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Lasmiditan Over Four Migraine Attacks in Chinese Population: Findings from CENTURION Study

Tingmin Yu[1], Li He[2], Xiaosu Yang[3], Quan Hu[4], Bin Zhang[4], Shiying Zhong[4], Shengyuan Yu[5]

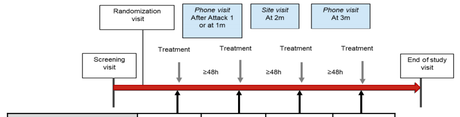
[1]Second Hospital of Jilin University, Changchun, China; [2]West China Hospital of Sichuan University, Chengdu, China; [3]Xiangya Hospital of Central South University, Changsha, China;
[4]Eli Lilly and Company, Indianapolis, USA; [5]Chinese PLA General Hospital, Beijing, China. Corresponding author: yusy1963@126.com

INTRODUCTION AND OBJECTIVE

- Lasmiditan is a selective serotonin (5-HT1F) receptor agonist (ditan), approved by the FDA for the acute treatment of migraine, with or without aura, in adults.[1]
- This Phase 3 placebo-controlled study (CENTURION) was designed to assess the efficacy, including first attack efficacy and consistency of response, and safety of lasmiditan in acute treatment of 4 migraine attacks with or without aura. Trial Registration Number: NCT03670810
- The primary endpoints were pain freedom at 2h (first attack) and pain freedom at 2h in at least 2 out of 3 attacks (consistency of efficacy).
- CENTURION was conducted in 17 countries including China. Additionally, the study designed a maximized extended enrollment (ME2) addendum to meet registration requirement in China after primary cohort completion.
- The objective of the present report is to present findings in the Chinese population, from both CENTURION primary cohort and China ME2 cohort.

[1]REYVOW® (lasmiditan) tablets [package insert]. Eli Lilly and Company, Indianapolis, IN; 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211280s000lbl.pdf.

STUDY DESIGN



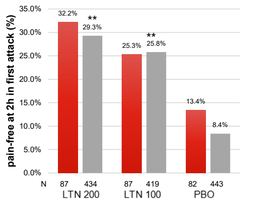
Randomized 1:1:1:1 to	Attack 1	Attack 2	Attack 3	Attack 4
LTN 100 (N=109)	LTN 100	LTN 100	LTN 100	LTN 100
LTN 200 (N=108)	LTN 200	LTN 200	LTN 200	LTN 200
Control (N=109)	PBO	PBO	LTN 50	PBO
	PBO	PBO	PBO	LTN 50

- Patient population: A history of disabling migraine (MIDAS[1] score ≥11) for at least 1 year; migraine onset before age 50; 3-8 migraine attacks/m but <15 headache days/m during the past 3m.
- End of study visit occurred at 7 days after treating the last migraine attack or at 4 months after randomization.
- All analyses in Chinese population were for descriptive purpose only. The P-value for treatment vs. placebo will not be displayed.

[1]MIDAS: Migraine Disability Assessment Test.

KEY RESULTS (Primary endpoints)

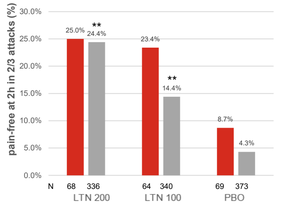
Pain freedom at 2h in first attack: *ITT population*



- Chinese ITT population (first attack)
- Primary cohort ITT population (first attack)

- ** P<0.001 vs. PBO
- *ITT population = patients who treated a migraine attack (mild, moderate or severe) and had any pain severity assessment ≤2h post dose.*

Pain freedom at 2h in at least 2/3 attacks: *ITT consistency population*



- Chinese ITT Consistency Population
- Primary cohort ITT Consistency Population

- ** P<0.001 vs. PBO
- *ITT consistency population = patients who experienced ≥2 successes or 2 failures during an ITT-evaluable attack.*

CONCLUSIONS

- In Chinese population, lasmiditan was numerically better than placebo for both primary endpoints and key secondary endpoints with an acceptable safety profile.
- These findings were generally consistent with that observed in CENTURION primary cohort.

