Safety and Efficacy of Concomitant Erenumab and INP104 Use From the Phase 3 STOP 301 Study in Migraine Patients

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Introduction

- Concomitant use of acute and preventive migraine therapies is common, as patients often continue taking acute therapies while on a preventive treatment aimed at reducing migraine attack (MA) frequency[1,2]
- Further, since breakthrough migraine attacks can occur while a patient is on preventive therapy, effective acute medications that can be used concomitantly without an increased risk of adverse events (AEs) are needed[2,3]
- Anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies such as erenumab are newer preventive migraine therapies that have been shown to be safe and effective in migraine patients[4]
- INP104 is drug-device product combining dihydroergotamine mesylate (DHE) with Precision Olfactory Delivery (POD®) technology to deliver DHE to the upper nasal space, and it has been approved for the acute treatment of migraine[3]
- Although the exploratory efficacy of INP104 as an acute therapy for migraine has been examined in a Phase 3 study, there remains a need to evaluate the potential impact of concurrent INP104 and erenumab use on efficacy and safety[3]

Objective

- This post hoc analysis of data from the Phase 3 STOP 301 study investigated the safety and exploratory efficacy of INP104 in migraine patients who concomitantly used erenumab and INP104 over 24 weeks

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)[3]
- The study comprised a 28-day screening period during which patients used their best usual care to acutely treat MAs, a 24-week treatment period during which patients used INP104 to acutely treat MAs, and a 2-week post-treatment follow-up period
- A subset of patients continued into a treatment extension to 52 weeks
- Daily eDiaries were completed to capture headache and migraine details, including most bothersome symptom (MBS) severity from screening through 24 weeks and, if applicable, 52 weeks

Study Patients

- Eligible patients:
  - Were adult males or females 18-65 years of age
  - Had a documented diagnosis of migraine with or without aura not qualifying as chronic migraine per the *International Classification of Headache Disorders*, version 3 beta
  - Were in general good health, with no significant medical history or clinical abnormalities at baseline
  - Experienced ≥2 MAs per month for the previous 6 months and during screening
  - Completed eDiary entries on ≥23 of the 28 days during screening

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 dose, given as one spray per nostril) 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
- Erenumab was the only approved CGRP monoclonal antibody at study initiation

Post Hoc Analysis

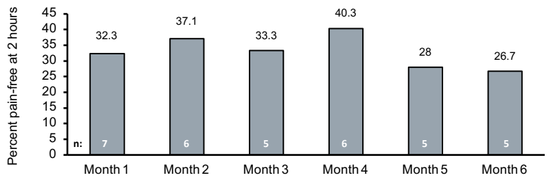
- This post hoc analysis of the STOP 301 trial evaluated the safety, tolerability, and exploratory efficacy of INP104 specifically in patients with migraine who concomitantly used erenumab as a preventive treatment during the study
- Assessments reported here include:
  - Safety: AE monitoring
  - Exploratory efficacy: Self-reported 2-hour pain freedom and MBS freedom

Results

Patient Demographics and Disposition

- 360 patients were screened and enrolled into the 24-week treatment period, with 354 self-administering ≥1 dose of INP104 over 24 weeks during STOP 301
- 8 patients used erenumab as a migraine preventive medication concomitantly and were included in the post hoc analysis

Figure 1. Self-reported Pain Freedom at 2 Hours Post-INP104 Treatment in Patients Using Erenumab Over 24 Weeks

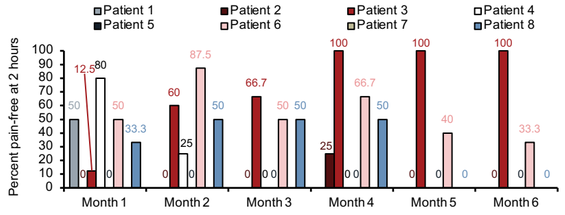


Note: Graphs include number of patients completing an eDiary entry.

