Re: Granulocyte–Macrophage Colony-Stimulating Factor Gene-Modified Autologous Tumor Vaccines in Non–Small-Cell Lung Cancer

Nemunaitis et al. (1) in their phase I/II study evaluated the feasibility, safety, and efficacy of vaccination with autologous tumor cells genetically modified with an adeno-viral vector to secrete human granulocyte–macrophage colony-stimulating factor (GM-CSF) in patients with early and advanced stage non–small-cell lung cancer. They found that three of 33 advanced-stage patients, two with bronchioloalveolar carcinoma, had durable complete tumor responses (lasting 6, 18, and >22 months). This exciting result may be related to activity of GM-CSF on recently defined cells termed “cancer stem cells.”

There is overwhelming evidence that virtually all cancers are clonal and represent the progeny of a single cell. The unclear point is which clonogenic cells within the tumor clone possess tumor-initiating cell function and are capable of maintaining tumor growth (2). Stem cells have the ability to divide almost indefinitely. The division can give rise to a new stem cell as well as to differentiated cells of the tumor. These cancer stem cells, which have not been characterized totally, may carry almost the same as antigens hematopoietic stem cells. GM-CSF may activate and repopulate these stem cells in addition to stimulating blood stem cells. Thus, differentiated cancer cells may become more antigenic for host as in the patients with a diagnosis of bronchoalveolar carcinoma. Activated cancer stem cells also become chemosensitive to various cell-cycle-specific chemotherapeutic agents. Therefore, use of GM-CSF with chemotherapy in practice may result in better outcome in epithelial cancers.

KADRI ALTUNDAG
OZDEN ALTUNDAG
MUSTAYA CENGIZ
MEHMET GUNDUZ
YAVUZ OZISIK
REFERENCES


NOTES

Affiliations of authors: Department of Medical Oncology, Hacettepe University Faculty of Medicine, Ankara, Turkey (KA, YO); Department of Medical Oncology, Numune Education and Research Hospital, Ankara, Turkey (OA); Department of Radiation Oncology, Hacettepe University Faculty of Medicine, Ankara, Turkey (MC); Department of Otolaryngology, Graduate School of Medicine and Dentistry, Okayama University, Shikata, Japan (MG).

Correspondence to: Kadri Altundag, MD, 8181 Fannin St., #728, Houston, TX 77054 (e-mail: drkadri@usa.net).

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