Exploratory Efficacy of INP104 in Migraine Patients by Prior Treatment

Tanya R. Bilchik, MD, FAHS[1]; Robert Vann, PhD[2]; Sutapa Ray, PhD[2]; Stephen B. Shrewsbury, MBChB[2]; Sheena K. Aurora, MD[2]*
[1]Yale School of Medicine, New Haven, CT, USA; [2]Impel NeuroPharma, Seattle, WA, USA
*Presenting author

Introduction

- Patient dissatisfaction with current acute therapies for migraine is an ongoing unmet need, and inadequate treatment may lead to increased disability and disease progression[1-3]
- Many evidence-based acute treatments are available and are either migraine non-specific (ie, non-steroidal anti-inflammatory drugs [NSAIDs], acetaminophen) or migraine specific (ie, triptans, dihydroergotamine mesylate [DHE], gepants, and ditans)[4]
- Triptans are considered a first-line therapy to acutely treat migraine; however, their efficacy and tolerability varies between different agents and within/between patients,[1,5,6] and specifically has a narrow dosing window
- Therefore, there is a need for new and effective acute therapies to resolve migraine symptoms, especially in patients who are not adequately managed by their current therapies and/or who have failed previous oral therapy
- INP104 is a drug-device combination product approved for the acute treatment of migraine that delivers DHE to the upper nasal space using Precision Olfactory Delivery (POD®)[7]
- Previously presented self-reported exploratory efficacy data for INP104 demonstrated that:[8]
  - During Weeks 1-12, 39% of migraine attacks (MAs) treated with INP104 were pain-free and 55% were most bothersome symptom (MBS)-free at 2 hours
  - During Weeks 13-24, 35% of MAs treated with INP104 were pain-free and 51% were MBS-free at 2 hours
- Because there are numerous acute therapies available, it is important to determine if the efficacy of INP104 is predicated by prior acute treatment history

Objective

- To assess the exploratory efficacy of INP104 treatment over 24 weeks based on acute medications used before INP104 treatment

Methods

Study Design

- STOP 301 was a pivotal Phase 3, interventional, open-label, single-group assignment study that assessed the safety, tolerability, and exploratory efficacy of INP104 (NCT03557333) and was conducted from July 2018 to March 2020
- The study included a 28-day screening period, where patients were on their best usual care, a 24-week treatment period for all patients, an optional treatment extension to 52 weeks, and a 2-week post-treatment follow-up period for all patients
- All patients were provided with up to 3 doses per week of INP104 to nasally self-administer (total of 1.45 mg in 2 sprays) with self-recognized MAs after the screening period
- Daily eDiaries were completed to capture headache and migraine details, headache medication usage, and MBS severity from screening through 24 weeks and 52 weeks, if applicable

Study Patients

- Males and 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, were eligible for this study
- Eligible 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 of screening
- Patients were in general good health, with no significant medical history or clinical abnormalities at baseline, excluding the migraine, which included no history of cardiovascular risk factors or diseases

Study Analysis

- In this post hoc analysis, pain and MBS freedom at 2 hours post-INP104 were assessed based on acute medications used
- Acute medications during the screening period included acetaminophen, barbiturates, combination analgesics, other ergotamine products, NSAIDs, opioids, other medications, and triptans
  - STOP 301 was performed before the launch of gepants and ditans
  - Patients were included in a screening medication group if they used the medication during the 28-day screening period, so patients and their MAs were counted in more than 1 group

Results

Patient Demographics and Disposition

- 354 patients administered ≥1 dose of INP104 over 24 weeks and comprised the 24-week full safety set (24-week FSS)
- 262 patients completed 24 weeks of treatment
- In this post hoc analysis, most patients used acetaminophen (n=163), NSAIDs (n=139), other medications (n=121), and/or triptans (n=101), followed by combination analgesics (n=57), opioids (n=9), barbiturates (n=6), and/or other ergotamine products (n=3) during the 28-day screening period (**Figure 1**)

Continued Next Page

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Figure 1: Acute Medications Used As Best Usual Care During the Screening Period

