Improvements in Productivity and Disability With INP104 as Assessed by the Migraine Disability Assessment Scale (MIDAS): Results From the Phase 3 STOP 301 Study

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Introduction

- Migraine is a highly prevalent disorder that causes recurrent, moderate-to-severe migraine attacks (MAs) lasting from 4-72 hours, which can come with intense pain and a variety of other symptoms[1]
- In addition to being a highly prevalent disorder, migraine remains one of the most frequent, leading causes of disability worldwide despite current treatments[2-5]
  - Migraine symptoms can be debilitating, often leading to significant physical, emotional, social, functional, and economic burden for patients[2,5-10]
  - Migraine-related disability can be assessed using reliable, validated measures, such as the Migraine Disability Assessment Scale (MIDAS)[11]
- There remains an unmet need for new and effective acute therapies that improve the migraine symptoms contributing to patient burden, particularly for those who are not adequately managed by their current therapies[12,13]
- INP104 is a drug-device combination product of dihydroergotamine (DHE) mesylate and Precision Olfactory Delivery (POD®) technology approved for the acute treatment of migraine[14,15]
- The primary results of the STOP 301 study have been previously reported, indicating that INP104 was well-tolerated and provided rapid symptom relief in patients with migraine[14]
- As part of the STOP 301 study, migraine-associated disability was assessed using the MIDAS questionnaire

Objective

- Scores for each item of the MIDAS questionnaire following long-term treatment with INP104 for the acute treatment of migraine are reported from the Phase 3 STOP 301 study

Methods

Study Design

- STOP 301 was a Phase 3, open-label, 24-week safety and exploratory efficacy study with a 28-week extension period for a subset of patients[14]
- Following a 28-day screening period, during which patients treated MAs with their standard usual care, eligible patients received INP104 (1.45 mg) to self-administer nasally with self-recognized MAs
- Patients were instructed to treat their MAs with ≤2 doses within 24 hours and ≤3 doses per 7 days

Study Population

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

MIDAS

- The MIDAS questionnaire[11] is a validated instrument measuring the headache-related disability affecting patients, with a grading system to categorize the degree of disability (Table 1)
- The questionnaire included 5 questions measuring the number of days within the past 3 months where patients felt limited in their daily activities at work, school, social, and leisure because of migraine
- Patients completed the questionnaire at baseline, Weeks 12 and 24, and if applicable, Weeks 36 and 52
- MIDAS total scores were determined based on the sum of questions 1-5 (for all nonmissing data)

MIDAS Scoring Categories

Score Range	Grade	Definition
0-5	I	Minimal or infrequent disability
6-10	II	Mild or infrequent disability
11-20	III	Moderate disability
21-40	IVa	Severe disability – subgroup a
41-270	IVb	Severe disability – subgroup b

MIDAS = Migraine Disability Assessment Scale.

Results

Patient Demographics and Disposition

- 360 patients were screened and enrolled, with 354 patients included in the 24-week full safety set (FSS; self-administered ≥1 INP104 dose over 24 weeks); 73 patients were included in the 52-week FSS
- 262 and 66 patients completed the 24- and 52-week treatment periods, respectively

Total MIDAS Scores Over 52 Weeks of INP104 Treatment

- Mean MIDAS total scores were 18.4, 17.4, 15.3, and 14.9 at Weeks 12, 24, 36, and 52, respectively, compared with 25.1 at baseline (Table 1, Figure 1)

Individual MIDAS Scores Over 52 Weeks of INP104 Treatment

- Treatment with INP104 improved several facets of migraine-related disability, as indicated by individual MIDAS question scores: (Table 1, Figure 2)
  - The mean number of school or workdays missed because of headache in the past 3 months was reduced from 2.4 at baseline to 1.8 and 1.7 at Weeks 24 and 52, respectively
  - The mean number of school or workdays with productivity reduced by half because of headache in the past 3 months was reduced from 5.6 at baseline to 3.9 and 3.3 at Weeks 24 and 52, respectively
  - The mean number of days of missed household work because of headache in the past 3 months was reduced from 7.2 at baseline to 5.3 and 4.4 at Weeks 24 and 52, respectively
  - The mean number of days when productivity in household work was reduced by half because of headache in the past 3 months was reduced from 6.5 at baseline to 3.9 and 3.1 at Weeks 24 and 52, respectively
  - The mean number of days of missed family, social, or leisure activities because of headache in the past 3 months was reduced from 3.4 at baseline to 2.6 and 2.4 at Weeks 24 and 52, respectively
- The mean number of headache days reduced from 15.9 at baseline to 10.1 and 10.5 days by Week 24 and Week 52, respectively (Table 1; Figure 3)
- The average headache pain intensity on a scale of 1 to 10 was 7.0 at baseline and 7.0 and 7.1 at Weeks 24 and 52, respectively (Table 1)

