The efficacy and safety of aminolevulinic acid 20% topical solution activated by pulsed dye laser and blue light for the treatment of facial cutaneous squamous cell carcinoma in situ

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INTRODUCTION

- Squamous cell carcinoma (SCC) is the second most common cutaneous malignancy[1]
- Aminolevulinic acid (ALA) 20% solution–photodynamic therapy (ALA-PDT) is approved for the treatment of actinic keratoses on the face, scalp, and upper extremities[2] and is a potential treatment option for SCC

OBJECTIVE

- This study evaluated the efficacy, tolerability, and safety of ALA-PDT in combination with pulsed dye laser (PDL) for the treatment of facial cutaneous SCC in situ (isSCC)

METHODS

Study design and participants

- A prospective, single-center, investigator-initiated, open-label pilot clinical trial (NCT02137785) was conducted at the Center for Clinical and Cosmetic Research in 2020–2021
- Patients with biopsy-confirmed isSCC on the face were included in the study
- Only lesions with a diameter of 0.4–1.3 cm were considered for the study
- Patients with infiltrative, severe, metaplastic, or recurrent isSCC were excluded from the study

Treatments and procedures

- ALA 20% topical solution was applied to the lesion and adjacent skin and incubated for 18–24 hours, followed by PDL treatment (pulse duration: 0.45 milliseconds, fluence: 13 J/cm^2, amount determined by the investigator) and then blue light illumination (BLU-U®; 10 J/cm^2 for 16 minutes 40 seconds)
- Patients underwent 2 ALA-PDL-PDT treatment sessions separated by a 30-day period
- The lesion was surgically excised for histological assessment 4–6 weeks following the second treatment

Assessments and endpoints

- The primary efficacy endpoint was the proportion of patients achieving histological clearance of isSCC at the end of treatment/surgical excision
- Tolerability was assessed from local skin reactions (LSRs) and patient-reported lesion site pain
  - Lesion site pain was measured using a visual analog scale ranging from 0 (no pain) to 10 (worst pain possible) within 15 minutes of each treatment session
- Safety was assessed from frequency of adverse events (AEs)

RESULTS

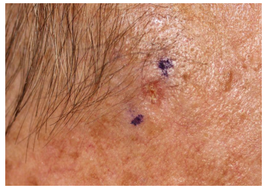
Efficacy

- Of 20 enrolled patients, 17 (85%) achieved histological clearance at the end of treatment
- After excluding two patients with residual isSCC exhibiting skip lesions, the histological clearance rate was 17/18 patients (94%)
- Images obtained during visit 1 (pretreatment; **Figure 1A**) and visit 10 (posttreatment; **Figure 1B**) show clinical clearance of isSCC with ALA-PDL-PDT

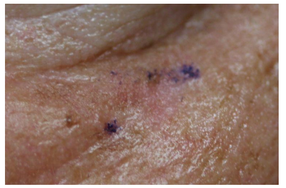
Figure 1. Imaging of isSCC in 2 patients obtained (A) before and (B) after treatment with ALA-PDL-PDT

A) Visit 1 (Pretreatment)

Patient A

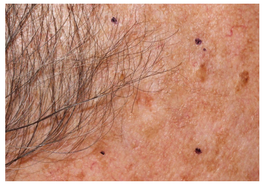


Patient B

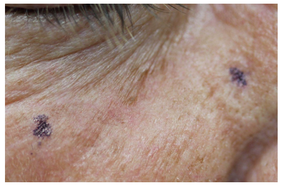


B) Visit 10 (Posttreatment)

Patient A



Patient B



ALA, aminolevulinic acid; PDL, pulsed dye laser; PDT, photodynamic therapy; isSCC, squamous cell carcinoma in situ.

Tolerability

- Median LSR scores peaked within 1 week following each treatment session and steadily decreased afterward (**Table 1**)
  - The most common LSRs were erythema and scaling
- The mean ± standard deviation posttreatment pain score was 2.95 ± 2.97

Table 1. Median local skin reaction scores for the lesion areas

	Visit number								
	1 (Pre-Tx #1)	3 (Tx #1)	4	5	6 (Pre-Tx #2)	7 (Tx #2)	8	9	10 EOT
Erythema	2	3	3	2	2	3	3	2	1
Flaking/scaling	1	1	1	1	1	0.5	1	0.5	0
Crusting	0	0	0	0	0	0	0	0.5	0
Swelling	0	0	0	0	0	0	0	0	0
Vesiculation/ pustulation	0	0	0	0	0	0	0	0	0
Erosion/ ulceration	0	0	0	0	0	0	0	0	0

Data shown as median LSRs for the lesion areas.
Responses were scored on a scale from 0 (not present) to 4 (high severity).
EOT, end of treatment; LSR, local skin reaction; Tx, treatment.

Safety

- The majority of treated patients (65%) did not experience any AEs
- Reported AEs included allergic contact dermatitis, blurry vision, right ear pain, right leg cellulitis, double vision, hypotension, and wound site infection
  - None of the reported AEs were serious or considered related to study treatment
- No patients withdrew from the study

CONCLUSIONS

- The primary and secondary efficacy endpoints of histological and clinical clearance were achieved in a majority of patients by the end of ALA-PDL-PDT treatment
- ALA-PDL-PDT was well tolerated and safe

REFERENCES

1) Voiculescu V, et al. *Dis Markers*. 2016;2016:4517492. **2)** LEVULAN® KERASTICK® (aminolevulinic acid HCl) for topical solution, 20%. Full prescribing information. Sun Pharmaceutical Industries, Inc. 2020.

ACKNOWLEDGMENTS

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DISCLOSURES

MN received a research grant from Sun Pharma. **HH**, **FY**, and **CS** report nothing to disclose.