 mg (N=750), lasmiditan 100 mg (N=1498), or lasmiditan 200 mg (N=1495), or placebo (N=1493), in the SAMURAI[2] or SPARTAN[3] study. Patients chose their most bothersome non-headache symptom from photophobia, nausea, and phonophobia.

*P<0.001 vs placebo. **P<0.05 vs placebo.

1. Ashina M, et al. *Headache*. 2019;Sep 17. doi: 10.1111/head.13636 [Epub ahead of print]. 2. Kuca B, et al. *Neurology*. 2018;91:e2222–e2232. 3. Goadsby PJ, et al. *Brain*. 2019;142:1894–1904.

Lasmiditan SAMURAI phase 3 study: safety results after first dose

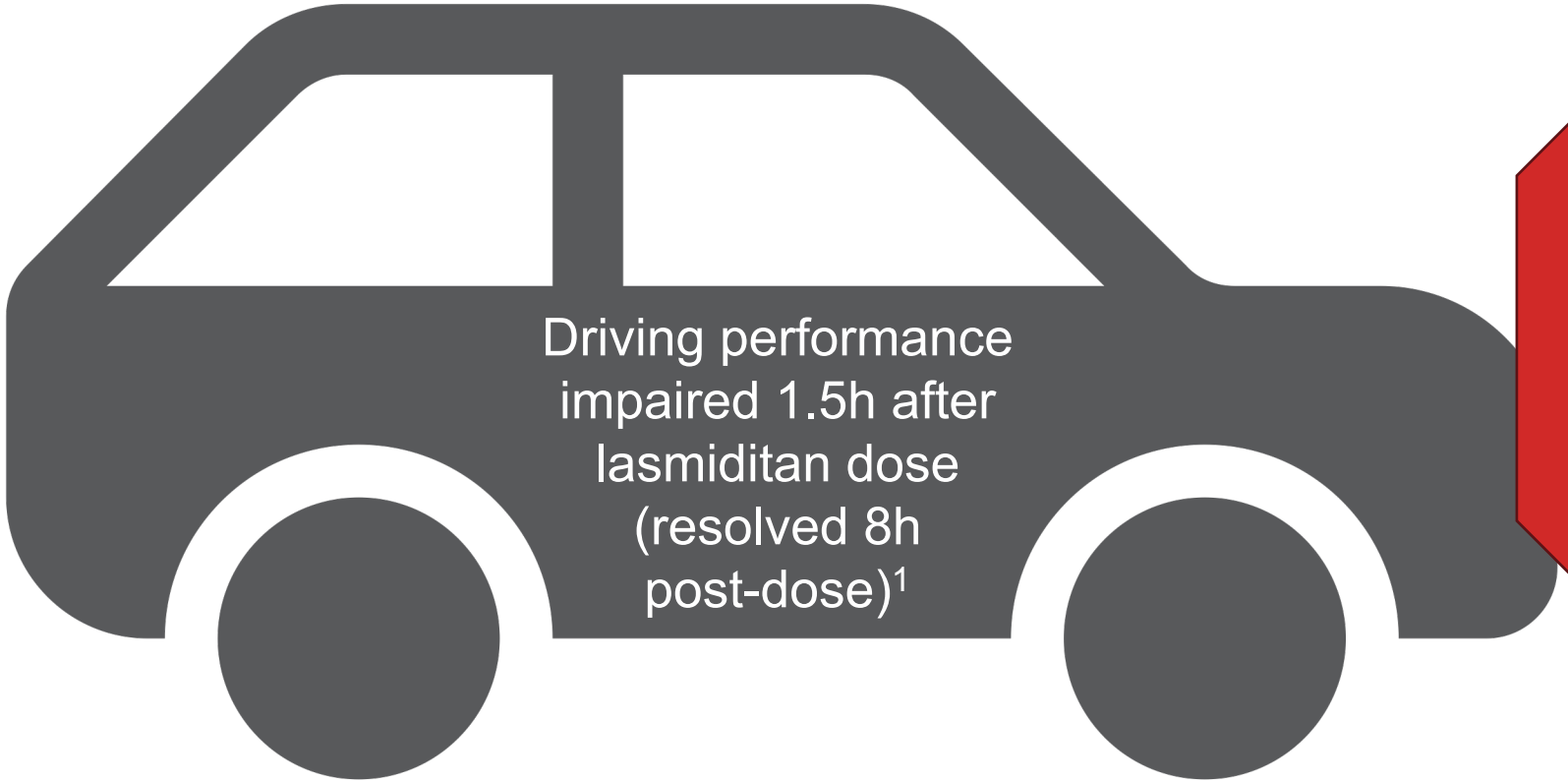
TEAE occurring in ≥2% of patients,* n (%)	Lasmiditan			Placebo (n=1262)
	50 mg (n=654)	100 mg (n=1265)	200 mg (n=1258)	
Dizziness	56 (8.6)	194 (15.3)	216 (17.2)	37 (2.9)
Paresthesia	16 (2.4)	73 (5.8)	91 (7.2)	19 (1.5)
Somnolence	35 (5.4)	65 (5.1)	75 (6.0)	27 (2.1)
Fatigue	18 (2.8)	52 (4.1)	50 (4.0)	8 (0.6)
Nausea	18 (2.8)	52 (4.1)	50 (4.0)	20 (1.6)
Muscular weakness	7 (1.1)	16 (1.3)	19 (1.5)	0
Hypoesthesia	2 (0.3)	17 (1.3)	20 (1.6)	3 (0.2)

- Most TEAEs in lasmiditan recipients were of mild or moderate severity[1]
- Dizziness had a median time to onset of 30–40 minutes and duration of 1.5–2 hours[2]

Integrated analysis[1] of data from 4439 patients who received at least one dose of study drug in the SAMURAI or SPARTAN study.
*In any lasmiditan group, and greater than placebo.
TEAE, treatment-emergent adverse event.

1. Krege JH, et al. *Cephalalgia*. 2019;39:957–966. 2. Tepper SJ, et al. *Headache*. 2019;59:1052–1062.

Driving impairment observed following lasmiditan dosing



Label Warning[2]

- Advise patients not to drive or operate machinery for at least 8 hours after each dose of lasmiditan
- Patients who cannot follow this advice should not take lasmiditan

1. Pearlman EM, et al. *Headache*. 2019;59(Suppl. 1):22–23. 2. Eli Lilly and Company. Reyvow US prescribing information (October 2019).

Lasmiditan integrated phase 3 studies: CV results

- 79% of patients who treated a migraine with study drug had ≥1 CV risk factor
- Likely CV TEAEs: lasmiditan 0.9%; placebo 0.4% (all mild-to-moderate)
  - Cardiac arrhythmias more often reported with lasmiditan vs placebo (0.9%* vs 0.2%; *P*=0.02)
  - Difference largely due to reports of palpitations, tachycardia, and increased heart rate
- No significant difference in frequency of likely CV TEAEs in the absence or presence of any CV risk factors
- The only likely CV TEAE seen across patients with ≥1, ≥ 2, ≥ 3, or ≥ 4 CV risk factors was palpitations

Integrated analysis[1] of data from 4439 patients who treated a single migraine attack with lasmiditan (all doses; N=3177) or placebo (N=1262) in the SAMURAI[2] or SPARTAN[3] study.

*Study size adjusted percentage.

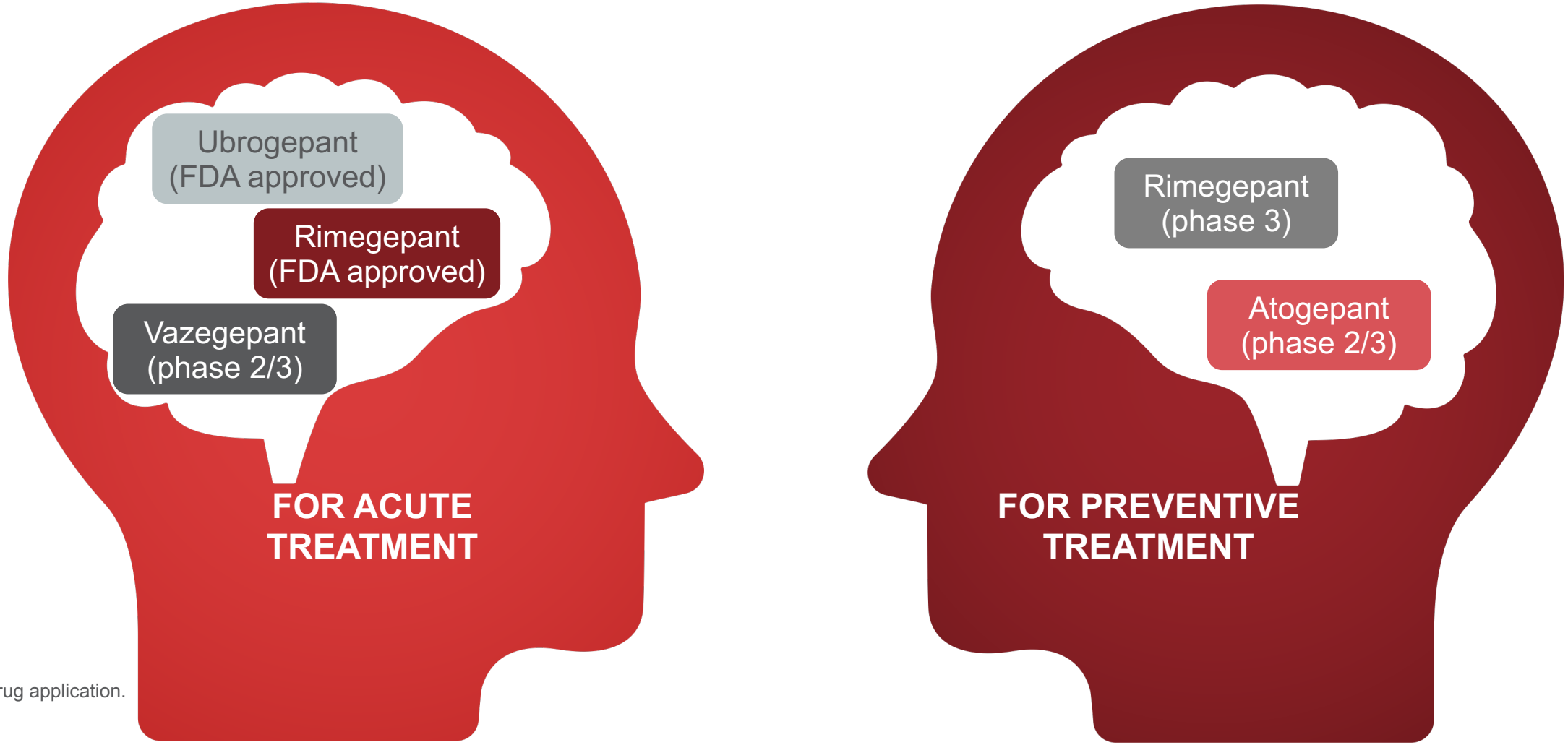
1. Shapiro RE, et al. *J Headache Pain*. 2019;20:90. 2. Kuca B, et al. *Neurology*. 2018;91:e2222–e2232. 3. Goadsby PJ, et al. *Brain*. 2019;142:1894–1904.

