

Immunotherapy for Glioblastoma: The Devil Is in the Details

TO THE EDITOR: In a recent issue of *Journal of Clinical Oncology*, Sampson et al¹ report encouraging progression-free survival and survival data using a vaccine that targets the tumor-specific epidermal growth factor receptor mutation, EGFRvIII. While selectively targeting a tumor-specific mutation with active immunotherapy has been the holy grail of this field for some time, the data presented by these authors also raises some concerns with regard to the value of single-arm phase II trials which have become perennial in neuro-oncology. While the authors' survival statistics are impressive, recent articles^{2,3} demonstrate that such data in the context of single-arm phase II trials can be misleading. In the Sampson et al¹ article, however, additional data is provided which further supports the potential efficacy of the vaccine – that is, the nearly universal elimination of the target antigen in patients whose tumors recur.

Radiation, by its very nature, and temozolomide, as more recently shown,⁴ are mutagenic. In the context of this trial, we must remember that these patients also received both of these standard-of-care therapies. Thus, it is possible that these potent mutagens cause either random or systematic mutations in EGFRvIII, resulting in its apparent absence. This finding might reduce the importance of this article. In contrast, if patients treated with standard-of-care radiation

and temozolomide maintain expression of EGFRvIII, then these authors have strong support for the activity of their vaccine, and the apparent increase in survival that they demonstrate has greater importance. I think it is important for the authors to comment on this issue and perhaps reply within the context of the *Journal*.

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AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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