INTRATUMORAL RUXOTEMITIDE (LTX-315) IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH UNRESECTABLE ADVANCED MELANOMA REFRACTORY TO PD-1/PD-L1 THERAPY: FINAL RESULTS FROM THE ATLAS-IT-05 STUDY

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Poster 3810
AACR Annual Meeting 2026
San Diego

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Introduction

- Ruxotemitide (LTX-315) is a first-in-class non-viral oncolytic peptide being developed for the intratumoral treatment of solid tumors (1).
- Its unique membranolytic action against cytoplasmic organelles results in necrosis-driven immunogenic cell death (Figure 1) (2,3).
- Previous clinical studies have shown regression of injected and non-injected lesions, enhanced CD8+ cytotoxic T lymphocyte infiltration in injected lesions, generation of systemic immune response, and significant expansion of tumor specific T-cell clones upon treatment (4-7).
- This study aims to assess the safety and efficacy of a ruxotemitide/pembrolizumab combination in patients with unresectable, advanced melanoma.

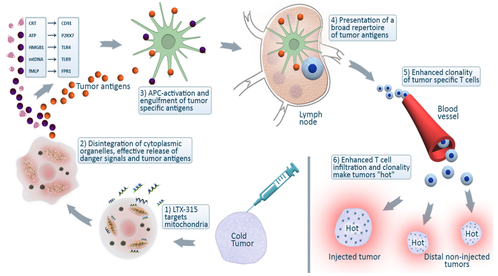

Figure 1: The unique mode of action of ruxotemitide resulting in effective release of potent immunostimulants and antigens

Methods

- A total of 23 patients were enrolled in this study (Figure 2).
- Inclusion criteria for the study included: Histologically confirmed, Stage IIIB-IVm1b unresectable melanoma, confirmed disease progression on or after prior treatment with PD-1/PD-L1 inhibitor, ≤3 prior lines of systemic treatment for metastatic disease, at least 1 superficial; non-visceral tumor accessible for injection, no ocular or mucosal melanoma diagnosis, adequate organ function and LDH ≤ 2 x ULN

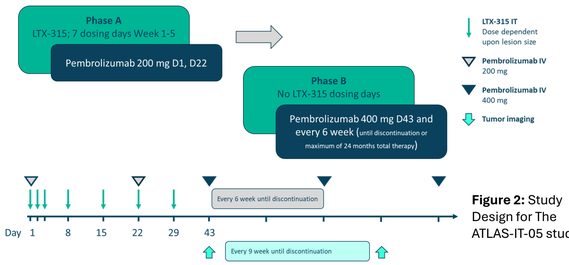

Figure 2: Study Design for The ATLAS-IT-05 study.

- **Endpoints:** Overall response rate (ORR)[a], clinical benefit rate (CBR)[b], progression-free survival (PFS), overall survival (OS), and safety (treatment-emergent adverse events [TEAEs]).

[a]Defined as the proportion of patients who achieved PR and/or CR per local investigator assessment using RECIST version 1.1.

[b]Defined as the proportion of patients who respond to treatment, estimated as the proportion of patients who achieve stable disease, PR, or CR per local investigator assessment using RECIST version 1.1.

Results

Demographics and Disease Characteristics

Table 1: Summary of demographics

Characteristic		N=23
Age, years; Median (Min, Max)		68.0 (42, 91)
Age Group, years; n (%)	≤65	10 (43.5)
	>65	13 (56.5)
Sex; n (%)	Male	13 (56.5)
	Female	10 (43.5)
Prior Lines of Therapy; n (%)	1	3 (13.0)
	2	7 (30.4)
	3	3 (13.0)
	4+	9 (39.1)
	Missing	1 (4.3)
Time From Initial Diagnosis to First Study Treatment months (n=20): Mean (±SD)		65.01 (75.601)
Histological Diagnosis, n (%)	Carcinoid	1 (4.3)
	Melanoma	22 (95.7)
Stage at Screening Visit; n (%)	Stage IIIB	1 (4.3)
	Stage IIIC	5 (21.7)
	Stage IIID	2 (8.7)
	Stage IV m1a	8 (34.8)
	Stage IVC	2 (8.7)
	Stage IV m1b	5 (21.7)
Metastatic Disease Sites, n (%)	Abdominal	1 (4.3)
	Bone	1 (4.3)
	Lung	5 (21.7)
	Lymph Nodes	17 (73.9)
	Other	14 (60.9)
BRAF Mutation Present, n (%)	Yes	7 (30.4)
	No	16 (69.6)
Total Number of Patients Enrolled		23
Patients Included in Safety Population		23
Patients Included in Efficacy Population		22

