

Letter to the Editor

## Whether Eculizumab Improves Quality of Life in Refractory Myasthenia Depends on the Definition of Refractoriness and Applied Scores

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With interest we read the article by Garzon-Arjuela *et al.*, about a meta-analysis of 9 studies on the impact of refractory myasthenia gravis treated with or without eculizumab on the quality of life (Garzón-Orjuela, N. *et al.*, 2019). The authors concluded that eculizumab improved the quality of life in patients with refractory myasthenia gravis (Garzón-Orjuela, N. *et al.*, 2019). The study has a number of shortcomings.

The first shortcoming is that the authors did not address how they defined refractoriness. We should know if they defined refractoriness as ineffectivity of immunosuppressive therapy, refractoriness to cholinergic medication, or refractoriness with regard to the serum levels myasthenia-associated antibodies.

The second shortcoming is that it was not assessed why myasthenia gravis was refractory. We should know in how many patients it was due to poor adherence, insufficient therapy, or due to wrong diagnosis.

The third shortcoming is that quality of life was assessed by three different tests (short form health survey, MG quality of life scale, Italian disease questionnaire) among the 9 included studies (Garzón-

Orjuela, N. *et al.*, 2019). As long as quality of life is variably defined in the 9 included studies, a common conclusion about the 9 studies has to be interpreted with caution.

The fourth shortcoming is that the duration of observation, number of follow-ups, and intervals between follow-ups was different in each of the 9 studies. A treatment effect on any drug may not only depend on the duration of observation and number of follow-up assessments but also on the time points at which re-evaluation took place.

A fifth shortcoming is that eculizumab was compared with placebo but not with another immunosuppressive therapy. It is conceivable that any immunosuppressive treatment for myasthenia gravis provides better quality of life, if tolerated, than not providing any immunosuppressive treatment at all to patients with myasthenia gravis.

A sixth shortcoming is that it was not mentioned how many patients had elevated titers of antibodies against the acetyl-cholin receptor, against MUSK, against RLP4, or against agrin. Specification of the myasthenia gravis subtype is crucial as each

subtypes may respond variably to immune-suppressive treatment including eculizumab (Evoli, A. *et al.*, 2019). In this regards we should know if patients without elevated antibody titers were included and if antibody titers truly declined upon application of eculizumab.

A seventh shortcoming is that the treatment the included patients were regularly taking was not provided. Knowing the current medication in refractory myasthenia gravis is crucial, to assess if refractoriness was due to drugs deteriorating myasthenia.

An eighth shortcoming is that the total number of patients included in this retrospective analysis was not mentioned. Furthermore, gender distribution was not provided. Since quality of life may not only be health-related (Nagane, Y. *et al.*, 2017), information about gender, the social status, income, and the education of the included patients should be provided.

Overall, this interesting study has a number of shortcomings as outlined above, which need to be addressed before final can be drawn and generalised. As long as comparability of included studies is not provided, general conclusions have to be regarded with caution.

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