Lasmiditan is Effective in the Acute Treatment of Migraine in Patients with Insufficient Response to Triptans: Findings from the CENTURION Study

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BACKGROUND

- Lasmiditan is a selective serotonin (5-HT1F) receptor agonist (ditan) approved for the acute treatment of migraine, with or without aura, in adults[1]
- The CENTURION trial was a Phase 3 placebo-controlled study of lasmiditan in acute treatment of 4 migraine attacks with or without aura
- In CENTURION, lasmiditan was superior to placebo for the primary endpoints of pain freedom at 2 hours (1st attack) and pain freedom at 2 hours in ≥2/3 attacks, as well as all key secondary endpoints[2]
- We present the efficacy findings from a pre-specified subset of the CENTURION population – patients who had an insufficient response to triptans (see below)

Pain Freedom and Pain Relief after First Dose *TIR ITT Population*

- Lasmiditan 200 mg (N=203)
- Lasmiditan 100 mg (N=183)
- Placebo (N=193)

Gated secondary endpoint
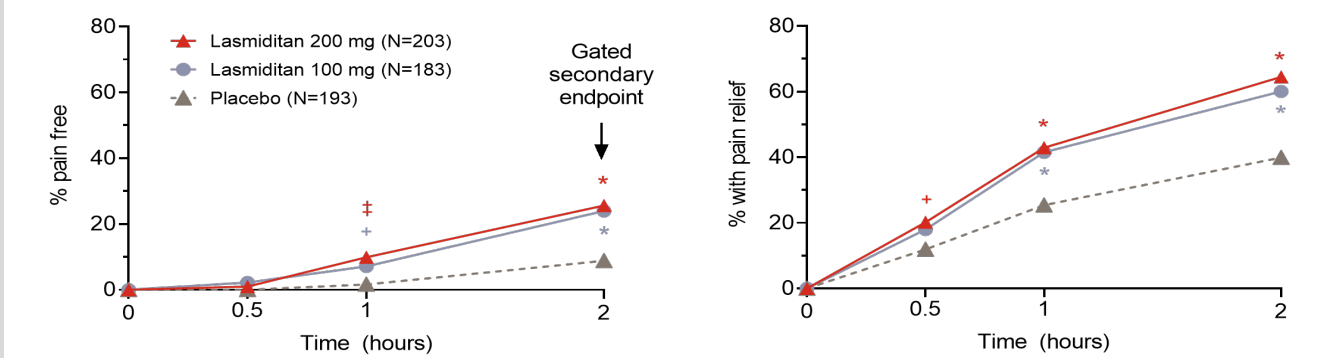
[+]p<0.05; [‡]p<0.05; [*]p<0.001 vs placebo (logistic regression with treatment and region as factors)

- Both lasmiditan doses showed statistically-significant benefit over placebo for pain freedom beginning at 1 hour, and for pain relief beginning at 0.5 hours (200 mg dose) or 1 hour (100 mg dose) in the TIR population

Other First Dose Findings *TIR ITT Population*

	Placebo (N=193)	Lasmiditan 100 mg (N=183)		Lasmiditan 200 mg (N=203)	
	n (%)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Sustained pain freedom 24h	7 (3.6)	26 (14.2)*	4.2 (1.8, 9.6)	30 (14.8)*	4.4 (1.9, 10.0)
Sustained pain freedom 48h	10 (5.2)	18 (9.8)[ns]	1.9 (0.9, 4.2)	28 (13.8)‡	2.9 (1.4, 5.9)
Disability free 2h	19 (9.8)	26 (14.2)[ns]	1.6 (0.8, 2.9)	38 (18.7)‡	2.2 (1.2, 4.0)
PGIC much/v much better 2h	27 (14.0)	49 (26.8)‡	2.3 (1.4, 3.9)	55 (27.1)*	2.4 (1.4, 4.1)
PGIC much/v much better 24h	40 (20.7)	58 (31.7)[ns]	1.6 (1.0, 2.7)	79 (38.9)*	2.4 (1.5, 4.0)
MBS free 2h	51 (29.1)	66 (40.0)†	1.6 (1.0, 2.5)	64 (34.8)[ns]	1.3 (0.8, 2.0)
Rescue medication 2-24h	50 (28.4)	31 (22.3)†	0.6 (0.4, 1.0)	30 (19.9)‡	0.5 (0.3, 0.8)

