Exploratory Efficacy of INP104 in Patients Using Concomitant Preventive Migraine Medications

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Introduction

- Acute therapies for migraine management are prescribed to reduce the pain, associated symptoms, and disability that accompanies migraine attacks (MAs)[1]
- Preventive therapies for migraine are recommended only for patients with MAs that significantly interfere with daily routines despite acute treatment; frequent attacks (≥4 monthly headache days); contraindication to, failure, or overuse of acute treatments; adverse events (AEs) with acute treatments; and patient preference[1]
- The goal of preventive treatment is to reduce MA frequency, and patients often continue taking acute therapies during this time;[1,2] therefore, concomitant use of acute and preventive migraine therapies is common
- Studies have reported that several acute therapies, including lasmiditan and ubrogepant, are similarly effective and safe in patients who have used and who have not used preventive therapies concomitantly[3-5], but there can be a risk of increased adverse events with the use of concomitant medications[2]
- INP104 is drug-device combination product that delivers dihydroergotamine (DHE) mesylate to the upper nasal space using Precision Olfactory Delivery (POD®) technology[6] and has been approved for the acute treatment of migraine
- The exploratory efficacy of INP104 as an acute therapy for migraine has been examined in a Phase 3 study[6], but the impact of concomitant use of preventive migraine therapies on the exploratory efficacy and safety of INP104 has not been explored

Objective

- This post hoc analysis of data from the Phase 3 STOP 301 study of INP104 for the acute treatment of migraine investigated the exploratory efficacy and safety of INP104 in patients who did or did not use concomitant migraine preventive medications over 24 weeks of treatment

Methods

Study Design

- STOP 301 was a Phase 3, open-label, single-group assignment study that assessed the safety, tolerability, and exploratory efficacy of INP104 (NCT03557333)
- The study consisted of a 28-day screening period when patients used their best usual care to acutely treat MAs, a 24-week treatment period for all patients when INP104 was used to acutely treat MAs, and a 2-week post-treatment follow-up period for all patients
- A subset of patients continued into a treatment extension to 52 weeks
- eDiaries were used to collect information, both daily and with every headache or migraine, on medication used and pain/most bothersome symptom (MBS) severity through 24 weeks and, if applicable 52 weeks

Study Treatment

- Following the screening period, all eligible patients were provided with up to 3 doses per week of INP104 to nasally self-administer (1.45 mg in a dosage of 2 sprays) with self-recognized MAs
- Concomitant preventive migraine medications were permitted during the study if stable (>30 days before screening) unless they were contraindicated for concomitant use with DHE mesylate

Study Patients

- Adult males or females aged 18-65 years with a documented diagnosis of migraine with or without aura not qualifying as chronic migraine based on the *International Classification of Headache Disorders,* 3rd edition beta
- Patients were required to be in general good health, have no significant medical history or clinical abnormalities at baseline, experience ≥2 MAs per month for the previous 6 months and during screening, and have completed eDiary entries on ≥23/28 days during screening

Post Hoc Analysis

- Exploratory efficacy end points of self-reported pain and MBS freedom at 2 hours post-INP104 as well as safety outcomes were evaluated based on concomitant preventive migraine medications used during the STOP 301 study
- Concomitant preventive migraine medication groups included none, topiramate, erenumab, and other
  - "Other" included propranolol, propranolol hydrochloride, amitriptyline, onabotulinum toxin A, bupropion, *Cannabis sativa, Curcuma longa,* duloxetine hydrochloride, estradiol, gabapentin, ibuprofen, labetalol, lamotrigine, loratadine, magnesium, nadolol, nortriptyline, nortriptyline hydrochloride, paroxetine hydrochloride, timolol, valproate semisodium, and zonisamide
- Patients who used >1 preventive medication were included under each applicable group; therefore, patients could be listed more than once

Results

Patient Demographics and Disposition

- 360 patients were screened and enrolled in the 24-week treatment period
- 354 self-administered ≥1 dose of INP104 over 24 weeks and comprised the 24-week full safety set (24-week FSS)
- For this post hoc analysis, 254, 31, 7, and 29 patients used none, topiramate, erenumab, or other migraine preventive medications concomitantly at Month 0 (ie baseline), respectively

Mean Number of INP104-treated MAs Based on Concomitant Preventive Migraine Medications Used Over 24 Weeks (Figure 1)

- None: 3.1 MAs at Month 1 vs 2.2 MAs at Month 6
- Topiramate: 3.0 MAs at Month 1 vs 2.0 MAs at Month 6
- Erenumab: 3.6 MAs at Month 1 vs 2.8 MAs at Month 6
- Other: 3.4 MAs at Month 1 vs 2.4 MAs at Month 6

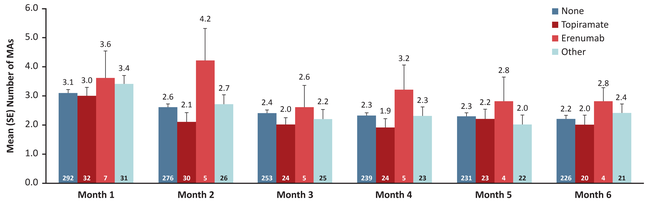
Exploratory Efficacy Based on Concomitant Preventive Migraine Medications Used Over 24 Weeks

