

REPLY

MSLT-I—response of clinical trial investigators

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We would like to thank Mark B. Faries, Alistair J. Cochran and John F. Thompson for their correspondence ([MSLT-I—response of clinical trial investigators. *Nat. Rev. Clin. Oncol.*; doi:10.1038/nrclinonc.2014.65-c1](#)),¹ in response to our News and Views article ([Why is sentinel lymph node biopsy ‘standard of care’ for melanoma? *Nat. Rev. Clin. Oncol.* **11**, 245–246; 2014](#)).²

The interpretation of the final results of the Multicenter Selective Lymphadenectomy Trial (MSLT-I) continues to be debated. All agree that sentinel-lymph-node biopsy (SLNB) in patients with melanoma has value as a staging tool that predicts prognosis, and can be used for this purpose if the patient and their physicians wish. The debate is focused on whether SLNB use can improve the overall survival of patients with melanoma. The essence of this debate devolves to the question of whether an elective lymph-node dissection (ELND; in this case directed by SLNB) can affect survival of patients with melanoma. This question has been addressed by four prior randomized studies, all of which failed to show an improvement in overall survival.^{3–6} Although all of these studies can be legitimately criticized (mostly for inadequate power), failing to show a survival benefit in a flawed study cannot allow one to conclude that benefit must be there. These prior studies provided the best data available before the results of the

MSLT-I trial were published, and they did not show a benefit. MSLT-I is also susceptible to criticism regarding the benefit of ELND because it defines lymph-node involvement in the two arms by different criteria when survival is compared in this subset of patients.⁷ Regardless, the primary end point of MSLT-I, melanoma-specific survival, was not significantly different after 1,270 patients were randomly assigned to observation or to SLNB and ELND, if node positive, and followed for over 10 years.⁷ Fortunately, the definitive study on this issue is underway; MSLT-II is randomizing patients with a positive SLNB to undergo or not undergo an ELND.⁸ If this trial shows an improvement in overall survival, then the value of SLNB in defining a population that can benefit from ELND will be established and this approach should become the standard of care. If the survival advantage of node-positive patients in MSLT-I is an accurate estimate of the size of the benefit of ELND, then it might only require approximately 250 patients in each arm of MSLT-II to show a significant benefit. With a targeted accrual of 1,925 patients, this study should be able to firmly close the door on a debate that has raged in various incarnations for over 30 years.

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Competing interests

The authors declare no competing interests.

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