The oncolytic peptide LTX-315 enhances T cell clonality and induces synergy with CTLA-4 blockade

REKDAL Ø.1 CAMILIO K.2 YUSKO E.3, VIGNALI M.4, SANDERS C.5, BENZENO S.5, NESTVOLD J.1, SAUNDERS A.5 YAMAZAKI T.1 ZITVOGEL L.1, SVENBJÖRNSSON B.1,2

Lytix Biopharma, Oslo, Norway; 1Adaptive Biotech, Seattle, United States; 2University of Oslo, Oslo, Norway; 3Gustave Roussy Cancer Campus, Villejuif, France, University of Tromsø, Tromsø, Norway.

Background
- LTX-315 induces complete regression and adaptive tumor-specific immune responses in several rodent tumor models [1].
- In some animal models LTX-315 has demonstrated abscopal effects, i.e. effects on non-treated lesions.
- LTX-315 targets and disintegrates the mitochondrial membrane and subsequently other cytoplasmic membranes resulting in the release of DAMPs (Damage-Associated Molecular Pattern molecules) such as ATP, cytochrome C and HMGB1 [1-5].
- Multi-domain proteins from the BCL-2 family seem to be partially involved in LTX-315 mediated killing [5].
- LTX-315 increases the T-cell clonality or non-infiltrated control tumors [c]. Immunolabeling with anti-CD3 showed many of the infiltrating immune cells to be CD3+ T cells [a], compared to low-tumor tissue necrosis [b]. Tumors injected with LTX-315 exhibited B16 tumors were surgically excised 24h and 120h post-injection with vehicle [a and b] or LTX-315 [c and d].

Aim
- Investigate whether LTX-315 enhances T cell inflammation in the tumor microenvironment and thereby expands the proportion of responders to checkpoint inhibitors.

Results

Fig. 1 LTX-315 induces complete regression of B16F1 tumors

Fig. 2 LTX-315 induced T-cell infiltration in treated B16 melanomas

Fig. 3 LTX-315 increases the T-cell clonality

Fig. 4 LTX-315 treatment of B16 melanomas inhibits lung tumor foci formation in the B16 metastasis model

Fig. 5 LTX-315 increased anticancer immunity mediated by CTLA-4 blockade

Fig. 6 LTX-315 enhances T-cell infiltration in Phase 1 cancer patients

Conclusions
- LTX-315’s ability to increase T-cell infiltration and T-cell clonality makes it ideal as a combination partner for other immunotherapies.
- Combination of LTX-315 and immune checkpoint inhibitors (anti-CTLA-4) demonstrate significant synergy.
- LTX-315 combined with either anti-PD1 or anti-CTLA-4 in a clinical setting is under planning.

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SAUNDERS A.1, YAMAZAKI T.4, ZITVOGEL L.4, SVEINBJØRNSSON B.1,5
1Lytix Biopharma, Oslo, Norway, 2Adaptive Biotech, Seattle, United States, 3University of Oslo, Oslo, Norway, 4Gustave Roussy Cancer Campus, Villejuif, France, 5University of Tromsø, Tromsø, Norway.

Lytx Biopharma AS | P.O. Box 6447 | NO-9294 Tromsø, Norway | E-mail: post@lytixbiopharma.com | Phone: +47 77 67 55 00 | Fax: +47 77 67 55 01