Best Overall Response

Table 2: Best overall response (Efficacy Population)

Tumor Response	N=22[a]; n (%)
Complete Response	0
Partial Response	3 (13.6)
Stable Disease	6 (27.3)
Progressive Disease	12 (54.5)
Not Evaluable	1 (4.5)
ORR (%, 80% CI[b], 90% CI[b])	13.6 (5.117–27.894, 3.822–31.591)
CBR (%, 80% CI[b], 90% CI[b])	40.9 (26.416–56.752, 23.272–60.484)

[A]One patient was excluded from efficacy analysis due to early withdrawal.
[B]Exact binomial CIs was calculated using the Clopper and Pearson method.
Note: ORR is defined as the proportion of patients who have best overall tumor response of CR and PR during the course of the study. CBR is defined as the proportion of patients who have best overall tumor response of stable disease, CR, and PR during the course of the study.

Overall Response of Individual Patients

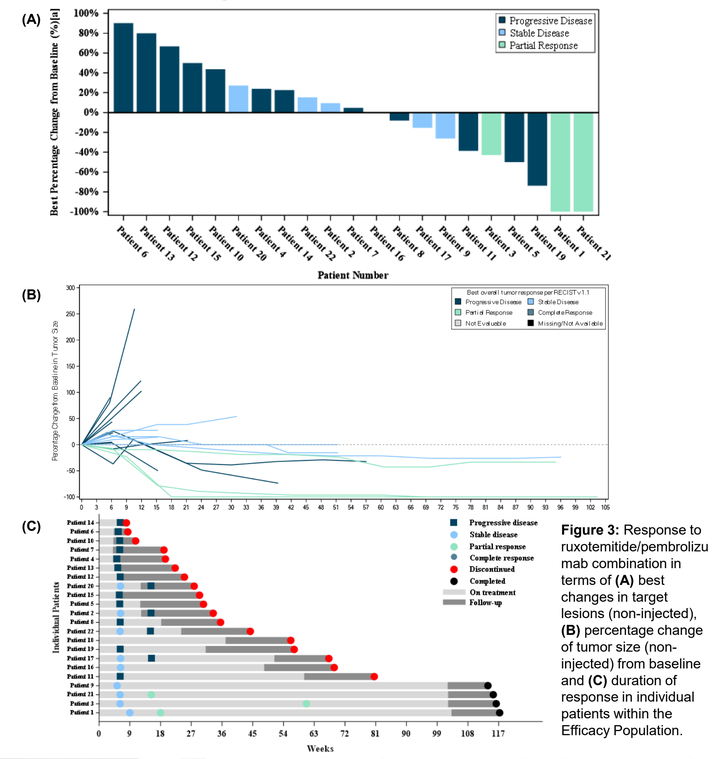

Figure 3: Response to ruxotemitide/pembrolizumab combination in terms of **(A)** best changes in target lesions (non-injected), **(B)** percentage change of tumor size (non-injected) from baseline and **(C)** duration of response in individual patients within the Efficacy Population.

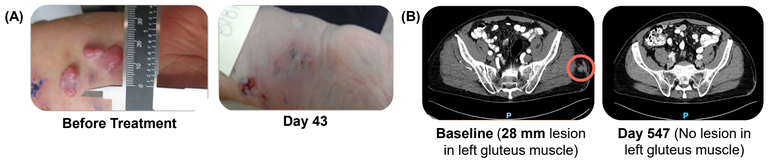

Figure 4: Examples of effects can be seen in **(A)** injected tumors and in **(B)** non-injected tumors where complete regression has occurred.

Progression-Free Survival and Overall Survival

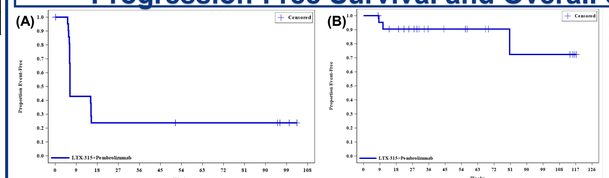

Figure 5: Rates of **(A)** PFS and **(B)** OS in the Efficacy Population.

