SURGICAL ONCOLOGY

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Current management of patients with melanoma who are found to be sentinel node-positive

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Key words
immunotherapy, lymph node dissection, Melanoma, molecular targeted therapy, sentinel lymph node biopsy.

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Accepted for publication 12 September 2019.

doi: 10.1111/ans.15491

Abstract

Background: The results of the DeCOG-SLT and MSLT-II studies, published in 2016 and mid-2017, indicated no survival benefit from completion lymph node dissection (CLND) in melanoma patients with positive sentinel nodes (SNs). Subsequently, several studies have been published reporting a benefit of adjuvant systemic therapy in patients with stage III melanoma. The current study assessed how these findings influenced management of SN-positive patients in a dedicated melanoma treatment centre.

Methods: SN-positive patients treated at Melanoma Institute Australia between July 2017 and December 2018 were prospectively identified. Surgeons completed a questionnaire documenting the management of each patient. Information on patients, primary tumours, SNs, further treatment and follow-up was collected from patient files, the institutional research database and pathology reports.

Results: During the 18-month study period, 483 patients underwent SN biopsy. A positive SN was found in 61 (13%). Two patients (3%) requested CLND because of anxiety about observation in view of unfavourable primary tumour and SN characteristics. The other 59 patients (97%) were followed with a four-monthly ultrasound examination of the relevant lymph node field(s). Two of them (3%) developed an isolated nodal recurrence after 4 and 11 months of follow-up. Fifty-seven patients (93%) were seen following the publication of the first two adjuvant systemic therapy studies in November 2017; 46 (81%) were referred to a medical oncologist to discuss adjuvant systemic therapy, which 32 (70%) chose to receive.

Conclusion: At Melanoma Institute Australia most patients with an involved SN are now managed without CLND. The majority are referred to a medical oncologist and receive adjuvant systemic therapy.

Introduction

Sentinel node (SN) biopsy (SNB) is routinely performed in patients with clinically localized intermediate and thick primary cutaneous melanoma. It offers prognostic and staging information and, combined with completion lymph node dissection (CLND), prolongs survival in SN-positive patients with intermediate thickness melanomas.[1] As no additional nodal metastases are found in approximately 80% of SN-positive patients and in view of the associated morbidity, the need for CLND was questioned.[2–4] In 2017, results of the second Multicenter Selective Lymphadenectomy Trial (MSLT-II) and the German Dermatologic Cooperative Oncology Group Selective Lymphadenectomy Trial (DeCOG-SLT) had shown that melanoma-specific survival is not significantly different when SN-positive patients are carefully observed with regular ultrasonography of their node field(s) and undergo a therapeutic dissection upon locoregional recurrence, compared to those

ANZ Journal of Surgery published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Surgeons

having an immediate CLND.[5,6] Although the median follow-up duration of both trials was limited (43 and 35 months respectively) and questions have been raised about the design and limited size of DeCOG-SLT, their conclusion that SN-positive melanoma patients can be safely observed instead of undergoing further surgery (CLND) is considered to be meaningful.[5,6]

There have also been important recent developments in adjuvant drug therapies, which reduce the risk of both locoregional and distant recurrence. In November 2017 the results of two phase three trials were published, followed by results of a third trial in May 2018, showing a relapse-free survival benefit from adjuvant PD-1 immunotherapy and BRAF/MEK targeted therapy in patients with stage III melanoma.[7–9]

To determine how these recent surgical and medical trial findings have impacted the management of SN-positive patients, we initiated a prospective study immediately following publication of the MSLT-II results.[5] The initial aims of the study were to determine the frequency and the reasons for undertaking of CLND in this setting, as well as to assess the use of adjuvant systemic treatment.

Methods

The study was conducted at Melanoma Institute Australia (MIA). It was approved by The University of Sydney Ethics Committee (identification number 2017/933) and all patients provided informed consent. Participating MIA surgeons signed a separate informed consent form.

