EURO PDT

20TH ANNUAL CONGRESS

PARIS

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THE EUROPEAN SOCIETY FOR PHOTODYNAMIC THERAPY

Paris, France

Friday 17 and Saturday 18, June 2022

BEST OF SLIDES 2022

EURO-PDT 2022 – Best of Slides

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Euro-PDT Board, June 2022

Plenary Session 1

DL-PDT and ADL-PDT – What do we know?

Chairs: Lasse R. Braathen, Nicole Basset-Seguin

Photodynamic Therapy

Lasse R.Braathen.MD.PhD.MHA.

Professor and Chairman Dermatology Emeritus.

Prof. and Chairman Emeritus, University of Bern, Switzerland Head Emeritus
Department for ENT, Rheumatology and Dermatology.
University and University Hospital North-Norway, Tromsö, Norway.

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EURO-PDT. An educational platform for PDT in Europe

- Aims:
  - Promote research, development and clinical use of PDT in Europe
  - Non-profit organisation
  - President: Prof. L.R.Braathen, Switzerland
  - Vice-President: Prof. R.-M. Szeimies, Germany
  - Board member: Dr. C. Morton. Scotland, UK

EURO-PDT

PDT Specialist Certificate.

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Info: www.euro-pdt.org

EuroPDT@gmail.com

What is new from the current guidelines? - Update 2022

Colin Morton, MD, MBChB, FRCP
Dermatology Centre, Stirling, Scotland

European Dermatology Forum Guidelines on Topical Photodynamic Therapy – Updated 2019/2020

Prof. Nicole Basset-Seguin
Prof. Lasse R. Braathen
Prof. Piergiacomo Calzavara-Pinton
Prof. Yolanda Gilaberte
Prof. Merete Haedersdal, Copenhagen
Prof. Gunther FL Hofbauer, Zurich
Prof. Robert Hunger, Bern
Prof. Sigrid Karrer, Regensburg
Dr. Colin. A. Morton
Prof. Stefano Piaserico
Prof. Rolf-Markus Szeimies
Dr. Claas Ulrich
Prof. Ann-Marie Wennberg

European Dermatology Forum

https://www.edf.one/home/Guidelines/Guidelines.html

European Dermatology Forum Guidelines on PDT 2020
Part 1 – Cancer Indications

C A Morton, R-M Szeimies, *N Basset-Seguin, et al*. Part 1. *J Eur Acad Dermatol Venereol* 2019;33:2225-38

Strength of Recommendation	Quality of Evidence	Indication
A	I	*Actinic keratoses (conventional/Daylight)* Squamous cell carcinoma in-situ Superficial and nodular BCC
B	I	NMSC in organ transplant recipients Prevention of NMSC in OTR Field cancerization
C	II iii	CTCL Extramammary Paget's disease
D	II iii	Invasive SCC

European Dermatology Forum Guidelines on PDT 2020 Part 2: Inflammatory/Infective Dermatoses

C A Morton, R-M Szeimies, *N Basset-Seguin, et al*. Part 2. *J Eur Acad Dermatol Venereol* 2020;34:17-29

Strength of Recommendation	Quality of Evidence	Indication
A	I	Photorejuvenation
B	I	Acne Refractory warts, plane/genital warts Cutaneous leishmaniasis Onychomycosis
C	II iii	Superficial fungal infections C II-III Deep cutaneous mycoses Hypertrophic and Keloid Scars Sebaceous gland hyperplasia
C	III	Lichen sclerosus Granuloma annulare Necrobiosis lipoidica Porokeratosis
D	I	Psoriasis

What's new- 2022?

EDF PDT and BCC guidelines:

- High quality evidence for use of PDT in approved indications – AK, Bowen's, BCC
- Consider where PDT best fits into your practice – offering choice to patients
- PDT in field cancerization/immunosuppressed
- Enlarging evidence base to consider combination therapy
- Substantial evidence for PDT in emerging indications

Global verification of a model for determining daylight photodynamic therapy dose

Paul O'Mahoney[1,2,3], Marina Khazova[4], Ethan LaRochelle[5], Brian Pogue[5], Sally H Ibbotson[1,2,3] and Ewan Eadie[2,3]

[1] School of Medicine, University of Dundee, Dundee, UK
[2]Photobiology Unit, NHS Tayside, Dundee, UK
[3] The Scottish Photodynamic Therapy Centre, Dundee, UK
[4] Public Health England, Didcot, UK
[5] Thayer School of Engineering at Dartmouth, Hanover NH, USA

GENERAL DERMATOLOGY

BJD
British Journal of Dermatology

Use of illuminance as a guide to effective light delivery during daylight photodynamic therapy in the U.K.

P. O'Mahoney,[1,2,3] M. Khazova,[4] M. Higlett,[4] T. Lister,[5] S. Ibbotson[1,2,3] and E. Eadie[1,2]

[1]Photobiology Unit, NHS Tayside, Ninewells Hospital, Dundee, U.K.
[2]The Scottish Photodynamic Therapy Centre, Dundee, U.K.
[3]University of Dundee, Dundee, U.K.
[4]Public Health England, Didcot, U.K.
[5]Salisbury NHS Foundation Trust, Salisbury, U.K

Table 1 Start and end treatment months and times of the day for daylight photodynamic therapy (dPDT) at each location, with respect to minimum conditions for dPDT – protoporphyrin-IX (PpIX)-weighted exposure dose > 4 J cm^{-2} and ambient temperature > 10 °C

		Start		End		Shortest time to achieve minimum dose	
	Latitude (°N)	Month	Time	Month	Time	Month	Time (min)
Lerwick	60·15	May	09:00–16:00	Oct	09:00–16:00	May	22·9
Inverness	57·48	Apr	09:00–16:00	Oct	09:00–16:00	Jul	21·4
Glasgow	55·85	Apr	09:00–16:00	Oct	09:00–16:00	Jul	21·3
Malin Head	55·35	Apr	09:00–16:00	Nov	09:00–16:00	Jun	20·4
Belfast	54·60	Apr	09:00–17:00	Nov	09:00–17:00	Jun	19·6
Leeds	53·80	Apr	09:00–16:00	Oct	09:00–16:00	Jul	19·6
Swansea	51·62	Apr	09:00–17:00	Dec	09:00–17:00	Jun	16·1
London	51·51	Mar	09:00–17:00	Dec	09:00–17:00	Jul	18·3
Camborne	50·21	Apr	09:00–17:00	Dec	09:00–17:00	Jun	16·2

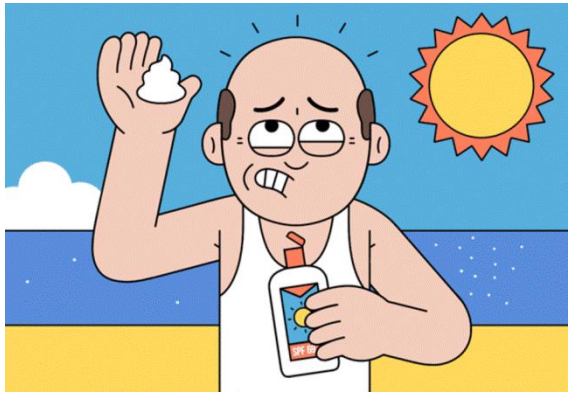
These recommendations are based on a 2-h exposure time. For the times of day presented, these represent the times in which treatment should take place, e.g. for Lerwick in May treatment should not start earlier than 09:00 and finish no later than 16:00. Shortest times to reach the minimum PpIX exposure dose in the months with the highest mean dose are included, i.e. on average, how long will it take to receive the minimum PpIX exposure dose in the corresponding month. These minimum times are indiscriminate of weather conditions.

O'Mahoney, P. et al. Use of illuminance as a guide to effective light delivery during daylight photodynamic therapy in the UK. British Journal of Dermatology. 2017;176(6):1607-1616

Weather and Daylight PDT - The Scottish Experience

Dr. Marese O'Reilly
Prof. Sally Ibbotson

Photobiology Unit, Dundee, Scotland



- Patients with superficial AK on sites that can be exposed to daylight
- April to September unless raining
- Apply non-reflectant sunscreen
- Lesion preparation 10-15 min later
- Apply prodrug (MAL or ALA) thinly without occlusion
- Attach HOBO device to clothing
- Within 30 min expose to daylight
- Continuous exposure for 2 h
- Wipe off excess prodrug
- Spend rest of day indoors
- Follow-up – may need to retreat at 1-3 months

Plenary Session 2

DL-PDT and ADL-PDT – What is new?

Chairs: Serge Mordon, Piergiacomo Calzavara-Pinton

Future of light devices for PDT

Pr. Dr. Serge Mordon

Fluorescence guided PDT for optimization of the outcome of skin cancer treatment

Kate C. Blanco[1], Lilian T. Moriyama[1], Natalia M. Inada[1], Ana G. Sálvio[2], Priscila F. C. Menezes[1], Everson J. S. Leite[3], Cristina Kurachi[1] and Vanderlei S. Bagnato[1]*

[1] Laboratório de Biofotônica, Instituto de Física de São Carlos (IFSC/Universidade de São Paulo), São Carlos, Brasil, [2] Hospital Amaral Carvalho, Jaú, Brasil, [3] Hospital Universitário Prof. Alberto Antunes of Universidade Federal de Alagoas, Maceió, Alagoas, Brasil

The photodynamic therapy (PDT) is an alternative technique that can be used for treating superficial basal cell carcinoma (sBCC), Bowen's disease and actinic keratosis with highefficiency. The objective of this study is to present a method where fluorescence imaging together with for PDT as a monitoring guidance in real time. Confirming that the lesion is well prepared and the photosensitizer shows a homogenous distribution, the outcome after few PDT sessions will be more predictable and the recurrence is minimized. Our proposition in this study is use the widefield fluorescence imaging to evaluate the PDT protocol *in situ* and in real time for each lesion. This evaluation procedure is performed in two steps: first with the monitoring of the production of protoporphyrin IX (PpIX) induced by methyl aminolevulinate (MAL), a derivative of 5-aminolevulinic acid (ALA) and second with the detection of PpIX photobleaching after illumination. The fluorescence images provide information correlated with distinct clinical features and with the treatment outcome. Eight BCC lesions are presented and discussed in this study. Different fluorescence patterns of PpIX production and photobleaching could be correlated with the treatment response. The presented results show the potential of using widefield fluorescence imaging as a guidance tool to customized PDT. This procedure is being incorporated to the main PDT skin cancer protocol applied in Brazil with an excellent outcome.