[†]p<0.05; [‡]p<0.01; [*]p<0.001 vs placebo; [ns]not significant (based on logistic regression with treatment and region as factors) Abbreviations: h, hour; MBS, Most Bothersome Symptom; OR, odds ratio; PGIC, Patient Global Impression of Change

- First dose findings in TIR population were similar to those for the non TIR population (interaction p-value >0.05 in all cases)
- Findings were similar when patients considered TIR based on tolerability issues/contraindications were excluded (no formal analysis)

CONCLUSION

- **Lasmiditan was efficacious across multiple clinically relevant endpoints in a pre-specified subset of patients with an insufficient response to triptans**

References
1. REYVOW® (lasmiditan). Package insert. Eli Lilly and Company; 2019.
2. Ashina M et al. Cephalalgia 2021; doi.org/10.1177/0333102421989232.
3. Lipton R et al Neurology 2015; 84: 688-695.
4. American Headache Society. Headache 2019; 59: 1-18.

Defining Triptan Insufficient Responder

Background
- No standard definition for triptan insufficient responders (TIR) exists
- Prior definitions have included both efficacy and tolerability considerations, and often rely on patients' self-reports rather than prospective identification

CENTURION Trial TIR Definition
- Pre-specified composite definition was based on review of the literature and input from an advisory board of migraine experts
- Patient considered TIR if they met any of the 3 criteria:
  - Currently taking a triptan and with score ≤5 based on 4 questions from the migraine Treatment Optimization Questionnaire 6 (mTOQ-6), indicating a poor/very poor response to current regimen.[3] The mTOQ is recommended by AHS to help identify patients who have failed to respond to or did not tolerate triptans;[4]
  - Did not achieve pain freedom at 2 hours post dose in ≥2 out of 3 attacks with their most recent triptan; or
  - Not currently taking a triptan and discontinued most recent triptan due to lack of efficacy, tolerability issues, or contraindications

Population Definitions
- Safety: Patients who took ≥1 dose of study drug
- ITT, intention-to-treat: Patients who took ≥1 dose of study drug to treat a migraine attack of at least mild pain severity and with any pain severity assessments at or before 2 hours post dose
- ITT consistency: Patients who experienced ≥2 successes or 2 failures during an ITT-evaluable attack

Baseline Demographics *Safety Population*

	Triptan naïve (N=538)	Triptan sufficient responders (N=300)	TIR (N=633)
Female	79%	85%	88%
Age, mean (SD), years	39 (12)	44 (12)	42 (12)
White	53%	91%	91%
Cardiovascular risk factors	52%	64%	62%
Region - Europe (76% of trial population)	53%	86%	91%
- North America (12%)	18%	8%	9%
- Asia (12%)	29%	5%	<1%
Migraine history, mean (SD), years	14 (12)	19 (13)	19 (13)
Number of migraines/m in past 3m, mean (SD)	4.8 (1.4)	5.0 (1.5)	5.0 (1.6)
Preventive treatment during study	16%	33%	36%
MIDAS total score, mean (SD)	30 (18)	30 (20)	34 (22)

