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Contents

EURO-PDT 2023 Best of Slides

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Euro-PDT Board, June 2023

Instructions

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Plenary session 1

PDT landscape 2023

Chairs: Lasse R. Braathen, Yolanda Gilaberte

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Welcome to EURO-PDT 2023

Lasse R. Braathen
Berne, Switzerland

EURO-PDT. An educational platform for PDT in Europe.

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

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New Insights in Pathology of AK

Thomas Dirschka
Wuppertal, Germany

Read the abstract

Can we define actinic keratoses?

- AK is a chronic and recurrent disease[1,2]
- AK is caused by long-term sun exposure[1,2]
- Everyday problem in dermatological offices[1,2]
- 40-60% of Australian adults and 38% of European adults have AK[1,3]
- Prevalence is rising[1,3,4]
- If untreated, AK can progress into SCC[5]
  - What are the risk factors?

AK, actinic keratosis; SCC**,** squamous cell carcinoma.

1. Chetty P, *et al. Dermatol Ther (Heidelb).* 2015;5:19–35; **2.** Uhlenhake EE, *et al. Clin Interv Aging.* 2013;8:29–35; **3.** Green AC, *et al. Curr Probl Dermatol*. 2015;46:1–7; **4.** Schaefer I, *et al. J Eur Acad Dermatol Venereol.* 2014;28:309–313; **5.** Cockerell CJ, *et al. Br J Dermatol.* 2003;149 Suppl 66:34–36.

1: Immunosuppression

~40% of AK patients develop invasive SCC under immunosuppression[1]

Organ-treatment patients have a **250 fold increased risk** for AK[1]

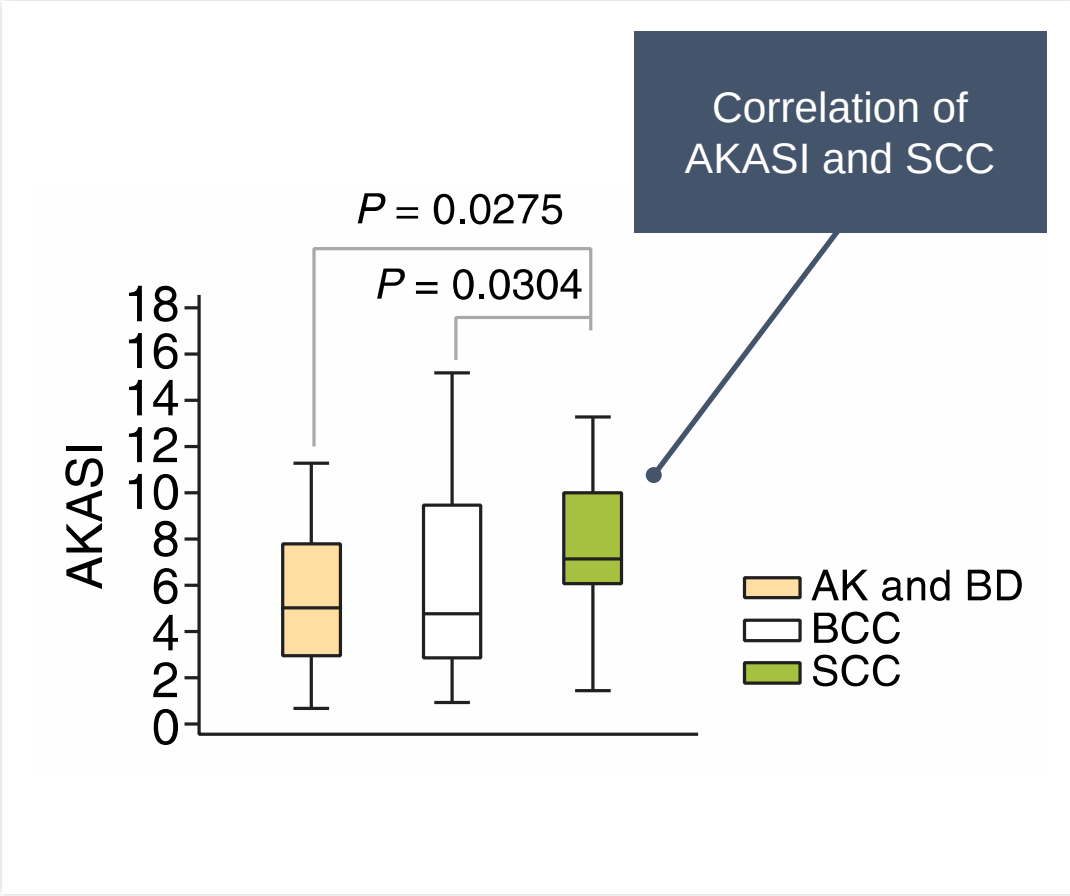
Organ-treatment patients have a **100 fold increased risk** to develop invasive SCC[1]

2: Field cancerisation (high AKASI)

ORIGINAL ARTICLE

Actinic keratosis area and severity index (AKASI) is associated with the incidence of squamous cell carcinoma

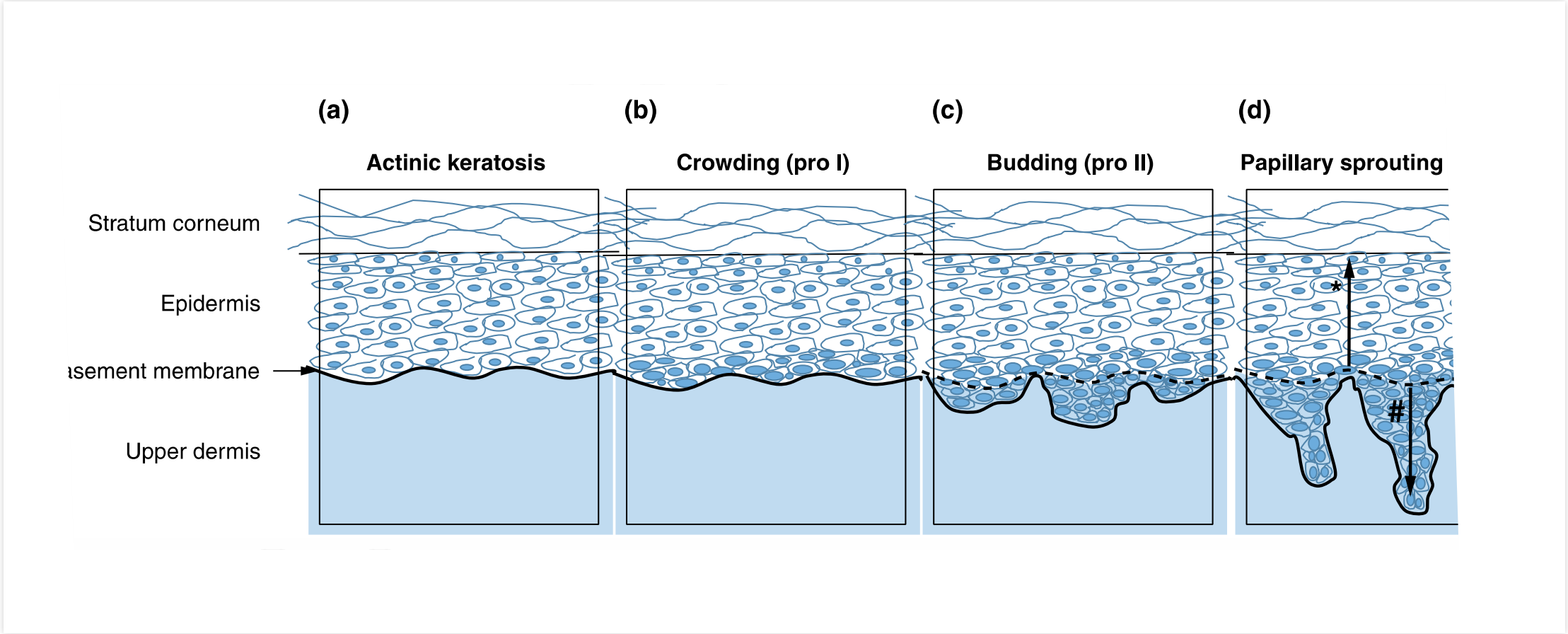
L. Schmitz,[1,*] T. Gambichler,[1] G. Gupta,[2,3] M. Stücker,[1] T. Dirschka[4,5]



AK, actinic keratosis; AKASI, actinic keratosis area and severity index; BCC, basal cell carcinoma; BD, bowen disease; SCC, squamous cell carcinoma.

1. Schmitz L, *et al. J Eur Acad Dermatol Venereol.* 2018,32:752–756.

3: Basal Proliferation (PRO III lesions)



PRO, basel growth pattern.

1. Schmitz L, *et al. J Eur Acad Dermatol Venereol*. 2018;32:745–751.

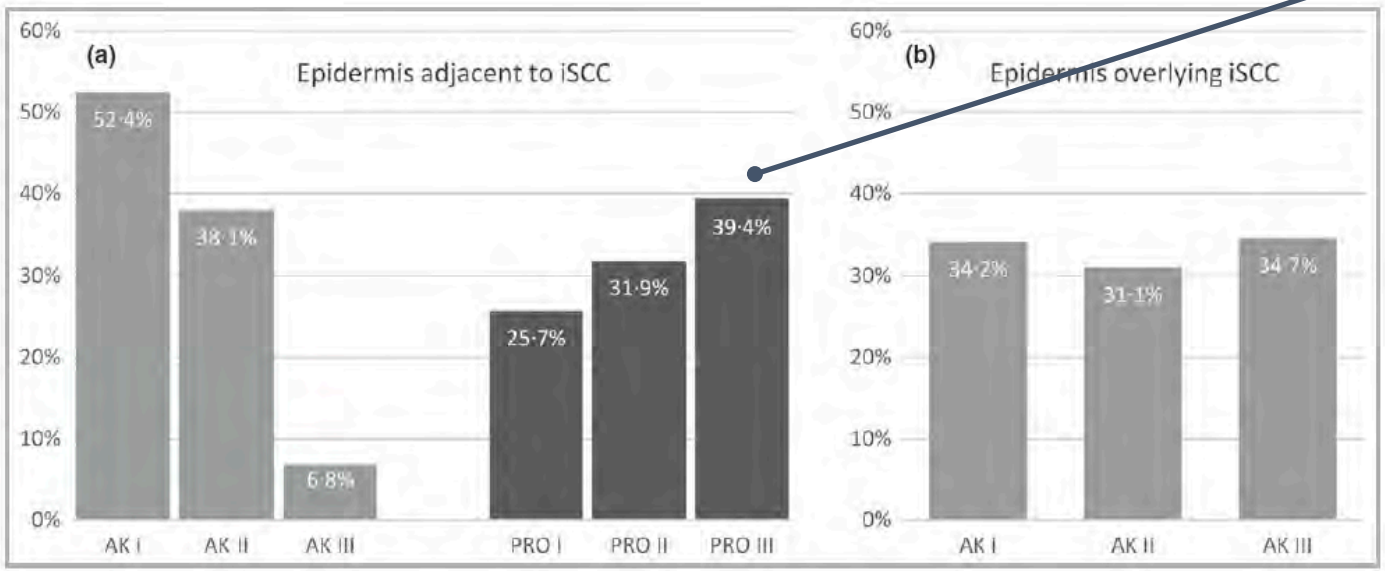
3: Basal proliferation (PRO III lesions) (1/2)

Cutaneous squamous cell carcinomas are associated with basal proliferating actinic keratoses*

L. Schmitz[1*], T. Gambichler[1], C. Kost[1], G. Gupta[2,3], M. Stücker[1], E. Stockfleth[1], T. Dirschka[4,5]

1Department of Dermatology, Venereology and Allergology, Ruhr-University, Bochum, Germany
2Department of Dermatology, University Hospital Monklands, Lanarkshire, UK
3School of Medicine, University of Glasgow, UK
4CentroDerm Clinic, Heinz-Fangman-Straße 57, Wuppertal, Germany
5Faculty of Health, University Witten-Herdecke, Alfred-Herrhausen-Straße 50, Witten, Germany

39.4% PRO III AKs adjacent to SCC



AK, actinic keratosis; iSCC, invasive squamous cell carcinoma; PRO, basal growth pattern; SCC, squamous cell carcinoma.

1. Schmitz L, *et al. Br J Dermatol.* 2019;180:916–921.

3: Basal proliferation (PRO III lesions) (2/2)

cancers

MDPI

Article

Basal Proliferation and Acantholysis May Represent Histological High-Risk Factors for Progression into Invasive Squamous Cell Carcinoma: A Comparison Study in Solid Organ Transplant Recipients and Matched Immunocompetent Patients

Conrad Falkenberg [1,*], Thomas Dirschka [2,3], Georgia Gilbert [4], Eggert Stockfleth [5], Bernhard Homey [1,†] and Lutz Schmitz [3,5,†]

This study showed that acantholytic AKs graded as AK I and PRO III are predominantly found in a population at high risk of iSCC

Thus, AKs with **marked basal proliferation** and **acantholysis** should be assumed to be histological **high-risk factors for the progression into iSCC**

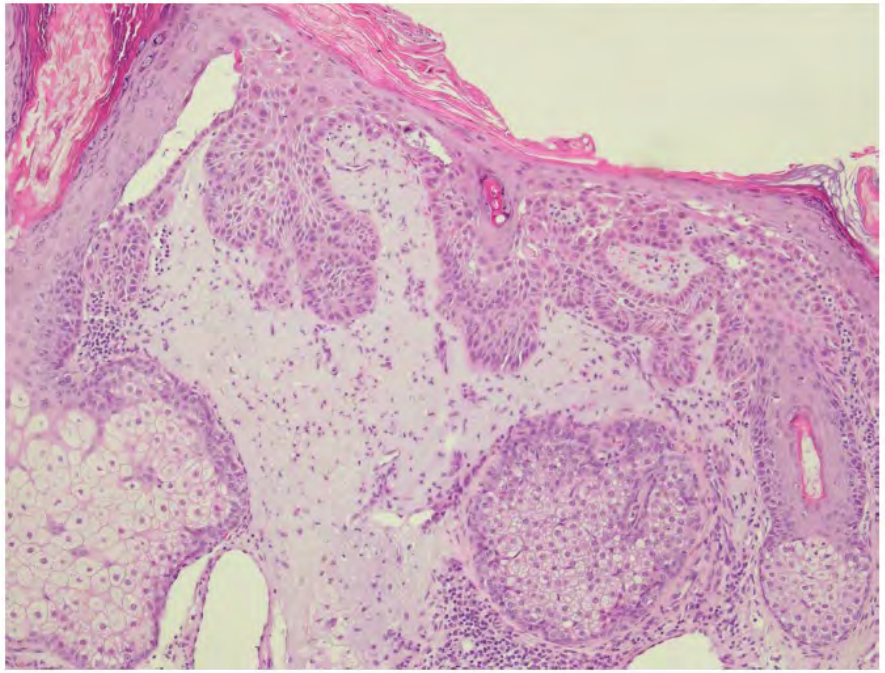


Figure 1. Histological section (H&E; original magnification ×40) of an actinic keratosis (AK) derived from a solid organ transplant recipient (sOTR) showing marked basal proliferation (PRO III), acantholysis, follicular involvement and pronounced solar elastosis. Marked basal proliferation (PRO III) and acantholysis were more prevalent in AKs from sOTRs than in the immunocompetent control group ($p < 0.0001$ and $p < 0.0001$, respectively).

AK, actinic keratosis; iSCC, invasive squamous cell carcinoma; PRO, basel growth pattern.

1. Falkenberg C, *et al. Cancers.* 2023;15:1765.

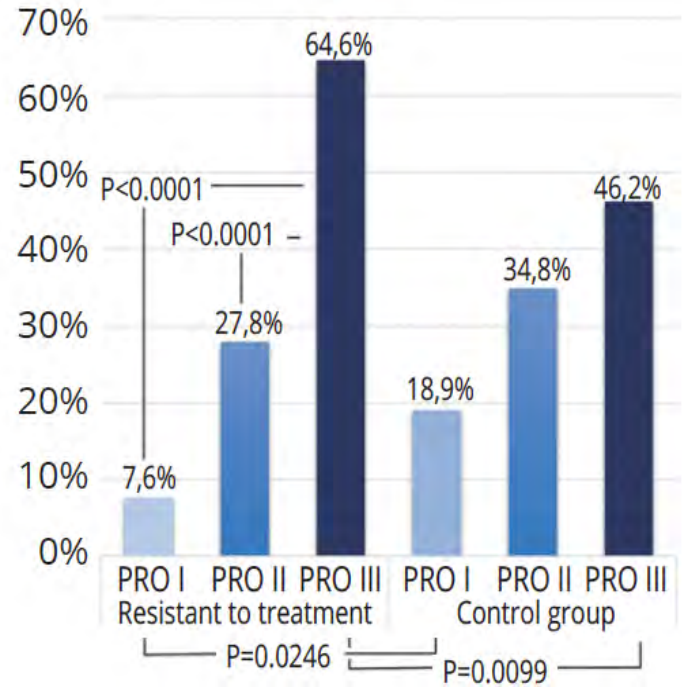
4: Treatment resistance

Investigation on treatment resistant actinic keratoses

211 AKs in 171 patients were biopsied and compared to AKs biopsied before any treatment

AKs without marked basal proliferation, PRO I change, were significantly less in the RG (7.6% vs. 18.9%, *p*=0.0246) compared to the CG

Comparison of clinical and histological features between treatment-resistant AKs and control group



AK, actinic keratosis; CG, control group; PRO, marked basal proliferation; RG, treatment-resistant AKs group.

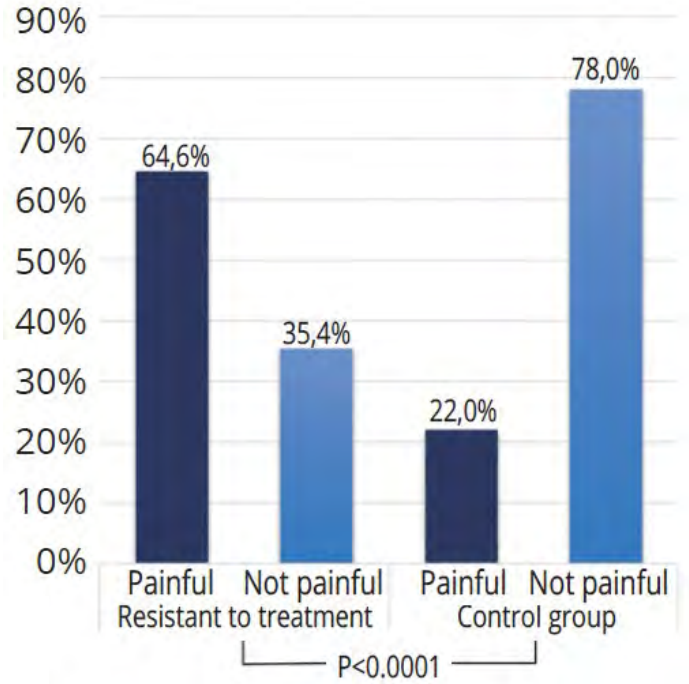
1. Schmitz L, *et al. Ital J Dermatol Venereol.* 2021;156:213–219.

5: Pain on palpation

Investigation on treatment resistant actinic keratoses 211 AKs in 171 patients were biopsied and compared to AKs biopsied before any treatment

Significantly more painful AKs in the RG (64.6%) compared to the CG (22.0%) (p<0.0001)

Comparison of clinical and histological features between treatment-resistant AKs and control group

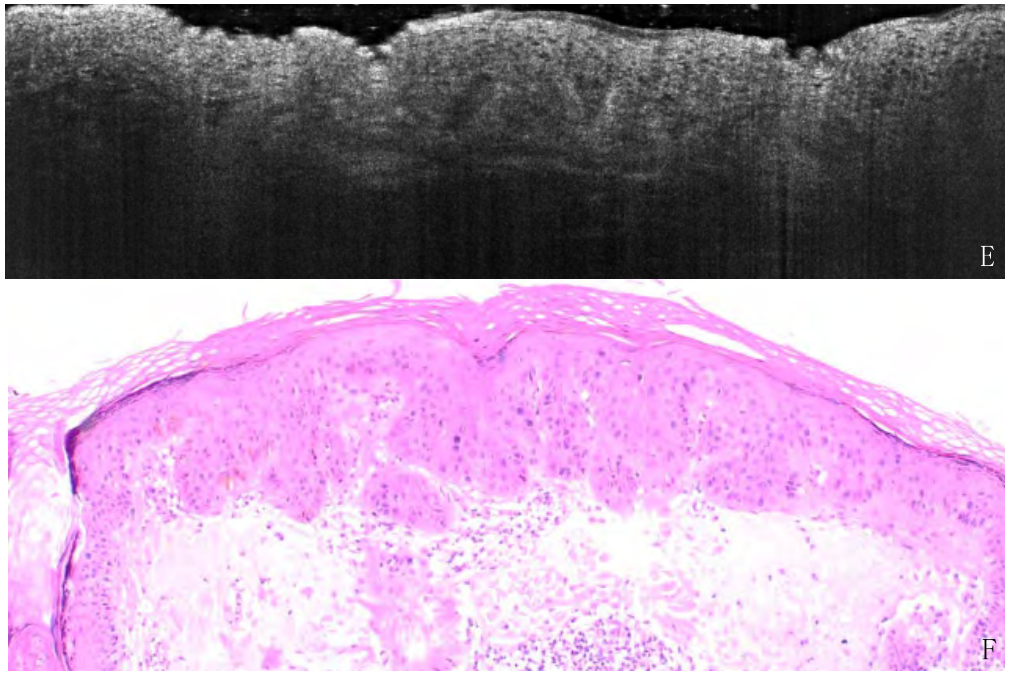


AK, actinic keratosis; CG, control group; PRO, marked basal proliferation; RG, treatment-resistant AKs group.

1. Schmitz L, *et al. Ital J Dermatol Venereol.* 2021;156:213–219.

6: LC-OCT → Diagnosis of proliferative actinic keratosis becomes possible

cancers MDPI



LC-OCT, line-field confocal optical coherence tomography.

1. Ruini C, *et al. Cancers (Basel).* 2021;13:2856.

7: Lessons from molecular pathology

KNSTRN-gene: Recent news on proliferative AK biomarkers

Entity/Grading		Samples N (%)	Mutation Analysis		
			Wild-type N (%)	p.Ala40Glu N (%)	p.Ser24Phe N (%)
HS		29 (100%)	27/29 (93.1%)	2/29 (6.9%)	0/29 (0%)
ADS		31 (100%)	26/31 (83.9%)	5/31 (16.1%)	0/31 (0.0%)
SCC		30 (100%)	21/30 (70.0%)	9/30 (30.0%)	0/30 (0.0%)
AK overall		109 (100%)	87/109 (79.8%)	20/109 (18.3%)	1/109 (0.9%)
AK Grading[1] [1]	AK I	34/109 (31.2%)	29/34 (85.3%)	5/34 (14.7%)	0/34 (0.0%)
	AK II	30/109 (27.5%)	25/30 (83.3%)	4/30 (13.3%)	1/30 (3.3%)
	AK III	45/109 (41.3%)	34/45 (75.6%)	11/45 (24.4%)	0/45 (0.0%)
PRO Grading[7]	PRO I	28/109 (25.7%)	27/28 (96.4%)	1/28 (3.6%)	0/28 (0.0%)
	PRO II	60/109 (55.0%)	47/60 (78.3%)	13/60 (21.7%)	0/60 (0.0%)
	PRO III	21/109 (19.3%)	14/21 (66.7%)	6/21 (28.6%)	1/21 (4.8%)

AK, actinic keratosis; ADS, actinically damaged skin; HS, healthy skin; KNSTRN, Kinetochore Localised Astrin (SPAG5) Binding Protein; PRO, basel growth pattern; SCC, squamous cell carcinoma.

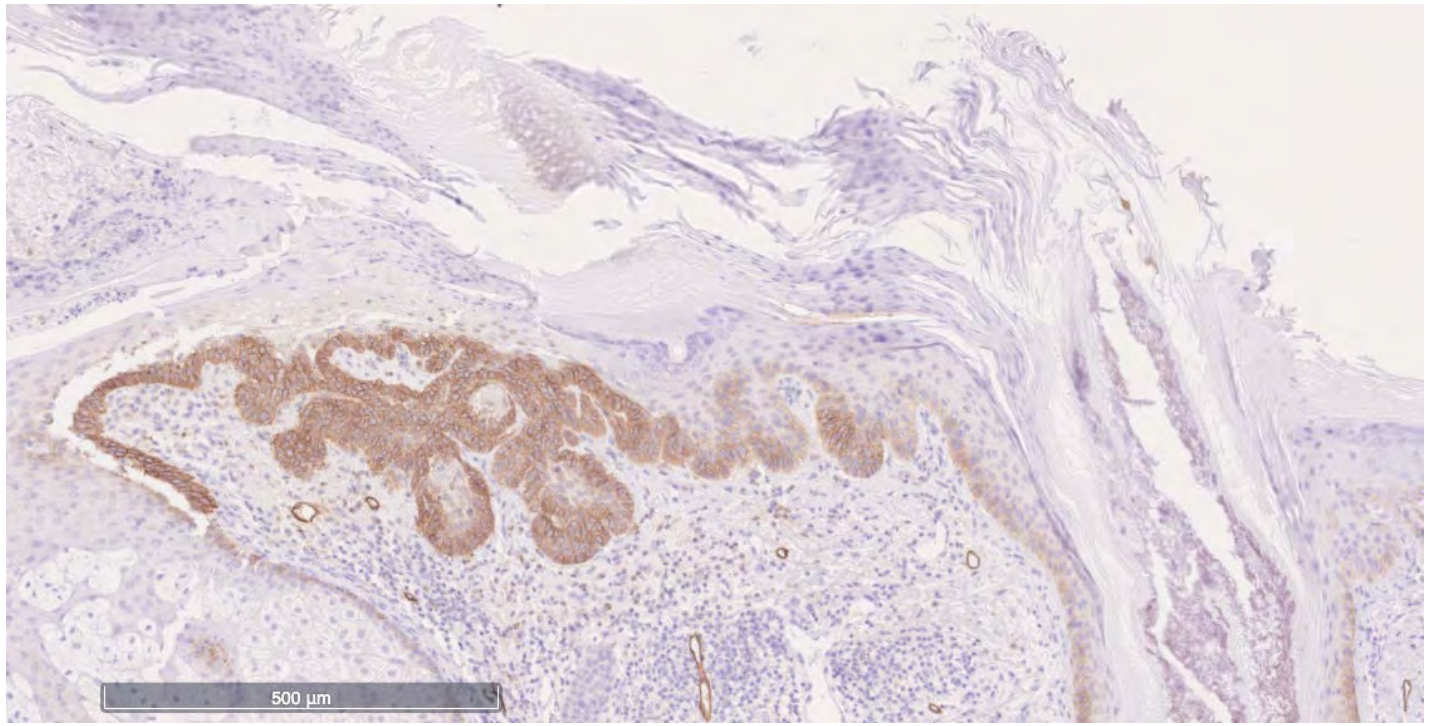
1. Schmitz I, *et al. J Eur Acad Dermato Venereol.* 2019;33:1535–1540.

8: Lessons from immunopathology

Latest research[1]

Immunohistological characterisation of proliferative actinic keratoses

AK type PRO III showed significant higher exprimation of D2-40 compared to non-proliferative AK (p<0.0056)



D2-40 (Podoplanin), x10
Source: CentroDerm Path

AK, actinic keratosis; PRO, marked basal proliferation.

1. contains contents of the dissertation of Vasileios Dervenis

Intermediate conclusion

Proliferation in AK plays a dominant role as risk factor of progression to squamous cell carcinoma![1]

Proliferation can be detected by:[1,2]

a) Biopsy
b) LC-OCT
c) Treatment resistance (indicator)
d) Pain on palpation (indicator)

Podoplanin is a marker that characterizes proliferative AK![3]

AK, actinic keratosis; LC-OCT, line-field confocal optical coherence tomography.

1. Ruini C, *et al. Cancers (Basel).* 2021;13:2856; **2.** Schmitz L, *et al. Ital J Dermatol Venereol.* 2021;156:213–219; **3.** data on file; contains contents of the dissertation of Vasileios Dervenis.

CENTRO DERM®

Presentation of suspected AK → Diagnosis and risk assessment → Suspicion of SCC / other differential diagnoses → Biopsy

Single AK lesions	Single AK lesions	Multiple AK lesions	AK in immuno-compromised patients	AK in special locations
Single widely scattered AK lesions per field or affected body area, no hyperkeratosis, no dynamic progression	Single widely scattered AK lesions per field or affected body area	Multiple AK lesions or clustered AK lesions in one body area or field Field cancerisation contiguous areas of chronic actinic damage	All severity degrees	1. Lower lip 2. Ears 3. Dorsum of hands / forearms 4. Lower legs

Provide information about AK (e.g. patient leaflet) & Advice on emollients and sun protection - Hyperkeratotic lesions: gentle curettage

Upon patient request	Destructive treatments	Conventional or daylight PDT	Conventional PDT or Laser assisted PDT	
- Self-monitor - Follow-ups - See GP or dermatologist if lesion grows / becomes hyperkeratotic	- Cryotherapy - Curettage - CO_2 / Er:YAG Laser Topical treatments - 5-FU/SA - 5 % 5-FU cream - 5 % Imiquimod cream	- ALA-PDT - MAL-PDT Topical treatments - 5-FU/SA - 5 % 5-FU cream - 5 % Imiquimod cream - 3.75 % Imiquimod cream - DFS Additional treatments for individual lesions - Cryotherapy - Curettage - CO_2 / Er:YAG Laser	- ALA-PDT - MAL-PDT Topical treatments - 5% 5-FU cream Additional treatments for individual lesions - Cryotherapy - Curettage - CO_2 / Er:YAG Laser	1. High risk! If conventional treaments fail → Vermillionectomy 2. High risk! If conventional treatments fail → Excision 3. Adequate removal of hyperkeratosis 4. Large areas Area restrictions of drugs, 5-FU cream possible

5-FU: 5-Fluorouracil
5-FU/SA: 0,5 % 5-Fluorouracil in 10 % hyaluronic gel
ALA: Aminolevulinic acid
DFS: 3 % Diclofenac sodium in 2,5 % hyaluronic gel
HA: Hyaluronic acid
MAL: Methyl aminiolevulinic acid
PDT: Photodynamic therapy
SA: Salicylic acid

Treatment-resistant AK → 2nd treatment cycle / change of treatment; if still treatment-resistant → Excision and histological work-up

Gupta G, Dirschka T., Rook's Textbook of Dermatology, 10th ed. in press

Future research

Hypothesis: If it is the case that proliferation plays an important role in progression of AK into SCC the best treatments would have to be those that directly influence proliferation

Which treatment works best for proliferating AK?

