

VP-315: An Investigational Non-surgical Immunotherapy in Subjects with Biopsy Proven Basal Cell Carcinoma

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Dr. Bhatia's Disclosures

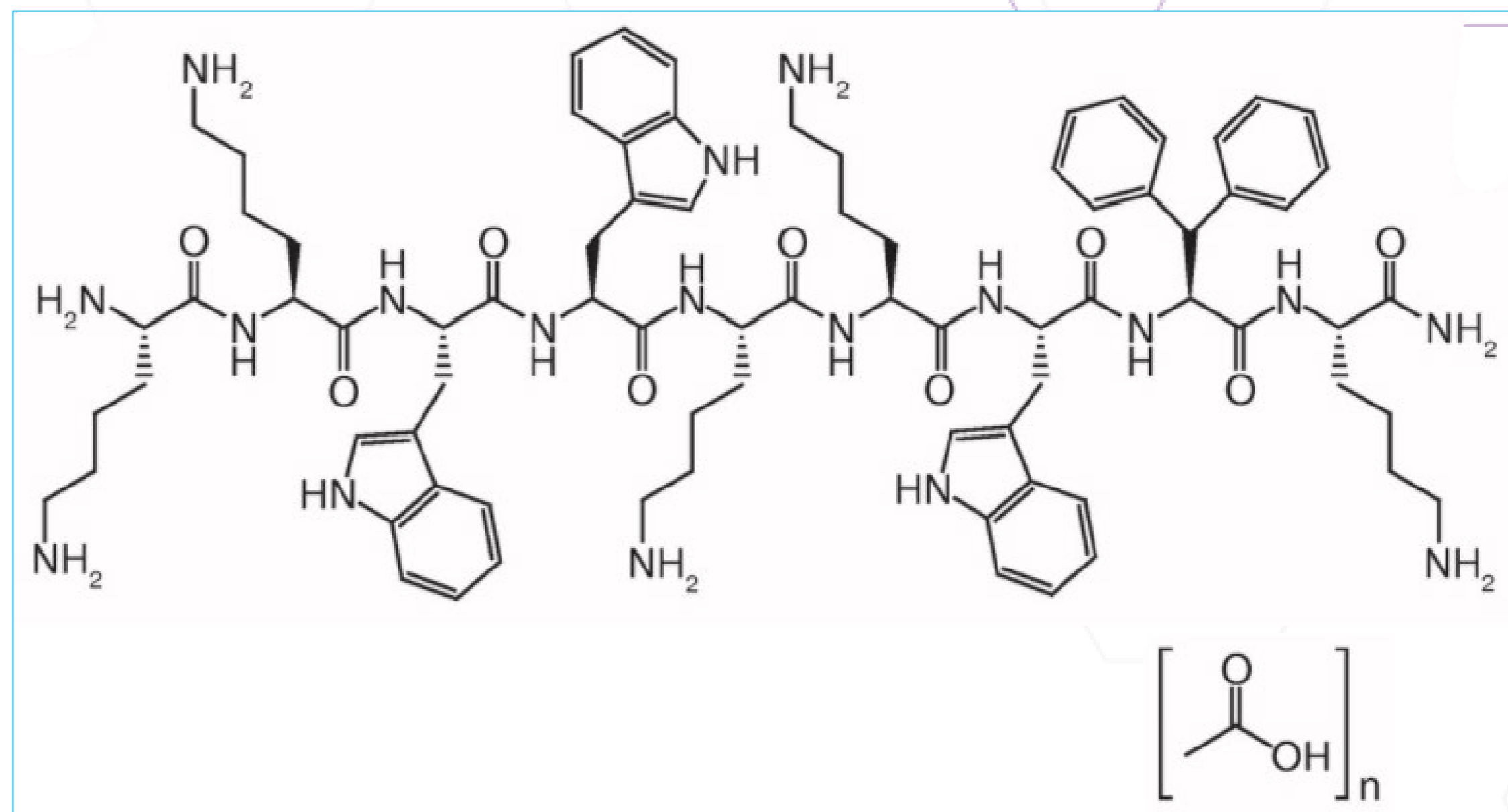
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- Copies of pdf or questions: bhatiaharbor@gmail.com

Background

- VP-315 is a *de novo* designed, intratumorally injected, oncolytic peptide that is currently under investigation as a non-surgical immunotherapeutic treatment option for patients with Basal Cell Carcinoma (BCC).
- BCC is usually treated with surgical intervention. However, some patients prefer not to undergo a surgical procedure and others may not be surgical candidates. A locally injected immunotherapy would provide a novel therapy that relies on the body's own immune system to target cancer cells, while sparing normal tissue.

VP-315 is a Synthetic Cationic Antimicrobial Peptide (CAP) Derived From Bovine Lactoferricin (LfcinB)

- Displays selective antimicrobial and anticancer properties and derived from the pepsin-mediated hydrolysis of the iron-binding bovine glycoprotein lactoferrin.
- LfcinB has a cyclic structure due to a disulphide bond between two Cys residues.
- Displays amphipathicity (can have both hydrophilic and hydrophobic parts).