Keywords: PpIX fluorescence, skin cancer, wide-field imaging, photodynamic therapy, photodiagnosis

Clinical evaluation of smartphone-based fluorescence imaging for guidance and monitoring of ALA-PDT

Shakir Khan,[a,c] M. A. Bilal Hussain,[a] Amjad P. Khan,[b] Hui Liu,[c] Shaista Siddiqui,[d] Srivalleesha Mallidi,[b] Paola Leon,[c] Liam Daly,[c] Grant Rudd,[c] Filip Cuckov,[c] Colin Hopper,[e] Stephen G. Bown,[e] Kafil Akhtar,[f] Syed Abrar Hasan,[g] Shahid Ali Siddiqui,[a] Tayyaba Hasan,[b,*] and Jonathan P. Celli[c,*]

[a]Aligarh Muslim University, Jawaharlal Nehru Medical College, Department of Radiotherapy, Aligarh, India
[b]Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, United States
[c]University of Massachusetts at Boston, Boston, Massachusetts, United States
[d]Aligarh Muslim University, Jawaharlal Nehru Medical College, Department of Radiodiagnosis, Aligarh, India
[e]University College London, London, England, United Kingdom
[f]Aligarh Muslim University, Jawaharlal Nehru Medical College, Department of Pathology, Aligarh, India
[g]Aligarh Muslim University, Jawaharlal Nehru Medical College, Department of Otorhinolaryngology (E.N.T.), Aligarh, India

Smartphone fluorescence imager for quantitative dosimetry of protoporphyrin-IX-based photodynamic therapy in skin

Alberto J. Ruiz,[a,*] Ethan Phillip M. LaRochelle,[a] Jason R. Gunn,[a] Sally M. Hull,[a] Tayyaba Hasan,[b] M. Shane Chapman,[c] and Brian W. Pogue[a,c,*]

[a]Dartmouth College, Thayer School of Engineering, Hanover, New Hampshire, United States

[b]Massachusetts General Hospital, Harvard Medical School, Wellman Center for Photomedicine, Boston, Massachusetts, United States

[c]Geisel School of Medicine, Department of Surgery, Hanover, New Hampshire, United States

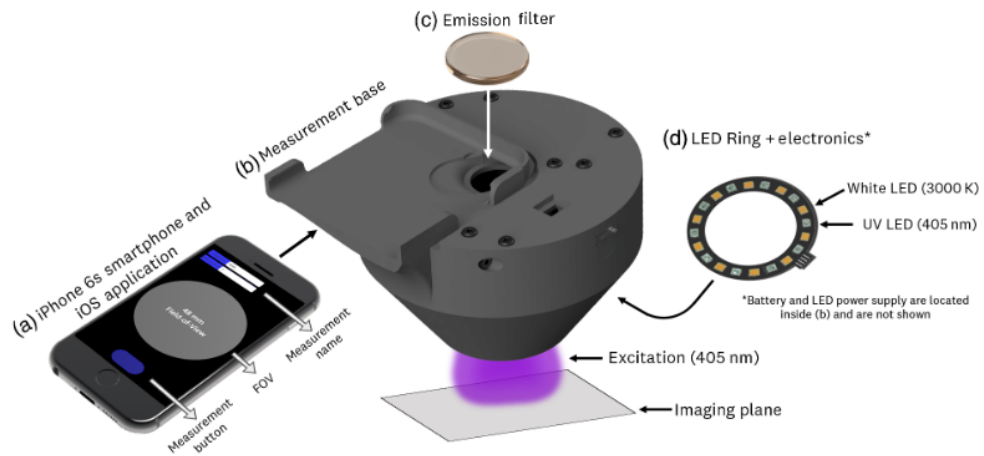


Fig. 1 Schematic representation of the dosimeter system: (a) iPhone 6s smartphone and custom iOS application for RAW image acquisition and image analysis; (b) 3D-printed measurement base for system integration and measurement distance and light leakage standarization; (c) 600-nm wavelength long-pass emission filter for PpIX signal isolation; and (d) 405-nm wavelenth LED ring and electronics for excitation and to provide rechargeability in a modular package. FOV, field of view.

Ambulatory photodynamic therapy

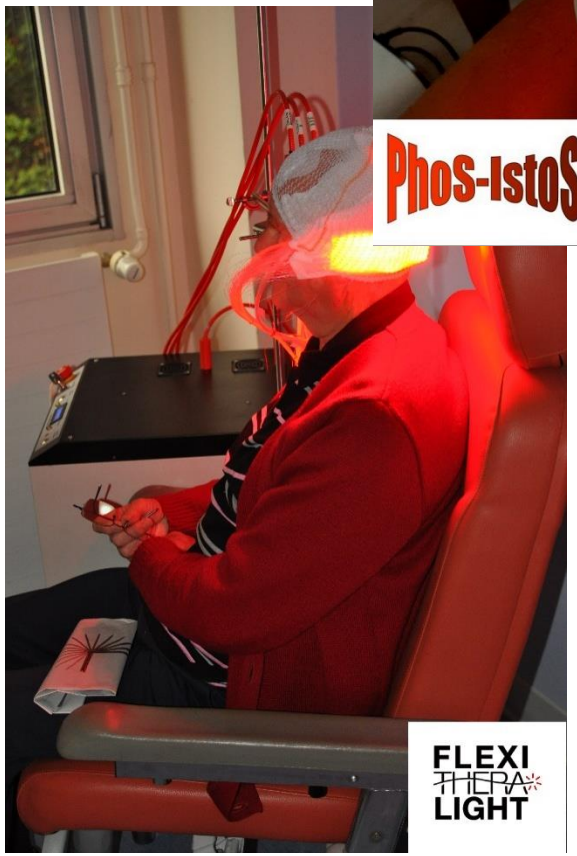
With the Ambulight, patients only need to spend a short amount of time in hospital while the cream is applied, and can then carry on with their daily routine.

Source: Ambulight

Moseley H, Allen JW, Ibbotson S, Lesar A, McNeill A, Camacho-Lopez MA, Samuel ID, Sibbett W, Ferguson J. Ambulatory photodynamic therapy: a new concept in delivering photodynamic therapy. Br J Dermatol. 2006 Apr;154(4):747-50.

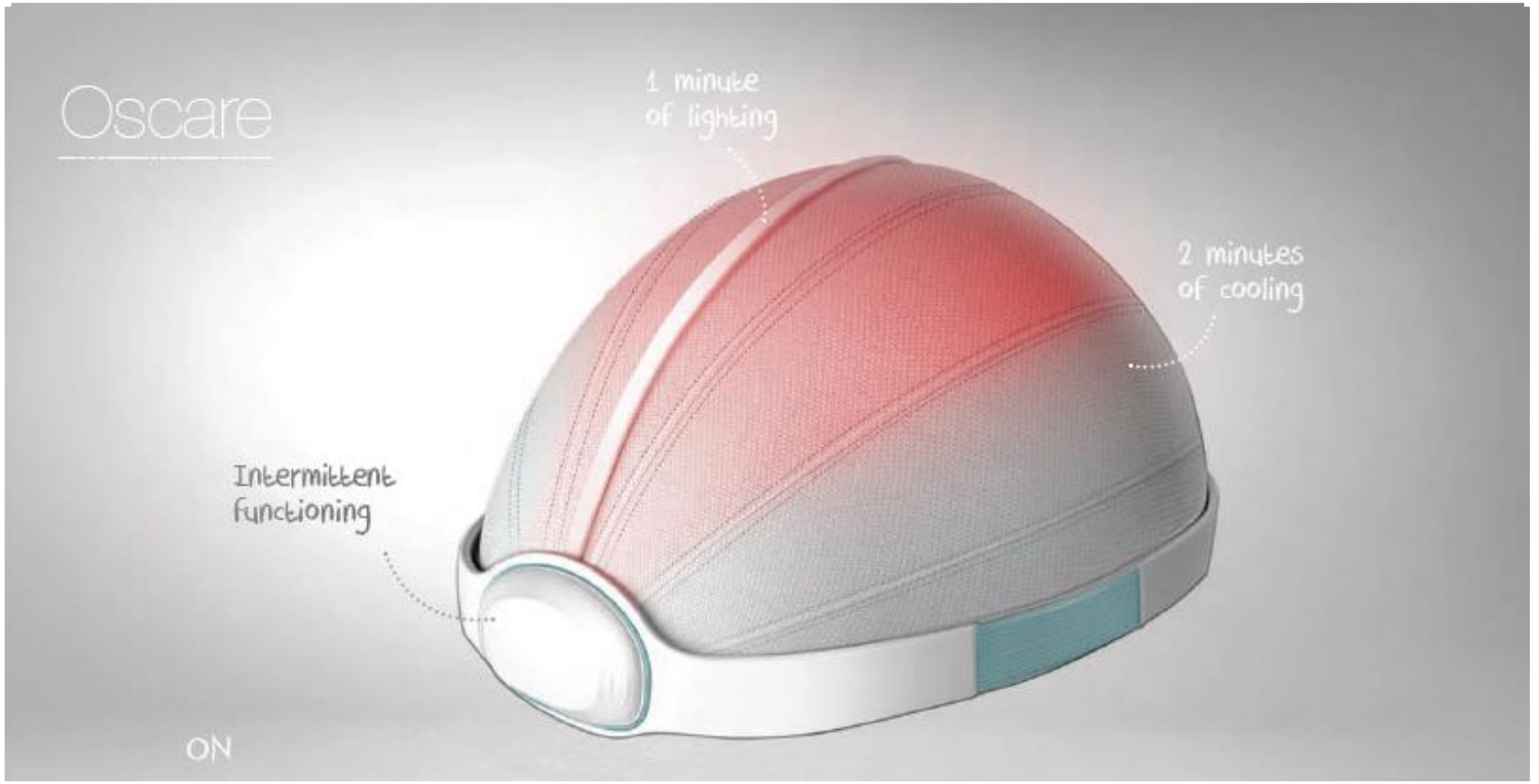
Attili SK, Lesar A, McNeill A, Camacho-Lopez M, Moseley H, Ibbotson S, Samuel ID, Ferguson J. An open pilot study of ambulatory photodynamic therapy using a wearable low-irradiance organic light-emitting diode light source in the treatment of nonmelanoma skin cancer. Br J Dermatol. 2009 Jul;161(1):170-3.

