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 ORIGINAL ARTICLE

Safety and Efficacy of Aminolevulinic Acid 20% Topical Solution Activated by Blue Light for Facial Cutaneous Squamous Cell Carcinoma In Situ

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ABSTRACT

Background: Squamous cell carcinoma in situ (isSCC) is an early-stage cutaneous malignancy that requires effective treatment to prevent progression to invasive SCC. Aminolevulinic acid photodynamic therapy (ALA-PDT) is a noninvasive treatment that selectively targets neoplastic cells. This study evaluated the effectiveness, safety, and tolerability of ALA-PDT for the treatment of patients with facial isSCC.

Methods: In this single-center, investigator-initiated, open-label study (NCT06159842), adult patients with biopsy-confirmed facial isSCC received 2 treatments with 20% ALA and blue light exposure, administered 28 days (± 3 days) apart. Lesions were excised for histopathological assessment 8 weeks after the second treatment. The primary endpoint was complete histological clearance at the end of treatment (EOT). Secondary outcomes included clinical clearance and tolerability.

Results: A total of 32 patients were enrolled in this study, of whom 30 completed the study. All patients achieved complete histological clearance at EOT. Clinical clearance was observed in all patients prior to excision, with 40% achieving clearance by day 49 and the remainder by day 69. Local skin reactions, including erythema and flaking, were mild and resolved over time. Only 1 patient experienced temporary hyperpigmentation. Pain scores remained low (mean, 2.71/10). Two patients reported adverse events considered unrelated to treatment.

Conclusions: ALA-PDT achieved 100% complete histological and clinical clearance with minimal adverse effects, demonstrating its potential as a safe, effective, and cosmetically favorable alternative to surgical excision for the treatment of facial isSCC. Further studies are needed to assess long-term recurrence rates and broader applications.

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INTRODUCTION

Nonmelanoma skin cancer is the most common form of cancer, with cutaneous squamous cell carcinoma (SCC) accounting for more than 20% of all skin cancers.[1,2] Although historically less prevalent than basal cell carcinoma (BCC), SCC carries a significant risk of metastasis and mortality and a poor prognosis.[3-6] Unfortunately, the incidence of SCC continues to rise, as observed in the Rochester Epidemiology Project conducted by the Mayo Clinic, which reported a 263% increase in the incidence of SCC between studies spanning the years 1976 to 1984 and 2000 to 2010.[7] In fact, recent studies have indicated that in areas of high sun exposure such as South Florida, SCC and its subtypes are significantly more prevalent than BCC.[8,9] Ultraviolet radiation exposure, especially ultraviolet A, is the primary risk factor for developing SCC; other risk factors include advanced age, fair skin, carcinogen exposure, chronic inflammation, and immunosuppression.[10,11] SCC often arises from precancerous lesions, including actinic keratoses (AKs) and SCC in situ (isSCC), also known as Bowen disease.[12] isSCC is a common superficial cutaneous malignancy with a reported rate of progression to invasive SCC of 3% to 5%.[13] Treatment of isSCC is crucial to prevent such progression.

Histopathological examination is the mainstay for the diagnosis of SCC, with certain histological features – such as poor differentiation, tumor depth >2 mm, and perineural invasion – indicating a higher risk for recurrence and metastasis.[11,14] The gold standards for the treatment of SCC are Mohs micrographic surgery (MMS), surgical excision, and radiation therapy (RT). MMS or RT may be indicated for high-risk SCC and SCC located

in the head, neck, or genital region.[15,16] For low-risk SCC or isSCC, standard excision with 4- to 6-mm clinical margins of normal-appearing skin is recommended, as per the 2025 National Comprehensive Cancer Network guidelines.[17]

Nonsurgical treatment options for isSCC include radiation therapy, electrocoagulation, cryosurgery, photodynamic therapy (PDT), and, in some cases, topical chemotherapy. Systemic chemotherapy is reserved for advanced SCC.[14,17]

Cure rates for AKs, isSCC, and invasive SCC vary widely by treatment modality. Clearance rates for AKs range from 24% to 91%, depending on the treatment used.[18-20] For isSCC, surgical excision achieves the highest clearance rate (~100%), with a low recurrence rate.[21] Invasive SCC is primarily treated with surgical excision or MMS, both of which offer >90% clearance and lower recurrence; however, challenges remain with incomplete deep margin resection, limited access to MMS, and surgical morbidity, especially for high-risk, anatomically complex, or cosmetically sensitive tumors.[22,23] There is an unmet need for nonsurgical treatments that can provide durable efficacy in isSCC while preserving cosmetic and functional outcomes, especially for lesions in cosmetically sensitive areas such as the face.