- The amphipathic secondary structure as well as the nature, size, and positioning of aromatic amino acids is of importance for anti-cancer activity.
- Data on lactoferricin derived, and also synthetic model peptides were found to be highly effective against both drug-resistant and drug-sensitive cancer cells and displayed a lower activity toward normal cells.

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

VP-315 Dual Mechanism of Action

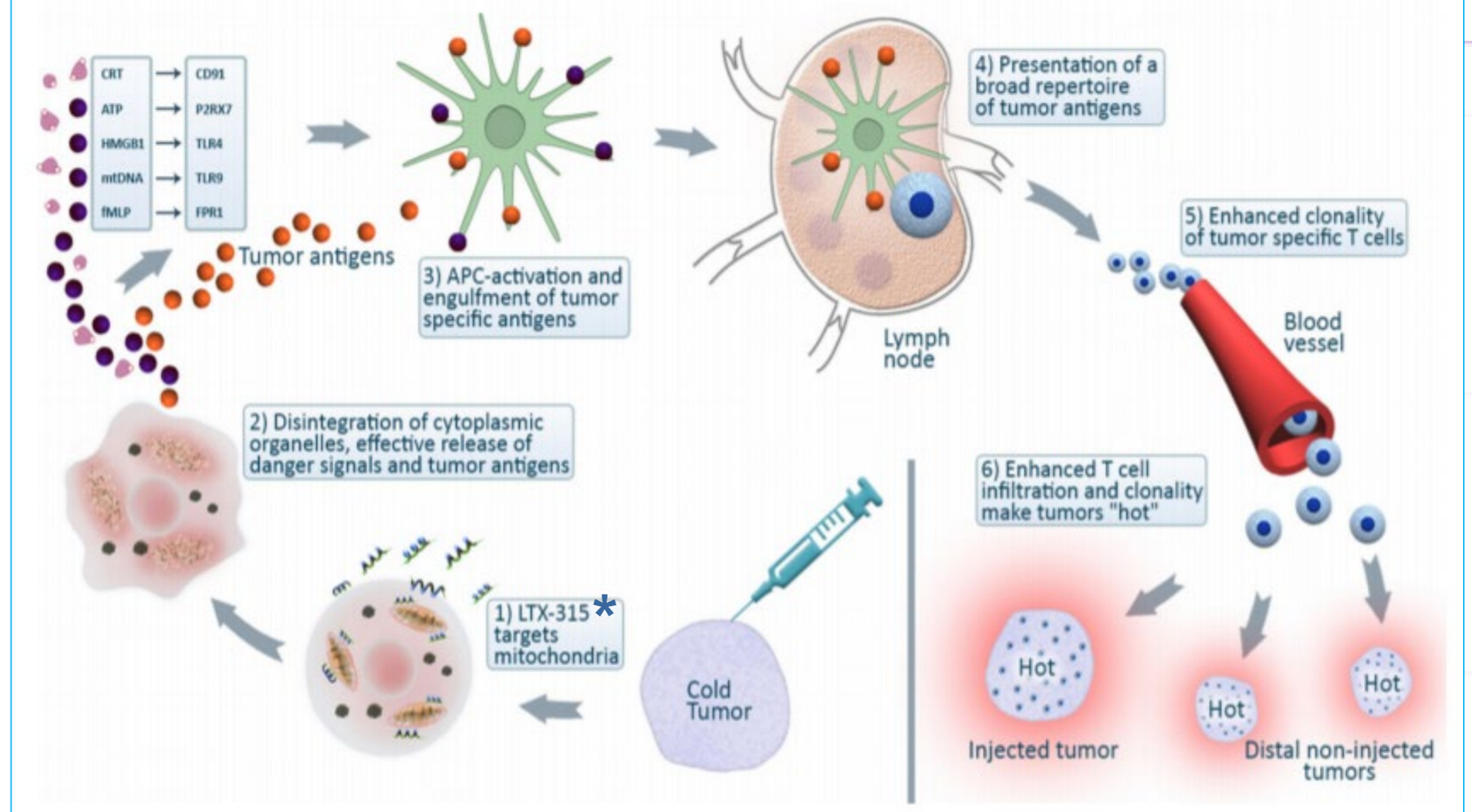
1. Direct Killing Activity

VP-315 enters cells by perturbing plasma membranes and targets mitochondria, and other organelles, causing cell death and release of danger signals (DAMPs) and a broad repertoire of tumor specific antigens (TSAs).

2. Immune System Activation

Release of DAMPS and TSAs activates the immune system to recognize, infiltrate, and attack cancer cells via dendritic and cytotoxic T cells. VP-315 has proven to be active in a panel of drug resistant cancer cells.

