Intra-tumoural treatment with LTX-315, an oncolytic peptide immunotherapy, in patients with advanced metastatic disease induces infiltration of CD8 effectors T-cells and regression in some injected tumors

JAMES SPIKER1, AHMAD AWAIDA1, PAUL F. BRUNSVIG2, REBECCA KRISTELEIT2, DAG ERIK JESSANG2, ANDREW SANDERS2, WENCHE MARIE OLSEN2, BERIT NICOLAISEN1, DYSTEIN REKDAL1, MARIE LARUELLE1, FEBY MARQUADJ1, JALAL VAKIL3, PHILIPPE AFTIMOS3, PHILIPPE BARTHELEMY4, SANJEEV DEVA4, NINA LOUISE JEBSEN4, JEAN-FRANCOIS BAURAIN4

1King’s College London, Guy’s Hospital, UK, 2Institut Jules Bordet, Université Libre de Bruxelles, Belgium, 3Orso University Hospital, Norway, 4University College London Hospital, UK, 5Haukeland University Hospital, Norway, 6Lytyx Biopharma, Norway, 7UL St. Luc, Belgium

Background

LTX-315, a first-in-class oncolytic peptide is developed from host defense peptides that have important functions in innate immune responses to microbial pathogens (1). Pre-clinical studies of LTX-315 demonstrate:
- Induction of immunogenic cell death.
- Release of potent immune stimulating molecules (2).
- Destruction of intracellular organelles resulting in the release of tumour antigens (3).
- Equally effective against drug-resistant and drug-sensitive tumour cells.
- Complete regression of injected and non-injected tumours (i.e. abscopal effect) (4).

A phase 1 clinical trial was initiated to evaluate the potential benefit of the oncolytic peptide LTX-315 as a novel intra-tumoural therapeutic strategy (5).

Rapid disruption of the cell membrane
- Effect on Meth A sarcoma cell

Mechanism of Action of LTX-315

Rapid release of intracellular contents

Primary targets

- Immature DC

Tumour cell engulfment

Activation and augmentation of tumourspecific CTLs

Study design

Primary Endpoints
- Safety: Dose limiting toxicities (DLT), adverse events, optimal dose and schedule
- Immunological markers in tumour tissue (i.e. tumour infiltrating lymphocytes)

Secondary Endpoints
- Local effects of LTX-315 in injected lesions (i.e. necrosis, inflammation)
- Immunological response of LTX-315 in peripheral blood (T lymphocytes, cytokines, CD8)
- Pharmacokinetic (PK) profile of LTX-315
- Anti-tumour activity of LTX-315 by immune-related response criteria (IRC) for non-injected lesions

Inclusion Criteria
- Histologically confirmed advanced/metastatic disease of any type
- At least one transcutaneously accessible lesion ≤10 cm in diameter
- ECOG Performance status (PS): 0 - 1

Exclusion Criteria
- Constitutional drug therapy within 4 weeks prior to study
- Immunosuppressive or passive therapy within 6 weeks prior to study
- External radiotherapy or cytotoxic chemotherapy within the last 4 weeks prior to study
- Immunotherapy or vaccine therapy within 6 weeks prior to study

Limiting Dose - DLT
- All lesions
- 4 mg OD
- 4 mg QD (N=3)
- 5 mg OD (N=3)
- 5 mg QD (N=3)
- 2x3 mg (N=2)
- 2x2 mg (N=2)
- 2x1 mg (N=2)

Overall conclusion
- This phase 1 study with LTX-315, an oncolytic peptide immunotherapy, is ongoing.
- The majority of LTX-315 related AEs are transient CTCAE grade 1-2 and include hypothyroidism, flushing, parasthesia and rash.
- No Dose Limiting Toxicities (DLTs)
- Tumour necrosis and increased TLS in injected lesions in some patients (6/15)
- No irRC responses were observed.
- Complete (1/15) and partial (2/15) regressions in 6 of 18 injected lesions; no change (44%) in 8 of 19 injected lesions.
- Stable disease (median duration 14 weeks) in non-injected tumour lesions (by IRC) in 6 of 9 evaluable patients (67%)
- The findings support the rationale and potential benefit of LTX-315 as a novel intra-tumoural immunotherapy.
- Phase II combination studies with LTX-315 in multiple solid tumours are planned for 2015.

References
2. Camus et al., Cancer Immun Therapeutics (2014)
4. Riedel et al., Oncoimmunology
5. Brummett et al., Abstract 3076 AIS 2014

Lytyx Biopharma A/S | P.O. Box 6447 | NO-9294 Tromsø, Norway | E-mail: post@lytyxbiopharma.com | Phone: +47 77 67 55 00 | Fax: +47 77 67 55 01