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Reply to: Letter re: Efficacy of isolated limb perfusion (ILP) in patients with Merkel cell carcinoma: A multicenter experience

We thank our colleagues Kroon and Thompson for their interest in our article and subsequently their suggestions regarding the treatment of advanced Merkel Cell Carcinoma (MCC) of the extremities [1].

We fully agree severe toxicity and mortality should be balanced carefully against efficacy, especially since neither Isolated Limb Perfusion (ILP) or Isolated Limb Infusion (ILI) seems to improve overall survival in MCC patients. However we do ask them to consider the following.

ILP is used to obtain locoregional control in locally advanced MCC patients and aims to preserve the affected limb. Although no survival benefit is seen, as a palliative treatment it aims to maintain quality of life. Especially considering the durable response rates in some patients, we consider ILP to be a valuable treatment option. We experienced durable responses in 2 patients (53 and 71 months) during a median follow-up (FU) of 24 months. For ILI, to our knowledge, no evidence for a durable response had been exposed. Zeitouni et al. [2] included 3 patients undergoing ILI with a median FU of 9 months, Turaga et al. [3] included 7 patients, with a median FU of 11 months and a median progression free survival of 6,5 months. Steinman et al. [4] indeed treated 2 MCC patients with ILI but one proved to be a non-responder and another non-evaluable. Also Kroon and Thompson do not state any duration on FU or PFS in the patients treated with ILI.

Even though ILP is considered a more complex procedure, it is performed relatively frequently and safely in experienced centers with beneficial effect on locoregional control in MCC patients, as well as sarcoma and melanoma patients. The experienced toxicity and mortality in our cohort is unfortunate and should absolutely be minimized. Overall, we believe the mortality rate could have been improved by better patient selection, since the deceased patient showed severe atherosclerosis of the treated limb [5].

Furthermore, locoregionally advanced MCC is rare and the body of evidence supporting specific treatments is small. Although, our cohort is the largest series of MCC patients treated with ILP, only 10 patients were included. As we already stated in our discussion 'no firm conclusions can be drawn regarding response and toxicity due to the small sample size'. Therefore, we explicitly refrain from designating a preferred treatment based on our data. This consideration should also apply to the data provided by Kroon and Thompson. Although they show results comparable to ILP for the less invasive ILI, it seems unwise to disregard the fact that a different outcome for only one single patient could significantly alter response and mortality rates for either treatment. That being said, we fully agree in considering ILI as treatment for advanced MCC confined to the extremities, especially due to aspects of the treatment as provided by Kroon and Thompson themself: it is a relatively simple and less invasive procedure; thus suitable for older patients with significant comorbidity.

To conclude, the care of MCC patients requires an expert center taking into consideration treatment and patients' characteristics in deciding on the best possible care. To state ILI should be preferred over ILP (or vice versa) in all patients with locally advanced limb MCC suggests little appreciation for this delicate process.

Conflict of interest

None.

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