New developments – Light Emitting Fabrics



- Mordon S, Vignion-Dewalle AS, Abi-Rached H, Thecua E, Lecomte F, Vicentini C, Deleporte P, Béhal H, Kerob D, Hommel T, Duhamel A, Szeimies RM, Mortier L. The conventional protocol vs. a protocol including illumination with a **fabric-based biophotonic device** (the Phosistos protocol) in photodynamic therapy for actinic keratosis: a randomized, controlled, noninferiority clinical study. Br J Dermatol. 2020 Jan;182(1):76-84. doi: 10.1111/bjd.18048
- Vicentini C, Vignion-Dewalle AS, Thecua E, Lecomte F, Maire C, Deleporte P, Béhal H, Kerob D, Duhamel A, Mordon S, Mortier L. Photodynamic therapy for actinic keratosis of the forehead and scalp: a randomized, controlled, phase II clinical study evaluating the noninferiority of a new protocol involving irradiation with **a light-emitting, fabric-b**ased device (the Flexitheralight protocol) compared with the conventional protocol involving irradiation with the Aktilite CL 128 lamp. Br J Dermatol. 2019 Apr;180(4):765-773
- Vignion-Dewalle AS, Abi Rached H, Thecua E, Lecomte F, Deleporte P, Béhal H, Hommel T, Duhamel A, Szeimies RM, Mortier L, Mordon S. **A New Light-Emitting, Fabric-Based Device** for Photodynamic Therapy of Actinic Keratosis: Protocol for a Randomized, Controlled, Multicenter, Intra-Individual, Phase II Noninferiority Study (the Phosistos Study). JMIR Res Protoc. 2019 Apr 26;8(4):e12990.
- Lecomte F, Thecua E, Ziane L, Deleporte P, Duhamel A, Maire C, Staumont-Salle D, Mordon S, Mortier L. Photodynamic Therapy Using a New Painless **Light-Emitting Fabrics Device** in the Treatment of Extramammary Paget Disease of the Vulva (the PAGETEX Study): Protocol for an Interventional Efficacy and Safety Trial. JMIR Res Protoc. 2019 Dec 3;8(12):e15026.
- Dubois M, Abi Rached H, Dezoteux F, Maire C, Vicentini C, Behal H, Thecua E, Lecomte F, Mordon S, Mortier L. Real-life evaluation of the treatment of actinic keratoses by **textile** photodynamic therapy (FLUXMEDICARE® device). Photodiagnosis Photodyn Ther. 2021 Jun;34:102213.

Future: Portable Device



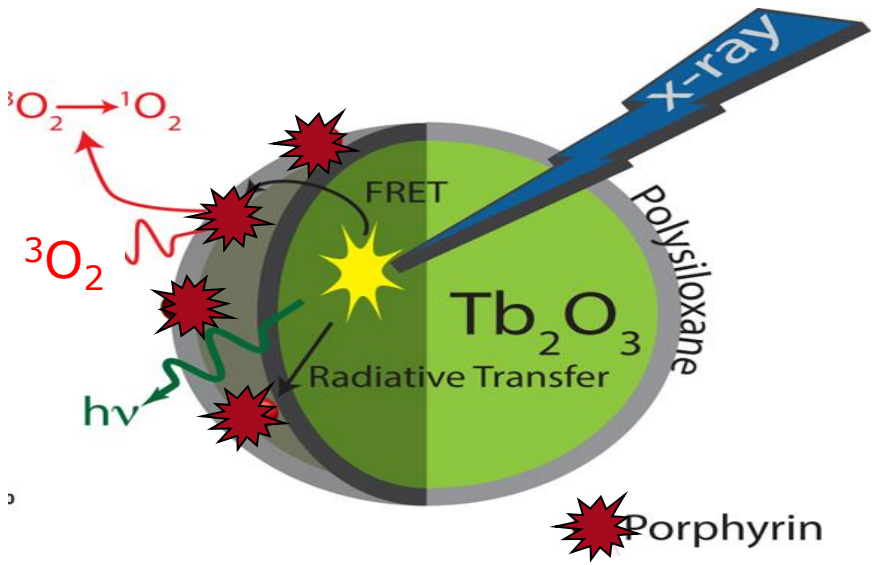
Thanks to a their high efficiency and very small footprint, these laser diodes can be embedded in the cap - The device can be easily monitored and controlled with a mobile phone

Photodynamic therapy and melanoma: latest progress

Céline FROCHOT, CNRS research director
LRGP, CNRS-University of Lorraine, Nancy, France

Batoul DHAIRI
Serge MORDON
Nadira DELHEM
Laurent MORTIER

PDT-X: X-ray induced PDT



Bulin A.L. *et al.* J Phys Chem, 2013
Rétif P. *et al.* Theranostic, 2015
Chouikrat R. *et al.* Phot Phot, 2017
Larue L. *et al.*, PPS, 2019
Daouk J. *et al.*, pharmaceuticals, 2021

PROJECT PDT-X

PDT-X to treat melanoma

L. Mortier and N. Delhem, Lille

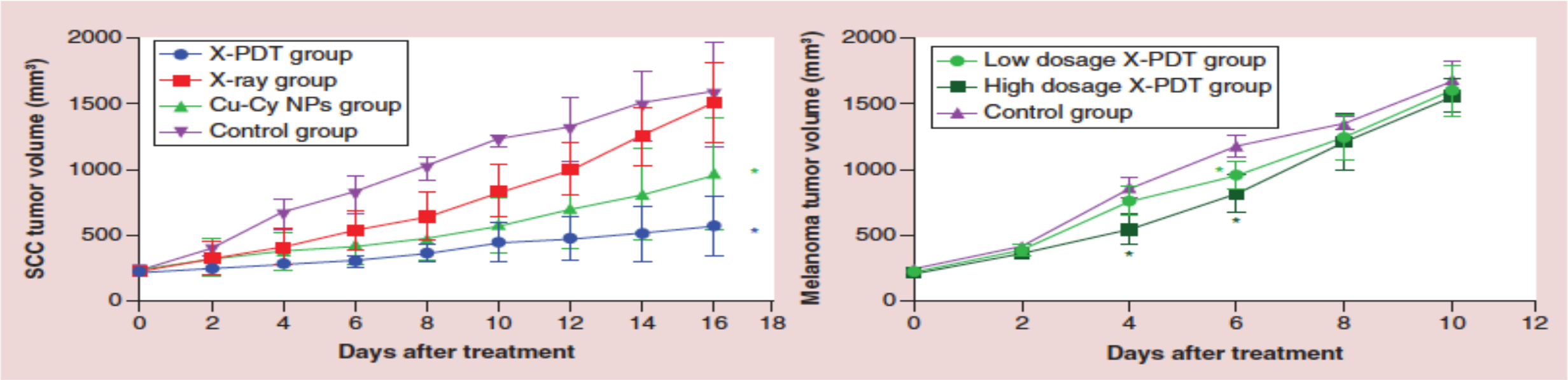
Nano Med Euro — Nano from research to patient and industry

ANR AGENCE NATIONALE DE LA RECHERCHE

Coll O. Tillement, F. Lux, Lyon
Coll Porphychem, Dijon
Coll J. Daouk, H. Schohn, M. Barberi-Heyob, Nancy

PDT-X and melanoma: 1 publication

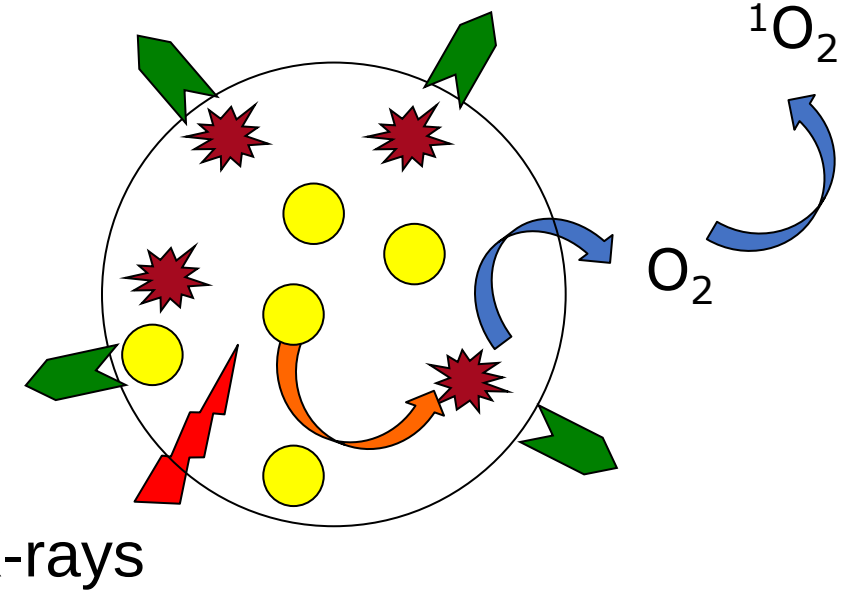
Copper-cysteamine NP



PDT-X (100 KVp, 200 cGy or 400 cGy) against squamous cell carcinoma and BF1610 melanoma

Shi et al., Nanomedicine,2019

X-rays instead of light



PROJECT
PDT-X

PDT-X to treat melanoma

Financial support

Laurent Mortier, Lille
Nadira Delhem, Lille

Sequential treatment with calcitriol and MAL DL-PDT for patients with multiple AK of the upper extremities

Stefano Piaserico
Clinica Dermatologica, Università di Padova

A randomized, half-side comparative study of DL-PDT vs. calcitriol plus DL-PDT in patients with multiple AKs of the upper extremities

