Gene Therapy Promising for Cutaneous Lymphoma

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KYOTO, JAPAN — Intratumoral interferon-gamma gene therapy delivered via an adenoviral vector induces systemic as well as local immune responses in patients with primary cutaneous T- or B-cell lymphoma, reported Dr. Mirjana Urosevic reported.

This novel approach to interferon-gamma gene transfer using an intralesionally injected adenoviral vector showed impressive safety and tolerability as well as promising efficacy in a multicenter combined phase I/II clinical trial, according to Dr. Urosevic of the University of Zürich.

Recombinant interferon-alfa and -gamma therapy have demonstrated efficacy in primary cutaneous lymphomas. However, it is accompanied by severe systemic toxicity, she said at an international investigative dermatology meeting.

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Dr. Urosevic and her coworkers believe that placing substantial quantities of the interferon-gamma gene within a tumor will result in production of sustained high levels of the cytokine by the patient's own cells without systemic toxicity.

Incorporating the interferon-gamma gene into an adenoviral vector offers a substantial bonus, she said: The vector itself appears to have therapeutic efficacy. The nonreplicating recombinant adenovirus Dr. Urosevic and her colleagues are using, known as TG1042, activates interferon-alfa genes, resulting in increased intralesional expression of interferon-alfa, supplementing the tumor-rejecting effects of the transgene-induced interferon-gamma.

She reported on 33 evaluable patients who received the investigational gene therapy at six centers in Switzerland, Germany, and France in an open-label clinical trial. Twenty-eight had cutaneous T-cell lymphoma and five had cutaneous B-cell lymphoma. All had advanced disease and previously had failed to respond to at least two first-line forms of therapy.

The injected tumors showed a partial response in 10 patients and a complete response in 9 others, for an overall 57% local clinical response rate. Half of the cutaneous T-cell lymphoma patients had a local therapeutic response, as did, notably, all five with cutaneous B-cell lymphomas, she said.

Fourteen patients experienced global responses, with regression of untreated as well as treated lesions. Seven of these patients had complete responses, while the rest demonstrated partial responses.

The treatment regimen consisted of once-weekly intratumoral injection of $3x10^{11}$ viral particles for 3 weeks, then a 2-week break, followed by a patient evaluation. If the patient was stable or had at least a partial response, then treatment resumed; if the disease progressed, treatment stopped. These three-injection cycles were repeated for up to 12 cycles, or 36 injections, Dr. Urosevic reported at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

All patients have mounted neutralizing antiadenovirus antibodies in response to the vector. However, these antibodies have not blocked the interferon response to the gene transfer or the vector itself, she said.

The study was sponsored by Transgene of Strasbourg, France. ■