Small-molecule CGRP receptor antagonists (gepants)

- Efficacy greater than placebo
- Do not cause vasoconstriction in cranial or coronary arteries[1,2]
  - No reports of serious CV adverse events in clinical trials
- Development of early agents in the class was discontinued for varying reasons
  - Olcegepant: IV only
  - Telcagepant: liver test abnormalities
  - MK-3207: liver test abnormalities
  - BI 44370 TA: no published data on the reason for discontinuation

1. Rubio-Beltran E, et al. *Cephalalgia*. 2020;40:357-366. 2. Conway CM, et al. *Headache*. 2019;59(Suppl. 1):176.

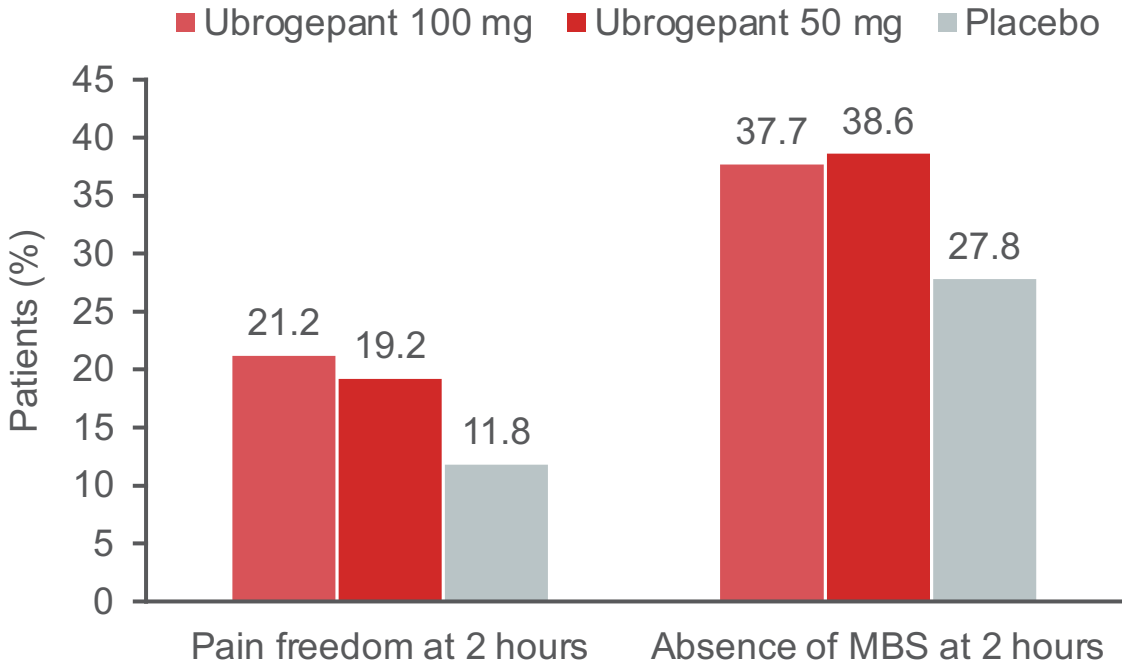
Gepants recently approved and currently in development



NDA, new drug application.

Ubrogepant phase 3 study in episodic migraine (ACHIEVE I)

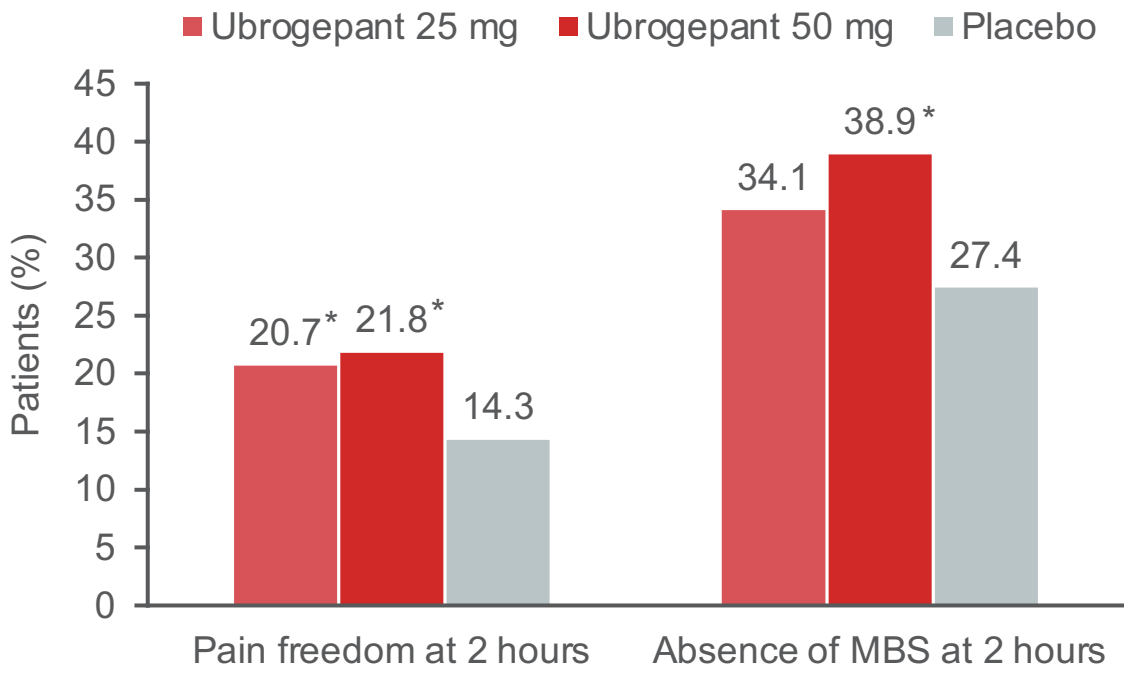
- Significantly superior to placebo on the coprimary efficacy endpoints*
- Most common AEs: nausea, somnolence, and dry mouth
  - No new or unexpected AEs*
  - No liver safety issues



**P*<0.02 vs placebo.
Patients (N=1113) were randomized to PO ubrogepant (50 or 100 mg) or placebo. MBS included photophobia, phonophobia, or nausea.
MBS, most bothersome symptom.

1. Dodick DW et al. *NEJM*. 2019;381:2230-2241

Ubrogepant phase 3 study in episodic migraine (ACHIEVE II)



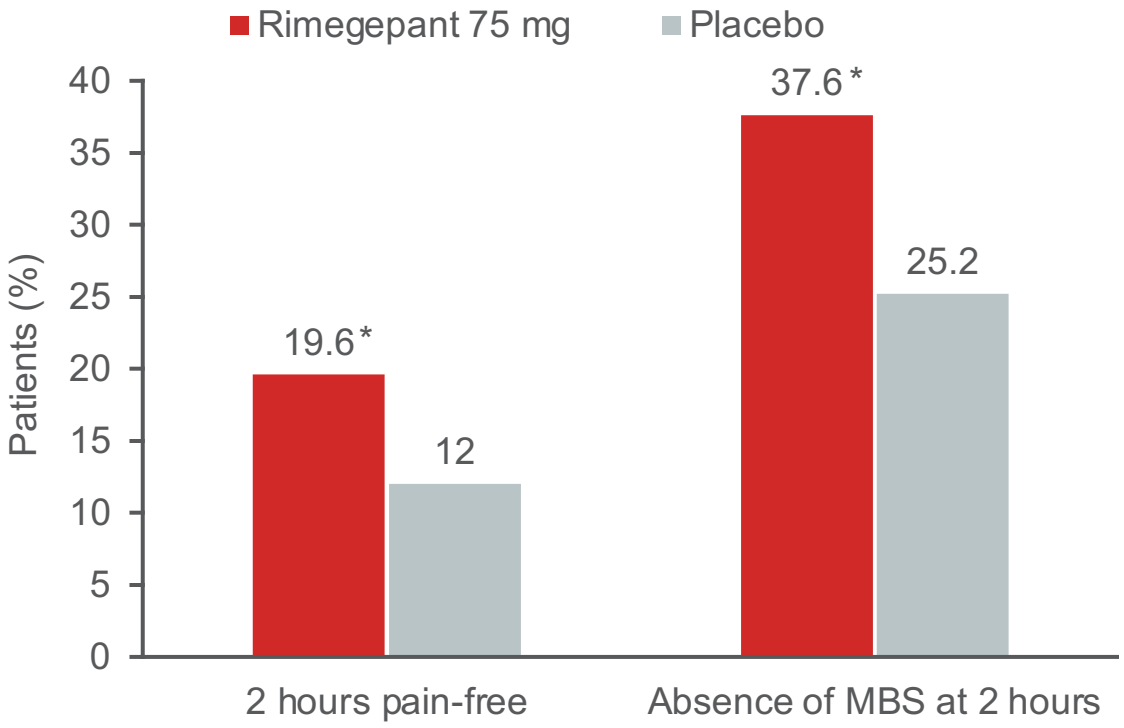
- Highly consistent with results from ACHIEVE I
- Patients in the 50 mg group showed sustained pain relief for 24 hours after treatment
- Most common AEs: nausea and dizziness
- No signal of hepatotoxic effects

*P<0.05 vs placebo.
Patients (N=1686) were randomized to PO ubrogepant (25 or 50 mg) or placebo. MBS included photophobia, phonophobia, or nausea.
MBS, most bothersome symptom.

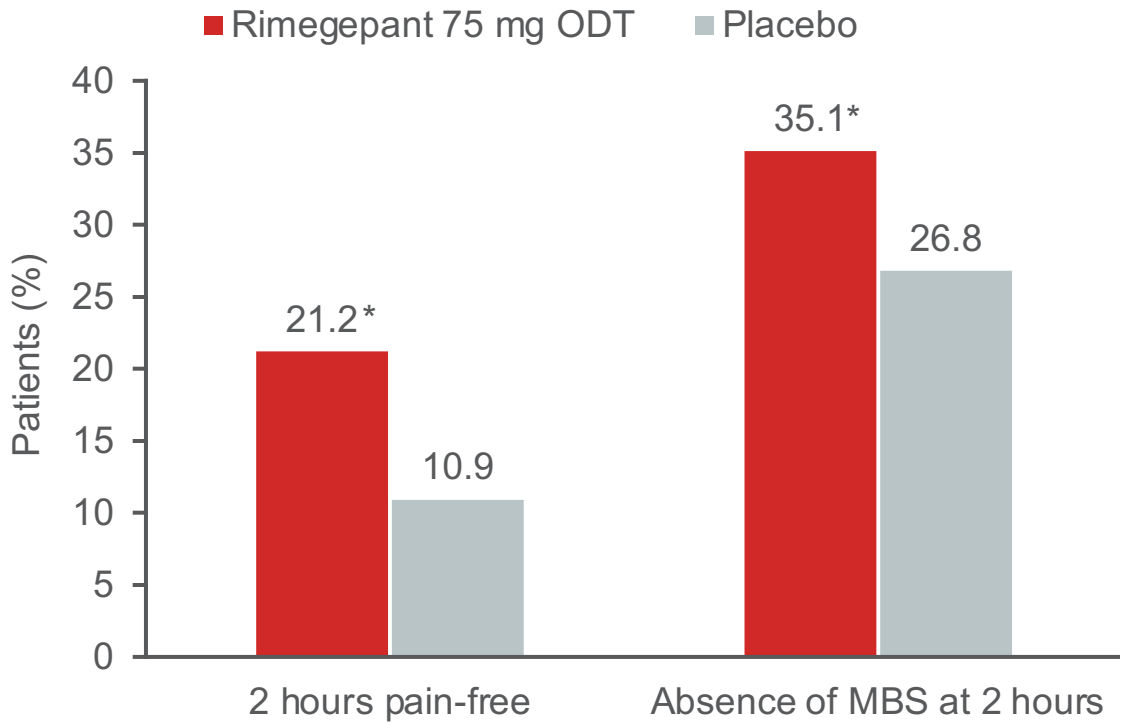
1. Lipton RB, et al. *JAMA*. 2019;322:1887–1898.

Rimegepant phase 3 studies: efficacy results

Conventional oral tablet (N=1072)[1]



ODT (N=1375)[2]



Positive treatment effects were observed as early as 1 hour post-dose[2]

*P<0.0001 vs placebo.
Patients were randomized to oral rimegepant 75 mg or placebo. MBS included photophobia, phonophobia, or nausea.
ODT, orally disintegrating tablet.

