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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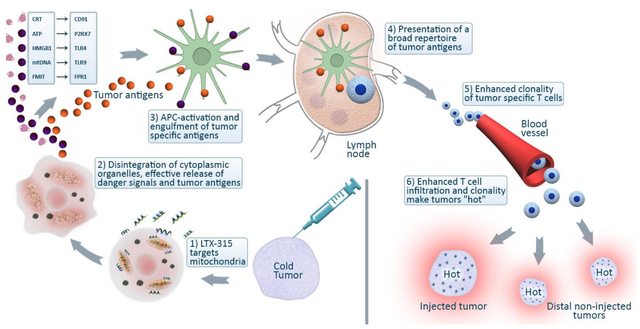
Aim

- Evaluate the safety and tolerability of intra-tumoral LTX-315 in monotherapy or in combination with either ipilimumab or pembrolizumab in patients with transdermally 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 transdermally accessible lesion of ≤ 10 cm in diameter

LTX-315 Monotherapy

LTX-315 dose per injection	No. of patients	Tumor type
Single/sequential lesion injection		
2-7mg (1-2 injections per lesion)	23	Melanoma (7); Breast (6); Sarcoma (3); H&N (3); Adrenal (1); Urethral (1); Desmoid (1); Pancreas
Multiple (≥ 1) lesion injection		
3mg (1-8 injections per lesion)	8	Head & Neck; Breast; Vaginal SCC; melanoma; sarcoma (2); Anal Ca; Desmoid
4mg (1-6 injections per lesion)	5	Head & Neck (2);Anal Ca; Sacroma; Gastric ca

LTX-315 + Ipilimumab

Metastatic melanoma (post-PD1/L1 treatment; multiple (≥ 1) lesion injection)

LTX-315 dose per injection	No. of patients
3mg (1-4 injections per lesion)	4

LTX-315 + Pembrolizumab

Metastatic Triple Negative Breast Cancer (2-5th line); multiple (≥ 1) lesion injection)

LTX-315 dose per injection	No. of patients
3mg (1-2 injections per lesion)	4
4mg (1-6 injections per lesion)	5

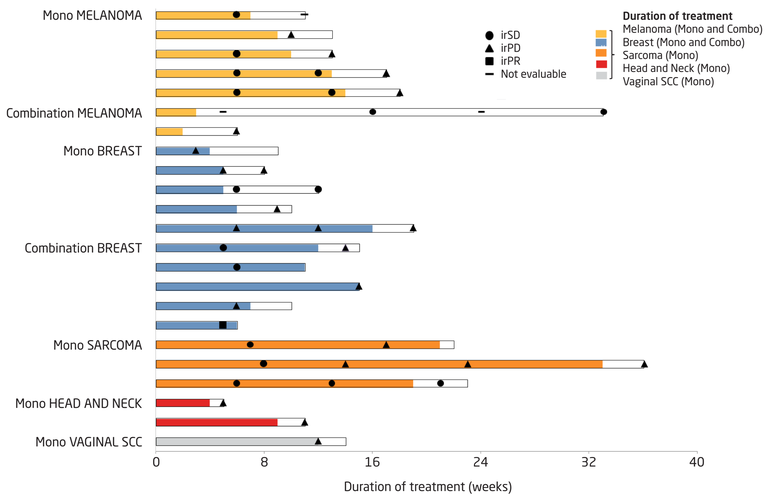
LTX-315: Safety (N=51)

LTX-315 Monotherapy (N=36)*		
LTX-315 related adverse event	Grade 1-2 (No. of pt (%))	Grade 3-4# (No. of pt (%))
Hypotension	10 (28%)	-
Parasthesia	8 (22%)	-
Rash	10 (28%)	-
Flushing	8 (22%)	-
Pruritis	4 (11%)	-
Tumor pain	2 (6%)	2 (6%)
Allergic reaction	1(3%)	4 (14%)
Pain (injection site)	2 (6%)	2 (7%)

LTX-315 Combination therapy (Ipilimumab/pembrolizumab) (N=15)		
LTX-315 related adverse event	Grade 1-2 (No. of pt (%))	Grade 3-4# (No. of pt (%))
Allergic reaction	4 (29%)	1 (7%)
Pain (injection site)	3 (20%)	1 (7%)
Tumor pain	2 (13%)	-
Fatigue	2 (13%)	-
Pneumonitis¥	-	1 (7%)

