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Predictors of 2-Hour Pain Freedom Among Patients Enrolled in 2 Phase 3 Studies of Lasmiditan for Acute Treatment of Migraine

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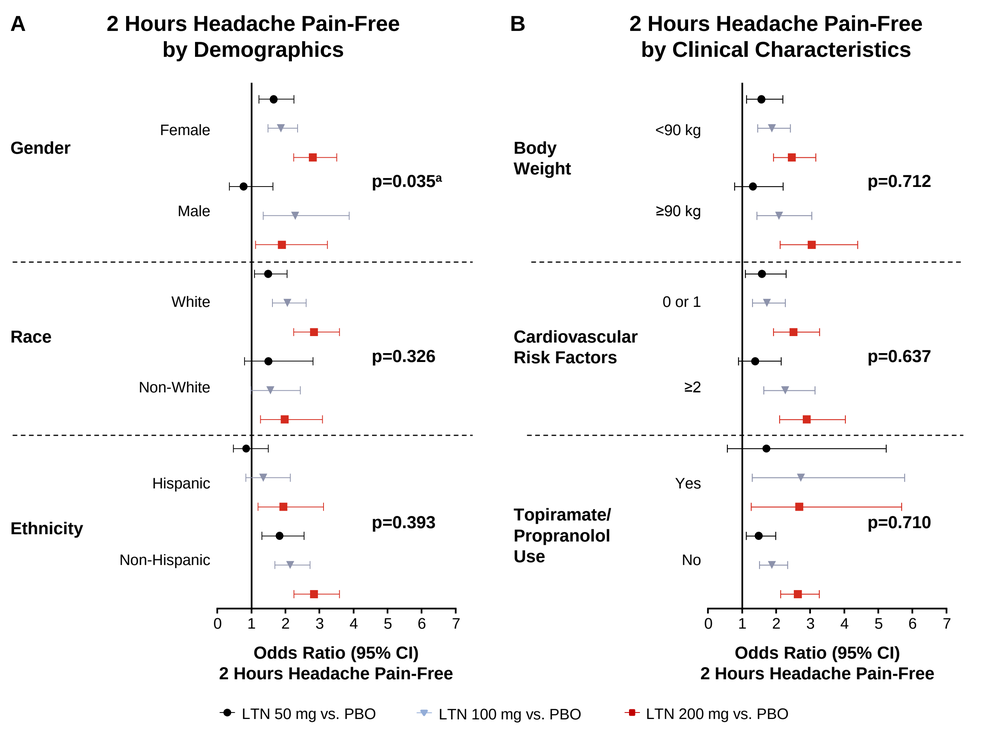
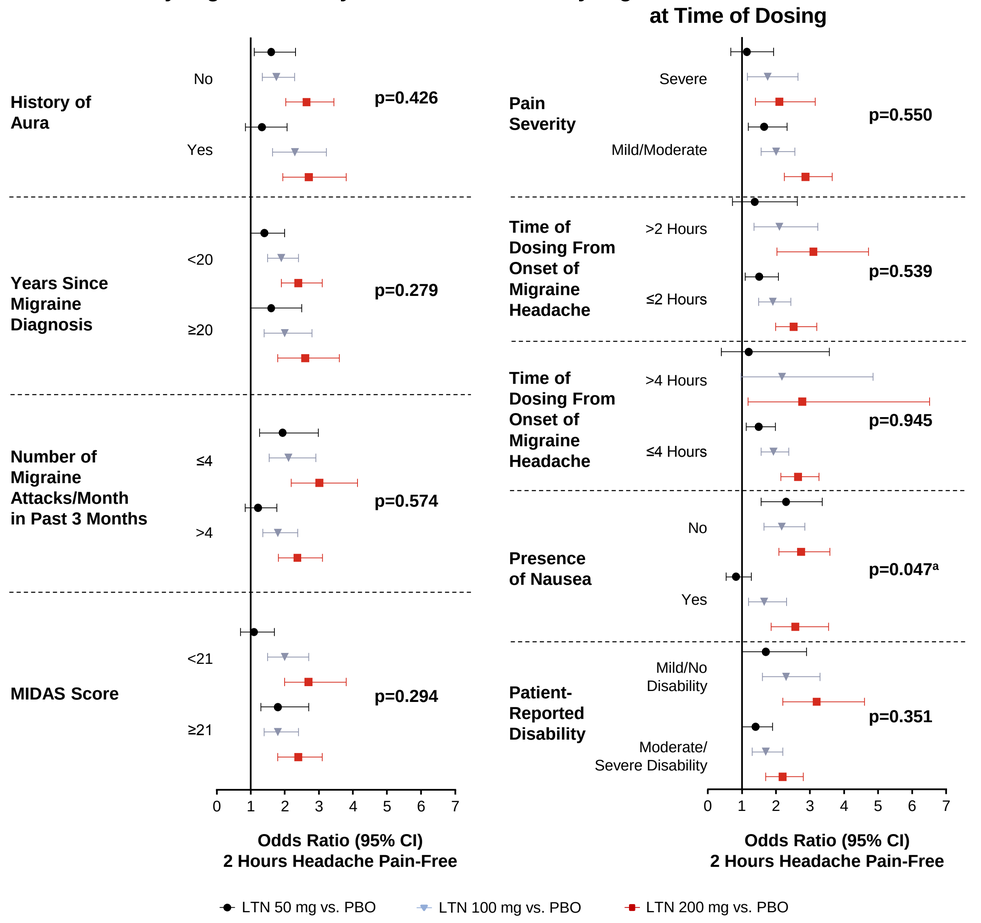
OBJECTIVE