1. Lipton RB, et al. *N Engl J Med.* 2019;381:142–149. 2. Croop R, et al. *Lancet*. 2019; 394:737–745.

Rimegepant phase 3 studies: safety results

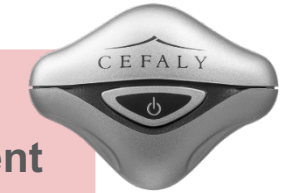
AEs, n (%)	Conventional tablet[1]		ODT[2]	
	Rimegepant (N=543)	Placebo (N=543)	Rimegepant (N=543)	Placebo (N=543)
Any AE	93 (17.1)	77 (14.2)	90 (13)	73 (11)
AEs reported in ≥1% of patients in either treatment group				
Nausea	10 (1.8)	6 (1.1)	11 (2)	3 (<1)
Urinary tract infection	8 (1.5)	6 (1.1)	10 (1)	4 (1)
Dizziness	NR	NR	6 (1)	7 (1)

- Liver function tests similar to placebo

Patients were randomized to oral rimegepant 75 mg or placebo.
NR, not reported.

1. Lipton RB, et al. *N Engl J Med.* 2019;381:142–149. 2. Croop R, et al. *Lancet*. 2019; 394:737–745.

Neurostimulation approaches for treatment of migraine



- Acute treatment
- Preventive treatment

Transcutaneous supraorbital nerve stimulation (external trigeminal nerve stimulation)

- Acute treatment
- Preventive treatment

Single-pulse transcranial magnetic stimulation

- Acute treatment
- Preventive treatment

Non-invasive vagus nerve stimulation

- Acute treatment

Remote electrical neuromodulation

Migraine and COVID-19

- Multiple headaches similar to ICHD-3 headache types may be present[1]:
  - Days 0-6: acute headache attributed to systemic viral infection, primary cough headache, tension-type headache, and headache attributed to heterophoria
  - Day 7+: headache attributed to hypoxia, headache attributed to other non-infectious inflammatory intracranial disease — aseptic meningeal inflammation due to cytokine storm?
- Telemedicine to avoid clinic and emergency department visits[2]
  - Acute treatment: NSAIDs and triptans are first-line, then gepants, lasmiditan, neuromodulation
  - NSAID "bridge" strategy for severe/continuous pain
  - Preventive: seek alternatives to onabotulinumtoxinA — CGRP mAbs, ACE inhibitors, ARBs
- Lift insurance restrictions on accessing migraine medications![2]

"Migraine patients decided to overcome all the logistical difficulties not to lose the clinical benefit they were experiencing and falling back into the abyss of their migraine attacks. . ."[3]

ICHD, International Classification of Headache Disorders.

1. Belvis R. *Headache*. 2020 May 15. doi: 10.1111/head.13841; 2. Szperka CL et al. *Headache*. 2020;0:1-10; 3. Silvestro M et al. *Headache*. 2020;60:988-989.

Acute Treatment Conclusions

- CV safety is an important consideration for both women and men
  - The patient's CV risk should be evaluated when initiating therapy and as the patient ages
  - Treatment options designed to be free of CV risk include investigational drugs and non-invasive neuromodulation devices
- Optimize acute migraine therapy for better effectiveness
  - Select a treatment based on the patient's individual needs
  - Educate the patient about the importance of taking medication early, when pain is still mild
  - Recognize the potential role and usefulness of neuromodulation
- Non-oral formulations may be needed for patients who desire faster onset of action, greater consistency, or better oral absorption

Migraine preventive treatment modalities

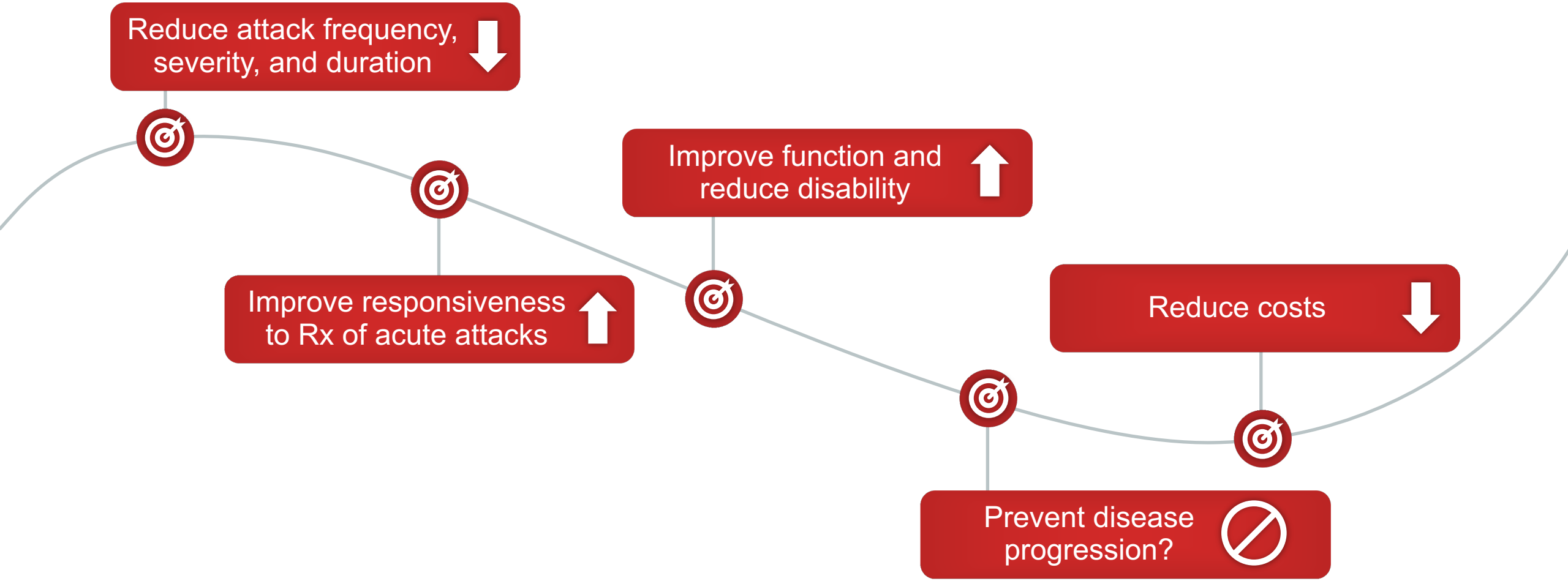
Pharmacotherapy

Behavioral therapy

Neuromodulation

Stay tuned for the sessions this afternoon!

Goals of preventive treatment



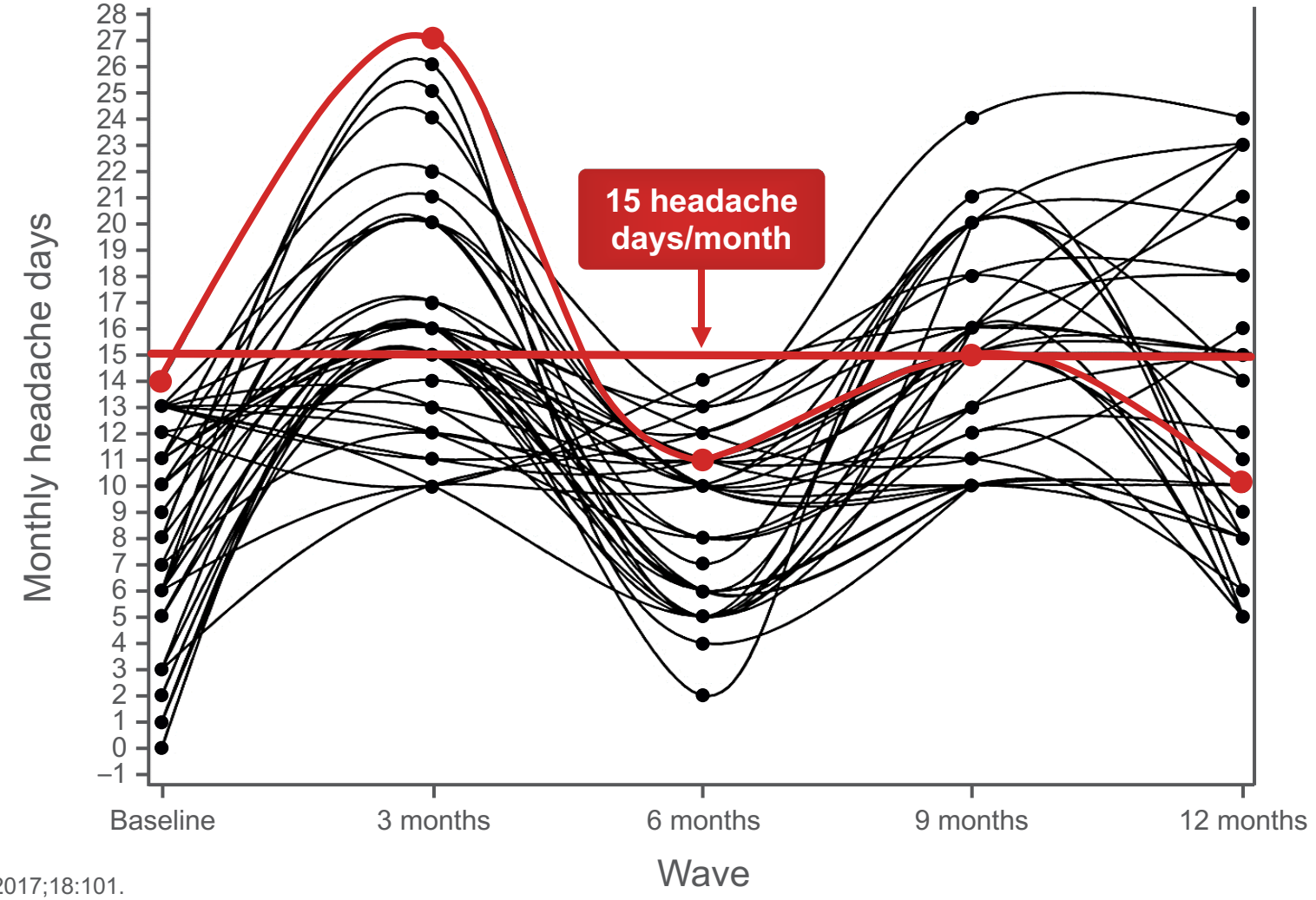
Rx, treatment.