LTX-315's unique mode of action results in effective release of potent immunostimulants and antigens



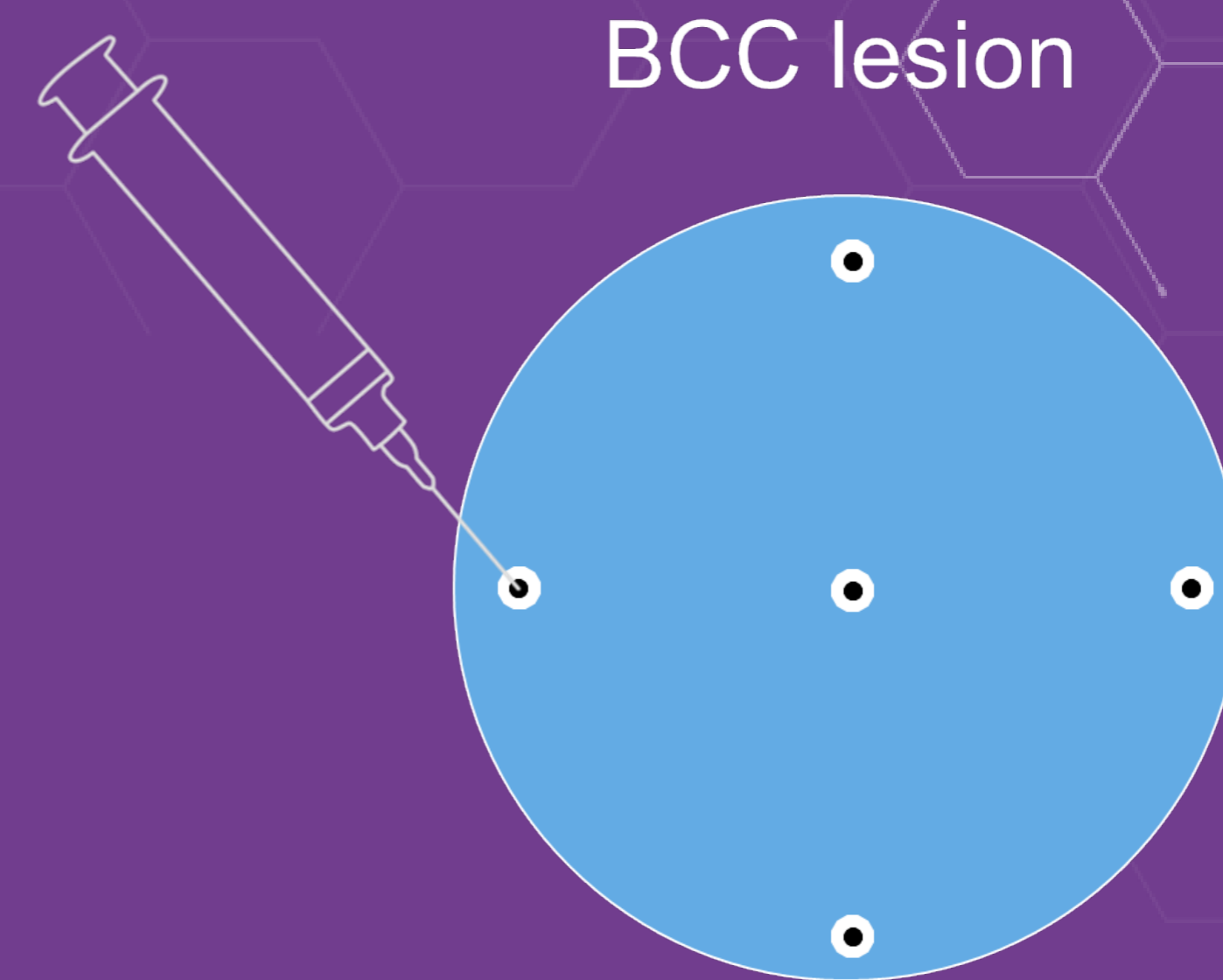
* LTX-315 is being studied in BCC as VP-315.

Study Objectives

- The primary objective of Part 1 of a 2 Part Study (N=10, total study N=80) was to assess the safety of ascending doses (2-8 mg) of VP-315, an investigational novel immunotherapy to treat BCC. We previously reported that no dose-limiting toxicities or serious adverse events, only expected cutaneous reactions, were observed over the entire dose range tested.
- NOTE: In April 2022, the first subject was dosed in Part 1 of a 3-part Phase 2, Multicenter, Open-label, Dose-escalation Proof-of-Concept Study with a safety run-in designed to assess the Safety, Pharmacokinetics, and Efficacy in Subjects with Biopsy Proven Basal Cell Carcinoma. In Part 1 of the trial, VP-315 demonstrated a favorable safety and tolerability profile with no reported serious adverse events. In June 2023, the protocol was amended to remove Part 3 of the trial by expanding Part 2.
- The exploratory objective of Part 1 of the study was to evaluate antitumor efficacy as determined by clinical and histological clearance of treated BCC lesions. We previously reported that there was consistent clinical evidence of tumor necrosis observed at the maximum 8 mg dose.
- The Part 1 clinical and histologic clearance results will be the focus of this presentation.

Methods

- ❑ Subjects received once daily dosing of VP-315, administered intratumorally, in up to 2 biopsy-proven BCC lesions for up to 6 treatments over a 2-week period. In Part 1 of the study, six subjects (1 lesion in each subject) were treated at the 8 mg dose.
- ❑ Post-treatment clinical assessment and excisions were performed at Day 49 (Range 35-70), followed by histological evaluation.



