Recurrence Rates for INP104 for the Acute Treatment of Migraine: Results From the Phase 3 STOP 301 Study

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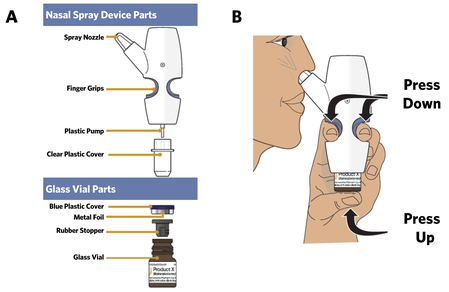
Introduction

- Recurrence of migraine headache is common with acute therapies, particularly with the triptan class[1-4]
- In some patients, recurrence of migraine may lead to an increased risk of new-onset chronic migraine and/or development of medication overuse headache due to repeat dosing of acute medications[5-7]
- Importantly, repeat dosing can impact cost[5]; and data on the efficacy and/or safety of repeat dosing are scarce
- Despite advances in the acute care of migraine, recurrence is still an important issue for physicians and their patients, and new therapies are needed to address this unmet need[1,2]
- To determine the sustained or prolonged efficacy of an acute therapy, varying study endpoints are often set by clinical trials, and can include return of migraine following pain relief or freedom; use of rescue medication; or sustained pain freedom or relief at various timepoints[1-3,8,9]
- Intravenous (IV) dihydroergotamine mesylate (DHE) has a long history as an efficacious acute therapy for migraine patients, including those who experience migraine recurrence[10,11]
- INP104 is an investigational, novel drug-device product that targets delivery of DHE to the upper nasal space using Precision Olfactory Delivery (POD®) technology (**Figure 1**)[12]
- Exploratory efficacy data for the first INP104-treated migraine from the recent Phase 3, STOP 301 study have been previously presented[13]
  - Pain freedom was self-reported in 38.0% of patients, most bothersome symptom (MBS) freedom in 52.1%, and pain relief in 66.3% at 2 hours for the first INP104-treated migraine[13]
  - Pain and MBS freedom were not very different whether patients administered INP104 within 2 hours of migraine initiation or beyond for their first treated migraine[13]

Figure 1. (A) INP104 Product and (B) Actuation of INP104



Objective

- Here we report recurrence rates; sustained pain freedom; and use of rescue medication for the first INP104-treated migraine to demonstrate single-dose efficacy associated with INP104 use from the STOP 301 study

Methods

Study Design

- STOP 301 was a Phase 3, interventional, open-label, single-group assignment study, assessing the safety, tolerability, and exploratory efficacy of INP104 over 24 and 52 weeks (NCT03557333)
- The study included a:
  - 4-week screening period, in which patients used their best usual care
  - 24-week treatment period for all patients, in which patients used INP104
  - Treatment extension to 52 weeks for a subset of the patients
  - 2-week post-treatment follow-up period
- After completing the screening period, all eligible patients were provided with up to 3 doses/week of INP104 to nasally self-administer (1.45 mg in a dose of 2 sprays) with self-recognized migraine attacks for either 24 and/or 52 weeks
- Patients completed daily eDiaries to capture headache and migraine details, headache medication usage, and MBS severity

Study Patients

- Patients were adult (18–65 years) males or females who had a documented diagnosis of migraine, with a minimum of 2 migraine attacks, with or without aura, each month not qualifying as chronic migraine during the previous 6 months per the *International Classification of Headache Disorders,* version 3 beta (ICHD-3β)
- Patients were in general good health, with no significant medical history or clinical abnormalities at baseline, which included no history of cardiovascular events

Study Outcome Measures

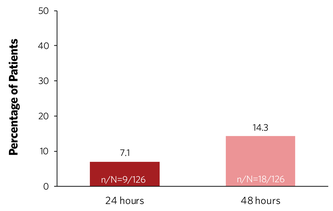
- Post hoc analyses of STOP 301 data were performed on self-reported exploratory efficacy data collected over 24 weeks
- Outcomes are reported for the 24-week full safety set (FSS; i.e., all patients who were enrolled and received ≥1 dose of INP104), which included 354 patients
- The eDiary did not capture 24- and 48-hour pain measurements if a patient was pain-free at 2 hours; therefore:
  - *Recurrence was defined as the percentage of patients who self-reported an onset of a new headache prior to 24 or 48 hours post-INP104 in patients who had self-reported pain freedom at 2 hours post-INP104*
  - *Sustained pain freedom was defined as the percentage of patients who self-reported no other headache at 24 and 48 hours post-INP104 in patients who had self-reported pain freedom at 2 hours post-INP104*
- After baseline, only non-ergot, non-triptan acute treatments were allowed as rescue medication for patients who still had headache pain, and only after 2 hours had elapsed since INP104 administration. A second dose of INP104 could also be used within 24 hours. The use of such rescue medications was recorded in the eDiary
  - *Rescue medication use was defined as the percentage of patients who self-reported using rescue medication following their first INP104-treated migraine*
  - Data included all treated migraine attacks regardless of availability of 2-hour pain and MBS results

Results

Recurrence

- Recurrence was self-reported in 7.1% (9/126) and 14.3% (18/126) of patients at 24 hours and 48 hours post-INP104, respectively, for the first treated migraine (**Figure 2**)

Figure 2. Recurrence Rates for the First INP104-Treated Migraine

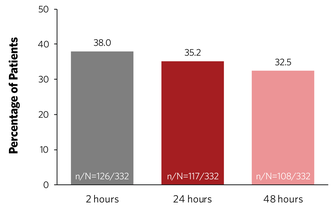


Note: Data are self-reported.

Sustained Pain Freedom

- Pain freedom was self-reported by 38% (126/332) of patients at 2 hours after treating their first migraine with INP104
- Sustained pain freedom was self-reported by 35.2% (117/332) and 32.5% (108/332) of patients at 24 and 48 hours post-INP104, respectively, for the first treated migraine (**Figure 3**)

Figure 3. Pain- and Sustained-Pain Freedom Rates for the First INP104-Treated Migraine

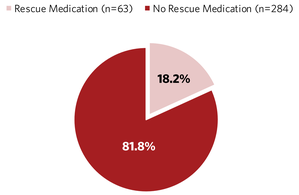


Note: Data are self-reported.

Rescue Medication

- Rescue medication use was self-reported by 18.2% (63/347) of patients for the first INP104-treated migraine (**Figure 4**)

Figure 4. Rescue Medication Use for the First INP104-Treated Migraine



Note: Data are self-reported.

Conclusion

- A post hoc analysis of exploratory efficacy data from the STOP 301 study was performed to evaluate single-dose efficacy of INP104 for the first treated migraine
  - Recurrence rates associated with INP104 were low; 7.1% and 14.3% at 24 hours and 48 hours, respectively
  - Sustained pain freedom was self-reported in 35.2% and 32.5% of patients at 24 and 48 hours post-INP104, respectively
  - 18.2% of patients self-reported using rescue medication post-INP104
- Data from this Phase 3 study demonstrate that a single dose of INP104 was associated with high rates of sustained efficacy for those who had received relief with INP104 for their first treated migraine
  - Results also align with previously presented data showing sustained efficacy of INP104 over multiple migraine attacks[13]

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