A Phase I study with LTX-315 – an immunogenic cell death inducer
- in patients with transdermally accessible tumours

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Background

Host defense peptides are naturally occurring cationic peptides that have an important function in innate immune responses to microbial pathogens [1]. Through structure-activity relationship studies we have designed the LTX-315, a short oncolytic peptide derived from a host defense peptide. Chemical structure of LTX-315

Study design

In nontoxic studies LTX-315 has demonstrated:

- Equally active against drug-resistant and drug-sensitive tumour cells [2].
- Complete regression in several different tumour models [3].
- Release of a number of danger signal molecules (DAMPs) [4].
- Protection against rechallenge, i.e. "memory" response [3].
- Rapid disruption of the cell membrane

Aim

A phase I dose escalating open label, single centre study was designed to evaluate safety profiles and determine recommended dose. Immunological responses to the injections were exploratory endpoints (5).

Safety results

Patients received weekly transdermally applied injections of LTX-315 into a transdermally accessible tumour for a maximum of 6 injections

Efficacy results

Breast cancer patient – Cohort 1

A reduction of tumour volume of 50% was also observed in the breast cancer patient (Baseline (14 x 6 mm)                  After 6 injections (10 x 4 mm)

References


Acknowledgement

Institutional administration of LTX-315 induces cellular lysis (necrosis), leading to release of intracellular content consisting of danger signals such as ATP and HMGB1 together with host defence peptides. These events initiate the maturation and recruitment of DCs into the tumour bed. Activated DCs are then primed for antigen processing and antigen presentation to T cells, creating tumour-specific cytotoxic CD8+ T cells that are capable of eradicating residual cancer cells.

Overall conclusion

- The main safety issues were primarily dose-related flushing and transient hypotension
- Tumour-infiltrating lymphocytes and tumour regression were observed in some patients
- The findings confirm the rationale and potential benefit of LTX-315 as a novel intradermal immunotherapy
- A Phase II/III study with LTX-315 is ongoing at four sites in Europe (ClinicalTrials.gov NCT01986426)

Aknowledgement

4. Dr. Christian Kersten, Southern Hospital Trust, Australia
5. LYTIX SFI Research

ClinicalTrials.gov NCT01058616

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