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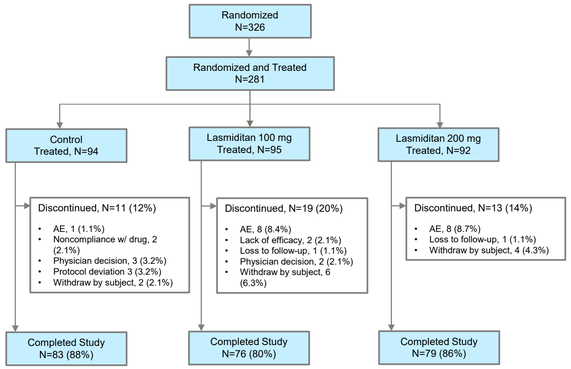
Disclosures: **QH**, **BZ**, and **SZ** are full-time employee at Eli Lilly and Company. **SY** serves as associated editor of the Journal of Headache and Pain and as Member of the International Headache Society. **TY**, **LH**, **XY**, and **SY** report financial relationships with Eli Lilly and Company for clinical research fee.

Results

Patient Flow



Baseline Characteristics: safety population

- Mean age 37.8 years; 72.2% female.
- Migraine history duration 12.7 years, average migraine per month in the past 3 months 4.3 attacks/month, MIDAS mean score 36.4.
- Baseline characteristics were well balanced across treatment groups.

- *Safety population = patients who take at least 1 dose of study drug.*

Pain Freedom

- Lasmiditan was numerically superior to placebo in pain freedom for:
  - Onset of pain freedom at 1h, with the efficacy sustained until 24h and 48h;
  - These results in Chinese population were consistent with in primary cohort.

Table 1: Gated secondary endpoints for pain freedom

	LTN 200 mg	LTN 100 mg	PBO
Chinese ITT population (first attack)			
N	87	87	82
Pain freedom at 1h, n(%)	13 (14.9%)	8 (9.2%)	4 (4.9%)
Sustained pain freedom for 24h, n(%)	15 (17.2%)	13 (14.9%)	8 (9.8%)
Sustained pain freedom for 48h, n(%)	16 (18.4%)	8 (9.2%)	6 (7.3%)
Primary cohort ITT population (first attack)			
N	434	419	443
Pain freedom at 1h, n(%)	55 (12.7%)	25 (6.0%)	9 (2.0%)
Sustained pain freedom for 24h, n(%)	75 (17.3%)**	57 (13.6%)**	19 (4.3%)
Sustained pain freedom for 48h, n(%)	67 (15.4%)**	39 (9.3%)*	19 (4.3%)

ITT: intention to treat; LTN: lasmiditan; PBO: placebo.
* P <0.01, ** P <0.001 vs. placebo.
ITT population = patients who treated a migraine attack (mild, moderate or severe) and had any pain severity assessment ≤2h post dose.

Pain Relief

- Lasmiditan was numerically superior to placebo in pain relief for:
  - Onset of pain relief at 1h;
  - Consistency of pain relief at 2h during at least 2 of 3 attacks;
  - These results in Chinese population were consistent with in primary cohort.

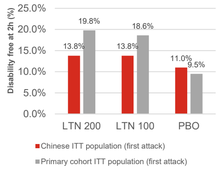
Table 2: Gated secondary endpoints for pain relief

	LTN 200 mg	LTN 100 mg	PBO
Chinese ITT population (first attack)			
N	87	87	82
Pain relief at 1h, n(%)	51 (58.6%)	45 (51.7%)	34 (41.5%)
Pain relief at 2h, n(%)	63 (72.4%)	63 (72.4%)	45 (54.9%)
Primary cohort ITT population (first attack)			
N	434	419	443
Pain relief at 1h, n(%)	205 (47.2%)**	204 (48.7%)**	130 (29.3%)
Pain relief at 2h, n(%)	283 (65.2%)**	274 (65.4%)**	183 (41.3%)
Chinese ITT consistency population			
N	65	60	59
Pain relief at 2h in at least 2/3 attacks	54 (83.1%)	44 (73.3%)	31 (52.5%)
Primary cohort ITT consistency population			
N	333	332	320
Pain relief at 2h in at least 2/3 attacks	222 (66.7%)**	207 (62.3%)**	118 (36.9%)

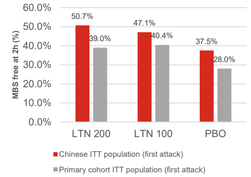
ITT: intention to treat; LTN: lasmiditan; PBO: placebo.
** P <0.001 vs. placebo.
ITT consistency population = patients who experienced ≥2 successes or 2 failures during an ITT-evaluable attack.

Other Key secondary endpoints

- Disability freedom at 2h in first attack



- Most bothersome symptom (MBS) freedom at 2h in first attack



Safety

- No new safety signal was observed in Chinese population (safety population).
  - No death.
  - 7 patients (2.5%) reported SAEs, these SAEs reported not related to study drug; only 1 treatment-emergent (occurred or worsen 0-48h post dose) SAE was reported by patient in lasmiditan 100 mg group.
  - 17 patients (6.1%) were discontinued from study due to AE.

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