When to consider prevention

1. Migraine significantly interferes with patients' daily routine, despite appropriate acute treatment
2. Frequent attacks (>1/week) with risk of progression
3. Acute medications ineffective, contraindicated, cause troublesome adverse effects, or overused
4. Patient preference
5. Special circumstances such as:
   - Hemiplegic migraine
   - Brain stem aura
   - Prolonged aura
   - Migrainous infarction

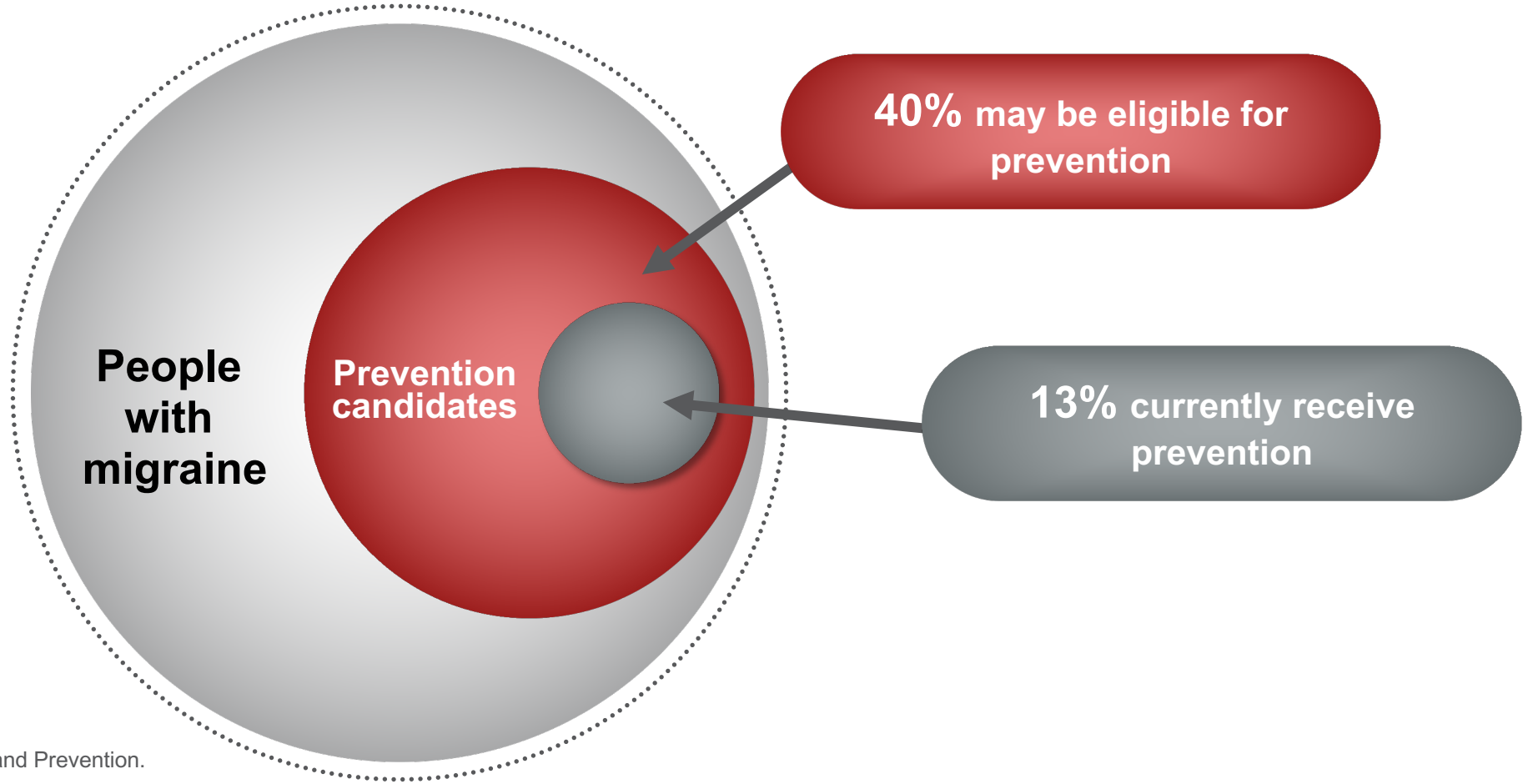
Silberstein SD. *Continuum (Minneap Minn)*. 2015;21(4 Headache):973–989. Lipton RB, et al. *Neurology*. 2007;68:343–349.

Headache frequency fluctuates within individuals



Serrano D, et al. *J Headache Pain*. 2017;18:101.

Migraine prevention is underutilized: AMPP study

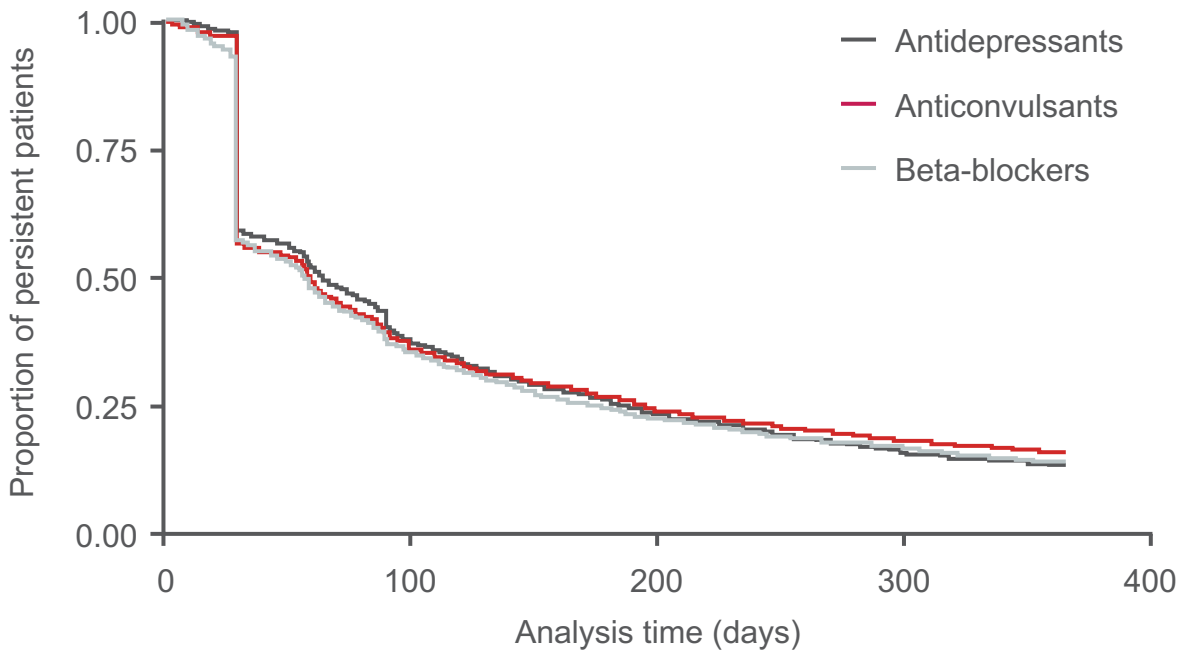


AMPP, American Migraine Prevalence and Prevention.

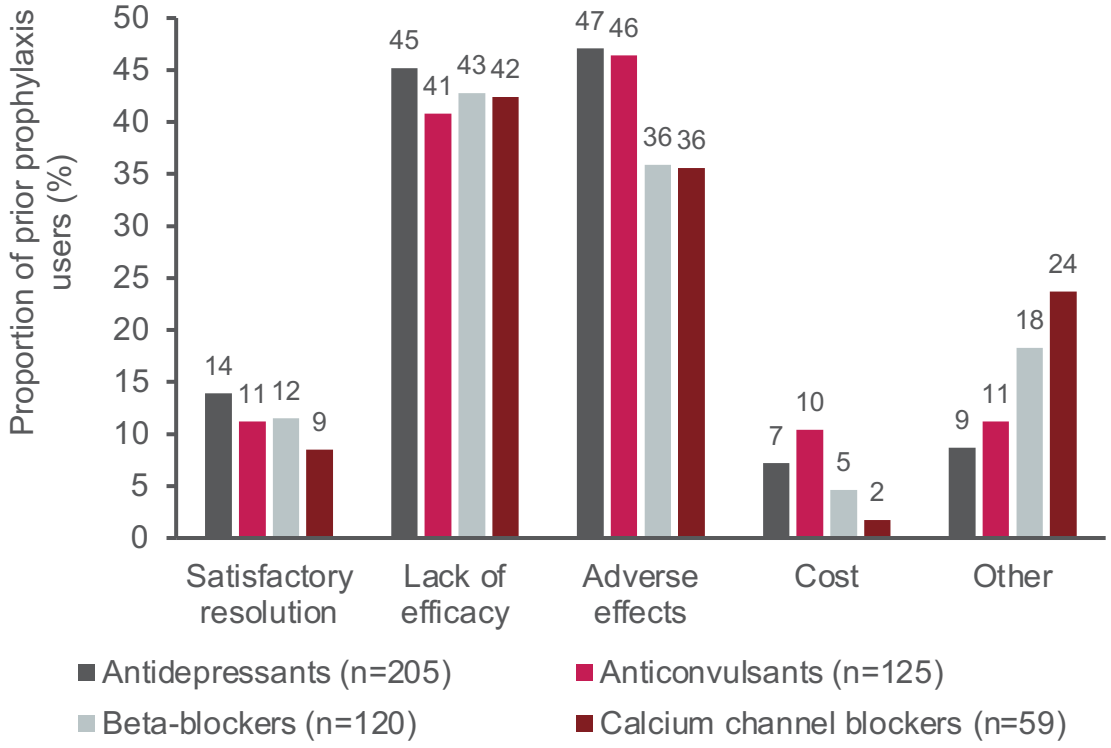
Lipton RB, et al. *Neurology*. 2007;68:343–349.

Persistence with oral migraine prevention is often poor due to low efficacy or intolerable adverse effects

Discontinuation of migraine prevention up to 12 months from initiation[1]



Patient-reported reasons for discontinuing migraine prevention[2]



1. Hepp Z, et al. *Cephalalgia.* 2017;37:470–485. 2. Blumenfeld AM, et al. *Headache.* 2013;53:644–655.

Migraine preventive medications

ANTIEPILEPTIC DRUGS

- Divalproex sodium*, valproate sodium*, topiramate*

BETA-BLOCKERS

- Propranolol*, timolol*, metoprolol, atenolol, nadolol

ANGIOTENSIN SYSTEM

- Candesartan, lisinopril

ANTIDEPRESSANTS

- TCAs, SNRIs

NEUROTOXINS

- OnabotulinumtoxinA (CM only)*

mAbs

- Erenumab*, fremanezumab*, galcanezumab*, eptinezumab*

OTHER

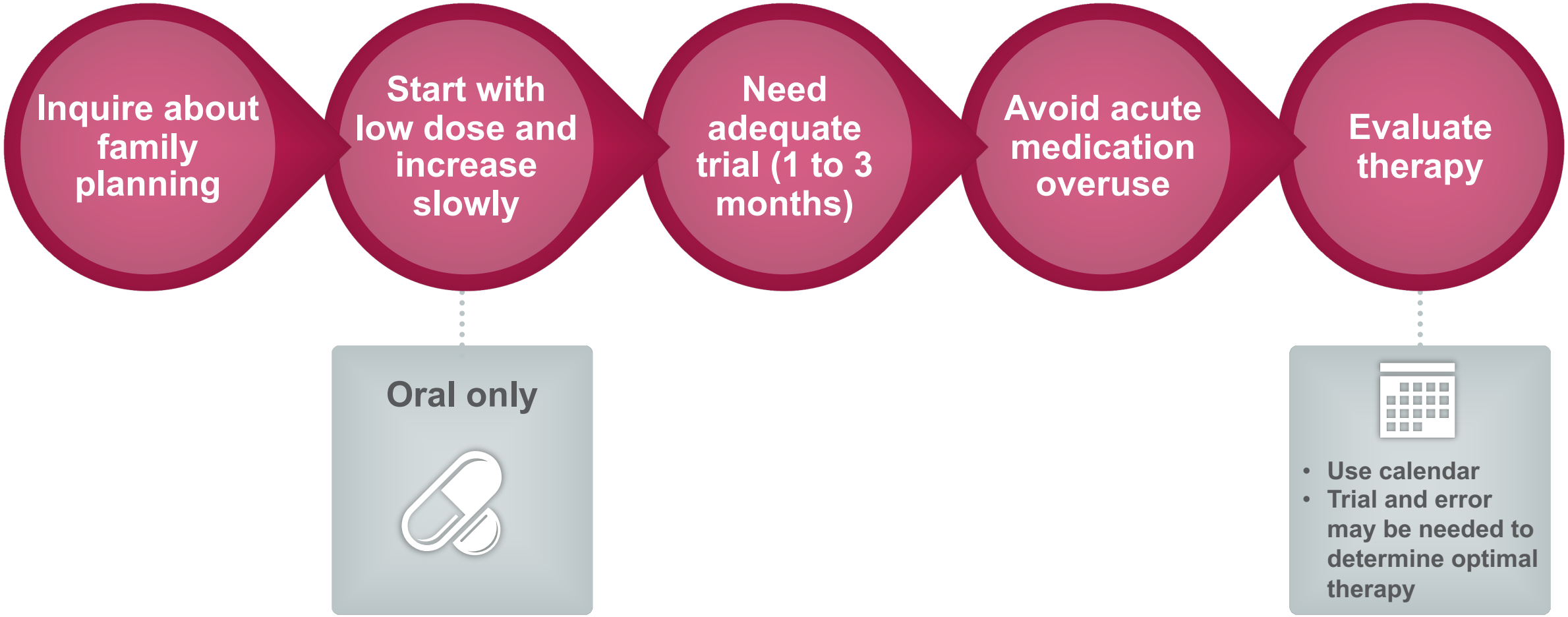
- Memantine
- Riboflavin
- Co-enzyme Q10
- Feverfew
- Magnesium
- Melatonin

*FDA approved

CM, chronic migraine; FDA, U.S. Food & Drug Administration; mAb, monoclonal antibody; SNRI, serotonin and norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.

