Intratumoral injection of DNA encoding human interleukin 12 into patients with metastatic melanoma: clinical efficacy

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Plasmid DNA encoding human interleukin 12 (IL-12) was produced under GMP conditions and injected into lesions of nine patients with malignant melanoma (stage IV) previously treated with both standard and nonstandard therapies. The treatment was based on efficacy in preclinical studies with melanoma in mice and gray horses. The DNA was applied in cycles, three injections per cycle, for up to seven cycles. Three therapy arms comprised low (2 mg), medium (4 mg), and high (10 to 20 mg) amounts of total DNA. The therapy was well tolerated. Three of nine patients experienced a clinical response: two stable disease and one complete remission. One patient receiving a low dose of DNA experienced a long-lasting stabilization of the disease for more than 3 years, whereas the other two responders received high doses of DNA. All patients but one (patient 9) experienced a transient response at the intratumoral injection site. Immunohistochemical staining of responder sections showed local reduction of angiogenesis and lymphocyte infiltrations. All patients, in particular the clinical and local responders (patients 3, 7, and 8), exhibited an antigen-specific immune response against MAGE-1 and MART-1, which in some cases preexisted. Biopsies of responders showed some increase in IL-12, IP-10, and IFN-γ. Serum levels revealed fluctuations. The results show that intratumoral injection of DNA produced some beneficial clinical effect. DNA encoding a cytokine may be useful as a therapeutic or adjuvant against various human cancers.

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