PDT has emerged as an effective and cosmetically favorable treatment for many dermatologic conditions, including AKs, BCC, isSCC, and warts.[20,24-27] It involves the application of a photosensitizing agent, such as aminolevulinic acid (ALA) or methyl aminolevulinate (MAL), which converts to its active form, protoporphyrin IX (PpIX), upon illumination. Activated PpIX generates reactive oxygen species, selectively destroying neoplastic cells.[28,29] For isSCC, PDT results in clearance rates ranging from 48% to 100% depending on the treatment regimen and follow-up period.[31-34]

ALA-PDT using a 20% 5-ALA solution with blue light (LEVULAN® KERASTICK® with BLU-U® Illuminator, Sun Pharmaceutical Industries, Inc.) is approved in the US for the treatment of minimally to moderately thick AKs on the face, scalp, and upper extremities.[35] The purpose of this trial is to evaluate the safety, tolerability, and efficacy of PDT consisting of topical PDT and blue light illumination in patients with isSCC on the face.

MATERIALS AND METHODS

Study Design and Population

This single-center, investigator-initiated, open-label study (NCT06159842) was conducted at the Center for Clinical and Cosmetic Research from August 2023 to September 2024. The study protocol was reviewed and approved by the US Institutional Review Board (IRB; IRB number U.S.IRB2023CCCR/01; approval date, July 30, 2024). The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. All patients provided written informed consent prior to study initiation.

Adult patients with histologically confirmed facial isSCC were enrolled consecutively in the study to reduce selection bias. Lesions must have been diagnosed and histologically confirmed within 6 months prior to screening. Only lesions measuring 0.4 to 1.3 cm in diameter were included. Lesions with histological features of nodular basal cell carcinoma, superficial basal cell carcinoma, other non-SCC tumors, severe squamous metaplasia, or infiltrative desmoplastic or micronodular growth patterns on biopsy, or a history of recurrence of the target isSCC, were excluded.

Treatment and Assessments

Prior to the application of 20% ALA hydrochloric acid (HCl), lesions were gently abraded using 4 x 4 gauze and wiped with alcohol wipes. Following lesion preparation, 20% ALA HCl was applied topically to the lesion and approximately 5 mm of the surrounding area. The treated area was then occluded with a bandage and incubated for 24 hours, as previously described,[36] during which patients were instructed to keep the treatment area dry and avoid direct sunlight. After the 24-hour incubation period, patients underwent PDT using blue light (BLU-U®) at an irradiance of 10 mW/cm^2, delivering a total fluence of 10 J/cm^2 for 16 minutes and 40 seconds. Each patient received 2 ALA-PDT sessions, administered 28 (± 3) days apart.

Eight weeks after the second treatment, the lesions were surgically excised, sectioned at 1-mm intervals using a "bread-loafing" technique, and stained with hematoxylin and eosin. A board-certified dermatologist, blinded to the clinical outcomes, examined the sections to assess for complete histologic clearance. Lesion size and eventual complete clinical clearance (CC), defined as no clinically visible lesion at the site, were assessed by the investigator at each visit.

Pigmentation changes at the lesion site (hyperpigmentation, hypopigmentation, and depigmentation) were semi-quantitatively evaluated at each visit by the investigator on a scale of 0 (none) to 3 (severe). Tolerability of the treatment was evaluated at each visit from local skin reactions (LSRs) on a scale of 0 (not present) to 4 (high severity) for erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, and erosion/ulceration. Patients also rated pain at the treatment site within 15 minutes after each ALA application and blue light illumination using a 10 cm visual analog scale (VAS) that ranged from 0 (no pain) to 10 (worst pain possible).

Outcomes

The primary endpoint of the study was the proportion of patients achieving complete histological clearance of isSCC at the end of treatment (EOT). The secondary endpoints were the proportion of patients with CC of the treated lesion as measured by investigator assessment and the aesthetic appearance of the treated lesion as reflected by LSR scores.

No formal sample size calculation was performed for this study; the number of patients was determined based on the investigators' clinical judgment.

