Reviewer's report

Title: Intravenous immunoglobulin in the treatment of primary trigeminal neuralgia refractory to carbamazepine: a study protocol (ISRCTN33042138)

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Reviewer: Prof Christoph Maier

Level of interest: not specified

Advice on publication: Other (see below)

General comment

It is a well written study protocol dealing with a new treatment approach of an important disease constellation, promising new insights into the mechanism of refractory pain generally. The available data regarding to the use of intravenous immunoglobulin (IVIG) for pain treatment lead to the need of a more complex study design, because the number of patients with analgesic response to IVIG is unknown (presumably low) and its effect does not follow a simple dose-response schema. The authors describe an adequate study protocol, using the time to exit as the primary endpoint. This purpose is in accordance with the recent recommendations of the EAMA. The protocol seems to be feasible by each a clinical and biometric point of view.

Some details should be improved:

1. Carbamazepine is the traditional substance used for the treatment of trigeminal neuralgia. However, today Gabapentine is more common due to its lesser adverse events and lower toxicity. Therefore patients with TN refractory to Gabapentine should be enrolled also, alternatively a pre-treatment with carbamazepine have to be included in the protocol, but this is not recommendable for clinical reasons.
2. (page 5) All patients, who terminate prematurely (not only these who withdraw related to analgesic non-response or adverse events) have to be included into an intent to treat analysis. Any further operative and also any interventional treatment of TN (e.g. balloon decompression, thermo-coagulation or injections of neurolytic agents) after enrolment have to be assessed as non-response.

Competing interests:
None declared.