SNB was generally recommended for patients who had a melanoma with a Breslow thickness of at least 1 mm and was discussed in patients with a thinner melanoma if adverse prognostic features such as ulceration and/or an elevated mitotic rate were present. A SN was defined as any lymph node receiving direct lymphatic drainage from the primary tumour.[10] The lymphoscintigraphy method, SNB technique and protocol for pathological evaluation of SNs have been described previously.[11,12]

Between July 2017 and December 2018 melanoma patients with a positive SN were identified from pathology reports. In patients with a positive SN, the advantages and risks of both the option of CLND and of observation with regular ultrasonography of the node field were discussed. Patient preference took precedence in the decision-making process. MIA surgeons filled out a questionnaire for each patient, recording whether CLND was performed and if so, for what reason(s) (Fig. S1). Referral to a medical oncologist and further treatment were evaluated. All patients were followed up three to four-monthly, with a physical examination. Additionally, an experienced radiologist performed an ultrasound examination of the relevant draining lymph node fields in patients who had not had a CLND. Patients who received adjuvant systemic therapy often had three-monthly positron emission tomography–computed tomography (PET/CT) scans instead.

Additional information on patient characteristics, primary tumour details, SNB outcomes, further treatment and follow-up were retrieved from the MIA research database, patient files and pathology reports. Follow-up data were obtained until 30 December 2018. Data were analysed using Excel and SPSS. Numbers were reported with percentiles, means with standard deviations, and medians with interquartile ranges.

Results

Five MIA surgeons participated in the study. A total of 483 patients underwent SNB during the 18 months of data acquisition following the publication of MSLT-II in June 2017. A positive SN was found in 61 of them (13%; Table 1). The median maximum diameter of the nodal melanoma deposits was 0.6 mm and 40 of the 72 SNs (56%) contained a metastasis <1 mm in diameter (Table 2).

Two of the 61 patients (3%) requested CLND after a detailed discussion about the risks and benefits of CLND and observation. Both were anxious about observation because of unfavourable prognostic characteristics. The first patient was a 62-year-old male with stage IIIC melanoma. He had a non-ulcerated primary tumour on the back with a Breslow thickness of 8.5 mm and a mitotic rate of 17/mm^2. Two SNs were harvested from the axilla, one of which was positive. The tumour deposit was 1.1 mm, it was located subcapsular, extending into the parenchyma, without extranodal extension. The other patient was a 56-year-old male who was stage IIIC as well with an ulcerated primary tumour on his shoulder with a Breslow thickness of 2.8 mm and a mitotic rate of 20/mm^2. Two of three axillary SNs were involved. The largest tumour deposit was 1.0 mm. Both patients underwent axillary dissection, yielding nine and 22 additional nodes, none containing further metastases.

Fifty-seven of the patients were treated following the publication of the adjuvant systemic therapy studies in November 2017. Forty-six of them (81%) were referred to a medical oncologist and 32 (70%) received adjuvant systemic therapy. Twelve of the treated patients had

Table 1 Baseline characteristics

Characteristics	Number of patients/ mean/median
SN-positive patients	61
Female | male, *n* (%)	28 (46) | 33 (54)
Mean age (SD)	57 (±14)
Stage at presentation	
IIIA	24 (39)
IIIB	10 (16)
IIIC	27 (44)
Primary tumour†	
Breslow thickness, *n* (%)	
≤1.0	3 (5)
>1.0–2.0	26 (43)
>2.0–4.0	17 (28)
>4.0	15 (25)
Ulceration, *n* (%)	22 (36)
Median mitotic rate per mm^2 (IQR)	4 (3–8)
Microsatellites, *n* (%)	3 (7)
Intravascular or intralymphatic invasion, *n* (%)	7 (16)
Location, *n* (%)	
Head/neck	7 (11)
Trunk	27 (44)
Upper extremity	12 (20)
Lower extremity	15 (25)

†Data missing for microsatellites and intravascular/intralymphatic invasion in 18 patients. IQR, interquartile range; SD, standard deviation; SN, sentinel node.

