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

We read with great interest the article entitled: "Efficacy of isolated limb perfusion (ILP) in patients with Merkel cell carcinoma (MCC): A multicenter experience", in which Van Veenendaal et al. reported the combined experience of two tertiary referral centers in the Netherlands, involving ten patients treated with ILP for locally advanced MCC confined to a limb [1]. There was an overall response (OR) rate of 87.5% in the eight evaluable patients, with a complete response (CR) rate of 62.5%. Median limb progression-free survival was 5 months, with two long-term responses (53 and 71 months respectively). Median overall survival was 54 months. Although these are excellent results, severe (Grade IV-V) limb toxicity following ILP occurred in 20% of their patients. A compartment syndrome developed in one patient and another patient had an above-knee amputation of the leg for critical ischaemia and ultimately died as a direct result of the severe limb toxicity.

Since locoregional procedures such as ILP do not increase overall survival, efforts should be made not only to achieve the greatest possible efficacy but also to limit regional toxicity. In our view, a 20% rate of severe regional toxicity following ILP and a 10% mortality rate is unacceptably high, and seriously overshadows the benefit achieved in those patients who had a favorable response.

Isolated limb infusion (ILI) is a relatively simple, minimally invasive alternative to the more complex ILP procedure, and is essentially a low-flow ILP performed via percutaneously placed catheters, without the need for oxygenation of the perfusate. ILI is a broadly applied alternative to the often more morbid ILP procedure, and is mostly used in patients with irresectable melanoma and soft tissue sarcoma confined to a limb. As suggested in the paper by Van Veenendaal et al. ILI can also be considered as an alternative to ILP in MCC [2–4]. In the literature, twelve cases of MCC treated by ILI have been reported, with results generally comparable to those reported after ILP (OR rates 78–100% and CR rates 33–75%) [2–4]. Patient morbidity and regional toxicity, however, were considerably lower than after ILP. Following ILI for MCC, median limb toxicity was Grade II, while no patients developing Grade IV or V limb toxicity.

At Melanoma Institute Australia we have also performed ILI procedures for MCC. We achieved an OR in 3 of 4 patients (75%) and a CR in one patient (25%), with Grade II limb toxicity observed in 2 patients and Grade III toxicity in the other 2 patients. Of significance, the patients were all very elderly, with a median age of 85 years (range 77–88 years), and none would have been considered a suitable candidate for ILP.

In their paper Van Veenendaal et al. concluded that ILP should be considered as an effective treatment modality for locally advanced MCC. They suggest that ILI could be a suitable alternative treatment option for older patients with multiple comorbidities or in patients expected to have difficult vascular access because of a previous lymph node dissection. However, we suggest that in view of the similar response rates and the much lower limb toxicity grades and the absence of reported mortality, ILI should be considered as the preferable alternative to ILP not only in these patient groups, but in all patients with locally advanced limb MCC.

## Conflict of interest

None.

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