A phase I, dose escalation study of LTX-315 as monotherapy or in combination with either ipilimumab or pembrolizumab, in patients with transdermally accessible tumors (NCT01986426)

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Background
LTX-315, a first in class oncolytic peptide is developed from host defense peptides that have an important function in innate immune responses to microbial pathogens (1).

Pre-clinical studies of LTX-315 demonstrate:
• Unique immunogenic cell death
• Targets and disintegrates intracellular organelles
• Release of patient immune stimulating molecules and tumor antigens (2)
• Increase infiltration of CD8+ T cells in both injected and non-injected tumors (3)
• Reduce number of Treg and MDSC in injected tumors
• Systemic tumor specific immune responses

LTX-315 demonstrates synergy with anti-CTLA4 or anti-PD-1 (4)

Study design
Arm A: Single lesion treatment arm
Patients with at least 1 injection tumor lesion, LTX-315 injection follows a sequential schedule with each lesion treated for 6 weeks (induction treatment) followed by bi-weekly maintenance treatment

Arm B: LTX-315 Monotherapy in patients with any solid tumor
Patients with different doses of LTX-315 starting with 3 mg. In all cases a minimum of one lesion is treated with a fixed dose of LTX-315 given as a single agent.

Arm C: LTX-315 in combination with ipilimumab in patients with unresectable/metastatic malignant melanoma
Patients with different doses of LTX-315, starting with 3 mg. In all cases a minimum of one lesion is treated with a fixed dose of LTX-315 in combination with standard approved ipilimumab (3 mg/kg 4 infusions).

Arm D: LTX-315 in combination with pembrolizumab in patients with unresectable/metastatic triple negative breast cancer
Patients with different doses of LTX-315, starting with 3 mg. In all cases a minimum of one lesion is treated with a fixed dose of LTX-315 in combination with pembrolizumab dose 200 mg (every 21 days).

Inclusion criteria
Arm A/B:
• Unresectable advanced or metastatic disease (any tumor type) and previously untreated patients with available standard of care (or not available standard of care) treatment or are not candidates for standard of care treatment

Arm A:
• At least one available lesion (cutaneous, subcutaneous or lymph node) for injection which is between 1 and 3 cm in diameter, and one bystander (non-injected) lesion

Arm C:
• Unresectable/metastatic diagnosis of malignant melanoma (histologically confirmed)

Arm D:
• Unresectable/metastatic diagnosis of triple negative breast cancer (histologically confirmed)

Exclusion criteria
Arm A/B:
• Known hypersensitivity to any of the excipients pembrolizumab infusion.

Arm A:
• Known hypersensitivity to any of the excipients ipilimumab infusion.

Arm C:
• Known hypersensitivity to any of the excipients pembrolizumab infusion.

Arm D:
• Known hypersensitivity to any of the excipients pembrolizumab infusion.

Conclusion
• LTX-315’s unique “release and reshape” property makes it ideal for combination with other types of immunotherapy.

Biopsy/Resection schedules
• All available biopsy/Resection schedules to include up to three core biopsies.

Recommended Phase II dose
The decision on the optimal phase II LTX-315 treatment regimen will be based on the results of the dose escalation cohorts from the following information:
• Safety parameters (DLT, AEs etc.)
• Immunological infiltrate and responses to LTX-315 as a monotherapy, in combination with ipilimumab or pembrolizumab.

References
3. Dose data on file, manuscript in preparation