Exploratory Efficacy for Concomitant Erenumab and INP104 Use

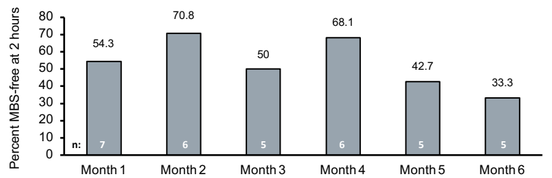
- At baseline, 2-hour pain freedom and MBS freedom were self-reported by 22.0% and 51.5% of patients on their best usual care, respectively
- At month 6, 26.7% and 33.3% of patients self-reported pain freedom and MBS freedom, respectively, at 2 hours post-INP104 use (n=5, with 3.2 total MAs and 3.0 INP104-treated MAs reported) (**Figure 1** and **Figure 3**, by patient data provided in **Figure 2** and **Figure 4**)

Figure 2. Self-reported Pain Freedom at 2 Hours Post-INP104 Treatment in Patients Using Erenumab Over 24 Weeks, by Subject



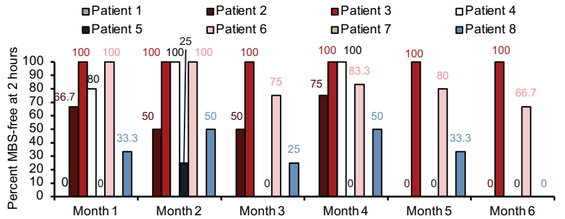
Note: Graphs include number of patients completing an eDiary entry. Entries with no data labels (non-zero) indicate no entry.

Figure 3. Self-reported MBS Freedom at 2 Hours Post-INP104 Treatment in Patients Using Erenumab Over 24 Weeks



Note: Graphs include number of patients completing an eDiary entry.
MBS=most bothersome symptom.

Figure 4. Self-reported MBS Freedom at 2 Hours Post-INP104 Treatment in Patients Using Erenumab Over 24 Weeks, by Subject



Note: Graphs include number of patients completing an eDiary entry. Entries with no data labels (non-zero) indicate no entry.
MBS=most bothersome symptom.

Safety Outcomes With Concomitant Erenumab and INP104 Use (**Table 1**)

- Over 24 weeks, 5 of the 8 patients who concomitantly used erenumab and INP104 reported no AEs
- The majority of AEs were mild or moderate in severity, with most AEs considered unrelated to treatment
  - 1 patient reported cervical muscle strain and sleep apnea (both mild and unrelated to treatment)
  - 1 patient reported 3 severe AEs, which included bronchitis and serious AEs of pulmonary embolism and visual disturbance; none of these were treatment related. The same patient also reported a moderate AE of influenza, also unrelated to treatment
  - 1 patient reported a moderate AE of allergic reaction to flea/tick spray unrelated to treatment, as well as a mild AE of abnormal olfactory test, considered possibly related to treatment

Table 1: Safety Outcomes in Migraine Patients With Concomitant Erenumab and INP104 Use

Patient	Reported Adverse Event	Severity	Relationship	Serious
1	--	--	--	--
2	Cervical muscle strain	Mild	Not related	No
	Sleep apnea	Mild	Not related	No
3	--	--	--	--
4	Bronchitis	Severe	Not related	No
	Influenza	Moderate	Not related	No
	Pulmonary embolism	Severe	Not related	Yes
	Visual disturbance	Severe	Not related	Yes
5	--	--	--	--
6	--	--	--	--
7	--	--	--	--
8	Allergic reaction to flea/tick spray	Moderate	Not related	No
	Abnormal olfactory test	Mild	Possible	No

Conclusions

- These data suggest that INP104 may be an effective and well-tolerated acute therapy for migraine patients who concomitantly use erenumab as a preventive therapy, with sustained benefits over 6 months
- Few AEs were reported with concomitant use of INP104 and erenumab, with the majority of AEs being mild or moderate and considered unrelated to treatment
- Limitations of this post hoc analysis include a small sample size

References

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2. Ferrari A, et al. *CNS Drugs*. 2018;32(6):567-578.
3. Smith TR, et al. *Headache*. 2021; 61(8):1214-1226.
4. Messina R, et al. *Cephalalgia*. 2023;43(3):333102423152169.

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Z Ahmed is a speaker for AbbVie and Biohaven Pharmaceuticals. RE Vann, C Fitzpatrick, S Ray, and SK Aurora are full-time employees of Impel Pharmaceuticals and are stockholders in Impel Pharmaceuticals. SB Shrewsbury was formerly a full-time employee of and an officer of Impel Pharmaceuticals. He remains a stockholder. This research was sponsored by Impel Pharmaceuticals. Editorial support was provided by IMPRINT Science and funded by Impel Pharmaceuticals. IMPEL and POD are registered trademarks of Impel Pharmaceuticals Inc.