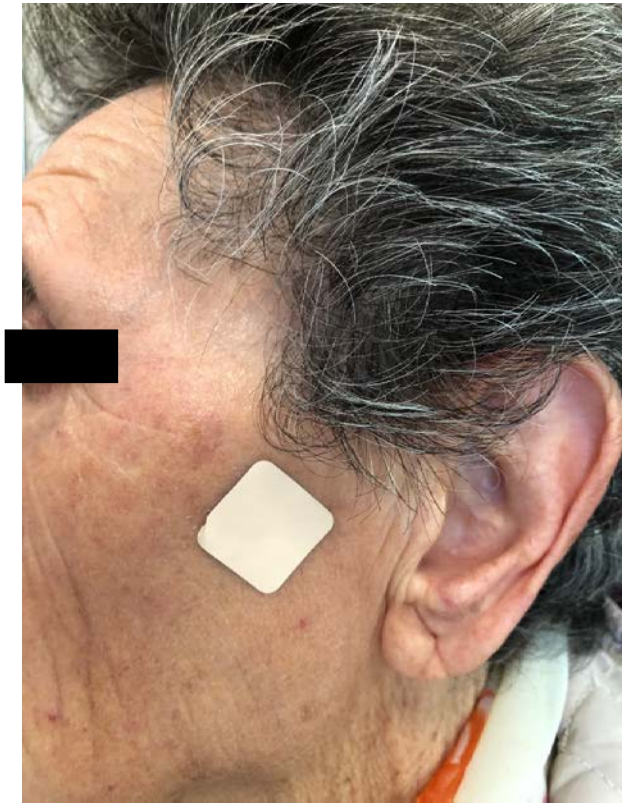
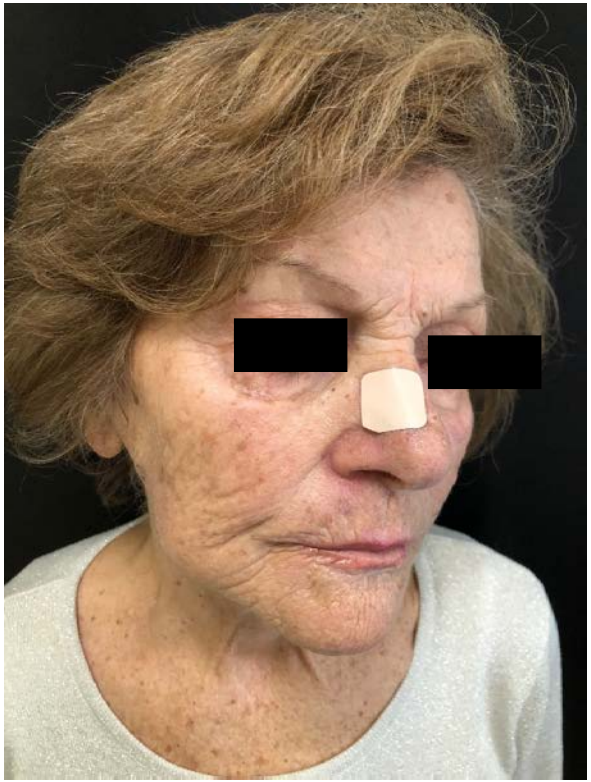
Novità in terapia fotodinamica per le cheratosi attiniche
Revisione della letteratura

Dott.ssa Nancy Dattola

Universita' degli studi di Roma "Tor Vergata"





PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed | pdt guidelines

Create RSS | Create alert | Advanced

Article types
Customize ...

Text availability
Abstract
Free full text
Full text

Publication dates
5 years
10 years
Custom range...

Species
Humans
Other Animals

Format: Summary | **Sort by**: Most Recent | **Per page**: 20 | **Send to**

Best matches for pdt guidelines:

European Dermatology Forum **Guidelines** on topical photodynamic therapy.
Morton C et al. Eur J Dermatol. (2015)

Photodynamic Therapy: A Clinical Consensus Guide.
Ozog DM et al. Dermatol Surg. (2016)

European **guidelines** for topical **PDT** part 1 JEADV 2013; 27: 536-544.
Skaria AM et al. J Eur Acad Dermatol Venereol. (2014)

Switch to our new best match sort order

Revisione letteratura

Therapy

Eur J Dermatol 2015; 25(4): 296-311

Colin MORTON[1]
Rolf-Markus SZEIMIES[2]
Alexis SIDOROFF[3]
Ann-Marie WENNBERG[4]
Nicole BASSET-SEGUIN[5]
Piergiacomo CALZAVARA-PINTON[6]
Yolanda GILABERTE[7]
Günther HOFBAUER[8]
Robert HUNGER[9]
Sigrid KARRER[10]
Percy LEHMANN[11]
Stefano PIASERICO[12]
Claas ULRICH[13]
Lasse BRAATHEN[9],
on behalf of the European Dermatology Forum