Table 2 Sentinel node characteristics

Characteristics	Number of patients/ mean/median
SN-positive patients	61
Location positive SN, *n* (%)	
Groin	17 (28)
Axilla	36 (59)
Neck	7 (11)
Interval node, *n* (%)	1 (2)
Number of SNs harvested	149
Positive SNs†	
Total number of positive SNs	72
Number of positive SNs, median (IQR; range)	1 (1–1; 1–3)
Largest deposit in mm, median (IQR; range)	0.6 (0.3–1.5; 0.02–4.0)
Metastasis penetrating depth in mm, median (IQR; range)	0.3 (0.1–1.1; 0.01–6.0)
Extranodal extension, *n* (%)	2 (3)
Location tumour in SN, *n* (%)	
Subcapsular	37 (63)
Subcapsular and parenchymal	20 (34)
Parenchymal	2 (3)

†Largest deposit unknown in four SNs, maximum metastasis penetrating depth unknown in 29 SNs, extranodal extension unknown in nine SNs, location tumour unknown in 13 SNs. IQR, interquartile range; SN, sentinel node.

stage IIIA melanoma, six stage IIIB and 14 stage IIIC. Twenty-four patients were treated with a PD1-inhibitor (pembrolizumab or nivolumab) and eight participated in an adjuvant therapy trial, in which they were randomized to receive nivolumab with or without ipilimumab. None received adjuvant targeted therapy with BRAF or MEK inhibitors because at the time it was not funded in Australia and no clinical trials involving BRAF/MEK inhibitors were open. Reasons for refraining from adjuvant systemic therapy were the fear for potential side effects, a low expected absolute benefit in some patients, cost of the drugs, ineligibility for trials, patient co-morbidity (combined with age), and inability or unwillingness to travel to the institute on a regular basis.

Neither of the two patients who had a CLND developed a recurrence. Eight of the patients who were observed did recur, four of them having received adjuvant systemic therapy (Table 3). Two observed patients developed an isolated recurrence in a lymph node field. Both had consulted a medical oncologist after SNB but had decided not to have adjuvant systemic therapy. One was a 61-year-old female with a stage IIIc primary melanoma on her forearm (Breslow thickness 7.1 mm, ulcerated). The retrieved SN contained a tumour deposit with a maximum diameter of 3 mm. After 4 months of follow-up, a nodal recurrence was found on physical examination and confirmed by fine-needle biopsy. She was treated with neoadjuvant immunotherapy followed by axillary CLND. The second patient who developed a nodal recurrence was a 50-year-old male who had stage IIIc melanoma on his thigh (Breslow thickness 6.5 mm, non-ulcerated). He had one positive SN, containing a tumour deposit with a maximum diameter of 2.1 mm. After 11 months of follow-up, a nodal recurrence was noted on a surveillance PET/CT scan performed prior to a routine clinical visit, when it was found to be clinically palpable. He underwent a CLND of the groin followed by adjuvant immunotherapy.

Table 3 Further management and follow-up

Further treatment and follow-up	*n*
Time from primary to last follow-up in months, median (IQR)	7 (3–12)
Time from SNB to last follow-up in months, median (IQR)	5 (2–11)
Patients lost to follow-up (>6 months since last follow-up),† *n* (%)	3 (5)
Patients with recurrences, *n* (%)	8 (14)
Type of recurrence	
Local recurrence	1
Nodal metastasis	2
In-transit metastasis	2
Distant metastasis	2
Local and in-transit metastases	1

†Two additional patients were not seen for over 6 months after they had moved overseas. They were referred to a local medical oncologist. SN, sentinel node.

All patients were alive at last follow-up, with a median time from primary to last follow-up of 7 months (interquartile range 3–12 months, range 1–16 months). Five observed patients (8%) did not attend follow-up at MIA for more than 6 months. Two of them had moved overseas with follow-up by a local specialist, while the three remaining patients (5% of the cohort) were truly lost to follow-up.

