Systemic anti-tumor effect and clinical response in a phase 2 trial of intratumoral palisomat interleukin-12 in patients with advanced melanoma.

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ABSTRACT

Background: Intratumoral IL-12 (pIL-12) promotes anti-tumor activity through multiple mechanisms, including augmentation of adaptive and innate immune responses. Intratumoral delivery of IL-12 via electroporation (EP) avoids systemic toxicity while promoting systemic antitumor immunity. This phase 2 study explored the systemic efficacy, clinical response and safety of pIL-12 in 12 patients (pts) (10 treatment cycles of 4 pIL-12 EP on days 1, 5, 8 in up to four lesions per cycle) in a maximum of 4 cycles. At 12-week intervals, 200 μg was assessed by a modification of RECIST for new lesions with metastasis, eventually selected for IL-12 EP.

Methods: This open-label, exploratory phase 2 study plan 4 treatment cycles (100 μg for IL-12) in pts with metastatic IL-12 resistant and safety of IL-12 plasmid EP (pIL-12) (28). Following 12 cycles of 4 (6), pIL-12 with aerosol epinephrine.

RESULTS

Population: 28 pts were randomized with stage IIIB-IV melanoma or cutaneous or intransit lesions accessible to treatment.

Treatment: One treatment cycle consists of one IL-12 EP cycle on days 1, 5, 8 in up to four lesions per cycle. A maximum of fourcycles.

End points: Local treatment with pIL-12 EP is well tolerated without severe systemic side effects. Local treatment and non-injected controls suggest systemic induction of systemic antitumor immune response Local and systemic immune therapies are consistent with the measured pharmacodynamic effect of IL-12. Based on these data, an expanded protocol to evaluate increased treatment frequency is planned for melanoma patients.

INTRODUCTION

Intratumoral IL-12 (pIL-12) shows promising antitumor activity through multiple mechanisms, including augmentation of adaptive and innate immune responses. Intratumoral delivery of IL-12 via electroporation (EP) avoids systemic toxicity while promoting systemic antitumor immunity. This phase 2 study explored the systemic efficacy, clinical response and safety of pIL-12 in 12 patients (pts) (10 treatment cycles of 4 pIL-12 EP on days 1, 5, 8 in up to four lesions per cycle) in a maximum of 4 cycles. At 12-week intervals, 200 μg was assessed by a modification of RECIST for new lesions with metastasis, eventually selected for IL-12 EP.

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