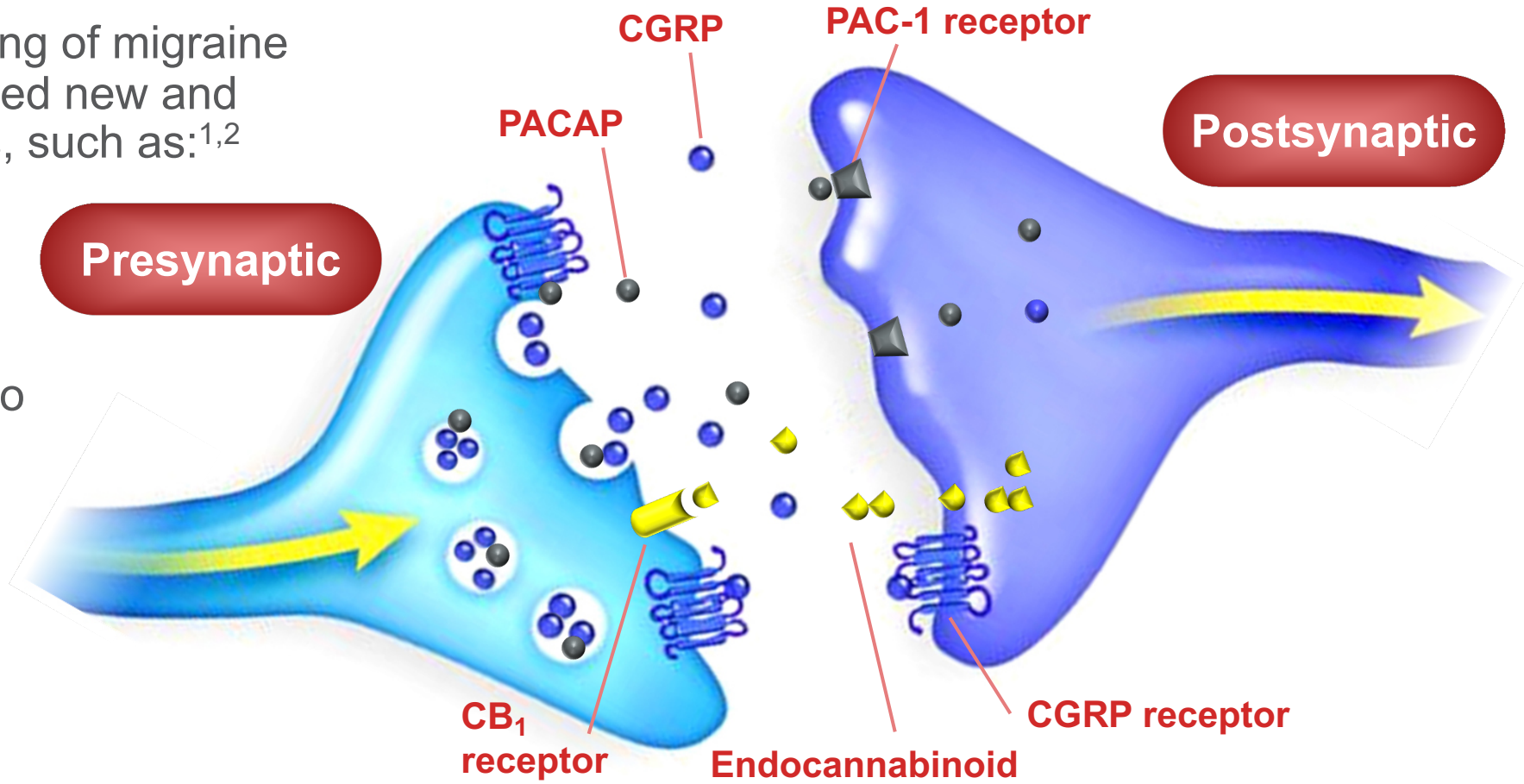
American Headache Society. *Headache*. 2019;59:1–18. Rau JC, Dodick DW. *Curr Treat Options Neurol.* 2019;21:17. Wells RE, et al. *Curr Pain Headache Rep*. 2019;23:10.

Traditional principles of preventive migraine drug treatment



New drug targets and development of novel pharmacotherapies

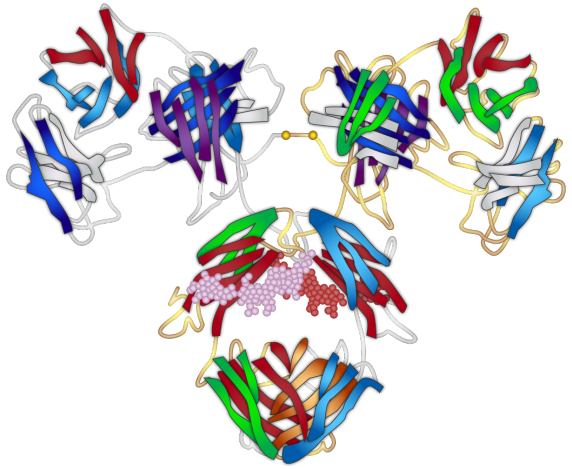
- Advances in the understanding of migraine pathophysiology have revealed new and emerging therapeutic targets, such as:[1,2]
  - CGRP
  - PACAP
  - Endocannabinoids
- mAbs are a new alternative to small molecules[3]



CB_1 receptor, cannabinoid receptor type 1; CGRP, calcitonin gene-related peptide;
PAC-1, pituitary adenylate cyclase-activating polypeptide type I receptor; PACAP, pituitary adenylate cyclase-activating polypeptide.

1. Charles A. *Lancet Neurol*. 2018;17:174–182. 2. Tassorelli C, et al. *Curr Opin Neurol*. 2019;Mar 14. doi: 10.1097/WCO.0000000000000688 [Epub ahead of print]. 3. Tso AR, Goadsby PJ. *Curr Treat Options Neurol*. 2017;19:27.

Small molecule vs antibody drugs



Small molecules	Monoclonal antibodies
Size <1 kD	Size ~150 kD
Orally administered	Must be injected
Many enter cells and cross the BBB*	Do not enter cells or cross the BBB†
Half-life hours to days	Half-life 1–4 weeks
Chemically synthesized	Manufactured in tissue culture
Hepatic metabolism and/or renal excretion	Reticuloendothelial system (peptidases)

*Not all small molecules cross the BBB in appreciable quantities. †Antibodies may cross the BBB in very small quantities (0.1% of serum concentration).

BBB, blood–brain barrier.

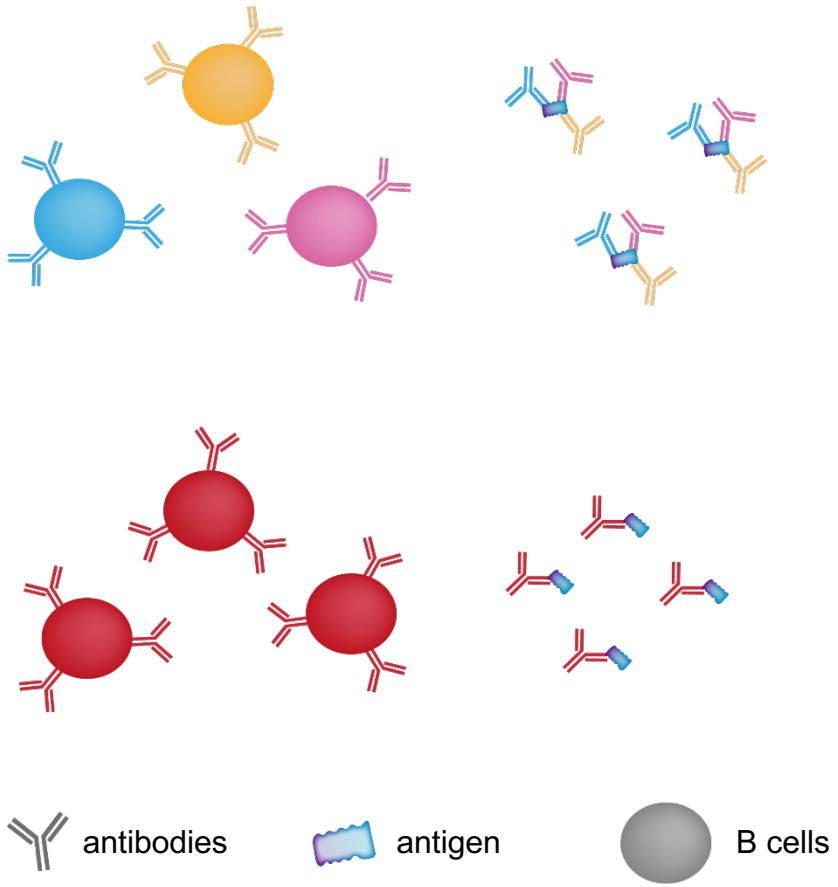
Polyclonal vs monoclonal antibodies

Polyclonal antibodies (pAbs)

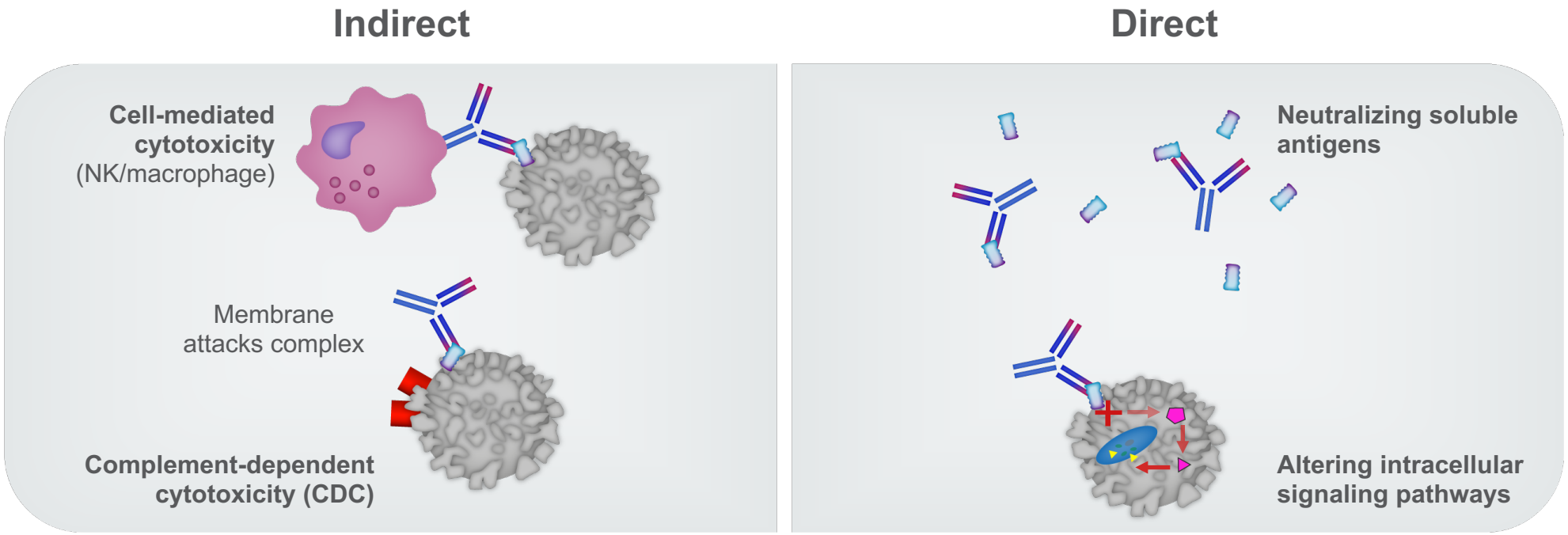
- Secreted from multiple B cells
  - Multiple antigen epitopes