Discussion

This study describes how the management of SN-positive patients at a large specialized melanoma treatment centre evolved following publication of the results of two landmark clinical trials in 2016 and 2017.[5,6] We are not aware of other recent studies on the management of SN-positive patients. In the 18 months following the publication of the MSLT-II results, only two of 61 SN-positive patients underwent CLND. Both expressed anxiety about observation because of the unfavourable prognostic primary tumour and SN characteristics, although MSLT-II showed no survival benefit from CLND in the subgroups with these features.[5]

Current surgical management at MIA is in accordance with the recently updated Australian Melanoma Management Guidelines that state 'CLND is no longer the preferred treatment for patients with a positive SLNB. CLND or active surveillance are equivalent in terms of 3-year melanoma-specific survival but CLND is more morbid'.[13] Before the MSLT-II publication, the guidelines recommended that all SN-positive patients should be offered CLND.[14] However, although it was considered standard management of SN-positive patients, CLND was not practiced as widely as might have been expected. Isaacs *et al*. reported that 38% of 599 SN-positive patients treated at MIA between 2004 and 2014 were monitored instead.[15] This was usually due to patients' preference rather than to their surgeon's recommendation. Patients with interval SLNs and multiple SLN fields were less likely to undergo CLND. Studies in the USA and Germany have reported similar outcomes, with 43% and 40%, respectively, of patients being monitored.[16,17]

The most important parameter in this decision-making process is survival. In the absence of a significant survival benefit from CLND,

Table 4 Overview of outcomes, advantages and disadvantages of completion lymph node dissection versus observation of SN positive patients

	Completion lymph node dissection	Observation
Overall survival[5,6]	No significant difference (even in subgroup analyses of sex, age, ulceration, Breslow thickness, primary site, number of positive SNs and largest SN metastasis) Trend towards better survival with CLND in patients with head and neck melanoma	
Distant-metastasis-free survival[5,6]	No significant difference	
Loco-regional recurrences[5,6]	No significant difference	
Nodal recurrence[5,6,18]	Less nodal recurrences	More nodal recurrences, but no loss of regional control with frequent ultrasound examinations
Distant recurrences[5,6]	No significant difference	
Prognostic information[5,6,19,20]	Information on non-SN tumour status, prognostic for systemic recurrence and survival Non-SNs positive in ±20% of the SN positive patients Change in AJCC-UICC tumour stage in 5–6% of the patients	No prognostic information on non-SN tumour status
Follow-up[5,21]	In Australia, recommended follow-up is four-monthly in the first 2 years, six-monthly in year 3, then annually for 5 more years. No surveillance ultrasound assessment necessary during follow-up[13]	In Australia, recommended follow-up is four-monthly in the first 2 years, six-monthly in year 3, then annually for 5 more years. Ultrasound assessment of the draining lymph nodes at every visit in the first 5 years
Acute surgical morbidity[14,22]	No significant difference in acute surgical morbidity in patients undergoing direct or delayed completion lymph node dissection	• Acute surgical complications in 14% of the patients having wide local excision • Acute surgical complications at SNB site in 10% of the patients undergoing SNB • Acute surgical complications in nodal region in 37% of the patients undergoing delayed CLND in case of nodal positivity
Lymphedema[5,14,23]	Lymphoedema in about 12% of the patients	• Lymphoedema in 0.3% of the patients after wide local excision • Lymphoedema in 1–6% of the patients after wide local excision and SNB • Lymphoedema in 20–24% of the patients after delayed CLND for nodal recurrence
Adjuvant systemic therapy	Available for all SN-positive patients, CLND no longer a prerequisite in most centres	

AJCC-UICC, American Joint Committee on Cancer - Union for International Cancer Control; CLND, completion lymph node dissection; SN, sentinel node; SNB, sentinel node biopsy.

it is understandable that most patients and surgeons opt for observation.[5,6] However, factors other than survival may also play a role in management decisions (Table 4). CLND provides additional staging information, with an increase in the AJCC-UICC stage in 5–6% of patients.[19,20] It offers prognostic information that is not available in patients who are observed, by providing the number of involved non-SNs, although it probably only detects 50% of the positive non-SNs.[5] Information on non-SN tumour status can help surgeons in subsequent management recommendations. For example, the prognosis of non-SN-positive patients is similar to the prognosis of patients with palpable nodal disease, making adjuvant systemic treatment even more important.[24–26]

