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A retrospective cohort study comparing persistence between rimegepant and lasmiditan for the acute treatment of migraine in the United States

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INTRODUCTION

- Migraine is a prevalent, disabling, chronic disease with significant burden on patients, caregivers, and the health care system.[1] Treatment is traditionally considered as either acute, taken as needed (PRN), to minimize symptom impact, or preventive, taken regularly to reduce attack frequency and severity.
- In recent years, novel drugs for the acute treatment of migraine with or without aura in adults have been licensed, including lasmiditan, a 5-HT1F receptor agonist (FDA approval in October 2019) and rimegepant, an orally disintegrating tablet 75 mg, calcitonin gene-related peptide antagonist (FDA approval for acute treatment in February 2020). In many countries, rimegepant is the first treatment approved for both acute and preventative treatment of migraine.
- In published Phase 3 clinical trials, both lasmiditan and rimegepant have proven to be effective and generally well-tolerated.[2,3] However, central nervous system depression and serotonin syndrome may occur with lasmiditan. Due to central nervous system side effects, the lasmiditan product label advises patients not to drive or operate machinery until 8-hours post dose.[4] Lasmiditan is also considered a Schedule V controlled substance with the potential for abuse, however the extent and direction of any impact on persistence is unknown.[4]
- Real world persistence of acute treatment is an important measure of the overall benefits of a treatment, and may provide insights into treatment tolerability, effectiveness over time, and satisfaction of patients. However, assessing persistence in PRN medicines is challenging due to intra- and inter-patient variability in frequency of use.
- There are no published studies comparing persistence of rimegepant with lasmiditan; comparative real-world evidence of these novel acute treatments will be useful to support clinical decision making.

Objectives

- The primary objectives of this study were to describe the cohorts diagnosed with migraine who are new users of rimegepant (quantity 8 tablets) or lasmiditan (any dose) and to compare persistence between these cohorts.
- The secondary objectives included subgroup analyses on persistence in those with an index dose of lasmiditan (50 mg or 100 mg), chronic migraine, or prior repeated use of controlled substances.

METHODS

Study design and data source – A retrospective cohort study of MarketScan Commercial Claims and Encounters and Medicare Supplemental administrative databases.

Cohort selection – Adult patients (age ≥18 y) diagnosed with migraine (G43.xxx) who newly initiated rimegepant (8 tablets, assumed acute use) or lasmiditan (50 mg, 100 mg or 200 mg) between March 2020 and December 2023, with a minimum of 12-months continuous enrollment pre- and post-index.

Outcomes – To address the challenges of assessing persistence for treatments taken PRN, this study defined persistence as having ≥1 refill (any number of tablets or dose) of the same molecule and route of administration as the index treatment within 12-months post-index. This approach meant patients with low frequency of treatment use were less likely to be considered as non-persistent.

Subgroups – Data were analyzed by specific index doses of lasmiditan (50 mg and 100 mg), by chronic migraine diagnosis, and by patients' prior repeated use of controlled substances.

Analysis – Baseline demographics and clinical characteristics were described. Comparative analyses were performed using inverse probability of treatment weighting (IPTW) to address differences between groups in sociodemographic and health characteristics and minimize confounding. Absolute values of standardized mean differences (SMDs) <0.1 indicated balance between groups after IPTW. The percentage of patients classified as persistent in IPTW cohorts were described and the odds ratio (OR), corresponding 95% CI and p-values were reported.

Sensitivity analysis– Performed to explore the sensitivity of results to persistence definition: 6- and 18-months follow-up and a requirement for ≥2 refills within 12-months of index to be classed as persistent.

RESULTS

Demographics and clinical characteristics, rimegepant vs lasmiditan cohort

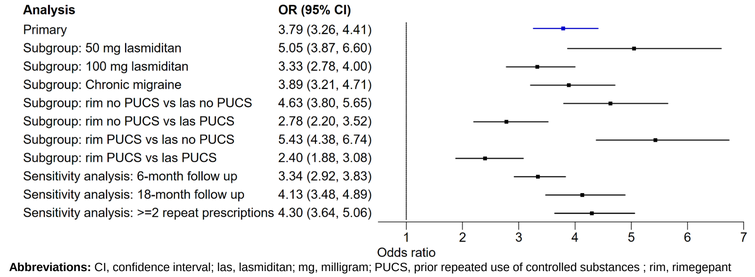
- The rimegepant and lasmiditan cohorts included 16,603 and 716 patients, respectively.
- Prior to IPTW adjustment and compared to the rimegepant cohort, the lasmiditan cohort was slightly older (mean age 45.5 vs 43.1 years), had fewer females (85.5% vs 87.7%;**Table 1**), had a higher proportion of comorbidities including ischemic cerebrovascular disease (8.7% vs 5.7%), structural heart disease (7.7% vs 5.0%), arrythmias (8.2% vs 5.2%), cardiac surgery (2.1% vs 0.8%), hypertension (38.1% vs 31.0%), depression (40.4% vs 31.2%) and anxiety related disorders (48.3% vs 41.1%). The lasmiditan cohort also had greater prior use of acute and preventive treatments and repeated prior use of controlled substances (**Table 1**).
- After adjustment with IPTW, sociodemographic and health characteristics were generally balanced between the two cohorts, other than small differences in mean age (SMD 0.10), ischemic heart disease (0.10), and diabetes mellitus (SMD -0.12) (**Table 1**).

