LETTER FROM DR. KENNETH WILSON

Re: Systemic therapy for patients at high risk for recurrent melanoma. Verma S., Quirt I., McCready D., Charette M., Iscoe N. and the members of the Melanoma Disease Site Group. *Curr Oncol* 2005; 12:31–6.

The conclusions reached in this review are based on incomplete data. In June 2002, the Melanoma Disease Site Group (DSG) sent me a draft manuscript of the above paper to review. I specifically recommended that the proposed guideline should reflect the fact that the E1684 trial is *negative* for overall survival benefit for high-dose interferon (HDIFN) at a median follow-up of 12.6 years (one-sided *p* value 0.09, as dictated by the protocol). Dr. John Kirkwood, principal investigator of the E1684 trial, provided a *p* value for overall survival in a letter to *J Clin Oncol* 2001 in response to a letter of mine seeking same. Unfortunately, Dr. Kirkwood, like the DSG, continues to interpret E1684 as a positive study, in spite of the insignificant *p* value with mature follow-up*. Although the E1684 investigators point to competing causes of death, they have not analyzed disease-specific mortality—or if they have, they have not reported it. They have reported analysis of distant disease-free survival, but this was not a protocol-specified endpoint. During manuscript review, I recommended that the DSG obtain the 12.6-year follow-up data of E1684 to add to their database and conduct joint analysis with other ECOG trials. The DSG have not acknowledged this important follow-up data on E1684 in their guideline. In fact, they reiterate that the ECOG 1684 trial detected a significant improvement in overall survival after "prolonged follow-up." This was in spite of being advised that analysis at a median follow-up of 12.6 years is negative ($p = 0.09$) for overall survival benefit. Consequently, we now have two mature ECOG studies of adjuvant HDIFN that are negative for overall survival benefit.

I believe that the results of E1694 are too preliminary to conclude that HDIFN is superior to GMK vaccine as adjuvant therapy of high-risk melanoma. The importance of mature follow-up is amply demonstrated by the E1684 experience. Indeed, the absence of published follow-up data on the E1694 trial makes one wonder whether the preliminary results are sustained.

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REPLY FROM DR. SHAILENDRA VERMA

Thank you for your comments. We acknowledge and concur with your opinion regarding the assertion that high-dose interferon is associated with a significant survival benefit. Our guideline has been corrected to reflect this, and the latest iteration states that "Our review of the available literature identified no systemic adjuvant therapy that confers a significant survival benefit in patients with high-risk resected primary melanoma. However high-dose interferon treatment should be considered in such patients as such therapy is associated with significant improvement in disease-free survival and reduction in 2-year mortality."

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* Wilson K. High-dose interferon versus GM2 vaccine in high-risk malignant melanoma [comment/reply]. *J Clin Oncol* 2001;19:4350.