# Improvements in Disability and the Interictal Period With INP104: Results From the Phase 3 STOP 301 Study

Grade I = minimal or infrequent disability (scores of 0-5); Grade II =

mild or infrequent disability (scores of 6-10); Grade III = moderate

disability (scores of 11-20); Grade IVa = severe disability (scores of

past 3 months that the patient experienced limitations in daily activities

21-40); Grade IVb = severe disability (scores of 41-270)

- It includes 5 scored questions that measure the number of days in the

- The MIDAS questionnaire was completed by patients during screening,

baseline, at Weeks 12 and 24, and, if applicable, at Weeks 36 and 52

Time between MAs was determined during screening and Weeks 1-24 of

INP104 treatment using Kaplan-Meier methods to estimate the median

Monthly frequency of MAs over 24 weeks by 4-week intervals

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# Introduction

- Migraine is a highly prevalent and debilitating condition that can result in significant functional, physical, emotional, economic, and social impairments<sup>1-6</sup>
- Migraine can place substantial burden on individuals during (ie, the ictal period) and in between (ie, the interictal period) migraine attacks (MAs)<sup>3,7,8</sup>
- The ictal burden is well-recognized and easily understood, while the interictal burden is complex, can extend past the days of the MA, and can impact other aspects of daily life<sup>3,7,8</sup>
- Several epidemiologic studies have reported that it is common to experience anticipatory anxiety or depression about future MAs, which may negatively affect quality of life<sup>3,5,7,8</sup>
- An increase in the frequency of MAs may also increase disease burden, anxiety, and headache-related disability; given the unpredictable nature of migraine, some patients may overuse acute medications during headache-free periods out of anticipation or fear of a migraine developing—a morbidity known as cephalalgiaphobia—which may further impact their interictal burden<sup>3-6, 9-13</sup>
- Therefore, the need exists for new and effective acute therapies that will rapidly resolve migraine symptoms and provide a sustained benefit to potentially reduce interictal symptoms
- INP104 is an investigational drug-device combination product for the acute treatment of migraine that delivers dihydroergotamine mesylate (DHE) to the previously underutilized upper nasal space using Precision Olfactory Delivery (POD®) technology<sup>14</sup>
- Previously presented exploratory efficacy data reported that INP104 was associated with improvements for both the first treated MA or across multiple MAs over 24 and 52 weeks<sup>14-16</sup>

# Objective

 This post hoc analysis investigated headache-related disability, time between MAs, and frequency of MAs over 24 weeks, which were exploratory outcome measures relevant to interictal burden, from the Phase 3, STOP 301 study of INP104 for the acute treatment of migraine

# Methods

### Study Design

- STOP (Safety and Tolerability of POD-DHE) 301 was a Phase 3, interventional, open-label, single-group assignment study that assessed the safety, tolerability, and exploratory efficacy of INP104 (NCT03557333)
- The study included a 4-week screening period, in which patients used their best usual care, a 24-week treatment period for all patients, a treatment extension to 52 weeks offered to the first 73 patients completing 24 weeks AND meeting compliance (and other) criteria, and a 2-week post-treatment follow-up period for all patients (**Figure 1**)
- Per FDA guidance, we were required to generate data in ≥150 patients using INP104 at least twice/month for 6 months and in an optional 50 patients (using INP104 twice/month for 12 months) for the 28-week extension
- After the screening period, all 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 MAs
- Daily eDiaries were completed to capture headache and migraine details, headache medication usage, and MBS severity from screening through 24 weeks and, if applicable, 52 weeks