European Dermatology Forum Guidelines on topical photodynamic therapy

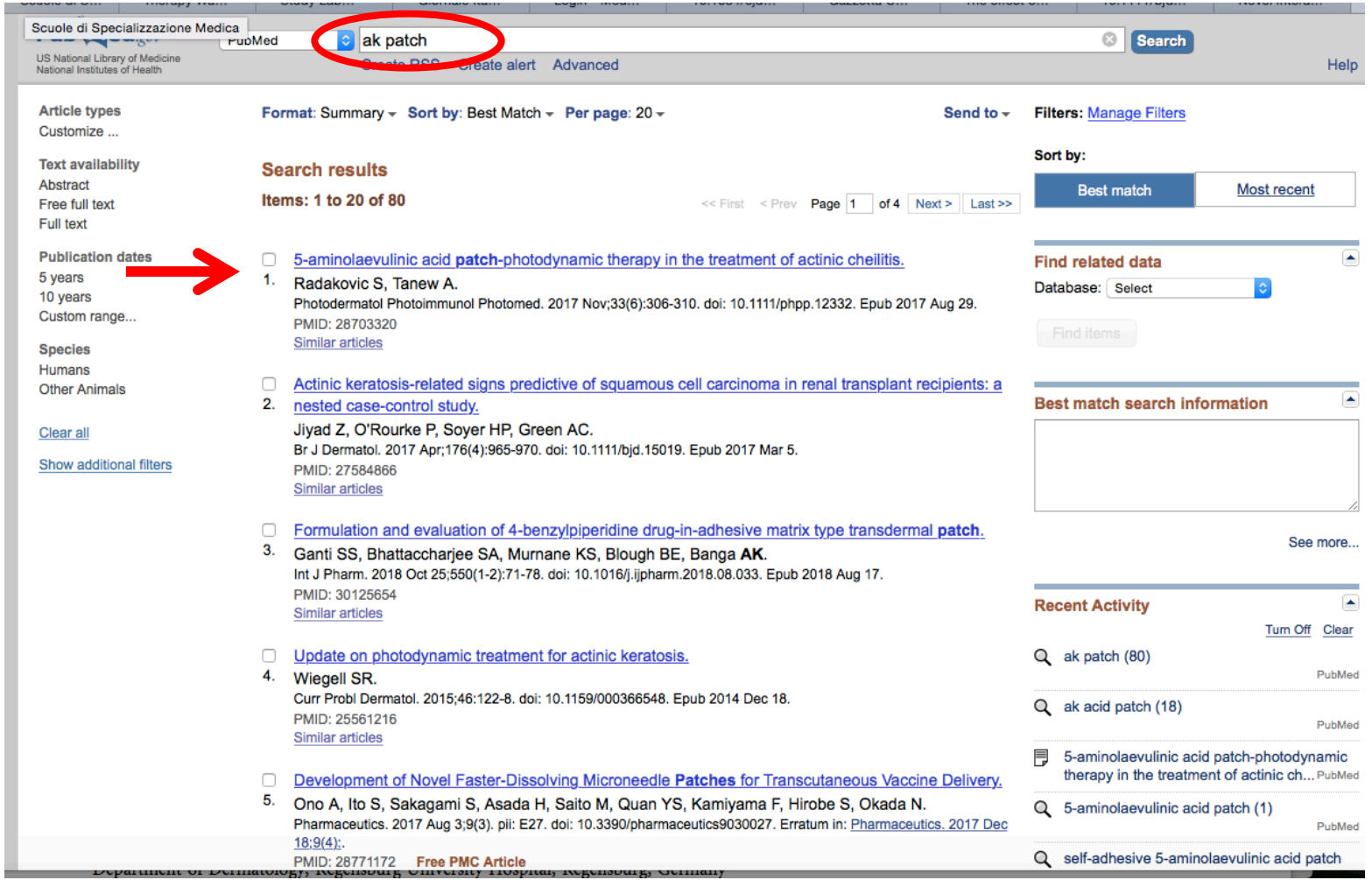
Topical photodynamic therapy (PDT) is a widely approved therapy for actinic keratoses, squamous cell carcinoma *in-situ*, superficial and certain thin basal cell carcinomas. Recurrence rates are typically equivalent to existing therapies, although inferior to surgery for nodular basal cell carcinoma. PDT can be used both as a lesional or as a field therapy and has the potential to delay/reduce the development of new lesions. PDT has also been studied for its place in the treatment of, as well as its potential to prevent, superficial skin cancers in immune-suppressed patients, although sustained clearance rates are lower than for immunocompetent individuals. Many additional indications have been evaluated, including photo-rejuvenation and inflammatory and infective dermatoses. This S2 guideline considers all current and emerging indications for the use of topical photodynamic therapy in Dermatology, prepared by the PDT subgroup of the European Dermatology Forum guidelines committee. It presents consensual expert recommendations reflecting current published evidence. An unabridged version of this guideline is available online at: http://www.euroderm.org/edf/index.php/edf-guidelines.

Key words: 5-aminolaevulinic acid, dermatology, guidelines, methyl aminolaevulinate, non-melanoma skin cancer, photodynamic therapy

European Dermatology Forum

[1] Department of Dermatology, Stirling Community Hospital, Stirling, FK8 2AU, UK
[2] Department of Dermatology & Allergology,

- Three agents are currently licensed for use in Europe: Methyl aminolaevulinate (160mg/g) (MAL**) Metvix® /Metvixia® (Galderma, Paris, France)** is used along with red light to treat non-hyperkeratotic actinic keratosis (AK), squamous cell carcinoma in-situ (SCC in-situ/Bowen's disease), superficial and nodular basal cell carcinomas (sBCC, nBCC)
- A patch containing **5-ALA (Alacare® (Galderma-Spirig AG, Egerkingen, Switzerland**) is approved for mild AK in a single treatment in combination with red light. Furthermore for AK, a nanoemulsion (Ameluz® (Biofrontera AG, Leverkusen, Germany)) is licensed for PDT in combination with red light for the treatment of mild and moderate AK.
- A 20% formulation of 5-ALA, Levulan (DUSA Pharmaceuticals, USA), is approved in N. America and certain other countries for AK, in a protocol that uses blue light


Scuole di Specializzazione Medica
US National Library of Medicine
National Institutes of Health
PubMed
ak patch
Search
Create alert
Advanced
Help
Article types
Customize ...
Text availability
Abstract
Free full text
Full text
Publication dates
5 years
10 years
Custom range...
Species
Humans
Other Animals
Clear all
Show additional filters
Format: Summary
Sort by: Best Match
Per page: 20
Send to
Filters: Manage Filters
Search results
Items: 1 to 20 of 80
<< First
< Prev
Page 1 of 4
Next >
Last >>
1. 5-aminolaevulinic acid patch-photodynamic therapy in the treatment of actinic cheilitis.
Radakovic S, Tanew A.
Photodermatol Photoimmunol Photomed. 2017 Nov;33(6):306-310. doi: 10.1111/phpp.12332. Epub 2017 Aug 29.
PMID: 28703320
Similar articles
2. Actinic keratosis-related signs predictive of squamous cell carcinoma in renal transplant recipients: a nested case-control study.
Jiyad Z, O'Rourke P, Soyer HP, Green AC.
Br J Dermatol. 2017 Apr;176(4):965-970. doi: 10.1111/bjd.15019. Epub 2017 Mar 5.
PMID: 27584866
Similar articles
3. Formulation and evaluation of 4-benzylpiperidine drug-in-adhesive matrix type transdermal patch.
Ganti SS, Bhattaccharjee SA, Murnane KS, Blough BE, Banga AK.
Int J Pharm. 2018 Oct 25;550(1-2):71-78. doi: 10.1016/j.ijpharm.2018.08.033. Epub 2018 Aug 17.
PMID: 30125654
Similar articles
4. Update on photodynamic treatment for actinic keratosis.
Wiegell SR.
Curr Probl Dermatol. 2015;46:122-8. doi: 10.1159/000366548. Epub 2014 Dec 18.
PMID: 25561216
Similar articles
5. Development of Novel Faster-Dissolving Microneedle Patches for Transcutaneous Vaccine Delivery.
Ono A, Ito S, Sakagami S, Asada H, Saito M, Quan YS, Kamiyama F, Hirobe S, Okada N.
Pharmaceutics. 2017 Aug 3;9(3). pii: E27. doi: 10.3390/pharmaceutics9030027. Erratum in: Pharmaceutics. 2017 Dec 18;9(4):.
PMID: 28771172 Free PMC Article
Sort by:
Best match
Most recent
Find related data
Database: Select
Find items
Best match search information
See more...
Recent Activity
Turn Off
Clear
ak patch (80)
PubMed
ak acid patch (18)
PubMed
5-aminolaevulinic acid patch-photodynamic therapy in the treatment of actinic ch... PubMed
5-aminolaevulinic acid patch (1)
PubMed
self-adhesive 5-aminolaevulinic acid patch

Similar articles

See more...

