**Background**

LTX-315 is a first in class oncolytic peptide with unique properties to convert "cold" tumors to "hot" as demonstrated by gene expression analysis of tumors post LTX-315 treatment. LTX-315's unique mode of action results in effective release of potent immunostimulants and antigens.

Pre-clinical studies of LTX-315 demonstrate:
- Unique immunogenic cell death mode of action by targeting the mitochondria (3,4).
- Safety profile (clinical, pre-clinical).
- Complete regression of injected and non-injected tumors (e.g., subcutaneous xenografts) (5-10).
- Safety in Monotherapy; all patients treated experienced an acute onset of anaphylaxis or hypersensitivity in ongoing patients to grade 1/2 with treatment and no sequelae.
- Extensive preclinical safety data supporting potential clinical development of LTX-315.
- Background

**Study design (NCT01986426)**

A phase 1 open label, multi arm, multi centre, multi dose study administering LTX-315 intravenously in single or multiple transdermally accessible lesions.

**Primary Endpoints**

- Safety (CTCAE, 4.0).

**Secondary Endpoints**

- Tumor size and gene expression in tumors and peripheral blood
- Tumor antigen activity of LTX-315 by CT scan assessment (IR)
- Patient Populations

- Tumor 
- Solid tumors
- Multiple lesions injected concurrently for 3 weeks (no maintenance)

**Study Arms**

- Two treatment arms:
  - Arm A: Single lesions injected sequentially (no maintenance) for 3 weeks followed by maintenance
  - Arm B: Multiple lesions injected concurrently for 3 weeks post maintenance

**Key inclusion criteria**

- Histologically confirmed advanced/metastatic disease (all tumors) not suitable for further conventional therapy.
- At least one transdermally accessible lesion ≤ 1.0 cm in diameter.
- ECOG Performance status (PS): 0 – 2.
- Meet minimum laboratory criteria

**Key exclusion criteria**

- Immunosuppressive or reciept therapy within 2 weeks prior to study entry
- External radiotherapy or systemic chemotherapy within the last 4 weeks prior to study entry
- History of allergies disease
- Known human immunodeficiency virus (HIV) infection or positive test for antibodies to HIV
- History of active or latent tuberculosis
- History of major medical or surgical condition
- Pre-existing local or regional CNS metastasis
- Active malignancy or history of malignancy
- History of prolonged bleeding time
- history of disease or event that in the opinion of the investigator would preclude treatment with LTX-315.

**Safety in Monotherapy; all patients**

- Thirty nine patients were enrolled and had at least one dose of LTX-315 in the monotherapy arms, thereof:
  - Arm A: 5 melanoimun patients in ITT population (melanomas 1G-5)
  - Arm B: 3 melanoma patients in ITT population (melanomas 6-8).

**Summary of melanoma patients**

<table>
<thead>
<tr>
<th>Case #</th>
<th>Sex</th>
<th>Age</th>
<th>Race</th>
<th>Disease</th>
<th>Treatment</th>
<th>ECOG PS</th>
<th>Best overall response</th>
<th>ImmunoSign® 21 gene signature</th>
<th>Immunostimulant &amp; Antigen</th>
<th>Safety &amp; Immunology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>64</td>
<td>White</td>
<td>Uveal</td>
<td>irPD 3/B</td>
<td>0</td>
<td>CR</td>
<td>12%</td>
<td>Anti-tumor T-cell response</td>
<td>Reduces the size of several non-injected lesion, indicating a systemic response</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>74</td>
<td>White</td>
<td>Skin</td>
<td>irSD</td>
<td>0</td>
<td>PR</td>
<td>14%</td>
<td>Anti-tumor T-cell response</td>
<td>Reduces the size of several non-injected lesion, indicating a systemic response</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>64</td>
<td>White</td>
<td>Unk</td>
<td>irSD</td>
<td>0</td>
<td>PR</td>
<td>14%</td>
<td>Anti-tumor T-cell response</td>
<td>Reduces the size of several non-injected lesion, indicating a systemic response</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>41</td>
<td>White</td>
<td>Ciliary</td>
<td>irSD</td>
<td>17/A</td>
<td>PR</td>
<td>14%</td>
<td>Anti-tumor T-cell response</td>
<td>Reduces the size of several non-injected lesion, indicating a systemic response</td>
</tr>
</tbody>
</table>

**Study Conclusion**

LTX-315: a first in class oncolytic peptide with unique properties to convert "cold" tumors to "hot". The findings described herein validate the clinical development of LTX-315, which is generally safe and tolerable; following incidents of anaphylaxis and allergy with minimal sequelae, the treatment approach is simple and meaningful progress is introduced. The majority of toxicities were self limited, and included immunologic hyperactivity (including uncharacterised anaphylaxis), nausea, vomiting, and diarrhea in connection with incidents of anaphylaxis. It is a tolerable agent.

The clinical design of LTX-315 will be optimised and advanced to position LTX-315 as a potentially new drug to be considered for use in the clinic. Further data are needed to assess the impact of LTX-315 in combination with other immunotherapies to decrease the potential for development of resistant disease.

**References**


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

AURELIEN MARABELLE1, JEAN-FRANCOIS BAURAIN2, AHMAD AWADIA, REBECCA KRISTELEIT3, DELPHINE LOIRAT2, DAG ERIK JØSSANG7, NINA LOUISE JEBSEN7, BALDUR SVEINBJØRNSSON8, VIBEKE SUNDVOLD GJERSTAD8, OLEUS UNIVERSITY HOSPITAL, OSLO, NORWAY; 3 INSTITUT JULES BORDET, UNIVERSITÉ LIBRE DE BRUXELLES, BRUSSELS, BELGIUM; 4 UNIVERSITY DE LIEGE, INSTITUTE OF IMMUNOLOGY, CATHOLIQUE DE LIEGE, BRUSSELS, BELGIUM; 5 UNIVERSITY COLLEGE LONDON HOSPITAL, LONDON, U.K.; 6 HAUKELAND UNIVERSITY HOSPITAL, BERGEN, NORWAY; 7 KINGS’S COLLEGE LONDON, GUY’S HOSPITAL, LONDON, U.K. 8 INSTITUTE OF ONCOLOGY, UNIVERSITY OF BERKELEY, BERKELEY, CALIFORNIA.

**RESULTS**

**LTX-315’s unique mode of action**

Ineffective release of potent immunostimulants and antigens

**Immunostimulant & Antigen**

- Anti-tumor T-cell response
- Reduces the size of several non-injected lesion, indicating a systemic response

**Safety & Immunology**

- Further conventional therapies.
- Following incidents of anaphylaxis and allergy with minimal sequelae, the treatment approach is simple and meaningful progress is introduced.
- The majority of toxicities were self limited, and included immunologic hyperactivity (including uncharacterised anaphylaxis), nausea, vomiting, and diarrhea in connection with incidents of anaphylaxis. It is a tolerable agent.

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**References**