RESULTS

Patients

Thirty-two patients with a mean (range) age of 75 (54–95) years and Fitzpatrick skin types I, II, or III were enrolled. Two patients did not complete the study; one died of causes unrelated to the study treatment, and the other sought treatment outside the study. Among the 30 patients who completed the study, 20 (67%) were male, and 10 (33%) were female. The locations of the isSCC lesions were as follows: 7 (23.3%) on the left cheek or temple, 10 (33.3%) on the right cheek or temple, and 13 (43.3%) on the forehead (glabellar region or eyebrow). Overall, 15 (50%) lesions were located on the left side of the face and 15 (50%) on the right; none were located in the midface. The mean lesion diameter was 0.73 cm (range, 0.4–1.2 cm; standard deviation [SD], 0.20 cm). The mean lesion width was 0.59 cm (range, 0.4–1.1 cm; SD, 0.19 cm).

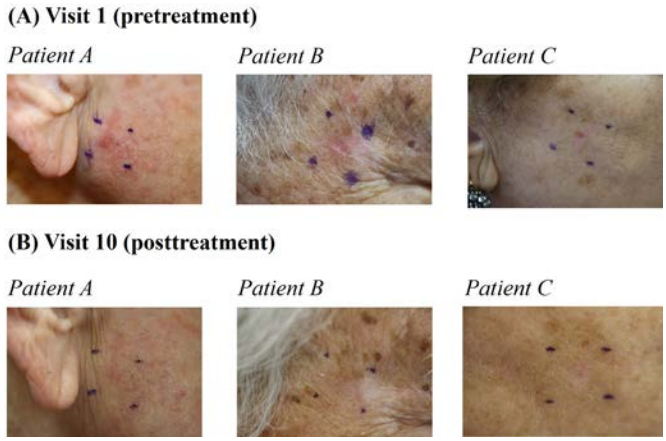
Effectiveness

All patients who completed the study (n = 30) achieved complete histological clearance of the treated isSCC lesion at EOT/surgical excision. All histological sections and surgical margins were free of neoplasm in every patient. Clinical clearance was also observed in all patients prior to surgical excision (Figure 1). One (3.3%) patient achieved CC by day 27, 12 (40%) by day 49, another 12 (40%) by day 58, and the remaining 5 (16.7%) by day 69. For context, the second blue light illumination occurred on day 29, and surgical excision was performed on day 58 (± 7 days after the second treatment).

Pigmentation Assessments

Almost all patients (29/30 [96.7%]) exhibited no changes in lesion pigmentation. One patient experienced mild hyperpigmentation 14 days after the first blue light treatment, which was resolved by the following visit 14 days later.

FIGURE 1. Imaging of facial isSCC before and after treatment with ALA-PDT.



ALA, aminolevulinic acid; isSCC, squamous cell carcinoma in situ; PDT, photodynamic therapy.

Local Skin Reactions

Erythema and flaking/scaling were the most common LSRs. Mean LSR scores for erythema and erosion/ulceration peaked on the day of each blue light treatment, one day after ALA application (visits 3 and 6; Table 1), whereas mean LSR scores for flaking/scaling peaked within 2 weeks after each blue light treatment. LSRs steadily decreased thereafter. Mean LSR scores were higher at visit 1 (pretreatment) than at visit 10 (EOT).

Tolerability

The mean pain score recorded by patients on the VAS within 15 minutes of each ALA application and each blue light treatment was 2.71 (range, 0–9; SD, 2.27).

TABLE 1.

Mean Local Skin Reaction Scores for the Lesion Areas						
Visit	Erythema	Flaking/Scaling	Crusting	Swelling	Vesiculation/Pustulation	Erosion/Ulceration
Visit 1 (pre-TX)	2.1	1.0	0.1	0	0	0
Visit 3 (TX1)	2.9	0.1	0	0	0	0.9
Visit 4 (FU1)	2.0	1.2	0.1	0	0	0
Visit 5 (pre-TX)	1.8	0.6	0	0	0	0
Visit 6 (TX2)	2.9	0.1	0.1	0	0	0.8
Visit 7 (FU2)	1.8	0.7	0.1	0	0	0
Visit 8 (FU3)	1.6	0.1	0	0	0	0
Visit 9 (FU4)	1.4	0.1	0	0	0	0
Visit 10 (EOT)	1.2	0	0	0	0	0

EOT, end of treatment; FU, follow-up; TX, treatment.

