Newer Therapies in the Management of Migraines

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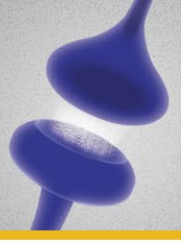
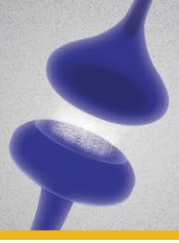
Disclosures



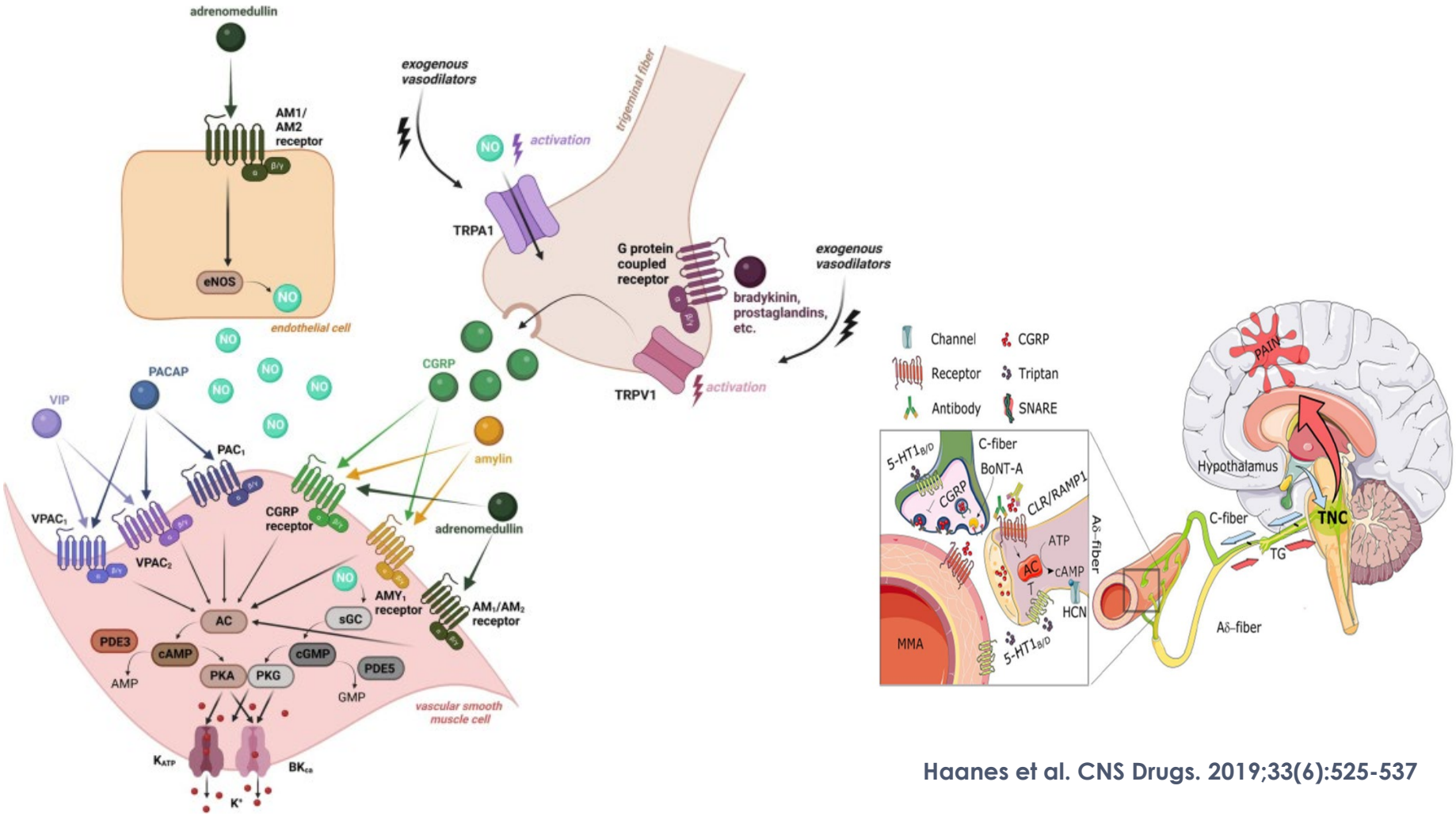
- Consultant, Advisor, Speaker
  - Allergan

Migraine Specific Medications



- No longer “borrowing” drugs indicated for other conditions
- From non-specific analgesics to Triptans, Gepants, Ditan
- From Antihypertensives, Antidepressants, Antiepileptics, to Monoclonal Antibodies and Small Molecules targeting CGRP, specifically developed for Migraine and other primary headache disorders (Cluster headache)

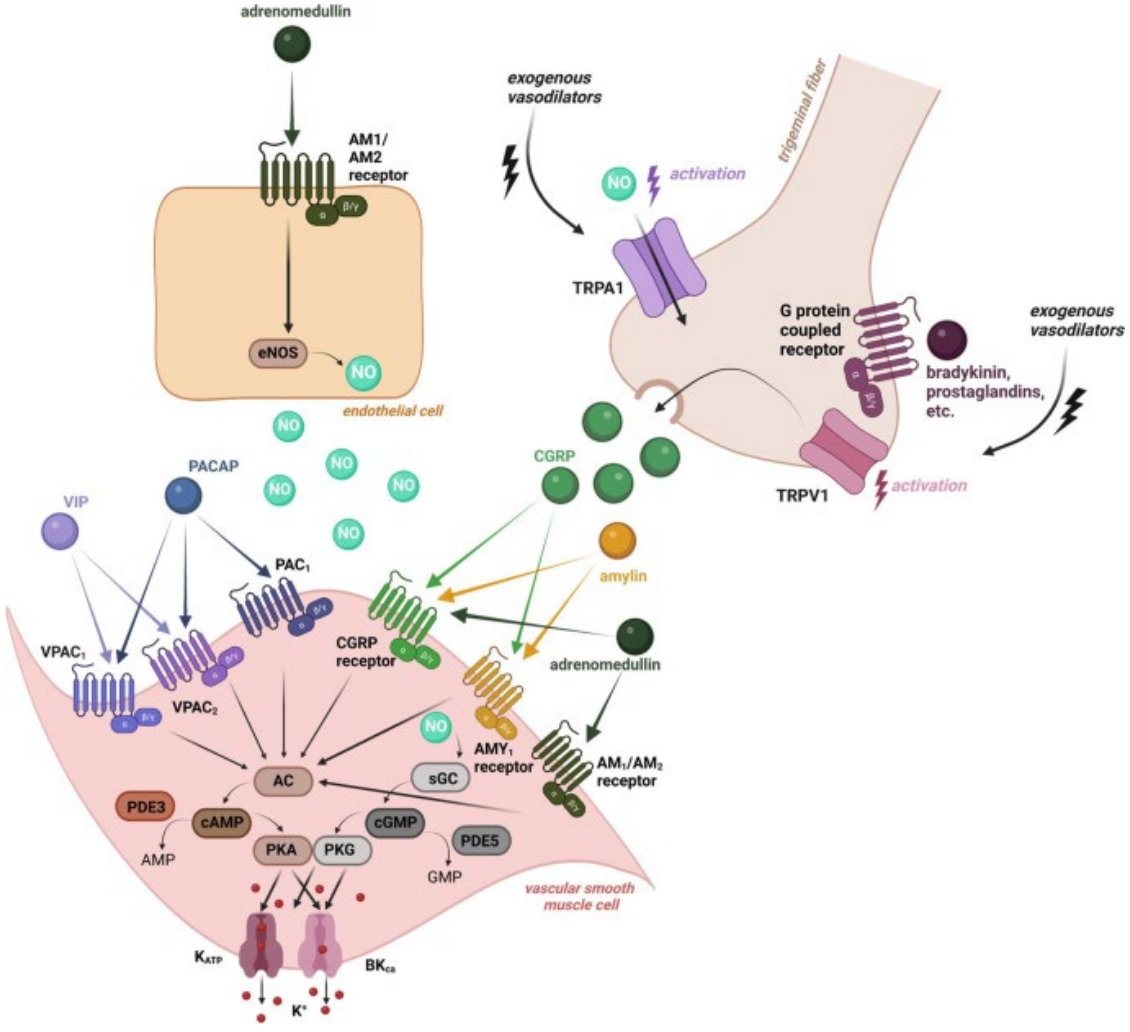
Migraine Mechanisms: Therapeutic Targets



Haanes et al. CNS Drugs. 2019;33(6):525-537

Al-Hassany et al. The Journal of Headache and Pain (2023) 24:76

Migraine Mechanisms: Therapeutic Targets



Al-Hassany et al. The Journal of Headache and Pain (2023) 24:76

AHS Position Statement: Background

- All migraine preventive therapies previously considered to be first-line treatments were developed for other indications and adopted later for migraine
- Adherence to these therapies is often poor due to issues with efficacy and tolerability
- Multiple new migraine-specific therapies have been developed based on a broad foundation of **pre-clinical and clinical evidence showing that CGRP plays a key role in the pathogenesis of migraine**
- These CGRP-targeting therapies have had a transformational impact on the management of migraine but are **still not widely considered to be first-line** approaches.

Evidence based Statement

- The evidence for the **efficacy, tolerability, and safety** of CGRP-targeting migraine preventive therapies (the monoclonal antibodies: erenumab, fremanezumab, galcanezumab, and eptinezumab, and the gepants: rimegepant and atogepant) is substantial, and vastly exceeds that for any other preventive treatment approach
- There is **consistency** across different individual CGRP-targeting treatments and is corroborated by extensive "real-world" clinical experience
- The data indicates that the efficacy and tolerability of CGRP-targeting therapies are equal to or greater than those of previous first-line therapies and that serious adverse events associated with CGRP-targeting therapies are rare.

AHS Position Statement

- **Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update**

- Andrew C. Charles MD, Kathleen B. Digre MD, Peter J. Goadsby MD, PhD, Matthew S. Robbins MD, Andrew Hershey MD, PhD, The American Headache Society. First published: 11 March 2024 https://doi.org/10.1111/head.14692

Prevention: Old versus New Therapies

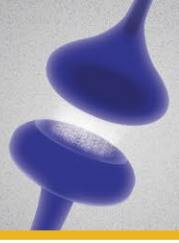
LESS THAN 1 IN 5 PATIENTS WITH FREQUENT MIGRAINE ATTACKS TAKE A PREVENTIVE TREATMENT[1]

With older migraine therapies, patients…

- …may cycle through oral medications to find the right type of treatment[2]
- …may titrate for several weeks to find an effective dose[3]
- …may have adverse events[3]
- …may be at risk of acute medication overuse[4]

1. Ashina S, Nicholson RA, Bush DC, et al. Identifying barriers to care-seeking, diagnosis, and preventive medication among those with migraine: results of the OVERCOME Study. 2. Eigenbrodt, A.K., Ashina, H., Khan, S. et al. Diagnosis and management of migraine in ten steps. Nat Rev Neurol 17, 501–514 (2021). 3. Ha H, Gonzalez A. Migraine headache prophylaxis. Am Fam Physician. 2019;99(1):17-24. 4. Ailani J, Burch RC, Robbins MS. The American Headache Society Consensus Statement: update on integrating new migraine treatments into clinical practice. Headache. 2021;61(7):1021-1039. doi: 10.1111/head.14153.

Newer Therapies



- Erenumab
- Galcanezumab
- Fremanezumab
- Eptinezumab

- Atogepant
- Rimegepant
- Ubrogepant

- Lasmiditan

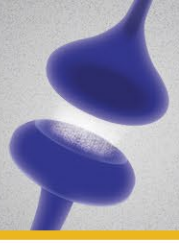
mAbs

- Erenumab (Aimovig)-SC
  - 70-140 mg q 28 days
- Galcanezumab (Emgality)-SC
  - Loading dose 240 mg, Maintenance dose 120 mg q 28 days
- Fremanezumab (Ajovy)-SC
  - 225 mg q 30 days or 675 mgquarterly
- Eptinezumab (Vyepti)-IV
  - 100-200-300 mg q 3 months

Small Molecules vs Monoclonal Antibody Drugs

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

Characteristics of mAbs developed for Migraine



Characteristic	Erenumab	Fremanezubab	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
Dose frequency	Monthly	Quarterly/ Monthly	Monthly	Quarterly
t1/2	28 days	31 days	27 days	31 days
Dose	70 or 140 mg monthly	225 mg monthly 675 mg quarterly	240 mg loading dose then 120 mg monthly	100 -200-300 mg quarterly

ERENUMAB (AIMOVIG, May 17, 2018)

Erenumab

- The most common adverse reactions in clinical studies (≥ 3% of Aimovig™-treated patients and more often than placebo) were injection site reactions and constipation.

