Phase I Study of Abagovomab in Patients with Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

To the Editor: In their article, Sabbatini et al. (1) describe the phase I data of abagovomab, a murine anti-idiotype antibody to the CA125-specific monoclonal antibody OC125. In their Introduction, they compare abagovomab’s mechanism of action to oregovomab’s, a murine Ab1 antibody to CA125. The authors describe treatment with oregovomab as “passive immunotherapy” and state that oregovomab is “unlikely to be associated with induction of CTL responses.” We respectfully disagree and would like to highlight some of the literature describing the immunostimulating properties of oregovomab. Unlike classical passive immunotherapy, oregovomab has been shown to generate CA125-specific immune responses via the formation of highly immunogenic complexes with circulating CA125, and to a lesser degree, via the activation of the idiotypic network (2). The antibody facilitates the uptake and immune processing of the CA125 antigen in dendritic cells and enhances the cross-presentation of the antigen into the HLA class I pathway, leading to CA125-specific CTL, T helper cell and antibody responses (3). Favorable clinical outcomes have been associated with the induction of antibodies to oregovomab and, in a limited series, with treatment-emergent induction of T cells specific for autologous tumor and CA125 (4). Due to the high human anti-mouse antibody levels that patients generate in response to murine antibody administration, considerable assay development has been undertaken for all assays, particularly for cytokine arrays, to ensure that the immune response measurements observed were real and not an artifact of human anti-mouse antibodies. In this context, we wonder if the cytokine analysis presented in this article had taken into account the potential interference of human anti-mouse antibody levels in the selected Luminex assay. Finally, we would like to request some clarification on the induction of CA125-specific B and T cell responses. Their Fig. 1 represents the frequency of Ab3 induction, which should not be equated with anti-CA125 antibody induction as not all Ab3 bind to the original antigen. We would appreciate if the authors could comment on the percentage of patients mounting antibodies in the cell-based assay and on the specificity of these antibodies. ELISPOT data are shown after a 14-day in vitro sensitization step with ACA125 and CA125. The data are encouraging; however, it would be informative if the responses were shown separately for ACA125– (antibody) and CA125– (antigen) specific components. In our experience, for example, a significant portion of oregovomab-treated patients mount T cell responses to the constant domains of the murine antibody, which has also likely been observed with abagovomab.

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