6. Photodynamic therapy with a 5-ALA **patch** does not increase the risk of conversion of actinic keratoses into squamous cell carcinoma: Results of a multicentre non-interventional study.
Reinhold U, Petering H, Dirschka T, Rozsondai A, Gille J, Kurzen H, Ostendorf R, Ebeling A, Stocker M, Radny P.
Exp Dermatol. 2018 Dec;27(12):1399-1402. doi: 10.1111/exd.13804.
PMID: 30326156
Similar articles

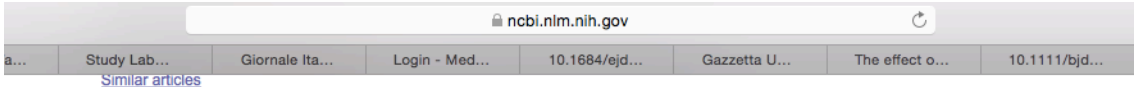
7. Sphingomyelin **patches** on pancreatic beta-cells are indicative of insulin secretory capacity.
Kavishwar A, Moore A.
J Histochem Cytochem. 2013 Dec;61(12):910-9. doi: 10.1369/0022155413502792. Epub 2013 Aug 6.
PMID: 23920110 **Free PMC Article**
Similar articles

8. [Actinic Keratosis].
Dejaco D, Hauser U, Zelger B, Riechelmann H.
Laryngorhinootologie. 2015 Jul;94(7):467-79; quiz 480-1. doi: 10.1055/s-0035-1554655. Epub 2015 Jun 30. Review. German.
PMID: 26125293
Similar articles

9. Quality of life in patients with recurrent aphthous stomatitis treated with a mucoadhesive **patch** containing citrus essential oil.
Kürklü-Gürleyen E, Öğüt-Erişen M, **Çak**ır O, Uysal Ö, **Ak** G.
Patient Prefer Adherence. 2016 May 27;10:967-73. doi: 10.2147/PPA.S106530. eCollection 2016.
PMID: 27313450 **Free PMC Article**
Similar articles

10. Fluorescence characteristics and pharmacokinetic properties of a novel self-adhesive 5-ALA **patch** for photodynamic therapy of actinic keratoses.
Fauteck JD, Ackermann G, Birkel M, Breuer M, Moor AC, Ebeling A, Ortland C.
Arch Dermatol Res. 2008 Feb;300(2):53-60. Epub 2007 Oct 25.
PMID: 17960406
Similar articles

11. A network meta-analysis of the relative efficacy of treatments for actinic keratosis of the face or scalp in Europe.
Vegter S, Tolley K.
PLoS One. 2014 Jun 3;9(6):e96829. doi: 10.1371/journal.pone.0096829. eCollection 2014.



Similar articles

12. A multicenter, open-label, pilot study evaluating the functionality of an integrated call center for a digital medicine system to optimize monitoring of adherence to oral aripiprazole in adult patients with serious mental illness.
Kopelowicz A, Baker RA, Zhao C, Brewer C, Lawson E, Peters-Strickland T.
Neuropsychiatr Dis Treat. 2017 Oct 19;13:2641-2651. doi: 10.2147/NDT.S143091. eCollection 2017.
PMID: 29089771 **Free PMC Article**
Similar articles

13. Optimization of photodynamic therapy with a novel self-adhesive 5-aminolaevulinic acid **patch**: results of two randomized controlled phase III studies.
Hauschild A, Stockfleth E, Popp G, Borrosch F, Brüning H, Dominicus R, Mensing H, Reinhold U, Reich K, Moor AC, Stocker M, Ortland C, Brunnert M, Szeimies RM.
Br J Dermatol. 2009 May;160(5):1066-74. doi: 10.1111/j.1365-2133.2009.09040.x. Epub 2009 Feb 16.
PMID: 19222455
Similar articles

14. Bucher's indirect comparison of daylight photodynamic therapy with methyl aminolevulinate cream versus diclofenac plus hyaluronic acid gel for the treatment of multiple actinic keratosis.
Calzavara-Pinton P, Zane C, Pacou M, Szeimies RM.
Eur J Dermatol. 2016 Oct 1;26(5):487-492. Review.
PMID: 27352420
Similar articles

15. Long-term follow-up of photodynamic therapy with a self-adhesive 5-aminolaevulinic acid **patch**: 12 months data.
Szeimies RM, Stockfleth E, Popp G, Borrosch F, Brüning H, Dominicus R, Mensing H, Reinhold U, Reich K, Moor AC, Stocker M, Ortland C, Brunnert M, Hauschild A.
Br J Dermatol. 2010 Feb 1;162(2):410-4. doi: 10.1111/j.1365-2133.2009.09377.x. Epub 2009 Jun 30.
PMID: 19804593
Similar articles

16. Gamma-band activity reflects attentional guidance by facial expression.
Müsch K, Siegel M, Engel **AK**, Schneider TR.
Neuroimage. 2017 Feb 1;146:1142-1148. doi: 10.1016/j.neuroimage.2016.09.025. Epub 2016 Sep 13.
PMID: 27637862
Similar articles

NeuroImage. 2017 Feb 1;146:1142-1148. doi: 10.1016/j.neuroimage.2016.09.025. Epub 2016 Sep 13.
PMID: 27637862
Similar articles

17. Effective photodynamic therapy of actinic keratoses on the head and face with a novel, self-adhesive 5-aminolaevulinic acid **patch**.
Hauschild A, Popp G, Stockfleth E, Meyer KG, Imberger D, Mohr P, Itschert G, Kaufmann R, Neuber K, Frambach Y, Gollnick H, Brunnert M, Stocker M, Ortland C, Karrer S.
Exp Dermatol. 2009 Feb;18(2):116-21. doi: 10.1111/j.1600-0625.2008.00770.x. Epub 2008 Jul 17.
PMID: 18643849
Similar articles

18. An adenylate kinase is involved in KATP channel regulation of mouse pancreatic beta cells.
Schulze DU, Düfer M, Wieringa B, Krippeit-Drews P, Drews G.
Diabetologia. 2007 Oct;50(10):2126-34. Epub 2007 Aug 18.
PMID: 17704905
Similar articles

19. Stromal Cell Subsets Directing Neonatal Spleen Regeneration.
Tan JK, Watanabe T.
Sci Rep. 2017 Jan 9;7:40401. doi: 10.1038/srep40401.
PMID: 28067323 **Free PMC Article**
Similar articles

20. Light **patch**: preliminary report of a novel form of blue light delivery for the treatment of actinic keratosis.
Zelickson B, Counters J, Coles C, Selim M.
Dermatol Surg. 2005 Mar;31(3):375-8.
PMID: 15841647
Similar articles

<< First < Prev Page 1 of 4 Next > Last >>

Back to top

BJD
British Journal of Dermatology

Long-term follow-up of photodynamic therapy with a self-adhesive 5-aminolaevulinic acid patch: 12 months data

R.-M. Szeimies, E. Stockfleth,* G. Popp,† F. Borrosch,‡ H. Brüning,§ R. Dominicus,¶ H. Mensing,**
U. Reinhold,†† K. Reich,‡‡ A.C.E. Moor,§§ M. Stocker,§§ C. Ortland,§§ M. Brunnert,¶¶ and A. Hauschild***

