Proof of Concept Study of VP-315, a Non-surgical Immunotherapy in Subjects with Biopsy Proven Basal Cell Carcinoma

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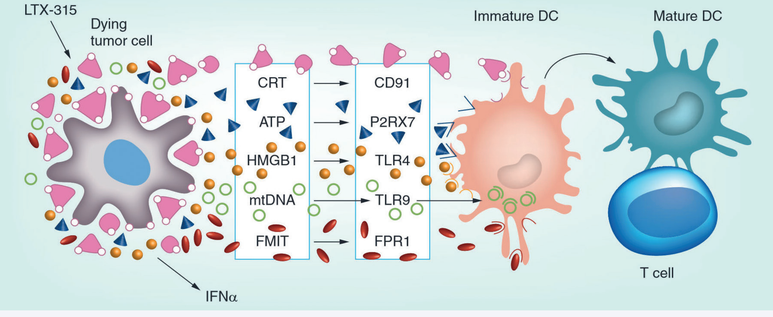
INTRODUCTION

- VP-315 is a de-novo designed, intratumoral injected, chemotherapeutic oncolytic peptide in development for basal cell carcinoma (BCC).
- VP-315 has proven to be effective against a panel of drug resistant cancer cells (including multidrug resistant phenotypes) and activates the adaptive immune system by inducing lysis and immunogenic cell death through release of potent immuno-stimulants and a repertoire of tumor antigens.[1,2]
- LTX-315 is being developed for BCC as VP-315.

Figure 1. LTX-315 (VP-315 for BCC) induces immunogenic cell death in cancer cells[1]



When treated with LTX-315, dying cancer cells release DAMPs such as calreticulin, ATP, HMGB1, mtDNA and formyl peptides. DAMPs bind to specific receptors on antigen-presenting cells such as dendritic cells and promotes their maturation and engulfment of tumor-antigens with subsequent presentation to T cells and execution of effective immune response.

DAMP: Damage-associated molecular pattern; FMIT: Mitochondrial N-formyl peptide; mtDNA: Mitochondria-derived DNA.

OBJECTIVES & ENDPOINTS

- Primary objectives of the study were to assess safety, tolerability, and maximum tolerated dose (MTD) of ascending dose strengths of VP-315 in adult subjects with biopsy proven BCC.
- Primary endpoints of the study included discontinuations due to adverse events (AEs), occurrence of dose-limiting toxicity (DLT), and assessment of expected cutaneous reactions related to treatment at different doses, including lesion necrosis.

METHODS

- This is Part 1 of a 3-part dose-escalation study.
- Part 1: N=10 (total study N=66).
- Subjects received treatment comprised of ascending once daily dosing, up to 3 consecutive treatment days in a 7-day treatment week, followed by no treatment for ≥ 4 days.
- Subjects were treated up to 6 treatments over a 2-week period, in ≤ 2 lesions.

DEMOGRAPHICS

Table 1. Summary of Demographics Baseline Characteristics*

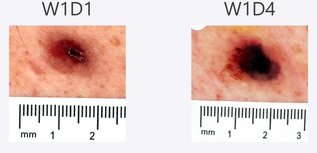
	N	%
Gender at birth (N=10)		
Female	5	50
Male	5	50
Age (N=10)		
Ranges	51-76	
FST (N=10)		
I	3	30
II	4	40
III	3	30
IV	0	0
V	0	0
VI	0	0
Body Area (N=12)		
Arm	2	16.7
Back	6	50
Chest	1	8.3
Clavicle	1	8.3
Neck	1	8.3
Shoulder	1	8.3

** FST=Fitzpatrick Skin Type.*
Two patients had 2 lesions treated.

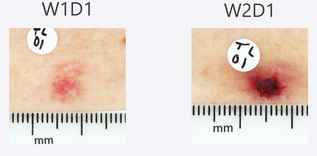
RESULTS

- All 10 subjects completed treatment with VP-315.
- The full target range of doses were well tolerated.
- A maximum dose of 8 mg did not reach a MTD in any subject.
- No subjects experienced DLTs.
- Most TRAEs were mild to moderate, and expected.
- Expected cutaneous reactions were observed.
- No treatment related SAEs were reported.

Images pre and post VP-315 Treatment



BCC, received 3 consecutive daily doses of 8 mg VP-315 with full necrosis observed on W1D4.



BCC, received 3 consecutive daily doses of 8 mg VP-315 and full necrosis observed on W2D1.

BCC=Basal Cell Carcinoma; W1D1=Week 1 Day 1; W1D4=Week 1 Day 4; W2D1=Week 2 Day 1.

RESULTS (CONT)

Table 2. Dose Escalation Scheme by Subject

Subject N=10	# Lesions Treated	Dosage Scheme (mg)	Total # of Treatments	Clinical Necrosis Achieved
1	Lesion 1	2mg, 3mg, 4mg, 5mg, 6mg, 7mg	6	No
2	Lesion 1	3mg, 4mg, 5mg, 6mg, 7mg, 8mg	6	No
3	Lesion 1	4mg, 5mg, 6mg,7mg, 8mg, 8mg	6	No
4	Lesion 1	5mg, 6mg, 7mg	3	Yes
	Lesion 2	6mg, 7mg, 8mg	3	Yes
5	Lesion 1	7mg, 8mg, 8mg	3	Yes
	Lesion 2	8mg, 8mg, 8mg	3	Yes
6	Lesion 1	8mg, 8mg, 8mg, 8mg	4	Yes
7	Lesion 1	8mg, 8mg, 8mg	3	Yes
8	Lesion 1	8mg, 8mg, 8mg	3	Yes
9	Lesion 1	8mg, 8mg, 8mg	3	Yes
10	Lesion 1	8mg, 8mg, 8mg	3	Yes

CONCLUSIONS

- VP-315 demonstrated a tolerable safety profile.
- Subjects receiving the higher range of dosing experienced a consistent response of clinical tumor necrosis.
- VP-315 warrants continued research as a potential non-surgical immunotherapy for BCC.

References

1. Sveinbjørnsson, Baldur et al. "LTX-315: a first-in-class oncolytic peptide that reprograms the tumor microenvironment." *Future Medicinal Chemistry* 9 12 (2017): 1339-1344.
2. Eike LM, Yang N, Rekdal Ø, Sveinbjørnsson B. The oncolytic peptide LTX-315 induces cell death and DAMP release by mitochondria distortion in human melanoma cells. *Oncotarget.* 2015 Oct 27;6(33):34910-23.

Disclosures

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