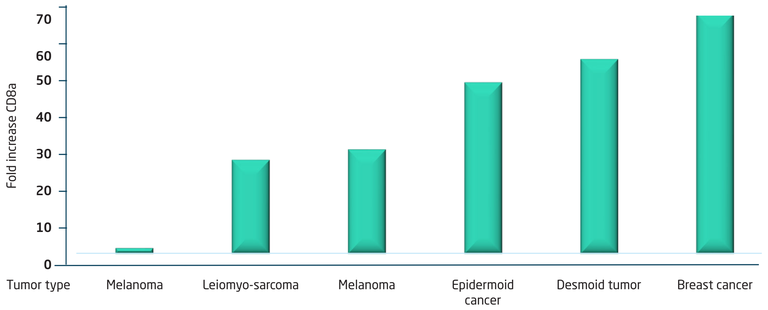
*AEs occuring in ≥ 2 patients per CTC Version 4.0
No grade 4 LTX-315 related AEs reported
¥ Reported as both LTX-315 and Pembrolizumab related

Immune related response (irRC) assessment



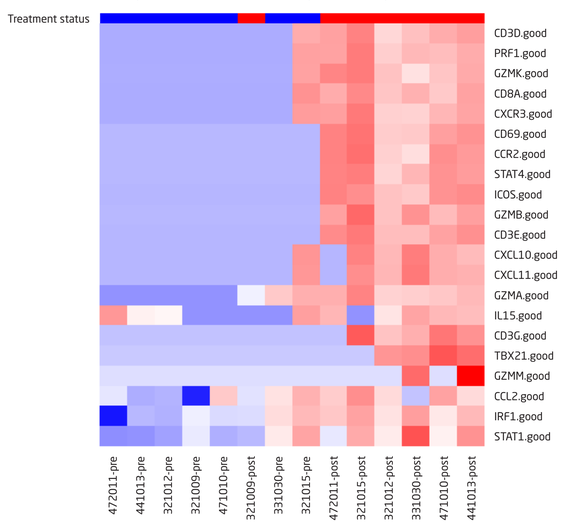
LTX-315 converts cold tumors to hot

Increase in CD8 gene expression in tumors upon LTX-315 treatment



Treatment	No. of patients treated	No. of patients with biopsies evaluable for CD8 IHC to date	No. of patients with increased CD8+ T cells in post treatment tumors
LTX-315	28	17	15 (88%)
LTX-315 + Pembrolizumab	9	5	4 (80%)

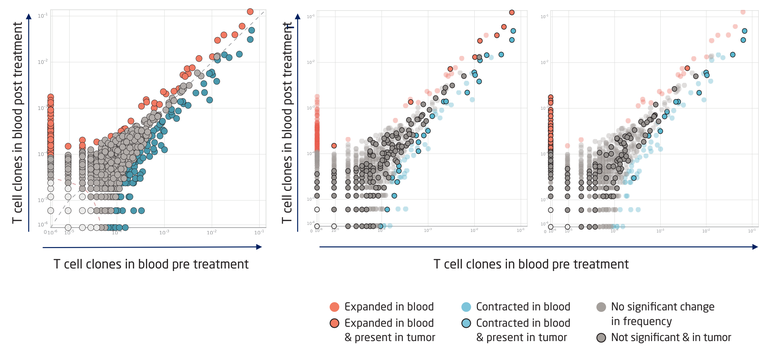
Gene expression in tumor pre and post treatment



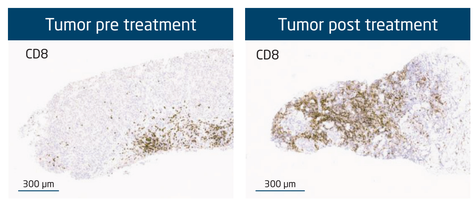
Hierarchical Clustering of Immunosign® 21 Immune Gene Signature (HalioDx) which profiles expressions of a pre-defined set of effector T cell, Th1, chemokine, and cytokine genes.

LTX-315 generates a systemic tumor specific immune response

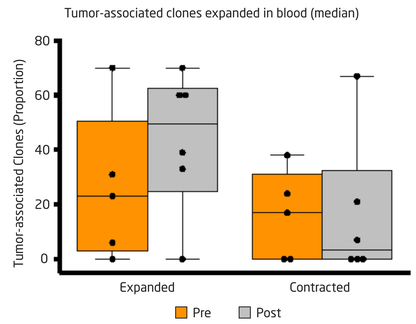
Case study: patient 471-016, Breast cancer, Monotherapy



- 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 23%.
- 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 evidences by increase of tumor infiltrating lymphocytes (CD8+ T cells) and gene expression analysis.
- TCR clonality analysis of blood and tumors 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 mono therapy (8/15 pts)
- Durable SD by irRC observed (1/4 pts) with LTX-315 + ipilimumab (32 wks, ongoing)
- Partial Remission (PR) by irRC observed (1/8 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

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