Complete regression and long-term specific protective immune responses obtained in rodent tumor models after intratumoral treatment with LTX-315

Ø. REKDAL, G. KVALHEIM, PD. LINE, B. ROLSTAD, K. CAMILIO, G. BERGE, J. NESTVOLD, MY. WANG, J. SHI, A. AREFFARD, B. SVEINBJÖRNSSON,
Oslo University Hospital, The Norwegian Radium Hospital, University of Oslo, University of Tromsø, Lytix Biopharma AS, NO-9294 Tromsø, Norway.

Background
LTX-315 was tested against drug-sensitive and drug-resistant cancer cell pairs from different origins, including direct killing of pathogens and immune-modulating properties. Some host defense peptides were re-challenged with HCC cells, both after complete regression (Fig 8) and immune-responses were obtained in all syngeneic models (Table 2).

A phase 1 study has been completed with LTX-315 (data under analysis) and an outline of a further clinical study is in progress.

Several host defense peptides have shown to confer a complete and permanent tumor regression of progressing tumors in naïve animals.

Figure 2. In vitro killing kinetic of LTX-315

Figure 3. LTX-315-induced release of the danger signal molecule HMGB1

Figure 4. Effect of LTX-315 in a rat transformed mesenchymal sarcoma model (rTMSC).

Figure 5. Infiltration of immune cells in LTX-315-treated tumors

Figure 6. LTX-315 treatment results in the release of cytokines induced in inflammatory responses

Figure 7. Transfer of immunity by splenocytes from animals cured by LTX-315

Figure 8. Protective immune responses in a rat hepatocellular carcinoma model

Fig 9. The effect of LTX-315 treatment combined with surgery in a rat hepatocellular carcinoma model.

Table 2. Effect of LTX-315 in rodent tumor models

Table: Activity is not affected by drug resistance

<table>
<thead>
<tr>
<th>Drug-resistant</th>
<th>Drug-sensitive</th>
<th>Normal cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Conclusion
LTX-315 may represent a new potential drug for treatment of chemoresistant solid tumors.

References
1. Utsugi et al., Cancer Res. 1991, 1;51(11):3062-6
4. Woehlecke et al., Biochem J. 2003, 1;376(Pt 2):489-95
6. Fischer 344 rats.
7. Complete regression and long-term specific protective immune responses obtained in rodent tumor models after intratumoral treatment with LTX-315.