Abbreviations: m, month; SD, standard deviation

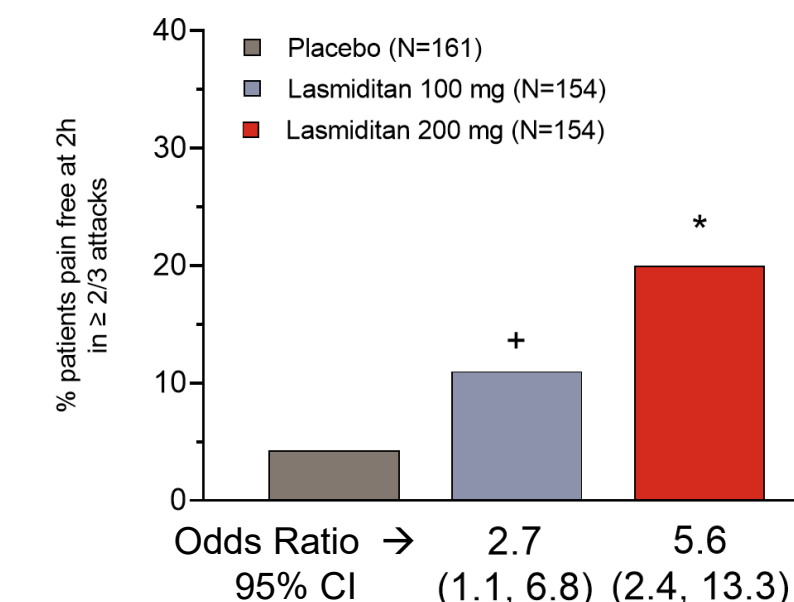**Triptan Experience in the TIR Population**

- Of the 633 TIR patients, the majority (76%) had tried 1 triptan, 17% had tried 2 triptans, 7% had tried 3 or more
- The reasons for being considered TIR are shown in the figure (right)
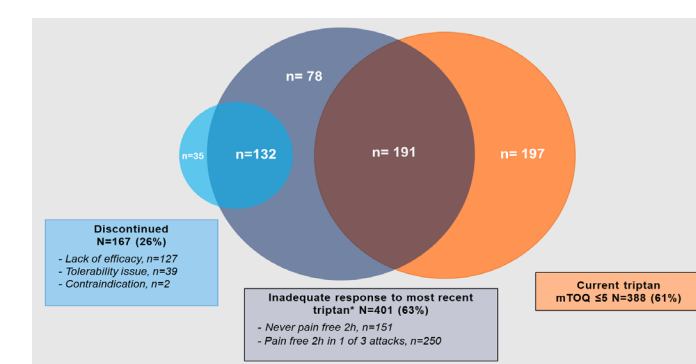
*based on response to q "How well did the patient's migraine pain respond to the medication" Response options:
- Never responded pain free at 2h
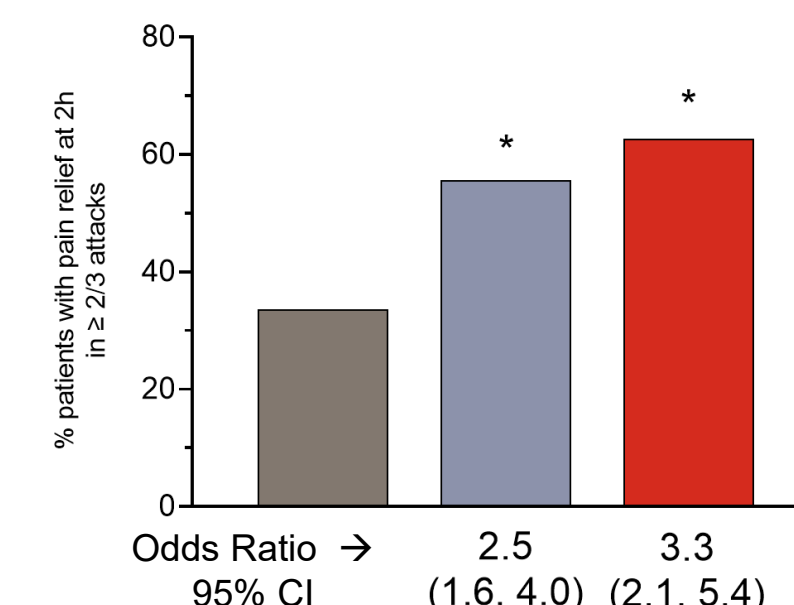- Responded pain free at 2h in 1/3 attacks