Safety

The treatment was well tolerated, with the majority of patients (28/30 [93.3%]) experiencing no adverse events (AEs). Reported AEs in 2 patients included newly diagnosed hypertension in one patient and worsening hypertension in another. Neither of these AEs was considered treatment related by the investigators, and they did not influence treatment administration or study outcomes.

DISCUSSION

ALA-PDT has emerged as a promising noninvasive treatment for superficial skin cancers. It has demonstrated efficacy for the treatment of isSCC as an alternative to current treatment modalities such as excisional surgery, 5-fluorouracil, and cryotherapy.[33,37,38] ALA-PDT is not approved by the US Food and Drug Administration for the treatment of isSCC.[35,39] Therefore, there is no standardized treatment protocol, and patient outcomes can vary due to the differences in photosensitizers, light sources and dosimetry, size and location of the lesions, and length of follow-up.[32,33,40,41]

Several studies show that ALA-PDT has clearance rates of 90% to 100% following 1 to 3 treatments in patients with isSCC.[38,42,43] In a retrospective study assessing the efficacy of ALA-PDT for the treatment of 58 patients with 68 isSCC lesions, 87.5% of lesions with a diameter of 2.0 cm or less cleared after 1 to 3 sessions of ALA-PDT using blue light. The initial complete response rate was 77.9%. The response rate was not associated with the number of PDT treatments, but it was linked to the location of the lesion on the face, tumor diameter of less than 2 cm, and longer ALA incubation time. Lesions with an incubation time of less than 3 hours had a response rate of 53.3%, while those with longer incubation had a response rate of 84.9%.[33] These studies highlight the correlation of a longer incubation period (>3 hours) with higher response rates, which was consistent with our study.

Another recent cohort study demonstrated that 85% of patients achieved histological clearance after 2 treatments using 20% ALA-PDT with pulsed dye laser for isSCC lesions on the face with a diameter of <2.0 cm. By the end of the treatment, only 2 patients experienced treatment failure, likely due to lesions in a cramped anatomical area (helix of ear and lateral malar cheek).[36] The study highlights the correlation of lesion characteristics, such as anatomical location and lesion size, with treatment success.

Although PDT has demonstrated similar efficacy to standard therapies, studies have shown that lesion size, incubation period, and anatomic location affect response rates.[33] Additionally, pretreatment abrasion, as recommended for the treatment of AKs, was not consistently documented in previous studies.[37,39,44] Our study used ALA-PDT with blue light to treat isSCC lesions located on the face after a 24-hour ALA incubation period. All patients achieved CC before eventual confirmation of complete histological clearance by the end of the treatment period. Our study thus supports existing literature, demonstrating the effectiveness of ALA-PDT treatment based on anatomic location, lesion diameter, and length of incubation and may highlight the importance of pretreatment abrasion.

Our findings also compare favorably with the reported efficacy of surgical excision and MMS, which are considered the gold standards for the treatment of isSCC and invasive SCC due to the high clearance and low recurrence rates achievable with these techniques.[45-47] In a retrospective study of 96 isSCC lesions, surgical excision with a 5-mm safety margin achieved a complete histological clearance rate of 94.4%, while smaller margins of <5 mm yielded clearance rates of 88.2% or lower. The overall recurrence rate after surgical excision was 2.1% over a mean follow-up of 35 months.[47]

In another study of 84 patients with isSCC lesions, standard excision achieved a 97.4% histological clearance rate over a follow-up of 12 months.[46] In contrast, MMS achieves better outcomes, with histologic clearance in all cases and a reported 5-year recurrence rate of 6.3%.[45] However, these surgical approaches may be associated with increased possibility of morbidity and less favorable cosmetic outcomes;[46,47] therefore, ALA-PDT may be preferable for patients with relatively small isSCC lesions in visible locations such as the face.