Importance of Hyperkeratosis?

Ahmadi S et al., JAMA Dermatol 2022; 158: 34-640
„In patients with severe AK (Olsen grade III), the risk was 20.9% (95% CI, 10.8%-38.1%)....“

Hyperkeratosis

ORIGINAL ARTICLE

Actinic keratosis: correlation between clinical and histological classification systems [1]

L. Schmitz,[1,2,*] P. Kahl,[3] M. Majores,[3] E. Bierhoff,[3] E. Stockfleth,[1] T. Dirschka[2,4]

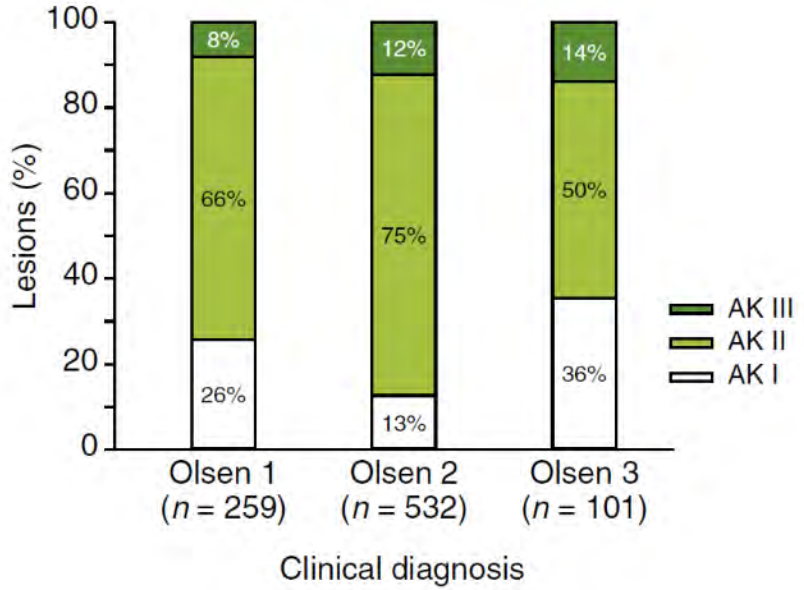


Figure 1 Histological classification of clinically diagnosed AK lesions (N = 892).

In >700 biopsies of AKs Olsen grade did not correlate with proliferation[2].

1. Schmitz L et al., J Eur Acad Dermatol 2016; 30: 1303-1307 **2.** Dirschka T *et al., unpublished, data on file*

How shall we conduct clinical AK trials?

Most important goal: to prevent progression into SCC!

We can not clear all lesions for ever!

→ If the number of Aks / area size are the most relevant factors, why shall we keep them small in clinical trials?

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Global Trends and Guidelines in PDT for skin cancer

Colin A. Morton
Stirling, United Kingdom

Read the abstract

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
Prof. Colin. A. Morton
Prof. Stefano Piaserico
Prof. Rolf-Markus Szeimies
Dr. Claas Ulrich
Prof. Ann-Marie Wennberg

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

BAD guideline PDT 2018: Key Recommendations:

Actinic keratosis

- ↑↑ Offer PDT to people with AK, particularly for cosmetically sensitive sites, multiple and large-area lesions.
  ↑ *Consider combining PDT with other treatment modalities if feasible for people with thick AK*

Squamous cell carcinoma in situ (Bowen disease)

- ↑↑ Offer PDT as a treatment option to people with SCC in situ, particularly for poorly healing or cosmetically sensitive skin sites, multiple/large-area lesions

Basal Cell Carcinoma

- ↑↑ Offer PDT to people with superficial BCC
- ↑ Consider PDT for people with thin (<2mm nodular BCC)

Skin cancer prophylaxis

- ↑ Consider field PDT as prophylaxis

Update of the British Association of Dermatologists' guidelines for BCC

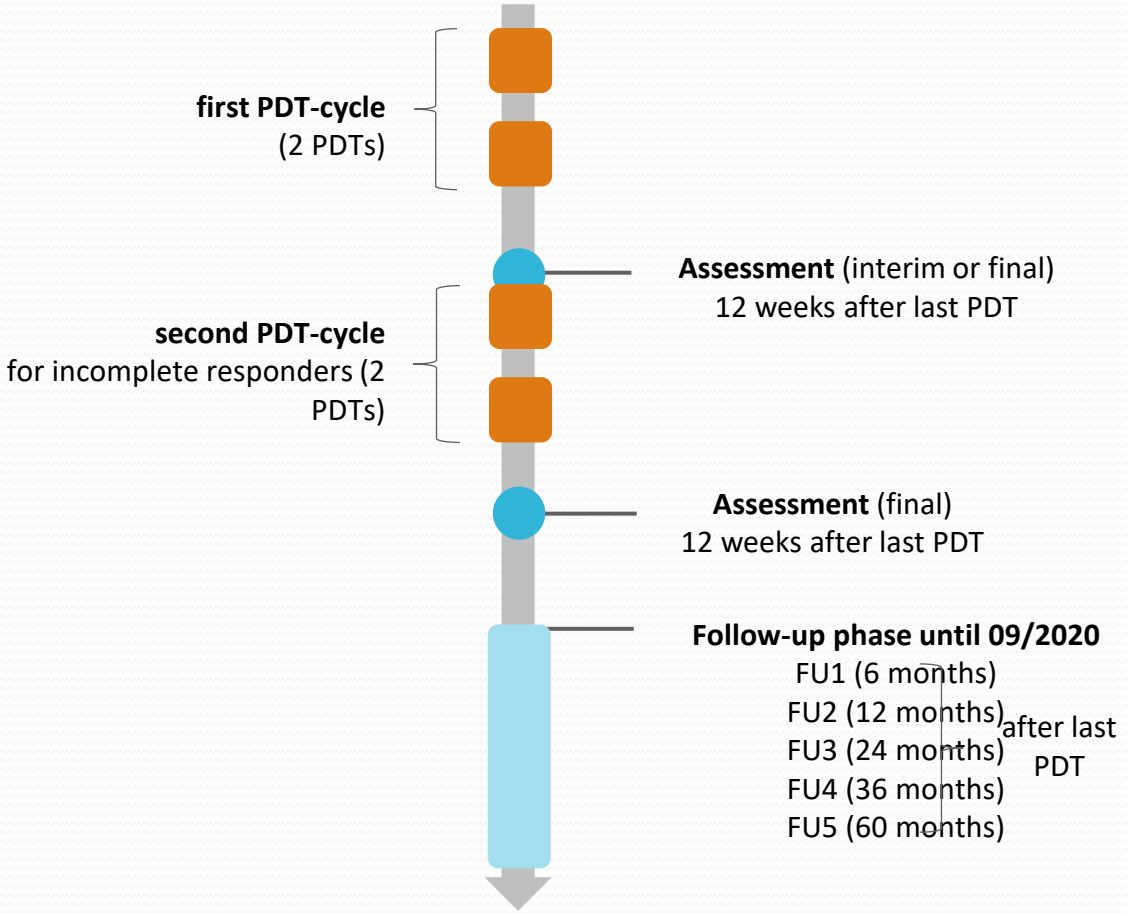
Nasr, I., McGrath, E.J., Harwood, C.A., et al. *Br J Dermatol.* 2021;185:899-920.

↑↑ Offer topical PDT for low-risk* BCC who are unsuitable for or decline standard surgical excision

*Low risk: up to 20mm on trunk/extremities (10mm on cheeks, forehead, scalp, neck, pretibia) primary superficial or nodular, immunocompetent, up to max 6mm histol depth

Red-light photodynamic therapy for non-aggressive BCCs: Pivotal phase III trial in Europe – ALA-BCC-CT008

- **Design:** randomised, observer-blind, comparator-controlled, interindividual, non-inferiority study in Germany and UK
- **Objective:** comparison of efficacy and safety in the treatment of non-aggressive BCCs with red-light PDT
  - BF-200 ALA: 78 mg/g aminolevulinic acid (ALA)
  - MAL cream: 160 mg/g methylaminolevulinate (MAL)
- **Duration:** treatment-phase from 2014 to 2015, follow-up phase until 2020
- **Patients:** 281 patients with one to three non-aggressive BCCs, up to 2 mm thickness
- **Primary endpoint:** overall patient complete clearance rate, 12 weeks after last PDT



modified according to Morton *et al.*, 2018.

ALA: aminolevulinic acid; BCC: basal cell carcinoma; FU: follow-up; MAL: methylaminolevulinate; PDT: photodynamic therapy.

References: NCT02144077; Morton *et al.*, Br J Dermatol. 2018; 179(2): 309-319.

Results to 12 months: Clearance rates

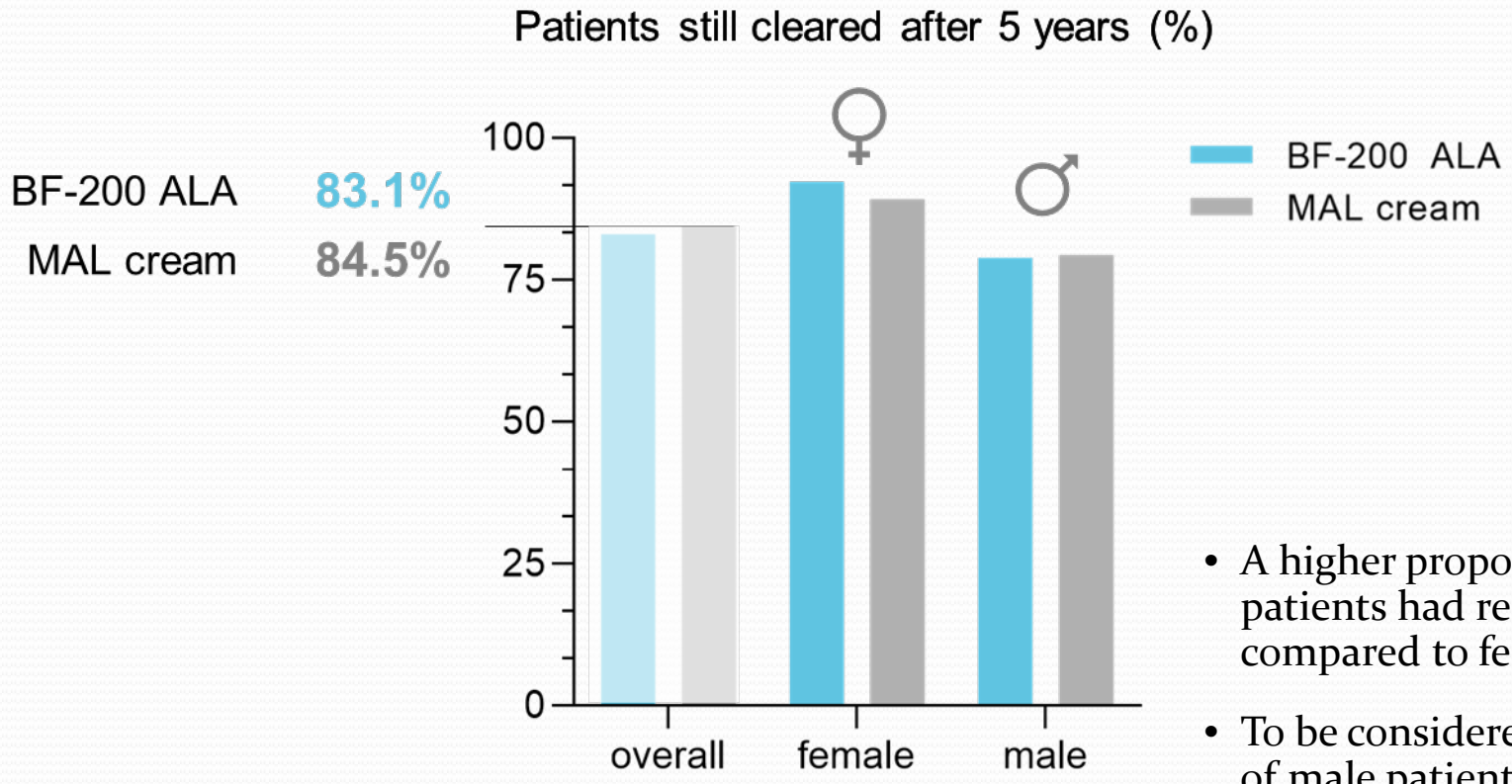
- Both patient and lesion complete clearance rates slightly higher for BF-200 ALA than for MAL
- High statistical significance for non-inferiority of BF-200 ALA (major statistical endpoint)
- Thicker and nodular BCCs responded better to BF-200 ALA than MAL

12 weeks after last PDT *	BF-200 ALA	MAL
patient complete clearance rate	93.4% (113/121)	91.8% (101/110)
• only superficial (sBCC)	94.7% (90/95)	96.4% (80/83)
• only nodular (nBCC)	85.7% (18/21)	76.2% (16/21)
• BCC face & scalp	76.9% (10/13)	71.4% (10/14)
• BCC trunk	97.4% (75/77)	95.9% (70/73)
lesion complete clearance rate	94.6% (140/148)	92.9% (118/127)
• 0-1 mm thickness • 1-2 mm thickness	96.4% 72.7%	95.7% 66.7%
lesion recurrence rate (6 months)	2.9% (4/140)	4.3% (5/115)
lesion recurrence rate (12 months)	6.7% (9/134)	8.2% (9/110)

ALA: aminolevulinic acid; BCC: basal cell carcinoma; MAL: methylaminolevulinate; nBCC: nodular BCC; PDT: photodynamic therapy; sBCC: superficial BCC. * Per protocol set.

References: NCT02144077. Morton CA et al. Br J Dermatol 2018;179(2):309-319.

High sustained patient clearance 5 years after last PDT



- A higher proportion of male patients had recurrent lesions compared to female patients.
- To be considered: proportion of male patients in BF-200 ALA arm (68.7%) was higher than in the MAL cream arm (47.9%).

* Per protocol set follow-up phase References: NCT02144077; Clinical study report ALA-BCC-CT008, final Addendum, data on file

What's new- 2023?

- PDT – Global research
- Booming business, but inequity of access
- Strong evidence base for place in skin cancer care
- New 5 year data supporting PDT for BCC
- Emerging indications including acne – lack of optimized protocols and approval as licensed treatment
- PDT – evolution in application: AK: Conventional, Daylight, Simulated Daylight, Home treatment and more!

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The Personalising Actinic Keratosis Treatment (PAKT) project - Final outcome

Rolf-Markus Szeimies
Recklinghausen, Germany

Read the abstract

What are the goals of PAKT?

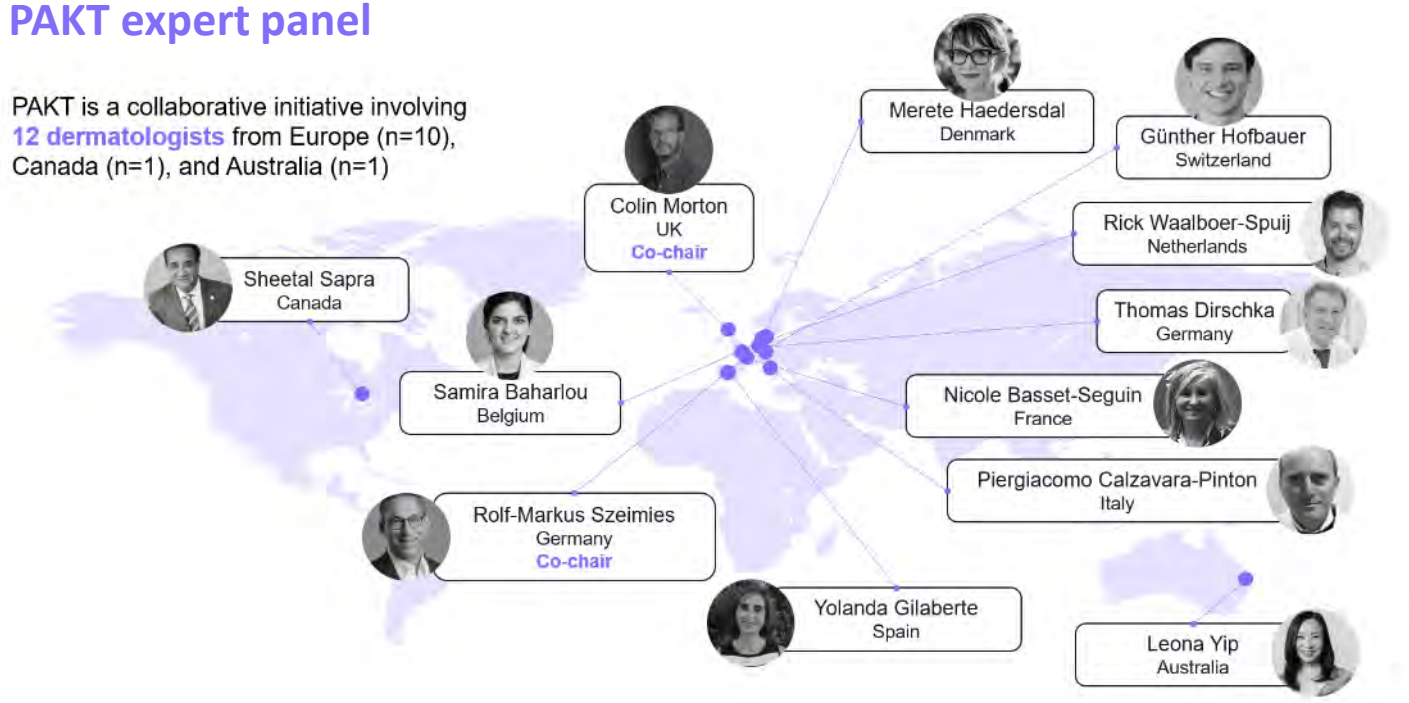
PAKT was established to identify current unmet needs in AK care and develop expert recommendations to address these needs

For patients with existing or at high risk of developing mild/moderate AK and field of cancerisation, the aims and objectives of PAKT are to develop:

- **Expert recommendations** to support **patient-centred treatment decisions,** considering:
  - The evolution and chronicity of disease once photodamage has been observed
  - Patient preferences along their personal treatment pathway
  - Populations particularly vulnerable to AK and progression to SCC
- A **tool** that aids HCPs in making **shared treatment decisions** with patients throughout the AK journey

PAKT expert panel

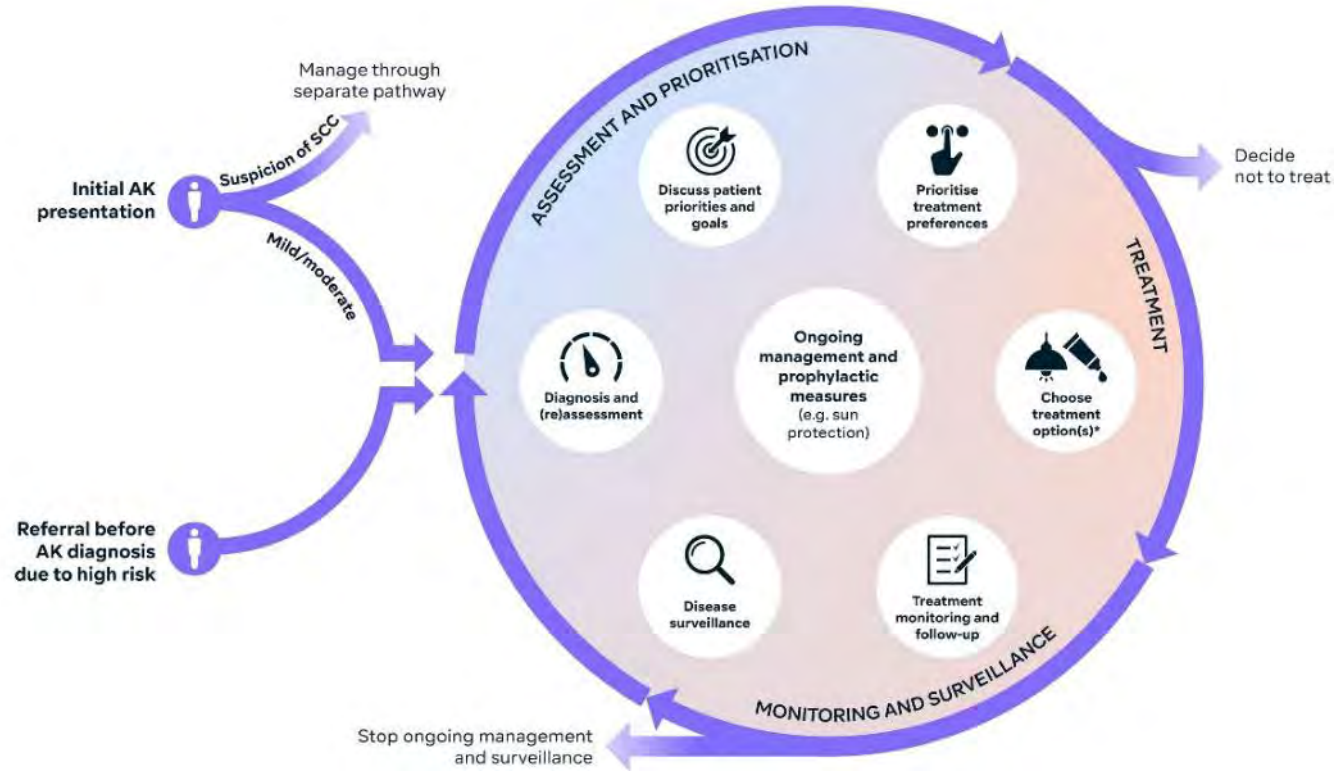
PAKT is a collaborative initiative involving **12 dermatologists** from Europe (n=10), Canada (n=1), and Australia (n=1)



AK, actinic keratosis; HCP, healthcare professional; PAKT, Personalising Actinic Keratosis Treatment; SCC, squamous cell carcinoma.

How can a clinical decision-making tool be used in practice?

Objective: Develop a tool that aids HCPs in making shared treatment decisions with patients throughout the AK journey



Practical use of the tool:

- ✓ **Drive treatment selection based on patient preference**
- ✓ **Personalised longitudinal care**
- ✓ **GP/primary care provider education**

Use of the tool extends beyond the clinic into educational applications which can support management of AK as a chronic disease

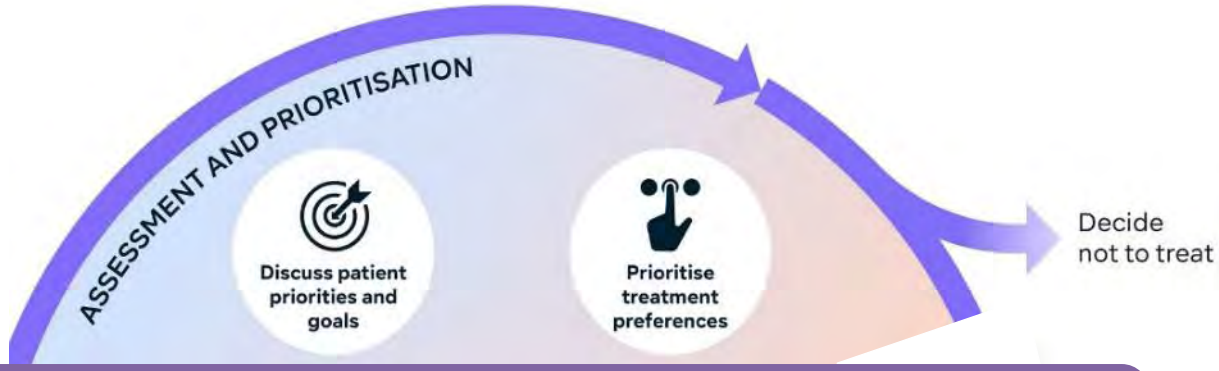
*Including co-prescriptions and adjunctive therapies.
AK, actinic keratosis; GP, general practitioner; HCP, healthcare professional; SCC, squamous cell carcinoma.

Assessment and prioritisation: Managing patient expectations is key

Treatment goals should be tailored according to the individual, considering **patient preference, adherence** and **response to treatment**

It is important to set **realistic expectations** of treatment outcomes

Treatment goals for **high-risk** patients include **reducing the risk of SCC progression** and **the disease impact** on the patient, and **clearing the field of cancerisation**



Establishing these goals at the beginning of the treatment journey can help drive patient-centric decision-making in latter stages

SCC, squamous cell carcinoma.

Treatment: Several factors relating to the patient and disease are important when determining suitable treatment

The most important factors influencing management include, **previous treatment experience**, **risk of progression to SCC** and **choice of lesion-directed vs field-directed treatment**

For patients at **high risk** of developing **AK** and **SCC** (e.g., immunosuppressed patients), consider **treatment modality**, **frequency** and **duration of treatment follow-up**

For treatment **satisfaction,** consider **patient's tolerance of treatment, shorter treatment duration**, **high lesion clearance rate** and **end cosmetic result**

Shared decision-making is key when determining a suitable treatment for patients

*Including co-prescriptions and adjunctive therapies.
AK, actinic keratosis; SCC, squamous cell carcinoma.

The process to develop treatment option schematics

How were the data calculated for the rated attributes of AK treatments?

To support the **'Choose treatment option(s)'** decision point, the PAKT panel were asked to rate therapies on a 6-point scale (0 'very poor' to 5 'excellent') on a range of **attributes** that matter in AK when selecting treatments:

- Good efficacy
- Good convenience
- Field-cancerisation management
- High tolerability
- Good cosmesis
- Short treatment duration

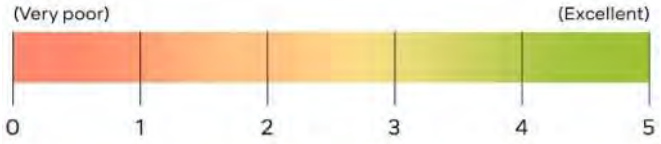
Treatment visualisation options were presented to the PAKT panel to provide feedback on the optimal approach to support key decision point five in the flowchart diagram, based on:

- Structure
- Content
- Overall usability
- Strengths
- Weaknesses

AK, actinic keratosis; PAKT, Personalising Actinic Keratosis Treatment.

Treatment option schematic: Heatmaps may be useful for patient consultations

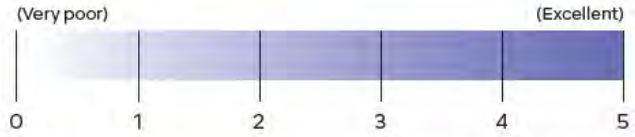
	Good efficacy	High tolerability	Good convenience	Short treatment duration	Good cosmesis	Field-cancerisation management
Red-light PDT with MAL 160 mg/g cream	4.3	2.5	3.3	4.3	4.3	3.8
5-FU 5% cream	4.3	2.5	2.8	2.3	3.2	4.3
Natural daylight PDT with MAL 160 mg/g cream	4.2	4.4	3.9	4.3	4.7	4.3
Artificial daylight PDT with MAL 160 mg/g cream	4.2	4.2	3.3	3.7	4.3	4.2
Red-light PDT with ALA 78 mg/g gel	4.2	2.3	2.9	4.5	4.4	4.3
Natural daylight PDT with ALA 78 mg/g gel	3.9	4.1	3.9	4.6	4.4	4.1
Imiquimod 5% cream	3.9	2.1	2.5	2.5	3.3	3.4
Cryotherapy	3.6	2.7	3.4	4.2	2.1	0.6
5-FU in salicylic acid 10% lacquer	3.6	2.9	3.0	2.7	3.1	1.1
Imiquimod 3.75% cream	3.4	2.4	2.5	2.5	3.2	3.4
Tirbanibulin 10 mg/g ointment	2.8	4.0	3.5	4.3	3.8	2.5
Diclofenac sodium 3% in HA 2.5% gel	1.2	4.6	3.0	0.7	3.4	2.1

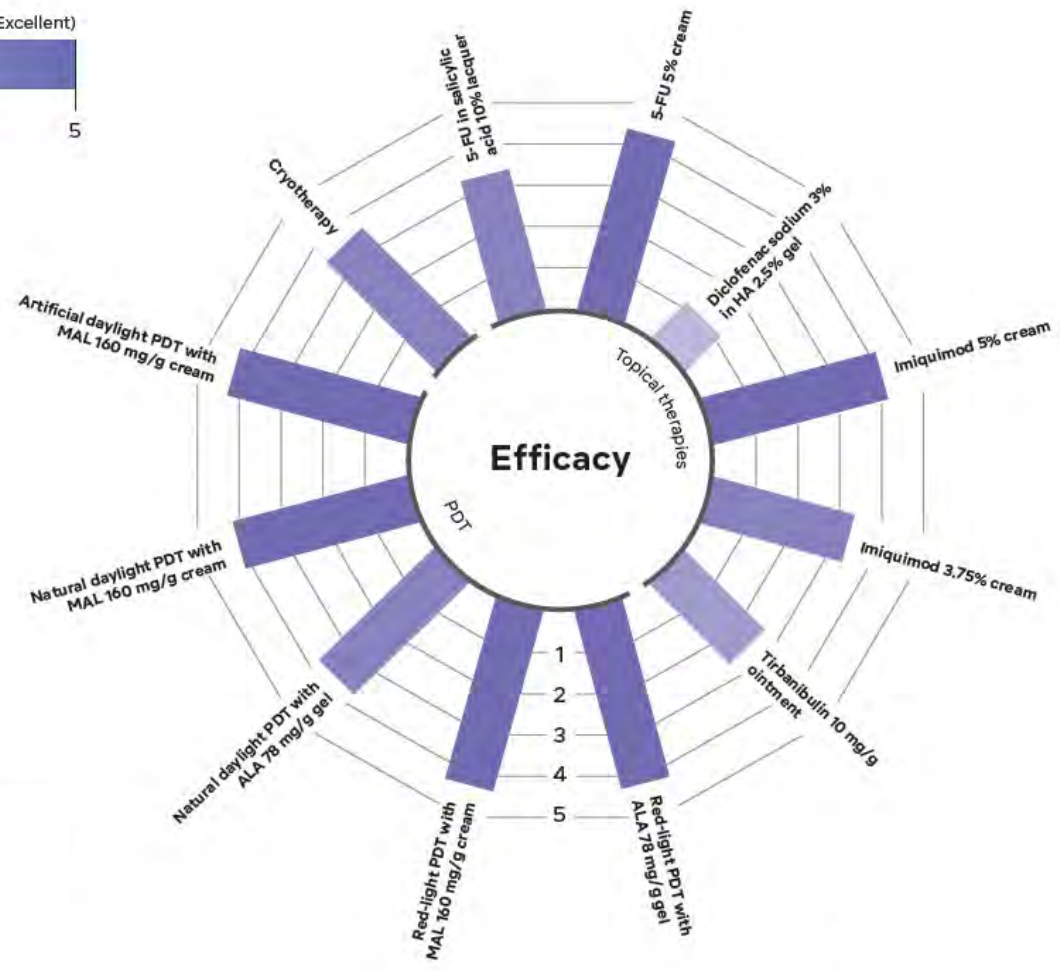


Expert panelists rated each treatment option based on combined knowledge from clinical evidence and their own clinical experience by answering the following question: 'Consider the treatments below. Based on your combined knowledge from clinical evidence (which includes published real-world evidence) and your own clinical experience, please rate each treatment on a scale from 0 (very poor) to 5 (excellent) for the listed factors.' Factors rated were: good efficacy, high tolerability, good convenience, short treatment duration, good cosmesis and field-cancerisation management. Values represent the weighted averages of all responses. Votes of N/A were excluded from the weighted average calculation.
ALA, aminolevulinic acid; FU, fluorouracil; HA, hyaluronic acid; MAL, methyl aminolevulinate; PDT, photodynamic therapy.