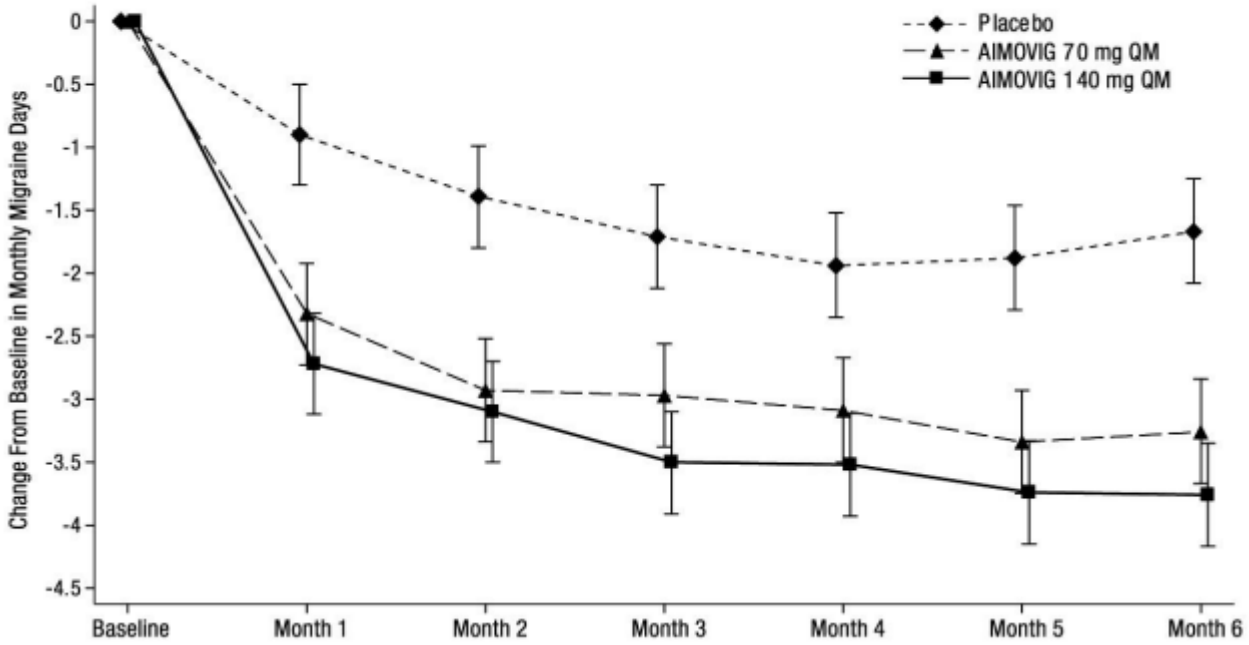
Erenumab (Aimovig) Efficacy Endpoints

Table 3: Efficacy Endpoints Over Months 4 to 6 in Study 1

	AIMOVIG 70 mg Once Monthly N = 312	AIMOVIG 140 mg Once Monthly N = 318	Placebo N = 316
Monthly Migraine Days (MMD)			
Change from baseline	−3.2	−3.7	−1.8
Difference from placebo	−1.4	−1.9	
p-value	< 0.001	< 0.001	
≥ 50% MMD responders			
% Responders	43.3%	50.0%	26.6%
Difference from placebo	16.7%	23.4%	
Odds ratio relative to placebo	2.1	2.8	
p-value	< 0.001	< 0.001	
Monthly acute migraine-specific medication days			
Change from baseline	−1.1	−1.6	−0.2
Difference from placebo	−0.9	−1.4	
p-value	< 0.001	< 0.001	

Erenumab (Aimovig) Change Study

Figure 1: Change from Baseline in Monthly Migraine Days in Study 1[a]



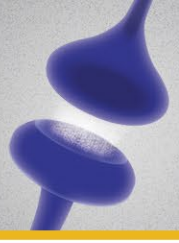
Erenumab (Aimovig) Adverse Reactions

Table 1: Adverse Reactions Occurring with an Incidence of at Least 2% for Either Dose of AIMOVIG and at Least 2% Greater than Placebo During the First 3 Months in Studies 1, 2, and 3

Adverse Reaction	AIMOVIG 70 mg Once Monthly N = 787 %	AIMOVIG 140 mg Once Monthly N = 507 %	Placebo N = 890 %
Injection site reactions[a,b]	6	5	3
Constipation	1	3	1
Cramps, muscle spasms	< 1	2	< 1

[a] Injection site reactions include multiple adverse reactions related terms, such as injection site pain and injection site erythema.
[b] The rate of injection site reactions reported in Table 1 is with the prefilled syringe.

Erenumab (Aimovig) post-marketing experience



6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of AIMOVIG. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity reactions, including rash, angioedema, and anaphylaxis *[see Warnings and Precautions (5.1)]*.

Gastrointestinal Disorders: Constipation with serious complications *[see Warnings and Precautions (5.2)]*, oral mucosal ulceration.

Skin and Subcutaneous Tissue Disorders: Rash, alopecia.

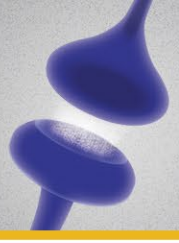
Vascular Disorders: Hypertension *[see Warnings and Precautions (5.3)]*.

FREMANEZUMAB (AJOVY, September 14, 2018)

Fremanezumab 225 mg per dose

May administer 3 injections every 3 months,
Quarterly dose 675 mg

Fremanezumab (Ajovy) Efficacy Endpoints



AJOVY® (fremanezumab-vfrm) injection

Both monthly and quarterly dosing regimens of AJOVY demonstrated statistically significant improvements for efficacy endpoints compared to placebo over the 3-month period, as summarized in Table 2.

Table 2: Efficacy Endpoints in Study 1

Study 1 Efficacy Endpoint	AJOVY 225 mg Monthly (N=287)	AJOVY 675 mg Quarterly (N=288)	Placebo (N=290)
Monthly migraine days (MMD)			
Baseline migraine days	8.9	9.2	9.1
Change from baseline	-3.7	-3.4	-2.2
Difference from placebo	-1.5	-1.2	
p-value	<0.001	<0.001	
≥50% MMD responders			
% responders	47.7%	44.4%	27.9%
Difference from placebo	19.8%	16.5%	
p-value	<0.001	<0.001	
Monthly acute headache medication days			
Change from baseline	-3.0	-2.9	-1.6
Difference from placebo	-1.4	-1.3	
p-value	<0.001	<0.001	

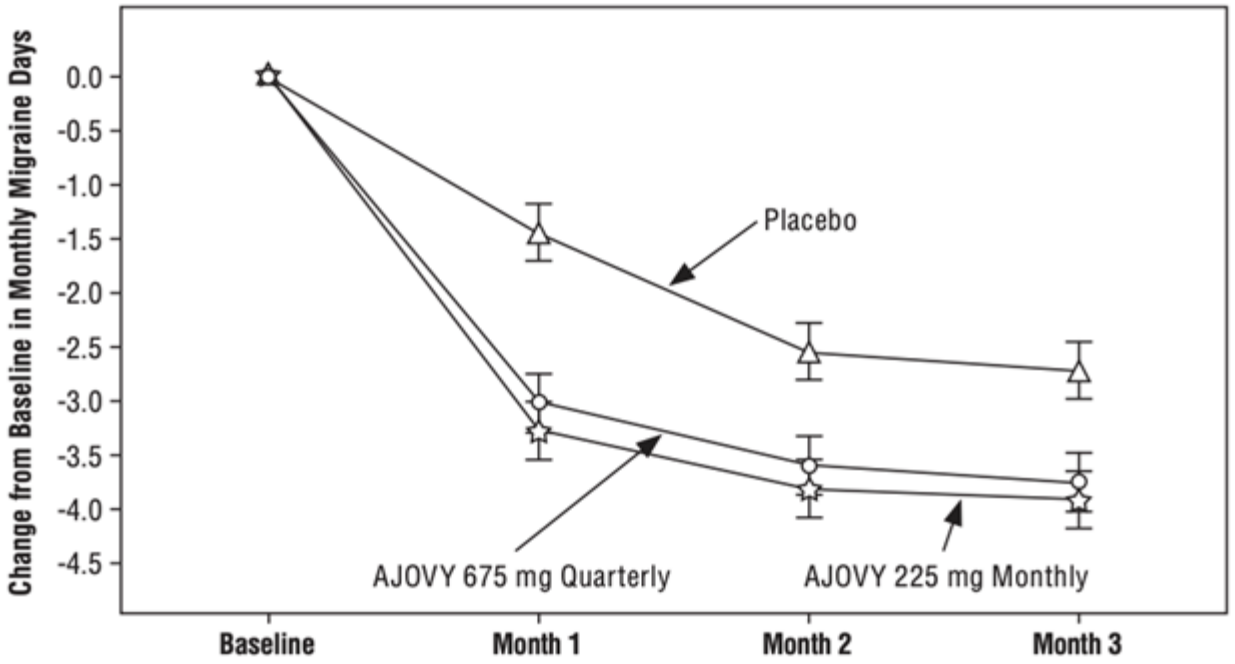
Fremanezubab (Ajovy) Efficacy Points

Table 3: Efficacy Endpoints in Study 2

Study 2 Efficacy Endpoint	AJOVY 225 mg[a] Monthly (N=375)	AJOVY 675 mg Quarterly (N=375)	Placebo (N=371)
Baseline headache days of any severity[b]	20.3	20.4	20.3
Baseline headache days of at least moderate severity[c]	12.8	13.2	13.3
Change from baseline in the monthly average number of headache days of at least moderate severity	-4.6	-4.3	-2.5
Difference from placebo	-2.1	-1.8	
p-value	<0.001	<0.001	
Change from baseline in the monthly average number of migraine days in patients	-5.0	-4.9	-3.2
Change from baseline in monthly average number of headache days of at least moderate severity at 4 weeks after 1st dose	-4.6	-4.6	-2.3
Percentage of patients with ≥ 50% reduction in monthly average number of headache days of at least moderate severity	40.8%	37.6%	18.1%
Change from baseline in monthly average number of days of acute headache medication	-4.2	-3.7	-1.9

Fremanezumab (Ajovy) Efficacy Study 1

Figure 1: Change from Baseline in Monthly Migraine Days in Study 1[a]



Fremanezumab (Ajovy) Adverse Reactions

Table 1: Adverse Reactions Occurring with an Incidence of At Least 2% for Either Dosing Regimen of AJOVY and At Least 2% Greater Than Placebo in Studies 1 and 2

Adverse Reaction	AJOVY 225 mg Monthly (n=290) %	AJOVY 675 mg Quarterly (n=667) %	Placebo Monthly (n=668) %
Injection site reactions[a]	43	45	38

[a] Injection site reactions include multiple related adverse event terms, such as injection site pain, induration, and erythema.