Department of Dermatology, Regensburg University Hospital, Franz Josef Strauss Allee 11, Regensburg, Germany
*Charité, Skin Cancer Center Charité Berlin, Chariteplatz 1, Berlin, Germany
†Hofackerstraße 19, Augsburg, Germany
‡Oyther Str. 24, Vechta, Germany
§Schönberger Str. 72–74, Kiel, Germany
¶Vollenstr. 8, Dülmen, Germany
**Dermatologisches Ambulatorium, Heegbarg 5, Hamburg, Germany
††Medical Centre Bonn, Friedensplatz 16, Bonn, Germany
‡‡SCIderm GmbH, Esplanade 6, Hamburg, Germany
§§photonamic GmbH & Co. KG, Theaterstr. 6, Wedel, Germany
¶¶M.A.R.C.O. Institute for Clinical Research and Statistics, Moskauer Str. 25, Düsseldorf, Germany
***Department of Dermatology, Venerology and Allergology, University of Kiel, Schittenhelmstr. 7, Kiel, Germany

Correspondence
Christoph Ortland.
E-mail: c.ortland@photonamic.de

Accepted for publication
24 June 2009

Key words
aminolaevulinic acid, actinic keratosis, photodynamic therapy

Conflicts of interest
RMS, AH, ES, ACEM, CO, MS and MB declared a conflict of interest—see note at end of article. The other authors have no conflict of interest to declare.

Summary

Background Photodynamic therapy with a self-adhesive 5-aminolaevulinic acid (5-ALA) patch shows high efficacy rates in the treatment of mild to moderate actinic keratosis (AK) in short term trials.

Objectives The purpose of the trial was to follow up patients after successful 5-ALA patch-PDT at 3 month intervals over a total period of 12 months. Patients who had received placebo-PDT or cryosurgery served for comparison.

Patients/methods Three months after therapy, 360 patients from two separate randomized parallel group phase III studies (one superiority trial vs. placebo-PDT, one noninferiority trial vs. cryosurgery) were suitable for the follow-up study. Patients had to show at least one successfully treated AK lesion after initial therapy. A total of 316 patients completed the follow-up.

Results Twelve months after a single treatment, 5-ALA patch-PDT still proved superior to placebo-PDT and cryosurgery ($P < 0{\cdot}001$ for all tests). On a lesion basis, efficacy rates were 63% and 79% for PDT, 63% for cryosurgery and 9% and 25% for placebo-PDT. Recurrence rates of patch-PDT proved superior to those of

Results

- The 5-ALA patch is intended to be directly applied to AK lesions without prior crust removal by curettage
- It is skin coloured, square and 4 cm2 in size
- The patch contains 8 mg 5-ALA (present as 5-ALA hydrochloride).
- **For PDT, 5-ALA or placebo** patches were applied to the lesions selected for study for 4 h without preparation of the lesions
- Placebo patches were of identical appearance to the 5-ALA patches but did not contain 5-ALA
- A maximum of 8 AK lesions was treated per PDT session

Results

- After patch removal, AK lesions were immediately illuminated with red light 37 J cm)2 at 630 3 nm; Aktilite CL 128 (Photocure ASA, Oslo, Nor- way) or Omnilux (Photo Therapeutics Inc., CA, U.S.A.).
- **Study lesions in the cryosurgery gro**up were frozen using one cycle with the liquid nitrogen open spraying procedure for a maximum time of 10 s after ice ball formation.
- 360 patients were eligible for the follow-up period of a maximum of 9months (i.e. 12 months after a single treatment).
- These patients had a total of 1619 cleared AK study lesions. Three hundred and sixteen patients completed the follow-up (Table 1).

Table 1 Disposition of patients during follow-up period. Numbers in parentheses indicate the number of patients showing at respective follow-up visit and are only given if different from the total number of patients under observation

	No. of patients			
Visit	1	2	3	4
Follow-up period (months)	Start	3	6	9
Time after initial treatment (months)	3	6	9	12
Superiority study				
5-ALA patch-PDT	64	62 (61)	54 (51)	53
Placebo PDT	12	12	11	10
Non-inferiority study				
5-ALA patch-PDT	132	131	126 (125)	121
Cryosurgery	130	130	121 (120)	113
Placebo PDT	22	19	19 (18)	19
Total	360	354	331	316

Efficacy

One year after a single therapy, the overall clearance rates were still high for the active treatment arms of both studies (Fig. 1). The 5-ALA patch-PDT proved statistically significantly

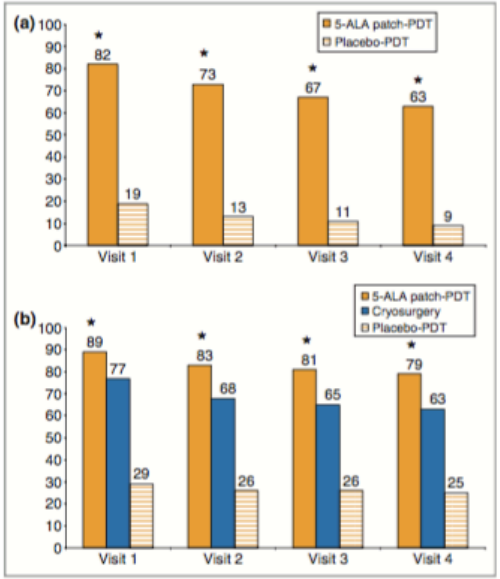


Fig 1. Overall clearance rates on a lesion basis at beginning of the follow-up period up to 12 months after a single therapy (Visit 1 indicating start of the follow-up period. Visits 2–4 were performed at intervals of 3 months). (a) Results of superiority study where 5-ALA patch-PDT was tested against placebo-PDT (*P < 0·001 vs. placebo-PDT). (b) Results of noninferiority study on the comparison of 5-ALA patch-PDT vs. cryosurgery and placebo-PDT (*P < 0·001 vs. cryosurgery and placebo-PDT).

Discussion

- A single course of 5-ALA patch-PDT has proved to be effective and better than standard and placebo treatment in short term studies with lesion clearance rates between 82% and 89%.
- This excellent efficacy of 5-ALA patch-PDT is linked to a convenient and easy way of treating AK; no curettage is necessary before applying the 5-ALA patch.
- The study results show that the thicker, moderate AK lesions respond as well to the 5-ALA patch PDT as mild AK lesions.
- It is hypothesized that the reason for this is the rapid flux of 5-ALA from the patch during the occlusion period.