- To identify characteristics associated with achieving 2-hour pain freedom following oral lasmiditan for the acute treatment of migraine, based on pooled data from the Phase 3 SAMURAI and SPARTAN studies

KEY RESULTS

No Patient Demographics (A), Clinical Characteristics (B), Migraine History (C), or Migraine Attack Characteristics (D) Analyzed Consistently Predicted Treatment Response



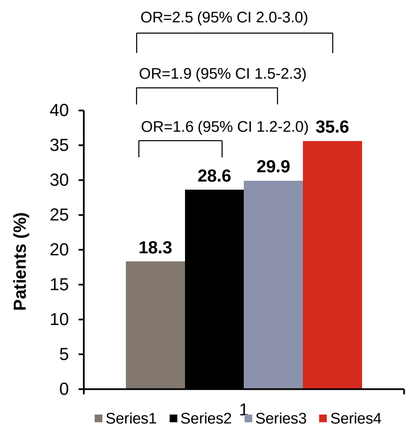


[a]p-Value not significant after tests for multiplicity.
Note: p<0.1 considered significant.
CI=confidence interval; LTN=lasmiditan; MIDAS=Migraine Disability Assessment; PBO=placebo.

Background

- Lasmiditan, a high-affinity, selective, 5-hydroxytryptamine 1F receptor agonist without vasoconstrictive activity, has proven to be effective in the acute treatment of migraine in 2 Phase 3 studies (SAMURAI [NCT02439320] and SPARTAN [NCT02605174])[1,2]
  - Significantly higher proportions of patients treated with lasmiditan were free from headache pain at 2 hours following dosing compared with placebo[3]

Pooled Pain Freedom at 2 Hours



CI=confidence interval; LTN=lasmiditan; OR=odds ratio; PBO=placebo.

Methods

Study Design

- SAMURAI and SPARTAN:
  - Main inclusion criteria: males or females (≥18 years) who had at least a 1-year history of disabling migraine with or without aura (International Headache Society diagnostic criteria 1.1 and 1.2.1),[4] a Migraine Disability Assessment (MIDAS) score ≥11,[5] onset before the age of 50 years, and 3-8 migraine attacks/month were eligible for enrollment
  - Study medication was to be taken within 4 hours of onset of migraine pain of at least moderate severity

	PBO	LTN 50 mg	LTN 100 mg	LTN 200 mg
SAMURAI	X		X	X
SPARTAN	X	X	X	X

Characteristics Investigated in the Analysis

- Patient demographics:
  - Gender (female vs. male)
  - Race (White vs. Non-White)
  - Ethnicity (Hispanic vs. Non-Hispanic)
- Clinical characteristics:
  - Body weight (<90 kg vs. ≥90 kg)
  - Number of cardiovascular risk factors (0 or 1 vs. ≥2)
  - Concomitant topiramate or propranolol use (yes vs. no)
- Migraine history:
  - History of aura (yes vs. no)
  - Years since migraine diagnosis (<20 vs. ≥20)
  - Number of migraine attacks/month in the past 3 months (≤4 vs. >4)
  - Baseline MIDAS (<21 vs. ≥21)
- Migraine attack characteristics at time of dosing:
  - Pain severity (severe vs. mild/moderate)[a]
  - Time of dosing from onset of migraine headache (≤2 vs. >2 hours, ≤4 vs. >4 hours)
  - Presence of nausea (yes vs. no)
  - Patient-reported disability (mild/no disability vs. moderate/severe disability)

[a]Despite instructions to treat when migraine pain was at least moderate severity, some patients were treated when pain was mild and were included in this analysis.