Table 1. Baseline characteristics before and after IPTW for the primary analysis

Characteristic	Primary analysis:12-month follow up					
	No weighting			IPTW weighted		
	Rimegepant cohort N = 16,603	Lasmiditan (any dose) cohort N = 716	SMD	Rimegepant cohort N = 16,603	Lasmiditan (any dose) cohort N = 716	SMD
Calendar year						
2020	3905 (23.52)	334 (46.65)	0.52	4073 (24.53)	191 (26.62)	0.06
2021	6501 (39.16)	227 (31.70)	-	6445 (38.82)	279 (39.01)	-
2022	6197 (37.32)	155 (21.65)	-	6086 (36.65)	246 (34.37)	-
2023	0 (0)	0 (0)	-	0 (0)	0 (0)	-
Age						
Mean (Std)	43.13 (11.51)	45.46 (11.46)	0.20	43.24 (11.52)	44.41 (11.34)	0.10
Sex						
Female	14567 (87.74)	612 (85.47)	-0.07	14550 (87.64)	629 (87.80)	0.00
Male	2036 (12.26)	104 (14.53)	-	2053 (12.36)	87 (12.20)	-
Menstrual migraine	462 (2.78)	17 (2.37)	0.03	459 (2.76)	15 (2.07)	0.05
Insurance						
Commercial	16421 (98.90)	702 (98.04)	-0.07	16415 (98.87)	707 (98.70)	-0.02
Medicare	182 (1.10)	14 (1.96)	-	188 (1.13)	9 (1.30)	-
Region						
Northeast	1985 (11.96)	72 (10.06)	0.25	1972 (11.88)	74 (10.28)	0.07
North Central	3545 (21.35)	196 (27.37)	-	3588 (21.61)	162 (22.57)	-
South	9108 (54.86)	322 (44.97)	-	9035 (54.42)	396 (55.27)	-
West	1952 (11.76)	126 (17.60)	-	1995 (12.01)	85 (11.88)	-
Unknown	13 (0.08)	0 (0)	-	12 (0.08)	0 (0)	-
Triptan contraindications and warnings						
Ischemic cerebrovascular disease	944 (5.69)	62 (8.66)	-0.12	966 (5.82)	49 (6.88)	-0.04
Other cerebrovascular or cardiovascular disease	524 (3.16)	36 (5.03)	-0.09	538 (3.24)	25 (3.54)	-0.02
Uncontrolled hypertension	4343 (26.16)	224 (31.28)	-0.11	4382 (26.39)	211 (29.49)	-0.07
Ischemic heart disease	615 (3.70)	41 (5.73)	-0.10	634 (3.82)	42 (5.89)	-0.10
Peripheral artery disease	408 (2.46)	16 (2.23)	0.01	407 (2.45)	22 (3.10)	-0.04
Contraindication considered as other significant cardiovascular disease						
Structural heart disease	827 (4.98)	55 (7.68)	-0.11	849 (5.11)	42 (5.91)	-0.04
Arrhythmias	868 (5.23)	59 (8.24)	-0.12	890 (5.36)	37 (5.19)	0.01
Cardiac surgery	129 (0.78)	15 (2.09)	-0.11	140 (0.84)	6 (0.85)	0.00
Other cardiac conditions	1063 (6.40)	52 (7.26)	-0.03	1070 (6.44)	46 (6.49)	0.00
Cardiovascular risk factors						
Hypertension	5145 (30.99)	273 (38.13)	-0.15	5197 (31.30)	248 (34.61)	-0.07
Hyperlipidemia	5216 (31.42)	252 (35.20)	-0.08	5244 (31.59)	251 (35.02)	-0.07
Diabetes Mellitus	2159 (13.00)	119 (16.62)	-0.10	2187 (13.17)	124 (17.38)	-0.12
Obesity	5019 (30.23)	224 (31.28)	-0.02	5024 (30.26)	230 (32.12)	-0.04
Smoking	781 (4.70)	44 (6.15)	-0.06	791 (4.76)	40 (5.62)	-0.04
Other comorbid conditions						
Depression	5174 (31.16)	289 (40.36)	-0.19	5242 (31.58)	238 (33.23)	-0.04
Anxiety and related disorders	6826 (41.11)	346 (48.32)	-0.15	6877 (41.42)	300 (41.90)	-0.01
Seizures	1322 (7.96)	69 (9.64)	-0.06	1335 (8.04)	66 (9.25)	-0.04
Prevention agents						
Beta blockers	3075 (18.52)	160 (22.35)	-0.09	3105 (18.70)	147 (20.47)	-0.04
Tricyclic antidepressants	2380 (14.33)	118 (16.48)	-0.06	2397 (14.44)	100 (13.94)	0.01
Anti-depressants	2389 (14.39)	164 (22.91)	-0.22	2453 (14.77)	118 (16.44)	-0.05
Anticonvulsants	3924 (23.63)	197 (27.51)	-0.09	3952 (23.80)	178 (24.91)	-0.03
Anti-CGRP monoclonal antibodies	4363 (26.28)	347 (48.46)	-0.47	4521 (27.23)	225 (31.40)	-0.09
Onabotulinumtoxin A	2142 (12.90)	191 (26.68)	-0.35	2246 (13.53)	119 (16.65)	-0.09
Acute agents						
Oral triptans	8486 (51.11)	375 (52.37)	-0.03	8493 (51.16)	379 (52.99)	-0.04
Nasal triptans	450 (2.71)	33 (4.61)	-0.10	465 (2.80)	14 (2.01)	0.05
Injectable triptans	476 (2.87)	50 (6.98)	-0.19	506 (3.05)	24 (3.29)	-0.01
Nasal dihydroergotamine	92 (0.55)	21 (2.93)	-0.18	112 (0.67)	7 (1.03)	-0.04
Injectable dihydroergotamine	77 (0.46)	14 (1.96)	-0.14	90 (0.54)	8 (1.07)	-0.06
Nasal NSAIDs	25 (0.15)	3 (0.42)	-0.05	27 (0.16)	2 (0.23)	-0.02
Injectable NSAIDs	90 (0.54)	27 (3.77)	-0.22	114 (0.69)	6 (0.85)	-0.02
Acetaminophen	2002 (12.06)	121 (16.90)	-0.14	2037 (12.27)	108 (15.11)	-0.08
Isometheptene combinations	2 (0.01)	0 (0)	0.02	2 (0.01)	0 (0)	0.02
Used >=2 triptans during pre- index	1672 (10.07)	112 (15.64)	-0.17	1712 (10.31)	71 (9.93)	0.01
Repeated use of controlled substances	3689 (22.22)	293 (40.92)	-0.41	3826 (23.04)	192 (26.75)	-0.09