DOI:10.1111/j.1600-0625.2008.00770.x
www.blackwellpublishing.com/EXD

Original Article

Effective photodynamic therapy of actinic keratoses on the head and face with a novel, self-adhesive 5-aminolaevulinic acid patch

Axel Hauschild[1], Georg Popp[2], Eggert Stockfleth[3], Karl-Gustav Meyer[4], Dirk Imberger[5], Peter Mohr[6], Götz Itschert[7], Roland Kaufmann[8], Karsten Neuber[9,†], Yvonne Frambach[10], Harald Gollnick[11], Marcus Brunnert[12], Marcus Stocker[13], Christoph Ortland[13] and Sigrid Karrer[14]

[1]Department of Dermatology, Allergology and Venerology, University of Kiel, Kiel, Germany;
[2]Private Practice, Hofackerstr. 19, D-86179 Augsburg, Germany;
[3]Dermatology Department, Skin Cancer Center Charité, Schumannstr. 20-21, D-10117 Berlin, Germany;
[4]Private Practice, Schönhauser Allee 71, D-10437 Berlin, Germany;
[5]Private Practice, Friedrichstr. 17, D-25980 Westerland, Germany;
[6]Elbe Kliniken, Buxtehude, Germany;
[7]Am Rathaus 2 A, D-25421 Pinneberg, Germany;
[8]Johann-Wolfgang-Goethe University, Frankfurt/Main, Germany;
[9]University Medical Center Hamburg-Eppendorf, Hamburg, Germany;
[10]University of Lübeck, Lübeck, Germany;
[11]Otto-von-Guericke-University, Magdeburg, Germany;
[12]M.A.R.C.O. Institute for Clinical Research and Statistics, Düsseldorf, Germany;
[13]photonamic GmbH & Co. KG, Wedel, Germany;
[14]Department of Dermatology, Regensburg University Hospital, Regensburg, Germany
Correspondence: Axel Hauschild, Department of Dermatology, Allergology and Venerology, University of Kiel, Schittenhelmstr. 7, D-24105 Kiel, Germany, e-mail: ahauschild@dermatology.uni-kiel.de, Phone +49 431 597-1852, Fax -1853
[†]*Karsten Neuber was an active investigator and passed away during preparation of the manuscript.*

Accepted for publication 21 May 2008

Background: Photodynamic therapy (PDT) is increasingly used for the treatment of actinic keratosis (AK).

Objectives: To investigate both the efficacy of different application times and the safety of a novel patch (PD P 506 A) containing aminolaevulinic acid in the PDT of mild to moderate AK.

Methods: Applications of PD P 506 A for 0.5, 1, 2 and 4 h were compared in a multicentre, randomized, blinded-observer, parallel-group study. After patch removal, study lesions were illuminated with red light ($\lambda_{em} \approx 630$ nm; 37 J/cm^2). Study lesions were not pretreated (e.g. by curettage) prior to PDT. Efficacy was evaluated 4 and 8 weeks after treatment. Safety and tolerability were determined through laboratory analyses and documentation of both local reactions and adverse events.

Results: A total of 149 patients were initially enrolled. Of these, 140 patients (520 lesions) completed the study according to protocol. Eight weeks after treatment, 86% of the AK lesions (74% of the patients) treated with 4-h patch application showed complete clearance. The complete clearance rates of lesions (patients) for the 2-, 1- and 0.5-h treatment arms were 73% (47%), 72% (50%) and 51% (24%), respectively. Statistically, the 4-h application was identified as the 'best treatment'. Patients with clearance seemed to experience local reactions to a greater extent than patients without clearance. Local reactions to study treatments did not exceed the expected range.

Conclusions: The results of this first clinical efficacy study suggest excellent therapeutic outcomes with a single PD P 506 A PDT with a 4-h application.

Key words: actinic keratosis – aminolaevulinic acid – clinical trial – photodynamic therapy

Table 1. Summary of (a) patient (n = 140) and (b) AK lesion characteristics (n = 520) (VfE sample)

	PD P 506 A application duration			
	0.5 h	1 h	2 h	4 h
(a)				
Number of patients	34	38	34	34
Age (years)				
Mean ± SD	71.6 ± 9.70	71.8 ± 8.98	69.7 ± 6.86	69.9 ± 7.73
Median (range)	73.0 (39–88)	70.0 (55–91)	68.5 (57–84)	69.5 (49–83)
Sex				
Female	9 (26%)	13 (34%)	9 (26%)	6 (18%)
Male	25 (74%)	25 (66%)	25 (74%)	28 (82%)
Time since AK diagnosis (months)				
Mean ± SD	55.3 ± 78.31	43.8 ± 43.10	55.5 ± 63.13	55.6 ± 68.56
Median (range)	36.0 (0–420)	32.0 (0–144)	36.0 (0–300)	38.0 (0–302)
(b)				
Number of lesions	128	138	124	130
Localization				
Scalp	43 (34%)	23 (17%)	37 (30%)	54 (42%)
Forehead	61 (48%)	78 (57%)	42 (34%)	49 (38%)
Cheek	12 (9%)	16 (12%)	18 (15%)	12 (9%)
Nose	8 (6%)	8 (6%)	8 (6%)	6 (5%)
Temple	3 (2%)	5 (4%)	8 (6%)	9 (7%)
Other	1 (1%)	8 (6%)	11 (9%)	0 (0%)
Severity				
Mild	68 (53%)	82 (59%)	70 (56%)	71 (55%)
Moderate	60 (47%)	56 (41%)	54 (44%)	59 (45%)
Diameter (mm)				
Mean ± SD	8.2 ± 3.49	9.3 ± 3.07	8.4 ± 3.35	8.5 ± 3.28
Median (range)	8.0 (2–18)	9.0 (3–17)	8.0 (2–16)	8.0 (2–18)

Table 2. Efficacy results. Frequency of clearance of AK lesions and patients (VfE sample)

	PD P 506 A application duration							
	Lesion-based analysis				Patient-based analysis			
	0.5 h	1 h	2 h	4 h	0.5 h	1 h	2 h	4 h
No. of lesions/patients	128	138	124	130	34	38	34	34
Clearance frequency 4 weeks after PDT (%)	47	56	60	72	26	39	44	53
Clearance frequency 8 weeks after PDT (%)	51	72	73	86	24	50	47	74

group). AEs not related to the study therapy occurring in two or more patients included the appearance of new AK outside of the treated areas (five patients), eczema on other parts of the body than the study lesions (three patients), and infections after excision of a skin lesion and after a biopsy (two patients). One serious AE, not related to therapy, occurred in the 2-h group. For laboratory parameters, no treatment group showed an increased rate of shifts from normal values to abnormally low or high values.

Local reactions at the study lesions are quantitatively displayed in Fig. 2. During PD P 506 A application, burning, pruritus and erythema were the main occurrences. No dose dependency was observed. All reactions were rated as mild or moderate except for one case of severe erythema (application time: 1 h). By contrast, the incidence of local reac-

- In all four treatment groups, the majority of lesions showed clearance 8 weeks after PDT (Table 2).
- Application of 4 h was the best treatment, with an estimated 86% clearance rate
- The 95% confidence interval for the clearance rate on a lesion basis for the 4-h application [0.75; 0.95] indicated superiority to the other treatment arms, and was statistically selected as the ‘best treatment’.