GALCANEZUMAB (EMGALITY, September 27, 2018)

- Galcanezumab 240 mg loading dose, then 120 mg every 28 days

- Also indicated for episodic Cluster headaches, 300 mg dose q 28 days during the active cycle

Galcanezumab (EMGALITY) Efficacy Endpoints

Table 2: Efficacy Endpoints in Studies 1 and 2

	Study 1		Study 2	
	EMGALITY 120 mg N = 210	Placebo N = 425	EMGALITY 120 mg N = 226	Placebo N = 450
Monthly Migraine Headache Days (over Months 1 to 6)				
Baseline migraine headache days	9.2	9.1	9.1	9.2
Mean change from baseline	-4.7	-2.8	-4.3	-2.3
Difference from placebo[a]	-1.9		-2.0	
≥50% Migraine Headache Days Responders (over Months 1 to 6)				
% Responders[a]	62%	39%	59%	36%
≥75% Migraine Headache Days Responders (over Months 1 to 6)				
% Responders[a]	39%	19%	34%	18%
100% Migraine Headache Days Responders (over Months 1 to 6)				
% Responders[a]	16%	6%	12%	6%
Monthly Migraine Headache Days that Acute Medication was Taken (over Months 1 to 6)				
Mean change from baseline (days)[a]	-4.0	-2.2	-3.7	-1.9
MSQ Role Function-Restrictive Domain Score (over Months 4 to 6)				
Baseline	51.4	52.9	52.5	51.4
Mean change from baseline[b]	32.4	24.7	28.5	19.7
Difference from placebo[a]	7.7		8.8	

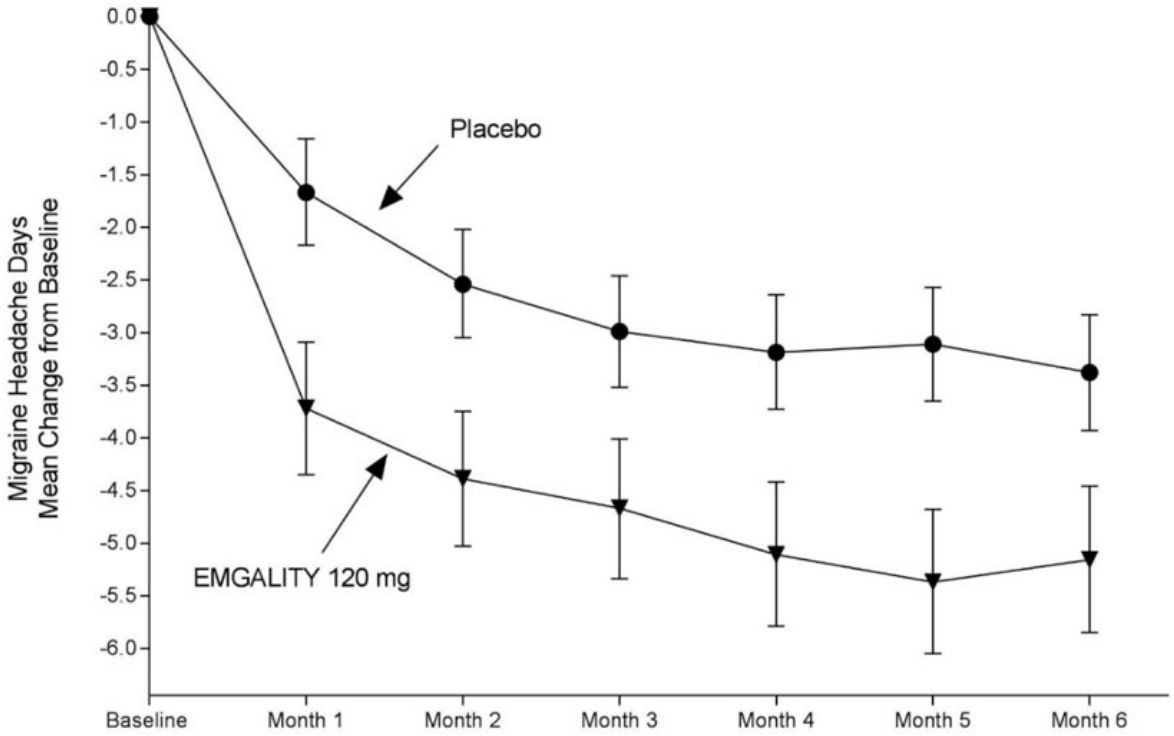
[a] p<0.001

[b] N = 189 for EMGALITY 120 mg and N = 377 for placebo in Study 1; N = 213 for EMGALITY 120 mg and N = 396 for placebo in Study 2.

Figure 1: Change from Baseline in Monthly Migraine Headache Days in Study 1[a]

Galcanezumab (Emgality) Change Study 1

Figure 1: Change from Baseline in Monthly Migraine Headache Days in Study 1[a]

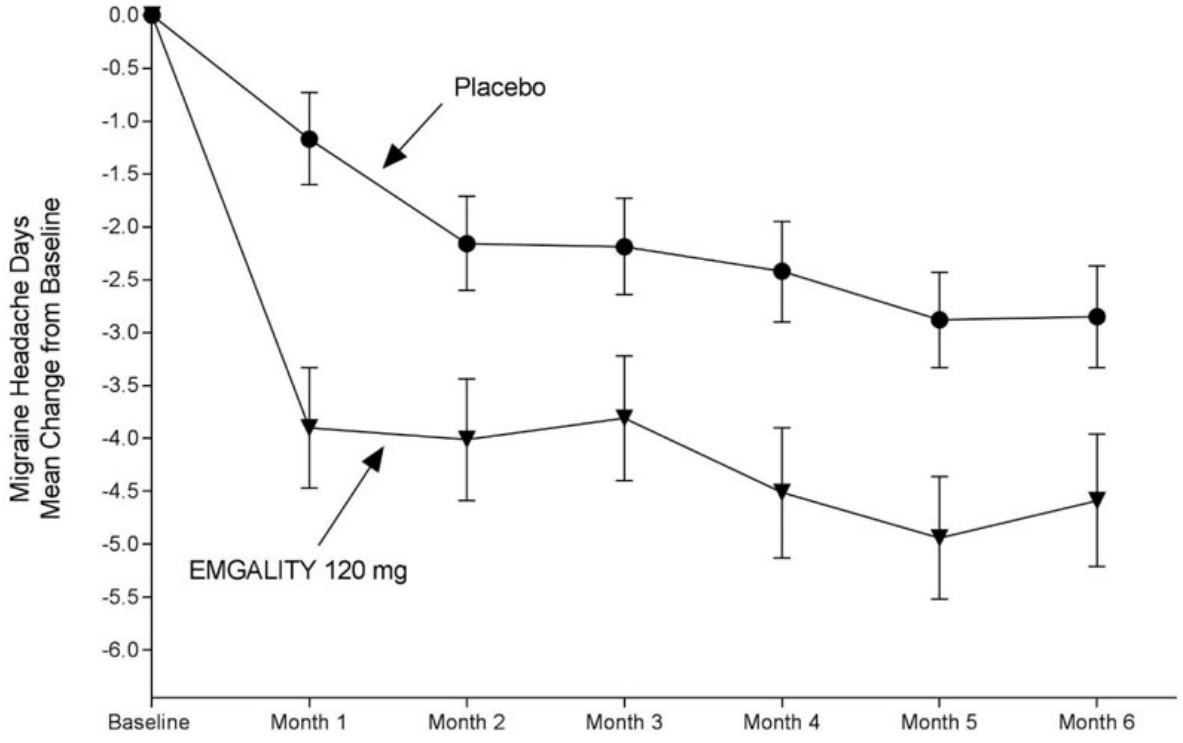


[a] Least-square means and 95% confidence intervals are presented.

Figure 2: Change from Baseline in Monthly Migraine Headache Days in Study 2[a]

Galcanezumab (Emgality) Change study 2

Figure 2: Change from Baseline in Monthly Migraine Headache Days in Study 2[a]



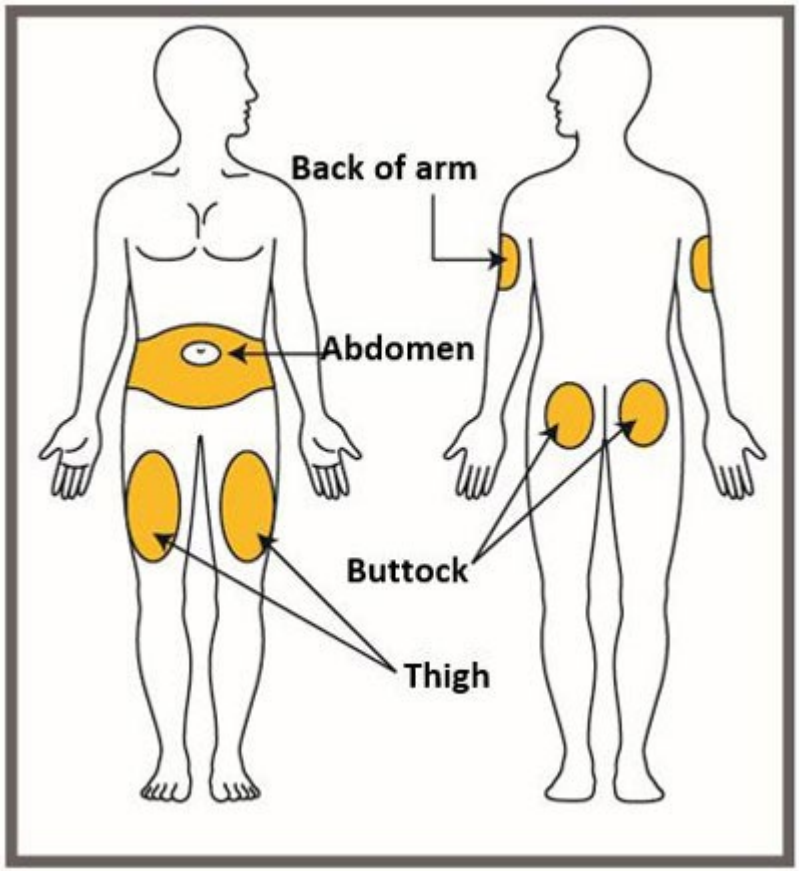
Emgality Adverse Reactions

Table 1: Adverse Reactions Occurring in Adults with Migraine with an Incidence of at least 2% for EMGALITY and at least 2% Greater than Placebo (up to 6 Months of Treatment) in Studies 1, 2, and 3

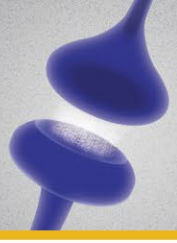
Adverse Reaction	EMGALITY 120 mg Monthly (N=705) %	Placebo Monthly (N=1451) %
Injection site reactions[a]	18	13

[a] Injection site reactions include multiple related adverse event terms, such as injection site pain, injection site reaction, injection site erythema, and injection site pruritus.

Injection sites



Adverse Events Common to ALL mAbs



- Most common: Injection site reaction
- Rash, swelling of face, lips, tongue or throat, trouble breathing, hives, redness in the face
- Constipation (Aimovig), maybe severe

ALL are well tolerated with similar efficacy and side effect profile

Eptinezumab (Vyepti, 2020)

- IV administration q 3 months
- 100 mg dose
- 200 mg dose
- 300 mg dose

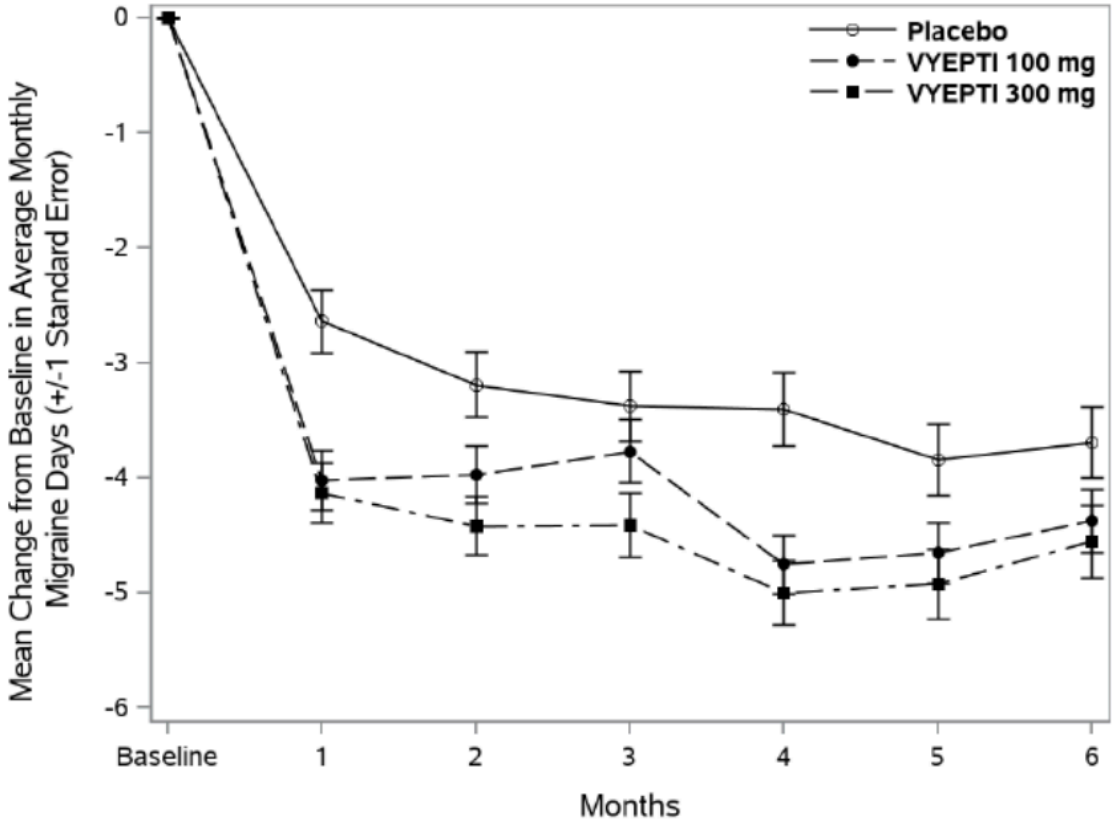
Eptinezumab (Vyepti) Efficacy Endpoints

Table 2. Efficacy Endpoint Results in Study 1

	VYEPTI 100 mg N=221	VYEPTI 300 mg N=222	Placebo N=222
Monthly Migraine Days (MMD) – Months 1-3			
Change from baseline	-3.9	-4.3	-3.2
Difference from placebo	-0.7	-1.1	
p-value	0.018	<0.001	
≥50% MMD responders – Months 1-3			
% Responders	49.8%	56.3%	37.4%
Difference from placebo	12.4%	18.9%	
p-value	0.009*	<0.001	
≥75% MMD responders – Months 1-3			
% Responders	22.2%	29.7%	16.2%
Difference from placebo	6.0%	13.5%	
p-value	NS**	<0.001	

