LTX-315, a first in class oncolytic peptide reshapes the tumor microenvironment in the majority of patients with advanced metastatic tumors: Results from an ongoing clinical phase I study

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Background
LTX-315 is a first in class oncolytic peptide with unique “release and reshape” properties. Pre-clinical studies of LTX-315 demonstrate:
- Unique immunogenic cell death mode of action by targeting the mitochondria
- Disinhibition of cytoplasmic organelles resulting in effective release of chemokines, danger signals and a broad repertoire of tumor antigens
- Reduced number of immunosuppressive cells
- Enhanced infiltration of T cells and T cell clonality
- Complete regression of injected and non-injected tumors (i.e. Abscopal effect)

A Phase I clinical trial was initiated to evaluate the potential benefit of the oncolytic peptide LTX-315 as a novel intralesional therapeutic strategy.

Aim
The aim of this study is to evaluate the safety and tolerability of intra-tumoral LTX-315 monotherapy and determine the recommended phase II dose and schedule.

LTX-315’s “Release and Reshape” MoA

Study Design
Primary Endpoints
- Safety (including DLTs, AEs, SAEs, lab assessments) of LTX-315
- Inflammatory markers in injected tumor tissue, such as tumor infiltrating lymphocytes

Secondary Endpoints
- Local effects of LTX-315 by assessment of:
  - Necrosis in index lesions determined by ultrasound and resection/biopsy
- Systemic immunological response with LTX-315 in peripheral blood

Safety Summary

- Doses of between 2-7mg per injection have been evaluated; no MTD was observed
- LTX-315-related adverse events (any grade) have been observed in 21 of 28 patients who received ≥ 1 LTX-315 injection
- 7 of 26 patients (25%) had CTC ≥ 3 grade 3 AEs including allergic reaction/anaphylaxis (4), pain on injection (2) and sepsis (1)
- 3 of 4 episodes of ≥ grade 3 LTX-315 related allergic reaction/anaphylaxis occurred; 3 occurred after > 10 weeks of treatment; one was a DLT and occurred in week 2

LTX-315 safety (n=28)

Immune related response (irRC) assessment

Stable disease (SD) median duration 11 weeks by irRC was observed in 8 of 15 evaluable patients (53%)

LTX-315 converts cold tumors to hot

- Biopsies of injected tumors taken at baseline and after treatment have been obtained in 13 patients. All biopsies were taken in up to 3 planes of orientation.
- Enhanced infiltration of CD8+ T-cells in injected lesions in 15 of 17 patients (88%)

Conclusion

- LTX-315 is generally safe and tolerable, the majority of toxicities are transient grade 1-2, and include hypotenison (asymptomatic) flushing, paresthesia and rash
- No MTD has been reached
- Regression in injected and non-injected lesions observed:
  - Stable disease (SD) median duration 11 weeks by irRC was observed in 8 of 15 evaluable patients (53%)
  - Abscopal effect observed
- Elevation of tumor infiltrating lymphocytes in injected lesions was observed in 15 of 17 (88%) evaluable patients
- The HaloDx Immune Gene Expression Signature Immunosign® 21 analysis of LTX-315 treated tumors shows:
  - Clear effect on key genes (effector T cell, Th1, orientation, chemokines and cytokines) involved in immune-mediated tumor regression
- LTX-315 converts cold tumors to hot, as evident by immune phenotyping using gene expression analysis
- Results support the rationale and potential benefit of LTX-315 as a novel intratumoral immunotherapy
- Combination testing of LTX-315 with immune checkpoint inhibitors is ongoing in melanoma and breast cancer

References
2. Sveinbjørnsson, B. et al.; Future Medicinal Chemistry (2017)