Assessing the Long-Term Effectiveness of Qtrypta® using Migraine-ACT: Correlation with e-Diary

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Introduction and Objectives

The Migraine-ACT Questionnaire

- The Migraine-ACT questionnaire was developed and validated as a rapid means of assessing the effectiveness of a patient's acute treatment of migraine therapy.[1,2]
- Migraine-ACT assesses four domains:
  - Global assessment of relief (2-hour pain freedom)
  - Headache impact
  - Consistency of response
  - Emotional response
- The Migraine-ACT questionnaire is shown in **Table 1.** The highest achievable score is 4, corresponding to "yes" answers to all 4 questions.
- One or more "no" answers may indicate the need to change treatment. An increasing number of "no" answers indicates increasing treatment needs.

Table 1. The Migraine-ACT Questionnaire

Please answer all four questions below as "yes" or "no", by placing a tick in the relevant box.

Question	Yes	No
When you take your treatment: Does your migraine medication work consistently, in the majority of your attacks?		
When you take your treatment: Does the headache pain disappear within 2 hours?		
When you take your treatment: Are you able to function normally within 2 hours?		
When you take your treatment: Are you comfortable enough with your medication to be able to plan your daily activities?		
Migraine-ACT Score (Total number of "yes" answers)		

About ADAM zolmitriptan (Qtrypta®, M207)

- Adhesive Dermally Applied Microarray (ADAM) is an investigational system that provides intracutaneous drug administration.
- In a pivotal phase 2b/3 randomized, double-blind, placebo-controlled study (ZOTRIP), ADAM zolmitriptan 3.8 mg met both co-primary endpoints (which were selected based on 2018 FDA Guidance Document for Clinical Trials Evaluating Drugs for Acute Migraine Treatment[3]) of pain freedom and freedom from patients' usual other most bothersome symptom (MBS) two hours post-dose.[4,5]

Methods

- This was an open-label, 12-month, long-term safety study of ADAM zolmitriptan (M207) for the acute treatment of migraine (NCT03282227).
- Adults were eligible to participate if:
  - They had a ≥1 year history of episodic migraine diagnosed according to IHS ICHD-3 beta criteria
  - In the last 6 months they experienced 2 to 8 migraines per month with no more than 15 headache days per month
- There was a screening period followed by a run-in period (14 to 21 days) to determine eligibility for treatment with study medication based on daily eDiary data collection.
- Participants self-administered ADAM zolmitriptan 3.8 mg to treat a qualifying migraine. Participants could treat multiple migraine attacks.
- The primary outcome measure was long-term safety as measured by incidence of adverse events over a 12 month period.
- Secondary outcome measures included pain freedom, freedom from most bothersome other headache-related symptom, pain relief, nausea freedom, photophobia freedom, and phonophobia freedom.
- Participants used a daily eDiary to record migraine symptoms and application site observations pre-dose, and 30 minutes, 2 hours, 12 hours, 24 hours, and 48 hours post-dose
- In addition to safety assessments, participants completed Migraine-ACT at each in-clinic visit (Weeks 4, 8, 12, 24, 36, and 48).
- Each participant's 2-hour pain scores (0=none, 1 = mild, 2 = moderate, 3 = severe) from the eDiary were averaged over the 28 days prior to a scheduled clinic visit.
- We compared the average 2-hour pain scores with the Migraine ACT scores at each visit.
- In-clinic assessed ACT data, and pain data in the 28 days prior to the visit when ACT was completed, must both have been present to be included in this analysis. ACT data were not included for those discontinuing prior to 24 weeks. For those discontinuing between 24 and 48 weeks, ACT data were mapped to the closest scheduled visit.

Results

- A total of 342 participants received study drug, 335 treated at least 1 migraine, 257 completed 6 months of the study and 128 completed 1 year. Data from 294 participants with both ACT and pain data were included in this analyses.
- Fifteen subjects withdrew for adverse events, one of whom experienced a serious, severe event that was unrelated to study drug.
- The most common adverse events were mild redness and swelling at the application site.
- Numerical Migraine-ACT results for each clinic visit are shown in **Figure 1;** the proportion of participants who scored ≥3 on the ACT survey are shown in **Table 2**.
- At their 48 week visit, 84-96% of participants answered yes for each of the Migraine-Act questions (**Table 3**).
- The relationship between e-diary 2-hour pain scores and Migraine-ACT scores is shown in **Figure 2**.

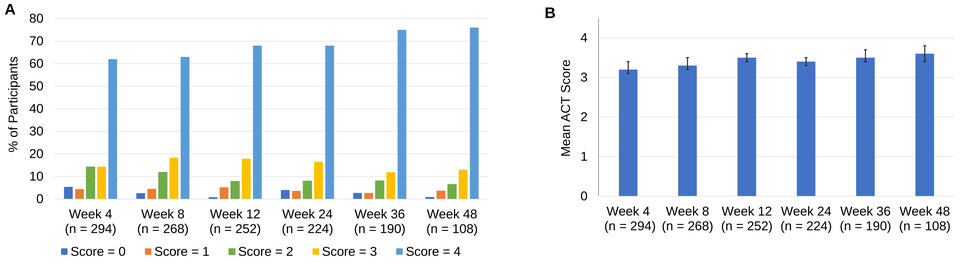

Figure 1. Migraine-ACT Scores at Each Clinic Visit
A) Number of "yes" answers on the ACT questionnaire
B) Mean ACT scores. Error bars: 95% confidence interval.

Table 2. Proportion of Participants who Scored ≥3 on the Migraine-ACT Questionnaire (n = 294)

	n	Scored ≥3 n (%)
Week 4	294	223 (76)
Week 8	268	217 (81)
Week 12	252	217 (86)
Week 24	224	189 (85)
Week 36	185	160 (87)
Week 48	108	96 (89)

Table 3. Proportion of Participants who Answered "Yes" for each Question of Migraine-ACT at 48 Weeks (n = 108)

Question	n (%)
Does your migraine medication work consistently, in the majority of your attacks?	104 (96)
Does the headache pain disappear within 2 hours?	92 (85)
Are you able to function normally within 2 hours?	91 (84)
Are you comfortable enough with your medication to be able to plan your daily activities?	101 (94)

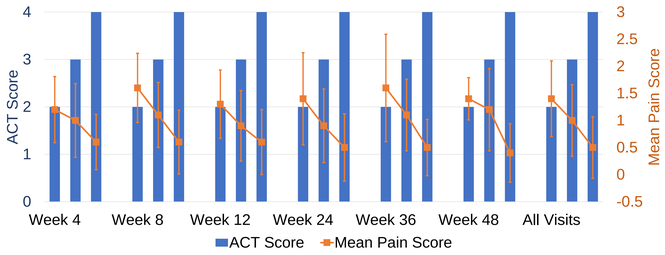

Figure 2. Relationship between E-Diary 2-hour Pain Scores and Migraine-ACT Scores
Mean e-diary pain scores at 2 hours post-dose for participants who answered "yes" to 2, 3, or 4 questions on the Migraine-ACT questionnaire.
Error bars: Standard deviation for mean pain score.

Discussion and Conclusions

- In this study population:
- Migraine-ACT Scores averaged greater than 3 throughout the trial, indicating excellent response to ADAM zolmitriptan 3.8 mg.
- A high percentage of participants scored either a 3 or 4 on the Migraine-ACT, suggesting optimal acute treatment and no need to change that treatment.
- Higher Migraine-ACT scores were associated with lower mean e-Diary pain scores, and this relationship was consistent throughout the trial.

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