Adverse events

- Five of 149 patients experienced an adverse event (AE)
- These were headache [one severe (0.5-h group), two moderate (2- and 4-h group)], moderate epistaxis (4-h group) and mild increase of alanine transaminase (0.5-h 4 h group)
- *AEs not related to the study therapy:*

AK outside of the treated areas (five patients),

eczema on other parts of the body than the study lesions (three patients)

infections after excision of a skin lesion and after a biopsy (two patients)

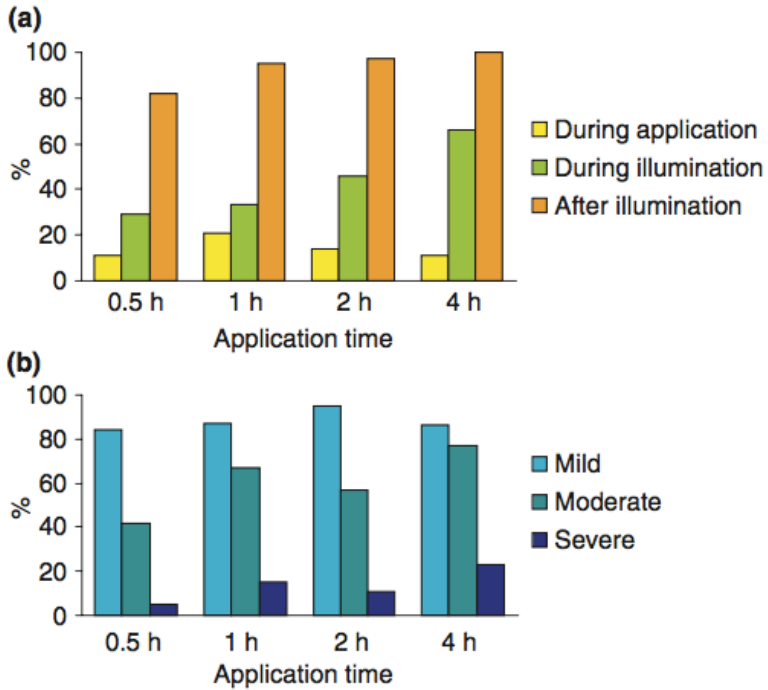


Figure 2. (a) Percentage of patients showing local reactions during application of PD P 506 A, during illumination with Aktilite® 128 CL and after illumination until the end of the observation period. (b) Percentage of patients showing mild, moderate and severe local reactions from the start of PD P 506 A application until the end of observation period.

The incidence of local reactions during illumination was dose-dependent and ranged from 26% in the 0.5-h group to 66% in the 4-h group.

The most frequent reactions were burning, pain and pruritus at the application site.

The incidence of mild local reactions was high in all treatment groups (‡ 84%)

The incidence of moderate or severe local reactions was lowest in the treatment group with 0.5-h and highest in the treatment group with 4-h application times

Arch Dermatol Res (2008) 300:53–60
DOI 10.1007/s00403-007-0787-0

HOT CLINICAL STUDY

Fluorescence characteristics and pharmacokinetic properties of a novel self-adhesive 5-ALA patch for photodynamic therapy of actinic keratoses

Jan-Dirk Fauteck · Günther Ackermann · Manfred Birkel · Marion Breuer · Anne C. E. Moor · Andrea Ebeling · Christoph Ortland

Received: 29 May 2007 / Revised: 29 June 2007 / Accepted: 21 August 2007 / Published online: 25 October 2007

Revisione letteratura

- Normally a precursor of the photosensitiser is applied topically and converted into protoporphyrin IX (PPIX) in the cells.
- By activating PPIX with light, the dysplastic cells will be destroyed.
- We report the results of two clinical studies investigating the properties of a novel self-adhesive 5-ALA-patch (PD P 506 A) intended for PDT of mild to moderate AK on the face and head.
- **The studies investigated the influence of patch application duration on PPIX-specific fluorescence and the pharmacokinetic properties of the 5-ALA patch.**
- **The PPIX fluorescence in AK lesions and normal skin after patch application (application for 2, 3, 4, 5 h) was investigated in 13 patients using DYADERM Professional (Biocam) 370–440 nm.**

Revisione letteratura

- In the subsequent pharmacokinetic study 12 patients were treated with 8 patches each (4 h application).
- 5-ALA and PPIX were analysed in plasma (over 24 h) and urine (over 12h). PPIX-specific fluorescence measured immediately after patch removal increased with increasing application duration to a maximum at 4-h application.
- The fluorescence in AK lesions was more intense than in normal skin.
- A small increase of 5-ALA plasma concentrations was observed in 10 of 12 patients after applying 8 patches for 4 h, which rapidly declined to normal values after patch removal.

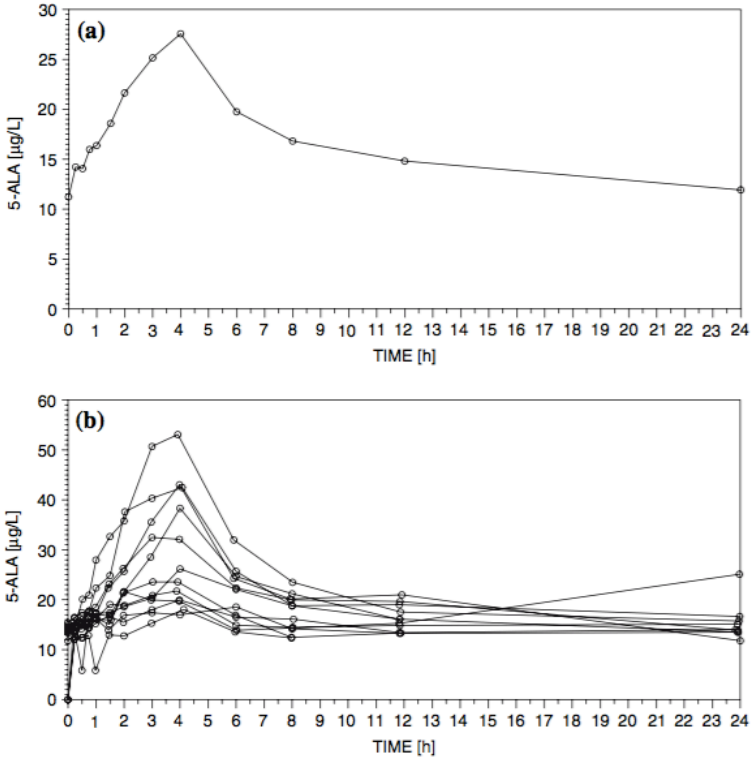


Fig. 2 **a** Geometric mean ($N = 12$) concentrations of 5-ALA (µg/l) versus time (h) following topical administration of 5-ALA patch. **b** All individual ($N = 12$) concentrations of 5-ALA (µg/l) versus time (h)

Table 1 Summary of patient characteristics of the safety samples of both studies

	FA study $N = 13$ (safety sample)	PK study $N = 12$ (safety sample)
Age (years)		
Mean ± SD	69.6 ± 9.87	69.8 ± 7.78
Median (range)	73 (49–80)	71 (50–81)
Sex		
Female	2 (15%)	2 (17%)
Male	11 (85%)	10 (83%)

FA Fluorescence Analysis; *PK* pharmacokinetic; *SD* Standard deviation

nificant difference.

By applying a repeated measurement model of analysis of variance, a statistically significant interaction between application duration and time was detected. Differences in mean fluorescence levels between the application durations changed over time. The mean profiles for fluorescence data are presented in Fig. 1a. Figure 1b presents the data in reference to the start of patch application. Since there is no difference in the fluorescence profiles depicted from start of the application for the application durations 3, 4 and 5 h, it can be postulated that a saturation of the biological system responsible for the conversion of 5-ALA to PPIX takes place.