Panelists suggested that the heatmap may be of use in **patient consultations for guiding treatment choice**, and could be utilised in **teaching settings**

Treatment option schematic: Radar plots may be suited to dermatologists

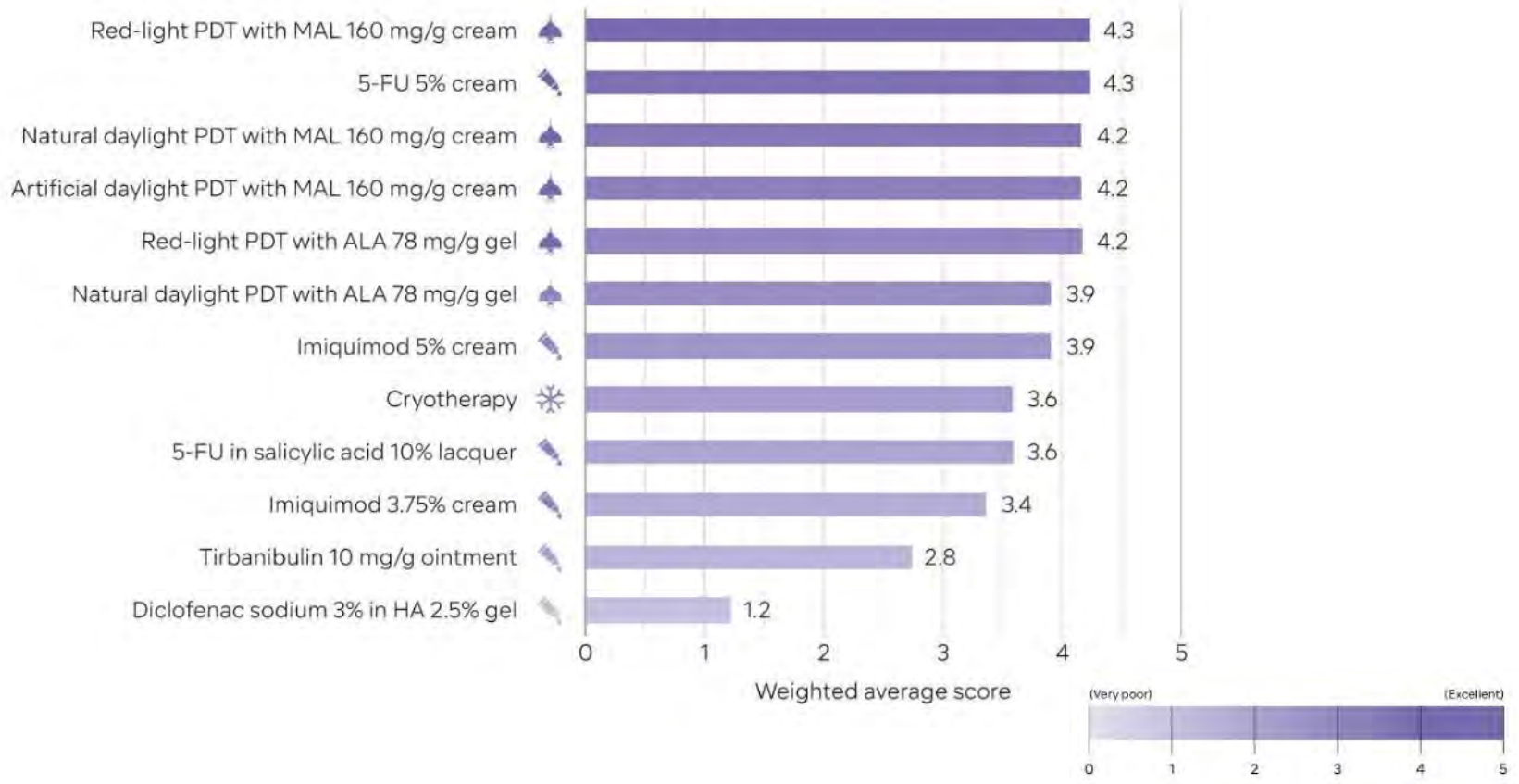




Panelists suggested that the radar plots may be best suited for **dermatologists or research scientists** due to level of detail and familiarity with format

ALA, aminolevulinic acid; FU, fluorouracil; HA, hyaluronic acid; MAL, methyl aminolevulinate; PDT, photodynamic therapy.

Treatment option schematic: Stacked bar charts may be useful for primary care physicians



Panelists suggested that the stacked bar chart may be useful for **dermatologists and primary care physicians**, and the structure is intuitive and easy to use

ALA, aminolevulinic acid; FU, fluorouracil; HA, hyaluronic acid; MAL, methyl aminolevulinate; PDT, photodynamic therapy.

Factors that affect monitoring: Follow-up and disease surveillance

Follow-up schedule considerations include **immunosuppression status**, previous **NMSC history** and previous **AK history**; **discontinuation** of treatment is guided by patient **preference**, **limited life expectancy** and **comorbidities** requiring treatment

Increasing follow-up frequency and/or duration should be guided by **immunosuppression status**, **disease severity**, **extent of field-cancerisation**, **extent of disease progression** and **history of NMSC**

At completion of follow-up appointments, disease surveillance appointments are guided by **previous NMSC history**, **immunosuppression status** and **disease severity**

AK, actinic keratosis; NMSC, non-melanoma skin cancer.

Patient perspectives on AK care:
Individual treatment goals and care aspects varied between patients

The panel surveyed **11 patients**

The majority of patients (9/10)* voted ‘agree’ or ‘strongly agree’ for the below statement:

“Your patient understands the chronic nature of their actinic keratosis and the requirement for repeated, ongoing management”

Treatment goals noted were:

Eradication of AK and **preventing progression to malignancy**, **minimising the disease** and **visible cosmetic results**

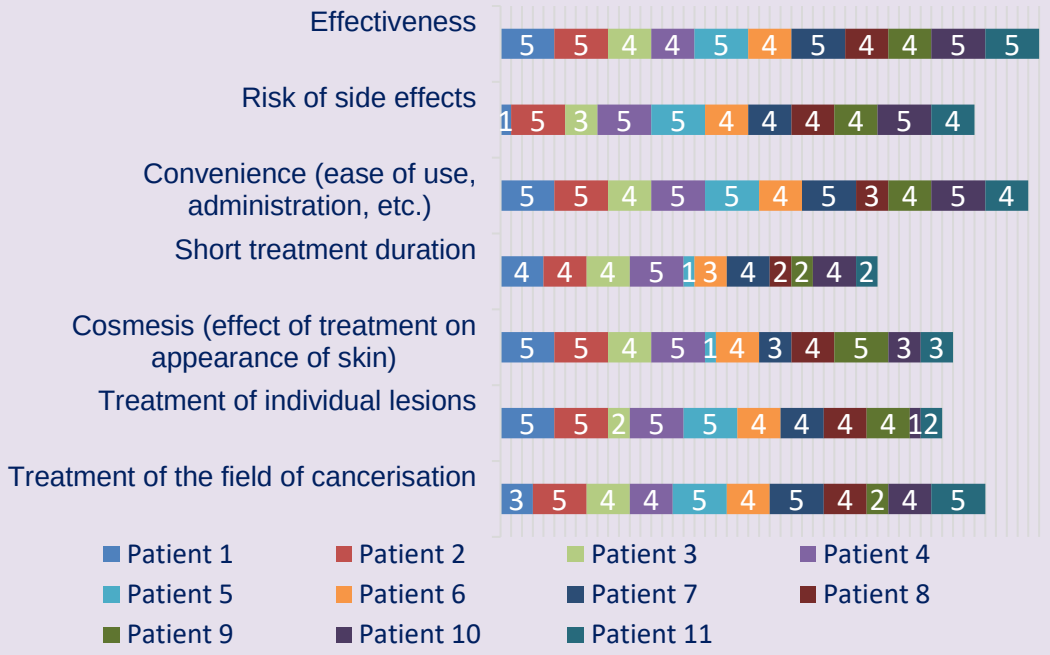
Aspects of care that should be discussed between HCPs and patients included:

Strategies for avoiding sun exposure, **duration of treatment cycles** and **post-treatment recovery**, explanation of the **impact of AK on life expectancy**, **treatment safety** and **frequency of follow-up appointments**

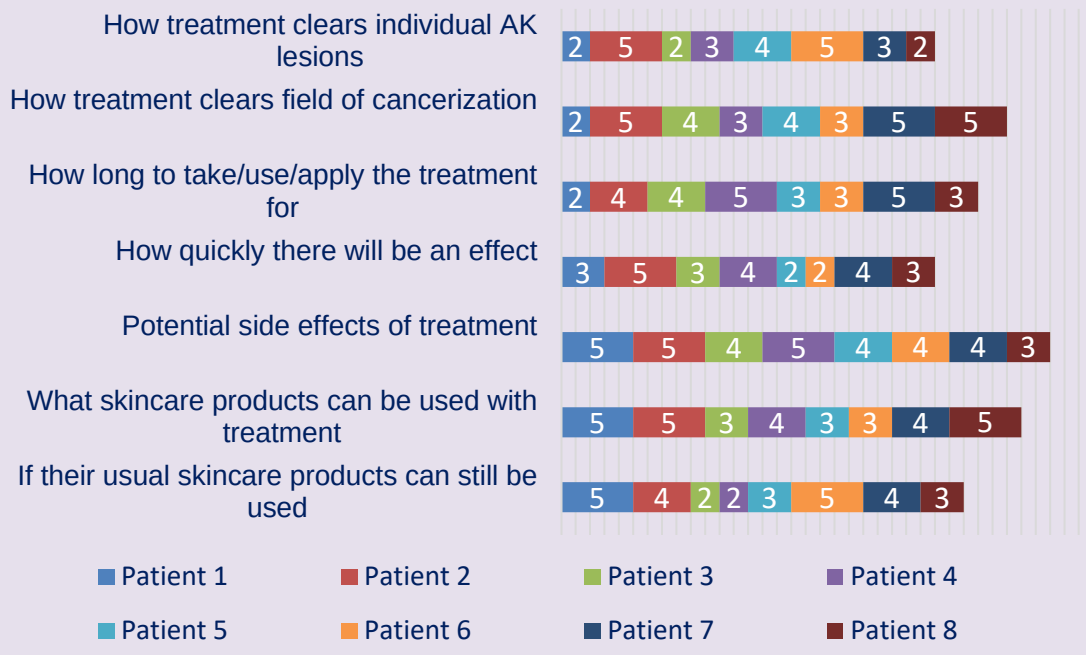
*Not all of the patients answered all questions.
AK, actinic keratosis.

Patients had differing views on aspects of treatment and decision-making

Importance of **different aspects of treatment** scored using a scale from 0 ('not very important') to 5 ('very important')



Importance of **different aspects when making treatment decisions** scored using a scale from 0 ('not very important') to 5 ('very important')*



*Not all of the patients answered all questions.
AK, actinic keratosis.

Strengths and weaknesses of the PAKT project

Strengths and weaknesses; including limitations of the Delphi process.

Strengths:

- Inclusion of experts from various countries who treat a range of patients in daily practice
- A particular strength of the Delphi process is that the group size does not depend on statistical power; instead, the group is selected for expertise
- Blinded voting reduced the potential for bias in the Delphi voting process

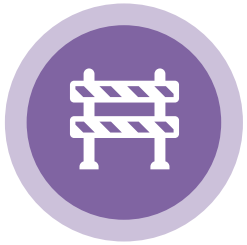
Weaknesses:

- Recommendations outlined are based on the experiences of the expert panel and reflect HCP perspectives on the important topics to discuss with patients, which could potentially differ from patient perspectives
- Although the PAKT tool integrates recommendations from an international group of experts, it only represents the healthcare systems in which the panel has experience and may not account for nuances in other regions

HCP, healthcare professional; PAKT, Personalising Actinic Keratosis Treatment.

Conclusions and recommendations

The PAKT panel has provided practical recommendations on **optimal, personalised** and **patient-centred** management of AK.



These recommendations aim to address some of the current unmet needs in AK including **personalising care** and **identifying barriers** to **optimal treatment outcomes**

A **novel clinical tool** based on these recommendations has been developed to facilitate **shared treatment decision-making** between HCPs and patients in daily practice, supporting **patient-centric management** throughout the AK journey

This tool can inform patient consultations and be used in educational settings to support **optimal, longitudinal** AK care

AK, actinic keratosis; HCP, healthcare professional; PAKT, Personalising Actinic Keratosis Treatment.

Look out for two new publications on actinic keratosis care!

1

'Expert recommendations on facilitating personalised approaches to long-term AK management: The Personalising Actinic Keratosis Treatment (PAKT) project'

- Expert **consensus recommendations** from the **PAKT panel** and a **novel clinical tool** to support patient-centred AK care in daily practice and improve understanding of disease chronicity
- Now available in ***Acta Dermato-Venereologica*** – **scan the QR code!**

2

'A Review of MAL-PDT for the Treatment Strategy of Actinic Keratosis: Broader Clinical Perspectives Beyond the Data and Guideline Recommendations'

- Targeted **review** of current evidence for different **MAL-PDT treatment strategies**, considering applications in **heterogenous AK populations**, such as organ transplant recipients
- Soon available in ***Dermatology and Therapy***

EUROPDT

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PDT for Prevention

Claas Ulrich
Berlin, Germany

Read the abstract

Declining Incidence of cSCC in the General Population

- Providing every patient in need with suitable, efficient and sustainable treatment for AK
  - Making AK treatments more attractive to patients and health care providers
    - Assure Reimbursement
    - Promote therapies which are *swift* and easy to use on *large fields* and in *all AK lesion* types
    - Allow individual adaption to special needs (elderly, singles, comorbidities etc)
  - High operational capacity (PDT > 10% of the AK market in GER)
  - Low recurrence rates of AK
  - Reduction of cSCC incidence in patients treated for AK
- Strategies to treat AK embedded into general program for optimized primary prevention (photoprotection) and early diagnosis/surveillance

EURO PDT

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PDT for Occupational Diseases

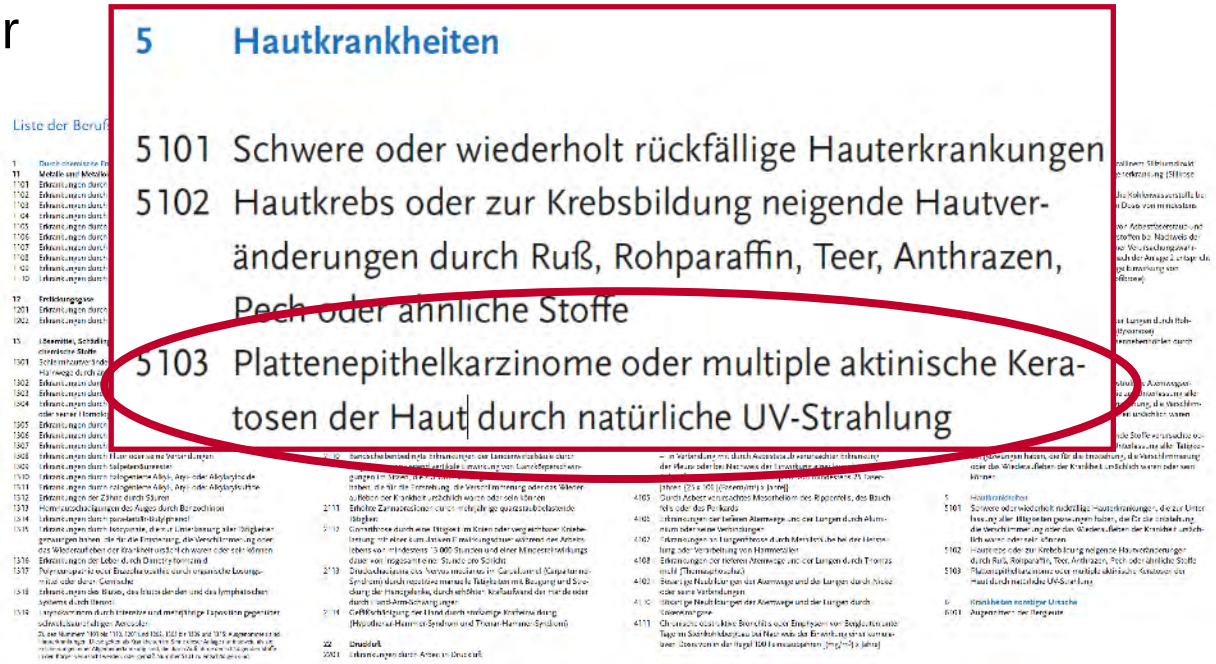
Berenice Lang

Mainz, Germany

Read the abstract

Occupational dermatology in Germany

- Occupational health and safety is insured under German law
- Occupational accidents but also „occupational diseases“
- Public accidental insurance institutions cover prevention and treatment of occupational disea
- Subspeciality for dermatologists with further education



5 Hautkrankheiten

5101 Schwere oder wiederholt rückfällige Hauterkrankungen

5102 Hautkrebs oder zur Krebsbildung neigende Hautveränderungen durch Ruß, Rohparaffin, Teer, Anthrazen, Pech oder ähnliche Stoffe

5103 Plattenepithelkarzinome oder multiple aktinische Keratosen der Haut durch natürliche UV-Strahlung

→ “SCC or multiple AK due to natural UV radiation“

Jobs with high exposure to UV radiation

- Construction industry
- Agriculture
- Vehicle drivers
- Security personnel
- Teachers
- Janitors
- Veterinarians
- Sailors
- …

Definition

- Multiple AK (> 5 per year or 4cm²) or SCC
  - „field cancerization“
- Appropriate occupational UV exposure
  - „Outdoor worker“
- Localization on exposed skin

„Typical“ patient with occupational field cancerization

- Long lasting medical history
- Multiple tumours and surgical interventions in medical history
- High need in therapy due to multiple lesions
- Severe UV damaged skin
- Still in job? Prevention?

→ **„high need“ patients**

Why do we treat field cancerization?

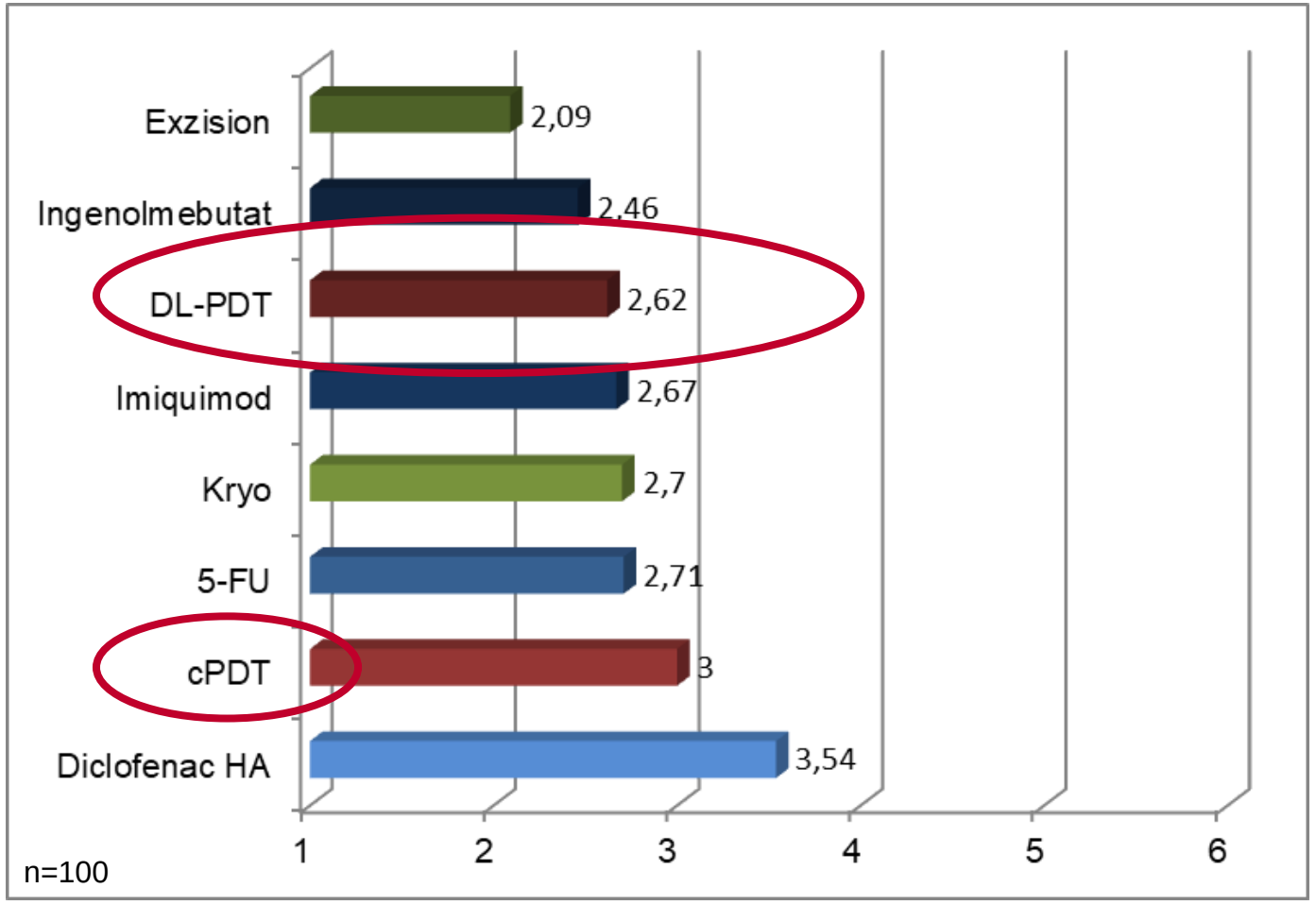
3 possibilities of AK “fate”:

- 1. Regression
- 2. Persistence as AK (in situ Carcinoma)
- 3. Progression into SCC

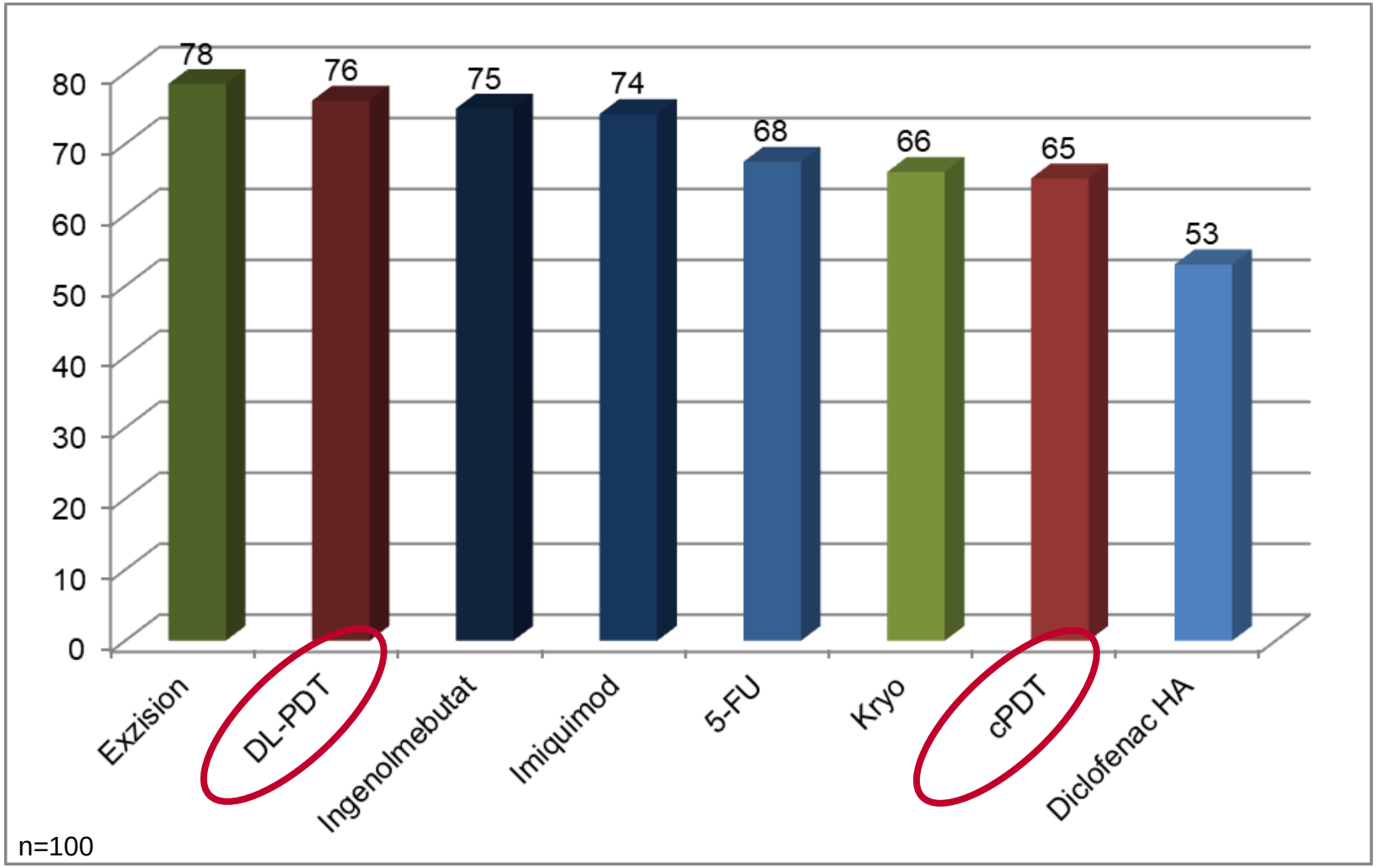
No predicting parameters for progression of AK into SCC

→ all lesions should be treated

„ How satisfied were you with the therapy?“



TSQM - Overall satisfaction



PDT in occupational dermatology

- High demand due to severe UV damaged skin
- Many cycles of treatment necessary
- Multiple sites = large area affected
- Patients still in the job

→ **„easy“ treatment option that is short and effective**

- Reimbursement by public accident insurance institutions
- All forms of PDT accepted

Summary

- „SCC and multiple AK due to natural UV radiation“ are classified as occupational disease in Germany
- Special patient population with high therapeutic needs
- (artificial) DL-PDT as effective and well tolerated treatment option for multiple cycles and large areas
- New: reimbursement by public accident insurance institutions is possible for all forms of PDT
- Outlook: „Preventive“ PDT?

Plenary session 2 DL-PDT and ADL-PDT - What is new? I

Chairs: Piergiacomo Calzavara-Pinton, Merete Haedersdal

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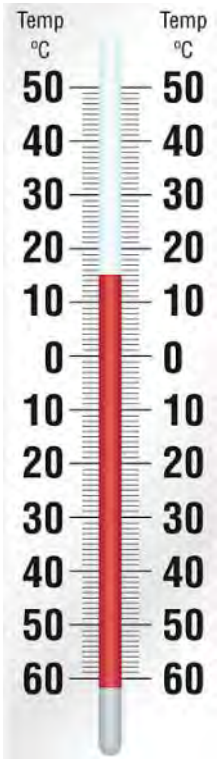
Daylight-PDT and Weather - always an easy one?

Sally Ibbotson
Dundee, United Kingdom

Read the abstract

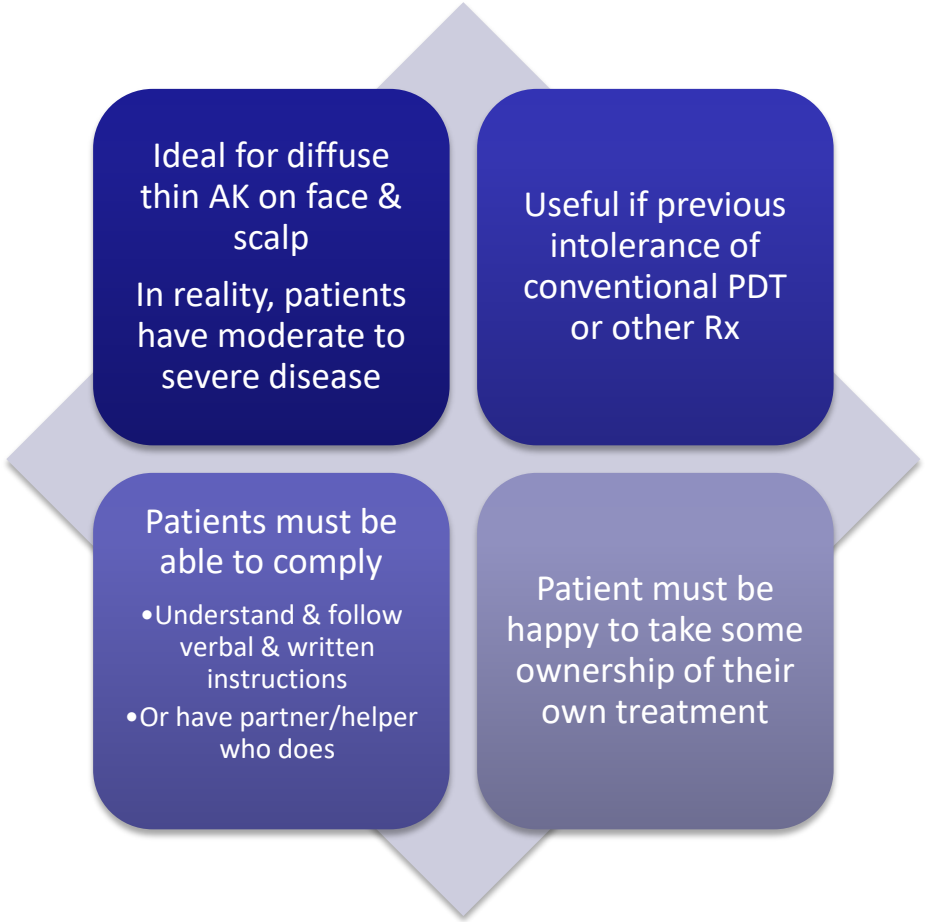
Requirements for daylight PDT



> 8 Jcm^{-2} PpIX effective dose

How feasible is daylight PDT in Scotland?

