Author's response to reviews

Title: Unmet clinical needs in chronic migraine: Rationale for study and design of COMPEL, an open-label, multicenter study of the long-term efficacy, safety, and tolerability of onabotulinumtoxinA for headache prophylaxis in adults with chronic migraine

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Version: 2  Date: 1 May 2014

Author's response to reviews: see over
Dear Dr. Shipley:

We are pleased to submit our article, “Unmet Clinical Needs in Chronic Migraine: Rationale for Study and Design of COMPEL: An Open-Label, Multicenter Study of the Long-Term Efficacy, Safety, and Tolerability of OnabotulinumtoxinA for Headache Prophylaxis in Adults With Chronic Migraine,” for consideration to be published as a Study Protocol Article in *BMC Neurology*.

We have added the following text about ethical approval: “The Central IRB for the COMPEL Study was reviewed and approved by the Quorum Review IRB in Seattle, WA”.

Chronic migraine is a disabling neurological disorder that affects approximately 2% of the general population; however, current prophylactic therapy options are unsatisfactory with regard to efficacy, safety, and tolerability, and none is currently approved for chronic migraine. OnabotulinumtoxinA has been reported to relieve pain in a variety of conditions, including migraine. Pivotal results from the PREEMPT (Phase III REsearch Evaluating Migraine Prophylaxis Therapy) clinical program have established onabotulinumtoxinA as a safe, well-tolerated, and effective headache prophylactic treatment of chronic migraine.

This paper will highlight the clinical rationale, study design, and treatment plan for the long-term evaluation of onabotulinumtoxinA in the treatment of chronic migraine. The Chronic migraine OnabotulinumtoxinA Prolonged Efficacy open Label (COMPEL) study, projected to be one of the largest and longest studies to be conducted in headache prophylaxis, will enroll adult patients with chronic migraine at international sites. Assessments of the efficacy, long-term safety, and tolerability of onabotulinumtoxinA as well as the effect of onabotulinumtoxinA on quality-of-life measures will be made in this study and COMPEL may provide an opportunity to evaluate the efficacy of onabotulinumtoxinA in a diverse, open-label population of chronic migraineurs.

Using a large database, a variety of outcome measures, and an extended time frame, the COMPEL study will seek to contribute substantially to the existing knowledge of the chronic migraine population and the long-term management of this debilitating disorder. The publication of the study design in *BMC Neurology* will allow physicians to understand the trial methodology and planned analyses.

We have suggested six potential reviewers based on their knowledge of the chronic migraine field and their understanding of onabotulinumtoxinA in this disorder. We have also suggested excluding four potential reviewers based on their differing opinions on the definition and classification of chronic migraine.

**Suggested reviewers:**
Roger Cady, Headache Care Center
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The principal author takes full responsibility for the data presented in this study, analysis of the data, conclusions, and conduct of the research. The principal author had full access to those data and has maintained the right to publish any and all data independent of any third party.

The Methods section includes a statement that an IRB or regional review board has approved the use of human subjects for this study.

The principal author declares that all authors and contributors have agreed to conditions noted on the Authorship Agreement Form.

**COMPETING INTERESTS**
Dr. Blumenfeld has received honoraria from Allergan, Inc., for consulting and speaking.
Dr. Aurora has received grant/research support and honoraria from Allergan, Inc., for consulting and speaking
Dr. Laranjo was an employee of and held stock in Allergan, Inc., at the time this paper was written. Dr. Papapetropoulos was an employee of and held stock in Allergan, Inc., at the time this paper was written.

Thank you for your consideration. I look forward to receiving your comments.

Sincerely,

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