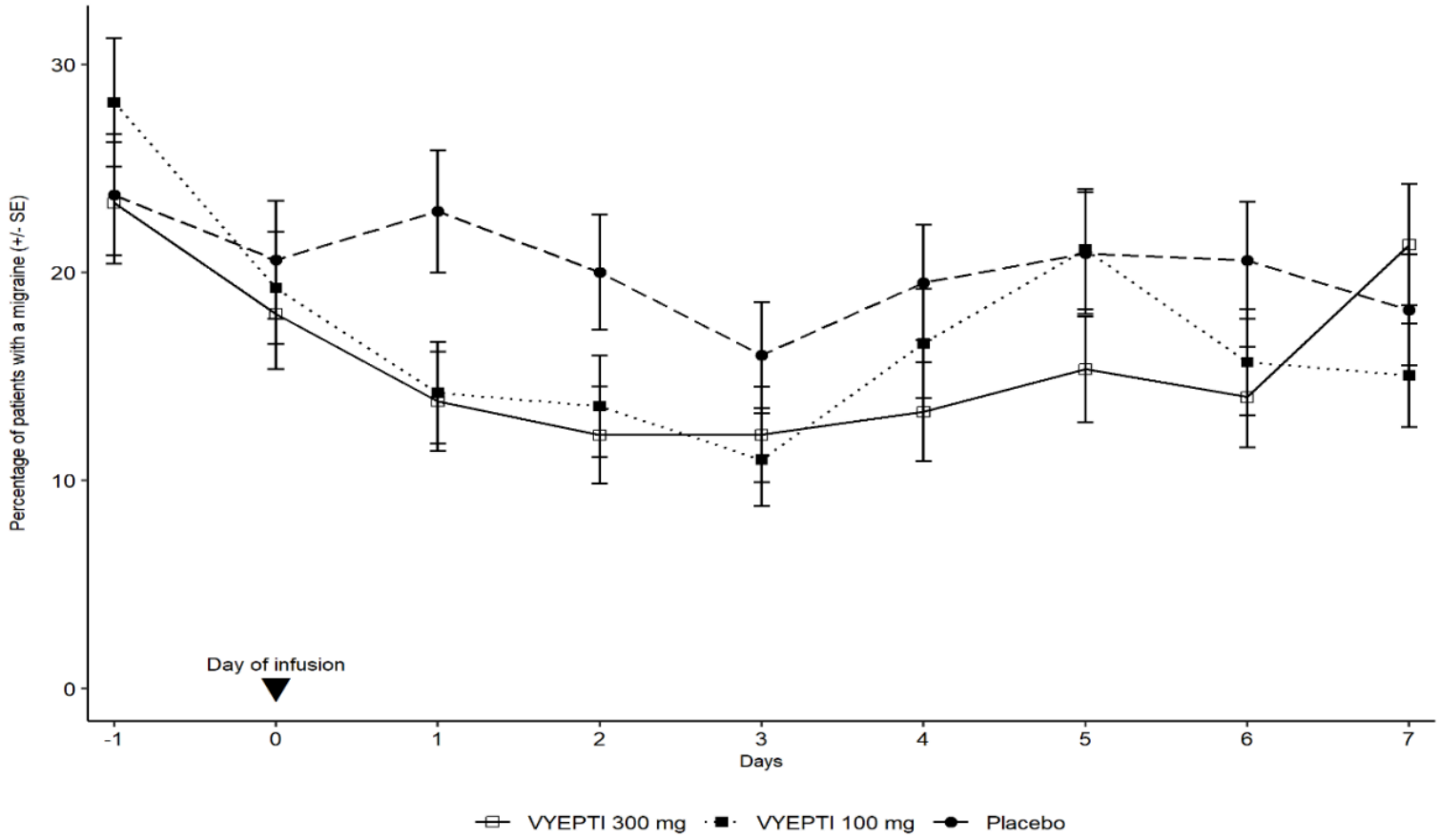
Eptinezumab (Vyepti) Change Study 1

Figure 1. Change from Baseline in Monthly Migraine Days in Study 1



Eptinezumab (Vyepti) Change Study 2

Figure 3. Percentage of Patients with a Migraine from Day -1 (Day Prior to Infusion) to Day 7 in Study 1



Eptinezumab (Vyepti) Adverse Reactions

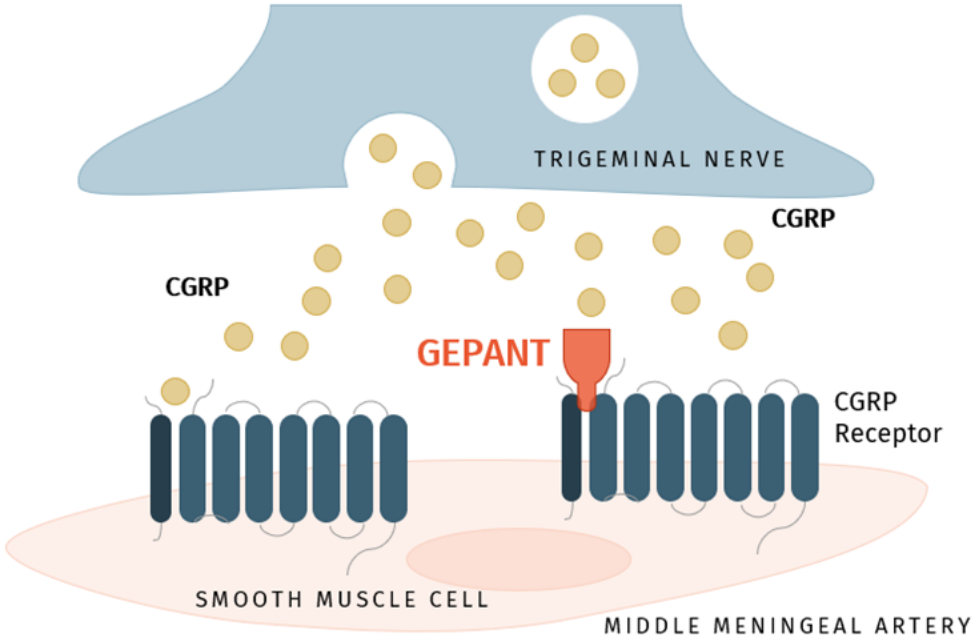
Table 1. Adverse Reactions Occurring with an Incidence of at Least 2% for VYEPTI and at Least 2% Greater than Placebo in Studies 1 and 2

Adverse Reactions	VYEPTI 100 mg N=579 %	VYEPTI 300 mg N=574 %	Placebo N=588 %
Nasopharyngitis	6	8	6
Hypersensitivity reactions*	1	2	0

* Hypersensitivity reactions includes multiple related adverse event terms, such as hypersensitivity, pruritus, and flushing/hot flush that occurred on the day of dosing.

Gepants

- Gepants bind to the same site on the CGRP receptor and block CGRP binding and receptor activation[1]
- Gepants have been approved for the acute treatment of migraine and preventive treatment of episodic migraine[2]:
  - No MOH warnings or precautions
  - No cardiovascular warnings or precautions
  - Not narcotics/not scheduled



1. Bell IM, J Med Chem, 2014. 2. Edvinsson L. CGRP receptor antagonists and antibodies against CGRP and its receptor in migraine treatment. Br J Clin Pharmacol. 2015. 3. Figure adapted from de Vries et al. Pharmacology & Therapeutics. 2020

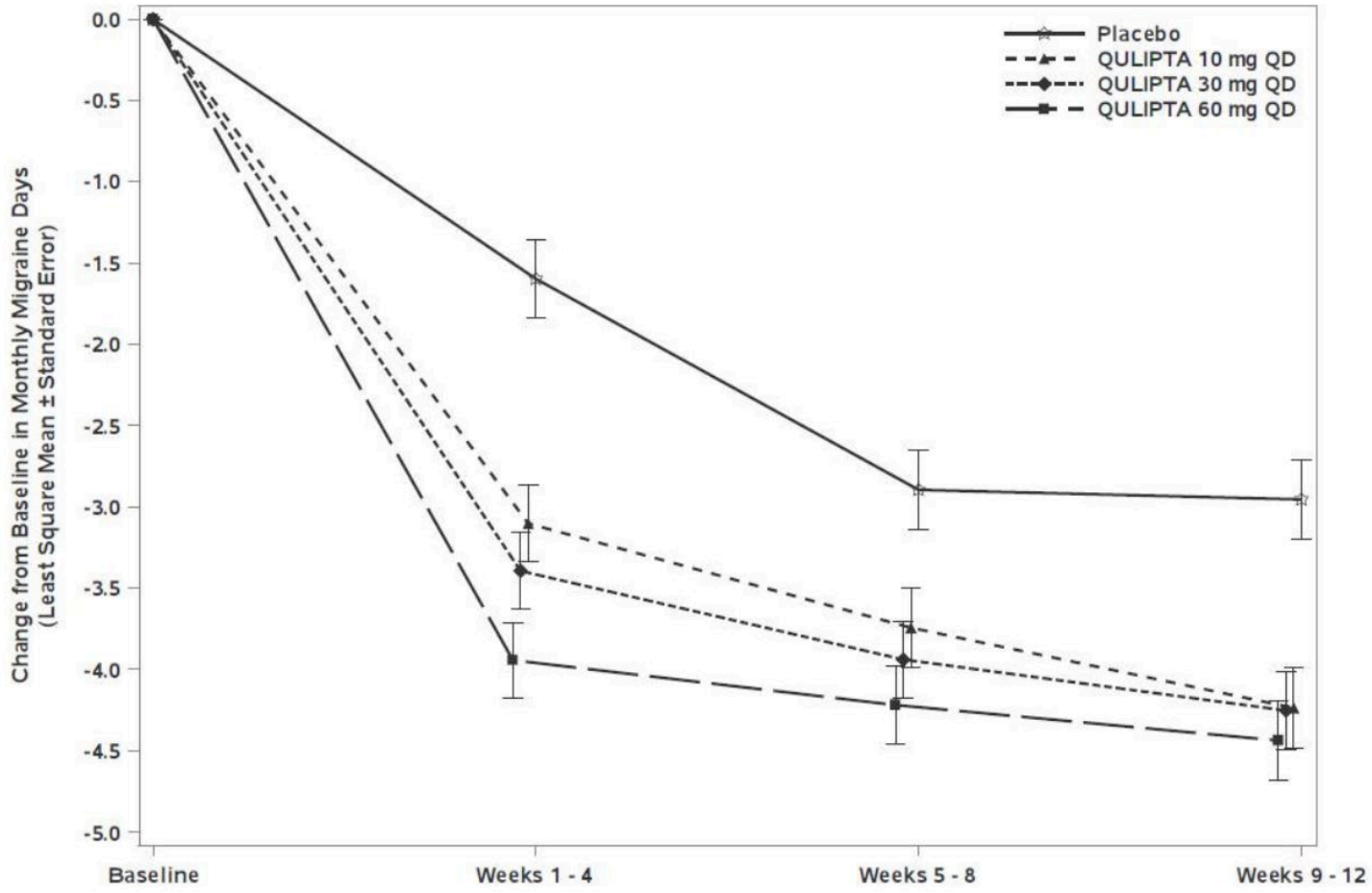
Atogepant (Qulipta) Efficacy Endpoints

Table 5: Efficacy Endpoints in Study 3

	QULIPTA 60 mg QD N=256	Placebo N=246
Monthly Migraine Days (MMD) across 12 weeks		
Baseline	19.2	18.9
Mean change from baseline	-6.9	-5.1
Difference from placebo	-1.8	
p-value	<0.001	
Monthly Headache Days across 12 weeks		
Baseline	21.5	21.4
Mean change from baseline	-7.0	-5.1
Difference from placebo	-1.9	
p-value	<0.001	