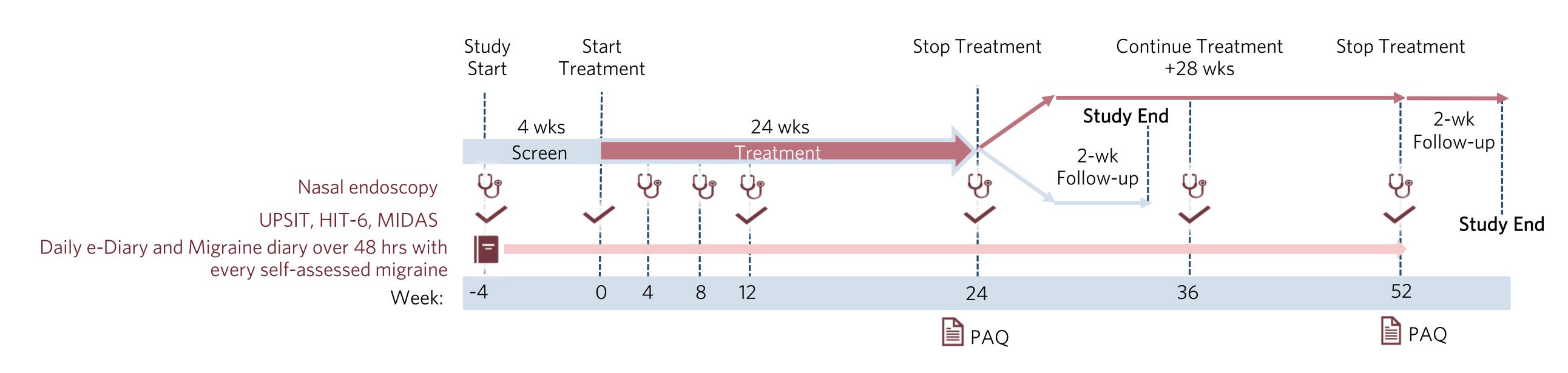
### Study Patients

- Eligible patients were adult males or females aged 18 to 65 years with a documented diagnosis of migraine with or without aura not qualifying as chronic migraine per 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 screening, and to have completed eDiary entries on ≥23 of the 28 days during screening for eligibility
- 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 of Exploratory Efficacy

- Migraine Disability Assessment (MIDAS)
- The MIDAS questionnaire is a validated, highly reliable instrument that measures headache-related disability with a grading system that categorizes disability as follows:

# Figure 1. Study Design



HIT-6 = Headache Impact Test-6; MIDAS = Migraine Disability Assessment; PAQ = patient acceptability questionnaire; UPSIT = University of Pennsylvania Smell Identification Test; wk = week.

### **Patient Demographics and Disposition**

interval length

Results

resulting from migraine

- 360 patients were screened and enrolled in the 24-week treatment period;
   354 comprised the 24-week full safety set (FSS; self-administered ≥1
   INP104 dose over 24 weeks) and 73 comprised the 52-week FSS
- 262 and 66 patients completed the 24- and 52-week treatment periods, respectively
- For the 24-week FSS, the mean MIDAS total score for patients was 25.1 at baseline
- Most frequent scores were Grade III (28.8%) and Grade IVa (27.7%), indicating moderate to severe disability at study initiation
- For the 52-week FSS, the mean MIDAS total score for patients was 24.6 at baseline
- Most frequent scores were Grade III (31.5%) and Grade IVa (31.5%), indicating moderate to severe disability at study initiation (**Tables 1 and 2**)

#### MIDAS Scores Over 24 and 52 Weeks

- For the 24-week FSS, the mean MIDAS total score at Weeks 12 and 24 was 18.4 and 17.4, with a mean change from baseline of -5.5 and -7.4, respectively
- Most patients had improved MIDAS scores of Grade III or better at Weeks 12 and 24
- At Weeks 12, 24, 36, and 52, the mean 52-week FSS MIDAS total score was 18.8, 20.3, 15.3, and 14.9, with a mean change from baseline of -5.8, -5.1, -7.8, and -8.9, respectively
- Most patients had MIDAS scores of Grade III or better at Weeks 12, 24, 36, and 52 (**Tables 1 and 2**)

#### Frequency of MAs Over 24 Weeks

- At baseline, the mean frequency of monthly MAs was 4.7
- The mean frequency of monthly MAs by 4-week intervals was 3.7, 3.0, 2.6, 2.5, 2.4, and 2.4 at Weeks 1-4, 5-8, 9-12, 13-16, 17-20, and 21-24, respectively (**Figure 2 and Table 3**)

#### Time Between MAs Over 24 Weeks

• During Weeks 1-24, the median time between MAs was 6 days, compared with 4 days at baseline (**Figure 3**)

Table 1. MIDAS Scores Over 24 and 52 Weeks

Period		24-Week FSS (N=354)	52-week FSS (N=73)
Baseline	n Mean (SD)	354 25.1 (22.3)	73 24.6 (20.2)
Week 12	n Mean (SD) Change from baseline, mean (SD)	283 18.4 (17.1) -5.5 (18.7)	73 18.8 (15.9) -5.8 (18.1)
Week 24	n Mean (SD) Change from baseline, mean (SD)	209 17.4 (16.5) -7.4 (17.6)	57 20.3 (16.2) -5.1 (18.6)
Week 36	n Mean (SD) Change from baseline, mean (SD)		69 15.3 (11.2) -7.8 (15.1)
Week 52	n Mean (SD) Change from baseline, mean (SD)		65 14.9 (12.0) -8.9 (15.8)

FSS = full safety set; MIDAS= Migraine Disability Assessment; SD = standard deviation

