# OnabotulinumtoxinA Improves Quality of Life in Chronic Migraine: the PREDICT Study

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**Supplemental Material**

**Supplemental Table 1.** Inclusion and Exclusion Criteria for the PREDICT Study

**Supplemental Table 2.** Outcome Measures and Data Collection Schedule for the PREDICT Study

**Supplemental Table 3.** Reasons for Discontinuation from the Study

**Supplemental Table 1.** Inclusion and Exclusion Criteria for the PREDICT Study

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| Inclusion criteria:1. Participant with a diagnosis of CM, as defined by the ICHD-3 (beta version34), who is eligible to receive onabotulinumtoxinA for injection treatment as per the approved Product Monograph33 and deemed medically necessary by the participating physician independently from this study, and is naïve to botulinum toxin treatment for CM.
2. Male or female that is ≥18 years of age on the day the informed consent form is obtained.
3. Participant using medication(s) with a known headache preventive effect may be included in the study if, in the opinion of the investigator, the dose has been stable, and the medication(s) has been well-tolerated for at least 12 weeks prior to baseline (visit 1).
4. Participant (and/or participant’s authorized legal representative) should understand the nature of the study and provide written informed consent prior to or at baseline (visit 1).
5. Participant is able to follow all study requirements/procedures and complete required visits.
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| Exclusion criteria:1. Participant has been diagnosed with the following complicated migraine disorders: hemiplegic migraine, basilar migraine, ophthalmoplegic migraine, or migrainous infarction.
2. Participant with a headache diagnosis of: chronic tension-type headache, hypnic headache, hemicrania continua, or new daily persistent headache.
3. Participant who is currently taking, or planning on taking, opioid-containing products for acute headache treatment or a pain condition on more than 8 days during the 28-day run-in-period (baseline period) and throughout the study, or is currently taking, or planning on taking, barbiturates (or combination) for acute headache or a pain condition.
4. Participant is concurrently participating in a clinical trial.
5. Participant with any contraindication to use onabotulinumtoxinA according to the approved Product Monograph33.
6. Participant planning elective surgery during the study period.
7. Female who is pregnant, nursing, or planning a pregnancy during the study period.
8. History of poor cooperation, non-compliance with medical treatment, or unreliability.
9. Any condition or situation which, in the physician’s opinion, places the participant at significant risk, could confound the study data, or may interfere significantly with participation in the study, including, but not limited to, unstable medical conditions.
10. Treatment with any other botulinum toxin product for any condition within 3 months of baseline (visit 1).
11. Participant who in the opinion of the investigator, has current uncontrolled active major psychiatric or depressive disorder(s).
12. Any medical condition that may put the participant at increased risk with exposure to onabotulinumtoxinA, including diagnosed myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis, or any other significant disease that might interfere with neuromuscular function.
13. Known allergy or sensitivity to the study medication or its components.
14. Inflammation or infection at anticipated injection sites at the time of onabotulinumtoxinA injection.
15. Participant with a BDI-II score of >2443.
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BDI-II, Beck Depression Inventory Score; CM, chronic migraine; ICHD-3, International Classification of Headache Disorders, 3rd edition (beta version).

**Supplemental Table 2. Outcome Measures and Data Collection Schedule for the PREDICT Study**

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| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Baseline**‡(Visit 1)  | **Tx1**(Visit 2) | **Tx2**(Visit 3) | **Tx3**(Visit 4) | **Tx4**(Visit 5) | **Tx7**(Visit 6) | **Final Visit**(Visit 7) |
| Demographics | X |  |  |  |  |  |  |
| Medical history | X |  |  |  |  |  |  |
| CM diagnosis (ICHD-3 beta)† | X |  |  |  |  |  |  |
| OnabotulinumtoxinA utilization |  | X | X | X | X | X |  |
| Headache diary† | X | X | X | X | X | X | X |
| Health-related quality of life (MSQ)† | X |  |  |  | X§ |  | X |
| Physician satisfaction (CGIC) † |  |  |  |  | X§ |  | X |
| Participant satisfaction (PGAT) † |  |  | X§ | X§ | X§ | X§ | X |
| Treatment emergent adverse events† | X | X | X | X | X | X | X |
| Withdrawal questionnaire |  |  |  |  |  |  | X¶ |

CGIC, Clinician’s Global Impression of Change; CM, chronic migraine; ICHD-3, International Classification of Headache Disorders, 3rd addition, beta version; MSQ, Migraine-Specific Quality of Life Questionnaire, version 2.1; PGAT, Patient Global Assessment of Treatment; TEAE, treatment-emergent adverse event; Tx, treatment session.