Our study demonstrated that complete clinical and histological clearance can be achieved using a nonsurgical, office-based protocol involving 24-hour ALA incubation and blue light illumination. Previous studies have also demonstrated the use of pulsed dye laser in addition to ALA-PDT with blue light, which was proved redundant by our protocol and data.[36] Our results are consistent with other published literature, specifically regarding clinical and histological clearance and safety profiles.[32,33,40,41] This may be attributable to our study design, which included pretreatment abrasion and a prolonged 24-hour ALA incubation. Treatment failure was not observed in our study, indicating a significant improvement in outcomes from previously published protocols that employed differing light sources, photosensitizers, and incubation times.[32-34,37]

The current 5-year cure rate for nonmelanoma skin cancer treated with MMS is >90%.[16,45,46] ALA-PDT would offer a safe, cosmetically appealing, more comfortable, and potentially less expensive alternative to MMS. Although all of our 30 patients had both clinical and histological clearance after 8 weeks, isSCC may recur 1 to 2 years after initial treatment.[32,33,37] Therefore, longer follow-up is needed to evaluate recurrence and other long-term outcomes after ALA-PDT in patients with facial isSCC.

CONCLUSION

Our study demonstrated that ALA-PDT is an effective, safe, and well-tolerated treatment strategy for facial isSCC. This approach achieved 100% clinical and complete histological clearance with minimal AEs and excellent cosmetic outcomes, reinforcing its potential as a noninvasive alternative to traditional surgical methods. While the results are promising, the study's limitations, including a small sample size and short follow-up period, highlight the need for further research. Future studies should explore the broader application of ALA-PDT, including efficacy on larger lesions, optimization of shorter incubation times, use on other anatomical sites, and long-term recurrence. In conclusion, ALA-PDT offers patients a safe and effective treatment option, particularly for lesions on cosmetically sensitive areas such as the face.

DISCLOSURES

MSN reports research grants from Biofrontera, Sirnaomics, and Sun Pharma, and is a consultant for Sirnaomics. AC, RJV, and VB have nothing to disclose.

