

BOTULINUM TOXIN IS A NECESSARY, SAFE AND EFFECTIVE TREATMENT OF CHRONIC MIGRAINE – NO

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Treatment options for chronic migraine are sparse. Thus, clinical trials investigating new treatment options are therefore endorsed in order to provide evidence-based data. Two double-blind, randomized, placebo-controlled clinical trials for the treatment of chronic migraine with onabotulinumtoxinA, the Phase III REArch Evaluating Migraine Prophylaxis Therapy (PREEMPT) 1 and 2 as well as the pooled data from the two trials were recently published. At a first glance it seems that chronic migraine in the PREEMPT studies adhere to criteria of the ICHD II, but it is not. It was shown that approximately 2/3 of all PREEMPT 1 and 2 included participants with chronic migraine had overused acute headache pain medication at baseline (which is not in line with the ICDH II criteria for chronic migraine). Those patients in the study, treated with onabotulinumtoxinA, might therefore be another entity than chronic migraine (e.g. medication overuse headache). Thus, the heterogeneity of the study participants raise questions in relation to efficacy of onabotulinumtoxinA on the Primary and secondary end point defined in the PREEMPT 1 and 2. Since enrollment of the PREEMPT 1 and 2 required that prophylactic medication was not taken 28 days prior to the baseline data collection, it is likely to assume that those enrolled had none or only a modest effect of previous tried prophylactic medications. This is important in the light that 79% of the reduction of headache days (primary efficacy variable) was due to placebo response.

Another important point to rise is the fact of two different primary endpoints in both PREEMPT 1 (mean change from baseline in frequency of headache episodes) and PREEMPT 2 (mean change from baseline in frequency of headache days). Subsequent to study initiation, but prior to study completion and treatment unmasking, the protocol and statistical analysis plan for PREEMPT 2 was amended to change the primary and secondary endpoints, making frequency of headache days the PREEMPT 2 primary endpoint. This fact leaves a bad taste, especially when it was clear that the primary endpoint in PREEMPT 1 did not reach statistical significance. In conclusion, clinical trials utilizing onabotulinumtoxin A as a preventive therapy for migraine has revealed mixed results. In part this reflects the inherent difficulties in study design such as defining different subpopulations of migraine sufferers and trial endpoints that are meaningful to patient populations. Recent studies of subjects with chronic migraine appear to have positive results. If confirmed this would be the first preventive medication indicated specifically for chronic migraine (with MOH).