Fargnoli MC & Piaserico S

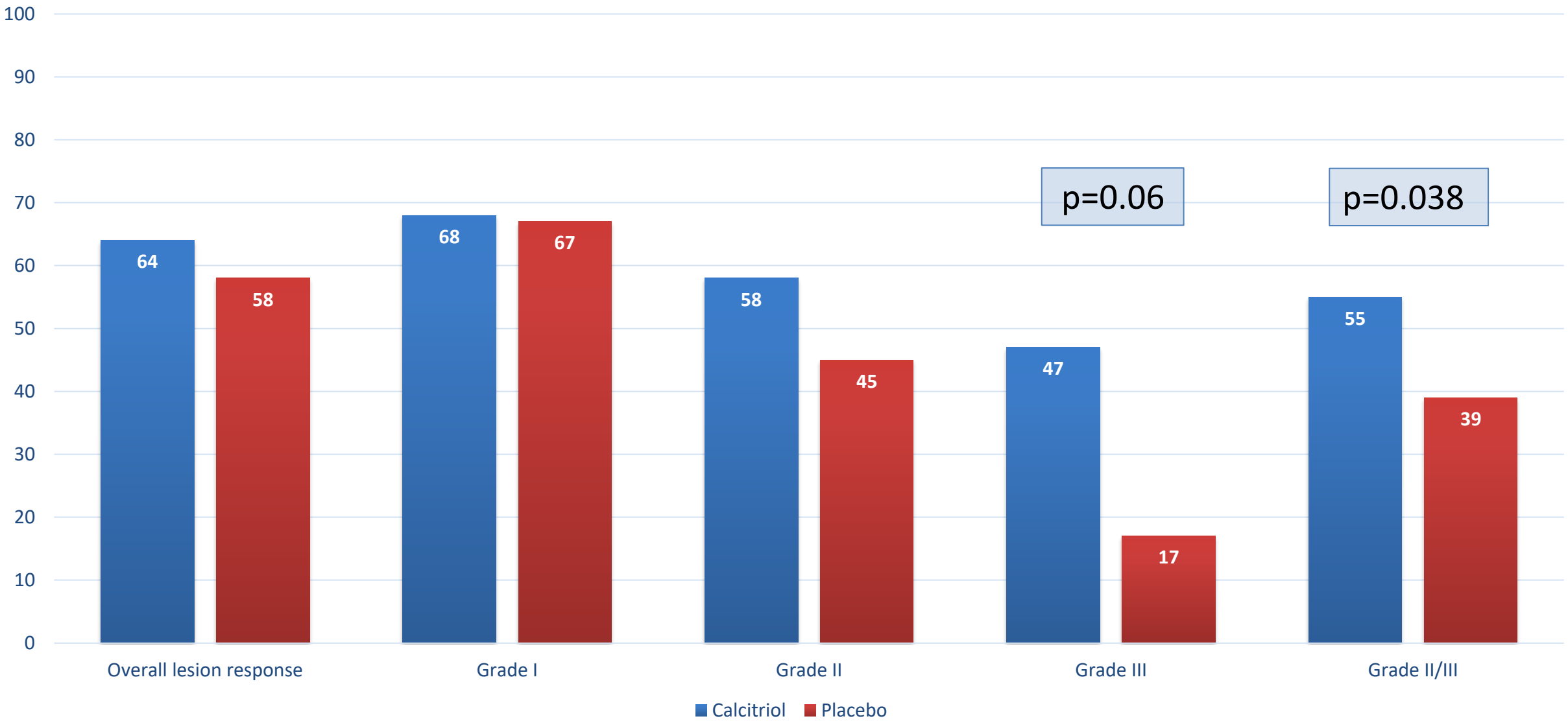
- A pilot, intra-patient, prospective study
- Aim:

  Investigate the clearance rate of multiple AKs on the dorsum of the hand or the forearms treated with 2 sessions of DL-PDT (1 week apart)

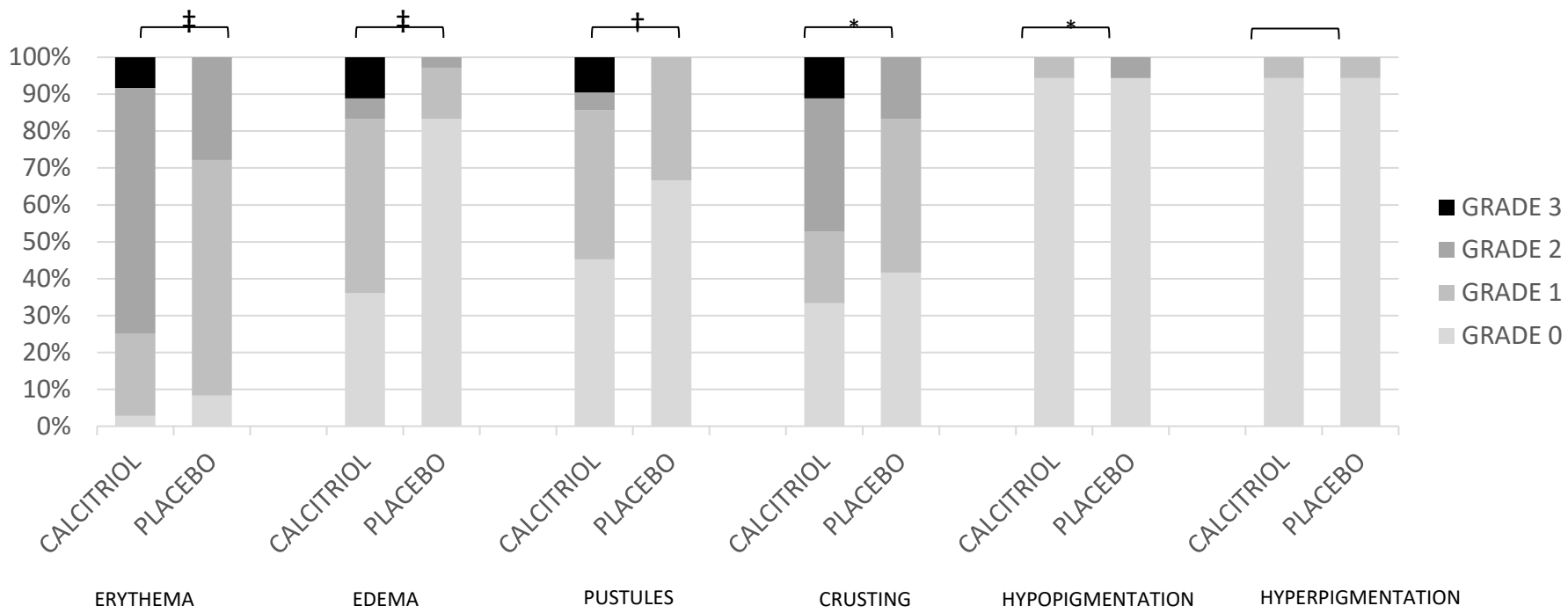
- One arm was pre-treated with 2 weeks of calcitriol (36 patients)
- The other arm was treated with a placebo cream.

Piaserico et al. Photodiagnosis and Photodynamic Therapy 2021

Results


100
90
80
70
60
50
40
30
20
10
0
64
58
68
67
58
45
47
17
55
39
p=0.06
p=0.038
Overall lesion response
Grade I
Grade II
Grade III
Grade II/III
Calcitriol
Placebo

Local skin reactions after the first session of DL-PDT



*<0.05, †<0.01, ‡<0.001.

- DL-PDT efficacy on difficult-to-treat areas (forearm and hands) can be increased by pre-treatment with calcitriol
- The effect size is +16% (lesional response) for grade II/III AKs
- Local skin reactions may be severe after DL-PDT

Sequential treatment of AK and photoaging by daylight-PDT and injectable NASHA gel as SkinBooster

Magda Belmontesi
Dermatologist Milan
Agorà Centro Clinico Formativo – Milan
Superior School Aesthetic Medicine Agorà – Milan
Italian Society Aesthetic Medicine SIME – Rome
Master II level Aesthetic Medicine Pavia University

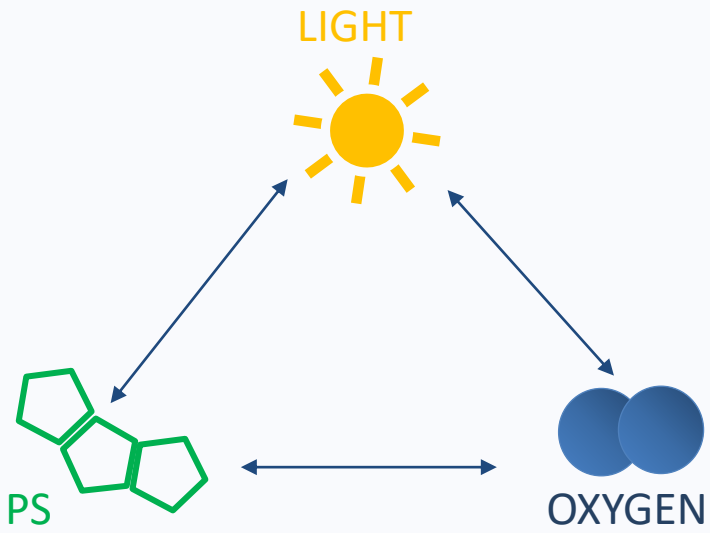
Patient expectations

- Treating AK
- Reducing photoaging damages
- Improving skin texture
- Getting «healthy look»
- No aggressive treatments, no downtime
- High tolerability

Sequential treatment DL-PDT and cross-linked-stabilized hyaluronic acid-gel injection in patients with AK lesions

1

DL-PDT photochemcial reaction[1]

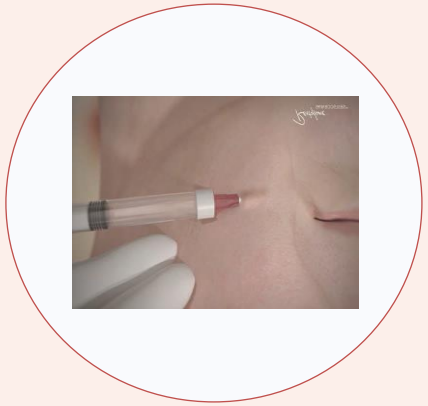


[Image adapted from Wan MT and Lin JY, 2014]

2

Injectable treatment with NASHA gel as skin booster[2]

- NASHA gel specifically designed to improve skin quality
- Patented NASHA technology:
  - Maintains natural **entanglements** of hyaluronic acid molecule
  - Only Minimal modification by 1,4-butanediol diglycidyl ether (BDDE)[3]