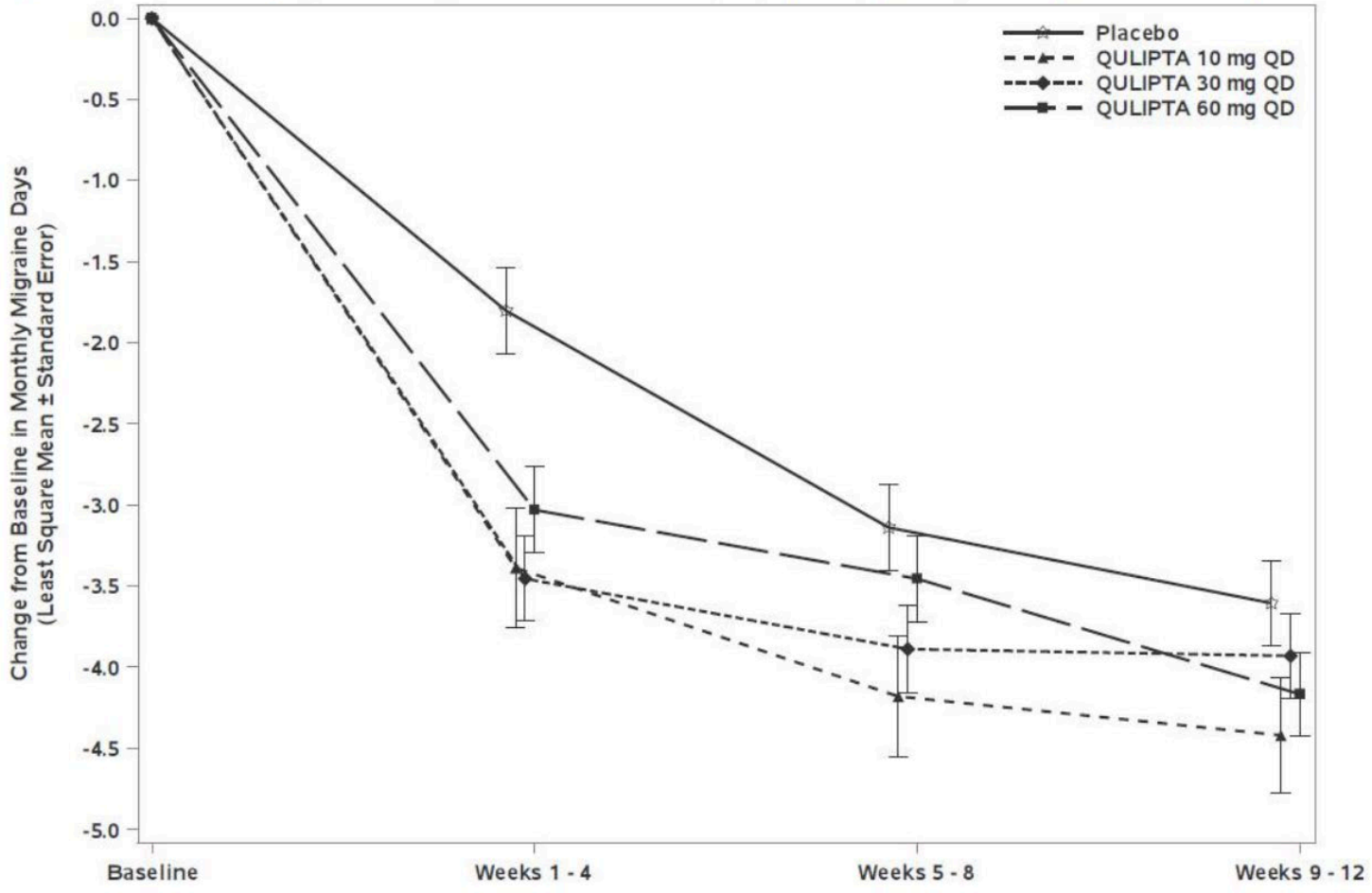
Atogepant (Qulipta) Change Study 1

Figure 1: Change from Baseline in Monthly Migraine Days in Study 1



Atogepant (Qulipta) Change Study 2

Figure 3: Change from Baseline in Monthly Migraine Days in Study 2



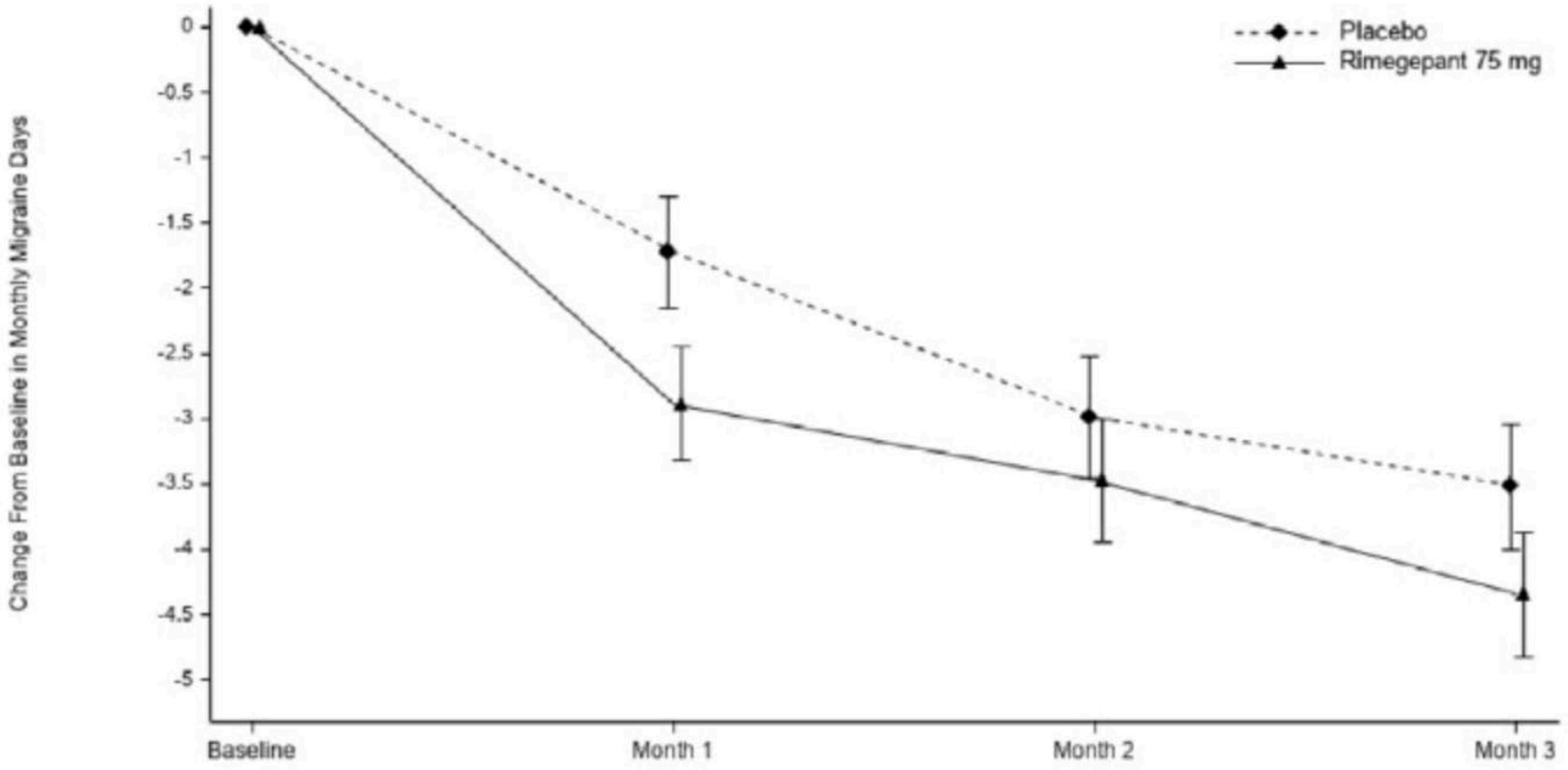
Atogepant (Qulipta) Adverse Reactions

Table 2: Adverse Reactions Occurring with an Incidence of At Least 2% for QULIPTA and Greater than Placebo in Studies 1, 2, and 3*

	Placebo (N= 663) %	QULIPTA 10 mg (N=314) %	QULIPTA 30 mg (N=411) %	QULIPTA 60 mg (N=678) %
Nausea	3	5	6	9
Constipation	2	6	6	8
Fatigue/Somnolence	4	4	4	5
Decreased Appetite	<1	2	1	3
Dizziness	2	2	2	3

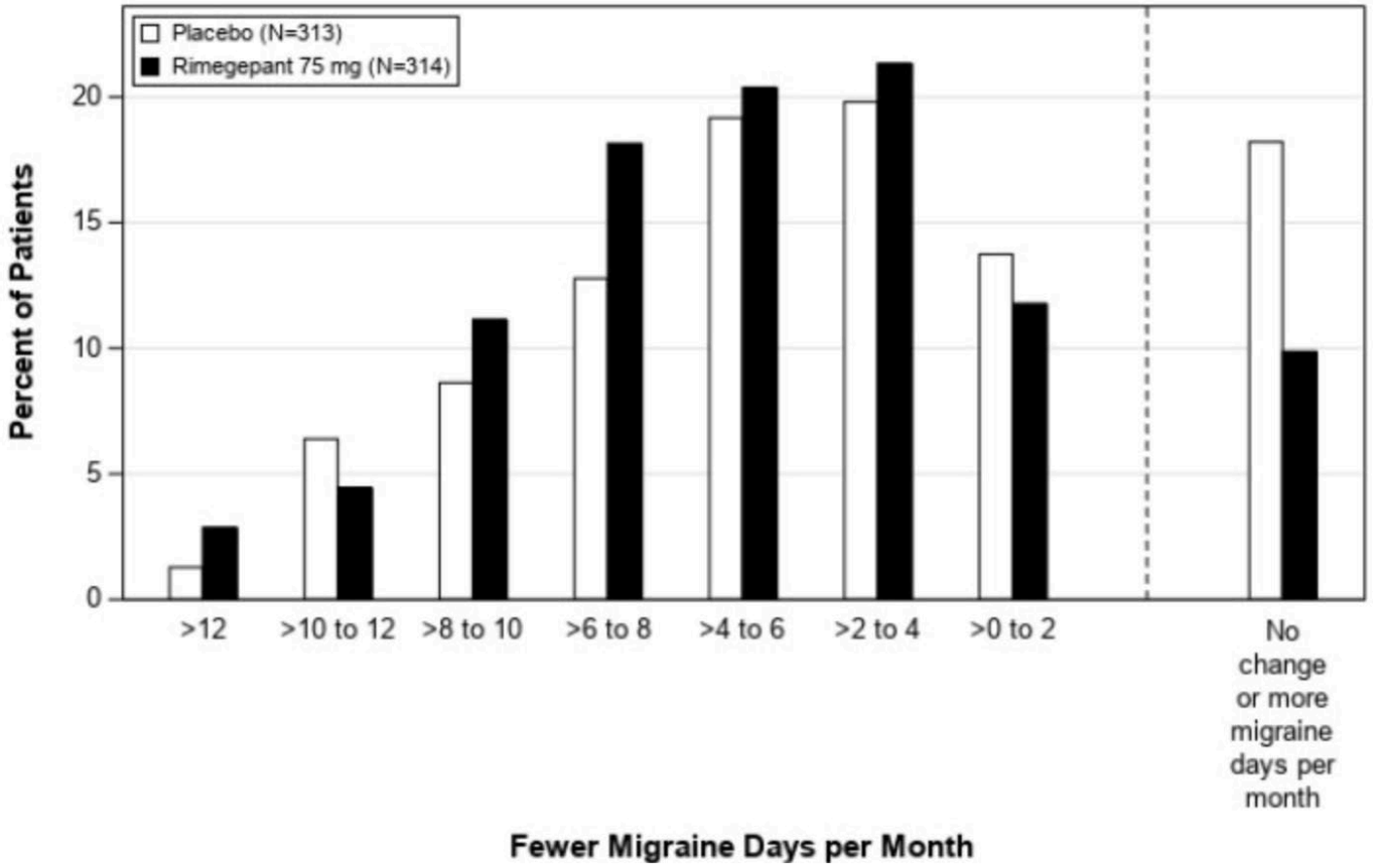
Rimegepant (Nurtec) Change Study 1

Figure 3: Change from Baseline in Monthly Migraine Days in Study 2[a]



Rimegepant (Nurtec) Change Study 2

Figure 4: Distribution of Change from Baseline in Mean Monthly Migraine Days at Month 3 by Treatment Group in Study 2[a]



Rimegepant (Nurtec) Adverse Reactions

The most common side effects of Nurtec ODT were nausea (2.7%) and stomach pain/indigestion (2.4%). These are not the only possible side effects of Nurtec ODT. Tell your HCP if you have any side effects.

