Results of a Phase 2 Multicenter Study to Evaluate the Efficacy of VP-315, an Investigational Therapy for Basal Cell Carcinoma

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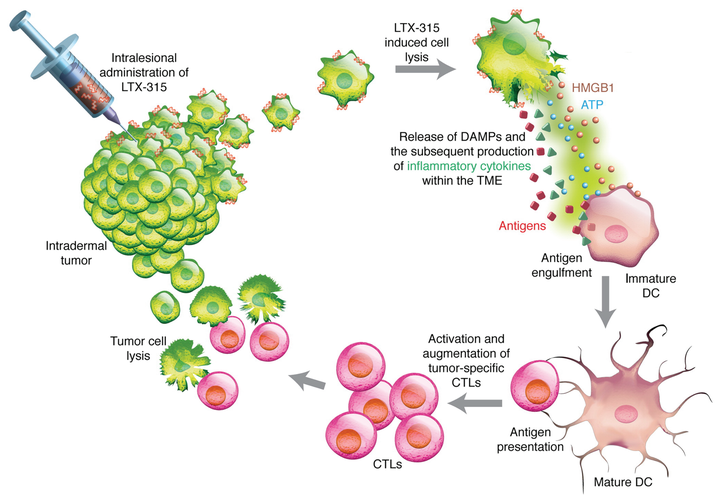
INTRODUCTION

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 activatate 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 secondary objective for Cohorts 1 and 2 was to evaluate the antitumor efficacy of 8 mg of VP-315. For Cohorts 4 and 5, to confirm the antitumor efficacy of 8 mg of VP-315 using the optimal dosing regimen.

METHODS

Eighty-two (82) subjects with up to 2 target BCC tumors (total 92 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.

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%).*

RESULTS

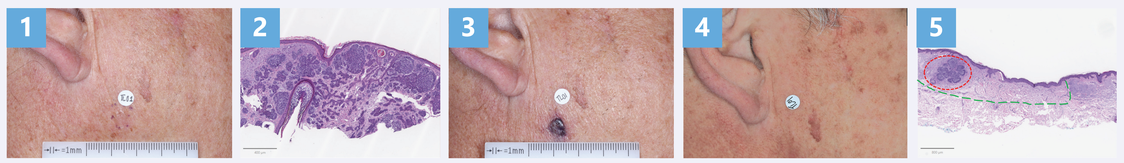
Eighty-two (82) subjects (n=92 tumors) completed treatment for BCC with VP-315 in Part 2. Approximately 52% of tumors achieved complete histologic clearance. All tumors treated had a reduction in tumor size. Overall tumor size reduction was 86%. Tumor size reduction in subjects who still had any residual tumor was 71%.

Table 2. Mean Percent Reduction in Tumor Clearance and Size

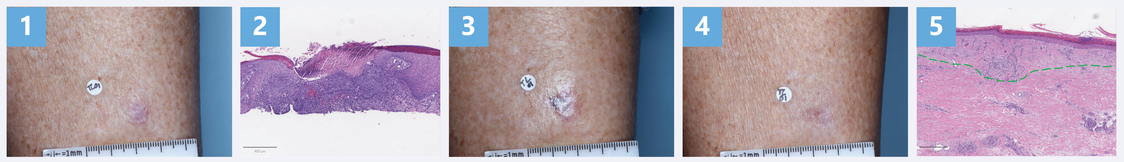
Tumors per Cohort	Complete Histologic Clearance by Tumor	Overall Percent Reduction of Tumor Size	Percent Reduction of Tumor Size with Remaining Tumor
Cohort 1 (n=7)	**71%**	**98%**	**93%**
Cohort 2 (n=3)	**33%**	**88%**	**83%**
Cohort 4 (n=38)	**53%**	**87%**	**73%**
Cohort 5 (n=44)	**48%**	**83%**	**67%**
Total (n=92)	**51%**	**86%**	**71%**

Case Studies

Cohort 4 Subject (69 yo, Male, Nodular, 85% reduction)



Cohort 5 Subject (59 yo, Female, Nodular, 100% reduction Complete Histologic Clearance)



1. *Initial Presentation (Prior to 1st Dose) - W1D1*

2. *Pre-Treatment Biopsy*

3. *Safety Visit – W1*

4. *End of Treatment Visit (Prior to Excision)*

5. *Histology from EOT Excision*

CONCLUSIONS

Complete histological clearance in a majority of VP-315-treated tumors could eliminate the need for surgical intervention in those patients in clinical practice. In subjects with residual tumor burden, the substantial reduction in tumor size after VP-315 treatment would markedly reduce the surgical incision area and the amount of potential post-surgical scarring. Based on the favorable results, further research using VP-315 as a potential non-surgical immunotherapy for BCC as a first-line therapy in a primary or neoadjuvant setting is warranted.

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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