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Response

We appreciate the pertinent and timely comments regarding our study. At the time Southwest Oncology Group (SWOG)-8642 was designed, enthusiasm for the use of interferon gamma (IFN γ) in the adjuvant setting was very high, and there was no clinical or scientific reason to expect that such therapy might actually be detrimental. Even today, with the wealth of preclinical and clinical information available regarding the effects of IFN γ, it remains hard to explain the lack of a beneficial effect in this and several other trials conducted in other cancers (*1-3*). We must, however, call attention to the fact that our trial did not clearly demonstrate that patients treated with IFN γ had poorer outcomes than patients on the observation arm. Although disease-free survival was somewhat poorer for IFN γ patients, the difference was not statistically significant (two-tailed $P = .38$ by logrank test for disease-free survival) (*1*). Therefore, we cannot conclude that the prometastatic effect of IFN γ observed in the preclinical models cited by our correspondents translates into a higher incidence of metastases in humans.

On the other hand, our study had limited statistical power to detect a detrimental effect of IFN γ (e.g., we could not reject the alternative hypothesis of a hazard ratio of 1.5 in the analysis of disease-free survival). Thus, while we found no significant evidence of a detrimental effect, our results do not rule out the possibility that IFN γ produced a small to moderate increase in the risk of recurrence or metastasis.

Dr. Lollini and his colleagues are conducting exactly the kind of comparative preclinical investigations of IFN alfa (IFN α) and IFN γ that are critically needed. This is particularly true in view of the observed beneficial effect of adjuvant interferon alfa-2b in melanoma (*4*) and highlights for us once again that the exact mechanisms by which IFN α led to an improvement (or by which IFN γ did not!) remain obscure. We hope that future preclinical studies will generate new leads for improving the results of adjuvant IFN γ therapy, in turn forming the basis of testable hypotheses for a new series of clinical trials.

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