Table 2 Summary of lesion characteristics of the safety samples of both studies

Application duration (h)	FA study $N = 13$ (52 lesions)				PK study $N = 12$ (96 lesions)
	2 h	3 h	4 h	5 h	4 h
Site					
Scalp	5 (38%)	6 (46%)	4 (31%)	6 (46%)	7 (7%)
Forehead	6 (46%)	4 (31%)	9 (69%)	5 (38%)	68 (71%)
Cheek	2 (15%)	3 (23%)	0	1 (7%)	19 (20%)
Ear	0	0	0	1 (7%)	1 (1%)
Temple	0	0	0	0	1 (1%)
Severity					
Mild	10 (77%)	8 (62%)	11 (85%)	9 (69%)	66 (69%)
Moderate	3 (23%)	5 (38%)	2 (15%)	4 (31%)	30 (31%)

FA Fluorescence Analysis; *PK* pharmacokinetic; *SD* Standard deviation

Local phototoxic reactions were prevented by applying a cover to the study lesions for the 48–72 h after removal of the 5-ALA-patch.

Results

The patient population as well as the selected study lesions shows comparable characteristics for both studies (Tables 1, 2). The majority of study lesions were located on the scalp and forehead. Most of the study lesions (70%) were of mild intensity.

Fluorescence analysis study (FA study)

Thirteen patients were recruited into the study. PPIX fluorescence data are based on the analysis of 48 AK study lesions and 24 normal skin areas (12 patients) which had been patched with the 5-ALA patch as specified in the study protocol and which provided valid fluorescence data. The patient who did not show valid fluorescence data was identified being a "PDT non-responder" retrospectively. All 13 patients were valid for safety evaluation.

Table 1 Summary of patient characteristics of the safety samples of both studies

Table 3 FA Study: fluorescence at the moment of patch removal (F_{0h}; $N = 12$) and summary statistics for primary variable

Study area	Application duration (h)	Fluorescence mean (SD)	Fluorescence median (range)
AK lesions	2	1.558 (0.403)	1.635 (0.81–2.17)
	3	2.496 (0.856)	2.580 (0.69–3.76)
	4	3.183 (1.041)	3.220 (1.55–4.95)
	5	3.407 (0.980)	3.260 (1.42–4.79)
Normal skin	2	0.823 (0.157)	0.805 (0.56–1.15)
	5	1.598 (0.649)	1.430 (0.75–2.77)

Baseline fluorescence was well comparable between study lesions. Mean values ranged from 0.66 to 0.70 for all except one AK lesions as well as normal skin areas.

The analysis of variance and multiple test procedure for treatment comparisons yielded the following results for the PPIX fluorescence in AK lesions (Tables 3, 4):

- The 2 h-duration is significantly different from each of the 3, 4 and 5-h durations
- The 3-h duration is significantly different from each of the 4 and 5-h durations
- The 4 and 5-h durations do not show a statistically significant difference.

By applying a repeated measurement model of analysis of variance, a statistically significant interaction between

Accepted: 6 July 2017
DOI: 10.1111/phpp.12332

ORIGINAL ARTICLE

WILEY Photodermatology, Photoimmunology & Photomedicine

5-aminolaevulinic acid patch-photodynamic therapy in the treatment of actinic cheilitis

Sonja Radakovic | Adrian Tanew

Department of Dermatology, Medical University of Vienna, Vienna, Austria

Correspondence
Sonja Radakovic, M.D., Department of Dermatology, Medical University of Vienna, Vienna, Austria.
Email: sonja.radakovic@meduniwien.ac.at

Funding information
Department of Dermatology, Medical University of Vienna, Vienna.

Summary

Background: Actinic cheilitis (AC) is a common disease caused by chronic ultraviolet exposure.

Objective: Alacare is a self-adhesive, skin coloured 5-aminolaevulinic acid (ALA) patch that has been developed for the treatment of mild to moderate actinic keratosis (AK). Considering the good results in the treatment of AK, the standardized delivery of ALA and the simple application Alacare patch- photodynamic therapy (PDT) appears as an interesting treatment option for AC.

Methods: We retrospectively assessed the efficacy, tolerability and cosmetic outcome of Alacare patch-PDT in eleven patients with AC. After occlusion with the Alacare patches for 4 hours, the AC lesions were illuminated with narrowband red light and a dose of 37 J/cm^2. All patients were clinically assessed for efficacy, side effects and cosmetic outcome at 3, 6, 9 and 12 months after treatment.

Results: Complete clinical response at the 3-month follow-up was achieved in eight of 11 patients (72,7%) and 12 of 15 AC lesions (80,0%), respectively. Up to the final 12-month follow-up, a recurrence was observed in two lesions. The complete clinical cure rate at 1 year after Alacare patch-PDT, thus, was 66,6% (10/15 lesions). The cosmetic outcome of the treatment was excellent in all cases.

Conclusion: Alacare patch-PDT was found to have substantial efficacy in the treatment of mild to moderate AC. Given its ease of use, absence of long-term side effects and the excellent cosmetic results Alacare patch-PDT might be considered as a promising new treatment option for the management of AC.

KEYWORDS
5-aminolaevulinic acid, actinic cheilitis, patch-PDT

to start treatment in case of activation of a latent herpes simplex infection.

The outcome was assessed clinically in comparison with baseline photographs at 3, 6, 9 and 12 months after PDT. Clinical cure was defined as a completely normal appearing lip surface without any signs of erythema, scaling, erosion or crusting. In case of incomplete response or recurrence of AC, a biopsy was taken to confirm the clinical diagnosis. Cosmetic changes such as fine lines and mottled pigmentation as well as the volume, roughness and dryness of the lips were also recorded at all follow-up visits.

3 | RESULTS

Complete clinical response at the 3-month follow-up was achieved in eight of 11 patients (72,7%) and 12 of 15 (80,0%) AC lesions. The latter included all five lesions treated with only one PDT session and seven of 10 lesions treated twice with PDT. Three patients with AC on the lower lip only showed a partial response after two PDT sessions. These poor responders were the two patients with a previous history of SCC and the patient with recurring AC.

Recurrence of one lesion each was observed at the 6-month (after 2 PDT) and 9-month (after 1 PDT) follow-up. No further recurrence was observed at the final visit. The complete clinical cure rate after a follow-up period of 12 months, thus, was 66,6% (10/15 lesions). All patients with partial response or clinical relapse were subsequently treated with imiquimod, KTP Laser or excision.

Photodynamic therapy-induced pain was the major side effect of treatment. Using the cold air blower during illumination, this side effect of PDT was sufficiently controlled in the first five patients (VAS score ranging between 2 and 5). It was only after the sixth patient who experienced very severe pain (VAS 8) that we decided to offer local anaesthesia for pain reduction to all subsequent patients. With that additional measure, the VAS during PDT was consistently below a VAS score of four. PDT was always followed by a moderate to severe local phototoxic reaction with swelling, blistering and erosions that proceeded to crust formation and scaling. Complete resolution of the local reaction occurred within 14 days after PDT. Five patients reported reactivation of herpesvirus infection within 1 week after PDT that was well controlled with immediate administration of valaciclovir.