Monoclonal antibodies (mAbs)

- Secreted from single B-cell line
  - One antigen epitope



Mechanisms of action of therapeutic mAbs may be indirect or direct



Induces complement or cell-mediated toxicity by Fc receptors (FcR)

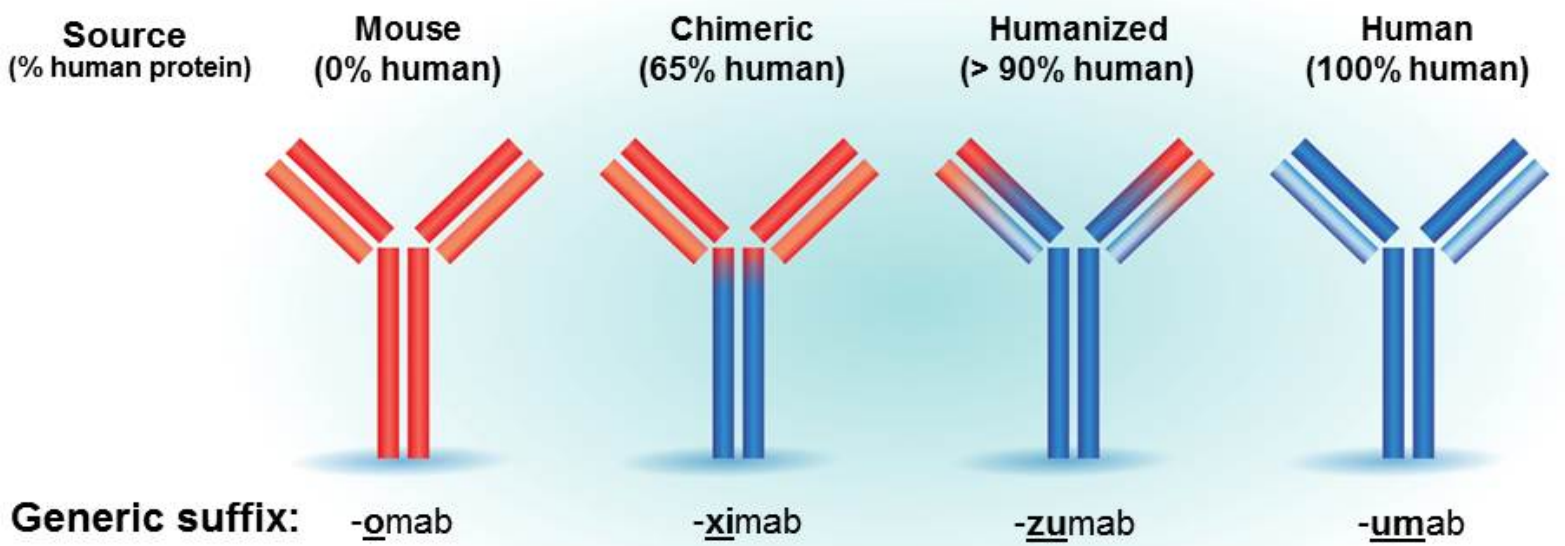
Binds to receptor or ligand

NK, natural killer.

Foltz IN, et al. *Circulation*. 2013;127:2222–2230. Silberstein S, et al. *Headache Currents*. 2015;55:1171–1182.

Naming conventions for therapeutic mAbs

Historical convention*



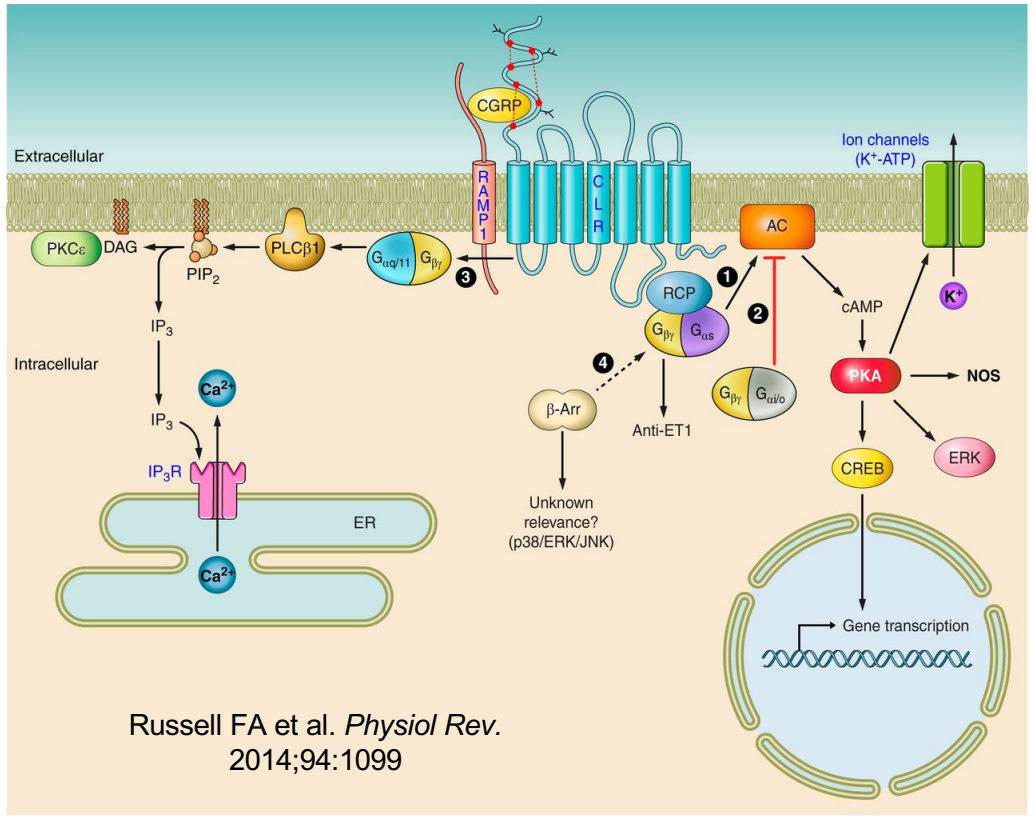
Revised nomenclature

The new nomenclature no longer recognizes the difference between humanized and human antibodies

*Existing names will not be retroactively changed.

CGRP mAbs for migraine prevention

- mAbs targeting CGRP ligand
  - Galcanezumab*
  - Eptinezumab*
  - Fremanezumab*
- mAbs targeting canonical CGRP receptor
  - Erenumab*



Russell FA et al. *Physiol Rev.* 2014;94:1099

*FDA approved.

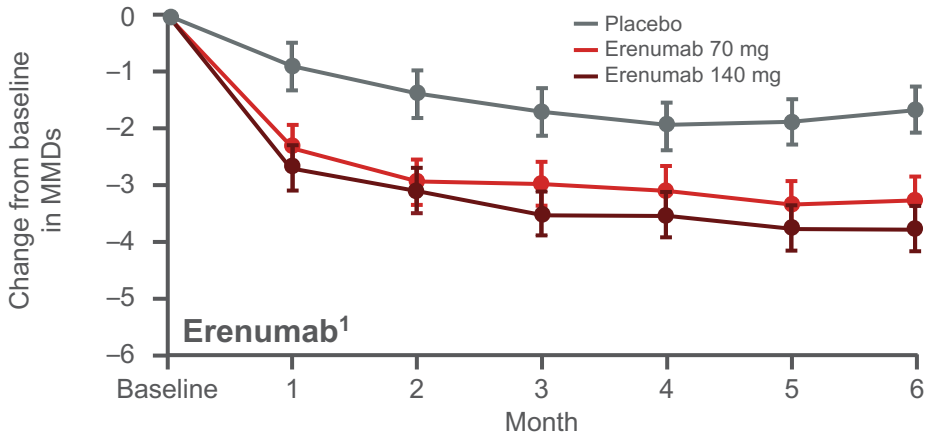
1. Tso AR, Goadsby PJ. *Curr Treat Options Neurol*. 2017;19:27.

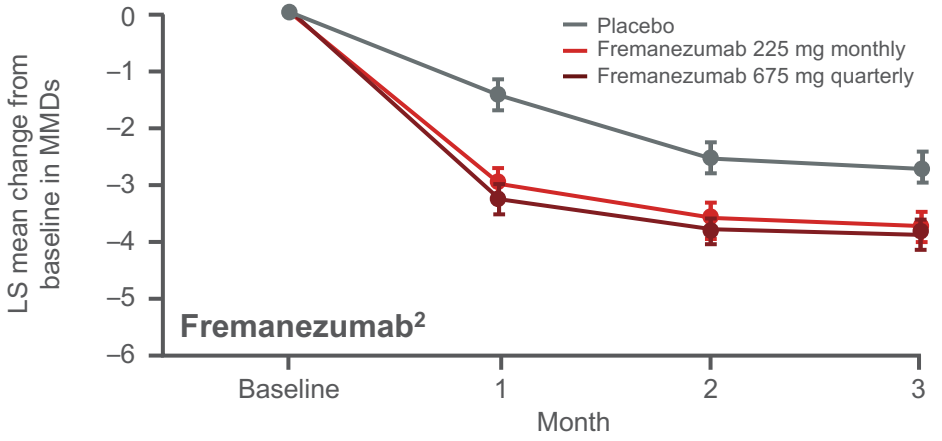
Characteristics of mAbs developed for migraine

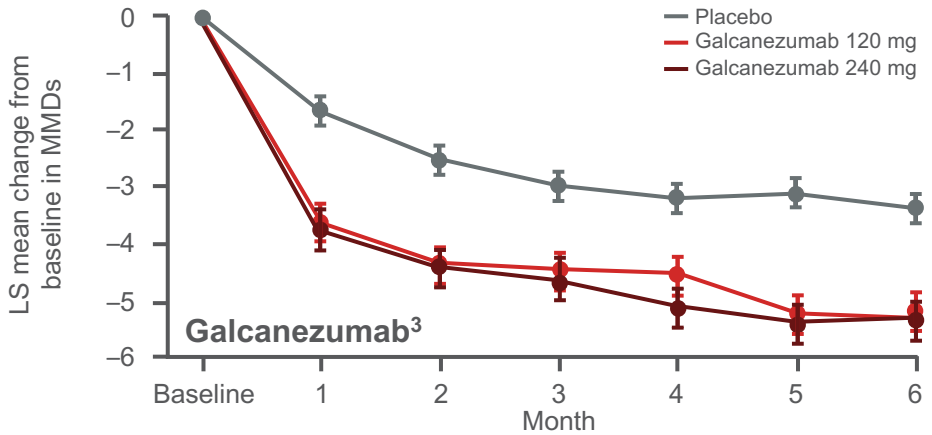
Characteristic	Erenumab	Fremanezumab	Galcanezumab	Eptinezumab
mAb type	Human IgG2	Humanized IgG2a	Humanized IgG4	Humanized IgG1
Target	CGRP receptor	CGRP ligand	CGRP ligand	CGRP ligand
Route of administration	SC	SC	SC	IV infusion
Dose frequency	Monthly	Quarterly/monthly	Monthly	Quarterly
Indication/ development stage	Migraine: approved	▪ Migraine: approved ▪ Post-traumatic headache: phase 2	▪ Migraine: approved ▪ Episodic cluster headache: approved	Migraine: approved
$t_{1/2}$	28 days	31 days	27 days	27 days
Study design – phase 3, placebo controlled (Rx/analysis wks)	12/12 24/last 12	12/12	24/24	24/12 12/12

