

June 2, 2016

Dear Editor:

I am pleased to submit a review article entitled "The Efficacy of Thioguanine Treatment in IBD: a Systematic Review" by Berrie Meijer, Chris Mulder and Nanne de Boer for consideration for publication in *World Journal of Gastroenterology*.

In this manuscript, we critically assess the available literature concerning the efficacy of thioguanine in IBD. Numerous literature reviews have been performed about safety issues, but literature concerning efficacy of thioguanine therapy in IBD has not been reviewed to date. For this reason, we only briefly discuss the safety profile (especially hepatotoxicity) of Thioguanine and we focus on the effectiveness of this therapy in this article.

Since thioguanine is considered as a rescue-treatment in IBD patients refractory to conventional thiopurines, our manuscript may serve as the basis for future trials. By March 1. 2016, Thioguanine has been officially registered as treatment modality for IBD in The Netherlands. With this manuscript, we show that thioguanine therapy is effective in about 65% of IBD patients refractory to conventional thiopurine therapy, thus protecting these patients from often expensive and potentially more harmful treatment. Whereas these numbers are based on solely observational (open-label) trials, randomized controlled trials are needed to confirm this efficacy.

We believe this manuscript forms a solid base for randomized (registration) trials to make thioguanine globally available for IBD patients.

This manuscript has not been published and is not under consideration for publication elsewhere.

Thank you for your consideration.

Yours sincerely,

On behalf of all authors,

Berrie Meijer, Ad van Bodegraven and Nanne de Boer

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