The cosmetic outcome of Alacare patch-PDT was excellent in eight patients as evidenced by an improvement in the perioral fine lines and an apparent increase in lip volume (Figure 2). These changes were also noticed by the patients themselves who, in addition, felt less roughness and dryness of the treated lips.

FIGURE 1 Even and intensive fluorescence of the lower lip under wood light illumination at 4 h after application of the 5-aminolaevulinic acid (ALA) patch

4 | DISCUSSION

Various treatment options are available for AC.[2] Data on PDT for this indication have so far been much less favourable than those obtained in the treatment of AK. A clinical cure in seven of 15 patients (47%) and histological cure in five of 13 biopsied patients (38%) was reported at 3 months after two sessions of methyl aminolevulinate photodynamic therapy (MAL-PDT).[4] Another study assessed the clinical and histological long-term outcome of 38 AC patients after two sessions of 20% ALA-PDT. At 3 months after PDT, complete clinical response was observed in 26 (68,4%) of the patients. The clinical and histological recurrence rate up to the final follow-up at 18 months after PDT were 15,4% and 34,6%, respectively. Thus the total clinical and histological clearance rate after 18 months were 58% and 45%.[7] In a subsequent study from the same group of investigators, two sessions of MAL-PDT were combined with 5% imiquimod (3 days per week for 4 weeks). The complete clinical response rate at 3 months after treatment was 79%. At the 12-month follow-up, the complete clinical and histological response were 80% and 73%, respectively, and clearly superior to the results obtained previously with ALA-PDT alone.[8] In contrast to these results are recent findings on 16 evaluable AC patients who were also treated with two sessions of MAL-PDT.

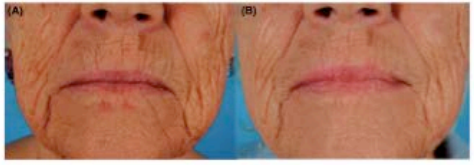
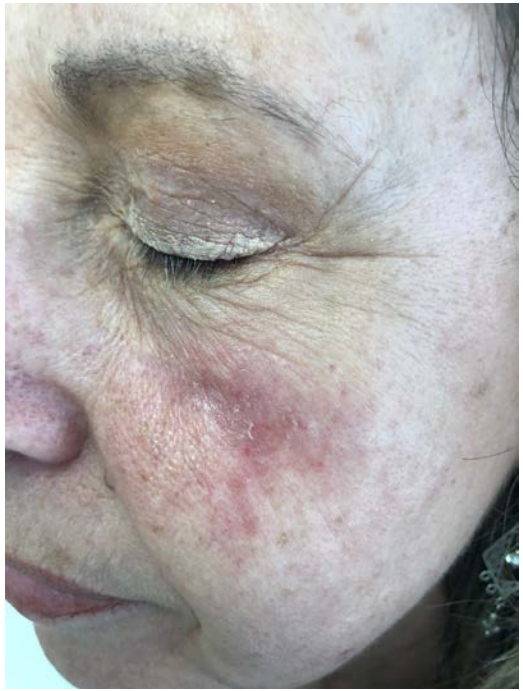
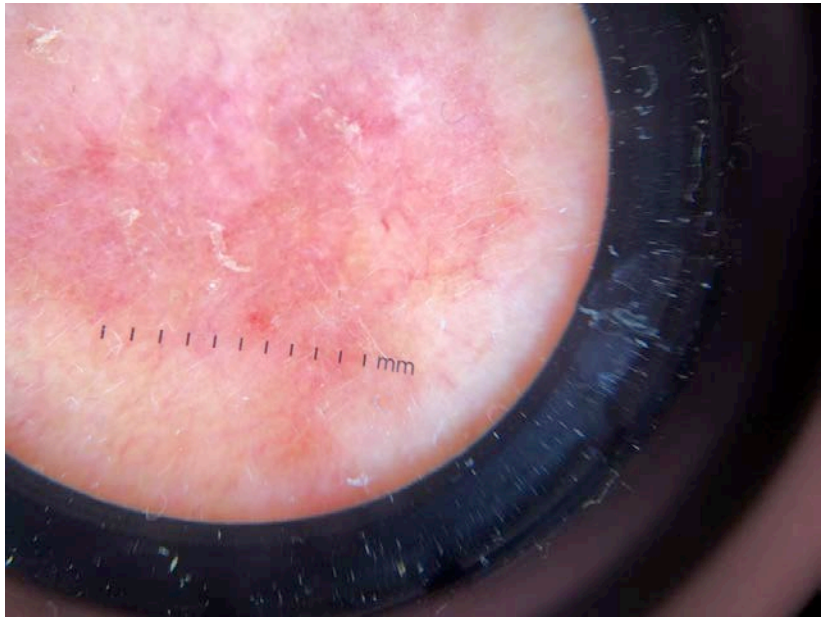


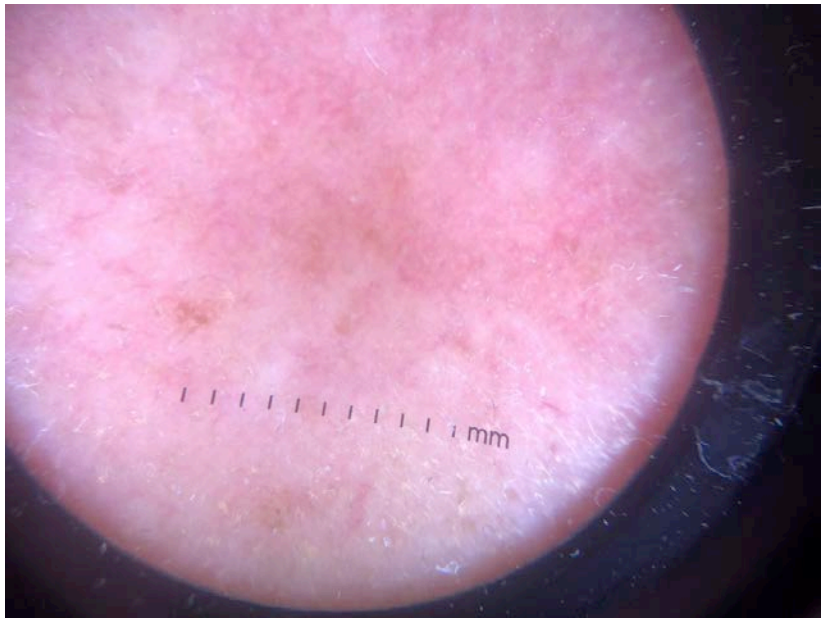
FIGURE 2 An 80-y-old female patient with actinic cheilitis of the lower lip before (A) and 6 mo after (B) one single 5-aminolaevulinic acid (ALA) patch-photodynamic therapy (PDT) treatment. Note the restoration of the normal lip surface and the excellent cosmetic result with reduction in the perioral lines and increase in lip volume

Donna, 58 anni T0





1 mese



Grazie per l'attenzione

- Grazie a ….
- Elena Campione
- Virginia Garofalo
- Sara Mazzilli
- Mauro Mazzeo

Grazie per l'attenzione

Domande?

No? Ottimo!

Ciao!