Enhanced antitumor activity achieved by combining the oncolytic peptide LTX-315 with anti-PD-L1 antibody

K. A. Camilio, B. Swinhorn, S. Maubant, G. Serin, J.-F. Mirjolet, F. Bichat, Ø. Rekdal
Lytx Biopharma AS, Norway; Department of Medical Biology, Faculty of Health Sciences, University of Tromso, Norway; Gudbrandsdøen, Dyrøy, France

For more information: contact@oncodesign.com / oystein.rekdal@lytixbiopharma.com

Background

The need for new and improved anticancer therapies is imperative, with an increased focus on immunotherapy and the combination of different treatments to achieve a synergistic antitumor effect and maximize the following immune engagement and activation.

LTX-315 (Oncopore™) is a novel oncolytic peptide derived from the naturally occurring host defense peptide, bovine lactoferrin [1]. LTX-315 interacts electrostatically with anionic components of negatively charged cancer cell membranes as well as intracellular targets such as mitochondria, causing cellular lysis and a subsequent release of endogenous cellular content including danger signals and tumor antigens [2-7].

Targeting immune checkpoints such as programmed cell death protein 1 (PD1), programmed cell death 1 ligand 1 (PD-L1) and cytotoxic T lymphocyte antigen 4 (CTLA4) has achieved noteworthy benefit in multiple cancers by blocking immuno-inhibitory signals and enabling patients to produce an effective antitumor immune response. Programmed cell death ligand 1 (PD-L1) is an immune checkpoint ligand expressed on immune cells, some normal tissues and many tumors. PD-L1 binds to PD-1 on lymphocytes to inhibit T cell receptor signaling and activation.

Aim

To investigate the antitumor effects of LTX-315 in combination with anti-PD-L1 Ab in the EMT-6 mouse breast carcinoma model.

Study design

Animals were randomized on D10 and treated during the treatment period. Mice were injected subcutaneously (SC) with EMT-6 tumor cells on D0 and then on D3.

Treatment with LTX-315 alone had no effect compared to untreated (tumor volumes of treated groups were not statistically different from the untreated group) (Figure 1A). Treatment with LTX-315 in combination with anti-PD-L1 Ab resulted in significant antitumor activity compared to either treatment alone (Figure 1B).

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Survival

Treatment with LTX-315 in combination with anti-PD-L1 Ab resulted in an increase of overall survival compared to either treatment alone.

Tumor free animals

The combination therapy resulted in more tumor free animals compared to either monotherapy, indicating an augmentation of the systemic antitumor response.

Conclusions

LTX-315 shows an enhanced antitumor effect when combined with anti-PD-L1 Ab compared to either of the compounds alone.

LTX-315 in combination with anti-PD-L1 Ab induced enhanced effect against non-treated tumors compared to anti-PD-L1 Ab alone.

The oncolytic peptide LTX-315 is a promising candidate for combination therapy with immune checkpoint inhibitors.

LTX-315 is currently in clinical phase I/IIa studies.

References

1. Haug et al. (2016)
2. Zhou et al. (2014)
3. Camilio et al. (2015)
5. Elke et al. (2015)
7. Zhou et al. (2016)

Figure 1. Survival analysis.

A) Mice were injected subcutaneously (SC) with EMT-6 tumor cells on D0 and then on D3.

B) Tumor growth inhibition (T/C %): last time point at which at least 80 % of mice from all analyzed groups were still alive.

Each point represents the median of the recorded tumor volume per group.

2. Zhou et al., Cancer Immun Immunother. 2014
3. Camilio et al., Oncotarget. 2015
4. Zhou et al., Oncotarget. 2015
5. Elke et al., Oncotarget. 2015
6. Forver, et al., Cell Cycle. 2015

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