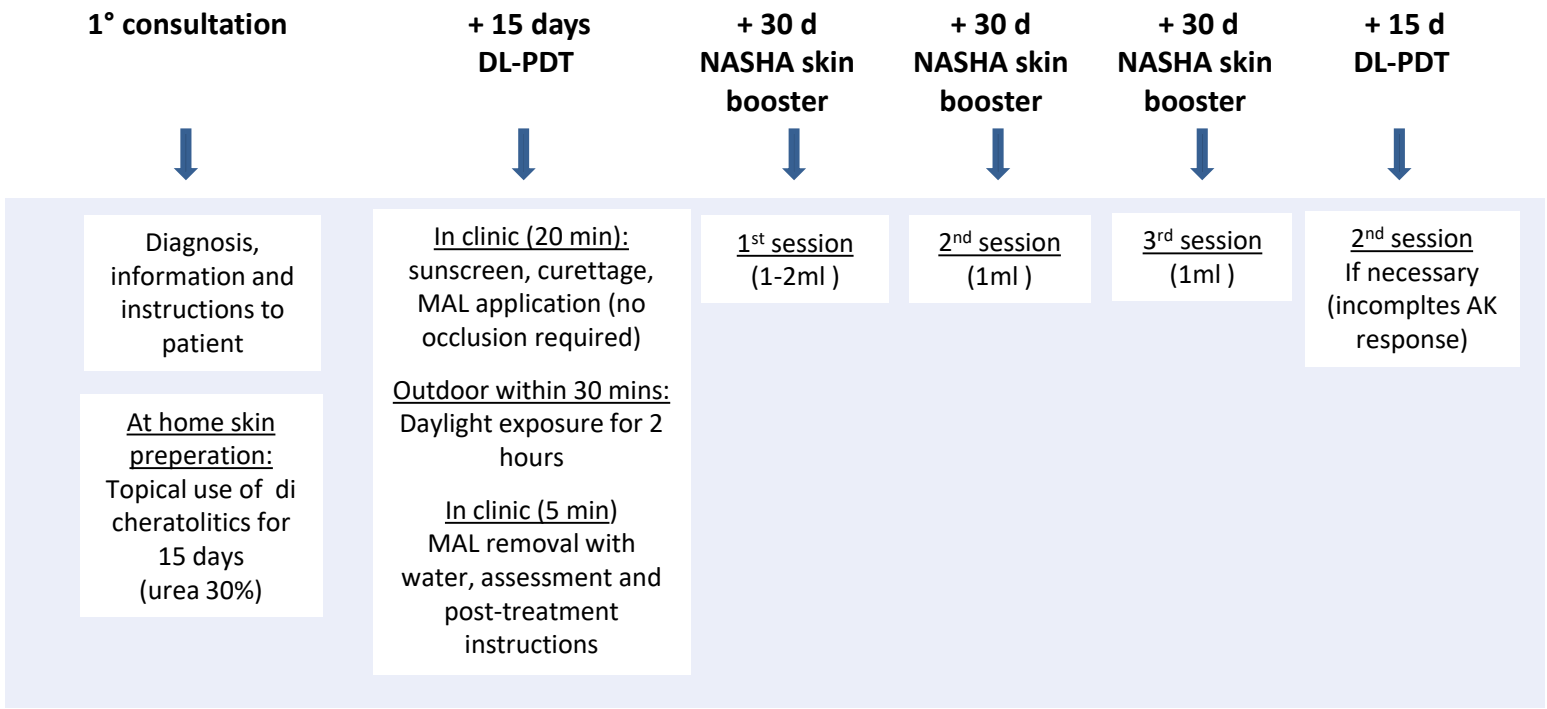


AK, actinic keratosis; **BDDE,** 1,4-butanediol diglycidyl ether; **DL-PDT,** daylight photodynamic therapy; **NASHA,** non-animal stabilized hyaluronic acid; **PS,** photosensitiser; **PDT,** photodynamic therapy.

1. Wan MT and Lin JY. *Clin Cosmet Investig Dermatol.* 2014;7:145-63. **2.** Kerscher M, *et al. Dermatol Surg.* 2008 May;34(5):720-6. **3.** Salti G and Fundaro S. *Ploymers* 2020;12:1644.

Sequential treatment of AK and photoaging by DL-PDT and injectable NASHA gel as a skin booster

Protocol used in study:*[1]



To treat AK lesions and field cancerization as well as improving skin quality

*This study tested the treatment using sequential sessions of DL-PDT and injectable NSBs on 4 patients with AK on head and neck. Two further sessions of NSBs were scheduled, 30 and60 days after the first injection, to improve the overall skin quality. Patients had multiple AKs (mostly grade 1) and moderate-to-severe photoaging on face and/or scalp were treated.[1]

AK, actinic keratosis; **DL-PDT,** daylight photodynamic therapy; **NSB,** NAHA gel skin booster; **NASHA,** non-animal stabilized hyaluronic acid; **PDT,** photodynamic therapy.

.1. Belmontesi M. *J Drugs Dermatol.* 2020;19(11):1065–8.

Conclusions

The combination of two minimally invasive, effective and well-tolerated therapies characterized by excellent compliance allowed:

- almost complete resolution of actinic keratosis and
- a clear improvement of skin texture,
- with noticeable reduction of the clinical signs of skin photoaging,
- meeting patient’s expectations

Successful treatment of palmoplantar dyshidrotic lesions of mycosis fungoides with conventional and daylight PDT

Gloria Juan Carpena, Juan Carlos Palazón Cabanes, Mar Blanes Martínez
Department of Dermatology, Dr. Balmis General University Hospital (Alicante)

Mycosis fungoides and cPDT

- **Used in:**
  - IA/IB stages (patches or plaques)
  - Uni or paucilesionals
  - Resistant localized lesions
  - Difficult or sensitive areas (face, neck, scalp, axilary and inguinal folds, breast, palms, soles or buttocks)

- **Case reports and case series** (lack of randomized controlled trials and prospective reports)

- **No standard protocols:**
  - MAL, 5-ALA
  - N of sessions/lesion: 1-11. More than 1 session
  - Periodicity: 1-8 weeks
  - More common schedule**: 6 sessions at 2 o 4-week intervals**

- **Objetive response 50-100%, complete response 63%**

Xue J, et al. Photodiagnosis Photodyn Ther. 2017;17:87–91.
Fernández-Guarino M, et al. Actas Dermosifilogr. 2010;101:785–791.
Kaufmann F, et al. J Eur Acad Dermatol Venereol. 2017;31:1633–1637.
Quéreux G, et al. J Am Acad Dermatol. 2013;69:890–897.
Kim ST, et al. Acta Derm Venereol. 2012;92:264–268.

Mycosis fungoides and PDT

PALMS AND SOLES

- Lower overall response rates to different treatments

Acta Derm Venereol 2012; 92: 264–268

INVESTIGATIVE REPORT

Photodynamic Therapy with Methyl-aminolaevulinic Acid for Mycosis Fungoides

Sang Tae KIM, Dong Young KANG, Jin Seuk KANG, Jae Woo BAEK, Young Seung JEON and Kee Suck SUH
Department of Dermatology, Kosin University College of Medicine, Busan, South Korea

Acta Derm Venereol. 2012;92:264–268.

Conventional PDT (cPDT)

PALMS: Complete response

SOLES: **PAIN** limited the treatment

SHORT REPORT

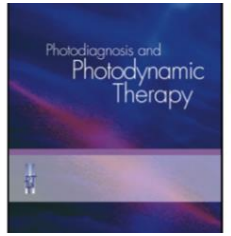
Unilesional plantar mycosis fungoides treated with topical photodynamic therapy – case report and review of the literature

F. Kaufmann,[1,2,3] N. Kettelhack,[1] N. Hilty,[4] W. Kempf[1,2,3,*]

J Eur Acad Dermatol Venereol. 2017;311633-1637.

Title: Photodynamic therapy: an option in mycosis fungoides.

Authors: Pileri Alessandro, Sgubbi Paola, Agostinelli Claudio, Infusino Salvatore Domenico, Vaccari Sabina, Patrizi Annalisa



Photodiagnosis Photodyn Ther. 2017 Dec;20:107-110

Daylight PDT

- 16% MAL, 5- ALA
- Mild-moderate AQ and field cancerization
- Exposition to daylight within < 30 min for 2 h between 9 - 18 h
- MAIN ADVANTAGE: **lower pain** (2 vs 6.6, 0.7 vs 4.4)* and easy to use

Daylight PDT (TFD-ld)

SOLES: complete response with minimal discomfort

Weigell SR et al. Br J Dermatol. 2008
Lacour JP et al. J Eur Acad Dermatol Venereol. 2015
Gilaberte Y et al. Actas Dermosifiliogr. 2015
Morton CA et al. J Eur Acad Dermatol Venereol. 2019

Conclusions

- We present a patient with palmoplantar lesions of MF resistant to multiple treatments treated with cPDT and dlPDT with good results
- Ours is the first published case of MF successfully treated with DL-PDT
- Dl-PDT, as well as cPDT, could be considered as a second-line option in the therapeutic arsenal against this condition

Plenary Session 3

PDT outside AK

Chairs: Yolanda Gilaberte, Merete Haedersdal

PDT combination therapies for AK/NMSC

Thomas Dirschka
CentroDerm, Wuppertal

Literature Search

Int. J. Mol. Sci. **2015**, *16*, 25912-25933; doi:10.3390/ijms161025912

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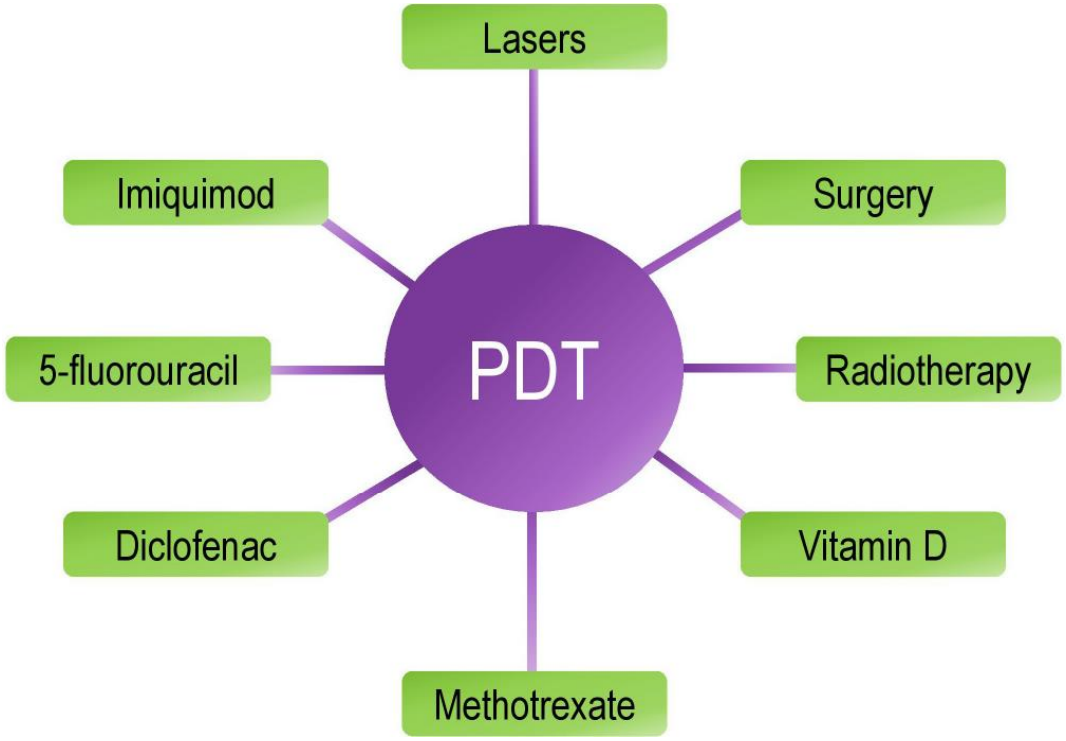
International Journal of
Molecular Sciences
ISSN 1422-0067
www.mdpi.com/journal/ijms