- Self-reported pain freedom at 2 hours post-INP104 (Figure 2)
  - None: 30.1% at baseline vs 36.1% at Month 6
  - Topiramate: 32.6% at baseline vs 31.1% at Month 6
  - Erenumab: 22.3% baseline vs 33.3% at Month 6
  - Other: 35.3% baseline vs 25.3% at Month 6
- Self-reported MBS freedom (Figure 3)
  - None: 47.4% at baseline vs 53.6% at Month 6
  - Topiramate: 50.7% at baseline vs 51.7% at Month 6
  - Erenumab: 47.4% baseline vs 41.7% at Month 6
  - Other: 49.4% baseline vs 38.3% at Month 6

Safety Outcomes Based on Concomitant Preventive Migraine Medications Used Over 24 Weeks (Table 1)

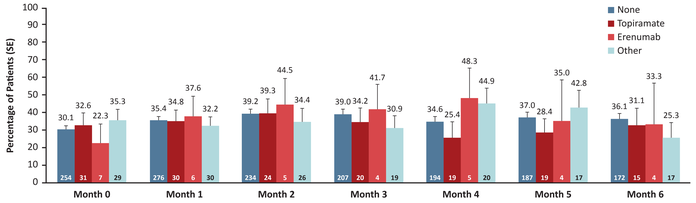
- Treatment-emergent adverse events (TEAEs)
  - None: 73.6%; topiramate: 62.5%; erenumab: 42.9%; other: 71.0%
- Serious TEAEs, none of which were considered related to INP104
  - None: 2.1% of patients had serious TEAEs, which included intestinal obstruction, clavicle fracture, rib fracture, status migrainosus, abortion spontaneous, and ovarian mass
  - Topiramate and Other: 0 serious TEAEs
  - Erenumab: 14.3% of patients had serious TEAEs, which included visual impairment and pulmonary embolism
- Severe TEAEs
  - None: 4.5% of patients had severe TEAEs, which included retinal detachment, vomiting, intestinal obstruction, nausea, gastroenteritis, infected bite, upper limb fracture, back pain, muscle spasms, carpal tunnel syndrome, dizziness, status migrainosus, abortion spontaneous, and nasal congestion
  - Topiramate: 3.1% of patients had severe TEAEs, which included dizziness
  - Erenumab: 14.3% of patients had severe TEAEs, which included visual impairment, bronchitis, and pulmonary embolism
  - Other: 0 severe TEAEs

Figure 1. Mean Number of INP104-treated MAs Based on Concomitant Preventive Migraine Medications Used Over 24 Weeks (FSS)



FSS = full safety set; MA = migraine attack; SE = standard error.

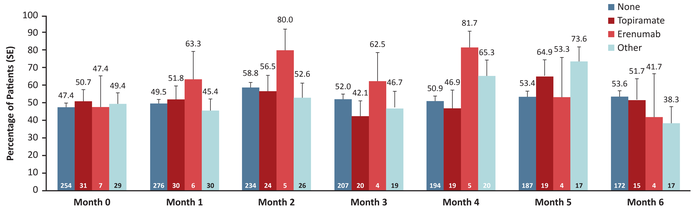
Figure 2. Pain Freedom at 2 Hours Post-INP104 Based on Concomitant Preventive Migraine Medications Used Over 24 Weeks (FSS)



Note: Data are self-reported. Patients who used >1 preventive medication were included under each applicable group; therefore, patients could be listed more than once.

FSS = full safety set; MA = migraine attack; SE = standard error.

Figure 3. MBS Freedom at 2 Hours Post-INP104 Based on Concomitant Preventive Migraine Medications Used Over 24 Weeks (FSS)



Note: Data are self-reported. Patients who used >1 preventive medication were included under each applicable group; therefore, patients could be listed more than once.

FSS = full safety set; MA = migraine attack; MBS = most bothersome symptom; SE = standard error.

Table 1. Safety Outcomes Based on Concomitant Preventive Migraine Medications Used Over 24 Weeks (FSS)

Concomitant Preventive Migraine Medications Used Over 24 Weeks				
	None (N=292)	Topiramate (N=32)	Erenumab (N=7)	Other (N=31)
TEAEs, n (%)	215 (73.6)	20 (62.5)	3 (42.9)	22 (71.0)
Serious TEAEs, n (%)	6 (2.1)	0 (0)	1 (14.3)	0 (0)
Severe TEAEs, n (%)	13 (4.5)	1 (3.1)	1 (14.3)	0 (0)

Note: Patients who used >1 preventive medication were included under each applicable group; therefore, patients could be listed more than once.

FSS = full safety set; TEAE = treatment-emergent adverse event.

Conclusion

- Despite using migraine-specific preventive therapies for migraine, patients continue to have acute attacks of migraine, highlighting an unmet need
- Exploratory efficacy of INP104 over 24 weeks of treatment demonstrated numerical improvements in self-reported pain and MBS freedom at 2 hours post-INP104 with most of the concomitant migraine preventive groups analyzed
- Safety measures were similar in patients who did or did not use concomitant migraine preventive medications over 24 weeks of treatment
- Results suggest that INP104 may be an effective and well-tolerated acute therapy for migraine in patients who are concurrently using preventive therapies

References

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