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REFERENCES

1. Ciążyńska M, Kamińska-Winciorek G, Lange D, et al. The incidence and clinical analysis of non-melanoma skin cancer. Sci Rep. 2021;11(1):4337.
2. Scrivener Y, Grosshans E, Cribier B. Variations of basal cell carcinomas according to gender, age, location, and histopathological subtype. *Br J Dermatol.* 2002;147(1):41-47.
3. Brougham ND, Dennett ER, Cameron R, Tan ST. The incidence of metastasis from cutaneous squamous cell carcinoma and the impact of its risk factors. *J Surg Oncol.* 2012;106(7):811-815.
4. Schmults CD, Karia PS, Carter JB, Han J, Qureshi AA. Factors predictive of recurrence and death from cutaneous squamous cell carcinoma: a 10-year, single-institution cohort study. *JAMA Dermatol.* 2013;149(5):541-547.
5. Knuutila JS, Riihilä P, Kurki S, Nissinen L, Kähäri VM. Risk factors and prognosis for metastatic cutaneous squamous cell carcinoma: a cohort study. *Acta Derm Venereol.* 2020;100(16):adv00266.
6. Que SKT, Zwald FO, Schmults CD. Cutaneous squamous cell carcinoma: incidence, risk factors, diagnosis, and staging. *J Am Acad Dermatol.* 2018;78(2):237-247.
7. Muzic JG, Schmitt AR, Wright AC, et al. Incidence and trends of basal cell carcinoma and cutaneous squamous cell carcinoma: a population-based study in Olmsted County, Minnesota, 2000 to 2010. *Mayo Clin Proc.* 2017;92(6):890-898.
8. Nestor MS, Zarraga MB. The incidence of nonmelanoma skin cancers and actinic keratoses in South Florida. *J Clin Aesthet Dermatol.* 2012;5(4):20-24.
9. Rogers HW, Weinstock MA, Feldman SR, Coldiron BM. Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the US population, 2012. *JAMA Dermatol.* 2015;151(10):1081-1086.
10. Xiang F, Lucas R, Hales S, Neale R. Incidence of nonmelanoma skin cancer in relation to ambient UV radiation in white populations, 1978-2012: empirical relationships. *JAMA Dermatol.* 2014;150(10):1063-1071. doi:10.1001/jamadermatol.2014.762
11. Voiculescu V, Calenic B, Ghita M, et al. From normal skin to squamous cell carcinoma: a quest for novel biomarkers. *Dis Markers.* 2016;2016:4517492.
12. Stratigos A, Garbe C, Lebbe C, et al. Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline. *Eur J Cancer.* 2015;51(14):1989-2007.
13. Morton CA, Birnie AJ, Eedy DJ. British Association of Dermatologists' guidelines for the management of squamous cell carcinoma in situ (Bowen's disease) 2014. *Br J Dermatol.* 2014;170(2):245-260.
14. Alam M, Armstrong A, Baum C, et al. Guidelines of care for the management of cutaneous squamous cell carcinoma. *J Am Acad Dermatol.* 2018;78(3):560-578. doi:10.1016/j.jaad.2017.10.007
15. Connolly SM, Baker DR, Coldiron BM, et al. AAD/ACMS/ASDSA/ASMS 2012 appropriate use criteria for Mohs micrographic surgery: a report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, and the American Society for Mohs Surgery. *J Am Acad Dermatol.* 2012;67(4):531-550.
16. Sharma A, Birnie AJ, Bordea C, et al. British Association of Dermatologists guidelines for the management of people with cutaneous squamous cell carcinoma in situ (Bowen disease) 2022. *Br J Dermatol.* 2023;188(2):186-194.
17. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Squamous Cell Skin Cancer Version 2.2025. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1465. Published February 7, 2025. Accessed June 23, 2025.
18. Swanson N, Abramovits W, Berman B, Kulp J, Rigel DS, Levy S. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: results of two placebo-controlled studies of daily application to the face and balding scalp for two 2-week cycles. *J Am Acad Dermatol.* 2010;62(4):582-590.
19. Jansen MHE, Kessels J, Nelemans PJ, et al. Randomized trial of four treatment approaches for actinic keratosis. *N Engl J Med.* 2019;380(10):935-946.
20. Piacquadio DJ, Chen DM, Farber HF, et al. Photodynamic therapy with aminolevulinic acid topical solution and visible blue light in the treatment of multiple actinic keratoses of the face and scalp: investigator-blinded, phase 3, multicenter trials. *Arch Dermatol.* 2004;140(1):41-46.
21. Park HE, Park JW, Kim YH, et al. Analysis on the effectiveness and characteristics of treatment modalities for Bowen's disease: an observational study. *J Clin Med.* 2022;11(10)
22. Stratigos AJ, Garbe C, Dessinioti C, et al. European consensus-based interdisciplinary guideline for invasive cutaneous squamous cell carcinoma: part 2. treatment-update 2023. *Eur J Cancer.* 2023;193:113252.
23. Moreno-Ramírez D, Silva-Clavería F, Fernández-Orland A, Eiris N, Ruiz de Casas A, Férrandiz L. Surgery for cutaneous squamous cell carcinoma and its limits in advanced disease. *Dermatol Pract Concept.* 2021;11(Suppl 2):e2021167S.
24. Chen J, Xie X, Liu Y, et al. Application of photodynamic therapy with 5-aminolevulinic acid and fractional CO2 laser for the management of recalcitrant plantar warts. *Photodiagnosis Photodyn Ther.* 2025;51:104407. doi:10.1016/j.pdpdt.2024.104407
25. Brian Jiang SI, Kempers S, Rich P, et al. A randomized, vehicle-controlled phase 3 study of aminolevulinic acid photodynamic therapy for the treatment of actinic keratoses on the upper extremities. *Dermatol Surg.* 2019;45(7):890-897. doi:10.1097/DSS.0000000000001760
26. Morton CA, Dominicus R, Radny P, et al. A randomized, multinational, noninferiority, phase III trial to evaluate the safety and efficacy of BF-200 aminolaevulinic acid gel vs. methyl aminolaevulinate cream in the treatment of nonaggressive basal cell carcinoma with photodynamic therapy. *Br J Dermatol.* 2018;179(2):309-319.
27. Cai H, Wang YX, Zheng JC, et al. Photodynamic therapy in combination with CO2 laser for the treatment of Bowen's disease. *Lasers Med Sci.* 2015;30(5):1505-1510. doi:10.1007/s10103-015-1754-1
28. Cohen DK, Lee PK. Photodynamic therapy for non-melanoma skin cancers. *Cancers (Basel).* 2016;8(10):90.
29. Collier NJ, Rhodes LE. Photodynamic therapy for basal cell carcinoma: the clinical context for future research priorities. *Molecules.* 2020;25(22):5398.
30. Piacquadio DJ, Chen DM, Farber HF, et al. Photodynamic therapy with aminolevulinic acid topical solution and visible blue light in the treatment of multiple actinic keratoses of the face and scalp: investigator-blinded, phase 3, multicenter trials. *Arch Dermatol.* 2004;140(1):41-6.
31. Sieroń A, Kawczyk-Krupka A, Cebula MA, et al. Photodynamic therapy (PDT) using topically applied δ-aminolevulinic acid (ALA) for the treatment of malignant skin tumors. *Photodiagnosis Photodyn Ther.* 2004;1(4):311-317.
32. Wu Y, Wang P, Zhang L, Wang B, Wang X. Enhancement of photodynamic therapy for Bowen's disease using plum-blossom needling to augment drug delivery. *Dermatol Surg.* 2018;44(12):1516-1524.