Return of their disease is a psychologically devastating experience for some patients and the risk of nodal recurrence is diminished after CLND.[5] Follow-up is less burdensome after CLND, as four-monthly ultrasound examination is not necessary. Furthermore, an early CLND causes less lymphedema compared to a delayed CLND and there is no indication for adjuvant radiotherapy at this early stage of nodal involvement.[14] Lastly, patients with head and neck melanoma were not represented in DeCOG-SLT and had a trend towards better survival with CLND in MSLT-II. If these patients have a nodal relapse, CLND is particularly challenging. These advantages of CLND generally do not outweigh the lack of a significant survival benefit and the morbidity associated with the early operation.

Some have misinterpreted the results of MSLT-II and advocated abandoning SNB.[27] However, the prognostic significance of SN-status, the improved staging and the survival benefit in node-positive patients are maintained. SNB is not obsolete. Indeed, it is more relevant as it provides the best opportunity for occult node positive patients to avoid CLND. SNB remains standard of care in Australia and internationally.[28,29]

It is important to note that only two patients in our study developed nodal recurrence, after 4 and 11 months; however, the follow-up time was relatively short, and more nodal recurrences may therefore become apparent over time.

There is accumulating evidence that adjuvant systemic therapy improves survival in melanoma patients with lymph node metastases. The preliminary results of the COMBI-AD trial showed that 1 year of adjuvant targeted therapy with a combination of dabrafenib and trametinib prolonged recurrence-free survival in stage III patients with a melanoma having the BRAF mutation.[7] The EORTC trial in stage III patients also demonstrated an improved recurrence-free survival with adjuvant pembrolizumab compared to placebo.[8] Results of the CheckMate 238 trial showed that recurrence-free survival with adjuvant nivolumab for 1 year was better than with ipilimumab in patients with stage IIIB, IIIC and stage IV disease, with less toxicity.[9] Local and distant recurrences were reduced on all trials to similar effect. It should be noted, however, that these three trials were conducted prior to

publication of the MSLT-II results, and thus all patients underwent CLND. Also, in the first two trials, patients with metastases ≤1 mm were excluded, as were patients with stage IIIA disease in the third trial. The median maximum diameter of SN metastases in our population was just 0.6 mm. Thus, although adjuvant drug therapy improves the short-term survival rate in patients with lymph node metastases, it remains to be determined whether this is true in the long-term for patients who have only a small tumour deposit in their SN. Nevertheless, the current evidence indicates that adjuvant systemic therapy should be considered in these patients. An ongoing trial, comparing nivolumab to nivolumab plus low-dose ipilimumab (CheckMate-915) does not mandate CLND. In the MSLT-II and DeCOG studies, patients were followed with frequent nodal ultrasound assessments. Patients receiving systemic therapy are often monitored with CT or PET/CT instead. Ultrasound examination is more sensitive and specific for detecting small lymph node metastases (≤10 mm diameter) whereas PET/CT is better than CT alone to screen for distant metastases, and will also detect nodal metastases >10 mm in diameter with reasonable reliability.[30] Because the risk of nodal metastasis is lower than the risk of systemic metastasis in patients receiving adjuvant systemic therapy, it is probably most cost-effective to undertake PET/CT surveillance in these patients.

In conclusion, this study shows that the management of melanoma patients with a positive SN at MIA changed remarkably over a recent 18-month period. Between 2004 and 2014, 62% of the SN-positive patients at MIA were managed with CLND.[15] After the results of MSLT-II and DeCOG-SLT were published, 97% of SN-positive melanoma patients no longer underwent CLND and had careful clinical follow-up with imaging of the relevant lymph node field(s). The majority of patients were referred to a medical oncologist to discuss the pros and cons of adjuvant systemic therapy, and 70% of them (32/46) chose to receive this. Compliance with the recommended follow-up schedule was high, and only two patients developed node field recurrences, both of which were resectable.