Rimegepant (Nurtec) Efficacy Endpoints

Table 1: Efficacy Endpoints for the Acute Treatment of Migraine in Study 1

	Study 1	
	NURTEC ODT 75 mg	**Placebo**
Pain Free at 2 hours		
n/N*	142/669	74/682
% Responders	21.2	10.9
Difference from placebo (%)	10.3	
p-value		<0.001
MBS Free at 2 hours		
n/N*	235/669	183/682
% Responders	35.1	26.8
Difference from placebo (%)	8.3	
p-value		0.001

* n=number of responders/N=number of patients in that treatment group

Ubrogepant (Ubrelvy) Efficacy points

Table 3: Migraine Efficacy Endpoints for Study 1 and Study 2

	Study 1			Study 2	
	UBRELVY 50 mg	**UBRELVY 100 mg**	**Placebo**	**UBRELVY 50 mg**	**Placebo**
Pain Free at 2 hours					
N	422	448	456	464	456
% Responders	19.2	21.2	11.8	21.8	14.3
Difference from placebo (%)	7.4	9.4		7.5	
p value	0.002	<0.001		0.007	
Most Bothersome Symptom Free at 2 hours					
N	420	448	454	463	456
% Responders	38.6	37.7	27.8	38.9	27.4
Difference from placebo (%)	10.8	9.9		11.5	
p value	<0.001	<0.001		<0.001	
Pain Relief at 2 hours					
N	422	448	456	464	456
% Responders	60.7	61.4	49.1	62.7	48.2
p value	<0.001	<0.001		<0.001	
Sustained Pain Freedom 2-24 hours					
N	418	441	452	457	451
% Responders	12.7	15.4	8.6	14.4	8.2
p value	*NS	0.002		0.005	

Ubrogepant (Ubrelvy) Adverse Reactions

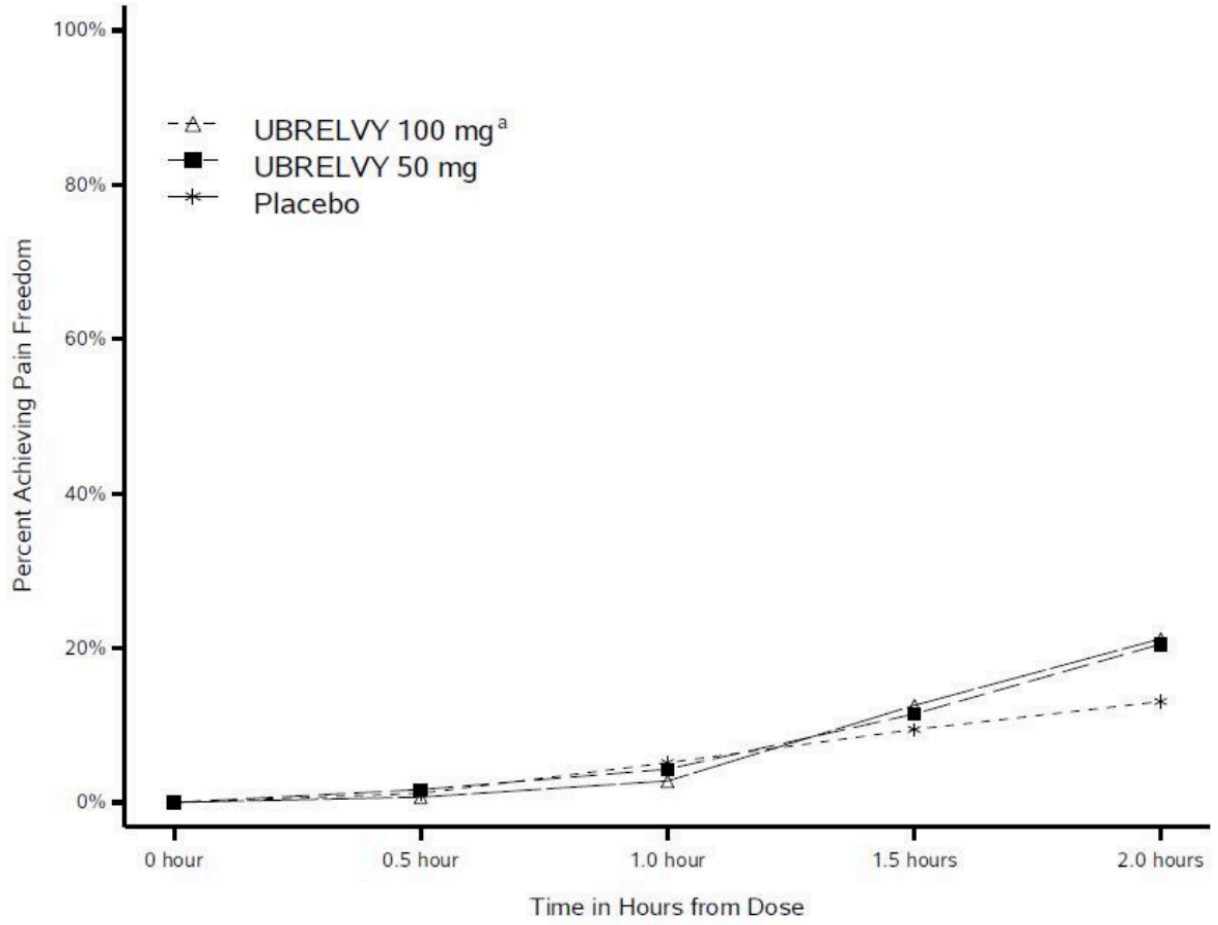
Table 2: Adverse Reactions Occurring in At Least 2% and at a Frequency Greater than Placebo in Studies 1 and 2

	Placebo (N= 984) %	UBRELVY 50 mg (N=954) %	UBRELVY 100 mg (N=485) %
Nausea	2	2	4
Somnolence*	1	2	3
Dry Mouth	1	<1	2

*Somnolence includes the adverse reaction-related terms sedation and fatigue.

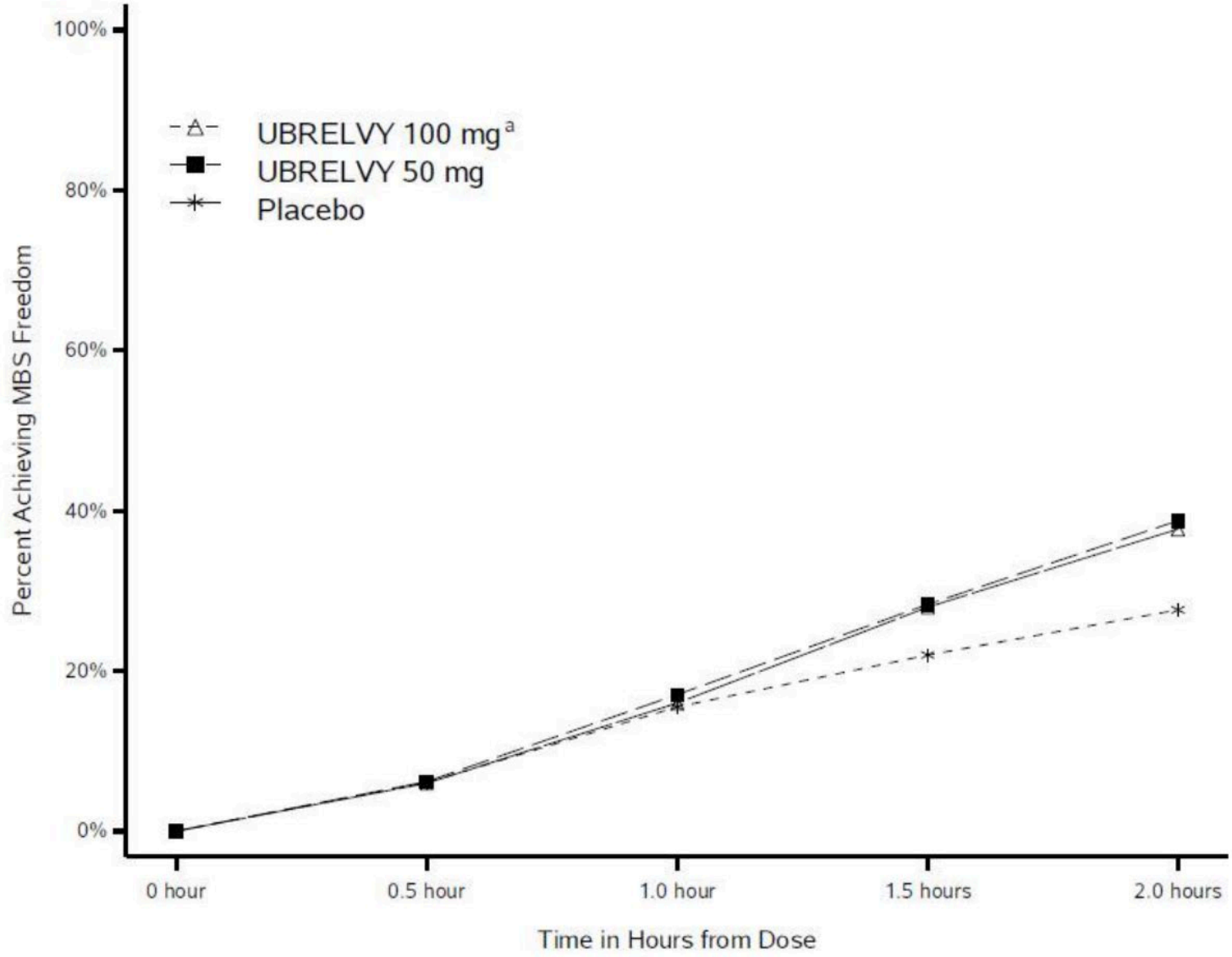
Ubrogepant (Ubrelvy) Change Study 1

Figure 1: Percentage of Patients Achieving Pain Freedom within 2 Hours in Pooled Studies 1 and 2



[a] The 100 mg arm was only included in Study 1.

Ubrogepant (Ubrelvy) Change Study 2



Zavegepant (Zavzpret) Efficacy Endpoints

Table 2: Efficacy Endpoints in Study 1

	ZAVZPRET 10 mg	Placebo
Pain Free at 2 hours		
n/N*	147/623	96/646
% Responders	23.6	14.9
Difference from placebo (%)	8.8	
p-value	<0.001	
MBS† Free at 2 hours		
n/N*	247/623	201/646
% Responders	39.6	31.1
Difference from placebo (%)	8.7	
p-value	0.001	

* n=number of responders/N=number of patients in that treatment group

† MBS = most bothersome symptoms of photophobia, phonophobia, or nausea.