†The *International Classification of Headache Disorders, 3rd edition* (ICHD-3, beta version 1) defines chronic migraine (CM) as headache occurring ≥15 days/month for >3 months, with at least 8 days/month fulfilling the criteria for migraine with or without aura. The *headache diary* aimed to quantify headache frequency, severity, duration (ie, whether a headache lasted >4 hours), and the use of abortive medications in between study visits and was to be completed daily by the study participants. The *Migraine-Specific Quality of Life* *Questionnaire, version 2.1* (MSQ 34) is a 14-item patient-reported questionnaire designed to measure health-related quality of life impairments attributed to migraine in the past 4 weeks across 3 domains (ie, role function restrictive, role function preventive, and emotional function) using a 6-point Likert-type scale, where 1 represents ‘none of the time’ and 6 represents ‘all of the time’. Raw MSQ scores were summed and rescaled to a 0-100 scale, with higher scores indicative of better quality of life. Changes in MSQ scores were compared against published minimal important differences for MSQ v2.137, defined as ‘the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management’50. The *Clinician’s Global Impression of Change* (CGIC) questionnaire is a physician-reported outcome that was utilized to determine the change in a participant’s health using a 7-point scale, where 1 represents ‘very much improved’ and 7 represents ‘very much worse’. Lower CGIC scores are indicative of a greater impression of change. The *Patient Global Assessment of Treatment* (PGAT) questionnaire is a participant-reported outcome designed to assess satisfaction with the impact of treatment on headache symptoms and activities of daily living using a 5-point Likert-type scale, where 1 represents ‘very dissatisfied’ and 5 represents ‘very satisfied’. Higher PGAT scores are indicative of greater satisfaction. *Treatment emergent adverse events* (TEAEs), defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment, were determined at each treatment visit, whereby the investigator (or designee) questioned the participant regarding adverse experiences that may have occurred since signing the consent form. All TEAEs (including severity, action taken, and relationship to study medication, as determined by the investigator or medical monitor) were recorded in the case report form. TEAEs were tabulated by system organ class and preferred term utilizing the Medical Dictionary for Regulatory Activities (MedDRA™ version 21.0). To assess possible distant spread of toxin (PDSOT), 40 MedDRA preferred terms that may be associated with botulinum toxin effects were identified. TEAEs associated with PDSOT were adjudicated by a panel of Allergan physicians.

‡Screening at baseline (visit 1) occurred 0-4 weeks prior to the first onabotulinumtoxinA treatment (visit 2). Baseline screening and visit 2 could be combined into one visit provided the participant had completed a headache diary for at least 28 days prior to the combined visit and participants received onabotulinumtoxinA treatment prior to completion of the study assessments.

§Data were collected prior to administering onabotulinumtoxinA at the visit.

¶The withdrawal questionnaire was only completed by individuals who discontinued the study.

**Supplemental Table 3.** Reasons for Discontinuation from the Study†

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| Total (n=184) | n (% of total) |
| Treatment did not work | 23 (12.5) |
| Cost of injection treatment |  5 ( 2.7) |
| Accessibility to clinic (distance from home) |  4 ( 2.2) |
| Moving or relocating away from clinic |  4 ( 2.2) |
| Changing to another treatment |  3 ( 1.6) |
| No longer have symptoms |  2 ( 1.1) |
| Cosmetic impairment |  1 ( 0.5) |
| Pain at injection sites |  1 ( 0.5) |
| Pregnancy/nursing |  1 ( 0.5) |
| Time consuming (need to return too frequently for re-treatment) |  1 ( 0.5) |
| Other reason‡ | 21 (11.4) |

n, number of participants.

†More than one reason for discontinuation could have been selected; categories were not mutually exclusive. Reason(s) for discontinuation were captured by the study site in the withdrawal questionnaire. Of the participants who discontinued the study (n=74), 61 participants completed the withdrawal questionnaire. Percentages are based on the number of participants in the analysis population (n=184; ie, those participants that received at least one treatment with onabotulinumtoxinA during the study).

‡The most common reason listed for ‘Other’ was lost to follow-up (n=8).