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Letter to the editor

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To the editor

We appreciate the comments from Jacoba van der Zee and Bin B.R. Kroon in response to our review article on the future directions in regional treatment strategies for melanoma and sarcoma of the extremity [1]. We acknowledge the work of the commentators on strategies to optimize the use of hyperthermia applied to isolated limb perfusion (ILP) [2, 3]. As stated in our article, we recognize that currently the application of mild hyperthermia (39°C–40°C) to ILP is advocated as a balance between optimizing response while maintaining acceptable levels of toxicity. Certainly the addition of mild hyperthermia to ILP is widely accepted because of the perception that heat improved response rates to ILP compared with historical controls while borderline true hyperthermia (40°C–41°C) and true hyperthermia (41°C–43°C) have been associated with unacceptable toxicity. Mild hyperthermia may also be important in isolated limb infusion (ILI) as subcutaneous temperatures >37.8°C in the limb at the conclusion of ILI were associated with a significant increase in survival and a trend toward prolongation of duration of response [4].

To date, however, there have been no randomized controlled trials comparing normothermic to mild hyperthermic or true hyperthermic ILP that unequivocally demonstrate a benefit for the addition of hyperthermia to ILP. The commentators own work concludes that the 39% complete response rate following normothermic ILP [5] was not significantly lower than that produced by most of the mild or true hyperthermic ILPs [3]. Thus, while the application of hyperthermia to augment response rates to regional chemotherapy is almost universially utilized as a component of ILP and ILI, there is no clinical data demonstrating its clear cut benefits. Indeed, the two proposed methods of hyperthermia discussed by van der Zee and Kroon in their letter are novel and warrant further investigation as does the whole field of hyperthermia as it pertains to optimally utilizing this form of therapy in conjunction with regionally administered chemotherapy. At the current time, strategies to optimize regional treatment for extremity melanoma, sarcoma and other malignancies that may recur in a multifocal pattern in the extremity focus on targeted agents and novel therapeutics. The scope of our review article was to specifically address these strategies which are readily applicable or are currently being utilized in clinical practice [1]. As such all the trials discussed in the review are open and currently accruing patients. Hyperthermia, to some degree is incorporated into all of these studies. While it is certainly true that optimizing delivery of hyperthermia to regionally treated patients may further improve responses, there are currently no regional therapy trials focusing specifically on this issue in melanoma or sarcoma.

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