Zavegepant (Zavzpret) Adverse Reactions

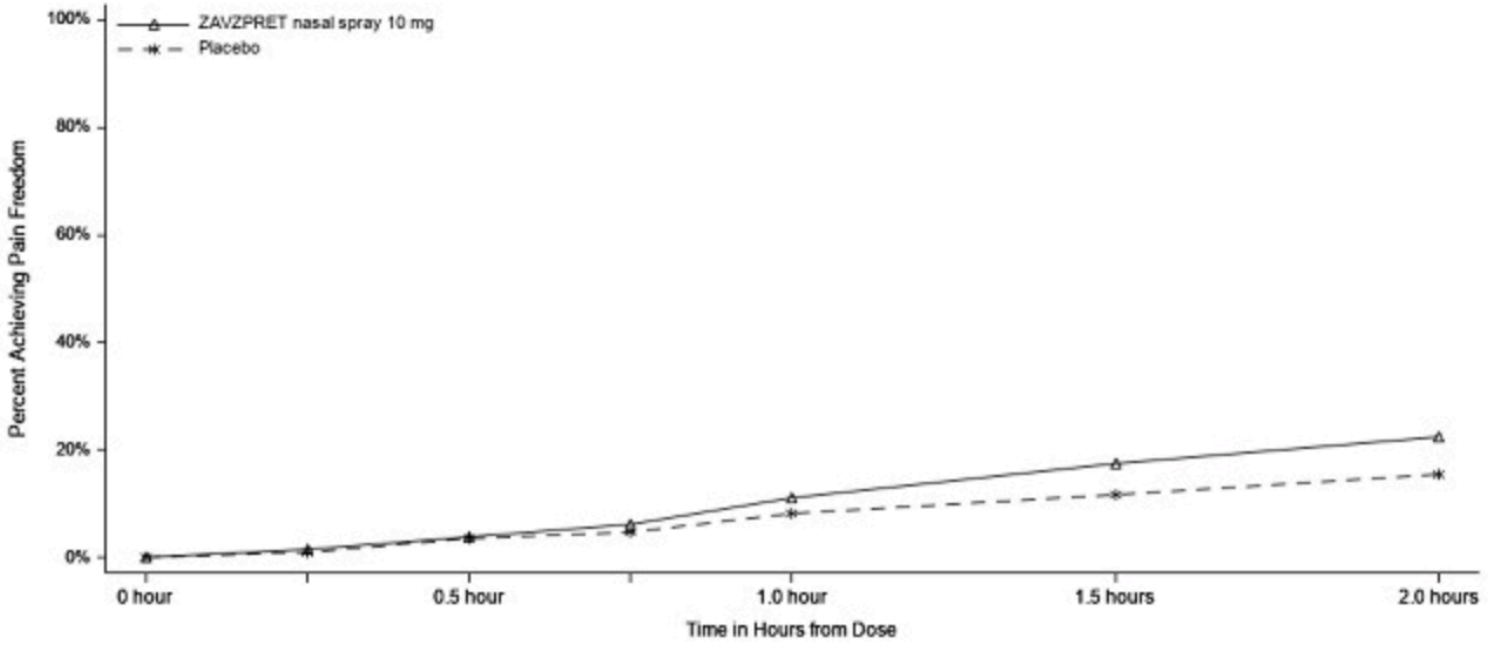
Table 1: Adverse Reactions Occurring in At Least 2% of Patients Treated with ZAVZPRET and at a Frequency Greater than Placebo in Study 1 and 2

Adverse Reaction	ZAVZPRET N=1023 %	Placebo N=1056 %
Taste Disorders*	18	4
Nausea	4	1
Nasal Discomfort	3	1
Vomiting	2	<1

* Taste disorders includes dysgeusia and ageusia

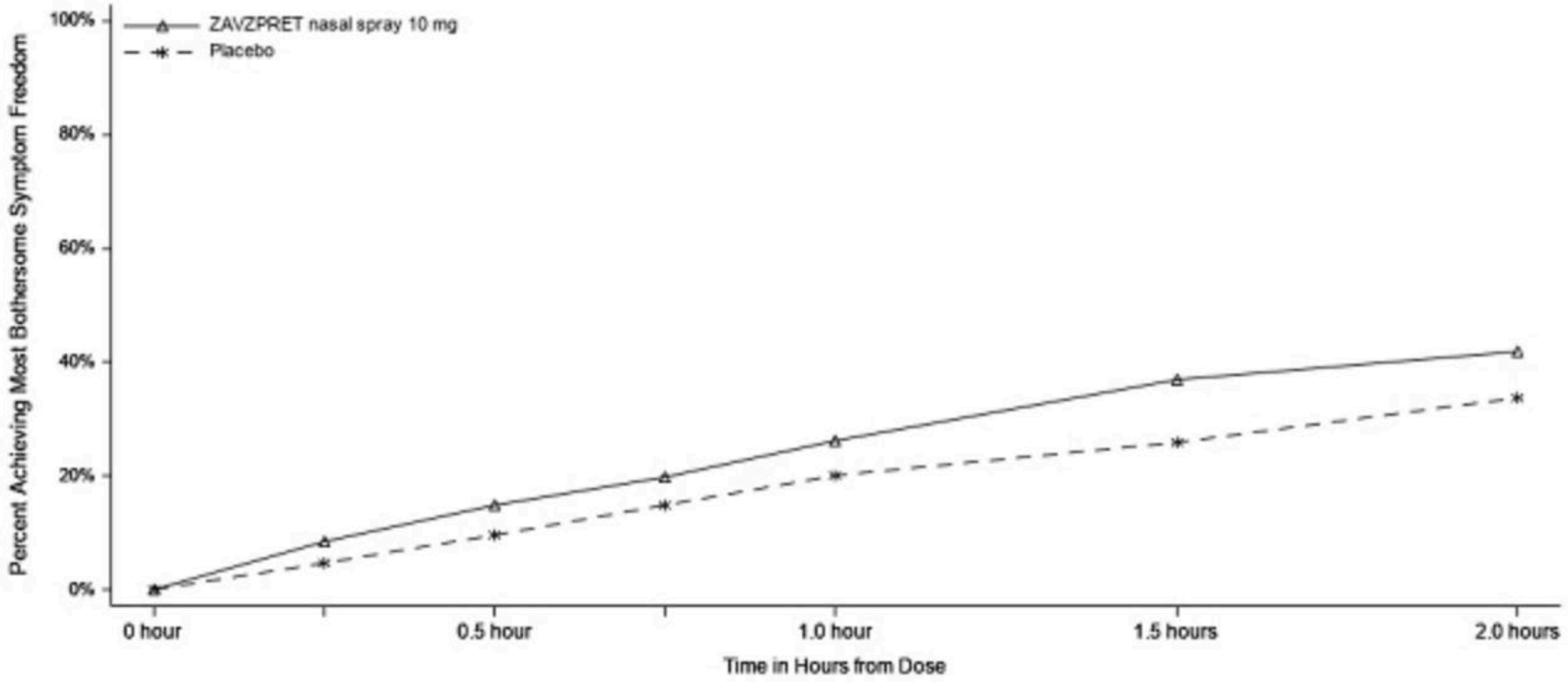
Zavegepant (Zavzpret) Change Study 1

Figure 3: Percentage of Patients Achieving Pain Freedom within 2 Hours in Study 2



Zavegepant (Zavzpret) Change Study 2

Figure 4: Percentage of Patients Achieving MBS Freedom within 2 Hours in Study 2



Lasmitidan (Reyvow)

Table 2: Migraine Efficacy Endpoints after Treatment for Studies 1 and 2

	Study 1			Study 2			
	REYVOW 100 mg	REYVOW 200 mg	Placebo	REYVOW 50 mg	REYVOW 100 mg	REYVOW 200 mg	Placebo
Pain Free at 2 hours							
N	498	503	515	544	523	521	534
% Responders	28.3	31.8	15.3	28.3	31.4	38.8	21.0
Difference from placebo (%)	13	16.5		7.3	10.4	17.8	
p-value	<0.001	<0.001		0.006	<0.001	<0.001	
MBS Free at 2 hours							
N	464	467	480	502	491	478	509
% Responders	41.2	40.7	29.6	40.8	44.0	48.7	33.2
Difference from placebo (%)	11.6	11.1		7.6	10.8	15.5	
p-value	<0.001	<0.001		0.014	<0.001	<0.001	

Pain relief at 2 hours, defined as a reduction in migraine pain from moderate or severe to mild or none, was also evaluated (see Table 3).

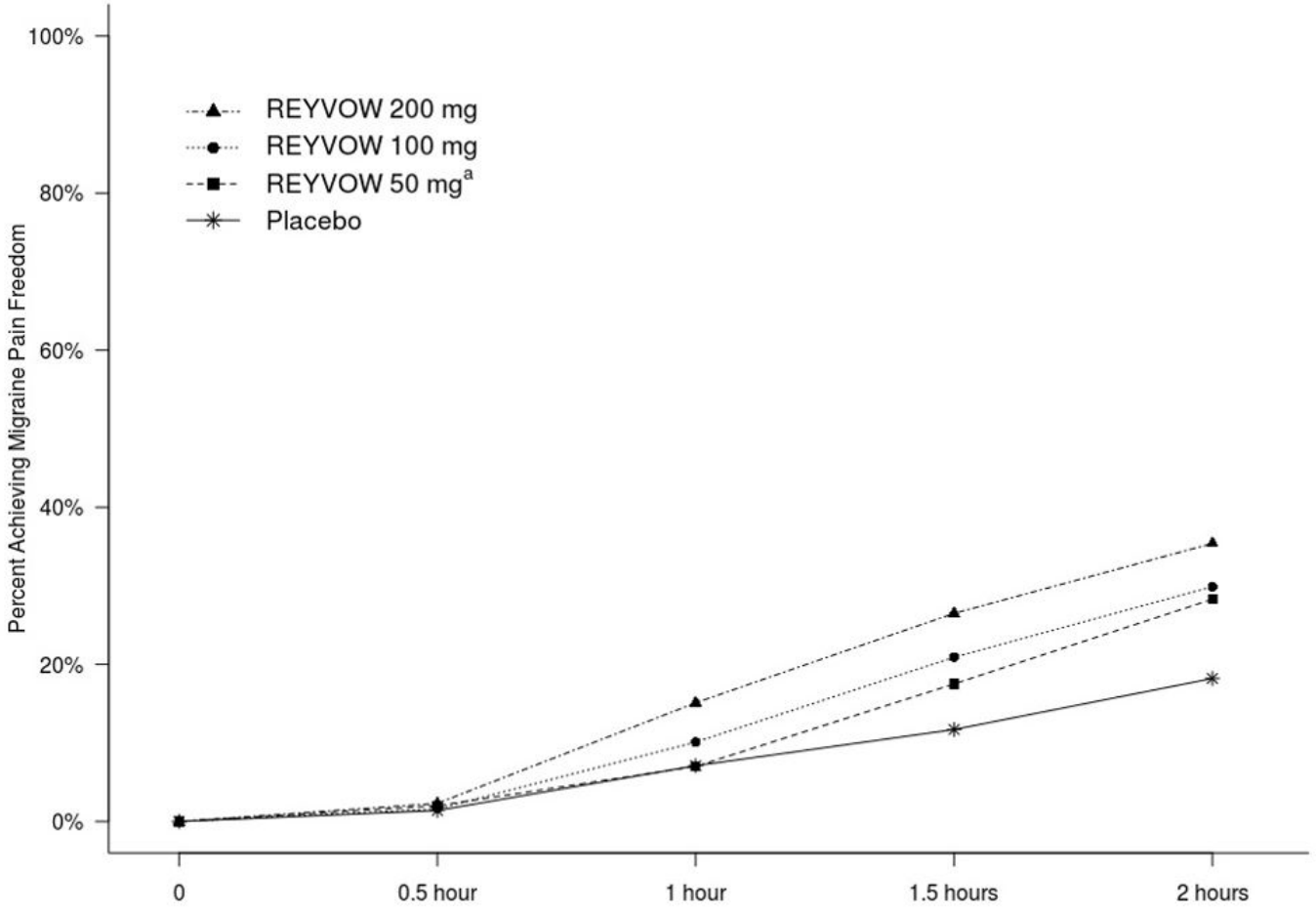
Table 3: Additional Migraine Efficacy Endpoint after Treatment for Studies 1 and 2

	Study 1			Study 2			
	REYVOW 100 mg	REYVOW 200 mg	Placebo	REYVOW 50 mg	REYVOW 100 mg	REYVOW 200 mg	Placebo
Pain Relief at 2 hours[a]							
N	498	503	515	544	523	521	534
% Responders	54.0	55.3	40.0	55.9	61.4	61.0	45.1
Difference from placebo (%)	14.0	15.3		10.8	16.3	15.9	

[a] The analysis of pain relief was descriptive and was not controlled for Type I error.