Abbreviations: CGRP, calcitonin gene-related peptide; IPTW, inverse probability of treatment weighting; NSAID, nonsteroidal anti-inflammatory drugs; SMD, standardized mean difference; std, standard deviation

Figure 1. Odds ratio and 95% confidence interval of persistence for rimegepant (quantity 8) compared with lasmiditan



Abbreviations: CI, confidence interval; las, lasmiditan; mg, milligram; PUCS, prior repeated use of controlled substances ; rim, rimegepant

Primary analysis

- The rimegepant cohort had a statistically significantly higher proportion of patients being persistent in the primary analysis compared to the lasmiditan cohort: OR: 3.79 (95% CI 3.26, 4.41) (**Figure 1**).

Subgroup analysis

- A significantly higher proportion of patients being persistent within the rimegepant cohort compared to the lasmiditan cohort was also reported for all subgroup analysis (**Figure 1**).

Sensitivity analysis

- Results were robust to sensitivity analyses exploring changes in follow-up duration (**Figure 1**).
  - 6-months follow-up available required for rimegepant vs lasmiditan: OR: 3.34 (95% CI 2.92, 3.83).
  - 18-months follow-up available required for rimegepant vs lasmiditan: OR: 4.13 (95% CI 3.48, 4.89).
- A sensitivity analysis requiring two repeat prescriptions within 12-months follow-up instead of one also showed significantly greater persistence for the rimegepant cohort vs lasmiditan: OR: 4.30 (95% CI 3.64, 5.06).

DISCUSSION

- This large observational study included adults diagnosed with migraine and enrolled in a US claims database who newly initiated either rimegepant or lasmiditan between March 2020 and December 2023.
- Analyses of IPTW-balanced cohorts indicate that rimegepant was associated with a statistically greater persistence than lasmiditan. This was seen regardless of lasmiditan index dose, chronic migraine diagnosis, or prior repeated use of controlled substances.
- Results were robust to sensitivity analyses, suggesting the definition of persistence did not impact the conclusions. Persistence on treatment for acute conditions such as migraine is likely influenced by many factors, including the effectiveness, tolerability, and safety profile of the treatments received.
- Given the evidence supporting rimegepant as an effective and generally well-tolerated acute migraine treatment, we hypothesize that the higher proportion of persistent patients in the rimegepant cohort may reflect an improved patient experience, potentially including improved tolerability.

Limitations

- Despite using IPTW, unadjusted confounding may remain.
- The definition of persistence used in this study does not distinguish between positive and negative reasons for discontinuing a treatment, and some patients may have stopped treatment as it was no longer required.
- Claims data do not capture the use of over-the-counter medications or medications that are paid for by the patient.

CONCLUSIONS

- **Rimegepant was associated with a statistically significant improvement in persistence compared to lasmiditan, regardless of lasmiditan index dose, chronic migraine diagnosis, prior repeated use of controlled substances. Results were robust to sensitivity analyses.**
- **These results may reflect a better response and/or tolerability of rimegepant treatment compared to lasmiditan in clinical practice.**

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CONFLICTS OF INTEREST

All authors are employees of and own stock/stock options in Pfizer.

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