EDITORIAL

OnabotulinumtoxinA Improves Quality of Life in Chronic Migraine: The PREDICT Study

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The PREDICT study was designed to assess the real-world and long-term health-related quality of life in adults with chronic migraine receiving onabotulinumtoxinA in Canada.[1] There have been several studies published on the long-term efficacy and safety of onabotulinumtoxinA after it was approved for clinical use in chronic migraine patients based on the result from the PREEMPT study.[2] One study was the COMPEL study in which it established significance with headache days reduction and improvement in disability based on the Headache Impact Test (HIT-6) and Migraine Disability Assessment Questionnaire (MIDAS) over a span of 108 weeks.[3] The REPOSE study demonstrated long-term (24 months) real-world data on effectiveness of onabotulinumtoxinA with sustained reduction in headache days frequency and significant improvement in quality-of-life measures.[4] However, these studies enrolled non-Canadian populations.

The PREDICT study is a multicenter, prospective study with data collected across headache/pain centers in Canada. Appropriate screening was performed with a 4-week baseline period. Treatments were based on the PREEMPT paradigm,[2] 155 units of onabotulinumtoxinA administered at 31 fixed sites with optional additional injections for a total dose of 195 units (follow the pain pattern). The PREDICT study was an observational study; hence, no formal sample size calculations were formed, or no formal hypothesis was tested.

The PREDICT study was able to demonstrate improvement in quality of life through a self-administered questionnaire known as Migraine-Specific Quality of Life Questionnaire (MSQ) which was a clinical outcome used in the REPOSE study.[4] The MSQ has its strength in exploring different domains, including role function restrictive, preventive, and emotional function. The PREDICT study further supports previous chronic migraine onabotulinumtoxinA studies, including reduction in headache days per month, reduction in moderate or severe headache days per month, and no new reported treatment-related adverse events.

As for the baseline demographics, it is comparable to other onabotulinumtoxinA studies for chronic migraine, including age, gender, age at diagnosis, and number of headache days per month,[3–5] with the exception of the following: There is a significant higher Caucasian representation (close to 95% vs. around 80% in other studies),[3–5] and 60% of the patients reported a positive family history of chronic migraine, which may be a reporting bias since the prevalence of chronic migraine in the general population is less than 2%.[6]

Other limitations to consider: the PREEMPT injection paradigm was not monitored and physicians could deviate from these recommendations. There was no placebo or comparator arm. There could be a significant recall bias and high drop-off rates since the PREDICT study was a long-term observational study. The participants remaining in the study at the later time points were likely to report a biased positive opinion on the treatment response. All three MSQ domains achieved more than the minimal important differences. However, not all outcomes were collected at each treatment visit. For example: MSQ and physician satisfaction were only collected at treatment 4 and final visit. Also, the impact on MSQ in patients who discontinued treatment was unavailable; hence, a conclusion could not be drawn toward response before treatment 4, between treatment 4 and final visit, and patients who discontinued midway.

The discontinuation rates for the pooled PREEMPT studies were 10%–12% for the 24-week double-blind phase and 25%–29% for the 56-week open-label phase.[2] In the PREDICT study, the total rate was 38% likely a result of the real-world study design and the length of the observation.

The majority of the participants were overusing acute medications (mean: 16.8 days per month). These participants likely had a coexisting diagnosis of medication overuse headache based on the International Classification of Headache Disorders 3rd edition.[7] The reduction of acute medication use was not reported. If this parameter was significant, it could have an impact on the MSQ outcome as well.

Patients who were taking oral preventatives were included in the study; however, the PREDICT study did not collect information on the potential changes or adjustment of oral preventatives within the 2-year period. An adjustment to an oral preventative may impact the clinical outcome. For example, an anti-depressant such as amitriptyline or nortriptyline may improve quality of life through better sleep and/or mood.

This study was sponsored by Allergan (now AbbVie) which is the manufacturer of onabotulinumtoxinA (Botox), and many authors of this study reported financial and/or nonfinancial conflicts of interest with Allergan (now AbbVie).

Overall, the PREDICT study was a well-designed study in consideration of the limitations stated and being an open-label observational long-term follow-up study. In the real-world setting, it is not uncommon that onabotulinumtoxinA is used to manage patients with chronic daily headaches, such as chronic migraine patients with everyday headaches. The outcome may not be a reduction in headache or migraine days, but possibly headache intensity and/or quality of life and disability. The

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impact on quality of life of chronic migraine in the Canadian population is limited and PREDICT results are relevant and applicable. As stated in the PREDICT study, future analysis from their data collection will explore the impact of onabotulinumtoxinA treatment for chronic migraine on health resource utilization and medication overuse in which these measures may also be appropriate for the real-world setting.

Conflict of Interest

Dr. Tommy Lik Hang Chan has no conflicts of interest (financial or nonfinancial) to disclose relevant to this study. Dr. Tommy Lik Hang Chan is on the advisory board for AbbVie Inc., Eli Lilly, Novartis, and Aralez Pharmaceuticals Canada. Dr. Tommy Lik Hang Chan has received grant support for education (no personal compensation) from Teva Pharmaceutical industries. Dr. Tommy Lik Hang Chan has received honoraria from Aralez Pharmaceuticals Canada, AbbVie, Lundbeck, and Novartis.

Availability of Material

The material analyzed during the current case is available from the author on a reasonable request.

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