Phase 2, Part 1 Study Results

Subject #	Body Lesion Location	Full Necrosis Observed	Residual Tumor (%)
1	R Upper Arm (R Clavicle)	YES	0% Residual Tumor
2	Left arm/Forearm	YES	70% Residual Tumor
3	Back LL	YES	0% Residual Tumor
4	Back LR	YES	0% Residual Tumor
5	Back LL	YES	0% Residual Tumor
6	Chest UL	YES	5% Residual Tumor

Clinical and Histologic Clearance Results

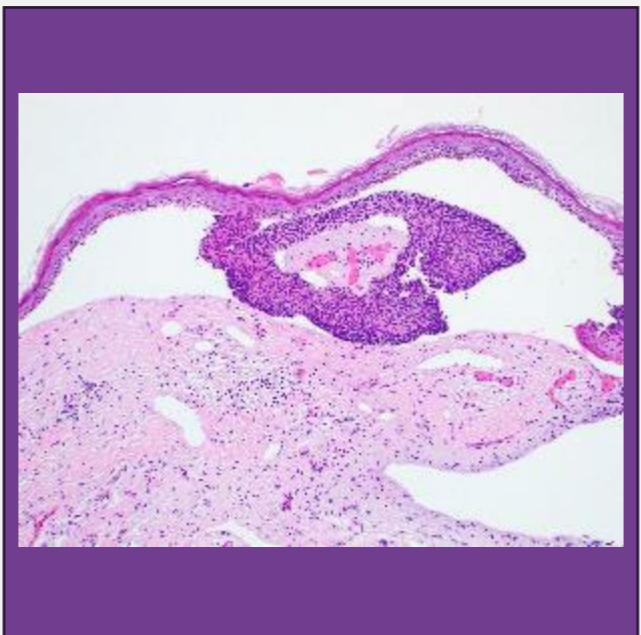
Subject 4 presented with BCC and received three consecutive daily doses of 8 mg VP-315. Complete lesion clearance achieved.

Subject 4

Initial presentation (W1D1)



Pre-treatment Biopsy



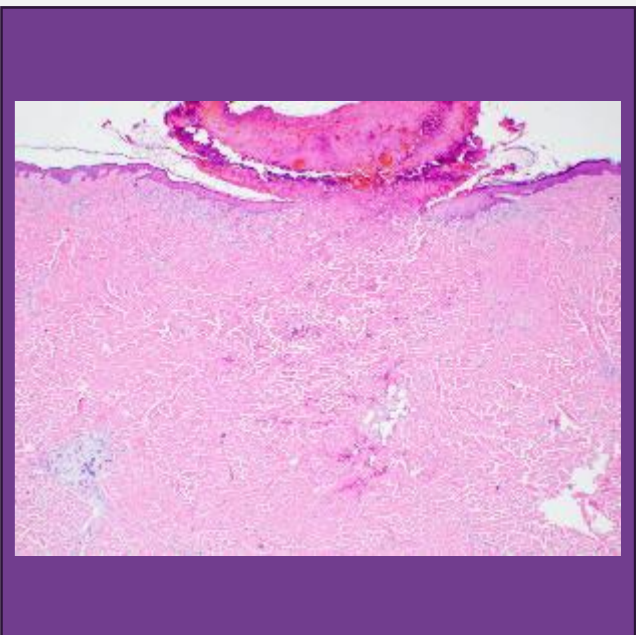
Full Necrosis induced* (W1D4)



End of Treatment Visit (Prior to Excision)