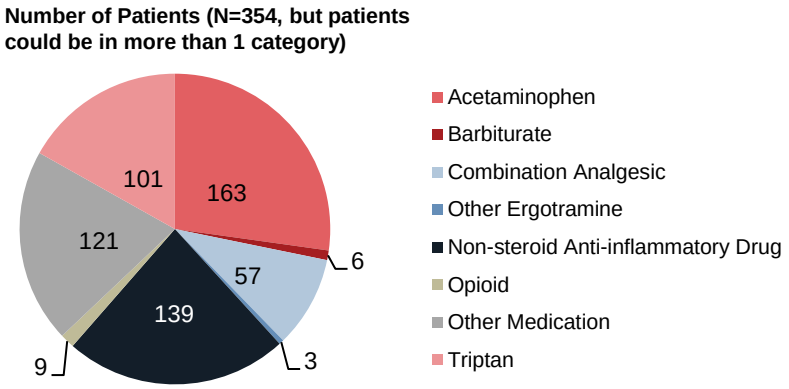
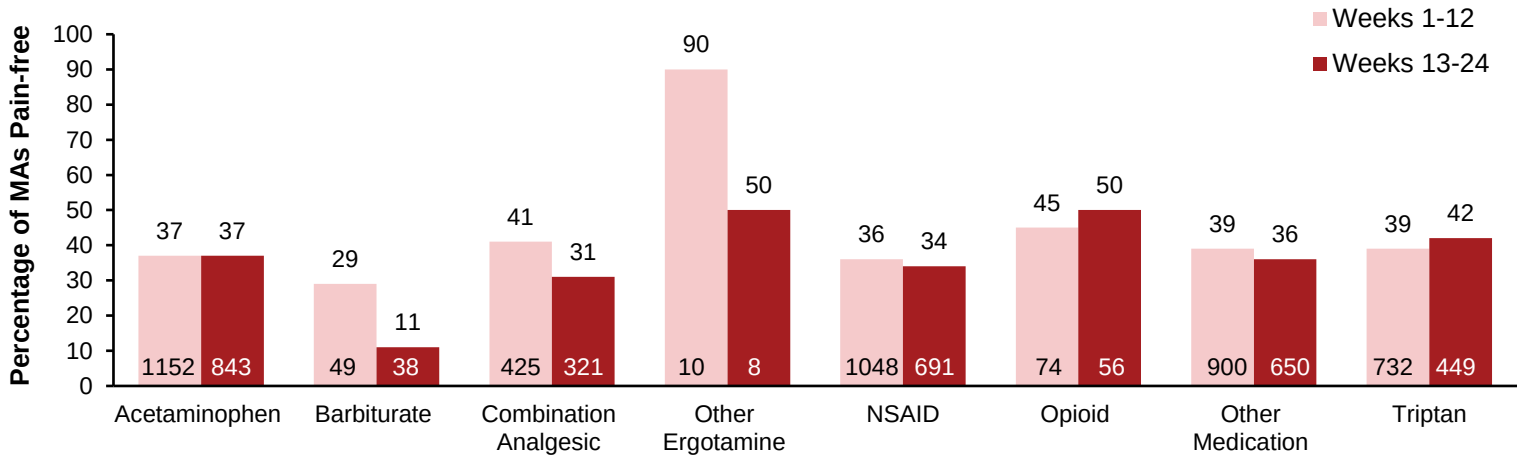


Figure 2: Pain Freedom at 2 Hours Post-INP104 by Acute Medications Used As Best Usual Care Before Treatment (N=354)



Note: Numbers at the bottom of bars represent the number of INP104-treated MAs with a non-missing 2-hour assessment. Patients were included in a medication group if they used the medication during the 28-day screening period, so patients and MAs were counted in more than 1 group. Data are self-reported.
MA = migraine attack; NSAID = non-steroidal anti-inflammatory drug.