Acknowledgement

AAGN has received research scholarships from the K.F. Heinfonds and Michaël Vlotenfonds in 2017.

Conflicts of interest

AMM has been on advisory boards for Bristol Myers Squibb, Merck Sharp and Dohme, Novartis, Roche and Pierre-Fabre. RPMS has been on advisory boards for Bristol Myers Squibb, Merck Sharp and Dohme, Novartis, Amgen; and has received a speaking honorarium from Bristol Myers Squibb. JFT has been on advisory boards for and received honoraria from Bristol Myers Squibb and Merck Sharp and Dome. He has been on advisory boards and received honoraria and travel support from Provectus Inc. and GlaxoSmithKline.

References

1. Morton DL, Thompson JF, Cochran AJ *et al*. Final trial report of sentinel-node biopsy versus nodal observation in melanoma. *N. Engl. J. Med.* 2014; **370**: 599–609.
2. van der Ploeg IM, Kroon BB, Antonini N, Valdes Olmos RA, Nieweg OE. Is completion lymph node dissection needed in case of minimal melanoma metastasis in the sentinel node? *Ann. Surg.* 2009; **249**: 1003–7.
3. Bilimoria KY, Balch CM, Bentrem DJ *et al*. Complete lymph node dissection for sentinel node-positive melanoma: assessment of practice patterns in the United States. *Ann. Surg. Oncol.* 2008; **15**: 1566–76.
4. Nagaraja V, Eslick GD. Is complete lymph node dissection after a positive sentinel lymph node biopsy for cutaneous melanoma always necessary? A meta-analysis. *Eur. J. Surg. Oncol.* 2013; **39**: 669–80.
5. Faries MB, Thompson JF, Cochran AJ *et al*. Completion dissection or observation for sentinel-node metastasis in melanoma. *N. Engl. J. Med.* 2017; **376**: 2211–22.
6. Leiter U, Stadler R, Mauch C *et al*. Complete lymph node dissection versus no dissection in patients with sentinel lymph node biopsy positive melanoma (DeCOG-SLT): a multicentre, randomised, phase 3 trial. *Lancet Oncol.* 2016; **17**: 757–67.
7. Long GV, Hauschild A, Santinami M *et al*. Adjuvant dabrafenib plus trametinib in stage III BRAF -mutated melanoma. *N. Engl. J. Med.* 2017; **377**: 1813–23.
8. Eggermont AMM, Blank CU, Mandala M *et al*. Adjuvant pembrolizumab versus placebo in resected stage III melanoma. *N. Engl. J. Med.* 2018; **378**: 1789–801.
9. Weber J, Mandala M, Del Vecchio M *et al*. Adjuvant nivolumab versus ipilimumab in resected stage III or IV melanoma. *N. Engl. J. Med.* 2017; **377**: 1824–35.
10. Nieweg OE, Tanis PJ, Kroon BBR. The definition of a sentinel node. *Ann. Surg. Oncol.* 2001; **8**: 538–41.
11. Li L-XL, Scolyer RA, Ka VSK *et al*. Pathologic review of negative sentinel lymph nodes in melanoma patients with regional recurrence. *Am. J. Surg. Pathol.* 2003; **27**: 1197–202.
12. Uren RF, Howman-Giles R, Chung D, Thompson JF. Guidelines for lymphoscintigraphy and F18 FDG PET scans in melanoma. *J. Surg. Oncol.* 2011; **104**: 405–19.
13. Cancer Council Australia. *Clinical Practice Guidelines for the Diagnosis and Management of Melanoma*. [Cited 25 Apr 2019.] Available from URL: https://wiki.cancer.org.au/australia/Guidelines:Melanoma
14. Faries MB, Thompson JF, Cochran A *et al*. The impact on morbidity and length of stay of early versus delayed complete lymphadenectomy in melanoma: results of the multicenter selective lymphadenectomy trial (I). *Ann. Surg. Oncol.* 2010; **17**: 3324–9.
15. Isaacs K, Pasquali S, Spillane A, Thompson T. Factors influencing choice of completion lymph node dissection after a positive sentinel lymph node in patients with melanoma: a large single institution experience (PT289). *Ann. Surg. Oncol.* 2017; **24**: S138.
16. Hewitt DB, Merkow RP, DeLancey JO *et al*. National practice patterns of completion lymph node dissection for sentinel node-positive melanoma. *J. Surg. Oncol.* 2018; **118**: 493–500.
17. Livingstone E, Windemuth-Kieselbach C, Eigentler TK *et al*. A first prospective population-based analysis investigating the actual practice of melanoma diagnosis, treatment and follow-up. *Eur. J. Cancer* 2011; **47**: 1977–89.
18. Coit D. The enigma of regional lymph nodes in melanoma. *N. Engl. J. Med.* 2017; **376**: 2280–1.
19. Verver D, van Klaveren D, van Akkooi ACJ *et al*. Risk stratification of sentinel node–positive melanoma patients defines surgical management and adjuvant therapy treatment considerations. *Eur. J. Cancer* 2018; **96**: 25–33.
20. Madu MF, Franke V, Bruin MM *et al*. Immediate completion lymph node dissection in stage IIIA melanoma does not provide significant additional staging information beyond EORTC SN tumour burden criteria. *Eur. J. Cancer* 2017; **87**: 212–21.