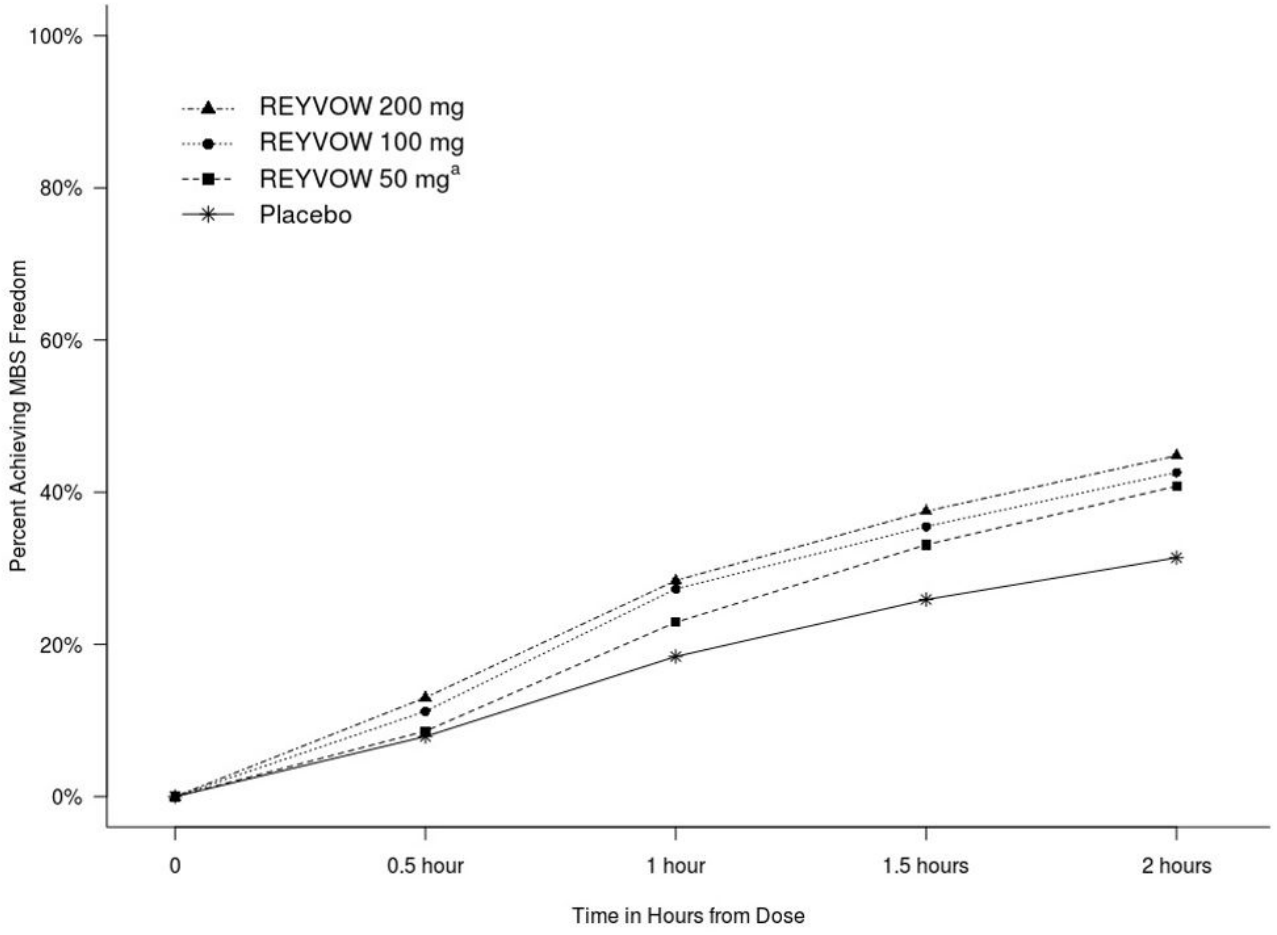
Lasmitidan (Reyvow) Pain freedom at 2 hours

Figure 1: Percentage of Patients Achieving Migraine Pain Freedom within 2 Hours in Pooled Studies 1 and 2



Lasmitidan (Reyvow) MBS

Figure 2: Percentage of Patients Achieving MBS Freedom within 2 Hours in Pooled Studies 1 and 2



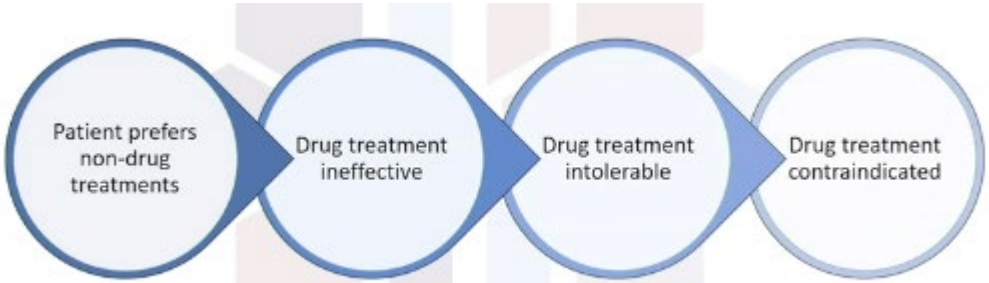
Lasmitidan (Reyvow) Adverse Reactions

Table 1: Adverse Reactions Occurring in ≥2% and at a Frequency Greater than Placebo in Studies 1 and 2

Adverse Reaction	REYVOW 50 mg N=654 %	REYVOW 100 mg N=1265 %	REYVOW 200 mg N=1258 %	Placebo N=1262 %
Dizziness	9	15	17	3
Fatigue[a]	4	5	6	1
Paresthesia[b]	3	7	9	2
Sedation[c]	6	6	7	2
Nausea and/or Vomiting	3	4	4	2
Muscle Weakness	1	1	2	0

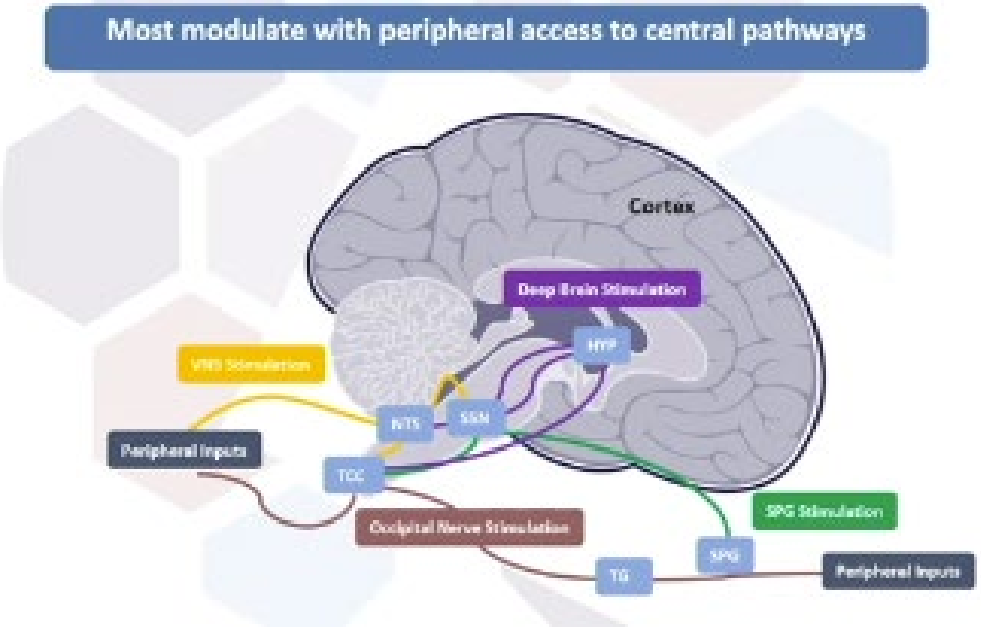
[a] Fatigue includes the adverse reaction related terms asthenia and malaise.
[b] Paresthesia includes the adverse reaction related terms paresthesia oral, hypoesthesia, and hypoesthesia oral.
[c] Sedation includes the adverse reaction related term somnolence.

AHS recommends non-drug Acute Treatment of Migraine When



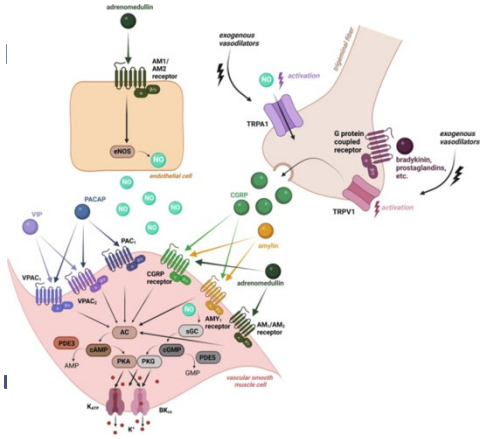
FDA Approved Neuromodulation in Migraine

How do neuromodulation devices work?

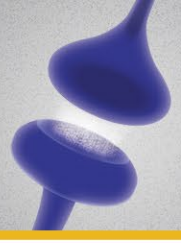


Emerging Targets for Migraine

- Pituitary adenylate cyclase activating peptide (PACAP38 and 27)
- Cannabinoids
- Insulin-like growth factor (IGF-1) nasal spray
- Liraglutide glucagon-like peptide-1agonist for IIH
- Selective nitric oxide synthase inhibitors
- Histamine receptor modulators
- 5-HT2B/2C receptor antagonist xc101-D13H for prevention
- Others



Headache Clinic Real Life Experience



- Remission
- Large improvement
- Moderate improvement
- Mild improvement
- No improvement (chronicity-comorbidities)

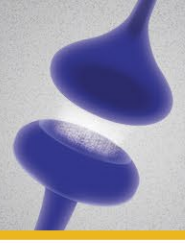
Which medicine did I use?

Chief Complaint: Headache

	4/30/2024 12:58 PM	1/29/2024 1:30 PM
Headache Questionnaire Answers		
In the past 30 days, how many days did you suffer from a headache?	4	30
In the past 30 days, how many days did you have headache that caused you to stay in bed, miss a social gathering and/or disappoint a close family member/friend?	0	2
In the past 30 days, how many times did you miss work/school and/or seek care at an urgent care or emergency department for the headache?	0	1

The patient presents for follow up. He has had a remarkable improvement going from daily headaches to 4 attacks per month quickly responsive to Nurtec. Not needed to use Relpax. In the interim, an MRI of the brain was negative. Very pleased with current regimen.

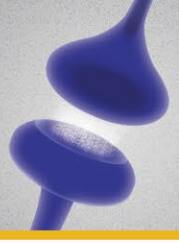
The other side of the coin…..



- Headache Questionnaire Answers:

4/30/24	4/14/24	1/18/24	10/26/23	9/19/23	8/11/23	6/30/23
In the past 30 days, how many days did you suffer from a headache?						
30	30	26	25	25	27	30
In the past 30 days, how many days did you have headache that caused you to stay in bed, miss a social gathering and/or disappoint a close family member/friend?						
5	6	7	15	15	15	27
In the past 30 days, how many times did you miss work/school and/or seek care at an urgent care or emergency department for the headache?						
5	6	0	10	10	12	27

Preventives Tried

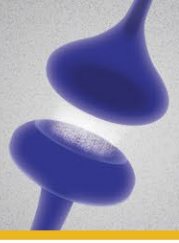


- Topamax 150 mg BID - not help
- Aimovig 70 mg - > 140 mg (Aug 2018 -) severe constipation
- Emgality- lost efficacy after several months of benefit
- Vyepti 300 mg, ineffective after 3 doses
- Vimpat - dizziness
- Cymbalta 60 mg BID - ineffective
- Clonazepam 2 mg - ineffective
- Timolol 10 mg BID - wt gain
- Verapamil - ineffective
- Elavil - sleepy Pamelor – photosensitivity
- Depakote- weight gain
- Effexor - ineffective
- Bystolic 15 mg - ineffective
- Qulipta 30 and 60 mg daily, - ineffective
- Ketamine infusions: initially helpful, then ineffective and poorly tolerated

Current Regimen

- Prevention:
  - Botox
  - Lamotrigine 100 mg daily
  - Duloxetine 120 mg daily
  - Baclofen 10 mg tid prn
  - Relivion and Nerivio (previously tried Gammacore and Cefaly)
- For acute attacks:
  - Indomethacin for paroxysmal hemicrania attacks
  - Ubrelvy, previously on Nurtec
  - Imitrex
  - no longer responding to Reyvow

Interventional Treatments



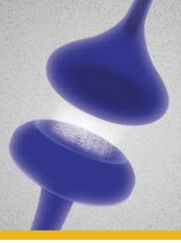
- She has tried several RFA procedures, GON blocks, dry needling, massage therapy, chiropractic treatment
- “Migraine Surgery" in Houston, this involved cutting muscles to "release nerves"
- Evaluated by Pain Medicine for ONS. History of previous surgery is a big confounding factor
- Psychological support since 2015

Intractable but…. is there hope?

- Headache Questionnaire Answers:

4/30/24	4/14/24	1/18/24	10/26/23	9/19/23	8/11/23	6/30/23
In the past 30 days, how many days did you suffer from a headache?						
30	30	26	25	25	27	30
In the past 30 days, how many days did you have headache that caused you to stay in bed, miss a social gathering and/or disappoint a close family member/friend?						
5	6	7	15	15	15	27
In the past 30 days, how many times did you miss work/school and/or seek care at an urgent care or emergency department for the headache?						
5	6	0	10	10	12	27

Thank you for your attention



- Questions?