Who do we treat with daylight PDT?



Our early experience of daylight PDT

- Low pain scores & acceptable inflammation
- 73% clear/at least a good partial response
- 74% very & 18% fairly convenient

(n=64; Cordey *et al., Scot Med J* 2017; 62:48-53)

Daylight PDT in Dundee

Similar latitude to Copenhagen – 56 degrees N.

2013-2021

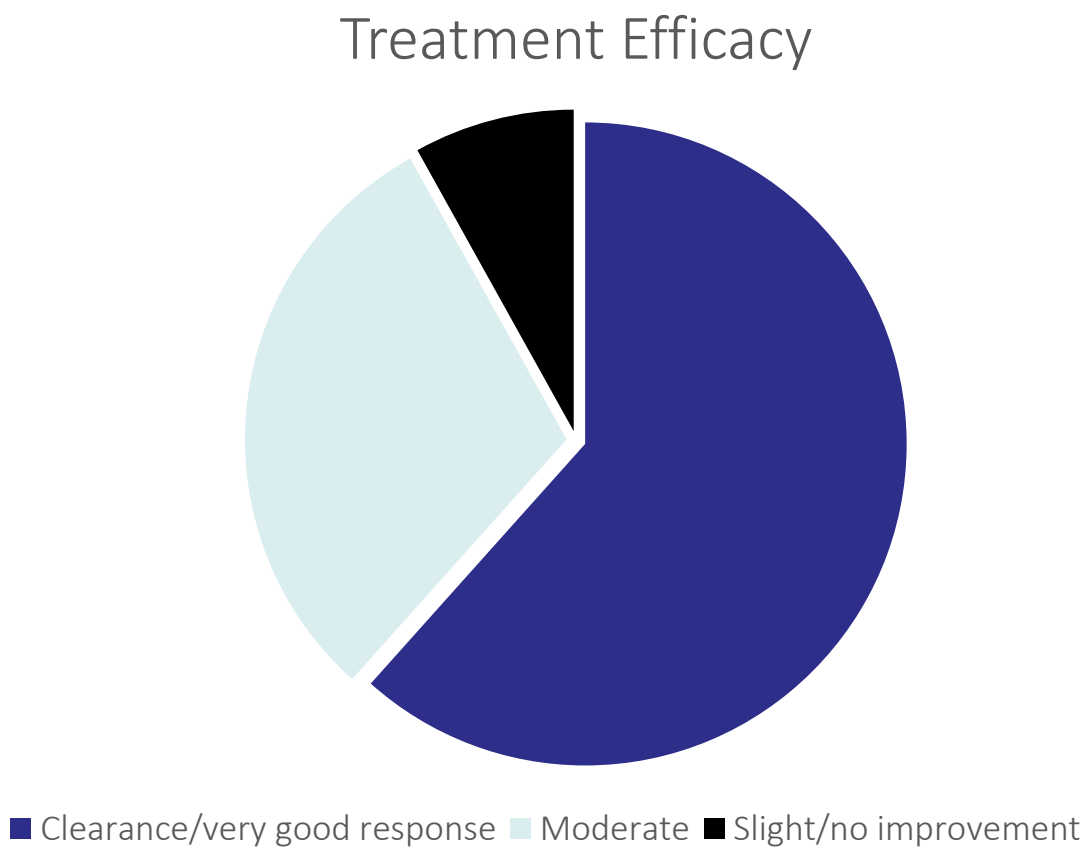
8 years

186 patient treatment courses

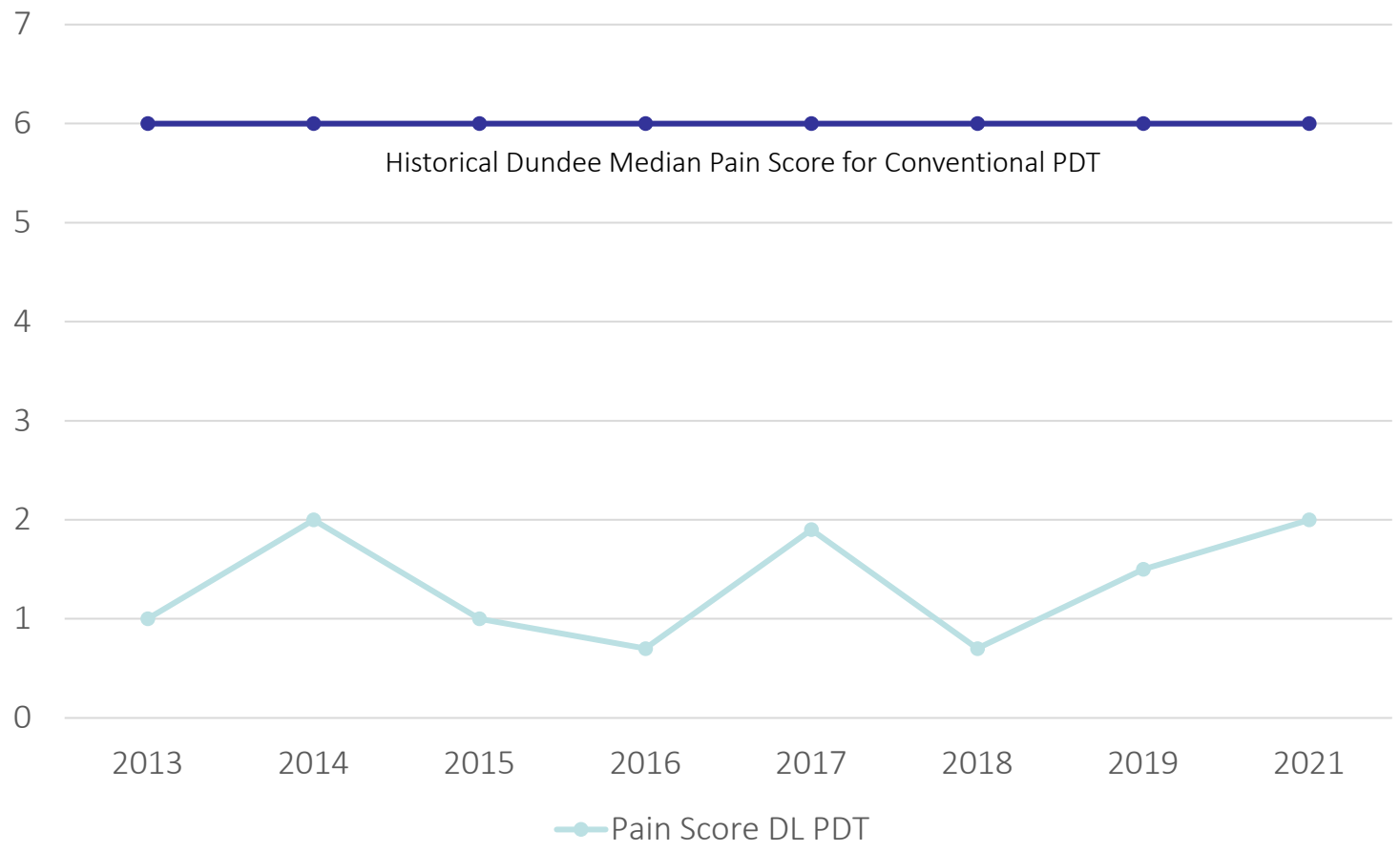
Median 3 (1-4) Rx at monthly intervals

Average age 75 years

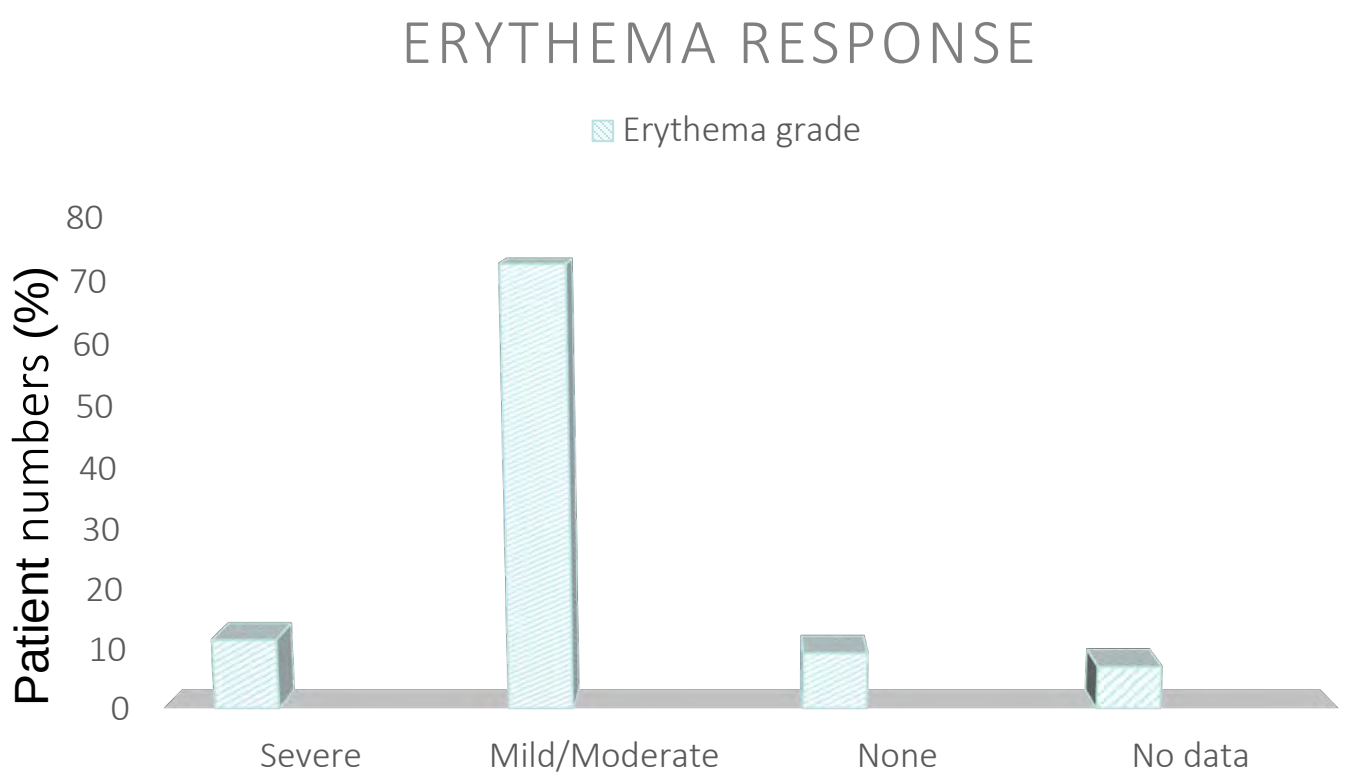
Daylight PDT outcomes



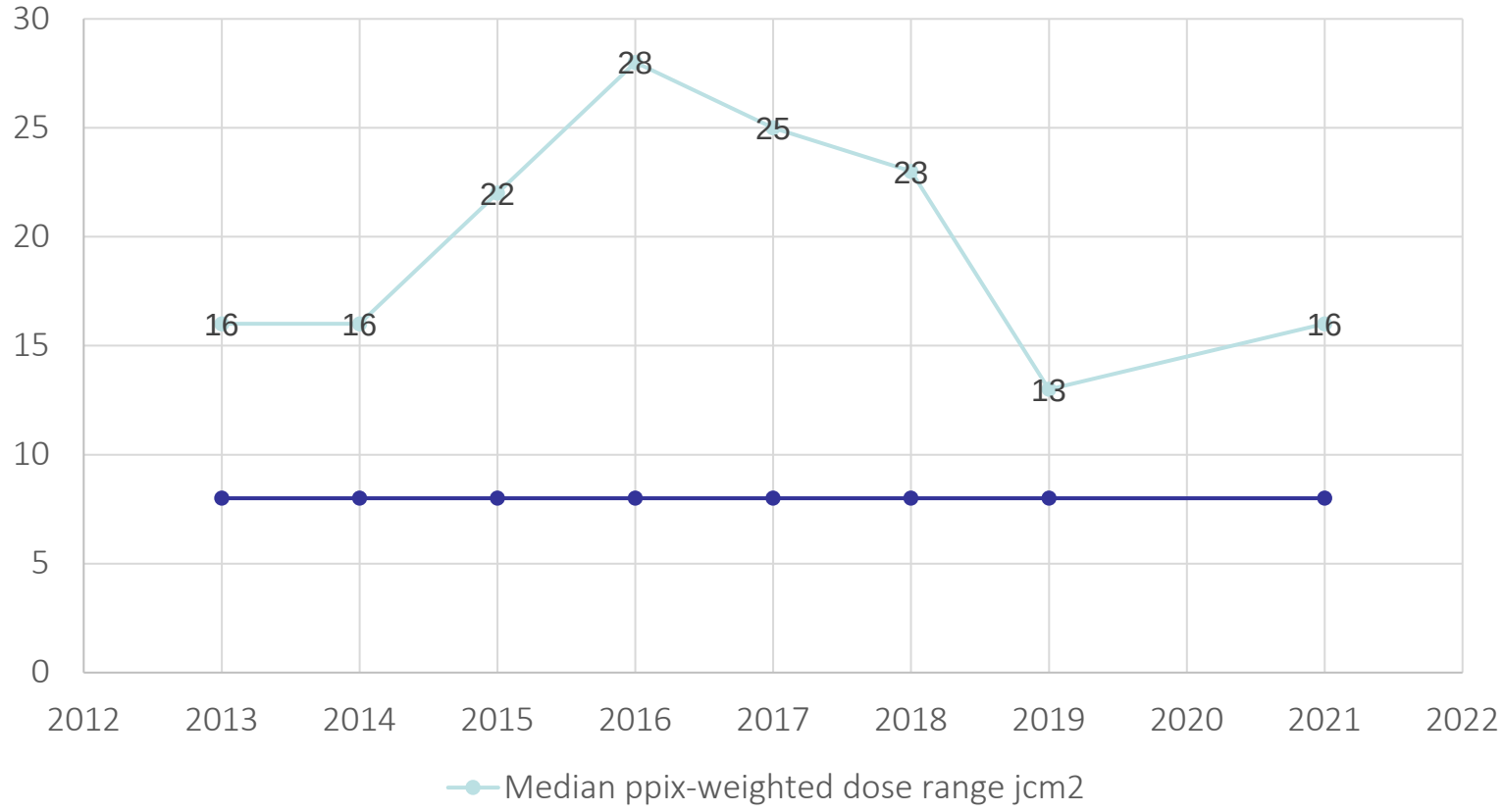
Median daylight PDT pain scores



Daylight PDT-induced erythema



Median PpIX-weighted dose range J/cm^2



Patient satisfaction

83% of patients expressed a preference for Daylight PDT over other treatment modalities for AK

Pilot of Home Daylight PDT 2021

Treatment Type	Home DL PDT	DL PDT
Patients treated	6	8
Response	0% clear	0% clear
	66% Excellent/Good	72% Excellent/Good
	17% Moderate	14% Moderate
	17% Slight	14% Slight
	0% No response	0% No response
Erythema	11% severe	4% severe
	84% mild to moderate	92% mild to moderate
	5% none	4% none
Median Pain Score (Range)	1.5	2.4
	(0-7.7)	(0-6.6)
Median PpIX-weighted Dose (Range) Jcm^{-2}	15	16
	(2-42)	(2-39)
Median Exposure Time (Range) Minutes	160	160
	(135-180)	(85-300)

Daylight PDT & the weather – is it always easy?

- Effective, well tolerated & feasible - even in Scotland!
- Particularly effective for thin field change AK
- High levels of patient satisfaction
- Careful selection of patients & lesions critical
- Sensible approach to weather needed
- Home DL PDT offers increased convenience but needs evaluating further
- Thicker lesions do not respond as well – compensate with:
  - Multiple treatments in summer
  - Good surface preparation
  - PDT passport for chronic disease management
  - Rotational approach
  - Realistic patient & clinician expectations

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Multilite-PDT for AK - a single center observational study

Sven Quist
Mainz, Germany

Read the abstract

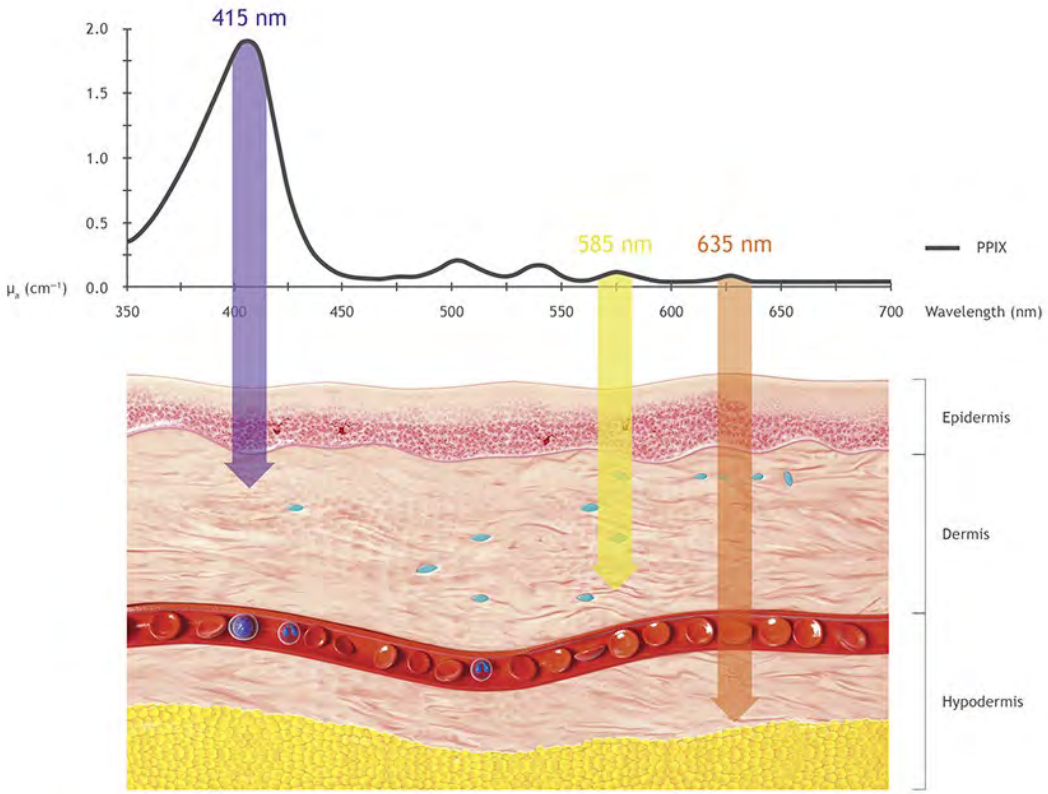
Multilite system – artificial light PDT

SPECIFICATIONS

Light source	LED — light-emitting diode
Wavelength	415 nm, 585 nm, 635 nm
Maximum dose per wavelength	415 / 585 / 635 nm: 98 / 48 / 120 J/cm²
Power density per wavelength	415 / 585 / 635 nm: 41 / 20 / 50 mW/cm²
Treatment area	500 cm²
Dimensions (H x L x B)	159 cm x 60 cm x 60 cm
Weight	27 kg
Indications	Photodynamic therapy → 415 nm, 585 nm, 635 nm Atopic dermatitis → 415 nm, 585 nm Eczema → 415 nm, 585 nm Acne → 415 nm

Protocols

Protocol	MAL/ALA incubation time	415 nm	585 nm	635 nm
35 min	60 min	26 min	6 min	3 min
80 min	30 min	67 min	9 min	4 min



Advantages

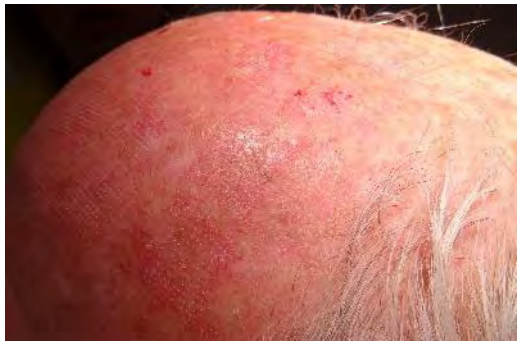
- Short protocol (10 min preparation incl. Laser treatment followed by 60 min incubation followed by 35 min irradiation ->1h 45 min)
- Low pain to no pain
- Area of 500 cm2 (or 2x500 cm2 or 2 parallel treatments with 500 cm2 with two Multilite)
- Easy to use (start and go)
- Flexible (easy movable, treatement sites include head, arms, legs, hands, trunk, back ect.)
- requires only minimal space

Indications

- **Actinic keratoses (head, arms, legs, back)**
- Bowens disease
- Initial SCCs
- BCCs (superifical, thin nodular)
- Folliculitis decalvans
- Skin rejuvination
- Acne
- Hand eczema (only 585 nm yellow)
- Alopecia areata (only 635 nm)

Protocol

removal
of crusts



FX-CO2
Laser abl.

MAL/ALA
60 min

art dayl.
PDT
Multilite
35/80 min

post-treatment
care and clincal
(LC-OCT)
re-examination
after 6 weeks

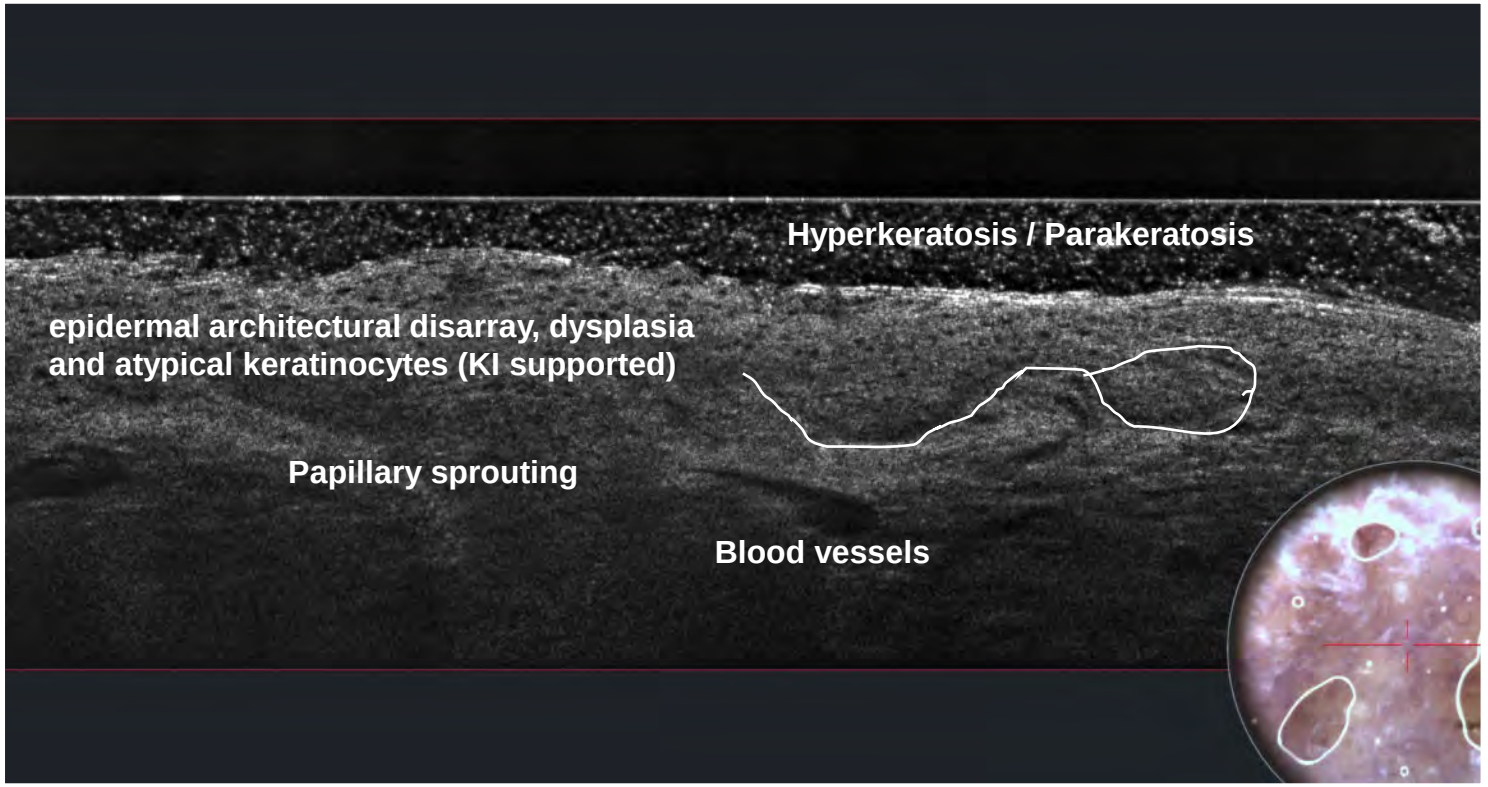
LC-OCT (combined OCT and laser micorscopy)

Str. corneum

Epidermis

Interface

Dermis



Results I

- 625 AK patients treated
  621 (99,4%) with the 35 min protocol,
  4 (0,6%) patients with the 80 min protocol

- pain level 1-4/10 with the 35 min protocol (dependent on the total number of AKs)
- pain level 0-1/10 with the 80 min protocol

- good results (almost clear/complete clearance in 91,3% of patients) after 3 months

Results II

- **8/625 (1,28%) of AK patients treated that presented treatment-resistant AK lesions (PDT alone or PDT+5-FU or PDT+Imiquimod) had histologically confirmed SCCs upon surgery**

- **11/625 (1,76%) of AK patients treated that had treatment-resistant AK lesions (PDT alone or PDT+5-FU or PDT+Imiquimod) had histologically confirmed carcinoma in situ pap III upon surgery**

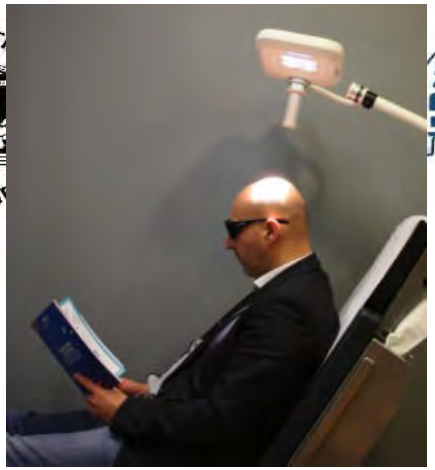
Options

- **If further artificial daylight PDT with the 35 min Multilite protocol is refused because of pain:**

- **switch to the 80 min protocol (4 patients)**

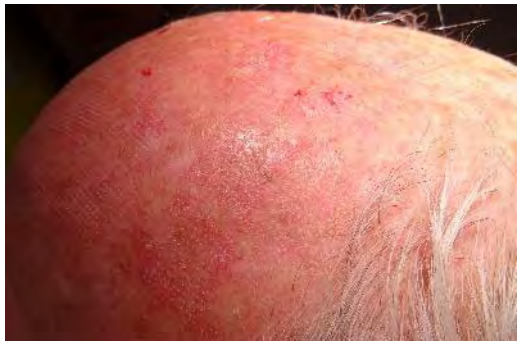
- **switch to Dermaris LED Daylight for the following PDT treatment (so far 14 patients)**

Protocol

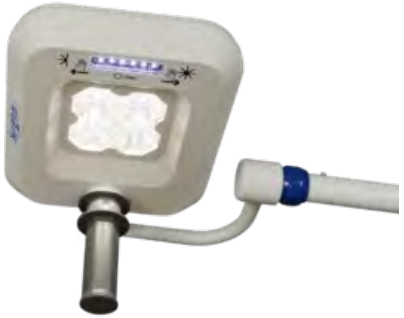


removal
of crusts

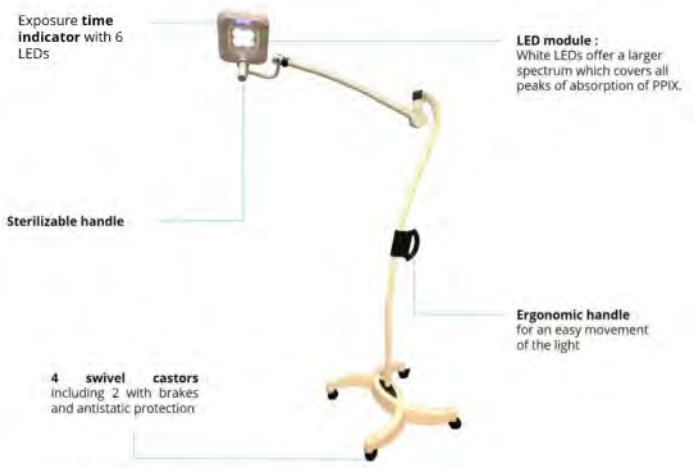
FX-CO2
Laser abl.