Results

Pain Freedom at 2 Hours Post-INP104 by Acute Medication Usage Before Treatment

- During Weeks 1-12 and Weeks 13-24, MAs self-reported as pain-free at 2 hours post-INP104 were (**Figure 2**):
  - 37% and 37% among acetaminophen users
  - 29% and 11% among barbiturate users
  - 41% and 31% among combination analgesics users
  - 90% and 50% among other ergotamine users
  - 36% and 34% among NSAID users
  - 45% and 50% among opioid users
  - 39% and 36% among users of other medications
  - 39% and 42% among triptan users
- During Weeks 1-12 and Weeks 13-24, pain freedom at 2 hours was self-reported by 39% and 35%, respectively, of ALL patients[8]

MBS Freedom at 2 Hours Post-INP104 by Acute Medication Usage Before Treatment

- During Weeks 1-12 and Weeks 13-24, MAs self-reported as MBS-free 2 hours post-INP104 were (**Figure 3**):
  - 54% and 50% among acetaminophen users
  - 43% and 29% among barbiturate users
  - 57% and 44% among combination analgesics users
  - 90% and 50% among other ergotamine users
  - 53% and 53% among NSAID users
  - 55% and 66% among opioid users
  - 54% and 54% among users or other medications
  - 55% and 59% among triptan users
- During Weeks 1-12 and Weeks 13-24, MBS freedom at 2 hours was reported by 55% and 51%, respectively, of ALL patients[8]

Continued Next Page

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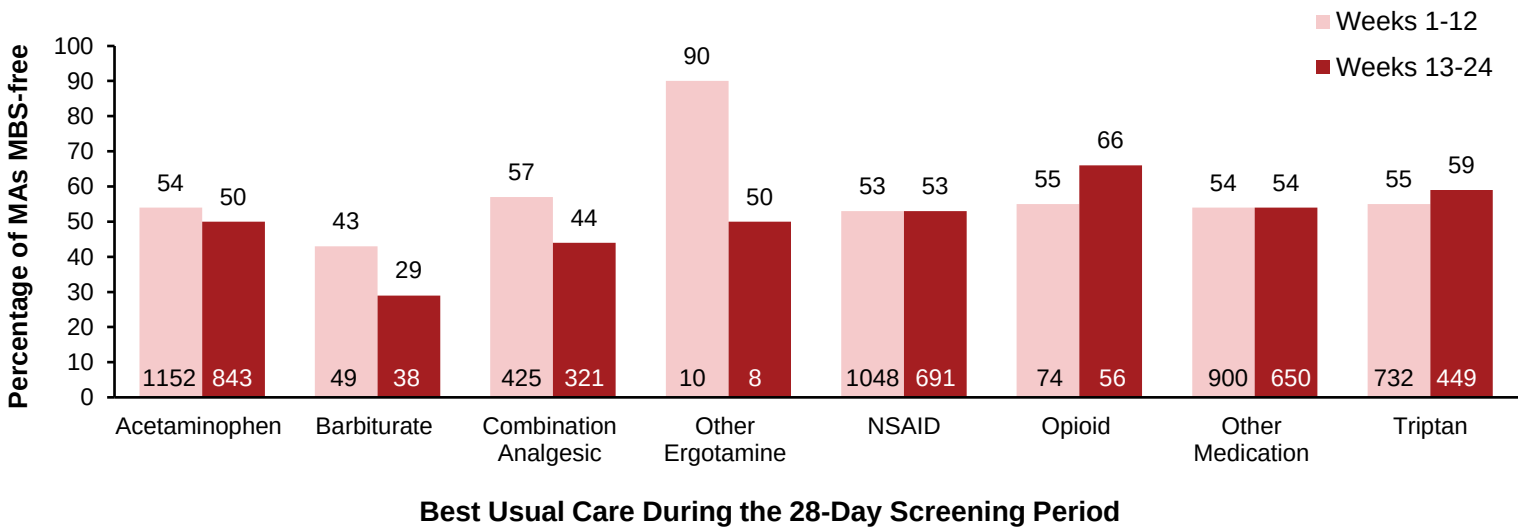
Figure 3: MBS Freedom at 2 Hours Post-INP104 By Acute Medications Used As Best Usual Care Before Treatment (N=354)



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MA = migraine attack; MBS = most bothersome symptom; NSAID = non-steroidal anti-inflammatory drug.

Conclusions

- Over 24 weeks, pain and MBS freedom at 2 hours post-INP104 were self-reported for MAs previously treated with several acute therapies before treatment initiation, which included the commonly used triptans, NSAIDs, and acetaminophen
- Pain and MBS freedom at 2 hours post-INP104 were similar at Weeks 1-12 and Weeks 12-24 for most prior acute treatment groups
- Results suggest that INP104 may be an effective acute treatment option for migraine patients regardless of their prior best usual care

References

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