33. Kibbi N, Zhang Y, Leffell DJ, Christensen SR. Photodynamic therapy for cutaneous squamous cell carcinoma in situ: impact of anatomic location, tumor diameter, and incubation time on effectiveness. *J Am Acad Dermatol.* 2020;82(5):1124-1130.
34. Souza CS, Felicio LB, Ferreira J, et al. Long-term follow-up of topical 5-aminolaevulinic acid photodynamic therapy diode laser single session for non-melanoma skin cancer. *Photodiagnosis Photodyn Ther.* 2009;6(3-4):207-213.
35. LEVULAN® KERASTICK® (aminolevulinic acid HCl) for topical solution, 20%. Full Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; 2024.
36. Nestor MS, Han H, Ceci FM, Lawson A, Gade A. Evaluating the safety and efficacy of aminolevulinic acid 20% topical solution activated by pulsed dye laser and blue light in the treatment of facial cutaneous squamous cell carcinoma in situ. *J Cosmet Dermatol.* 2023;22(9):2471-2475.
37. Salim A, Leman JA, McColl JH, Chapman R, Morton CA. Randomized comparison of photodynamic therapy with topical 5-fluorouracil in Bowen's disease. *Br J Dermatol.* 2003;148(3):539-543.
38. Morton CA, Whitehurst C, Moseley H, McColl JH, Moore JV, Mackie RM. Comparison of photodynamic therapy with cryotherapy in the treatment of Bowen's disease. *Br J Dermatol.* 1996;135(5):766-771.
39. AMELUZ® (aminolevulinic acid hydrochloride) topical gel. Full Prescribing Information. Woburn, MA: Biofrontera, Inc.; 2024.
40. Clark C, Bryden A, Dawe R, Moseley H, Ferguson J, Ibbotson SH. Topical 5-aminolaevulinic acid photodynamic therapy for cutaneous lesions: outcome and comparison of light sources. *Photodermatol Photoimmunol Photomed.* 2003;19(3):134-141.
41. Grapengiesser S, Ericson M, Gudmundsson F, Larkö O, Rosén A, Wennberg AM. Pain caused by photodynamic therapy of skin cancer. *Clin Exp Dermatol.* 2002;27(6):493-497.
42. Morton CA, Whitehurst C, McColl JH, Moore JV, MacKie RM. Photodynamic therapy for large or multiple patches of Bowen disease and basal cell carcinoma. *Arch Dermatol.* 2001;137(3):319-324.
43. Morton CA, Whitehurst C, Moore JV, MacKie RM. Comparison of red and green light in the treatment of Bowen's disease by photodynamic therapy. *Br J Dermatol.* 2000;143(4):767-772.
44. Heusinkveld LE, Bullock TA, Negrey J, Warren CB, Maytin EV. Sandpaper curettage: a simple method to improve PDT outcomes for actinic keratosis. *Photodiagnosis Photodyn Ther.* 2022;40:103050.
45. Leibovitch I, Huilgol SC, Selva D, Richards S, Paver R. Cutaneous squamous carcinoma in situ (Bowen's disease): treatment with Mohs micrographic surgery. *J Am Acad Dermatol.* 2005;52(6):997-1002.
46. Ahmady S, Nelemans PJ, Kelleners-Smeets NWJ, et al. Surgical excision versus topical 5% 5-fluorouracil and photodynamic therapy in treatment of Bowen's disease: A multicenter randomized controlled trial. *J Am Acad Dermatol.* 2024;90(1):58-65. doi:10.1016/j.jaad.2023.08.076
47. Westers-Attema A, van den Heijkant F, Lohman BG, et al. Bowen's disease: a six-year retrospective study of treatment with emphasis on resection margins. *Acta Derm Venereol.* 2014;94(4):431-435.

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