MAL/ALA
10 up to 30 min



Dermaris LED PDT 2h



post-treatment
care and clincal
(LC-OCT)
re-examination
after 6 weeks

Results III

- **14 patients treated**
- **pain level 0/10 over the 2h treatment period**
- **clinical results in evaluation**

Summary

- Artificial daylight PDT with the Multilite system is feasible and effective
- Associated with low pain (80 min lower than 35 min protocols)
- Flexible and easy to use, large areas can be covered (x 500 cm2)
- save (expected side effects from Artificial daylight PDT)
- Compared to other artificial daylight PDT options shorter treatment time-frame in the clinic, around 1h 45 min in total for the patient, 35 min irradiation and 10 min preparation for the staff

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THE EUROPEAN SOCIETY FOR PHOTODYNAMIC THERAPY

Barcelona, Spain

Friday 9 and Saturday 10, June 2023

PDT for Actinic Cheilitis

Ana Julia Garcia Malini

Huesca, Spain

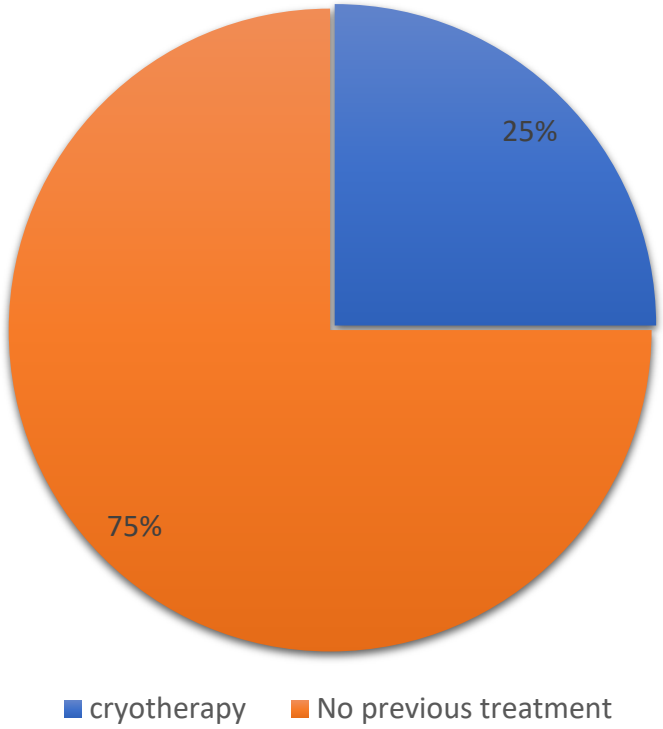
Read the abstract

AC and PDT : material and methods

- A retrospective observational study
  - Hospital Universitario San Jorge, Huesca, Spain
- All patients diagnosed with AC and treated with PDT (MAL) between 2008 and 2022.
- Data from the clinical history and the PDT database
- Statistical analyses SPSS software v20.0

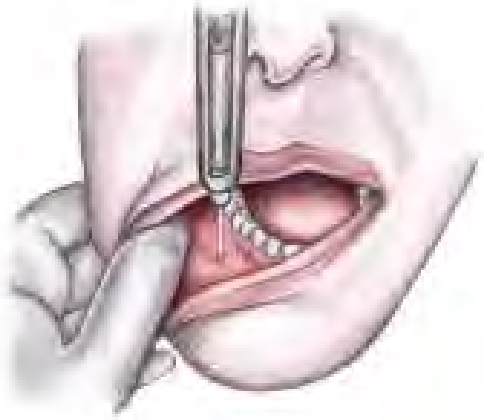
AC and PDT : results

- 12 patients
  - 10 males (83,3%)
  - 2 females(16,7%)
- Average age: 76,5 years old (40-88)
- Previous treatmets
  - 25% cryotherapy

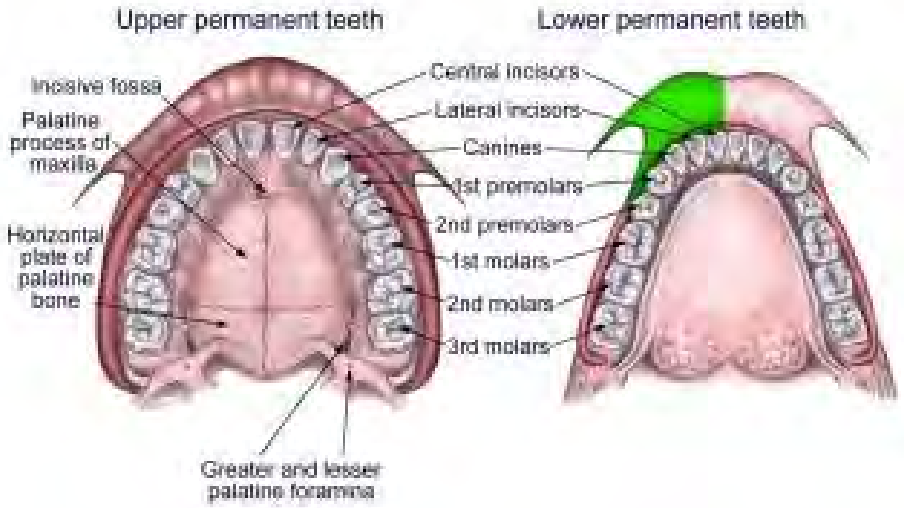


AC and PDT : results

- Biopsy
  - Yes: 16,7% (n=2)
  - No: 83,3% (n=10)

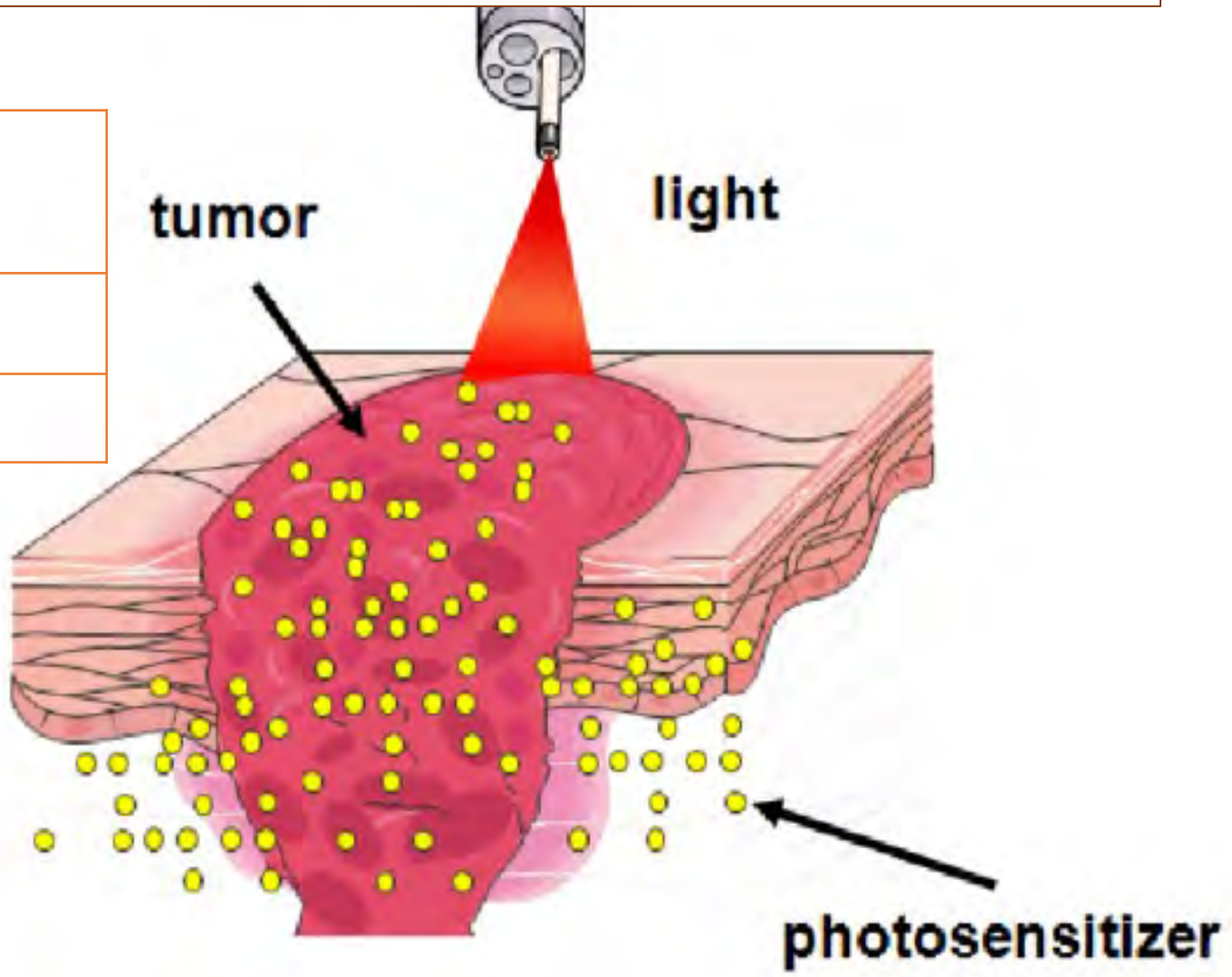


- Preparation prior PDT
  - 50% (n=6) Mental nerve block
  - 25% (n=3) Oral analgesia
  - 8,3% (n=1) Mental nerve block and oral analgesia
  - 16,7% (n=2) No anesthesia



AC and PDT : results

Number of sessions	Number of patients	%
1	9	75%
2	3	25%



MAL: 100% (n=12)
One session every 4 weeks

AC and PDT : results

- Treatment response

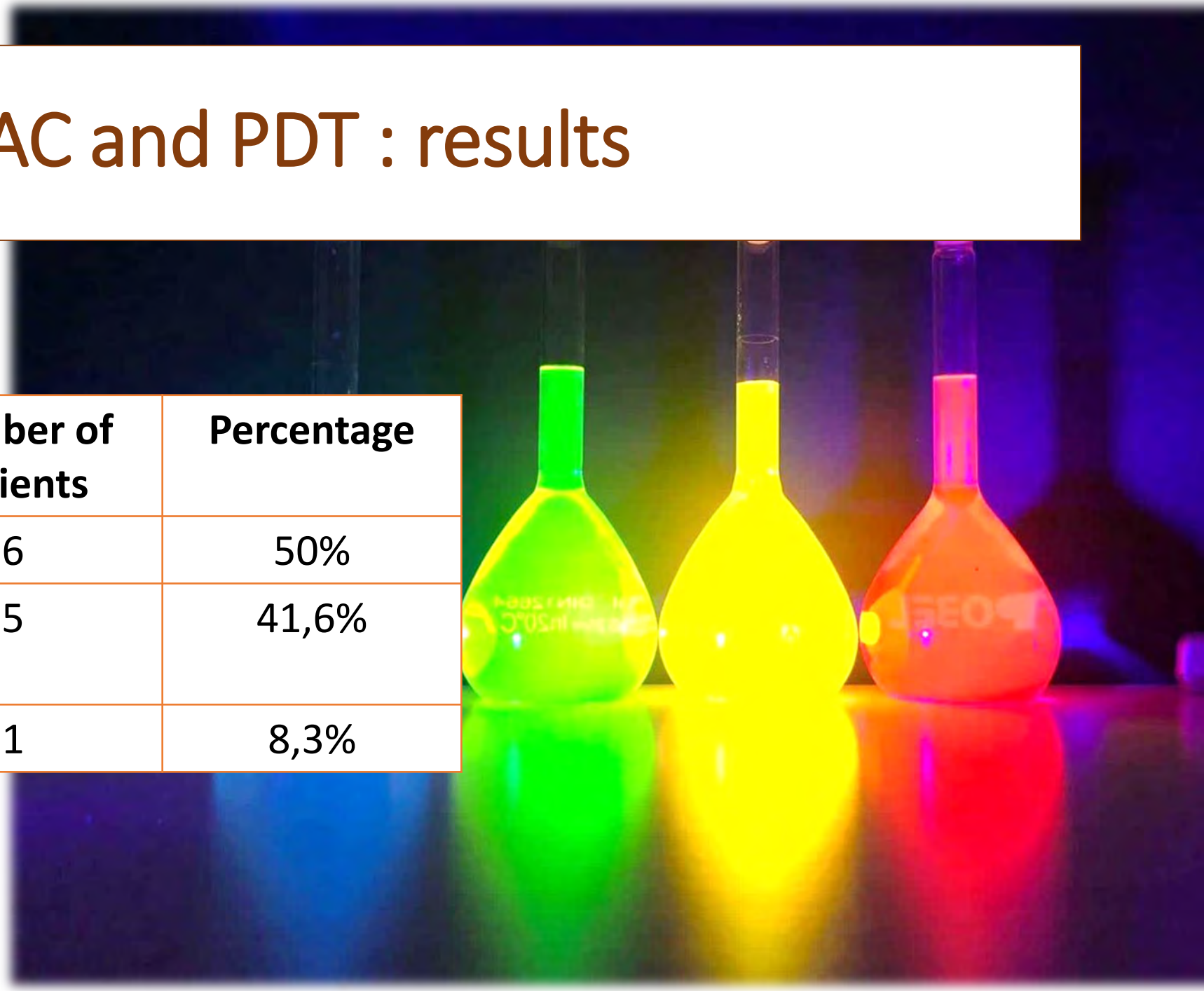
Response	Number of patients	Percentage
Resolution	**11**	91,7%
No resolution	**1**	8,3%

No association was found between number of session, previous preparation, and fluorescence and treatment response

AC and PDT : results

- Fluorescene

Fluorescence	Number of patients	Percentage
Positive	6	50%
Weakly positive	5	41,6%
Negative	1	8,3%



AC and PDT : results

- **Follow up**
  - **Mean: 37,5 months**
  - **Range: 6-72 months**
- **Tolerance**

None of the patients had to stop the illumination.

Pain	Number of patients	%
Mild	7	58,3
Moderate	5	41,7

AC and PDT: limitations

- Restrospective study
- Abscense of standarized protocol
- Number of patients

AC and PDT: Conclusions

- C-PDT is highly effective therapeutic strategy for AC
- Another option to treat AC, with good cosmetic results and long-term persistence of efficacy

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Friday 9 and Saturday 10, June 2023

What's new with PDT Light, a painless and effective Treatment of Light Skin Cancer?

Martin Braun
Überlingen, Germany

Read the abstract

„PDT light“, for this actual review we analyzed again all our treated cases

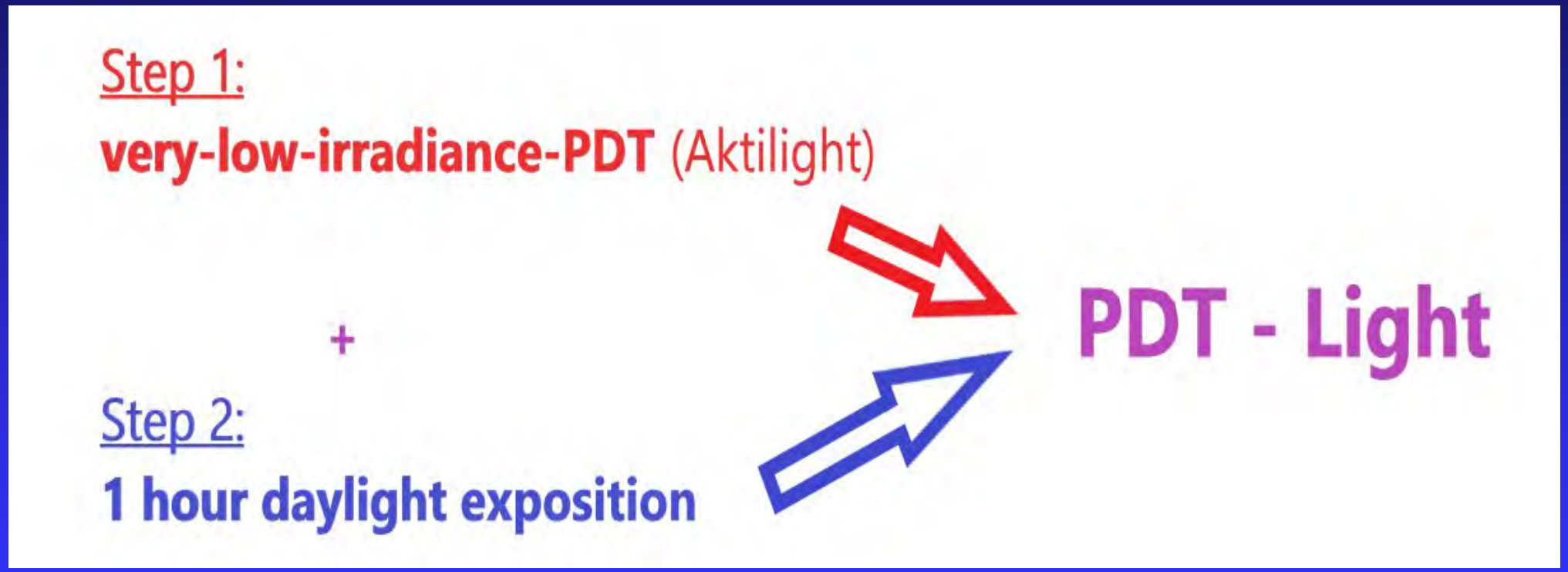
- We implemented into our study 2 follow-up margins:
- Follow-up 1 (FU1): at least 6 months after last treatment.
- Follow-up 2 (FU2): at least 12 months after last treatment.

- Average time of FU1: 8.1 months, FU2: 14.2 months
- Each patient, who did not appear at least 6 months after last PDT, was excluded from our study.

Thus, from originally 178 patients treated with PDT-Light, 129 were kept in the study.

BODENSEE LASERKLINIK Dr. Martin Braun

What is “PDT Light?” It is combination of low-irradiance-PDT and a shortened daylight PDT:



Therefore it can be performed only in the warm season (10° + C, no rain)

BODENSEE LASERKLINIK Dr. Martin Braun

Our concept of low irradiation-PDT, we started about 2016:

We decreased the light dose to not more than 12 or 14 J/ cm² (in the face), with a maximal illumination time of 2:36 – 3:02 min.

12	14	16	J/cm²
2:36	3:02	3:28	min.

BODENSEE LASERKLINIK Dr. Martin Braun

Theoretical background of PDT Light: According to Valentine & Ibbotson, 50 % of PpIX is reduced after 117 seconds (= 1:57 min.),

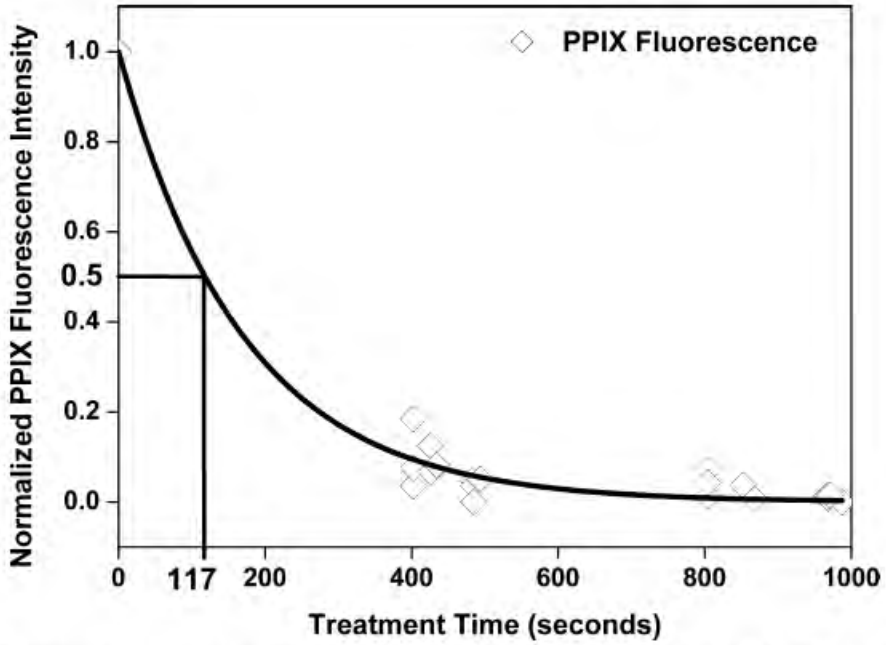


Figure 2. Reduction in mean normalized protoporphyrin IX (PPIX) fluorescence intensity during photodynamic therapy (PDT), recorded from 10 patients, allows for the monitoring of *in vivo* photobleaching. Diamonds (◇) are representative of data from individual lesions (superficial basal cell carcinoma treated with aminolevulinic acid-PDT). A best-fit exponential is shown, and the time for fluorescence reduction to 50% is indicated.

= after a dose of 9 Joule/cm²

dose J/cm²	4	6	8	10
time (min.)	0:52	1:18	1:44	2:10

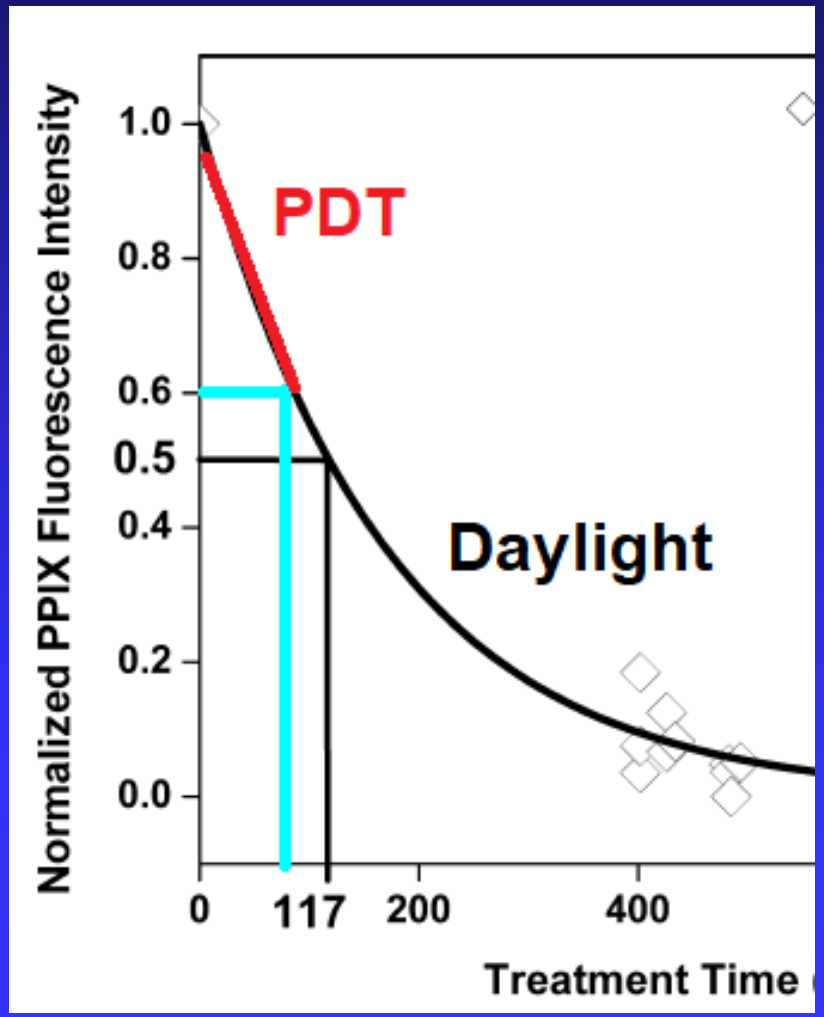
Photochemistry and Photobiology, 2011, 87: 242–249

A Quantitative Comparison of 5-Aminolaevulinic Acid- and Methyl Aminolevulinate-Induced Fluorescence, Photobleaching and Pain During Photodynamic Therapy

Ronan M. Valentine*[1,2], Sally H. Ibbotson[2], C. Tom A. Brown[1], Kenny Wood[1] and Harry Moseley[2]
[1]School of Physics and Astronomy, University of St. Andrews, St. Andrews, Fife, UK
[2]Photobiology Unit, University of Dundee, Ninewells Hospital & Medical School, Dundee, UK
Received 15 July 2010, accepted 27 September 2010, DOI: 10.1111/j.1751-1097.2010.00829.x

BODENSEE LASERKLINIK Dr. Martin Braun

Adapting this figure for our purpose, according to Valentine & Ibbotson, „PDT light“ has reduced PpIX..



...by ca. 40 %, when illumination time was approx. 1:18 min (dose 6 J/cm²).

dose J/cm²	4	6
time (min.)	0:52	1:18

The rest has to be done by the daylight.

Photochemistry and Photobiology, 2011, 87: 242–249

A Quantitative Comparison of 5-Aminolaevulinic Acid- and Methyl Aminolevulinate-Induced Fluorescence, Photobleaching and Pain During Photodynamic Therapy

Ronan M. Valentine*[1,2], Sally H. Ibbotson[2], C. Tom A. Brown[1], Kenny Wood[1] and Harry Moseley[2]
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Received 15 July 2010, accepted 27 September 2010, DOI: 10.1111/j.1751-1097.2010.00829.x

BODENSEE LASERKLINIK Dr. Martin Braun

I can absolutely confirm the conclusion, to which my collegues come:

Considerable pain reduction with low-irradiance (li)-PDT compared to high irradiance-PDT with a similar treatment outcome,
as well by a 2-step-illumination-strategy.

And there is another advantage of unique value: These patients come back for further treatments to our offices, if they need!

BODENSEE LASERKLINIK
Dr. Martin Braun

„PDT light“, our therapy in 2019:
A report of 152 cases, reviewed in 2023

- 152 cases, 129 patients,
- illumination with Aktilite-LED + 1 h daylight
- fluence 74 mW/cm²,
- average illumination time 1:02 min.
- average dose 4.56 J/cm²,
- only cold-air-anesthesia, no drugs, no LA
- performed from March to November

BODENSEE LASERKLINIK
Dr. Martin Braun

Parameters of treatment:

	size/F cm² total	Size case cm²	SSE	No. VAS all cases	Avrg VAS/ area	J/cm² total	J/cm² per case (avrg)	No. treat-ments total	No. treat-ments p. case/area
Scalp	185	3,5	2	75	1,41	242	4,56	73	1,38
Forehead	165	9,7	1	22,5	1,25	65	3,61	27	1,59
Temple	168	9,9	0	18	1	95	5,58	23	1,35
Cheek	463	22	2	23	1,09	117	5,57	28	1,33
Eyelid	103	7,9	0.5	18	1,5	52	4,33	16	1,25
Nose	90	6,4	3	15	1,07	51	3,64	19	1,36
Lips/Perioral	15	3,8	0	5,5	1,37	11	2,75	5	1,25
Ear	25	3,6	0.5	2,5	0,36	27	3,86	9	1,29
Neck	4	4	0	0	0	2	2,00	1	2
Hands/arms	109	36,3	0	0	0	18	6,00	3	1
Trunk	30	30	0	1	1	8	8,00	1	1
Lower extremity	5	5	0	1	1	5	5,00	1	1
Sum		142,1	8,5	181,5		693	54,90	206	
Average		**11,84**	**5,55%**	**1,19**		**4,56**		**1,35**	

BODENSEE LASERKLINIK Dr. Martin Braun

„PDT light“, clearance rates at follow-up 1 (FU1) (avrg. 8.1 months): excellent = 78%, good = 11.6%

	Cases FU1	FU1 average months	Cl.A FU1 cases	Cl.A FU1 %	Cl.B FU1 c.ses	Cl.B FU1 %	Cl. A+B FU1 c.ses	Cl. A+B FU1%
Sum	152	8.1	121	78.1%	18	11.6	139	91.5%

- Clearance class A (Cl.A) = excellent: 80-100% clearance
- Clearance class B (Cl.B) = good: 60-79 % clearance
- Clearance class C = fair: 40-59 % clearance
- Clearance class D = moderate: 20-39% clearance
- Clearance class E = poor: 0-19%% clearance

BODENSEE LASERKLINIK Dr. Martin Braun

„PDT light“, clearance rates at follow-up 2 (FU2 - 14.2 months):

	Cases FU2	FU2 average months	Cl.A FU2	Cl.A FU2 %	Cl.B FU2 c.ses	Cl.B FU2 %	Cl. A+B FU2 c.ses	Cl. A+B FU2%
Sum	26	14.2	18	69.2%	4	15.4%	22	84.6%

- Clearance class A (Cl.A) = excellent: 80-100% clearance
- Clearance class B (Cl.B) = good: 60-79 % clearance
- Clearance class C = fair: 40-59 % clearance
- Clearance class D = moderate: 20-39% clearance
- Clearance class E = poor: 0-19%% clearance

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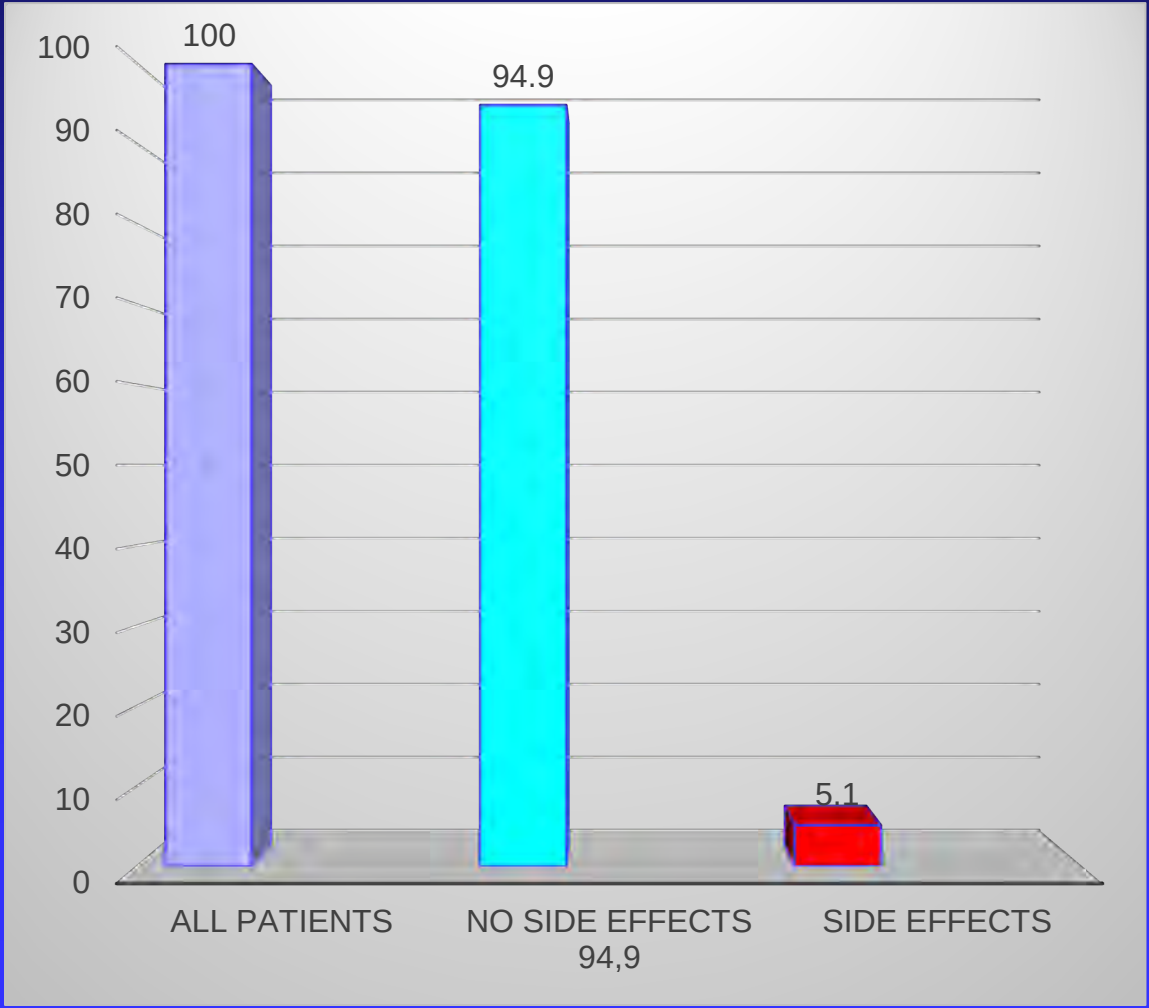
„PDT light“, low rate of side effects: 5.1 %
94,9 %: no side effects



In more 76 % of the cases only 1 therapy session was needed for healing.
The average number of treatments per case was 1.35 with no significant difference between different localisations.

