Early Prediction of Response to INP104 for the Acute Treatment of Migraine

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Introduction

- Migraine is a highly prevalent and debilitating condition, and it can result in significant patient burden[1-4]
- The main goals of acute treatment include rapid relief of pain and associated symptoms with minimal recurrence, reduced use of additional rescue medications, restoration of function, reduced need for subsequent resource use, and minimized occurrence of adverse events[5]
- However, many patients with migraine report dissatisfaction with the available acute treatments and may cycle through many therapies before achieving effective and adequate relief[6-8]
- Therefore, understanding the early prediction of response to acute therapies for migraine may help patients and health care providers optimize the acute management of migraine
- INP104 is drug-device combination product that delivers dihydroergotamine mesylate (DHE) to the upper nasal space using Precision Olfactory Delivery (POD®) technology,[9] and has been approved for the acute treatment of migraine
- Previously reported data from the Phase 3 STOP 301 study showed that INP104 was well tolerated and associated with improvements in several outcomes of exploratory efficacy for the first INP104-treated migraine attack (MA) as well as across multiple MAs over 24 and 52 weeks[9,10]

Objective

- This post hoc analysis of data from the Phase 3, STOP 301 study of INP104 for the acute treatment to migraine aimed to determine if early treatment response to INP104 could predict response over subsequent MAs

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 comprised a 28-day screening period in which patients used their best usual care, a 24-week treatment period for all patients, a treatment extension to 52 weeks for a subset of the patients, and a 2-week post-treatment follow-up period for all patients
- Following the screening period, all patients were provided with up to 3 doses per week of INP104 to nasally self-administer (1.45 mg in a dose of 2 sprays) with self-recognized MAs
- Daily eDiaries were completed to capture headache and migraine details, headache medication usage, and most bothersome symptom severity from screening through 24 weeks and, for a subset, an extension to 52 weeks

Study Patients

- Eligible patients were 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, version 3 beta
- Patients were required to have experienced ≥2 MAs per month for the previous 6 months and during the 28-day screening period, and to have completed eDiary entries on ≥23 of 28 days during screening for eligibility
- Patients were in good general health, with no significant medical history or clinically significant abnormalities at baseline

Study Analysis

- Patients with ≥4 INP104-treated MAs over 24 weeks were included in this post hoc analysis
- The percentage of patients who were overall ≥75% responders during Weeks 1-24 based on self-reported pain level after treatment for their first, first 2, and first 3 INP104-treated MAs during Weeks 1-4 was evaluated. This was neither a primary, secondary, nor exploratory outcome measure in this trial
  - 75% responder rate = at least three-quarters of a patient's MAs were self-reported as pain being mild or none 2 hours after INP104
  - Pain level = none, mild, moderate, or severe

Results

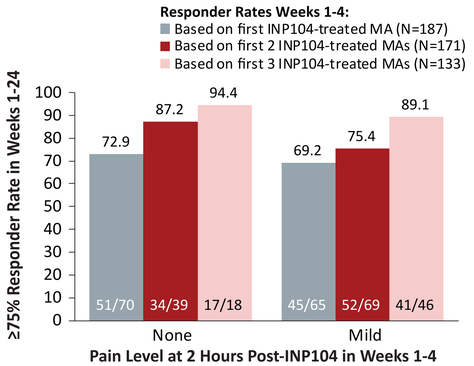
Patient Disposition

- 360 patients were screened and enrolled into 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)
- 188 patients from the 24-week FSS had ≥4 INP104-treated MAs

≥75% Responder Rates During Weeks 1-24 by Pain Level After Treatment During Weeks 1-4 Across the First 3 INP104-treated MAs

- For those patients with a pain level of NONE for their first, first 2, and first 3 INP104-treated MAs during Weeks 1-4, 72.9%, 87.2%, and 94.4%, respectively, self-reported ≥75% responder rates during Weeks 1-24 (Figure 1)
- For those patients with a pain level of MILD for their first, first 2, and first 3 INP104-treated MAs during Weeks 1-4, 69.2%, 75.4%, and 89.1%, respectively, self-reported ≥75% responder rates during Weeks 1-24 (Figure 1)

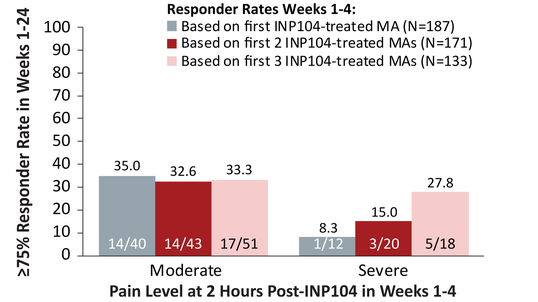
Figure 1. Responder Rates (Weeks 1-24) Based on Pain Level of None and Mild During Weeks 1-4



Note: Data are self-reported; numbers in the bars denote n/N.
FSS = full safety set; MA = migraine attack.

- For those patients with a pain level of MODERATE for their first, first 2, and first 3 INP104-treated MAs during Weeks 1-4, 35.0%, 32.6%, and 33.3%, respectively, self-reported ≥75% responder rates during Weeks 1-24 (Figure 2)
- For those patients with a pain level of SEVERE for their first, first 2, and first 3 INP104-treated MAs during Weeks 1-4, 8.3%, 15.0%, and 27.8%, respectively, self-reported ≥75% responder rates during Weeks 1-24 (Figure 2)

Figure 2. Responder Rates (Weeks 1-24) Based on Pain Level of Moderate and Severe During Weeks 1-4



Note: Data are self-reported; numbers in the bars denote n/N.
FSS = full safety set; MA = migraine attack.

Conclusions

- Patients who self-reported mild or no pain after treatment for their first 2 INP104-treated MAs are likely (>75%) to be a ≥75% responder over Weeks 1-24
- Patients who self-reported mild or no pain at 2 hours after treatment for their first 3 INP104-treated MAs are extremely likely (>89%) to be a ≥75% responder over Weeks 1-24
- Results suggest that if INP104 provides pain relief for the first 2-3 MAs, it is highly likely a patient will be an INP104 responder with long-term use, which is informative for clinical decision-making

References

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