Current role of sentinel lymph node biopsy in early-stage melanoma

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There has been significant evolution in the management of surgically resectable melanoma the past five years with the success of adjuvant therapy for stage 3, and more recently, high-risk stage 2 melanoma. In the context of these recent changes, the role of sentinel lymph node biopsy (SLNB), which has been debated for many years, has come under the spotlight again.

The issues underlying the differing opinions regarding SLNB are borne out in the MSLT-1 and MSLT-2 studies of SNLB and completion lymph node dissection (CLND). The MSLT-1 trial found that, although a positive sentinel node was a poor prognostic sign, SLNB did not independently improve 10 year melanoma-specific survival. MSLT-1 did, however, confirm sentinel node status as the most important prognostic factor in intermediate-thickness melanomas, and in patients without clinically detected lymph node involvement, it remains the best single predictor of melanoma-specific survival.

The impact of nodal involvement is reflected in the eighth edition of the American Joint Committee on Cancer (AJCC) melanoma staging. In this most recent staging system, an accurate stage cannot be allocated to a patient with melanoma >1.0mm Breslow thickness in the absence of the results of SLNB assessing clinically occult nodal disease. A comparison of 10 year survival rates for stages IA and IIC is illustrative as survival was 93% and 39%, respectively, using the AJCC seventh edition (which did not require SLNB) compared to 98% and 75% with the eighth edition. Accurate nodal staging offers improved prognostication within this heterogeneous group of patients. For instance, the presence of sentinel lymph micrometastases in a patient with a 2mm Breslow thickness ulcerated cutaneous melanoma decreases 10 year survival from 89% to 60%, mandating significant changes in follow-up and adjuvant treatment.

The subsequent MSLT-2 trial showed that completion lymph node dissection (CLND), following a positive sentinel lymph node, did not improve melanoma-specific survival. It was, however, associated...
with an increased rate of complications compared with ultrasound observation, especially lymphoedema which occurred in 24% versus 6%. These trials show that, although SLNB does not have an independent therapeutic benefit in early-stage melanoma, it does provide vital prognostic information.

Recent trials of PD-1 inhibitor immunotherapy and BRAF/MEK tyrosine kinase inhibitors in stage 3 melanoma proved definitively the benefit of adjuvant therapy. The KEYNOTE-054 and the CheckMate-238 trials showed that one year of adjuvant pembrolizumab and nivolumab significantly reduced relapse in stage 3 melanoma. Inclusion in these trials was based on the AJCC staging and required lymph node metastasis. Adjuvant immunotherapy has become a cornerstone in the treatment of early-stage disease as these trials show sustained benefit in relapse-free survival (RFS hazard ratio of 0.56). Adjuvant immunotherapy has become standard of care in Australia, USA, and Europe for patients with stage 3B melanoma and above (assessed by SLNB status) but is still not funded by PHARMAC in New Zealand.

Furthermore, the recent KEYNOTE-716 trial in high-risk stage 2 melanoma (pT3b–pT4b) also showed a benefit in adjuvant therapy. However, the absolute risk of disease recurrence was far less in stage 2 (16.9% at 12 months without treatment), compared with stage 3 disease (39.2% at 12 months without treatment). When weighing the relative benefits and risk of adjuvant therapy, SLNB provides fundamental prognostic information to inform patient and clinician choice.

One of the criticisms of SLNB is that it does not account for distant haematogenous spread, and is of limited utility. This is a valid critique, but there are no clinically validated prognostic risk models superior to SLNB. Until we have improved risk assessment tools, such as molecular assessment of the primary melanoma or composite tools (not currently available), validated in adjuvant clinical trials, it is our position that SLNB remains a critical element in the management of early-stage melanoma. The prognostic information SLNB provides allows patients and their doctors to make informed decisions about adjuvant therapy, especially given the current cost of adjuvant therapy in New Zealand.
LETTER

COMPETING INTERESTS
Nil.

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REFERENCES