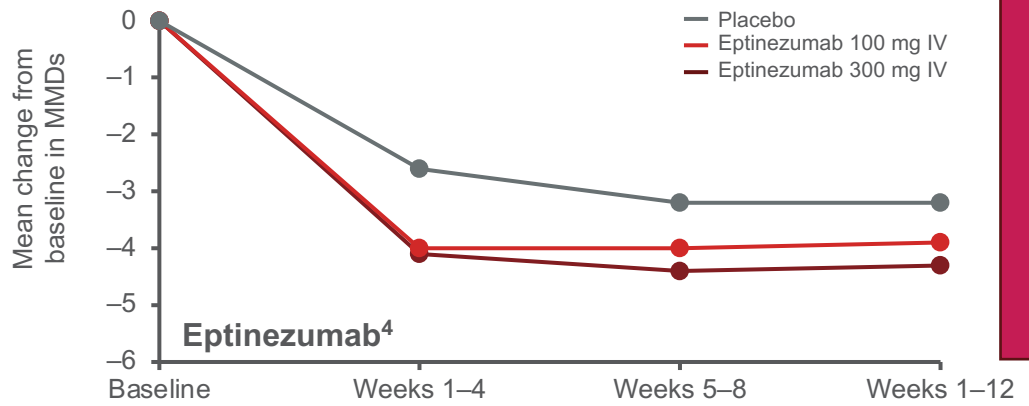
Ig, immunoglobulin; IV, intravenous; SC, subcutaneous; $t_{1/2}$, half-life.

Phase 3 trials in EM: reduction of mean MMDs









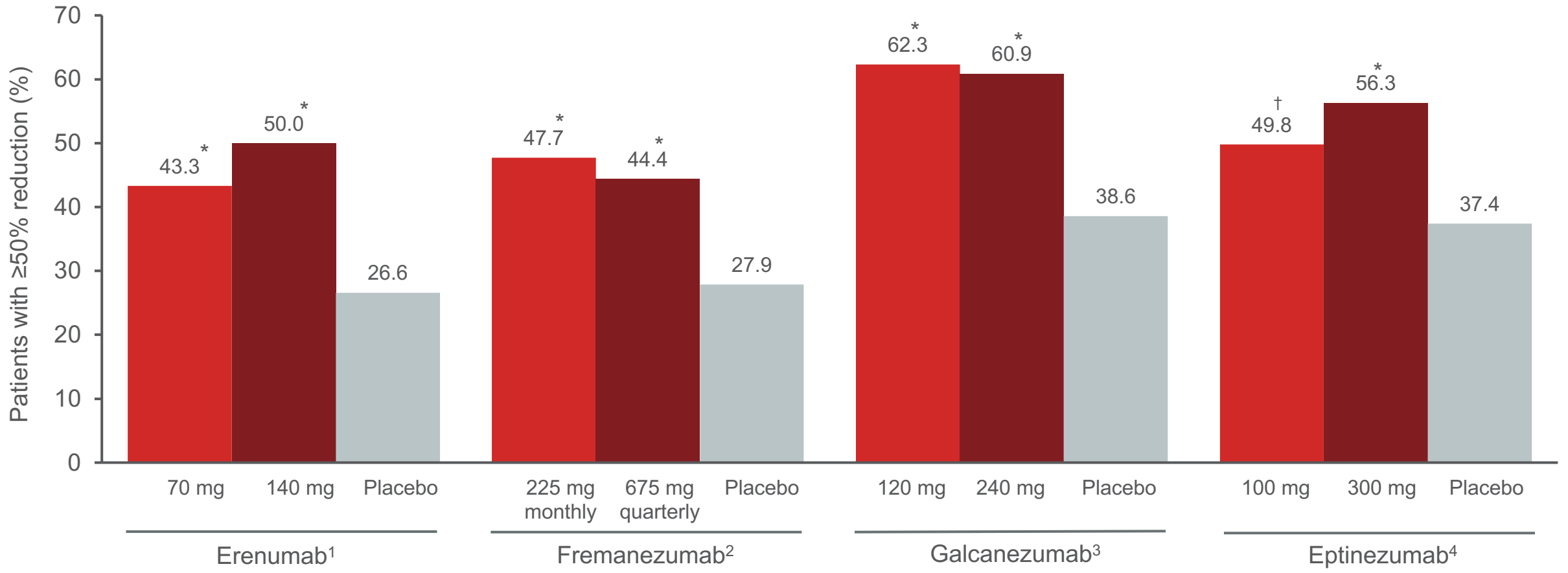
No comparative studies, but anti-CGRP mAbs effective in patients with prior treatment failures[5,6]

Also effective in the setting of medication overuse[7]

EM, episodic migraine; LS, least-squares; MMD, monthly migraine day.

1. Goadsby PJ, et al. *N Engl J Med*. 2017;377:2123–2132. 2. Dodick DW, et al. *JAMA*. 2018;319:1999–2008. 3. Stauffer VL, et al. *JAMA Neurol*. 2018;75:1080–1088. 4. Saper J, et al. *Cephalalgia*. 2017;37(1S):377. 5. Goadsby PJ, et al. *Cephalalgia.* 2019;39:817–826. 6. Ferrari MD, et al. *Lancet.* 2019;394:1030–1040. 7. Tepper SJ, et al. *Neurology*. 2019;92:e2309–e2320.

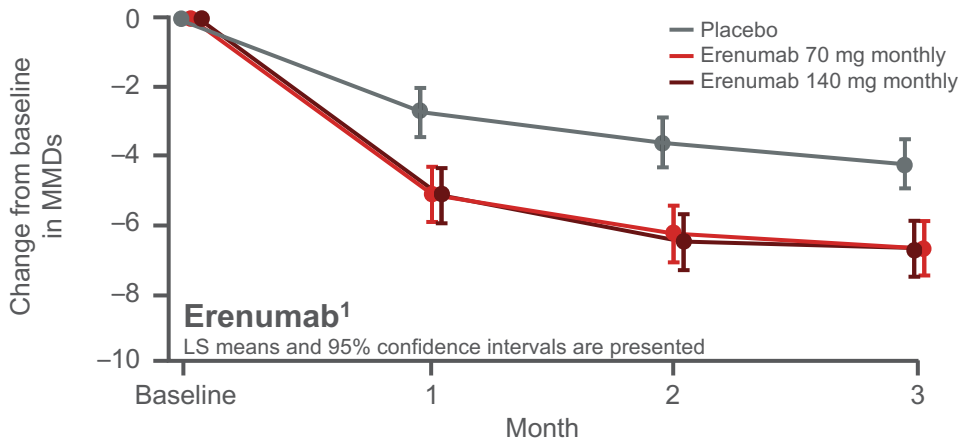
Phase 3 trials in EM: reduction in mean MMDs ≥50%

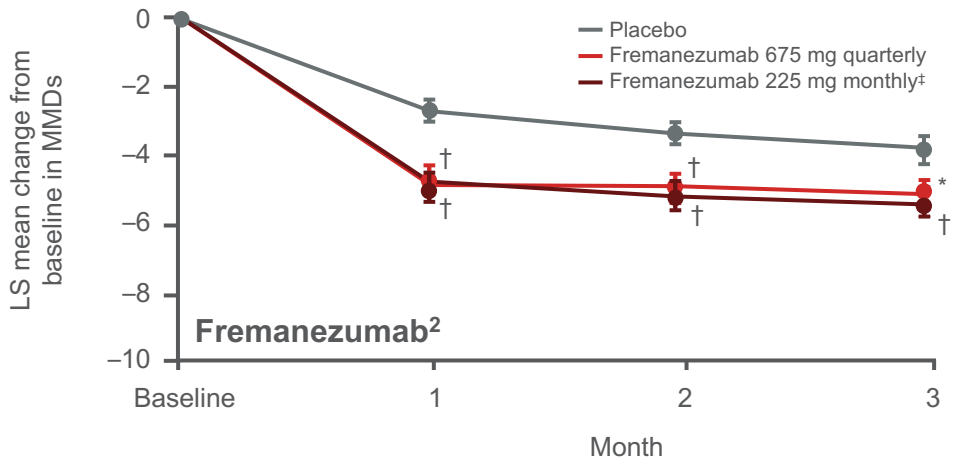


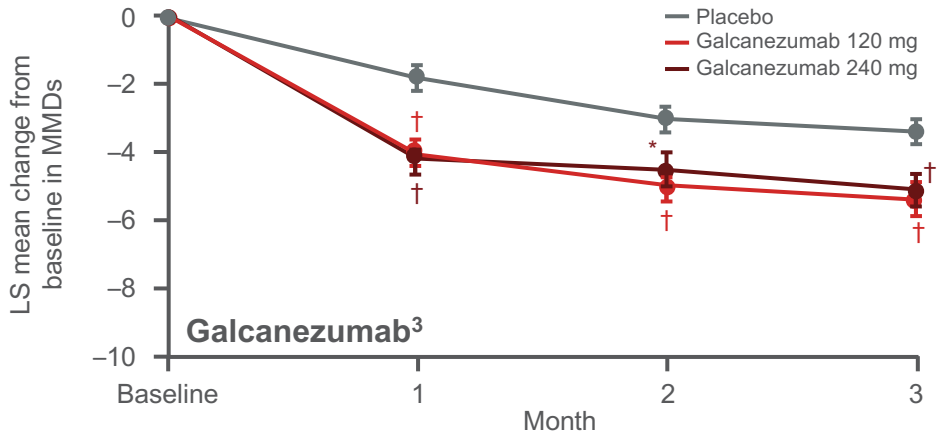
*P<0.001 vs placebo. †P<0.01 vs placebo.

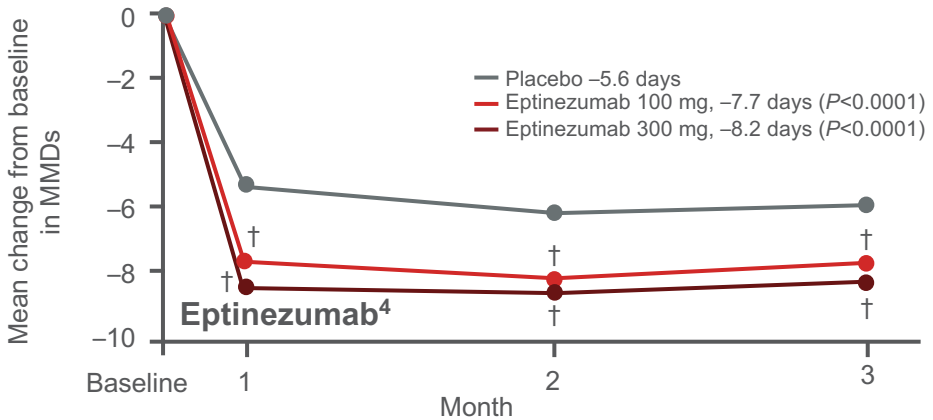
1. Goadsby PJ, et al. *N Engl J Med*. 2017;377:2123–2132. 2. Dodick DW, et al. *JAMA*. 2018;319:1999–2008. 3. Stauffer VL, et al. *JAMA Neurol*. 2018;75:1080–1088.
4. Saper J, et al. *Neurology*. 2018;90(15 Suppl):S20.001.