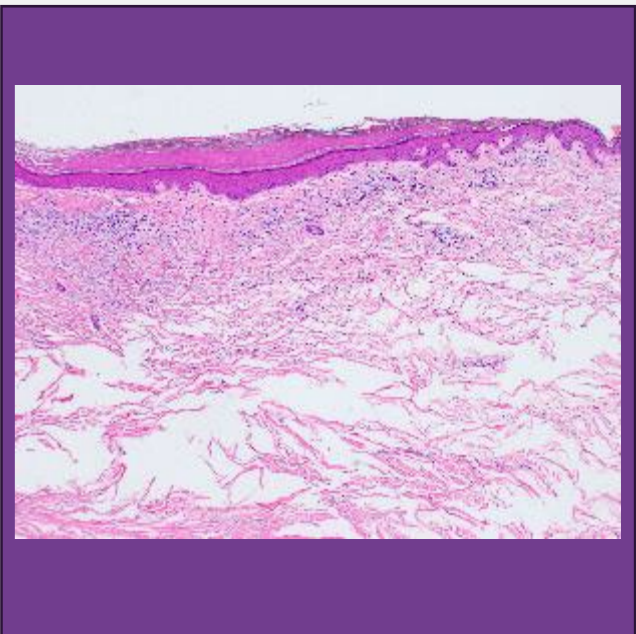
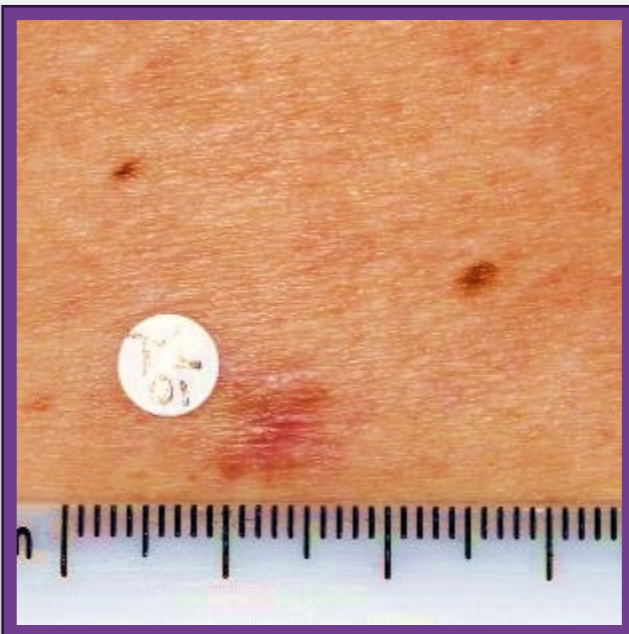
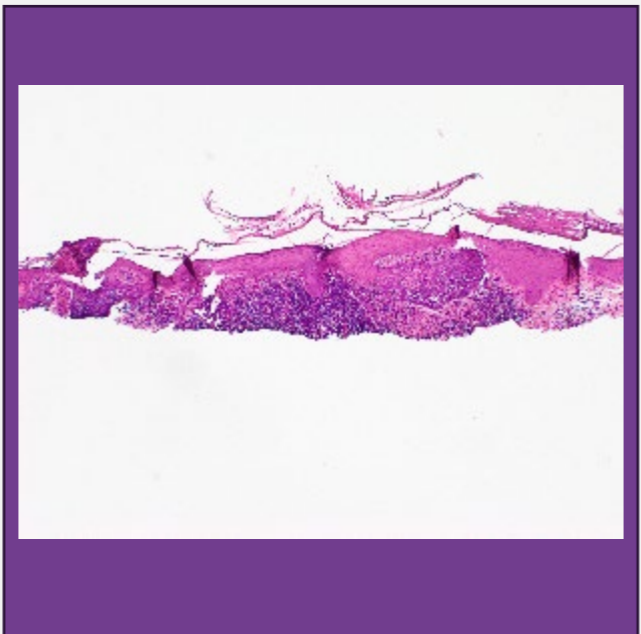
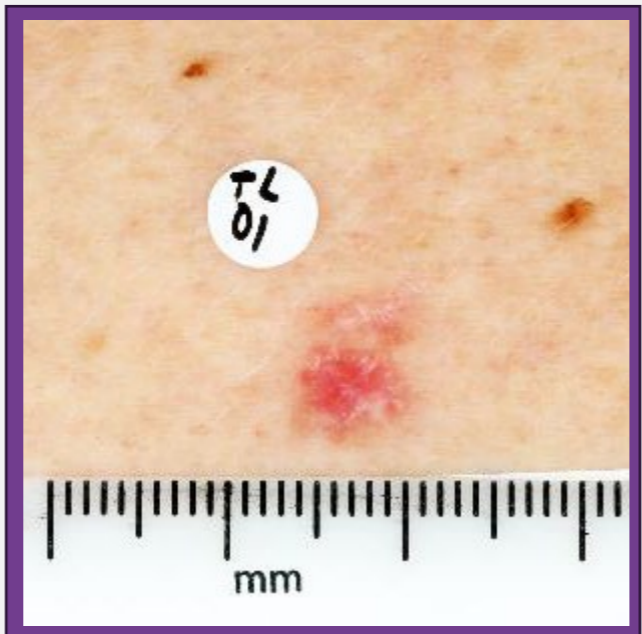