BODENSEE LASERKLINIK
Dr. Martin Braun

PDT: after my opinion these conditions are most important for:

1. a satisfied patient ,
2. a good result, and
3. an economic management:

- VAS-adjusted type of PDT: “Light”, DL, or artificial DL
- limited size of treated area (< 25 cm²)
- (the very low irradiation time is one of the advantages of „PDT-Light“)

BODENSEE LASERKLINIK Dr. Martin Braun

„PDT light“, when the weather is bad? Then we switch to a 2-step irradiation-protocol:

1. PDT with Aktilite
   3-6 J (39 sec– 1.18 min.)
2. immediately after that:
   PDT with Treviolux Medlight (Indoor-Daylight Compact-PDT, 630 nm):
   4,5-6 J, 10-16 mW, 7:30 - 10:00 min. – in my case: 5:53 min.

Time con-sumption for both procedures:
8.30 - 12 min.
– in my case:
7:30 min.

„PDT light“, our results in 2019:

VAS Score (all patients, taken immediately after illumination):

Nearly no pain

- Average VAS score: **1.19**

BODENSEE LASERKLINIK Dr. Martin Braun

„PDT light“, the advantages (1):

- Very low pain percentage (VAS 1.19)
- Better control of therapy than daylight-PDT (only half probability = 1 h of unexpected circumstances, i.e. upcoming rain at the open whilst outside)
- Less side-effects * than c- and DL-PDT

* (to be proved by further studies)

BODENSEE LASERKLINIK Dr. Martin Braun

„PDT light“, more advantages (2):

- **Less time consumption in your office, compared to DL-PDT and indoor-PDT** (because no UV-screen has to be applied, you have the patient NOT sitting in your office for 15 or 20 minutes until the UV-Screen has been absorbed into the skin)

„PDT light“, conclusion:

Nevertheless I would be very happy to evaluate further on our yearly ca. 350 PDT-patients.

But unfortunately, we are lacking of man-and-woman-power, and we have no idea how to find interested students, working on that fascinating topic!

BODENSEE LASERKLINIK Dr. Martin Braun

„PDT light“, the advantages:

Summary:

with our 152 cases treated in 2019, we could confirm the hopeful results of PDT-Light, I presented 2020 at Sevilla.

BODENSEE LASERKLINIK Dr. Martin Braun

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Artificial daylight: IndoorLux experience

Wim Venema
Assen, Netherlands

Read the abstract

Artificial daylight sources

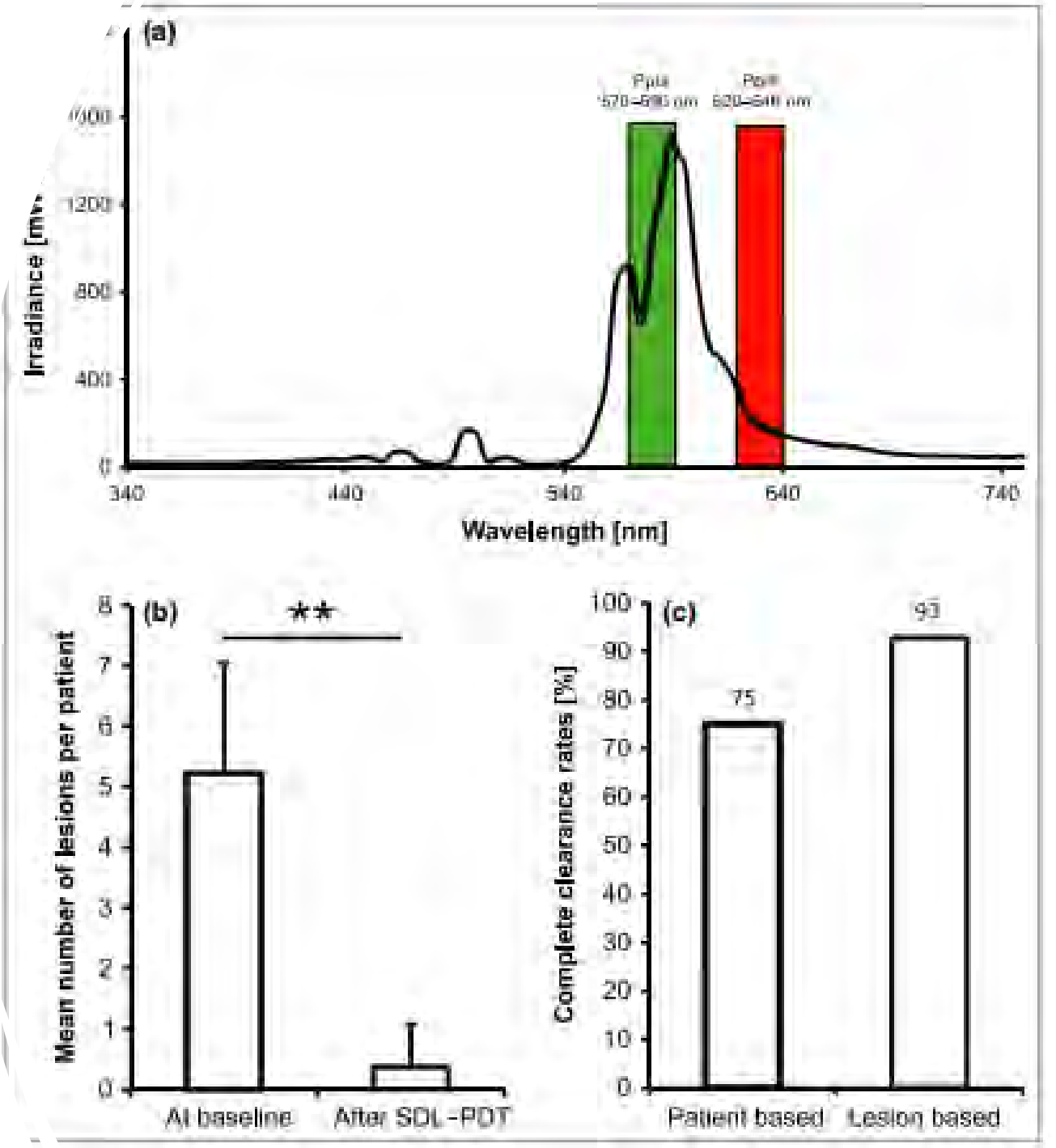
* Manufacturer product profiles

	Light spectra (nm)	Intensity (LUX)	Duration of treatment	Treatment area	Color of light
Smpc	**400-750**	**Min. 12.000**	2 uur		
Dermaris*	400-800	20.000		314 cm2 20 cm diameter	White
Multilite*	415-635	12.000-30.000		500 cm2	Blue, Yellow red
Medisun Daylight 1200-9000*	400-800	12.000		Face scalp	White
Indoor LUX*	570-630	32.000		Face scalp	Green, Yellow Red

SDL-PDT

- Simulated-daylight photodynamic therapy with BF-200 aminolaevulinic acid for actinic keratosis: assessment of the efficacy and tolerability in a retrospective study

- British Journal of Dermatology (2015) 1



Non-inferiority to DL-PDT ?

DL-PDT protocol (1/2 h)

No pre-treatment

Control after 3months

Comparing with recent DL-PDT

Outlines

- 28 participants (only male)
- Light to severe actinic keratosis on the scalp
- Average age 77
- 82 % was previously treated for AK

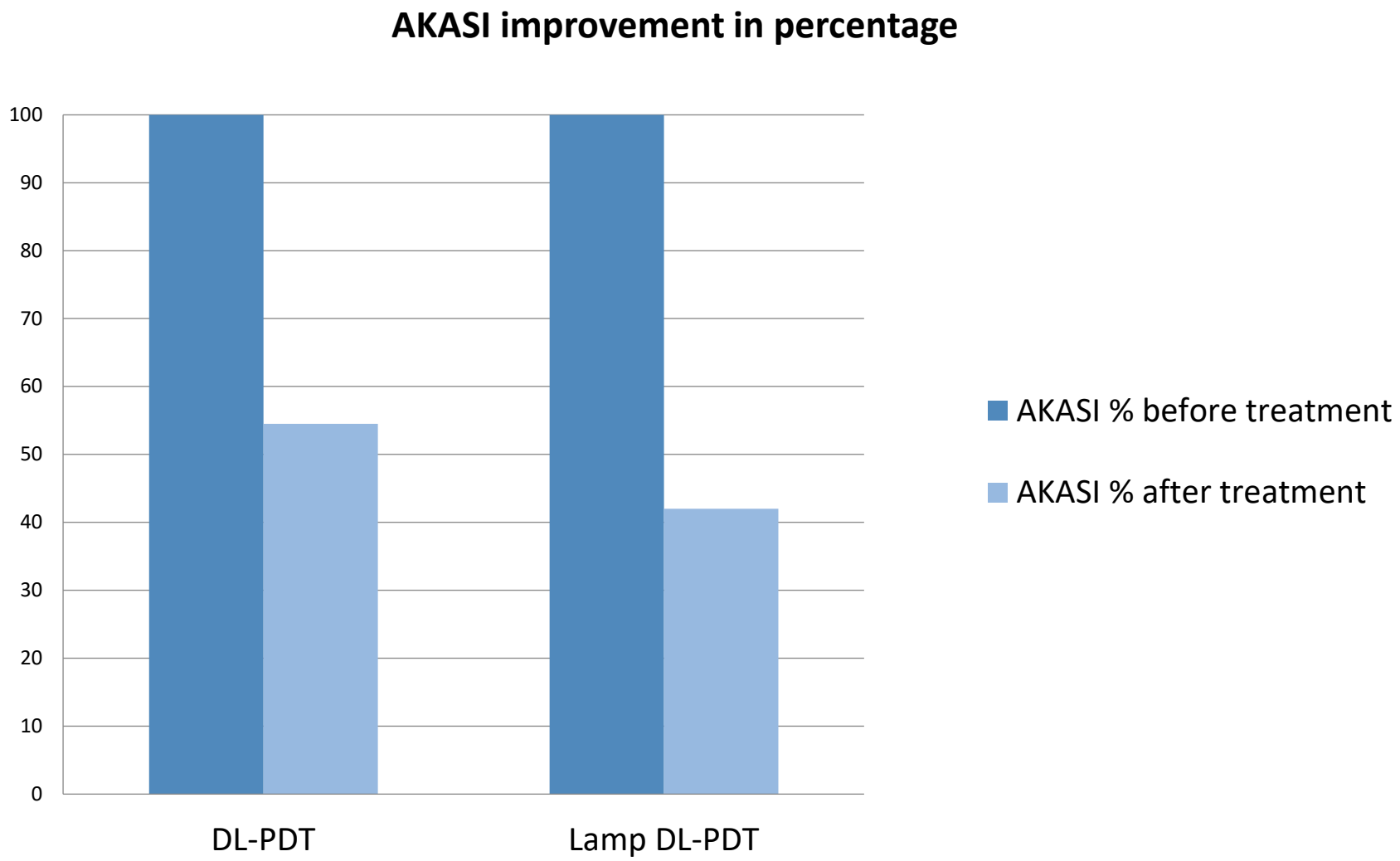
- Compared percentage improval AKASI
- VAS (1-10)
- Patient satisfaction (1-10)

AKASI comparison to DL-PDT

- Daylight photodynamic therapy for severe facial and scalp actinic keratosis: a prospective non-sponsored single-centre study employing the actinic keratosis area and severity index (AKASI)

- JORDAN, GHORESCH, EBERLE
- Eur J Dermatol 2019

DL-PDT versus indoorLux SDL-PDT



Pain and treatment-satisfaction

- Overall VAS-score 1
- Overall treatment satisfaction 8

Track record > 1000 treatments

- Indoorlux as other forms of ADL

- Advantage:
- Treatment throughout the year
- Reproducibilty

- Peer contact

Plenary session 3 DL-PDT and ADL-PDT - What is new? II

Chairs: Stefano Piaserico, Muriel Creusot

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Barcelona, Spain
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Homebased Photodynamic Daylight Therapy, My daily practice approach at the UZ Brussels

Samira Baharlou
Brussels, Belgium

Read the abstract

DAYLIGHT PDT APP BENELUX (NL + FR)

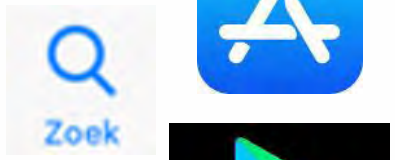
Goal

Optimize Daylight PDT treatment for patients

Search term

-TPD à la lumière du jour

- Daglicht PDT



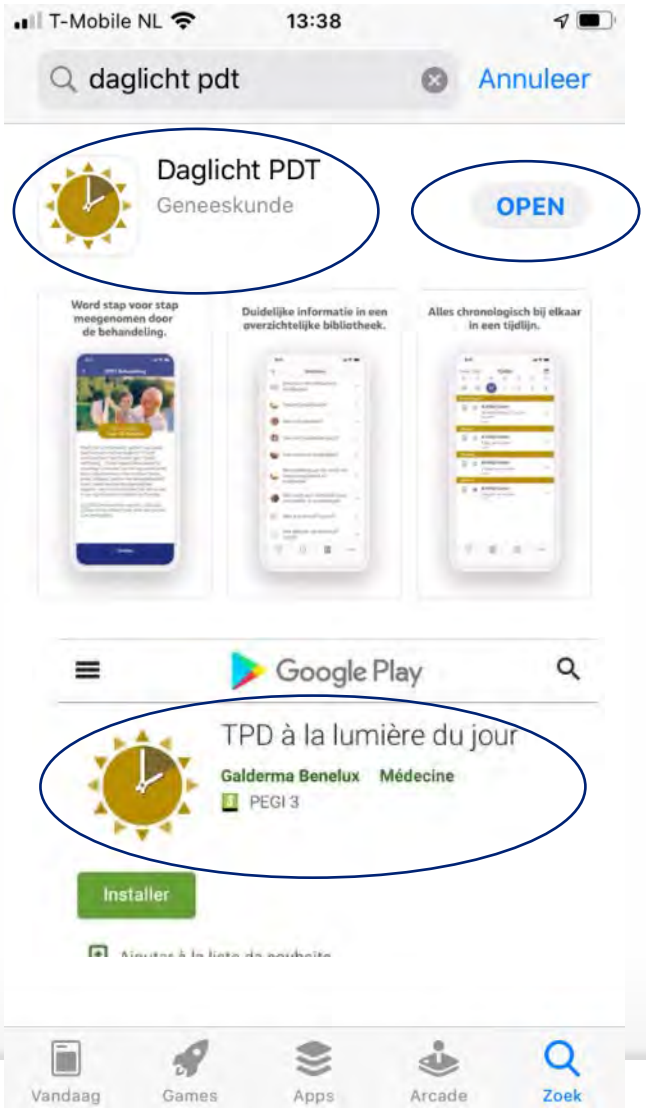
Extra tools

Information about skin cancer & sun protection

Useful links to

-Patient information websites

-Dermatology associations



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START TREATMENT

Push start button when the Metvix cream is put on

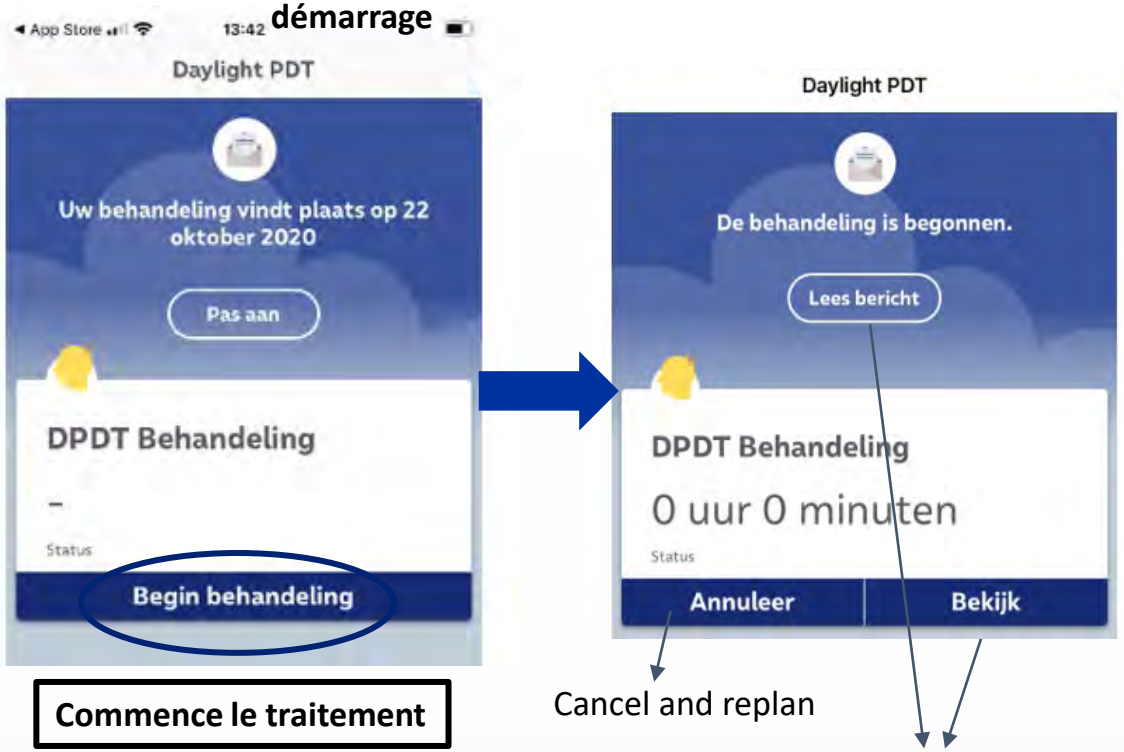
→ Starts messages during the illumination

To summarize actions for the patient:

→Plan treatment date

→Start treatment (nurse can also activate)

Lorsque le traitement a commencé, appuyez sur le bouton de démarrage



Commence le traitement

Cancel and replan

Read relevant message

VUB VRIJE UNIVERSITEIT BRUSSEL

NOTIFICATIONS DURING AND AFTER TREATMENT

Patient gets 4 notifications during the treatment and 1 afterwards

-Directly after “start”: The treatment has started (be outside within 30 minutes)

-After 30 minutes: Are you in good contact with daylight?

-After 1.5 h: The last treatment tips and tricks (still in good contact with daylight, short pause,…)

-After 2.5 h: Tips and tricks after treatment (please go inside soon, remove the cream…)

-After 24 h: Protect your skin

Le traitement a commencé

Les derniers conseils et astuces thérapeutiques.

INFORMATION FOR THE PATIENT/LIBRARY (III)

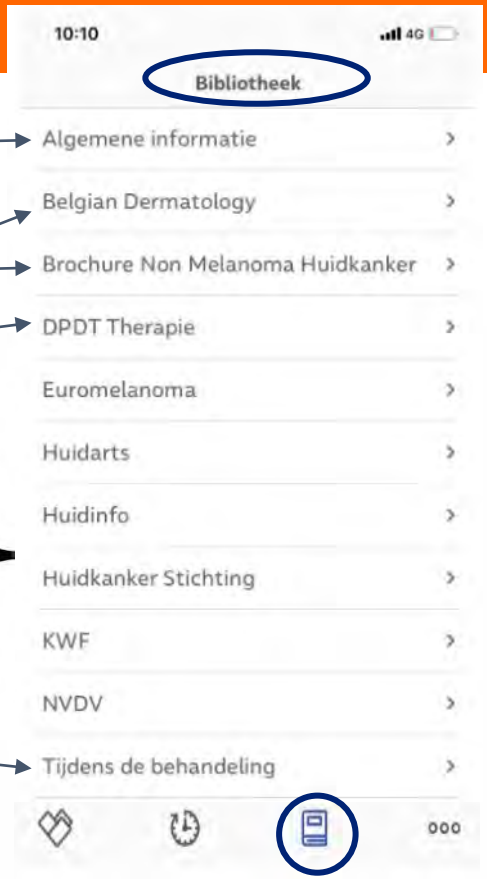
General information about PDT and Daylight PDT

Information anout sun protection/Actinica (leaflet)

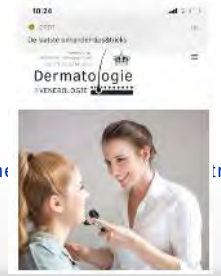
Extended Messages before treatment (4x)

Links to relevant websites

→ Euromelanoma and Be Dermatology in both languages



Extended me treat



VRIJE UNIVERSITEIT BRUSSEL

pharmaceutics

MDPI

Review

Combination-Based Strategies for the Treatment of Actinic Keratoses with Photodynamic Therapy: An Evidence-Based Review

Stefano Piaserico *, Roberto Mazzetto, Emma Sartor and Carlotta Bortoletti

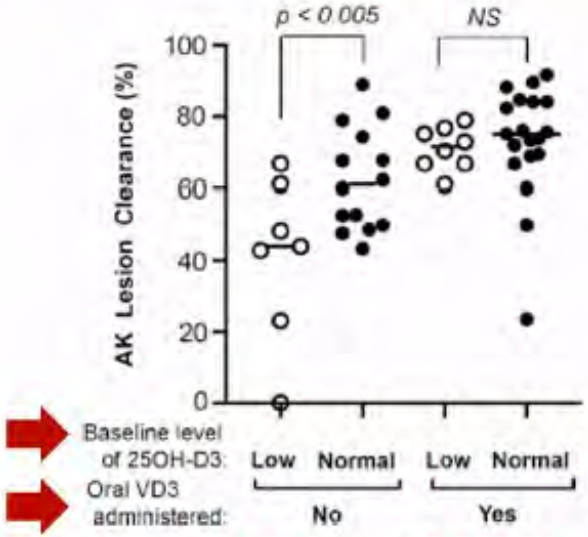
Dermatology Unit, Department of Medicine, University of Padua, 35121 Padua, Italy
* Correspondence: stefano.piaserico@unipd.it; Tel.: +39-049-8212914; Fax: +39-049-8212502

Abstract: Photodynamic therapy (PDT) is a highly effective and widely adopted treatment strategy for many skin diseases, particularly for multiple actinic keratoses (AKs). However, PDT is ineffective in some cases, especially if AKs occur in the acral part of the body. Several methods to improve the efficacy of PDT without significantly increasing the risks of side effects have been proposed. In this study, we reviewed the combination-based PDT treatments described in the literature for treating AKs; both post-treatment and pretreatment were considered including topical (i.e., diclofenac, imiquimod, adapalene, 5-fluorouracil, and calcitriol), systemic (i.e., acitretin, methotrexate, and polypodium leucotomos), and mechanical–physical (i.e., radiofrequency, thermomechanical fractional injury, microneedling, microdermabrasion, and laser) treatment strategies. Topical pretreatments with imiquimod, adapalene, 5-fluorouracil, and calcipotriol were more successful than PDT alone in treating AKs, while the effect of diclofenac gel was less clear. Both mechanical laser treatment with CO_2 and Er:YAG (Erbium:Yttrium–Aluminum–Garnet) as well as systemic treatment with Polypodium leucotomos were also effective. Different approaches were relatively more effective in particular situations such as in immunosuppressed patients, AKs in the extremities, or thicker AKs. Conclusions: Several studies showed that a combination-based approach enhanced the effectiveness of PDT. However, more studies are needed to further understand the effectiveness of combination therapy in clinical practice and to investigate the role of acitretin, methotrexate, vitamin D, thermomechanical fractional injury, and microdermabrasion in humans.

Citation: Piaserico, S.; Mazzetto, R.; Sartor, E.; Bortoletti, C. Combination-Based Strategies for the Treatment of Actinic Keratoses with

NEW: ORAL VITAMINE D & PDT

Vit D deficiency is associated with lower AK clearance and pretreatment with high dose Vit D3 significantly improves lesion clearance



Vit D3 cps, 10.000 UI
- 1cp/d for 5 days
- 1cp/d for 14 d if low

No difference in side effects

Table 2. Facial AK clearance rates after PDT in relation to Vitamin D status prior to treatment, and with or without oral VD3 pretreatment

	Group 1 (PDT only)	Group 2 (VD3 + PDT)
Vitamin D deficient (< 31 mg/dL)		
No. of patients (n)	7	8
25OH-D3 values (mg/dL), range	14.9 to 29.3	14.2 to 28.7
AK clearance (%, mean ± SD)	**40.9** ± 48	**71.0** ± 6.0
Vitamin D sufficient (> 31 mg/dL)		
No. of patients (n)	22	21
25OH-D3 values (mg/dL), range	32.0 to 83.3	31.0 to 100
AK clearance (%, mean ± SD)	**62.6** ± 14.2	**73.1** ± 15.9
Are the Vitamin D deficient and replete groups statistically different?		*No, p = 0.71*
All patients	29	29
AK clearance (%, mean ± SD)	**54.4** ± 22.8	**72.5** ± 13.6
Statistical comparison of AK clearance between Groups 1 and 2 **	—	*p < 0.002*

Bullock TA et al. JAAD 2022

NEW: TOPICAL CALCIPOTRIOL (CAL-DL-PDT)

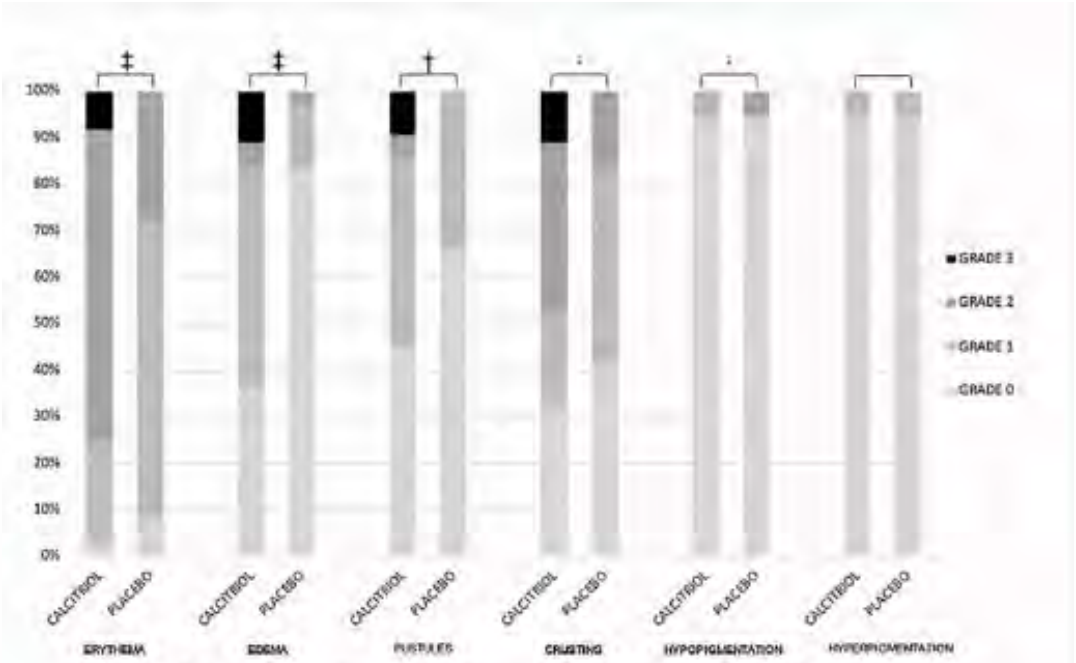


Fig. 4. Local skin reactions after the first session of DL-PDT; *<0.05, †<0.01, ‡<0.001.

CAL-DL-PDT is more effective than P-DL-PDT for thicker "difficult to treat" AKs on the upper extremities but is associated with increased local skin reactions

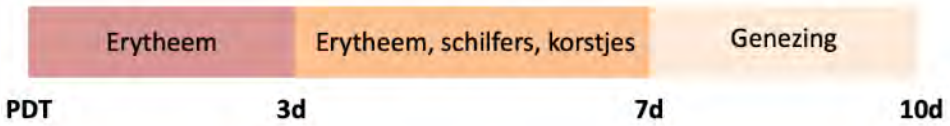
LIFT method
Lesion **i**ntensified **t**reatment

LIFT treatment of hyperkeratotic AKs (with FXL + DL-PDT)

SIDE EFFECTS& ADVERSE EVENTS

PHOTODYNAMIC THERAPY

- Temporary photosensitivity to light (48 hours)
- Temporary pain
- Localized erythematous reaction (4 to 7 days)
  - Edema, vesicles or crusting
- Pruritus (7 days)
- Sterile pustule development
  - Persistent: consider S. Aureus or MRSA
- Flares of herpes labialis
- Hypo- or hyperpigmentation (darker skin types)
- Contact allergy (topical photosensitiser)



AFTERCARE

AFTER PHOTODYNAMIC THERAPY

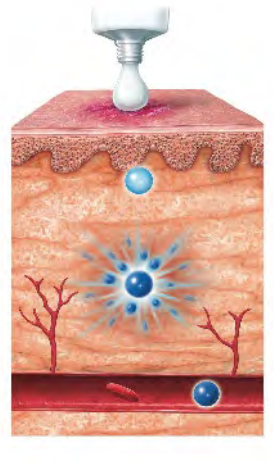
- Avoid sun exposure
- Pain traitment: Paracetamol

  No ibuprofen: supresses inflammatory response ?

- Application of petroleum jelly daily /hydration
- Topical corticosteroids 24h

  Decrease of erythema with compromising efficacy ?

