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Conflicts of interest: none declared.

Response to: Routine usage of sentinel node biopsy in melanoma management must cease

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Dear Editor, I read with interest the communication by Dixon and colleagues.[1] I share their concern over patients being told that therapies are available to them only if they have a sentinel node biopsy (SNB). SNB does more than offer a subset of patients added prognostic information.[2] What the Multicenter Selective Lymphadenectomy Trial (MSLT)-I emphatically demonstrated is that SNB is a useful staging tool to stratify patients. Those with a positive SNB do significantly worse than those with a negative result. Furthermore, micrometastases in a lymph node left alone are highly likely to become macroscopic, prompting a therapeutic lymph node dissection.[2]

We do not know whether the prognostic advantage alluded to in the article of Dixon *et al.* is ultimately due to the SNB alone, or to the adjunct of a completion lymph node dissection (CLND). Aside from this, we await the results of MSLT-II to help us rationalize the use of CLND. If the issue is the ethics surrounding how clinicians recruit patients to trials that require an SNB, then that is reasonable, but perhaps the title 'Coercion into melanoma trials using SNB must cease' is more apt.

Trial data would be fundamentally flawed if the participants did not have an accurate disease stage. The available précis online for trial NCT01972347 describes an interest in patients with macroscopic nodal disease, not the necessity of SNB plus CLND.[3] The assertions that these trials recruit 'low-risk patients...as long as they have a positive SNB' is counterintuitive. The very fact they have a positive SNB means they are not 'low risk', they will do significantly worse than the same patient with a negative SNB.

The binary argument around SNB is dated. The key discussion now is whether the patient wants to know whether it is better to have potential positive nodes resected early (i.e. an SNB, which carries low morbidity of 2–6%),[4] or later, when the majority of these micrometastases have developed into palpable disease. The latter option carries greater morbidity and requires more adjuvant treatment (probably because of more extranodal extension), but does not dilute the survival.[2]

I wonder whether some of the authors' angst is generated by anecdotal observation of such behaviour, which I agree prompts questions of probity. I do not think SNB should be used as a 'deal breaker' if certain therapeutics may benefit patients later in their disease course. However, this should not generate a view on the validity and clinical use of what SNB offers patients with melanoma, and the notion that it should cease.

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Authors' response to a reply to: Re: Routine usage of sentinel node biopsy in melanoma management must cease

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Dear Editor, We thank Mr Saleh for his comments[1] and are pleased he agrees that acceptance into melanoma therapeutic

trials should not be contingent on undergoing sentinel node biopsy (SNB). However, we disagree with his assertion that SNB still has a viable role in melanoma management.

Suppose SNB followed by completion lymphadenectomy was a drug therapy for melanoma, subjected to a 10-year randomized controlled trial involving 2000 patients where a survival benefit was not found. The manufacturer would not seek its formal approval for usage. We would not still be discussing the drug. SNB with completion lymphadenectomy has failed to demonstrate a survival benefit in such a trial, the Multicenter Selective Lymphadenectomy Trial (MSLT)-I.[2] Yet SNB is still commonly offered to our patients. We await but cannot presume the findings of the forthcoming MSLT-II data.

Further, suppose we regard SNB as an investigation rather than a therapy? Saleh and others consider SNB to be a 'staging procedure'. We were taught from medical school that an investigation is intended to guide treatment. In contrast to BRAF testing, positive SNB results offer patients no alternative therapies of proven benefit. At present, staging with SNB does not assist in guiding management. SNB is an imperfect test, with biopsy-negative patients still frequently progressing to metastatic disease. Further, early nodal melanoma metastases can be detected by ultrasound without needing invasive surgery.[3]

The MSLT-I trial[4] showed SNB to have a 10·1% complication rate. Other data report complication rates of over 15%. We have identified that these complications are at times serious.[5] Saleh's suggestion of a complication rate of 2–6% cherry picks the data and misrepresents SNB risks.

Saleh suggests a benefit in finding involved nodes early rather than late. This concept was extensively covered in the Cochrane analysis of SNB for melanoma.[6] A morbidity benefit was not supported by the data. The authors concluded, 'Currently this evidence is not sufficient to document a benefit of SLNB when compared to observation in individuals with primary localised cutaneous melanoma.'[6]

SNB does not pass as either a beneficial test or a treatment. It can be difficult to accept that an intervention well-intentioned physicians have offered patients has not benefited them. When such interventions are found not to help our patients, we must discard them and move on.

We are scientists. Fine tuning management based on evidence-based medicine sets us apart from so many other healthcare providers. We fail to show that distinction when we continue to recommend (and potentially personally benefit from) an intervention that has not been found to benefit our patients.

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A reply to: 'Impact of biologic therapies on risk of major adverse cardiovascular events in patients with psoriasis: systematic review and meta-analysis of randomized controlled trials'

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Dear Editor, We read with interest the recent article by Rungapiromnan *et al.* that utilized a meta-analysis to compile data from 38 randomized controlled trials (RCTs) to determine whether there is an association between biological therapies and major adverse cardiovascular events (MACEs) in patients with plaque psoriasis.[1]

In that study, only 10 MACEs were reported over nine of the RCTs examined. The reported absolute values of the Peto odds ratios are worthy of attention. The overall pooled analysis of the nine trials found a combined Peto odds ratio of 1·45 (95% confidence interval 0·34–6·24, $P = 0·62$), with seven of the nine RCTs exhibiting a Peto odds ratio > 3. It is preferable not to perform a pooled analysis that combines data on different biological therapies. For instance, tumour necrosis factor (TNF) inhibitors may lower the risk of MACEs, whereas ustekinumab may not.[2,3] Currently, there are limited data on the effect of interleukin (IL)-17 inhibitors on the risk of MACEs. Moreover, the nine RCTs included in the meta-analysis consisted of small sample sizes, ranging from 59 to 483 patients, with short time courses of treatment. With the