Histology from EOT Excision




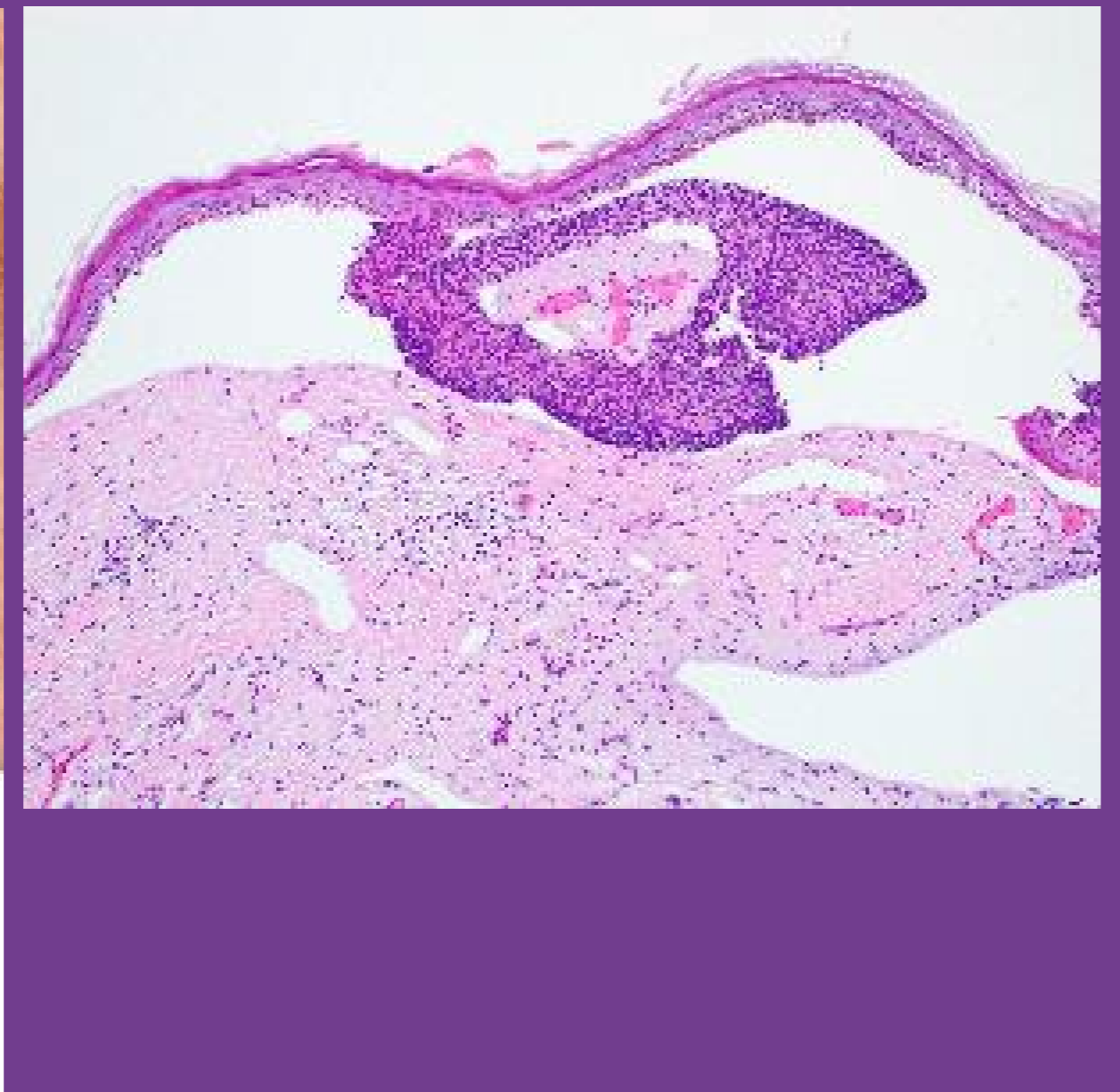

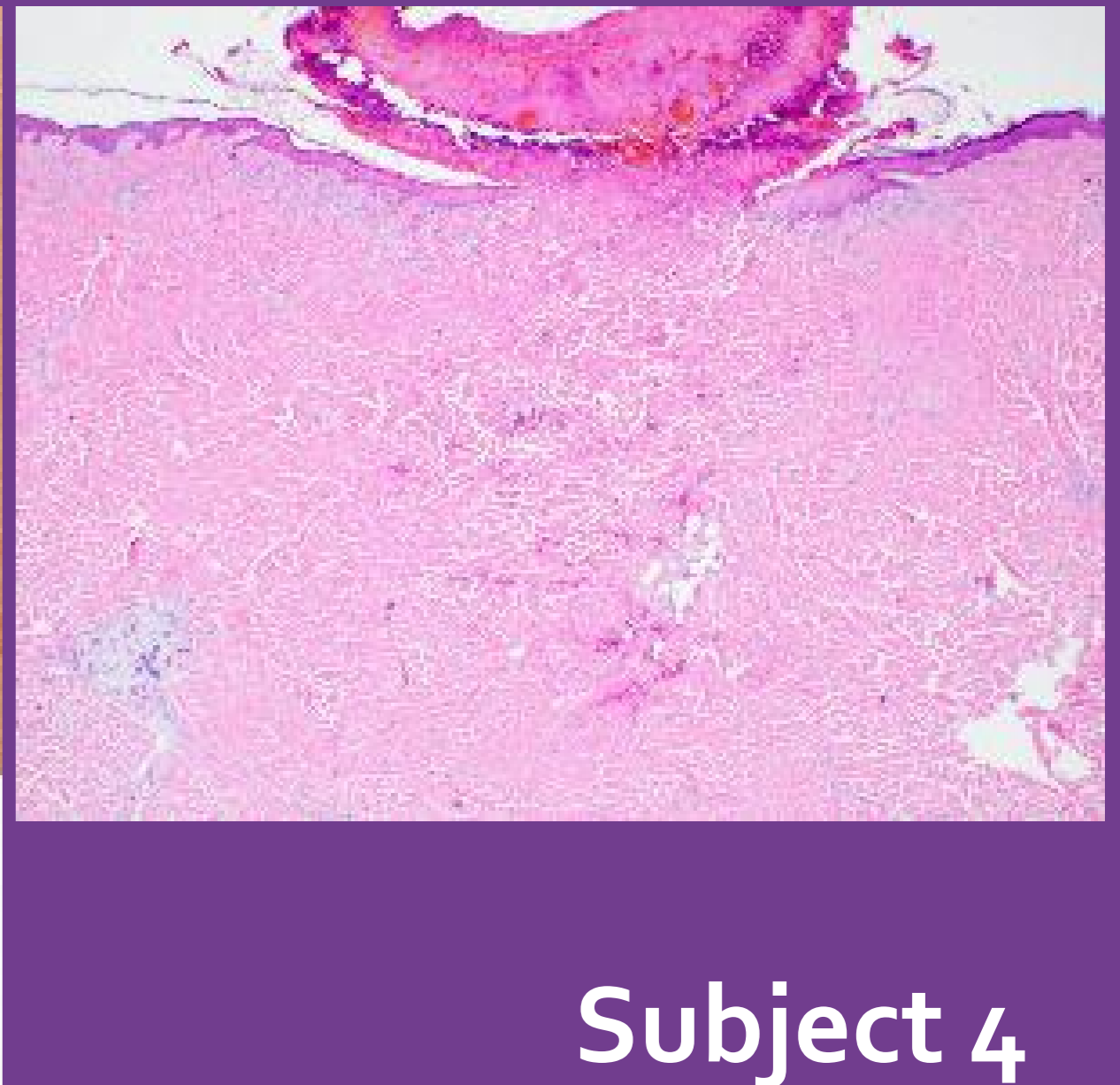
Subject 5 presented with BCC and received three consecutive daily doses of 8 mg VP-315. Complete lesion clearance achieved.