Safety

Table 3: TEAEs (related and unrelated to ruxotemitide) affecting >10% of patients

Dose: 5 mg (N=23)			
TEAEs	**Grades 1-2**	**Grades 3-4[a]**	**All Grades**
Injection site pain	19 (82.6)	6 (26.1)	21 (91.3)
Injection site erythema	10 (43.5)	1 (4.3)	10 (43.5)
Fatigue	8 (34.8)	1 (4.3)	8 (34.8)
Constipation	7 (30.4)	0	7 (30.4)
Hypotension	6 (26.1)	0	6 (26.1)
Injection site swelling	6 (26.1)	0	6 (26.1)
Pruritus	5 (21.7)	1 (4.3)	6 (26.1)
Abdominal pain	5 (21.7)	0	5 (21.7)
Anaemia	5 (21.7)	1 (4.3)	5 (21.7)
Nausea	5 (21.7)	0	5 (21.7)
Alanine aminotransferase increased	4 (17.4)	0	4 (17.4)
Anxiety	4 (17.4)	0	4 (17.4)
Asthenia	3 (13.0)	1 (4.3)	4 (17.4)
Decreased appetite	4 (17.4)	0	4 (17.4)
Diarrhoea	4 (17.4)	0	4 (17.4)
Myalgia	4 (17.4)	0	4 (17.4)
Oedema peripheral	4 (17.4)	1 (4.3)	4 (17.4)
Urinary tract infection	4 (17.4)	0	4 (17.4)
Vomiting	4 (17.4)	0	4 (17.4)
Abdominal pain upper	3 (13.0)	0	3 (13.0)
Arthralgia	3 (13.0)	0	3 (13.0)
Aspartate aminotransferase increased	3 (13.0)	0	3 (13.0)
Blood lactate dehydrogenase increased	3 (13.0)	0	3 (13.0)
Cough	3 (13.0)	0	3 (13.0)
Dry skin	3 (13.0)	0	3 (13.0)
Flushing	3 (13.0)	0	3 (13.0)
Gamma-glutamyltransferase increased	3 (13.0)	0	3 (13.0)
Headache	3 (13.0)	0	3 (13.0)
Hypertension	1 (4.3)	2 (8.7)	3 (13.0)
Pain in extremity	3 (13.0)	0	3 (13.0)
Pyrexia	3 (13.0)	0	3 (13.0)
Rash maculo-papular	3 (13.0)	0	3 (13.0)
Ruxotemitide-related TEAEs			
Injection site pain	19 (82.6)	6 (26.1)	21 (91.3)
Injection site erythema	10 (43.5)	1 (4.3)	10 (43.5)
Fatigue	7 (30.4)	0	7 (30.4)
Injection site swelling	6 (26.1)	0	6 (26.1)
Pruritus	4 (17.4)	1 (4.3)	5 (21.7)
Hypotension	4 (17.4)	0	4 (17.4)
Flushing	3 (13.0)	0	3 (13.0)
Oedema peripheral	3 (13.0)	0	3 (13.0)

[a]No Grade 4 or Grade 5 TEAEs were noted in the Safety Population.

Conclusions

- Intratumoral treatment with ruxotemitide/pembrolizumab combination demonstrated encouraging antitumor activity in patients with advanced or metastatic melanoma refractory to prior anti-PD-1/PD-L1 therapy.
- Objective responses were observed, and disease stabilization was achieved in a meaningful proportion of patients, with several durable responses ongoing at the time of analysis.
- The combination was generally well tolerated, with a safety profile consistent with the known profiles of ruxotemitide and pembrolizumab, and no new safety signals identified.
- These findings support further clinical investigation of ruxotemitide in combination with PD-1 blockade, including exploration in earlier lines of therapy (neoadjuvant melanoma).

References: 1. Haug, B.E. *et al* Journal of Medicinal Chemistry (2016); **2.** Eike, L-M. *et al* Oncotarget (2015); **3.** Zhou, H. *et al* Cell Death Disease (2016); **4.** Kepp, O. *et al* Journal of Immunotherapy of Cancer (2026); **5.** Jebsen, N *et al* Journal of Medical Case Reports (2019); **6.** Spicer, J. *et al* Clin Cancer Res (2021); **7.** Nielsen, M *et al* Oncoimmunology (2023)