Review

Combined Treatments with Photodynamic Therapy for Non-Melanoma Skin Cancer

Silvia Rocío Lucena [1], Nerea Salazar [1], Tamara Gracia-Cazaña [2,3], Alicia Zamarrón [1], Salvador González [4,5], Ángeles Juarranz [1,†] and Yolanda Gilaberte [3,6,†,*]



Online version at http://www.minervamedica.it

Italian Journal of Dermatology and Venereology 2021 April;156(2):213-9
DOI: 10.23736/S2784-8671.21.06892-9

ORIGINAL ARTICLE

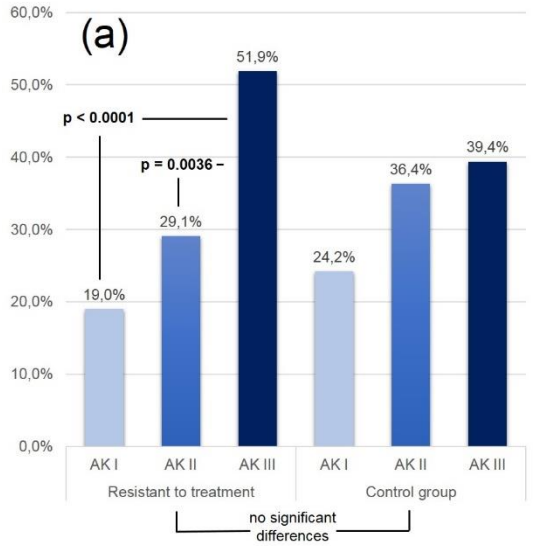
Treatment-resistant actinic keratoses are characterized by distinct clinical and histological features

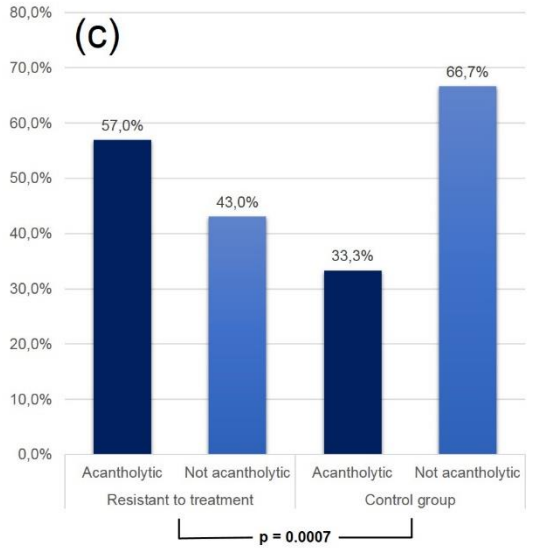
Lutz SCHMITZ [1, 2] *, Amrei BREHMER [3, 4], Conrad FALKENBERG [5], Thilo GAMBICHLER [1], Markus V. HEPPT [6], Theresa STEEB [6], Girish GUPTA [7, 8], Josep MALVEHY [9], Thomas DIRSCHKA [4, 10]

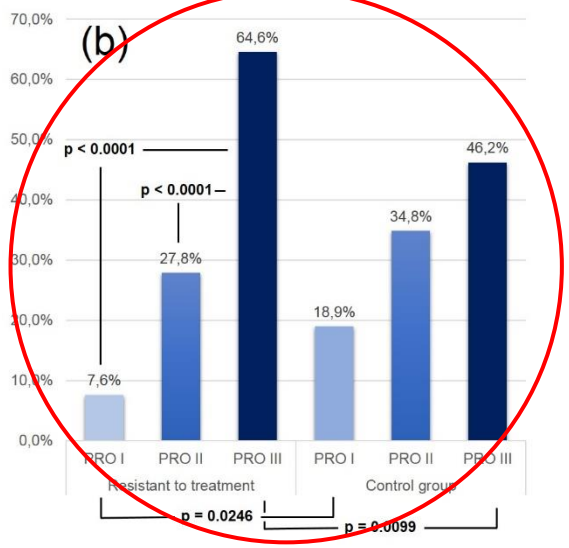
[1]Department of Dermatology, Venereology and Allergology, Ruhr-University, Bochum, Germany; [2]Institute of Dermatopathology, MVZ Corius DermPathBonn, Bonn, Germany; [3]Department of Dermatology, Klinikum Dortmund gGmbH, Dortmund, Germany; [4]Faculty of Health, University Witten-Herdecke, Witten, Germany; [5]Department of Dermatology, Faculty of Medicine, Heinrich-Heine-University, Düsseldorf, Germany; [6]Department of Dermatology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany; [7]Department of Dermatology, Lauriston Building, Edinburgh, UK; [8]School of Medicine, University of Glasgow, Glasgow, UK; [9]Department of Dermatology, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University Hospital of Barcelona, University of Barcelona, Barcelona, Spain; [10]CentroDerm Clinic, Wuppertal, Germany

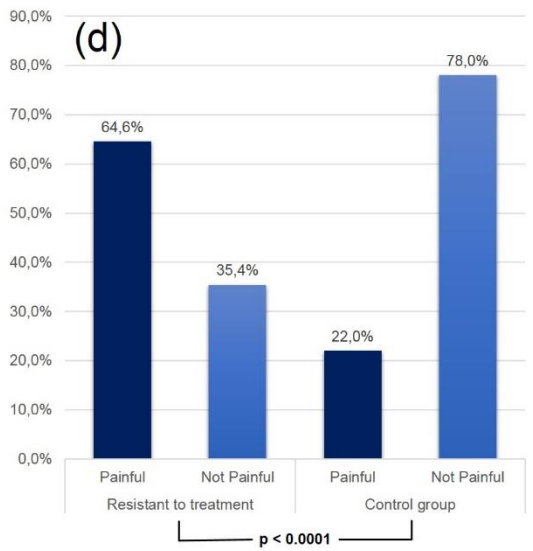
*Corresponding author: Lutz Schmitz, Institute of Dermatopathology, MVZ Corius DermPathBonn, Trierer Str. 70-72, 53155 Bonn, Germany.
E-mail: lutz.schmitz@dermpath-bonn.de

211 treatment resistant Aks in 171 patients have been biopsied and were compared to AK before treatment









Conclusions

- Clinical trials comparing AK combination treatments have substantial deficiencies:
  - Lesion count not standardized
  - Area size not determined
  - Point of time to look at treatment success not standardized

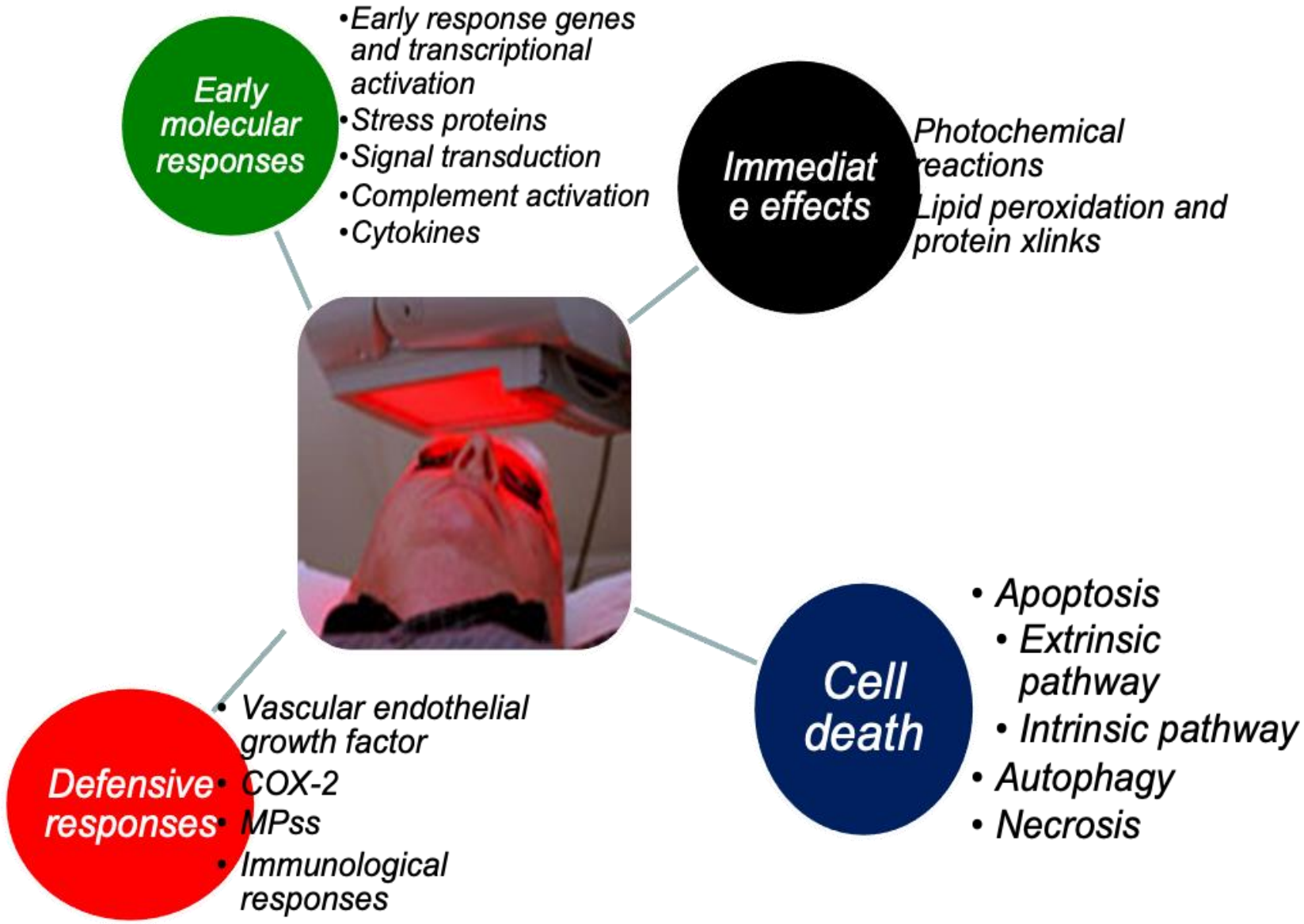
- The pure number of cleared lesions does not provide information on SCC promotion
  - Treatment resistant AK carry a elevated risk to turn into SCC

- PDT can be of value as diagnostic tool to separate less-aggressive vs. more aggressive AK

- Although most trials show increased treatment response the relevance of pure increase of cleared lesions remains unclear!