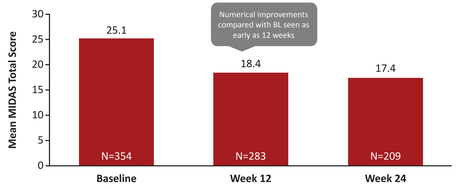
Table 1. Summary of Scores for Each Item of the MIDAS Questionnaire Following Long-term Treatment With INP104

MIDAS Questions (Mean)	Baseline (n=354)	Week 12 (n=283)	Week 24 (n=209)	Week 36* (n=69)	Week 52* (n=65)	
MIDAS total score	25.1	18.4	17.4	15.3	14.9	↓
Headache days in the past 3 months	15.9	11.3	10.1	9.1	10.5	↓
School and work days missed because of headache in the past 3 months	2.4	1.7	1.8	1.5	1.7	↓
School and work days with productivity reduced by half because of headache in the past 3 months	5.6	4.6	3.9	3.4	3.3	↓
Days of missed household work because of headache in the past 3 months	7.2	5.2	5.3	4.2	4.4	↓
Days where productivity in household work was reduced by half because of headache in the past 3 months	6.5	4.5	3.9	3.5	3.1	↓
Days of missed family, social, or leisure activities because of headache in the past 3 months	3.4	2.5	2.6	2.7	2.4	↓
Average headache pain intensity on a scale of 1 to 10	7.0	7.3	7.0	7.0	7.1	+/-

*Note: The 52-week data set included only the subset of patients who continued in the extension period, which had a sample target population of ≥50 patients per FDA guidance.[14]

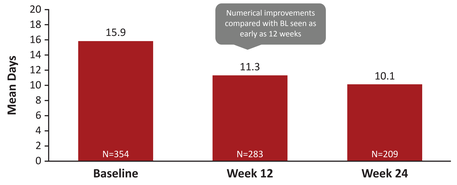
FDA = Food and Drug Administration; MIDAS = Migraine Disability Assessment Scale.

Figure 1. Mean MIDAS Total Scores Over 24 Weeks of INP104 Treatment



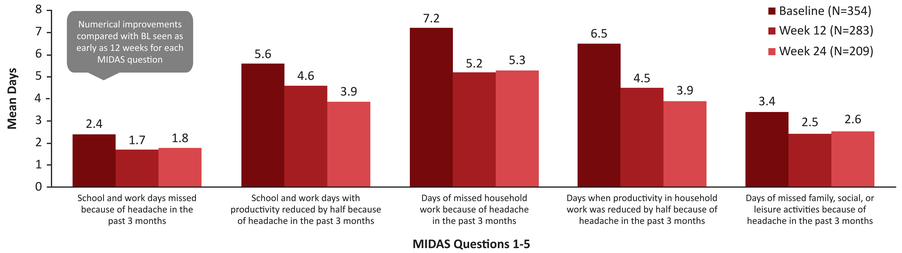
BL = baseline; MIDAS = Migraine Disability Assessment Scale.

Figure 3. Mean Number of Headache Days Over 24 Weeks of INP104 Treatment



BL = baseline; MIDAS = Migraine Disability Assessment Scale.

Figure 2. Mean Individual MIDAS Question Scores Over 24 Weeks of INP104 Treatment



BL = baseline; MIDAS = Migraine Disability Assessment Scale.

Conclusion

- Long-term INP104 use was associated with improvements in total MIDAS scores and across multiple domains of migraine-related disability, as measured by the individual items included in the MIDAS questionnaire at each postbaseline visit
  - INP104 led to a decrease in the number of headache days over 24 and 52 weeks, providing patients with a reduction in overall patient burden
  - Clinically meaningful improvements to patients' ability to participate in school, work, household activities, and leisure activities were observed over 52 weeks
- Taken together, these data suggest that the acute treatment of migraine with INP104 can reduce the burden of migraine-associated disability for patients as well as decrease the number of headache days over time

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