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

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**Aim**
- Evaluate the safety and tolerability of intra-tumoral LTX-315 in monotherapy or in combination with either ipilimumab or pembrolizumab in patients with transversally accessible tumors.
- Determine the recommended phase II dose and schedule.

LTX-315 is a first in class oncolytic peptide with unique “release and reshape” MoA

**Study Design**

**Primary Endpoints**
- Safety (including DLTs, AEs, SAEs, lab assessments) of LTX-315

**Secondary Endpoints**
- LTX-315 related immune parameters in tumor and peripheral blood
- Anti-tumor activity of LTX-315 by CT scan assessment (immune-related response criteria (irRC))

**Patient population**
- Advanced/metastatic disease (all tumor types)
- At least one transversally accessible lesion of ≤ 10 cm in diameter

**LTX-315 Monotherapy**

<table>
<thead>
<tr>
<th>LTX-315 dose per injection</th>
<th>No. of patients</th>
<th>Tumor type</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 mg (2-6 injections per lesion)</td>
<td>21</td>
<td>Breast (5); Pancreas (6); Neuroendocrine (1); Adrenal (1); Uterine (1); Prostate (2); Nasopharynx (1)</td>
</tr>
<tr>
<td>0 mg (no injections)</td>
<td>2</td>
<td>Breast (2)</td>
</tr>
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**LTX-315 + Ipiilimumab**

<table>
<thead>
<tr>
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<th>No. of patients</th>
<th>Tumor type</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 mg (2-6 injections per lesion)</td>
<td>4</td>
<td>Breast (3); Pancreas (1)</td>
</tr>
</tbody>
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**LTX-315 + Pembrolizumab**

<table>
<thead>
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<th>No. of patients</th>
<th>Tumor type</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 mg (2-6 injections per lesion)</td>
<td>5</td>
<td>Breast (5)</td>
</tr>
</tbody>
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**LTX-315: Safety (N=51)**

**Immune related response (irRC) assessment**

**LTX-315 generates a systemic tumor specific immune response**

Case study: patient 471-016, Breast cancer, Monotherapy

- 128 T cell clones expanded in blood post treatment.
- Clones expanding in blood were predominantly detected in post-treatment tumor samples.

**T cell clones expanded in blood are detected in post-treated tumors**

- Clones expanding in blood are detected in post-treatment tumor biopsies; median 49%, 6 patients analyzed.
- In contrast, the expansion of pre-treatment tumor associated clones is less in all but one patient; median 29%.
- Contracted clones in blood were not detected in the tumor in 2 of the 6 patients.

**Study Conclusions**

- LTX-315 converts “cold” tumors to “hot”, as evidenced by increase of tumor infiltrating lymphocytes (CD8+ T cells) and gene expression analysis.
- TCR clonality analysis of blood and tumor samples show that LTX-315 generates a systemic anti-tumor T cell response.
- LTX-315 is generally safe and tolerable. No MTD has been reached.
- Stable disease (SD) by irRC observed with LTX-315 monotherapy (8/15 pts).
- Durable SD by irRC observed (1/4 pts) with LTX-315 + ipilimumab (32 wks, ongoing).
- Partial Remission (PR) by irRC observed (1/6 pts) with LTX-315 + pembrolizumab (10 wks, ongoing).
- Results support the rationale and potential benefit of LTX-315 as a novel intratumoral immunotherapy. A phase II multi-arm combination trial is planned in 2018.