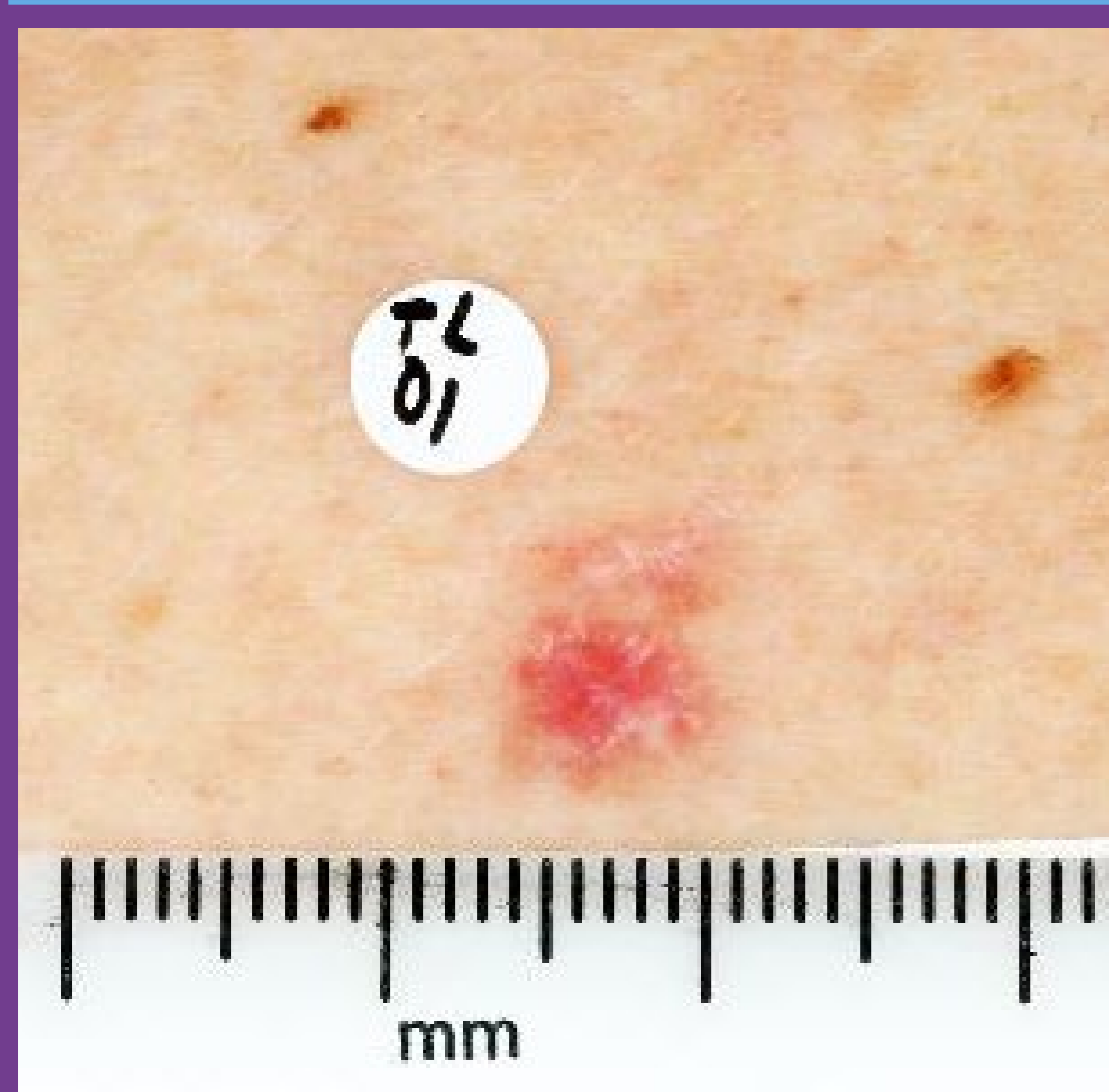

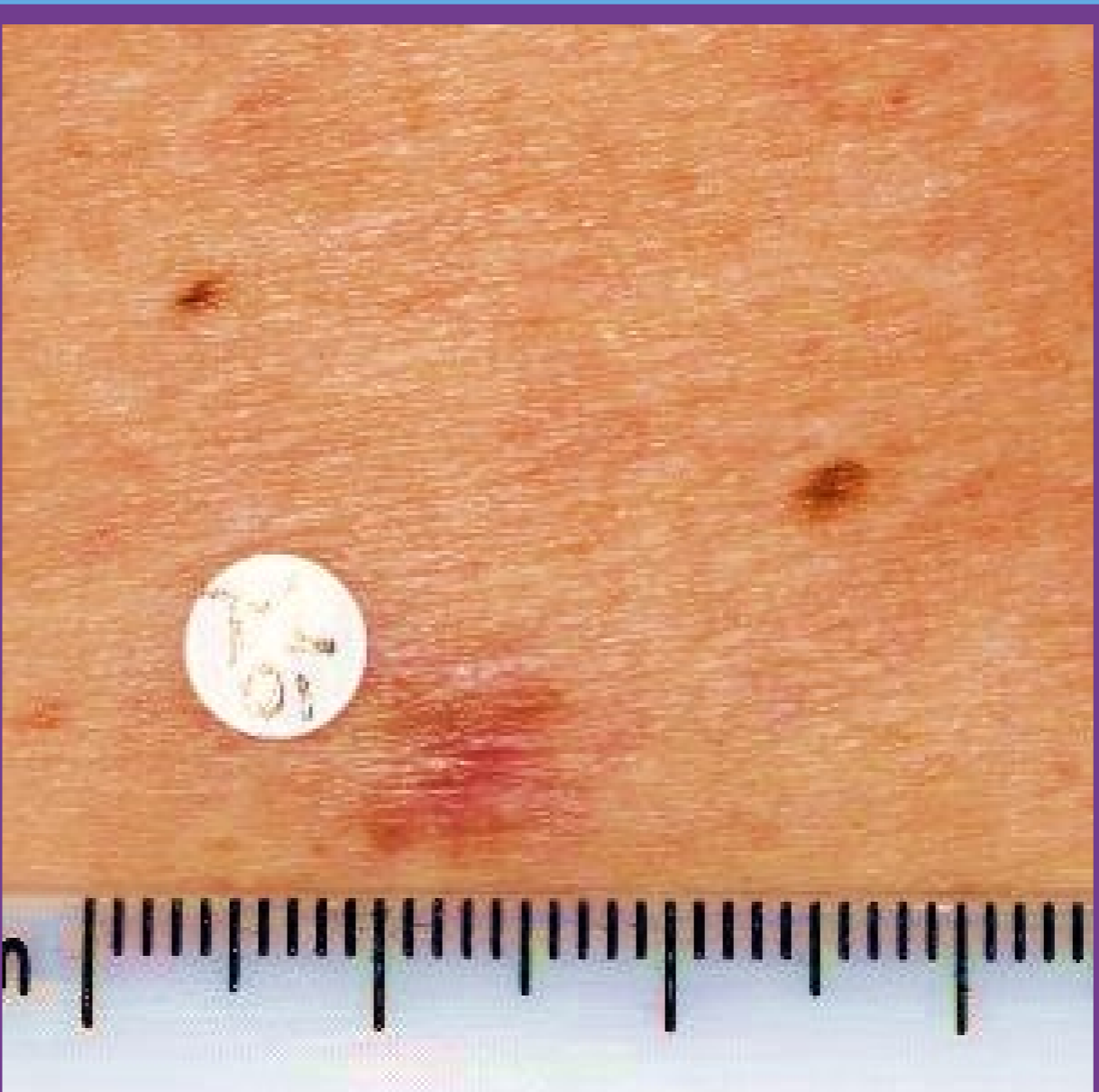

Subject 5



*Visual confirmation of necrosis or a DLT resulted in termination of dosing. Full necrosis was achieved in all six lesions. No subjects experienced DLTs.

Clinical and Histologic Pre and Post Treatment 🔍

Pre-treatment	Pre-treatment	EOT	EOT
			
Subject 4			

			
Subject 5			

Conclusions

- Consistent clinical and histologic clearance of treated BCC lesions was observed by Day 49 post-treatment with the 8 mg dose of VP-315, with 4 out of 6 subjects (67%) showing complete clearance.
- Optimization of the 8 mg dosing regimen is under investigation in Part 2 of the study.
- These early encouraging results from Part 1 support VP-315 as a potential non-surgical therapeutic approach for BCC.

Questions?