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Letter to the Editor

[Translated article] Response of the authors to the Letter to the Editor regarding the article *Analysis of retreatment with monoclonal antibodies in chronic/episodic migraine: Real-world data*

Respuesta de los autores a la Carta al Editor sobre el artículo Analysis of retreatment with monoclonal antibodies in chronic/episodic migraine: Real world data

Dear colleagues,

First of all, we appreciate your attentive reading and analysis of the paper titled *Analysis of retreatment with monoclonal antibodies in chronic/episodic migraine* recently published in Farm Hosp. You highlight critical aspects of the use of monoclonal antibodies (anti-CGRP) in clinical practice and make some relevant reflections on our study.

In relation to your comment about the use of temporary treatment interruption or "therapeutic rest" to reduce costs and the risk for adverse reactions, we agree that it is an increasingly tested approach for the management of different chronic diseases. As you noted, our study revealed that discontinuance of erenumab and fremanezumab caused a worsening of the clinical symptoms of migraine, and most patients required retreatment within 4 months. As you also mention, switching anti-CGRP antibodies has been suggested as an alternative when a patient is no longer responsive to a specific antibody. However, the evidence supporting this approach is still limited, and further additional studies are needed to comparatively assess its effectiveness in a consistent manner.

Regarding the methodological limitations that you noted in relation to the study design (retrospective, single-arm study), we acknowledge that the absence of a comparator group is a common challenge of real-life studies. As you rightly point out, the natural fluctuations of migraine and the regression toward the mean phenomenon may mask the true association between treatment discontinuance and clinical worsening. However, the goal of this study was to provide a preliminary evaluation based on observational data and respond to the growing demand from clinicians for information about retreatment. We agree with you that controlled, randomized studies are certainly needed to establish a more solid cause-effect relationship.

With regard to the placebo effect and progressive loss of efficacy in the long term, these factors should be considered for the long-term evaluation of monoclonal antibody treatments for migraine. Our analysis revealed a satisfactory response in 2 of 3 patients following retreatment. This finding suggests that, although some patients may experience a loss of response, reintroduction of this treatment is still a feasible approach in most cases. Previous studies demonstrate that the decrease in plasma concentrations of anti-CGRP antibodies after treatment interruption may correlate with clinical worsening, which warrants retreatment.

Of note, although several papers have been published on the effects of retreatment throughout the course of the disease, effects are most frequently assessed 3–4 months after initiation of retreatment. Such is the case of our study, which is a limitation. No studies are available either involving a follow-up period after treatment interruption longer than 5 months, which coincides with the 5-month half-life of anti-CGRP antibodies. Therefore, long-term treatment and temporary withdrawal studies are needed to establish the potential of these drugs to modify the course of the disease[1].

As suggested by the promising results obtained in a recent Italian multicentric study conducted by Barbanti et al[2], several 12-month cycles of treatment alternated with a short period of discontinuation emerges as an alternative approach.

Finally, in relation to your suggestion of developing predictive tools to better identify patients who will benefit from temporary treatment discontinuation, we definitely agree with you in the need for a more personalized approach. The use of automatic learning models to predict patient response to anti-CGRP treatment is a promising approach that could improve patient selection not only for treatment initiation but also for temporary withdrawal and retreatment.

In response to your final question on clinical decisions in our center after the study, our multidisciplinary team agreed to suspend treatment discontinuance for one year and provide chronic treatment.

We strongly appreciate your letter and recommendations. We hope our communication will contribute to improve our understanding and management of migraine, especially regarding the use of monoclonal antibodies.

CRediT authorship contribution statement

Patricia García-Lloret: Validation, Writing – original draft.

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