Is there a place for PDT in inflammatory dermatoses?

Piergiacomo Calzavara Pinton
Dermatology Department, University of Brescia, Italy



A broad variety of molecular mechanisms has motivated the use of ALA/ MAL-PDT for the treatment of more than 60 inflammatory, infectious and oncologic skin disorders

Molecular mechanisms of PDT

B Ortel, C R Shea, P Calzavara-Pinton; FBS 2009

DOI: 10.1111/jdv.16044 JEADV

GUIDELINES

European Dermatology Forum guidelines on topical photodynamic therapy 2019 Part 2: emerging indications – field cancerization, photorejuvenation and inflammatory/infective dermatoses

C.A. Morton,[1] R.-M. Szeimies,[2,3,*] N. Basset-Séguin,[4] P.G. Calzavara-Pinton,[5] Y. Gilaberte,[6] M. Hædersdal,[7] G.F.L. Hofbauer,[8] R.E. Hunger,[9] S. Karrer,[2] S. Piaserico,[10] C. Ulrich,[11] A.-M. Wennberg,[12] L.R. Braathen[13]

OFF LABEL	RECOMMENDATION	EVIDENCE
SKIN AGING	A	I
ACNE	B	I
SEBACEOUS GLAND HYPERPLASIA	C	II-III
HYPERTROPHIC AND KELOID SCARS	C	II-III
LICHEN SCLEROSUS	C	III
GRANULOMA ANNULARE/ NECROBIOSIS LIPOIDICA	C	III
POROKERATOSIS	C	III
PSORIASIS	D	I

Dermatology

Review Article

Dermatology 2021;237:262–276
DOI: 10.1159/000507926

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Published online: June 18, 2020

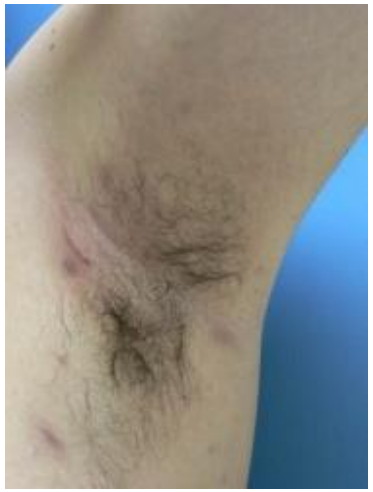
A Critical Reappraisal of Off-Label Use of Photodynamic Therapy for the Treatment of Non-Neoplastic Skin Conditions

Giuseppe Monfrecola[a] Matteo Megna[a] Chiara Rovati[b] Mariachiara Arisi[b] Mariateresa Rossi[b] Irene Calzavara-Pinton[b] Gabriella Fabbrocini[a] Piergiacomo Calzavara-Pinton[b]

OFF LABEL	RECOMMENDATION	EVIDENCE
SKIN AGING	A	I
ACNE	B	I
SEBACEOUS GLAND HYPERPLASIA	C	III
HYPERTROPHIC AND KELOID SCARS	C	III
LICHEN SCLEROSUS	C	III
GRANULOMA ANNULARE	C	III
NECROBIOSIS LIPOIDICA	D	III
ROSACEA	D	III
PSORIASIS	D	I

Suppurative hidradenitis: Conventional PDT

Pts number	13
Gender (M/F)	1/5
Mean age (range)	34.2 (21-52)
Groins	7
Armpits	4
Mild/ moderate/ severe	6/3/4
No exposures	4.8±2
Interval (days)	41.3±53.9
Follow-up (mos)	2.6±0.5



Calzavara-Pinton et al. 2013

Suppurative hidradenitis

PDT combined with surgery

Patient satisfaction and quality of life after surgery combined with 5-aminolevulinic acid–based photodynamic therapy for hidradenitis suppurativa

Li Y, et al. JAAD2021

Table I. Surgical option and nursing method of different stage HS

	Surgical method	PDT method	Wound care
Stage I	Direct resection and suture	4 times after surgery with an interval of 1 week.	Routine cleaning and disinfection
Stage II	Extensive resection, and the suture was performed 3 days after the surgery	1 PDT was performed on the wound surface during the surgery. 3 subsequent PDT were performed 1 week later with an interval of 1 week.	Clean secretions twice a day, refill with rivanol gauze, and the wound was covered with sterile gauze dressing
Stage III	Excision, reconstructive open space. The suture was performed 3 days after the last PDT.	Intraoperative photodynamic irradiation of the wound. 3 subsequent PDT at an interval of 1 week.	Clean secretions twice a day, refill with rivanol gauze, and the wound was covered with sterile gauze dressing.

Table II. Dermatology Quality Life Index and Vancouver Scar score of patients

	Stage I	Stage II	Stage III	Total	*P* value
No. patients	10	15	7		
Dermatology Quality Life Index*					
Before	10.7 ± 1.9	13.73 ± 2.42	21.14 ± 1.92	14.41 ± 3.81	<.05
After	2.3 ± 0.56	4.07 ± 1.81	5.43 ± 2.04	3.78 ± 1.73	
How satisfied or dissatisfied are you with your treatment result?†	1.70 ± 0.56	1.67 ± 0.44	1.71 ± 0.61	1.69 ± 0.52	>.05
Would you recommend this therapy to a friend or relative?†	1.60 ± 0.60	1.60 ± 0.56	1.57 ± 0.49	1.590.56	>.05
Vancouver Scar score	2.90 ± 0.36	4.26 ± 1.48	7.71 ± 1.18	4.59 ± 1.92	<.05
Recurrence	0	2	2	4	<.05

*Scores range from 0 (no effect on patient's life) to 30 (extremely large effect on patient's life)
†Responses were scored on a scale from 1 (very satisfied) to 5 (very dissatisfied).

Suppurative hidradenitis: intralesional PDT

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journal homepage: www.jdsjournal.com

Treatment of hidradenitis suppurativa with intralesional photodynamic therapy with 5-aminolevulinic acid and 630 nm laser beam

María Jesús Suárez Valladares*, Noemi Eiris Salvado, Manuel Angel Rodríguez Prieto

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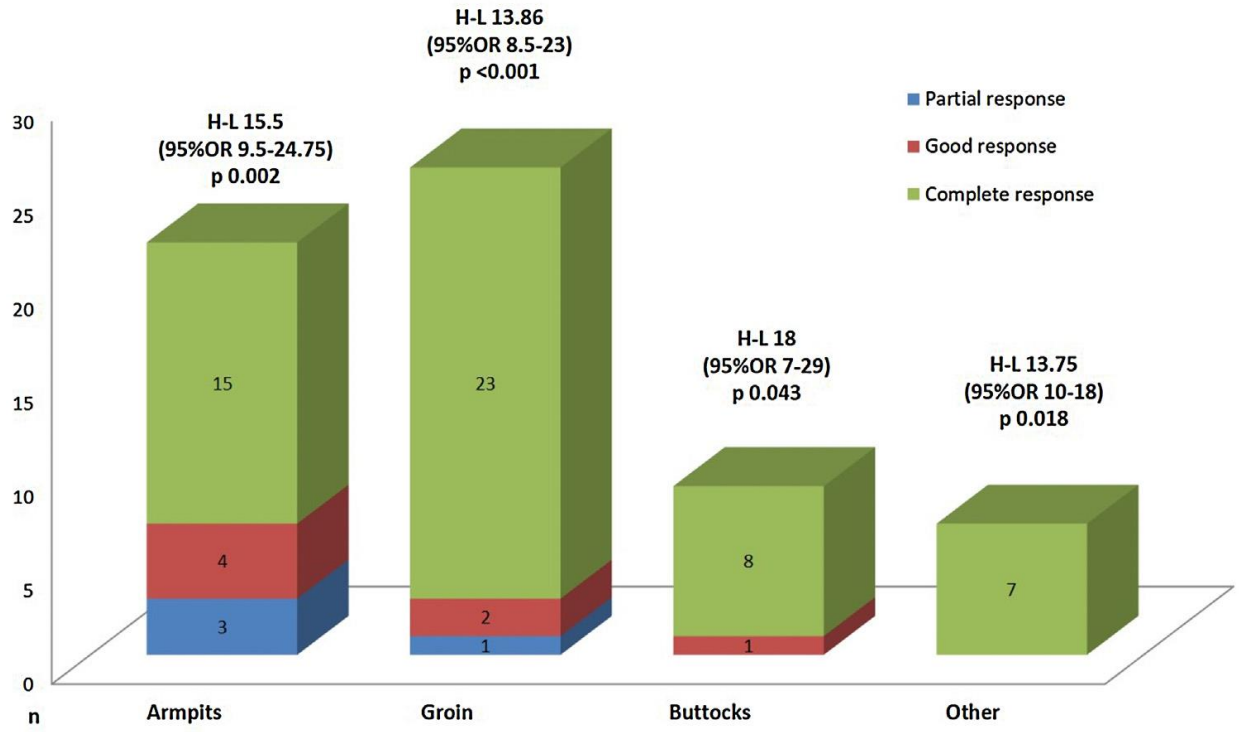


Sebaceous gland hyperplasia:
Strength of Recommendation C, Quality of Evidence II-III

Five patients with sebaceous gland hyperplasia received stan-dard MAL-PDT protocol with marked improvement in 2 and moderate response in 2. (Calzavara-Pinton PG, et al 2013).

