A PHASE I STUDY OF THE ONCOLYTIC PEPTIDE LTX-315 GENERATES DE NOVO T-CELL RESPONSES AND CLINICAL BENEFITS IN PATIENTS WITH ADVANCED SARCOMA

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Background

LTX-315 is a first-in-class oncolytic peptide with unique properties to convert "cold" tumors to "hot" (1,2)

Key trials of LTX-315 demonstration:

- Unique immunological cold-to-hot dual mechanism of action by targeting the mitochondria (3-4)
- Disruption of chemokine expression, resulting in effective release of chemokines, danger signals, and a broad repertoire of tumor antigens (3-4)
- Reduced number of immunosuppressive cells (3-4)
- Damped expression of key T-cell co-inhibitors (3-4)
- Complete regression of injected and non-injected tumors (i.e. abscopal effect) (3-4)

Aim

- Evaluate the safety and tolerability of intra-tumoral LTX-315 in patients with transmissible melanomas.
- Evaluate efficacy.
- Determine the recommended phase II dose and schedule.
- Evaluate immune responses in tumor and peripheral blood samples pre and post-treatment.

LTX-315’s unique mode of action results in effective release of potent immunostimulators and antigens

Study design (NCT01986426)

A phase 1 open label, multi-arm, multi-centre, multi-dose study administrating LTX-315 intravascularly to single or multiple transmissively accessible lesions

- Primary Endpoint: Safety, tolerability, and CT scan results in target and parallel lesion.
- Secondary Endpoints: T cell clonality, Gene expression, local tumour therapy.

Patient Population

- Inclusion criteria:
  - Advanced/metastatic sarcoma
  - At least one transdermally accessible lesion
  - At least one transmissively accessible lesion

Study Arms

- Two monotherapy arms:
  - Arm A: Single lesion injected sequentially for 7x followed by maintenance
  - Arm B: Multiple lesions injected concurrently for 3x (pre maintenance)

Key inclusion criteria

- Histologically confirmed adenocarcinoma/malignant disease (all tumors) not suitable for surgery or metastatic treatment
- At least one transmissively accessible lesion of ≥1 cm in diameter
- ECOG Performance status: 0-3
- Meet minimum baseline laboratory criteria

Key exclusion criteria

- Immunosuppressive or recruteur therapy within 2 weeks prior to study entry
- External radiotherapy or systemic chemotherapy within the last 4 weeks prior to study entry
- History of peritonitis
- History of hemoglobin expression, significant CNS metastases
- Pregnant or nursing
- Any prior or active haemopathy B or C

Safety in Monotherapy: all patients

No severe toxicity or related SAEs (NCT03725605).

- All patients were enrolled and evaluable for safety and efficacy assessment.
- Thirty-nine patients were enrolled and had at least one dose of LTX-315 in the monotherapy arms.
- Arm A: 3 Sty patients in ITT population (sarcoma 4:2)
- Arm B: 2 ST patients in ITT population (sarcoma 4:5)

Study Parameter

- Substantial increase in 24 gene signature clonal activity after primary surgical resection.
- Substantial increase in immnosignatures after primary surgical resection.
- Substantial increase in GZMM T-cell clonality in PBMC post treatment.

Results sarcoma patients

Thirty nine patients were enrolled and at least one dose of LTX-315 in the monotherapy arms, thereof:

Arm A: 3 STY patients in ITT population (sarcoma 4:2)
Arm B: 2 STY patients in ITT population (sarcoma 4:5)

- LTX-315 T cell therapy treatment is intended to treat population ALL PATIENTS TREATED WITH LTX-315 MONOTHERAPY

- Best overall response (irRC) and best response in one non-injected lesion

Case #3: LTX-315 local treatment leads to systemic response

- Patient with recurrent metastatic leiomyosarcoma after primary surgical resection
- Treatment with local intratumoral LTX-315, injection in the gluteal muscle lesion
- Disease control ≥14 days, No SDs, grade 2 hypotension post dosing

Summary of sarcoma patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Arm A (n=3)</th>
<th>Arm B (n=2)</th>
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</thead>
<tbody>
<tr>
<td>Response (n=3)</td>
<td>3/3 (100%)</td>
<td>2/2 (100%)</td>
</tr>
<tr>
<td>Overall response</td>
<td>3/3 (100%)</td>
<td>2/2 (100%)</td>
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</tbody>
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THERAPY FOR SARCOMA

Ongoing Trial: LTX-315 in combination with Adoptive T cell therapy for sarcoma patients (NCT03725605)

Study Conclusion

LTX-315:

- In generally safe and tolerable, following incidents of anaphylaxis and allergic reactions, none of which was serious and all of which resolved with standard support measures.
- LTX-315 is being developed as a novel approach to treat sarcoma, which is currently the standard treatment for sarcoma.
- LTX-315 demonstrated a significant increase in immune parameters in tumor and peripheral blood.
- LTX-315 generated a de novo T-cell response in sarcoma patients.
- LTX-315 significantly expanded T-cell clones in injected lesion.
- LTX-315 induced an immune response in sarcoma patients.
- LTX-315 generated a de novo T-cell response in sarcoma patients.
- LTX-315 generated a de novo T-cell response in sarcoma patients.

References