### Table 2. Category of MIDAS Scores Over 24 and 52 Weeks

Period		24-Week FSS (N=354)	52-Week FSS (N=73)
Baseline, n (%)	n I II IVa IVb	354 38 (10.7) 51 (14.4) 104 (28.8) 98 (27.7) 65 (18.4)	73 4 (5.5) 10 (13.7) 23 (31.5) 23 (31.5) 13 (17.8)
Week 12, n (%)	n I II IVa IVb	283 45 (15.9) 62 (21.9) 88 (31.1) 65 (23.0) 23 (8.1)	73 8 (11.0) 17 (23.3) 24 (32.9) 19 (26.0) 5 (6.8)
Week 24, n (%)	n I II IVa IVb	209 39 (18.7) 43 (20.6) 72 (34.4) 38 (18.2) 17 (8.1)	57 7 (12.3) 10 (17.5) 22 (38.6) 12 (21.1) 6 (10.5)
Week 36, n (%)	n I II IVa IVb		69 9 (13.0) 16 (23.2) 28 (40.6) 13 (18.8) 3 (4.3)
Week 52, n (%)	n I II IVa IVb	Disability Assessment; SD = sta	65 8 (12.3) 20 (30.8) 23 (35.4) 12 (18.5) 2 (3.1)

FSS = full safety set; MIDAS= Migraine Disability Assessment; SD = standard deviation

Figure 2. INP104 Reduced Migraine Frequency Over 3 Months and Reduction Was Sustained at 6 Months (24-Week FSS, N=354)

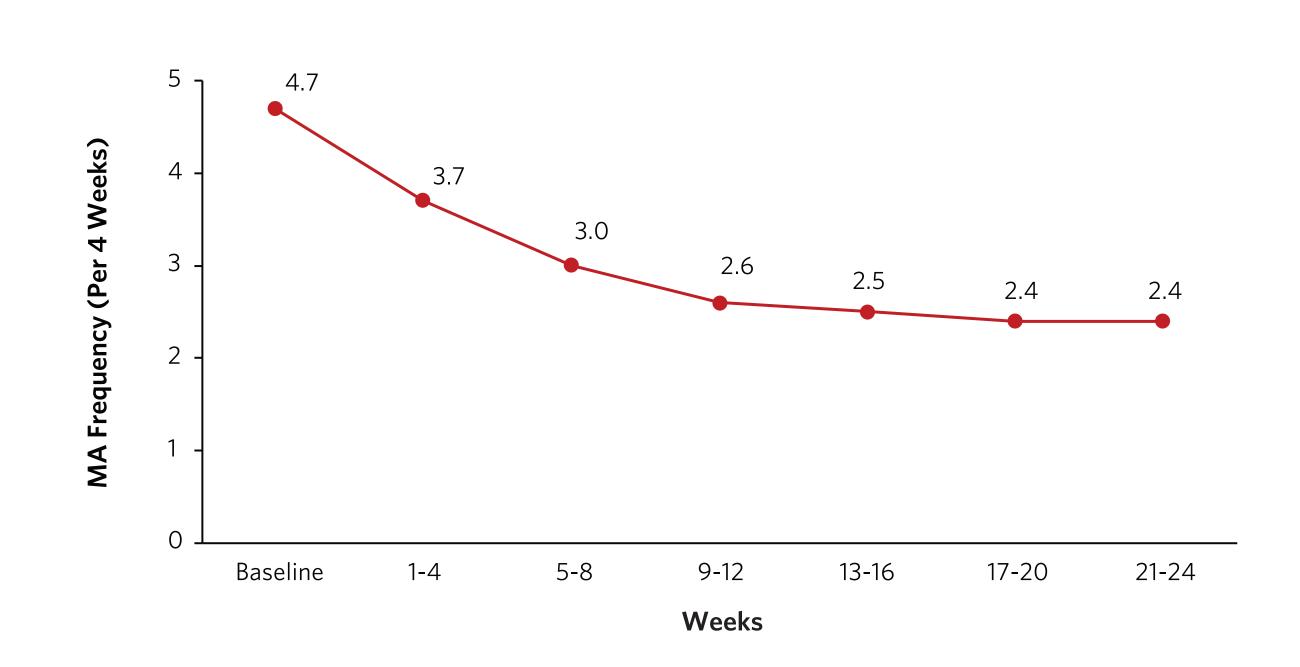


Table 3. Frequency of Monthly MAs Over 24 Weeks

FSS = full safety set; MA = migraine attack.