Pivotal phase 2/3 trials in CM: reduction of mean MMDs









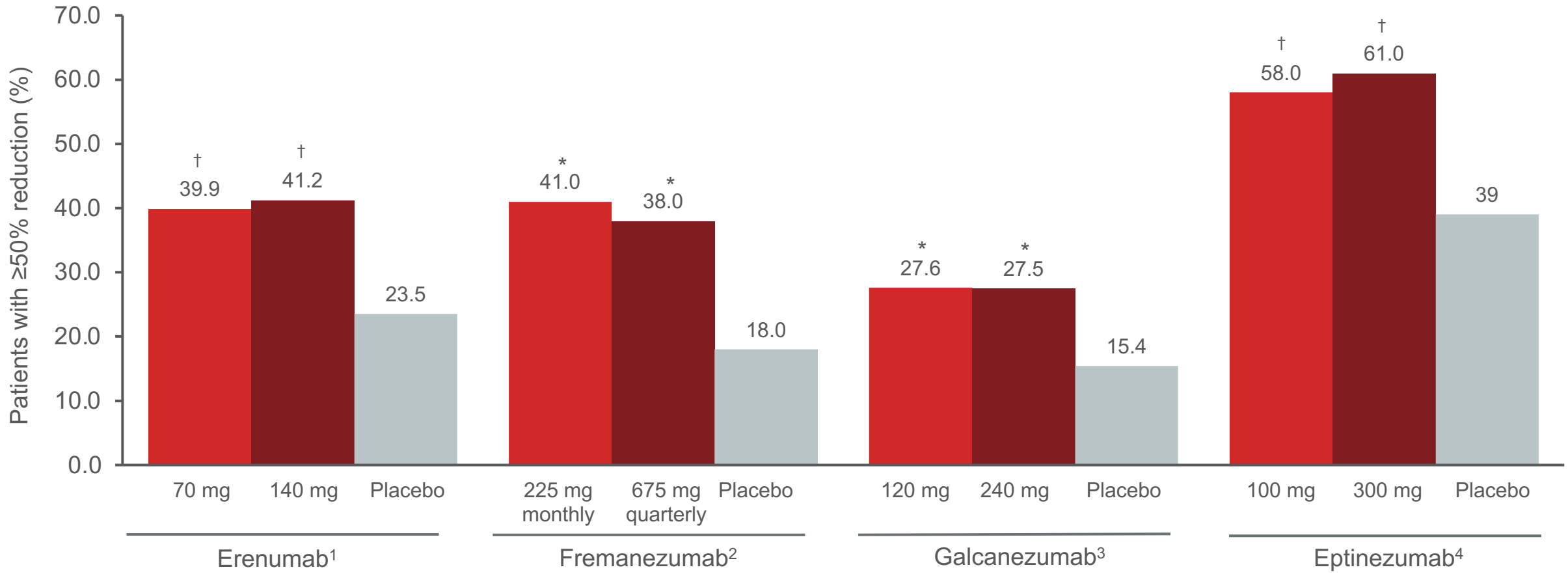
No comparative studies, but anti-CGRP mAbs effective in patients with prior treatment failures[5,6]

Also effective in the setting of medication overuse[7]

*P<0.01 vs placebo. †P<0.001 vs placebo. ‡The fremanezumab monthly group received 675 mg at baseline and 225 mg at weeks 4 and 8.

1. Tepper S, et al. *Lancet Neurol*. 2017;16:425–434. 2. Silberstein SD, et al. *N Engl J Med*. 2017;377:2113–2122. 3. Detke HC, et al. *Neurology*. 2018;91:e2211–2221. 4. Smith J, et al. *Headache*. 2017;57(Suppl 3):130. 5. Ashina M, et al. *Cephalalgia*. 2018;38:1611–1621. 6. Ferrari MD, et al. *Lancet.* 2019;394:1030–1040. 7. Aurora SK, et al. *Headache*. 2019;59(Suppl. 1):23.

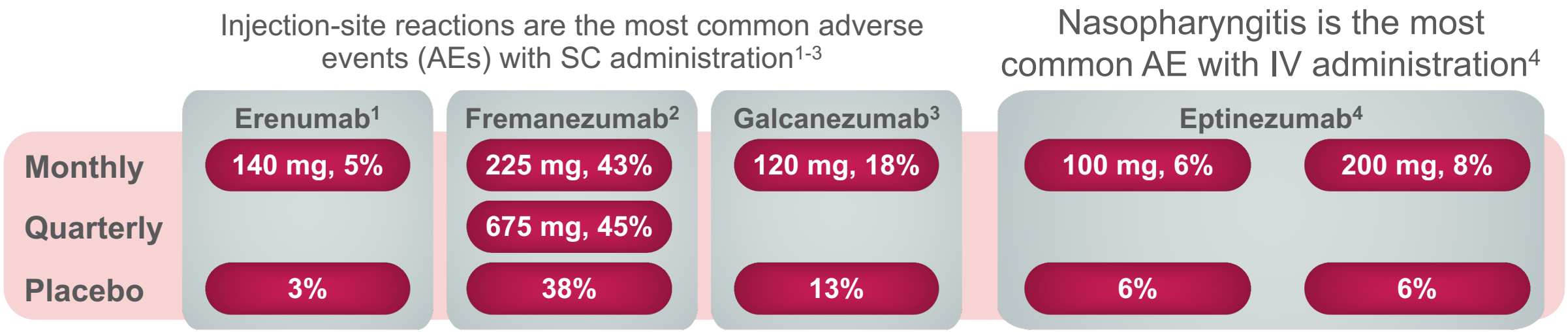
Phase 2/3 trials in CM: achievement of ≥50% reduction in mean MMDs



*P<0.001 vs placebo. †P<0.0001.

1. Tepper S, et al. *Lancet Neurol*. 2017;16:425–434. 2. Silberstein SD, et al. *N Engl J Med*. 2017;377:2113–2122. 3. Detke HC, et al. *Neurology*. 2018;91:e2211–2221.
4. Smith J, et al. *Headache*. 2017;57:(Suppl. 3):130.

Safety and tolerability of CGRP mAbs



- Label warnings
  - Hypersensitivity reactions reported with erenumab, fremanezumab, galcanezumab, and eptinezumab[1-4]
  - Constipation with serious complications and hypertension reported with erenumab[1]
- No serious CV AEs reported in placebo-controlled clinical trials; however, a recent case report suggested a possible association between CGRP inhibition and ischemic stroke in a patient receiving erenumab[5]

1. Aimovig US prescribing information. 2. Ajovy US prescribing information. 3. Emgality US prescribing information. 4. Vyepti US prescribing information. 5. Aradi S et al. *J Stroke Cerebrovasc Dis*. 2019;28:104286.

Long-term safety and tolerability of CGRP mAbs

Interim analysis of erenumab open-label extension study (median exposure 4.9 years)

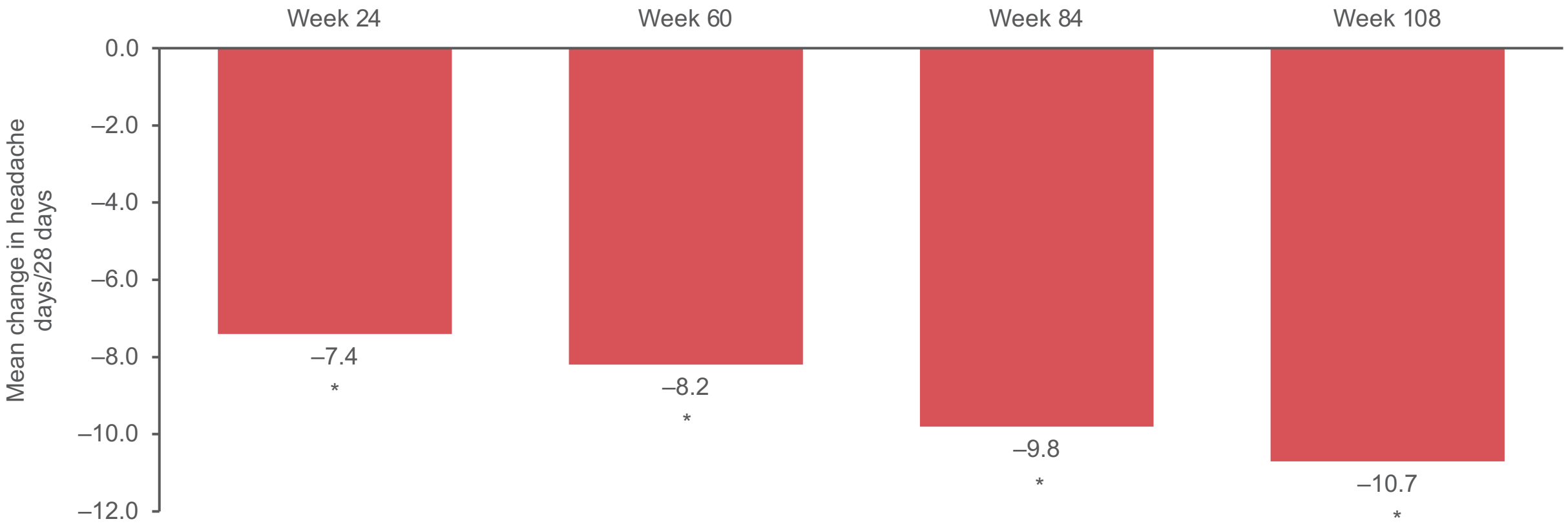
- Exposure-adjusted AE rate: 124.9/100 patient-years
- Constipation rate/100 patient-years:
  - erenumab 70 mg, 1.3
  - erenumab 140 mg, 2.6
- In total, 19 patients (5.0%) discontinued due to an AE
- Most frequent AEs (rate/100 patient-years):
  - Nasopharyngitis (10.9)
  - Upper respiratory tract infection (6.8)
  - Influenza (4.7)
- Serious AE rate: 3.8/100 patient-years

Ashina M, et al. *Headache*. 2019;59(Suppl. 1):25.

Summary of CGRP mAbs

- Safe, well tolerated, and effective
- Onset within first week
- Long half-life supports infrequent dosing
- Onset of effect is usually rapid; however, some patients who eventually respond do not show a response during the first month
- Safety in pregnancy and lactation unknown

Long-term effects of onabotulinumtoxinA for CM prevention in the open-label COMPEL study (N=716)[1]



Adults with CM received 155 U of onabotulinumtoxinA (31 sites in a fixed-site, fixed-dose paradigm across seven head/neck muscles) every 12 weeks (±7 days) for nine treatment cycles (108 weeks).

*P<0.0001 vs baseline.

1. Blumenfield AM, et al. *J Headache Pain*. 2018;19:13.

OnabotulinumtoxinA: safety & tolerability for CM (PREEMPT studies)

Event, n (%)		Safety population (N=716)
TEAE	≥1 TEAE	436 (60.9)
	Serious TEAE	75 (10.5)
	TEAE in those who discontinued treatment	32 (4.5)
TRAE	≥1 TRAE	131 (18.3)
	Serious TRAE	1 (0.1)
	TRAE in those who discontinued treatment	13 (1.8)
TRAE with incidence ≥2%	Neck pain	29 (4.1)
	Eyelid ptosis	18 (2.5)
	Musculoskeletal stiffness	17 (2.4)
	Injection site pain	14 (2.0)

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*P<0.0001 vs baseline.
TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
Blumenfield AM, et al. *J Headache Pain*. 2018;19:13.

Preventive Treatment Conclusions

- All preventive treatments are underused (pharmacologic, device, behavioral)
- Need for prevention should be calculated based upon headache day frequency and associated disability
- Traditional preventive pharmacologic therapies are effective, but discontinuation rates are high due to both efficacy and tolerability
- mAbs offer advantages (eg, fewer adverse effects and better compliance) over traditional preventive treatment options
- Behavioral therapies are effective for migraine prevention
  - They can be used independently or in conjunction with pharmacologic therapies
  - Superior outcomes are typically achieved when modalities are combined