ACKNOWLEDGEMENTS

We do not have any acknowledgements.

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doi: 10.1111/ajd.13797

Letter

To the editor

We thank Dr Brown *et al.* for their interest in our article in which, based on our clinical experience and review of the literature, we proposed practical clinical strategies for the application of imiquimod for patients with lentigo maligna (LM), if it is considered the most appropriate treatment option for them. Whilst there are some points on which we agree with Dr Brown *et al.*, others argue against imiquimod for managing LM.

Despite its high prevalence, more evidence is needed to determine the optimal treatment of LM. A recent Cochrane review[1] concluded that there is a lack of high-quality evidence for both surgical and non-surgical modalities for treating melanoma *in situ* (including LM). Nevertheless, we highlight in our article that surgery is the recommended primary treatment modality for LM, as per international guidelines, because it allows a pathological evaluation of dermal invasion and margins. Despite this, a recent survey of European practitioners revealed the use of multiple management approaches for LM, including non-surgical treatments such as topical imiquimod.[2] Furthermore, some patients with recurrent or complex LM or those with significant comorbidities cannot be easily managed with surgery. It remains our view that such LM patients are best managed in a multidisciplinary specialist setting, a point with which Dr Brown *et al.* agrees. For these reasons, we state in our article that, at the current time, treatment with imiquimod should be considered only for patients with recurrent or complex LM who cannot be managed easily with surgery or in whom there are relative contraindications for surgery such as significant comorbidities. In our experience, such complex LM patients have high recurrence rates when treated with surgery (38% recurrence at 10 years)[3] because adequate margins are difficult to obtain.[4] These data emphasise the need to investigate the efficacy and tolerance of other treatment modalities for such patients, including imiquimod and radiotherapy, as highlighted in our article.

We agree with Dr Brown *et al.* that the use of imiquimod for treating LM is not listed on PBS. As we stated in our article, whilst retrospective evidence and cohort studies suggest it may be effective, this is not yet proven in well-designed prospective clinical trials, and we await the results of the RADICAL trial with great interest. However, we disagree that there is a vacuum of data on the use of imiquimod to treat LM: three systematic reviews analysing published data on the use of imiquimod to treat LM reported similar histological clearance rates of approximately 76% (despite heterogeneous series and lack of a long-term follow-up).[5–7] A recent report from Chamber M *et al.* reported a long-term follow-up and found recurrences occurred in only 10.1% of patients (mean time to recurrence 2.9 years (SD: 2.7 years)).[8]

To maximise compliance, its potential efficacy and to obtain robust data, it is important that an optimal protocol and procedure for the application of imiquimod for treating LM is followed. Indeed, we consider it likely that variability in the imiquimod application procedures may have impacted the results obtained in different studies published to date.[5–7] Based on clinical experience, our multidisciplinary team of experts have developed a consensus that we believe should be considered the best guidance for the practical application of imiquimod for managing complex LM patients until further data are available from prospective clinical trials. Whilst treatment

[Correction added on 13 February 2022, after first online publication: The sentence has been rephrased from "much of their letter appears to represent a diatribe against imiquimod for managing LM." to "others argue against imiquimod for managing LM".]

* This work was supported by the Cancer Australia Priority-driven Collaborative Cancer Research Scheme – (1083221), Melanoma Institute Australia and the Royal Australian and New Zealand College of Radiologists (2014/RANZCR/005). We acknowledge the Cancer Australia for the support of Melanoma and Skin Cancer Trials (MASC Trials) through the Support for Cancer Clinical Trials Program.

** Disclosures: RAS has received fees for professional services from Provectus Biopharmaceuticals Australia, Qbiotics, Novartis, Merck Sharp & Dohme, NeraCare, AMGEN Inc., Bristol-Myers Squibb, Myriad Genetics and GlaxoSmithKline. All other authors declare no conflict of interest related to this article.

failure may be assessed after 6 months, these data will require a long-term follow-up since LM may have a very long evolution, and recurrences may occur after more than 5 years.

The management of LM patients, particularly those with multiple recurrences, can be challenging, and we believe imiquimod is a potential treatment option in carefully selected patients, preferably in a multidisciplinary setting. We hope that the optimisation of the imiquimod application protocol including with the diary and follow-up will facilitate better compliance and efficacy of this form of treatment.

ACKNOWLEDGEMENT

Open access publishing facilitated by The University of Sydney, as part of the Wiley - The University of Sydney agreement via the Council of Australian University Librarians.

Pascale Guitera[1,2,3,*] | Andreanne Waddell[4] | Elizabeth Paton[5] | Gerald B Fogarty[1,3,6] | Angela Hong[1,3,6] | Richard A Scolyer[1,3,7,**] | Jonathan R Stretch[1,3] | Brett A O'Donnell[8] | Giovanni Pellacani[9]

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