LTX-315, an oncolytic peptide converts immunogenically "cold" tumors to "hot" in a majority of patients with advanced or metastatic tumours: results from an ongoing phase I study

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Background: Intratumoral LTX-315 disintegrates cytoplasmic organelles with release of tumor antigens in preclinical models accompanied by increase in tumor-infiltrating lymphocytes (TILs). LTX-315 induced complete regression in several rodent models, with systemic immune responses. LTX-315 is strongly synergistic preclinically with immune checkpoint inhibitors (ICI). We are conducting a phase 1 trial to evaluate LTX-315 in combination therapy.

Methods: Patients with advanced metastatic solid tumours received injections of LTX-315 into a single accessible tumour over 6 weeks. Additional injections could be administered thereafter every 2 weeks. Biopsies of injected lesions were taken at baseline, and on treatment.

Results: 28 have been enrolled to date, median age is 58 (range 32-80) and median prior treatments 2 (range 1-14). LTX-315 monotherapy was administered at doses of 2-7mg to a median of 1.8 tumour lesions (range 1-6) for a median of 9 weeks (range 1-33). In 24 patients all LTX-315-related adverse events were CTC grade 1 or 2, most commonly local erythema, flushing, pruritis and hypotension, most resolving within minutes of injection. Related grade 3 (3 patients) or 4 (1) allergic/anaphylaxis adverse event occurred and resolved without sequelae. Best response in 44 injected lesions in 20 evaluable patients included 2 complete responses, $\geq$ 50% reduction in 5 tumours, and 20 stable (injected). Significant increases in TILs occurred in 67% (14 of 21) patients with biopsies of injected tumours available. Regression of distant non-injected tumour has been observed clinically on biopsy (abscopal effect). No RECIST response in non-injected tumours has been observed in 16 evaluable patients. Stable disease (median duration 14 weeks) occurred in 50% of patients as best response (melanoma (4), sarcoma (3), breast (1)).

Conclusions: This phase 1 study demonstrates that intratumoural LTX-315 has a manageable safety profile and induces increases in TILs in heavily pre-treated patients. Partial and complete regression was seen in some injected tumours. Evaluation of LTX-315 in combination with ICIs in breast and melanoma is ongoing.