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Thalidomide: an effective anabolic agent in gastrointestinal cancer cachexia: authors' reply

SIRS, In the letter by Wilkes and Freeman, the authors mentioned that our article[1] fails to adequately explore the beneficial effects of thalidomide in patient with cancer cachexia. We did not discuss the potential effect of thalidomide in detail, because only the uncontrolled observational study of Khan *et al*.[2] and the study of Bruera *et al*.,[3] which did not focus on nutritional parameters, had been available during the preparation of this article. Gordon *et al*.[4] published their randomized prospective study on the role of thalidomide in cancer cachexia after we had completed the research.

The study by Gordon *et al*.[4] demonstrates a potential benefit of thalidomide in a small group ($N = 17$ at 4 weeks and $N = 12$ at 8 weeks) of patients with end-stage pancreatic cancer on preservation of body weight and lean body mass, but no clear benefit with regard to quality of life was observed.[4]

The potential mechanism by which thalidomide may work includes: inhibition of angiogenesis (anticancer effect), decrease in adhesion molecules, inhibition of cyclo-oxygenase 2, modulation of NFκB action and inhibition of proinflammatory mediators, especially tumour necrosis factor (TNF)-α.[5] In this context it has to be mentioned that the inflammatory and neurohumoral response with the consecutive catabolic metabolism in stress situations-like cancer or infections is part of a physiological response to maintain lifesaving functions. This endogenous mobilization of substrates allows the organism to survive in times when exogenous food supply is reduced or failed. The catabolic response cannot be stopped by energy and substrate support alone.[6] In addition, we should be aware that pharmacological attempts to reverse the immunological–metabolic response to severe infection or injury by anti-TNF-α antibody or growth hormone therapy may led to negative clinical outcome.[7, 8]

As we discussed in this review, treatment of cancer cachexia consists of a multimodal approach including an intelligent modulation of the immunological–metabolic pathways in combination with adequate supply of protein and energy. We agree with Wilkes and Freeman, which the study by Gordon *et al*.[4] suggests, that in this context thalidomide has promising features. Therefore, thalidomide may be a potential novel approach in the treatment

of cancer cachexia, but now we have to test whether thalidomide can fulfil this approach in larger clinical trials with defined clinical outcomes.

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