Intra-patient Consistency
TIR ITT Consistency Population

- Placebo (N=161)
- Lasmiditan 100 mg (N=154)
- Lasmiditan 200 mg (N=154)

Odds Ratio 95% CI: 2.7 (1.1, 6.8); 5.6 (2.4, 13.3)

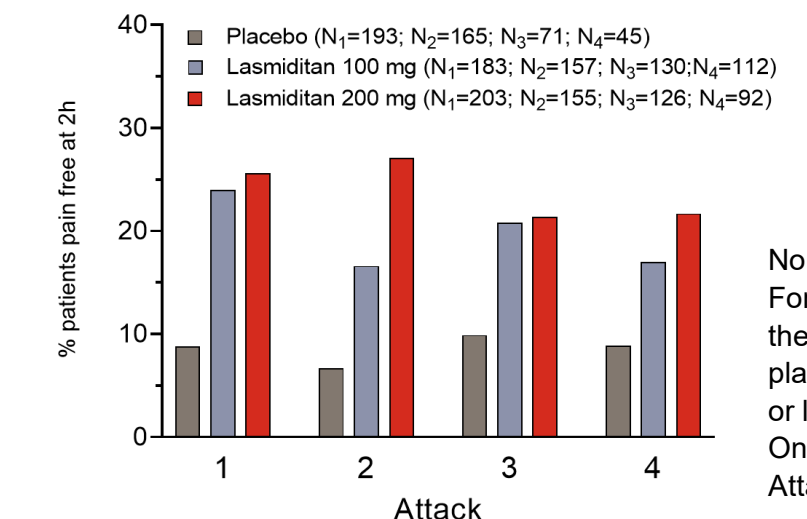Odds Ratio 95% CI: 2.5 (1.6, 4.0); 3.3 (2.1, 5.4)

- Intra-patient consistency findings for the TIR population were similar to those for the non TIR population (interaction p-value >0.05 both cases) and when patients considered TIR based on tolerability issues/contraindications were excluded

[†]p<0.05; [*]p<0.001 vs placebo

Population Consistency
TIR ITT Population

- Placebo (N1=193; N2=165; N3=71; N4=45)
- Lasmiditan 100 mg (N1=183; N2=157; N3=130; N4=112)
- Lasmiditan 200 mg (N1=203; N2=155; N3=126; N4=92)

No formal statistical comparisons. For Attacks 3 and 4, patients in the control group received either placebo/lasmiditan 50 mg or lasmiditan 50 mg/placebo. Only placebo data are shown for Attacks 3 and 4.
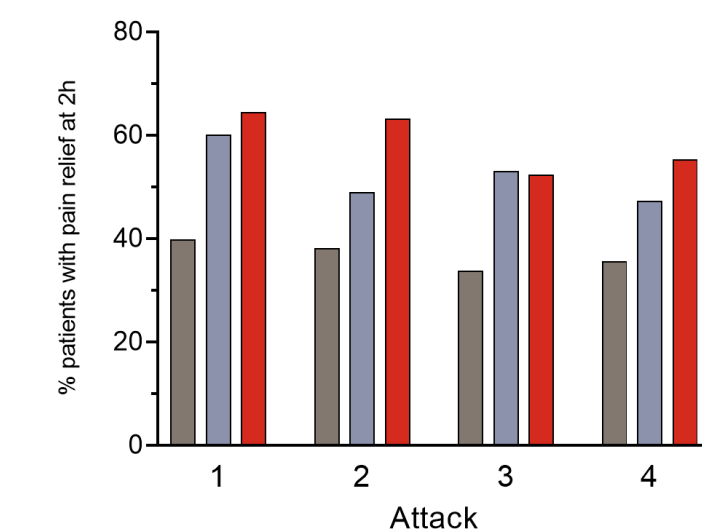
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