21. Coit D, Thompson J, Albertini M *et al*. *Melanoma Version I.2017 – NCCN. Clinical Practice Guidelines in Oncology*, Vol. **1**. 2017; 2016.
22. Morton DL, Cochran AJ, Thompson JF *et al*. Sentinel node biopsy for early-stage melanoma: accuracy and morbidity in MSLT-I, an international multicenter trial. *Ann. Surg.* 2005; **242**: 302–11.
23. Wrightson WR, Wong SL, Edwards MJ *et al*. Complications associated with sentinel lymph node biopsy for melanoma. *Ann. Surg. Oncol.* 2003; **10**: 676–80.
24. Leung AM, Morton DL, Ozao-Choy J *et al*. Staging of regional lymph nodes in melanoma: a case for including nonsentinel lymph node positivity in the American Joint Committee on Cancer (AJCC) staging system. *JAMA Surg.* 2013; **148**: 879–84.
25. Balch CM, Gershenwald JE, Soong SJ *et al*. Multivariate analysis of prognostic factors among 2,313 patients with stage III melanoma: comparison of nodal micrometastases versus macrometastases. *J. Clin. Oncol.* 2010; **28**: 2452–9.
26. Reintgen M, Murray L, Akman K *et al*. Evidence for a better nodal staging system for melanoma: the clinical relevance of metastatic disease confined to the sentinel lymph nodes. *Ann. Surg. Oncol.* 2013; **20**: 668–74.
27. Bigby M, Zagarella S, Sladden M, Popescu CM. Time to reconsider the role of sentinel lymph node biopsy in melanoma. *J. Am. Acad. Dermatol.* 2019; **80**: 1168–71.
28. Faries MB, Cochran AJ, Thompson JF. Re: "Time to reconsider the role of sentinel lymph node biopsy in melanoma". *J. Am. Acad. Dermatol.* 2019; **pii**: S0190-9622(19)30508-0.
29. Wong SL, Faries MB, Kennedy EB *et al*. Sentinel lymph node biopsy and management of regional lymph nodes in melanoma: American society of clinical oncology and society of surgical oncology clinical practice guideline update. *J. Clin. Oncol.* 2018; **36**: 399–413.
30. Xing Y, Bronstein Y, Ross MI *et al*. Contemporary diagnostic imaging modalities for the staging and surveillance of melanoma patients: a meta-analysis. *J. Natl. Cancer Inst.* 2011; **103**: 129–42.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Figure S1. Questionnaire.