Immune system–boosting agent CpG-B reduced early-stage melanoma recurrences

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Among patients with clinically stage 1 or stage 2 melanoma, those treated with the immune system–boosting agent CpG-B were less likely to experience recurrence of their disease than those who received placebo, according to results from two randomized, placebo-controlled phase II clinical trials presented at the CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference, held Sept. 16–19.

"Even though stage 1 and stage 2 melanomas can be removed surgically, in a considerable proportion of patients cells from the tumor have already spread and eventually lead to tumor recurrence," said Tanja D. de Gruijl, PhD, professor and head of the immunotherapy lab in the Department of Medical Oncology at the VU University Medical Center Cancer Center Amsterdam in the Netherlands. "We set out to investigate whether intradermal [within the skin] injection of the immune-stimulatory compound CpG-B around the site of surgical removal of the primary tumor could boost patients' antimelanoma immune responses and provide local and systemic protection against early metastatic events that could otherwise lead to tumor recurrence.

"We found that there was a significant prolongation of recurrence-free survival among the patients who had received CpG-B compared with the patients who received saline placebo," continued de Gruijl. "The apparent clinical effect was much stronger than we had anticipated and underlines the powerful ability of the immune system, provided it is properly activated, to control melanoma."

CpG-B is a reagent that closely resembles a stretch of bacterial DNA, explained de Gruijl. It is perceived by the human immune system as a sign of danger that calls for an immune response.

From 2004 to 2007, de Gruijl and colleagues enrolled 52 patients with clinically stage 1 or stage 2 melanoma in the two clinical trials. Patients were assigned intradermal injection of either CpG-B or saline. Injections were administered directly adjacent to the site of surgical excision of the primary melanoma tumor, seven and two days before re-excision and sentinel lymph node biopsy, which de Gruijl explained are part of the standard of care at VU University Medical Center Cancer Center Amsterdam.

The researchers found that after a median follow-up of 76.5 months, two of the 30 patients assigned CpG-B and nine of the 22 patients assigned placebo had experienced melanoma recurrence.

"Our results imply that local conditioning of the melanoma excision site by simple intradermal administration of an immune-stimulatory compound like CpG-B can lead to boosting of a systemic antimelanoma immune response that affords protection against recurrences in the long term, with minimal transient side effects," said de Gruijl. "We plan to conduct a large, randomized phase III clinical trial of intradermal CpG-B versus saline to confirm our findings of prolonged long-term recurrence-free survival."

According to de Gruijl, the major limitations of the study are that the data are the combined results of two phase II clinical trials with low numbers of enrolled patients and that different CpG-B doses were used in the two clinical trials. The low patient numbers mean that a large, randomized phase III clinical trial is needed to confirm the current promising findings, she added.