Statistical Methods

- With the exception of the analysis, "Time of dosing from onset of migraine headache ≤4 hours vs. >4 hours," the analyses were conducted on the modified intention-to-treat (mITT) population, which included patients who took a dose of study drug within 4 hours of onset of migraine headache and had an efficacy measure (or outcome) recorded in the eDiary
- Logistic regression modeling was used to identify statistically significant predictors associated with response
- p-Values were determined from tests of subgroup-by-treatment interaction, with terms for study, subgroup (patient phenotype or migraine attack characteristic), treatment, and interaction
  - p<0.1 was considered significant

Results

Baseline Demographic and Patient Characteristics Were Balanced Between Treatment Groups

Characteristics (mITT Population)	PBO N=1064	LTN 50 mg N=556	LTN 100 mg N=1035	LTN 200 mg N=1046
Age, years, mean (SD)	42.45 (12.60)	42.85 (13.28)	42.79 (11.99)	41.36 (12.15)
Female, n (%)	906 (85.2)	473 (85.1)	862 (83.3)	869 (83.1)
Body weight, kg, mean (SD)	82.7 (21.7)	81.2 (20.7)	83.8 (23.8)	85.5 (24.2)
Race, White, n (%)	862 (81.0)	452 (81.3)	821 (79.3)	823 (78.8)
Ethnicity, Hispanic, n (%)	182 (17.1)	115 (20.7)	178 (17.2)	179 (17.1)
≥1 baseline cardiovascular risk, n (%)	847 (79.6)	430 (77.3)	818 (79.0)	803 (76.8)
Topiramate or propranolol use, n (%)	107 (10.1)	48 (8.6)	93 (9.0)	92 (8.8)

LTN=lasmiditan; mITT=modified intention-to-treat; PBO=placebo; SD=standard deviation.

Migraine History Characteristics Were Balanced Between Treatment Groups

Characteristics (mITT Population)	PBO N=1064	LTN 50 mg N=556	LTN 100 mg N=1035	LTN 200 mg N=1046
Migraine history duration, years, mean (SD)	18.50 (12.66)	18.62 (12.87)	19.32 (13.20)	18.17 (12.61)
Migraine attacks/month in the past 3 months, mean (SD)	5.32 (2.10)	5.23 (1.95)	5.16 (1.81)	5.18 (1.81)
History of aura, n (%)	360 (33.8)	194 (34.9)	362 (35.0)	347 (33.2)
MIDAS total score, mean (SD)	31.98 (23.63)	32.53 (23.84)	30.65 (20.33)	31.95 (22.01)

LTN=lasmiditan; MIDAS=Migraine Disability Assessment; mITT=modified intention-to-treat; PBO=placebo; SD=standard deviation.

Migraine Attack Characteristics Were Balanced Between Treatment Groups

Characteristics (mITT Population)	PBO N=1064	LTN 50 mg N=556	LTN 100 mg N=1035	LTN 200 mg N=1046
Migraine attack severity, n (%)				
Severe	310 (29.1)	152 (27.3)	291 (28.1)	295 (28.2)
Moderate	739 (69.5)	392 (70.5)	730 (70.5)	729 (69.7)
Mild	14 (1.3)	12 (2.2)	14 (1.4)	22 (2.1)
None	1 (0.1)	0	0	0
Time to treatment from migraine attack pain onset, hours, mean (SD)	1.05 (1.91)	0.97 (1.76)	1.07 (2.06)	1.12 (1.66)
Presence of nausea, n (%)	470 (44.2)	245 (44.1)	445 (43.0)	451 (43.1)
Patient-reported migraine attack-related disability, n (%)				
Mild/no disability	201 (25.1)	151 (27.2)	244 (30.7)	233 (29.5)
Moderate/severe disability	601 (74.9)	405 (72.8)	551 (69.3)	557 (70.5)

LTN=lasmiditan; mITT=modified intention-to-treat; PBO=placebo; SD=standard deviation.

CONCLUSIONS

- The efficacy of lasmiditan on pain freedom at 2 hours was similar for subgroups defined by the patient demographics, clinical characteristics, migraine history, and migraine attack characteristics that were analyzed

References
1. Kuca B et al. *Neurology* 2018;92:e2222-e2232.
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3. Doty EG et al. *Cephalalgia* 2019;39:957-66.
4. Headache Classification Subcommittee of the International Headache Society. *Cephalalgia* 2004;24:9-160.
5. Lipton RB et al. *Headache* 2001;41:854-61.

Abbreviations: CI=confidence interval; LTN=lasmiditan; MIDAS=Migraine Disability Assessment; mITT=modified intention-to-treat; OR=odds ratio; PBO=placebo; SD=standard deviation.

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