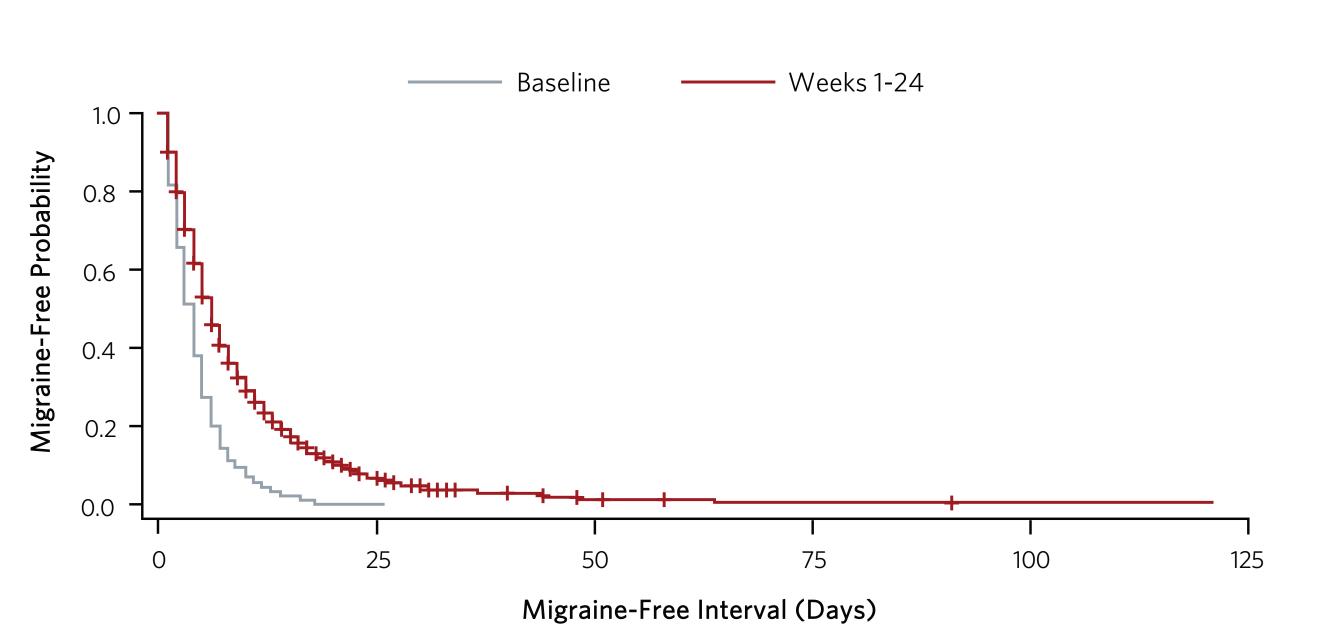
## (24-Week FSS, N=354)

Period		24-Week FSS (N=354)	Week 24 Completers (n=262)
Baseline	n	354	262
	Mean (SD)	4.7 (2.30)	4.6 (2.32)
Weeks 1-4	n	347	262
	Mean (SD)	3.7 (2.05)	3.8 (2.10)
Weeks 5-8	n	325	262
	Mean (SD)	3.0 (2.08)	3.2 (2.04)
Weeks 9-12	n	297	262
	Mean (SD)	2.6 (1.97)	2.7 (1.95)
Weeks 13-16	n	289	262
	Mean (SD)	2.5 (1.89)	2.6 (1.87)
Weeks 17-20	n	276	262
	Mean (SD)	2.4 (1.89)	2.5 (1.88)
Weeks 21-24	n	268	262
	Mean (SD)	2.4 (1.85)	2.4 (1.84)

Note: Patients are only summarized within the months that they have completed. FSS = full safety set; MA = migraine attack; SD = standard deviation.

Figure 3. Time Between MAs Over 24 Weeks (24-Week FSS, N=354)

#### INP104 Treatment Resulted in Increased Interval (Median of 2 Days) Between MAs Over 24 Weeks



# Conclusion

- Use of INP104 was associated with improvements in migraine-related disability as assessed by the MIDAS questionnaire
- The mean MIDAS total score in both 24-week and 52-week FSS decreased at each post-baseline visit, with mean total scores suggestive of moderate residual disability
- Over 24 weeks, the frequency of monthly MAs decreased and the time between MAs was longer with INP104 use compared with baseline when patients used their best usual care
- A limitation of this study was the open-label design, which does not include a placebo control group for comparison; however, comparing INP104 with a patient's best usual care at baseline is reflective of a real-world setting
- Data reported here suggest that repeated acute use of INP104 may have positive effects on interictal burden by reducing migraine-associated disability, prolonging the headache-free period, and decreasing the number of MAs over time

### References

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