Results of a Phase 2 Multicenter Study Evaluating the Safety and Tolerability of VP-315, an Investigational Therapy for Basal Cell Carcinoma

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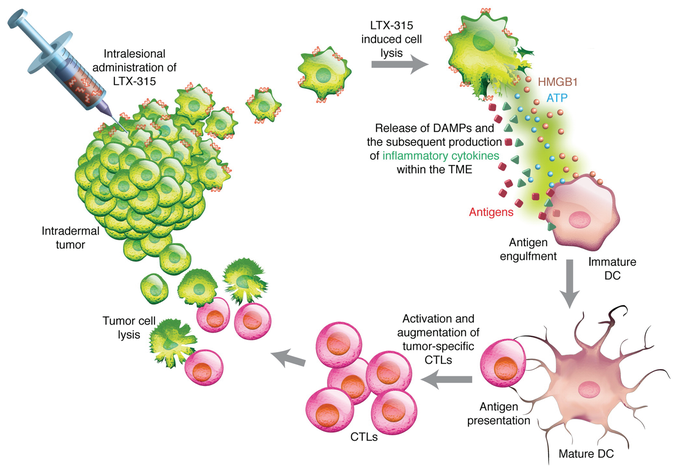
INTRODUCTION

- VP-315 is an intratumorally injected, chemotherapeutic oncolytic peptide in development as a non-surgical immunotherapeutic agent to be utilized as first-line therapy in a primary or neoadjuvant setting for patients with basal cell carcinoma (BCC).
- Intratumoral injection of VP-315 induces lysis and tumor cell death releasing a repertoire of potent tumor antigens that then activate the adaptive immune system.



ATP=adenosine triphosphate; DAMPs=danger-associated molecular pattern molecules; DC=dendritic cell; CTLs=cytotoxic CD8+T lymphocytes,. HMGB1=high mobility group box protein 1; TME=tumor microenvironment

LTX-375 is being studied as VP-315 in BCC.

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OBJECTIVE

In part 2 of this study, the primary objective for Cohorts 1 and 2 was to determine the optimal regimen for dosing 8 mg of VP-315 based on safety and tolerability. For Cohorts 4 and 5, to gain additional information on the safety, tolerability, and dosing regimen of VP-315 to support a pivotal study protocol design.

METHODS

- Eighty-two (82) subjects with up to 2 target BCC tumors were treated intratumorally with VP-315 for up to 2 weeks. Cohort 3 was not enrolled based on results from Cohorts 1-2. Each 7-day treatment week was comprised of 2 or 3 consecutive treatment days followed by a no-treatment period of at least 4 days. In Cohort 4, each BCC was treated for 2 consecutive days. In Cohort 5, each BCC was treated for 3 consecutive days. A subject could have up to two target (treated) tumors.
- Safety and tolerability were assessed by documenting the occurrence of Treatment Related Adverse Events (TRAEs), including those of special interest, Treatment Related Serious Adverse Events (TRSAEs), discontinuations due to AEs and expected treatment-related cutaneous reactions including tumor necrosis.

Table 1. VP-315 Study Design – Part 2

Cohorts	W1D1	W1D2	W1D3	W1D4	W2D1	W2D2	W2D3	W2D4*
Cohort 1 Loading Dose (n=6)	4 mg loading	8 mg	8 mg	Safety	8 mg	8 mg	8 mg	Safety
Cohort 2 No Loading Dose (n=3)	W1D1	W1D2	W1D3	W1D4	W2D1	W2D2	W2D3	W2D4
	8 mg	8 mg	8 mg	Safety	8 mg	8 mg	8 mg	Safety
Cohort 4 2-day Dosing Regimen (n=36)**	Lesion #1 Treatment				Lesion #2 Treatment			
	W1D1	W1D2	W1D3	W2D1	W2D1	W2D2	W2D3	W3D1
	30/70 8 mg	30/70 8 mg	Safety	Limited Safety	30/70 8 mg	30/70 8mg	Safety	Limited Safety
Cohort 5 3-day Dosing Regimen (n=37)**	Lesion #1 Treatment					Lesion #2 Treatment				
	W1D1	W1D2	W1D3	W1D4	W2D1	W2D1	W2D2	W2D3	W2D4	W3D1
	30/70 8 mg	30/70 8 mg	30/70 8 mg	Safety	Limited Safety	30/70 8 mg	30/70 8 mg	30/70 8 mg	Safety	Limited Safety

** Cohort 3 was not enrolled based on results from Cohorts 1-2.*
*** 8 mg total dose split into 2 injections, 30% given initially followed 15-30 minutes later (70%).*

METHODS (CONT.)

Table 2. Baseline Demographics

	Cohort 1 (N=6)	Cohort 2 (N=3)	Cohort 4 (N=36)	Cohort 5 (N=37)	Total (N=82)
Gender					
Female	3	1	19	16	39
Male	3	2	17	21	43
Age	63.66	65.00	64.63	65.32	64.72
Ranges	48-74	61-72	44-87	44-88	44-88
FST					
I	0	0	2	8	10
II	6	3	26	22	57
III	0	0	7	7	14
IV	0	0	1	0	1
V	0	0	0	0	0
VI	0	0	0	0	0

	Cohort 1 (N=6)	Cohort 2 (N=3)	Cohort 4 (N=36)	Cohort 5 (N=37)	Total (N=82)
Body Area					
Arm	1	0	9	8	18
Back	6	0	7	14	27
Chest	0	1	7	7	15
Clavicle	0	0	1	0	1
Neck	0	0	1	5	6
Shoulder	0	0	8	6	14
Abdomen	0	2	2	0	4
Leg	1	0	1	5	7
Face	0	0	4	1	5

RESULTS

All 82 subjects completed one of the VP-315 treatment regimens for BCC. TRAEs were mostly mild to moderate. AEs included injection site pain (mild 13.4%, moderate 12.2%, severe 1.2%), hypertension (mild 4.9%), hypotension (mild 4.9%), erythema (mild 1.2%, moderate 2.4%), and headache (mild 2.4%). Expected cutaneous reactions were observed. No TRSAEs were reported.

Table 3. Preliminary Treatment Emergent Adverse Events

(Excluding Cutaneous Injection Site Reactions), (N=82 Subjects)

	Mild n (%)	Moderate n (%)	Severe n (%)
Injection site pain	11 (13.4)	10 (12.2)	1 (1.2)
Hypertension	4 (4.9)	0 (0.0)	0 (0.0)
Hypotension	4 (4.9)	0 (0.0)	0 (0.0)
Erythema	1 (1.2)	2 (2.4)	0 (0.0)
Headache	2 (2.4)	0 (0.0)	0 (0.0)

CONCLUSIONS

VP-315 treatment was shown to be safe and well tolerated when administered once daily 2-3 times per week per tumor for up to 2 weeks using a split-dose approach. Given its favorable safety profile, VP-315 warrants continued research as a potential non-surgical immunotherapy for BCC as a first-line therapy in a primary or neoadjuvant setting.

References

1. Sveinbjørnsson B, et al. *Future Med Chem.* 2017;9(12):1339-44.
2. Eike LM, et al. *Oncotarget.* 2015;6(33):34910-23.

Disclosures

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