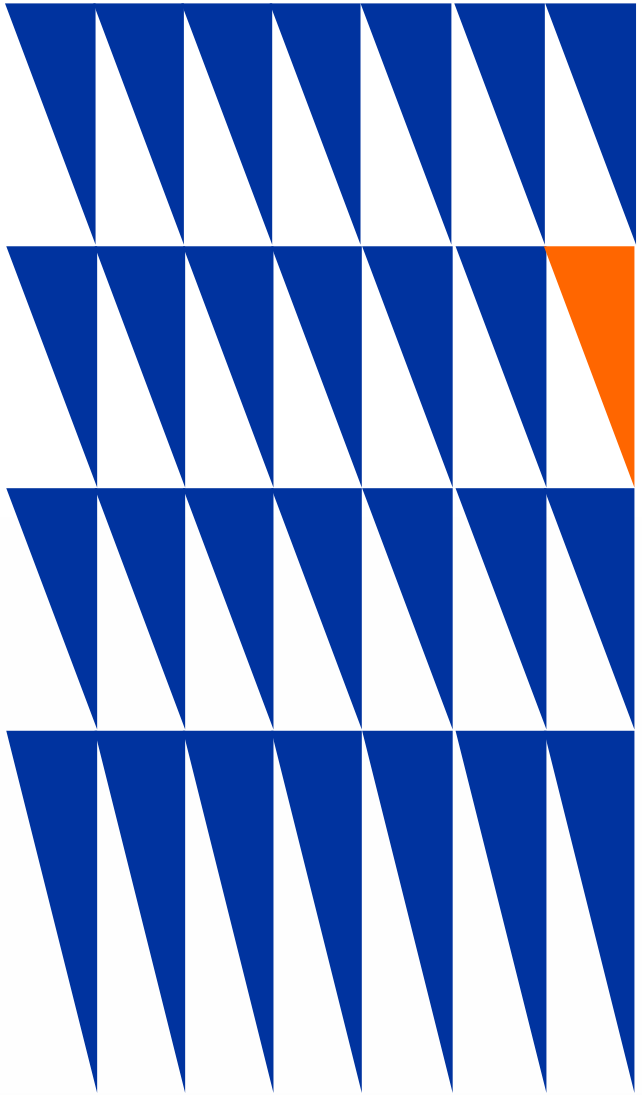
- Local cooling
- Cover the area while going outdoors (first 48h)



CONTRAINDICATIONS

PHOTODYNAMIC THERAPY

- Hypersensitivy to components of topical photosensitizer
- Porphyria
  - Porphyria cutanea tarda
- Photodermatoses
  - Lupus erythematosus, vitiligo
- Pregnancy or breastfeeding
  - No data available
- Children
  - Safety of PDT not established



CONCLUSION

- ✓ C- and DL-PDT remain gold standards in Belgium
- ✓ HB-DL-PDT is an important "new" modality

Reimbursement restrictions
No financial valorisation for the dermatologist
Restricted patient selection

- ✓ HB-DL-PDT/ as effective and safe as C-& DL-PDT for treating AK
- ✓ High patient satisfaction for DL–PDT & HB-DL-PDT
- ✓ Support via DL–PDT application
- ✓ Combination-Therapies are promising
- ✓ New indications in the future?

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Barcelona, Spain
Friday 9 and Saturday 10, June 2023

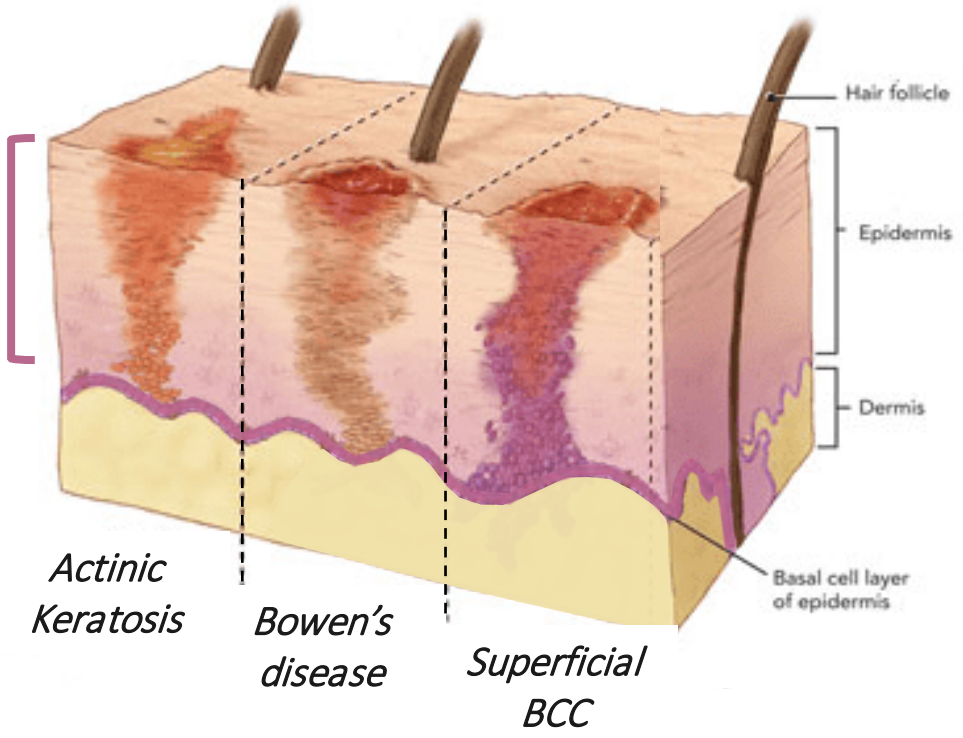
Is it still necessary to use dedicated red LED sources for PDT of deep lesions?

Serge Mordon
Ascain, France

Read the abstract

Is it still necessary to use dedicated red LED sources for deep lesions?

How deep should the light reach for PDT treatment of superficial BCC and in situ SCC ?



Non-Melanoma Skin Cancers (NMSC) that can be treated with PDT are ***only located in epidermis and deep epidermis***

There is NO NEED to reach hypodermis for PDT treatment

E. La Rochelle et al. (2019)		*Measurement from surface of corneal layer to surface of lesion (µm)*	*Measurement from surface of corneal layer to base of lesion (µm)*
(A)	*Actinic keratosis*	189	222
(C)	*Squamous cell carcinoma in situ*	305	1038
(E)	*Basal cell carcinoma, superficial type*	214	403

Corresponding to 0.2 to 1 mm depth in damaged skins

Is it still necessary to use dedicated red LED sources for deep lesions?

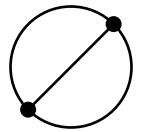
No, sup. BCC and Bowen's disease can be similarly treated with AD-PDT light sources after :

8 min

37 J/cm²

Same **PpIX weigthed dose** as **37 J/cm²** of C-PDT with AKTIILITE in depth after …

Dermaris



174 min

Is it still necessary to use dedicated red LED sources for deep lesions?

No, sup. BCC and Bowen's disease can be similarly treated with AD-PDT light sources after :

8 min

37 J/cm²

Same **PpIX weigthed dose** as **37 J/cm²** of C-PDT with AKTIILITE in depth after …

Power x 6

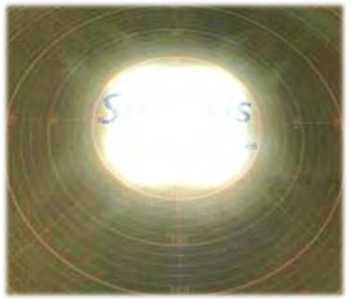
Dermaris

20 cm

Dermaris +

8 cm

174 min



30 min

Is it still necessary to use dedicated red LED sources for deep lesions?

No, sup. BCC and Bowen's disease can be similarly treated with AD-PDT light sources after :

2 min

9.25 J/cm²

H.C. Wulf et al. (2021)

Same **PpIX weigthed dose** as **9.25 J/cm²** of C-PDT with AKTIILITE in depth after …

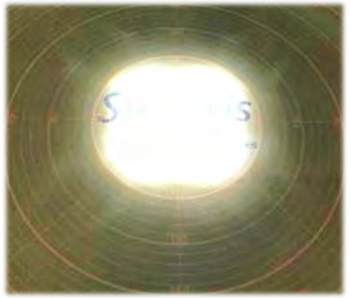
Dermaris

20 cm

44 min

Dermaris +

8 cm



8 min

Is it still necessary to use dedicated red LED sources for deep lesions?

Clinical Studies

› Photodermatol Photoimmunol Photomed. 2022 Jul;38(4):322-327. doi: 10.1111/phpp.12750. Epub 2021 Nov 24.

An open-label prospective study to assess short incubation time white LED light photodynamic therapy in the treatment of superficial basal cell carcinoma

Rebecca Hellen [1], Eilis Nic Dhonncha [1], Alison Havelin [1], Ann Kavanagh [1], Blaithin Moriarty [1], Paul Collins [1]

Case Reports › Acta Derm Venereol. 2019 Jun 1;99(7):701-702. doi: 10.2340/00015555-3174.

Successful Treatment for Extensive Bowen's Disease using Daylight-mediated Photodynamic Therapy

Roba Safar [1], Alya Alkhars, Matthias Tallegas, Nina Korsaga-Some, Laurent Machet

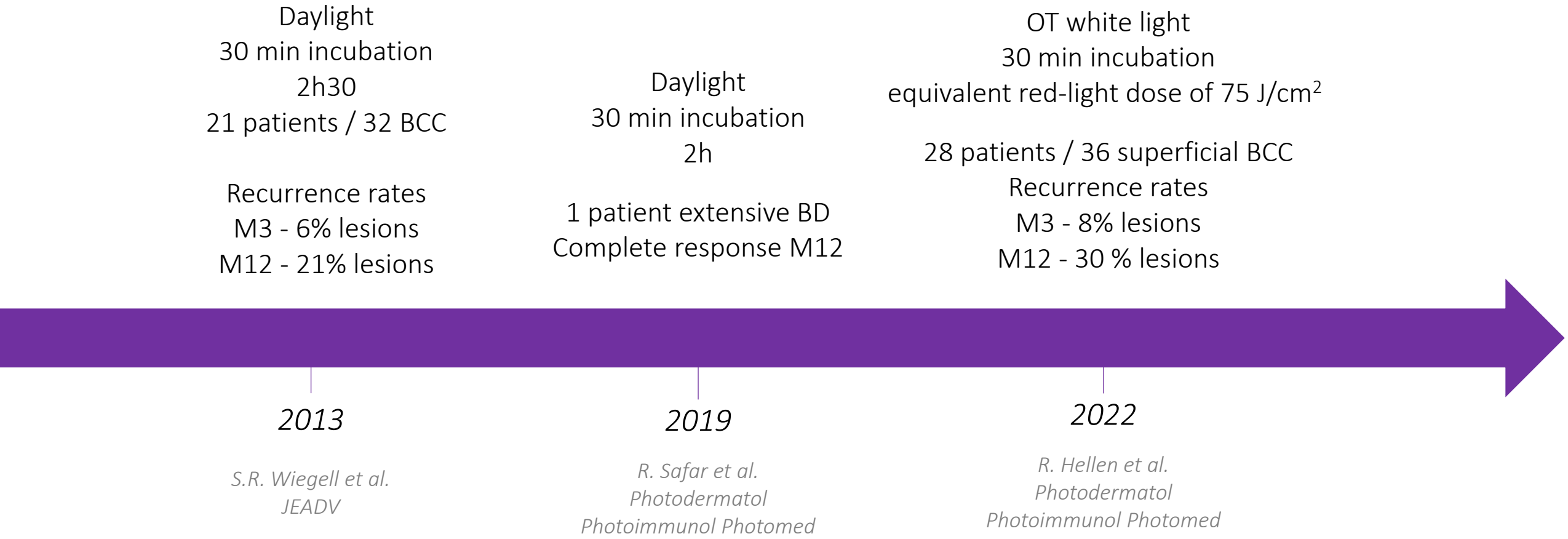
› J Eur Acad Dermatol Venereol. 2014 Feb;28(2):169-75. doi: 10.1111/jdv.12076. Epub 2013 Jan 7.

Daylight-mediated photodynamic therapy of basal cell carcinomas - an explorative study

S R Wiegell [1], V Skødt [2], H C Wulf [1]

Is it still necessary to use dedicated red LED sources for deep lesions?

Clinical Studies



Is it still necessary to use dedicated red LED sources for deep lesions?

Conclusion

- White is not a color, but is only the superposition of all the colors
- The new medical white LED delivers an important amount of red.
- Recent clinical studies clearly demonstrate that artificial White LED can be used to treat deep lesions.

The author would like to acknowledge Elise Thecua

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Barcelona, Spain

Friday 9 and Saturday 10, June 2023

Pre- and Post-treatment procedures for PDT

Jens Malte Baron
Aachen, Germany

Read the abstract

Recent European expert and S2K guideline recommentations for pre- and post- PDT treatments

Received: 9 September 2022 | Accepted: 4 January 2023

DOI: 10.1111/jdv.18855

JEADV

REVIEW ARTICLE

Expert recommendations on supportive skin care for non-surgical and surgical procedures

Jean-Michel Amici[1] | Olivier Cogrel[2] | Marie Jourdan[3] | Catherine Raimbault[4] | Ludivine Canchy[5] | Delphine Kerob[5] | Diane C. Madfes[6] | Yan Tian[7] | Elena Araviiskaia[8]

JDDG Journal of the German Society of Dermatology

DDG Deutsche Dermatologische Gesellschaft

Guideline | Open Access

S2k guideline: Laser therapy of the skin

Uwe Paasch Miriam Zidane, Jens Malte Baron, Thorsten Bund, Hans-Joachim Cappius, Michael Drosner, Konstantin Feise, Tanja Fischer, Gerd Gauglitz, Peter Arne Gerber ... See all authors

First published: 13 September 2022 | https://doi.org/10.1111/ddg.14879

Pre- treatment procedures for PDT

Pre-PDT preparation recommendations

Non-surgical procedure	Invasiveness and recovery period[a]	Preparation[b]
Photodynamic Therapy (PDT)	*Moderately invasive* with 2–3 days recovery period: photodynamic therapy, photodynamic rejuvenation	Apply a keratolytic ointment or cream the night before treatment to facilitate easier crust removal Tape stripping, microdermabrasion or laser ablation or gentle curettage can also be used to reduce hyperkeratosis and prepare the skin for the photosensitizing agent

J Eur Acad Dermatol Venereol 2023 Mar;37 Suppl 3:16-33. doi: 10.1111/jdv.18855

GUIDELINES

European Dermatology Forum guidelines on topical photodynamic therapy 2019 Part 1: treatment delivery and established indications – actinic keratoses, Bowen's disease and basal cell carcinomas

C.A. Morton,[1] R.-M. Szeimies,[2,3,*] N. Basset-Seguin,[4] P. 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]

JEADV 2019, 33, 2225–2238

Lesion preparation

Protocols for topical PDT in Europe conventionally recommend some form of lesion preparation to enhance photosensitizing agent absorption and light penetration in MAL-PDT and nanoemulsion ALA-PDT. Studies using a novel ALA plaster for mild and moderate thickness AK do not require prior preparation with results consistent with standard protocols.[13,39] Tape-stripping, microdermabrasion or laser ablation, or gentle curettage can also be used to reduce hyperkeratosis.

Pre-PDT preparation recommendations

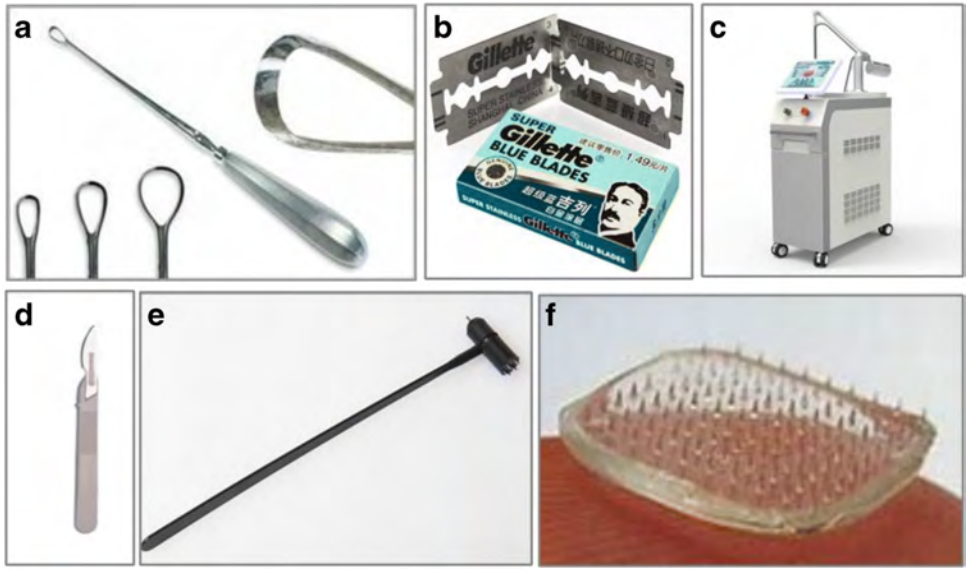
Lasers in Medical Science (2021) 36:1369–1377
https://doi.org/10.1007/s10103-020-03233-6

REVIEW ARTICLE

The application of physical pretreatment in photodynamic therapy for skin diseases

Dihui Liu[1,2] · Shuang Zhao[1] · Jinmao Li[1] · Mingliang Chen[1] · Lisha Wu[1,3,4]

Type	Author	Kind of disease	Number of PDT	Efficacy (%)
Curettage	Tamara et al. [17]	nBCC (*n* = 285); sBCC (*n* = 119) pBCC (*n* = 25)	2–3	OR: 93.3 (1 year); OR: 76.8 (1 year) OR: 76.2 (1 year)
	Lu et al. [18]	Perianal CA (*n* = 40; 522 lesions)	3	CR: 100; RR: 15 (3 months)
Superficial shaving	Liu et al. [19]	BD (*n* = 10; 44 lesions)	3	CR: 100 (3 months); RR: 0 (1 year)
	Zhao et al. [20]	VIN (*n* = 17)	3	CR: 94 (1 year); RR: 23.5 (1 year)
	Huang et al. [21]	Planter warts: SS-PDT group (*n* = 46; 271 lesions); cryotherapy group (*n* = 26; 147 lesions)	3	SS-PDT vs cryotherapy group (OR: 91.3 vs 23.1 (6 months); RR: 8.7 VS 76.9 (6 months))
	Wu et al. [22]	Periungual warts (*n* = 23; 61 lesions)	3	CR: 61 (3 months); RR: 9 (1 year)
Laser	Ko et al. [23]	BD (*n* = 21; 58 lesions)	Er:YAG- AFL-PDT: 1; MAL-PDT: 2	Er:YAG AFL-PDT: CR: 93.8; RR: 6.7 (1 year) MAL-PDT: CR: 73.1; RR: 31.9 (1 year)
	Togsverd-Bo et al. [24]	AK (*n* = 16; 542 lesions)	1	CR: AFL-dPDT: 74; dPDT: 46; cPDT: 50; AFL: 5
	Togsverd-Bo et al. [25]	AK (*n* = 15; 212 lesions)	1	AFXL-PDT vs PDT: AK (II-III:88 vs 59; I:100 vs 80)
Surgery resection	Lu et al. [26]	BCC (*n* = 32); BD (*n* = 13); SCC (*n* = 5); Paget (*n* = 8);	3	CR:100; RR: 0 (6 months); RR: 12.5 (1 year)
Plum-blossom needling	Wu et al. [27]	BD (*n* = 24; 43 lesions)	≤ 6	PBN-ALA-PDT: CR: 78; RR: 0 (6 months) ALA-PDT: CR: 40; RR: 11.76 (6 months)
Microneedle	Caccavale et al. [28]	Resistant plantar or palmar warts (*n* = 13; 137 lesions)	3–5	CR: 92.3 (4.3 months);



Lasers in Medical Science (2021) 36:1369–1377

Pre-treatment procedures for PDT

JDDG
Journal of the German Society of Dermatology

DDG Deutsche Dermatologische Gesellschaft

Guideline | Open Access

S2k guideline: Laser therapy of the skin

Uwe Paasch, Miriam Zidane, Jens Malte Baron, Thorsten Bund, Hans-Joachim Cappius, Michael Drosner, Konstantin Feise, Tanja Fischer, Gerd Gauglitz, Peter Arne Gerber ... See all authors

First published: 13 September 2022 | https://doi.org/10.1111/ddg.14879

Laser S2k guideline: recommendations for the treatment of actinic keratosis

Recommendations for the treatment of actinic keratosis/ field cancerization	Strength	Consensus
LADD-PDT using a fractional 10,600 nm CO_2 laser combined with red light (635 nm), artificial daylight (415 nm, 585 nm, 635 nm), or daylight *is recommended* for field cancerization.	↑↑	100 %
LADD-PDT using a fractional 2,940 nm Er:YAG laser combined with red light (635 nm), artificial daylight (415 nm, 585 nm, 635 nm), or daylight *is recommended* for field cancerization.	↑↑	100 %

J Dtsch Dermatol Ges 20(9):1248-1267, 2022

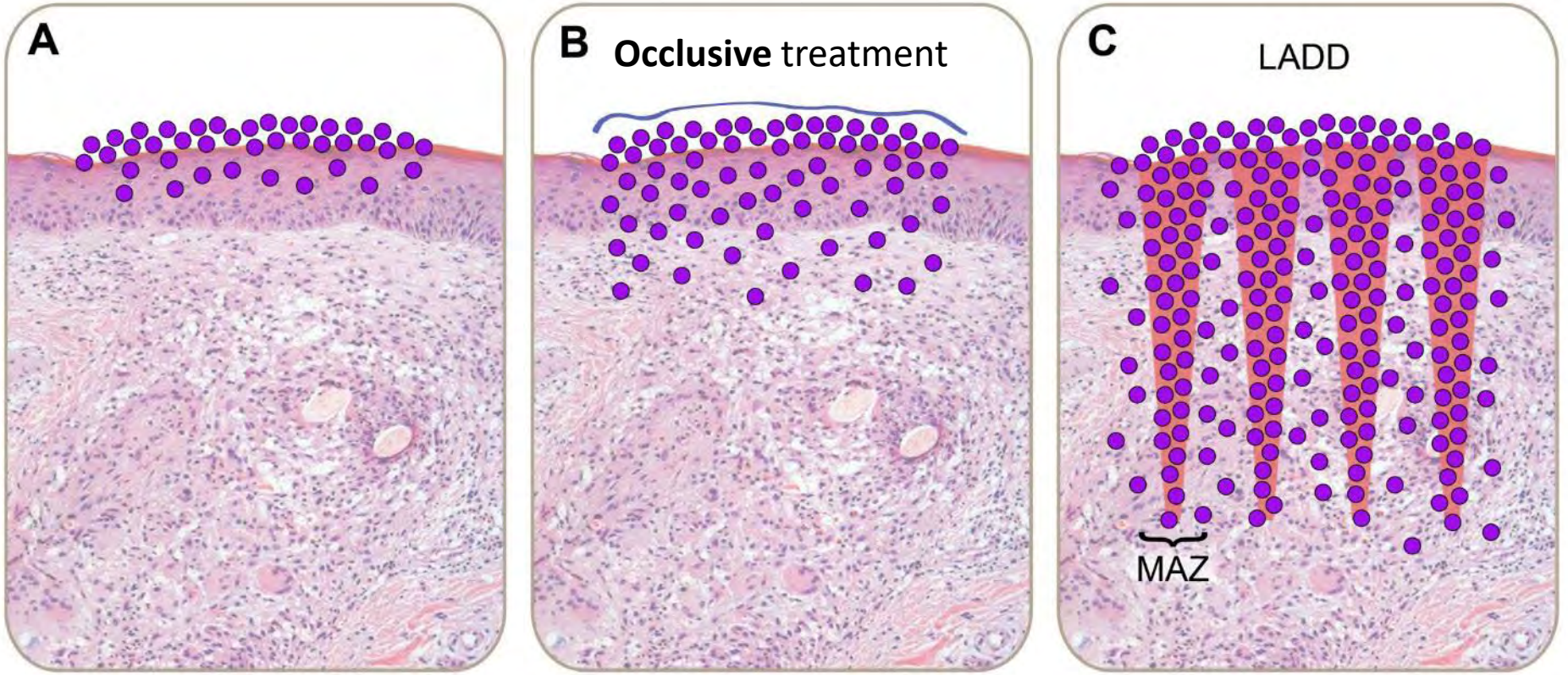
Laser guideline: treatment of cheilitis actinica

Cheilitis actinica

Recommendations for the treatment of cheilitis actinica	Strength	Consensus
Ablative Lasers:		
LADD-PDT using a fractional 10,600 nm CO_2 laser combined with red light (635 nm), artificial daylight (415 nm, 585 nm, 635 nm), or daylight *may be recommended.*	↑	83 %
Ablative use of a 2,940 nm Er:YAG laser *may be considered.*	0	100 %
Ablative use of a 10,600 nm CO_2 laser (scanned continuous wave) *may be recommended.*	↑	100 %

J Dtsch Dermatol Ges 20(9):1248-1267, 2022

Laser assisted drug delivery (LADD)

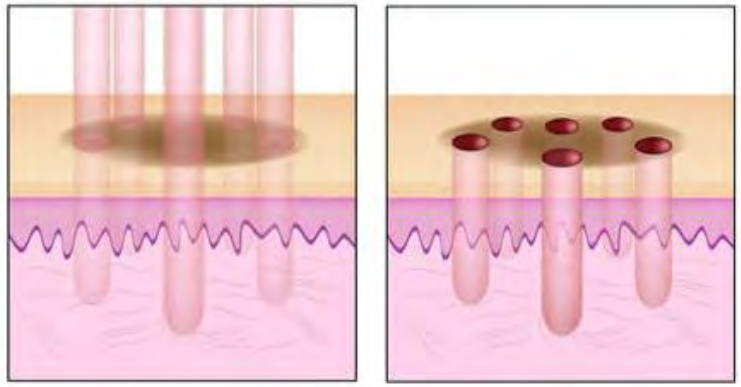


Braun SA & Gerber PA, *JDDG (accepted)*
Braun SA & Gerber PA, *Cosm Med 2014*
Bunert N & Gerber PA, *Haut 2014*
Haedersdal M et al. Lasers Surg Med. 2010

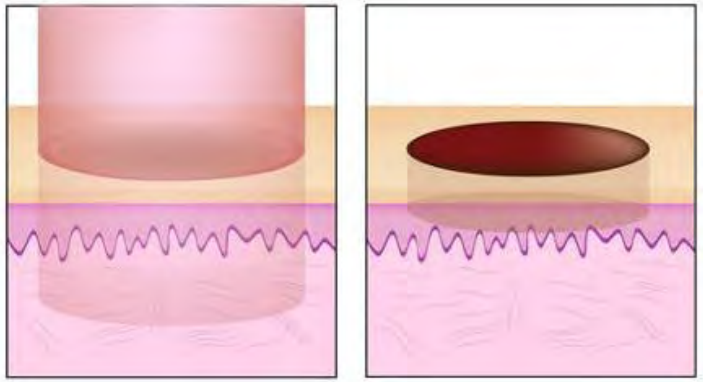
MTZ forms a **reservoir** from which the drug is slowly released

Fractional/ areal laser treatment

fractional treatment



areal treatment

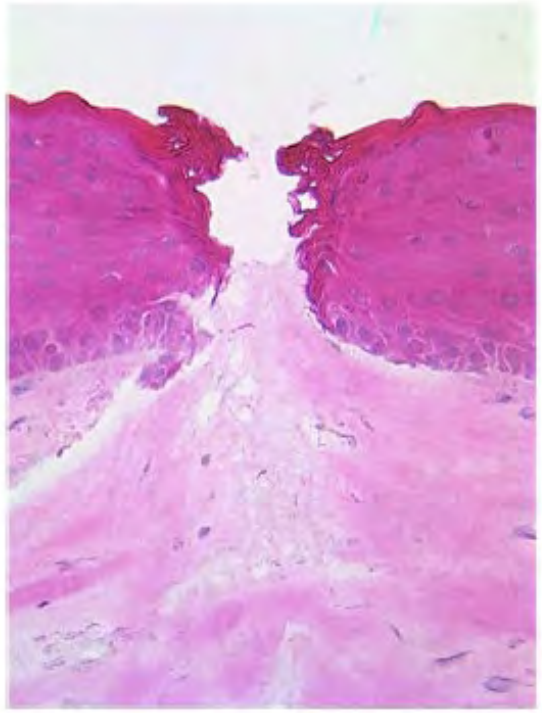


Arrays of **m**icroscopic **t**reatment **z**ones **separated** by **intact tissue**

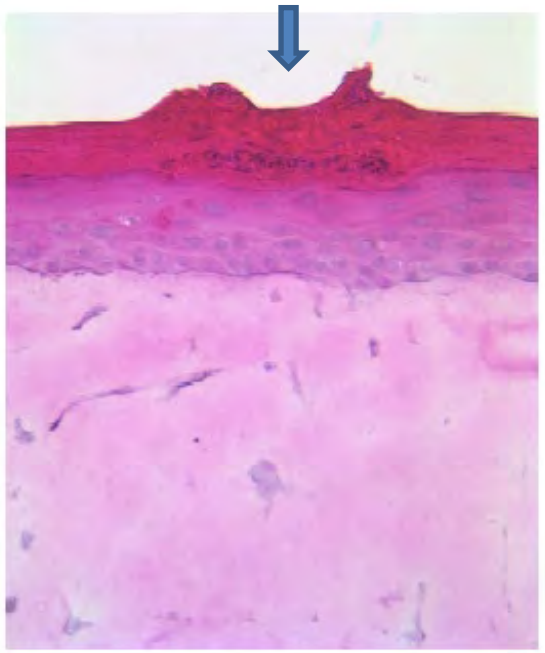
Penetration of topically applied active ingredients

H&E staining 3D skin model **on day 0** and **day 3 after treatment** with **fractional CO_2 laser** (microscanner, 10mJ, 300Hz, d10%)

