

IN REPLY: We appreciate the interest of Shaw et al in our article on desmoplastic melanoma (DM).¹ Because tumor thickness remains the single most important prognostic variable associated with primary melanomas, it is notable that median tumor thickness of DM patients in our series, other published series, and the group presented by Shaw et al, is significantly greater than in non-DM patients. A valuable perspective on DM biology is therefore obtained by comparing DM patients with non-DM patients who are matched for tumor thickness. The additional matching of non-DM control patients for age, sex, and year of diagnosis aids in reducing variables between the two groups under comparison. The size of our database precludes matching for additional variables, including, as pointed out by Shaw et al, mitotic rate and anatomic site; however, these variables carry significantly less prognostic value. The strategy of using controls matched for important prognostic variables reduces—but does not eliminate—biases introduced by variables other than histology. As such, nowhere did we state that observed differences between the groups are attributable solely to differences in histology.

Our data suggest that DM and non-DM patients matched for tumor thickness differ in their stage at presentation. The observation that the incidence of lymph node and distant metastases at presentation is lower in DM patients despite matching for tumor thickness indicates an important difference in tumor biology between DM and non-DM patients. As suggested by Shaw et al, an additional analysis using a control group matched for stage at presentation would be of interest. Nonetheless, it is reasonable to conclude that the biology of DM influences stage at presentation relative to thickness-matched non-DM controls.

These observations notwithstanding, Shaw et al suggest that the difference in stage at presentation between DM and non-DM patients in our study “casts considerable doubt on the comparative survival outcomes,” relative to their own statement that 280 DM patients enjoyed superior 5-year survival compared with 7,767 other melanoma patients in the Sydney Melanoma Unit (Camperdown, Australia) database. (Notably, Shaw et al provide no information to suggest comparable stage at presentation of their DM and non-DM patients.) As is shown in Tables 4 and 5 of our article, there is no significant difference in the number of patients that developed distant metastases. Since cancer death is a direct result of distant metastasis, this supports the validity of our observation of similar survival rates between non-DM and DM patients with primary lesions of similar thickness.

Shaw et al appear to be concerned that our non-DM group fared worse as a result of biases introduced when selecting this control

group. However, it is notable that the 5-year survival rate of 76.9% in the non-DM group that we reported is close to 5-year survival rates of 70% observed in 5,739 stage II patients in the American Joint Committee on Cancer staging database,² and 80% observed in patients with melanomas measuring 2.5 to 2.7 mm in thickness in the Massachusetts General Hospital (Boston, MA) melanoma database. Moreover, it is reasonable to conclude that had we identified and used a non-DM control group with even earlier stage disease at presentation than the current control group, the 5-year survival of the this non-DM group would stay the same or improve. Consequently, the DM patients would not end up with a 5-year survival superior to non-DM patients.

Regarding the concern that bias is introduced by inclusion of patients with multiple primaries in the survival analyses, exclusion of these patients does not alter our conclusion. The 5-year survival rates of DM and non-DM patients who had only a single primary melanoma are 81% and 82%, respectively ($P = .85$ by log-rank analysis).

We do not advocate withholding of sentinel node biopsy solely on the basis of DM histology. Rather, the rate of positive nodes in DM patients should be integrated with other clinical information to arrive at an appropriate recommendation for each individual patient. DM is an interesting entity that is relevant to all who study and treat melanoma. While we have elucidated similarities and differences in clinical behavior between DM and non-DM, further study is warranted to reveal the biologic mechanisms underlying these observed differences.

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Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.