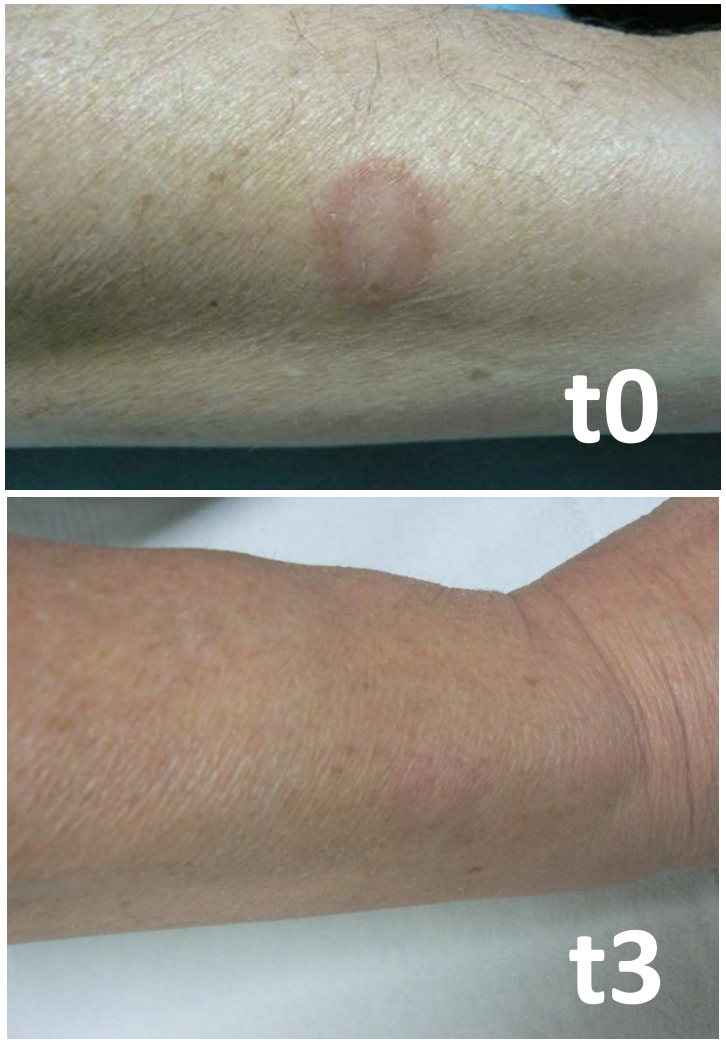
Table 1
Studies on the use of aminolevulinic acid photodynamic therapy for sebaceous skin

Reference	ALA incubation time (h)	No. of treatments	Light source	Results	Follow-up (mo)
Horio et al [20]	4 (under occlusion)	3	Halogen, >620 nm	Small and large lesions decreased in size and reduced sizes persisted for 12 mo; temporary erythema, edema, hyperpigmentation.	12
Alster et al [52]	1	1, 2	PDL (595 nm)	7 of 10 patients cleared with 1 treatment, 3 patients cleared after 2 treatments; transient erythema, edema, focal crusting.	3
Goldman [54]	0.25	2–4	IPL or blue	Acne and SH lesions cleared after 2–4 treatments.	—
Richey et al [53]	0.75–1	3–6	Blue	70% lesion clearance after 6 mo; 10%–20% recurrence 3–4 mo after final treatment; temporary erythema, edema, hyperpigmentation.	6
Gold et al [55]	0.5–1	4	Blue, IPL	55% reduction in lesions with blue light, 53% with IPL; temporary mild erythema and blisters.	1, 3

Abbreviation: IPL, intense pulsed light.

Adapted from Nestor MS, Gold MH, Kauvar AN, et al. The use of photodynamic therapy in dermatology: results of a consensus conference. J Drugs Dermatol 2006;5(2):148; with permission.

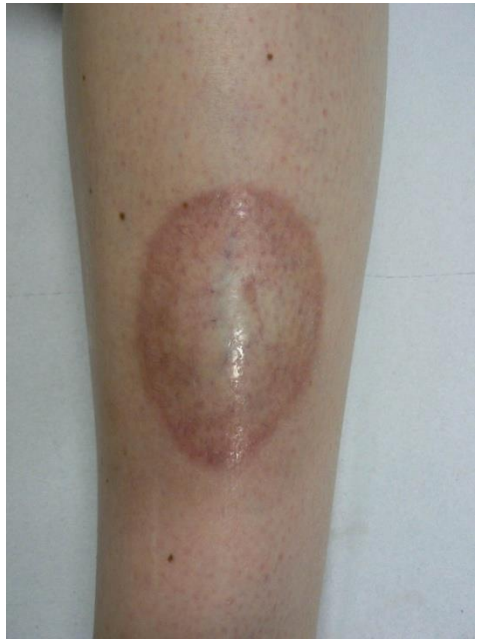
Granuloma annulare:
Strength of recommendation C; Quality of evidence III

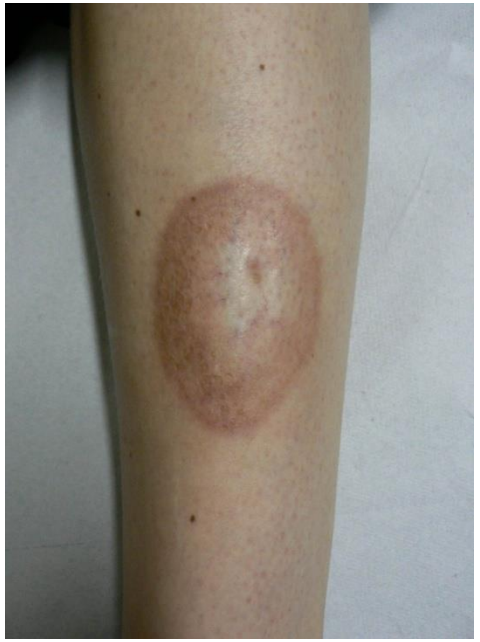


Complete healing in two patients, marked improvement in 2, poor/ no response in 3 with 2-3 ALA-PDT sessions .
(Weisenseel P, et al. 2008)

A complete/ marked improvement in 7/ 13 patients with a mean of 2.8 MAL-PDT treatments.
(Calzavara-Pinton PG, et al. 2013)

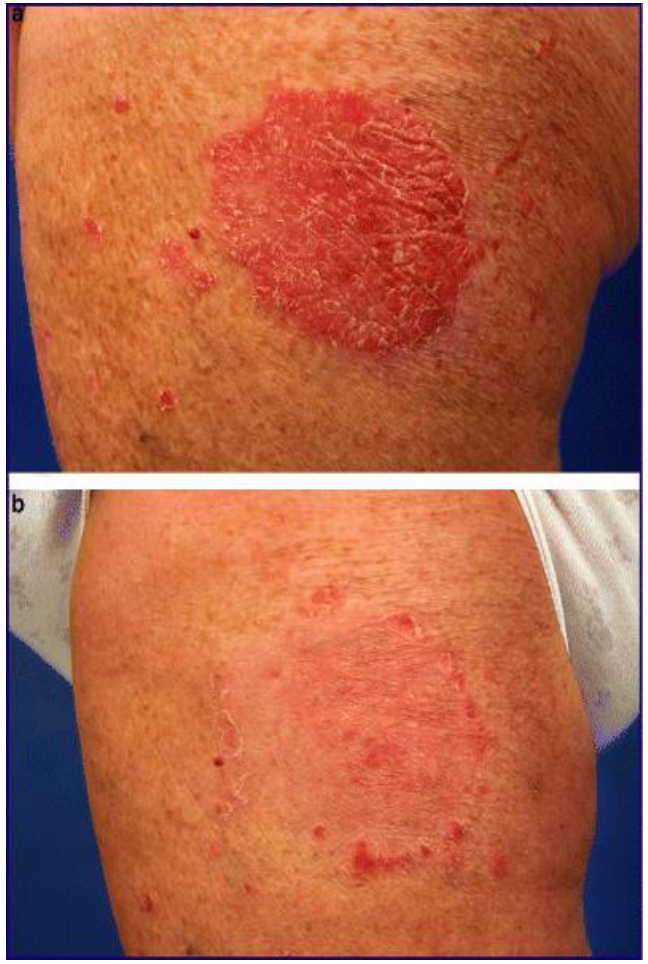
Necrobiosis lipoidica:
Strength of recommendation C; Quality of evidence III





1 patient had a complete response, 6 a partial response and 11 no/poor response after 9-14 ALA-PDT treatments.
(Berking C et al. 2009)
3/8 patients had a partial response after a mean of 10 MAL-PDT sessions.
(Calzavara-Pinton PG, et al. 2013)
43/ 65 patients had a complete/ partial response with MAL-PDT after superficial curettage
(Kaae J, et al. 2018).

Psoriasis:
Strength of recommendation D; Quality of evidence I



In 12 patients, the mean improvement was 37.5%, 45.6% and 51.2% in the 0.1%, 1% and 5% ALA-treated groups, respectively. Treatment was frequently interrupted due to severe burning and pain

(A randomized, observer-blinded study by Radakovic-Fijan, S et al. 2005).

6/17 patients showed short-term improvement following MAL-PDT, whilst psoriatic lesions worsened in 2 patients.

(A retrospective study by Calzavara-Pinton PG, et al. 2013)

Tinea capitis caused by Microsporum canis treated with MAL-daylight-PDT and ketoconazole shampooing

Yolanda Gilaberte, Paulina Cerro, Betsabé Melcón, Carmen Aspiroz
Department of Dermatology, Miguel Servet University Hospital Ophtalmology and Microbiology Services Royo Villanova Hospital, IIS Aragón. Zaragoza. Spain

EURO PDT 20TH ANNUAL CONGRESS PARIS
PLATINUM SPONSOR GALDERMA EST. 1981

Homebase DLPDT protocol

- Signed inform consent for off label used
- Shave the area and remove scales with 70% alcohol
- MAL 16% crema (Metvix®) (2 cm around) incubated for 30 minutes
- Daylight exposure: 2 hrs
- Wash the area and protection from the light for 24-48 hours
- **Side effects:** mild erythema after the PDT session

MAL

+

Follow-up….

- 10 days after last PDT session the lesion recurred
- Culture was positive (a few colonies)
- Ketoconazole shampoo is recomended in the guidelines of *tinea capitis* added to oral antifungals in order to decrease arthrocconidia, reducing transmisibility

MAL

+

+

KETOCONAZOLE 2% shampoo
Twice per week

Limitations of antimicrobial PDT

- Possibility of regrowth of microorganisms not inactivated during the PDT session
- In *tinea capitis* recurrence is probably due to persistence of the fungus in areas of the scalp where MAL was not applied
- Several sessions are need
- Cost of the treatment

Conclusions

- ALA or MAL PDT can be useful in the treatment of *tinea capitis* especially in:
  - Children with comorbidities
  - Failure of antifungals
  - Maybe especially convenient for kerion
- Combination with antifungals is needed:
  - Ketoconazole shampoo
  - Systemic antifungal for a short time
- Daylight PDT is a very friendly treatment for children
- Treatment could be made at homebase
- More studies are needed to define the protocol

The Euro-PDT Board acknowledge all the contributors an sponsors to the 2022 Euro-PDT meeting, including Galderma as platinum sponsor.

LR Braathen, RM Szeimies, CA Morton, Euro-PDT Board, June 2022