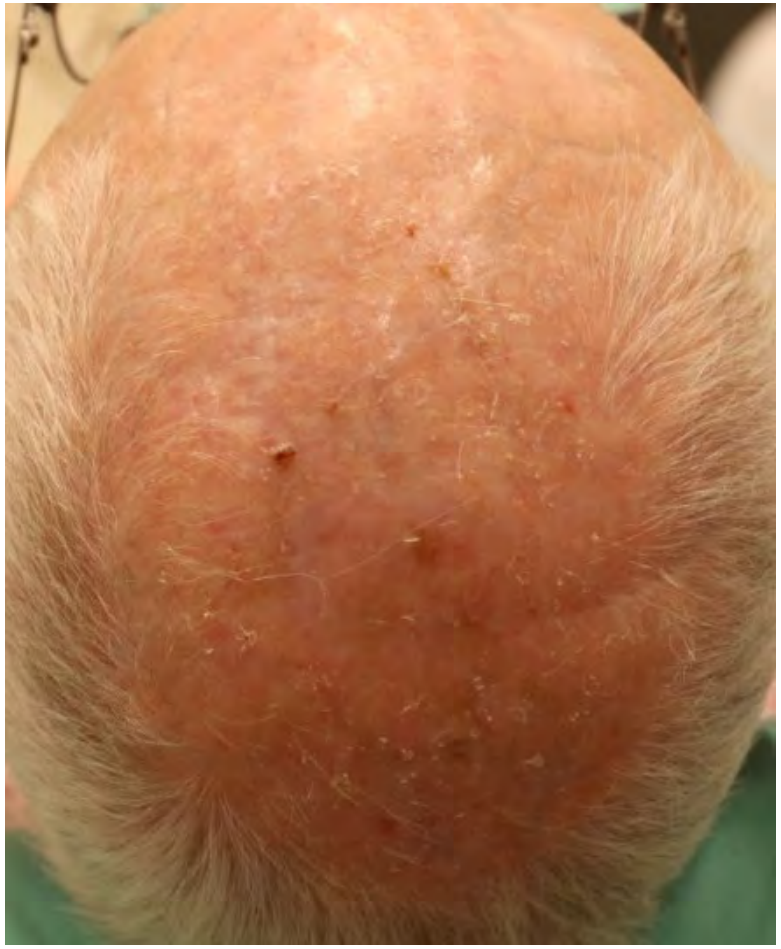
day 0



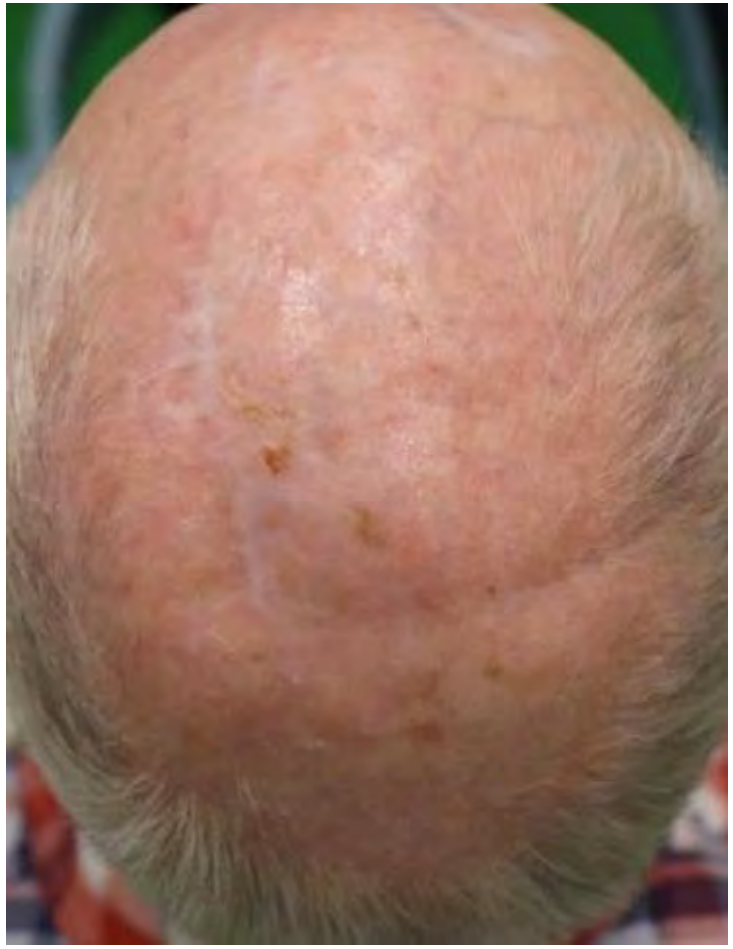
day 3



Laser assisted drug delivery (LADD)- daylight PDT



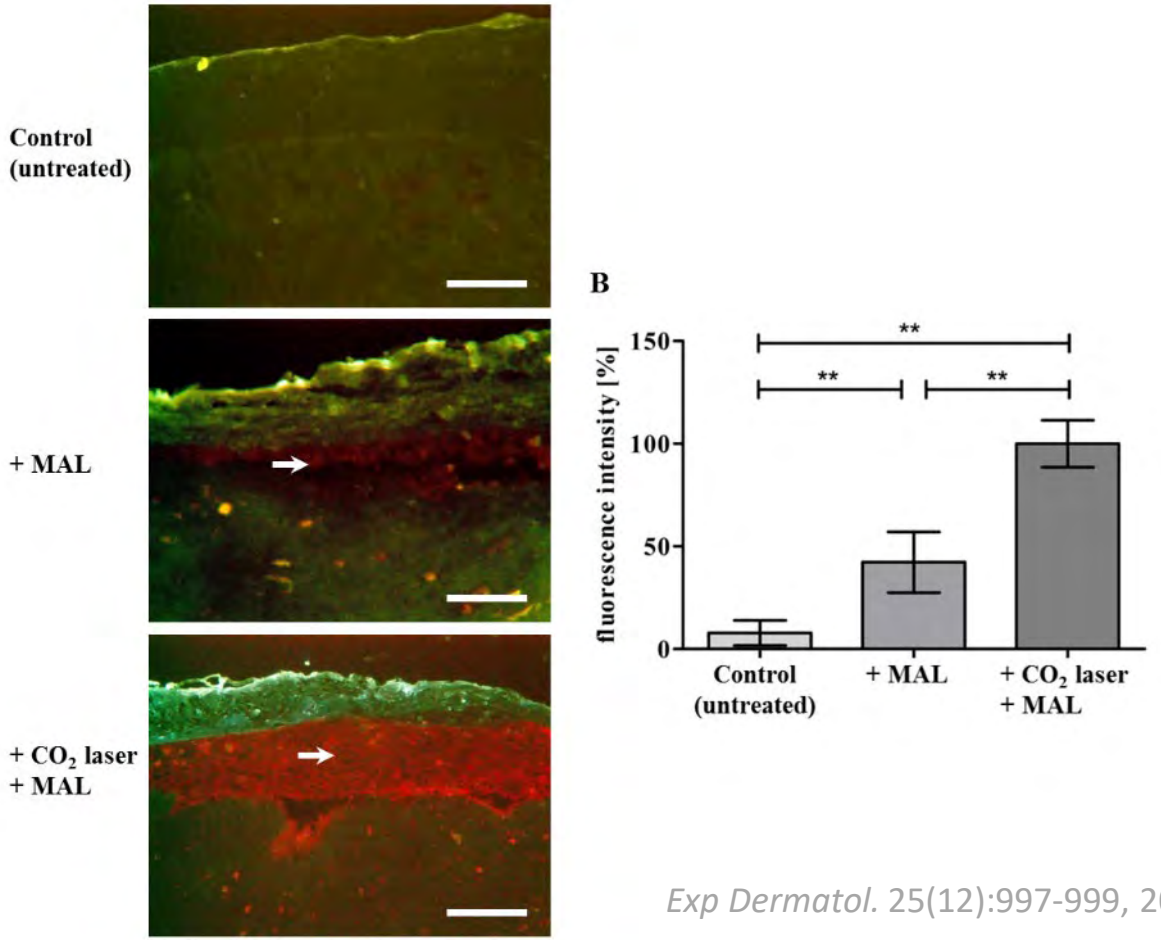
Initial findings (**d0**)



after 5 weeks

Laser assisted drug delivery (LADD)- cPDT

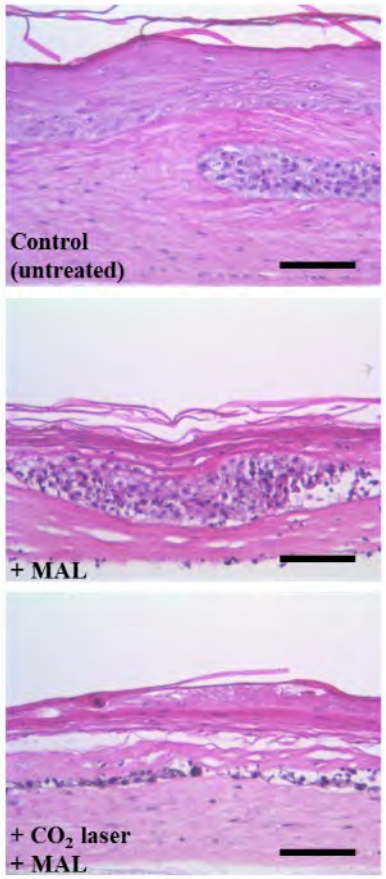
pretreatment of **AK skin model** with **fractional CO_2 laser** significantly **improves uptake** of **5-methyl-aminolevulinic acid** (MAL)

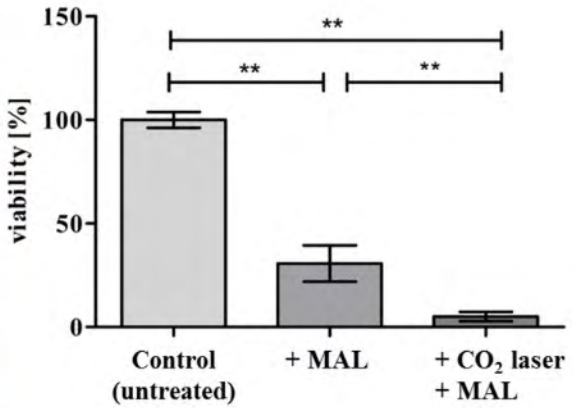


Exp Dermatol. 25(12):997-999, 2016

Laser assisted drug delivery (LADD)- cPDT

Pretreatment of **AK skin models** with a **fractional laser improves** the effect of **PDT** with **5-methyl-aminolevulinic acid (MAL) + red light** (630nm) on **tumor cells**





Exp Dermatol. 25(12):997-999, 2016

Laser assisted drug delivery (LADD)- PDT

Pretreatment with ablative fractional carbon dioxide laser improves treatment efficacy in a synergistic PDT protocol for actinic keratoses on the head

C. Falkenberg [a,b,1,*], L. Schmitz [c,d,1], K. Dicke [a,b], V. Dervenis [a], R.M. Szeimies [e], T. Dirschka [a,b]

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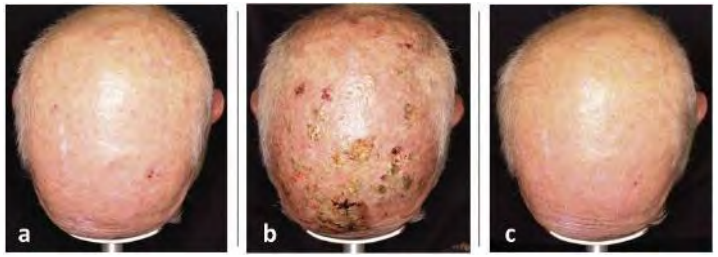
[c] Department of Dermatology, Venerology and Allergology, Ruhr-University, Bochum, Germany
[d] Institute of Dermatopathology, MVZ Cerius DermPathBonn, Bonn, Germany
[e] Clinic for Dermatology and Allergology, Klinikum Vest, Recklinghausen, Germany



ARTICLE INFO

Keywords:
Actinic keratosis
AKASI
ALA
Fractional CO_2 laser
NMSC
Photodynamic therapy

ABSTRACT

Background: A recently proposed synergistic photodynamic therapy protocol (s-PDT) combining advantages of both conventional- and daylight-PDT proved to be an effective and almost painless treatment for patients with actinic keratoses (AKs). This study investigated the safety and efficacy of an additional ablative fractional CO2-laser (AFXL) pretreatment.

Methods: 28 patients with AKs on the head received s-PDT using 5-aminolevulinic acid. AFXL pretreatment was conducted using the following parameters: pulse energy 8 mJ, spot density 50 spots/cm^2, power 30 W, beam size 4–18 mm. Outcome was assessed by AK area and severity index (AKASI) and lesion count (LC) before and 3 months after treatment. Safety was monitored by blood pressure and pulse measurements. Intensity of pain was determined by use of a visual analog scale (VAS).

Results: Most patients (96.4 %) showed a significant AKASI reduction ($P < 0.0001$) 3 months after PDT (median AKASI 1.6 [0–2.4]) compared to baseline (5.3 [4–7.75]). Median reduction rate was 75.5 % (61.3 %–100 %). Eleven patients (39.3 %) achieved AKASI 100, three (10.7 %) AKASI 75 and ten (35.7 %) AKASI 50. Blood pressure and pulse did not change significantly throughout treatment. Median VAS for pain during irradiation was 0 (0–0), 0 (0–2) and 0 (0–2) at the beginning, in the meantime and at the end, respectively. Compared to data without AFXL pretreatment, this study showed significantly higher AKASI and LC reduction rates (75.5 % vs. 63.7 % [$P = 0.023$] and 91.3 % vs. 80.4 % [$P = 0.043$]).

Conclusions: S-PDT with AFXL pretreatment represents a safe and almost painless treatment for patients with AKs on the head and improves treatment efficacy.

Photodiagnosis and Photodynamic Therapy 34 (2021) 102249

Laser assisted drug delivery (LADD)- PDT

Journal of the American Academy of Dermatology
Volume 79, Issue 5, November 2018, Pages 860-868

Original article

Ablative fractional laser–assisted photodynamic therapy provides superior long-term efficacy compared with standard methyl aminolevulinate photodynamic therapy for lower extremity Bowen disease

Ho-Jin Kim MD, Ki-Hoon Song MD, PhD

A total of 60 patients with 84 BD lesions were randomly assigned to a single session of AFL-MAL-PDT or two sessions of MAL-PDT with a 1-week interval between sessions. In patients with lower extremity BD lesions, AFL-MAL-PDT showed significantly higher long-term efficacy and lower recurrence rates than standard MAL-PDT

Post- treatment procedures for PDT

Post-PDT treatment recommendations

Non-surgical procedure	Immediately after procedure	Post-procedure care[c]
Photodynamic Therapy (PDT)	Strict avoidance of sun exposure (driving or walking in the sun) for 48 h Exposure to intense visible light (e.g. surgical lighting or a high-power dentist lamp) should be avoided for 48 h Apply soothing spray or lotion, mist with thermal water, or apply icepacks to soothe and refresh Dab any weeping to reduce risks of infection Apply repairing balms or ointments to repair the epidermis or in some cases antibiotic ointment to prevent infection Avoid make-up application immediately after the procedure	Strict photoprotection for 15 days Cleanse gently every day with a mild cleanser or micellar water Apply repairing balms or ointments to repair the epidermis or in some cases antibiotic ointment to prevent infection morning and evening for 5 days Continue anti-herpetic treatment in case of lip treatment for 5 days

J Eur Acad Dermatol Venereol 2023 Mar;37 Suppl 3:16-33. doi: 10.1111/jdv.18855.

General recommendations on aftercare following ablative laser treatments (S2k laser treatment guideline)

Procedure after ablative laser treatments

Follow-up after ablative laser procedures should be tailored to the phases of wound healing.
According to current evidence, this strategy should therefore include the following steps [46]:

- Protection against infections
- Protection against free radicals
- Modulation of inflammation
- Support of cell proliferation and acceleration of migration
- Promotion of remodeling

Specific recommendations for treatment after ablative laser therapy

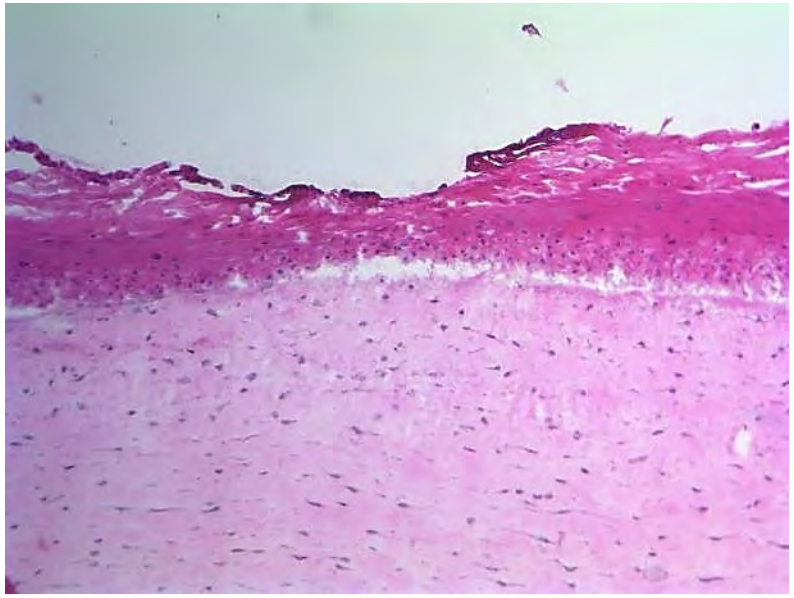
ablative laser treatment
Ointment containing **dexpanthenol**
Cream containing **panthenol**, madecassoside and copper-zinc-manganese
0.02% **triamcinolone** acetonide cream
Vitamin C, E and ferulic acid serum (**antioxidant**)
Clobetasol propionate 0.05% ointment
Sun protection products also with **protection** against **UVA**

J Dtsch Dermatol Ges 20(9):1248-1267, 2022

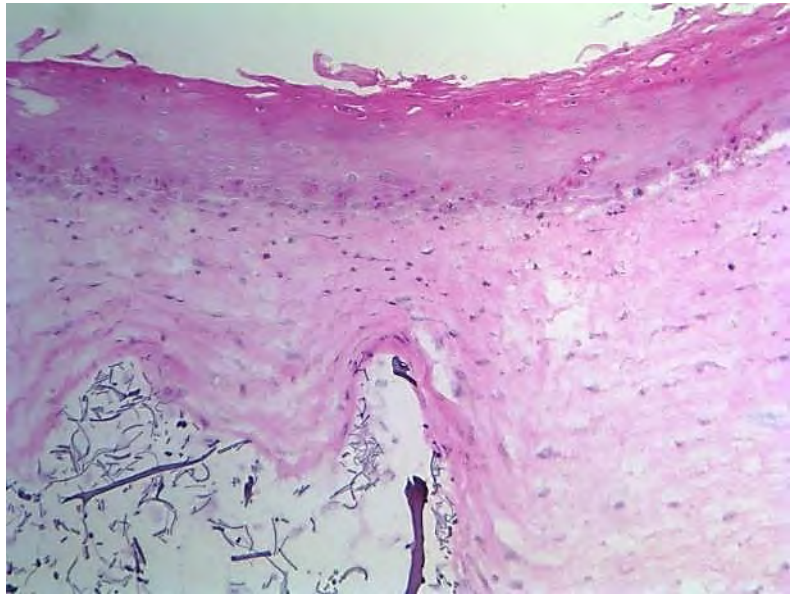
Post-treatment after LADD- ADL PDT with ointment containing dexpanthenol

Er:YAG (N10% 20J); then topical 1h 5-methyl-aminolevulinic acid, followed by 1h irradiation with 20J/cm^2 ADL; histological examination **after 24h**

without aftercare treatment



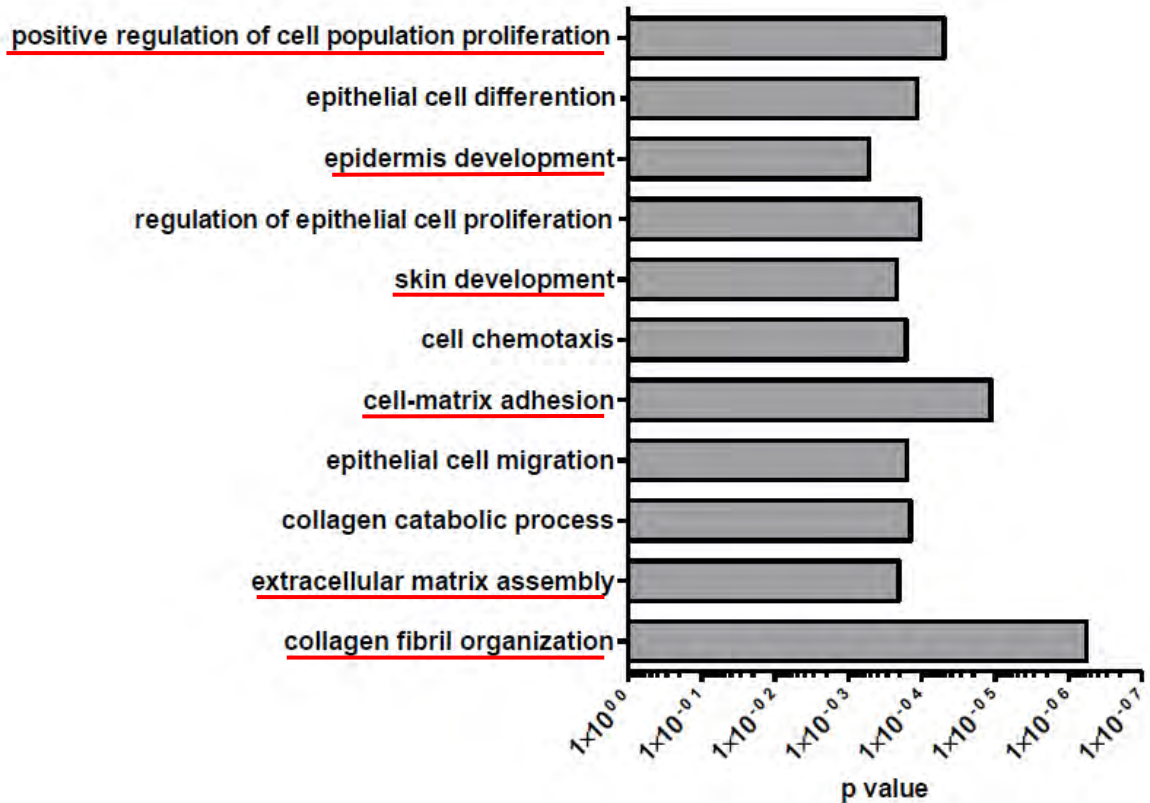
with dexpanthenol containing ointment



Post-treatment after LADD- ADL PDT with ointment containing dexpanthenol

Er:YAG N10% 20J; then topical 1h 5-methyl-aminolevulinic acid, followed by 1h irradiation with 20J/cm^2 ADL; **GO analysis** of **NGS data** after **24h**

Follow-up treatment with **ointment containing dexpanthenol**



Summary

- A **European group of experts** in cosmetic surgery and dermatology recently recommended **supportive skin care management** to **prepare, cleanse** and **protect** the **skin** and **post-procedure skin care** with **healing** and **anti-inflammatory ingredients** to **speed up regeneration** and **wound healing** whilst **minimizing scarring** and **downtime**

- According to a recent German **S2K guideline**, using laser-assisted drug delivery, the so-called **laser-assisted PDT** achieves **better healing rates** and **longer freedom** from **recurrence**

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Barcelona, Spain

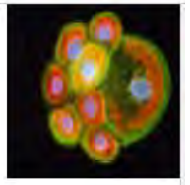
Friday 9 and Saturday 10, June 2023

Nurses for Daylight-PDT

Paola Pasquali

Barcelona, Spain

Read the abstract



Topical photodynamic therapy: an introduction for nurses

Paula Oliver

Skin cancer is important to healthcare professionals and to the public, as it is common, preventable and treatable. There are three main types of skin cancers: malignant melanoma, and the two non-melanoma skin cancers (NMSCs): basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). NMSCs are most common in the elderly and and on exposed body parts, such as the face, neck, ears, forearms and hands. While these are rarely fatal, they can result in considerable morbidity.

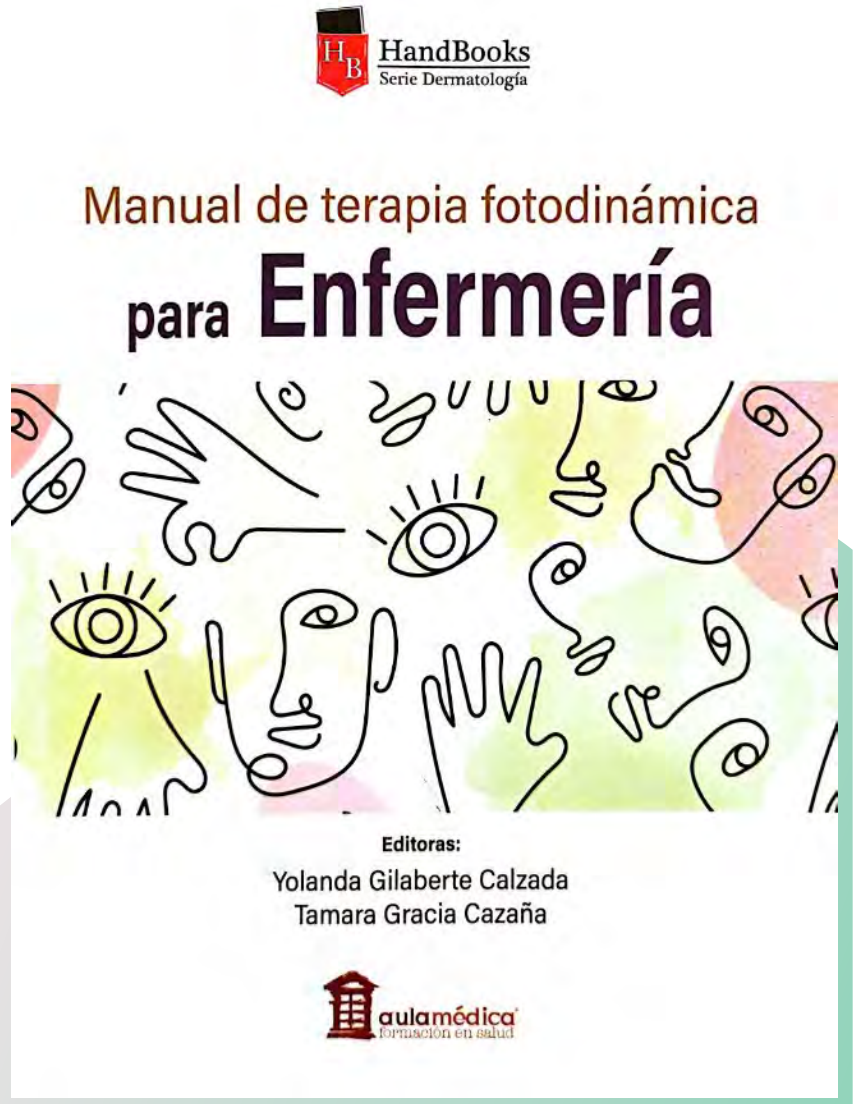
Indications for use for topical photodyamic therapy

Actinic keratosis (AK), is a common pre-cancerous state caused by exposure to sunlight.

Abstract

Non–melanoma skin cancers are the most common cancers in the UK. Although an estimated 50 000 cases were registered in 1999 across England and Wales, there is likely to be significant under-reporting of cases. However, the cancer registries do not include pre-cancerous lesions of the skin and therefore the number treated will greatly outnumber the cancers (National Institute for Health and Clinical Excellence, 2006). Topical photodynamic therapy (PDT) is one of several effective treatments for pre-malignant and malignant non–pigmented skin cancers. The treatment is non-invasive and can be administered by nurses in a clinical setting. PDT is a two-step process involving the application of a light-activated substance followed by exposure to light to activate this substance. The treatment results in the elimination of tumour cells while leaving the healthy skin unharmed. This article provides an introduction to PDT for nurses who may in the future be involved in setting up a PDT service within their practice area.

Key words: Skin and skin disorders ■ Skin cancer ■ Nurse-led clinics



- Basics of PDT
- Types of PDT
- Protocols
- How to organize (space/time/material)
- Pre and Post-treatment
- How to manage complications
- Pain managment

TIME AND DEDICATION

- Evaluate pts requirements and needs
- Identify health issues
- Create the best posible atmosphere
- Organize the procedure
- Monitor, accompany and follow-up

Photodiagnosis and Photodynamic Therapy
Volume 30, June 2020, 101749

Knowledge, practice and attitude about photodynamic therapy use among practicing nurses: A large scale cross-sectional data on implementation of photodynamic therapy education

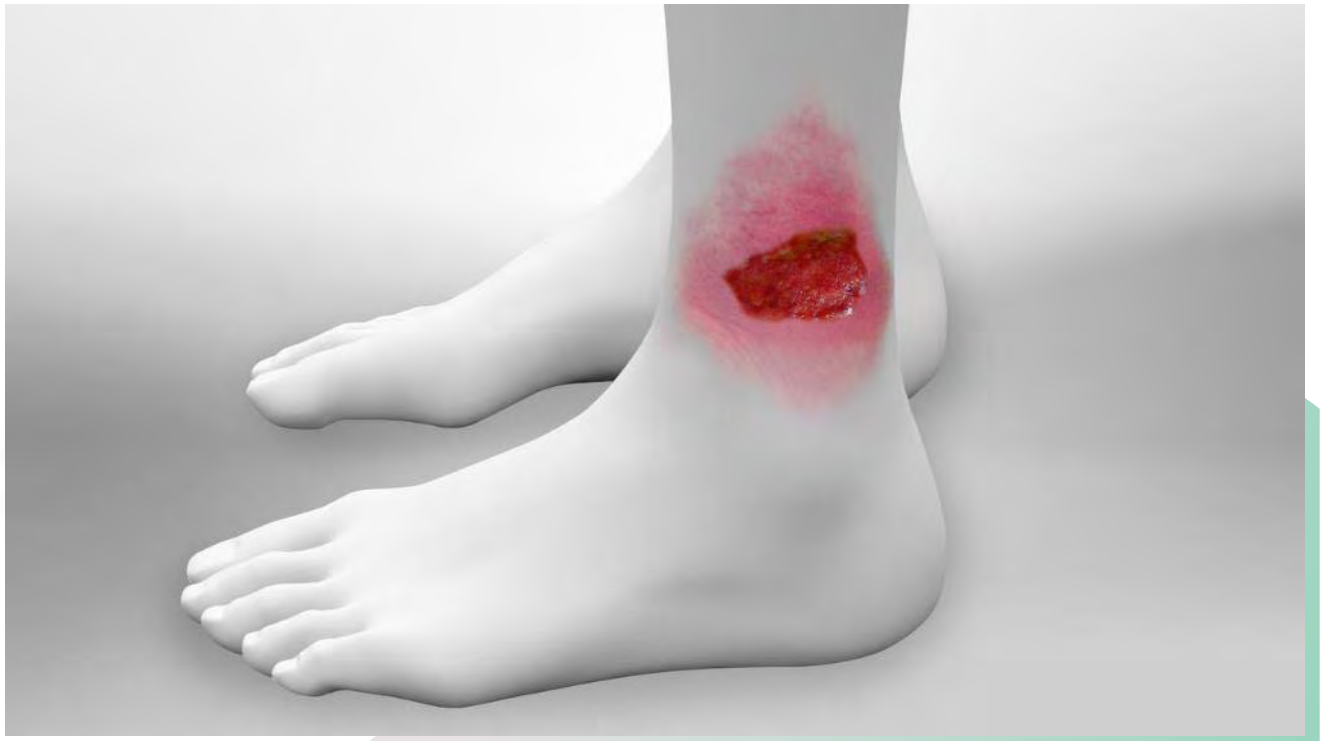
Mohammed Mahmoud Al-Momani

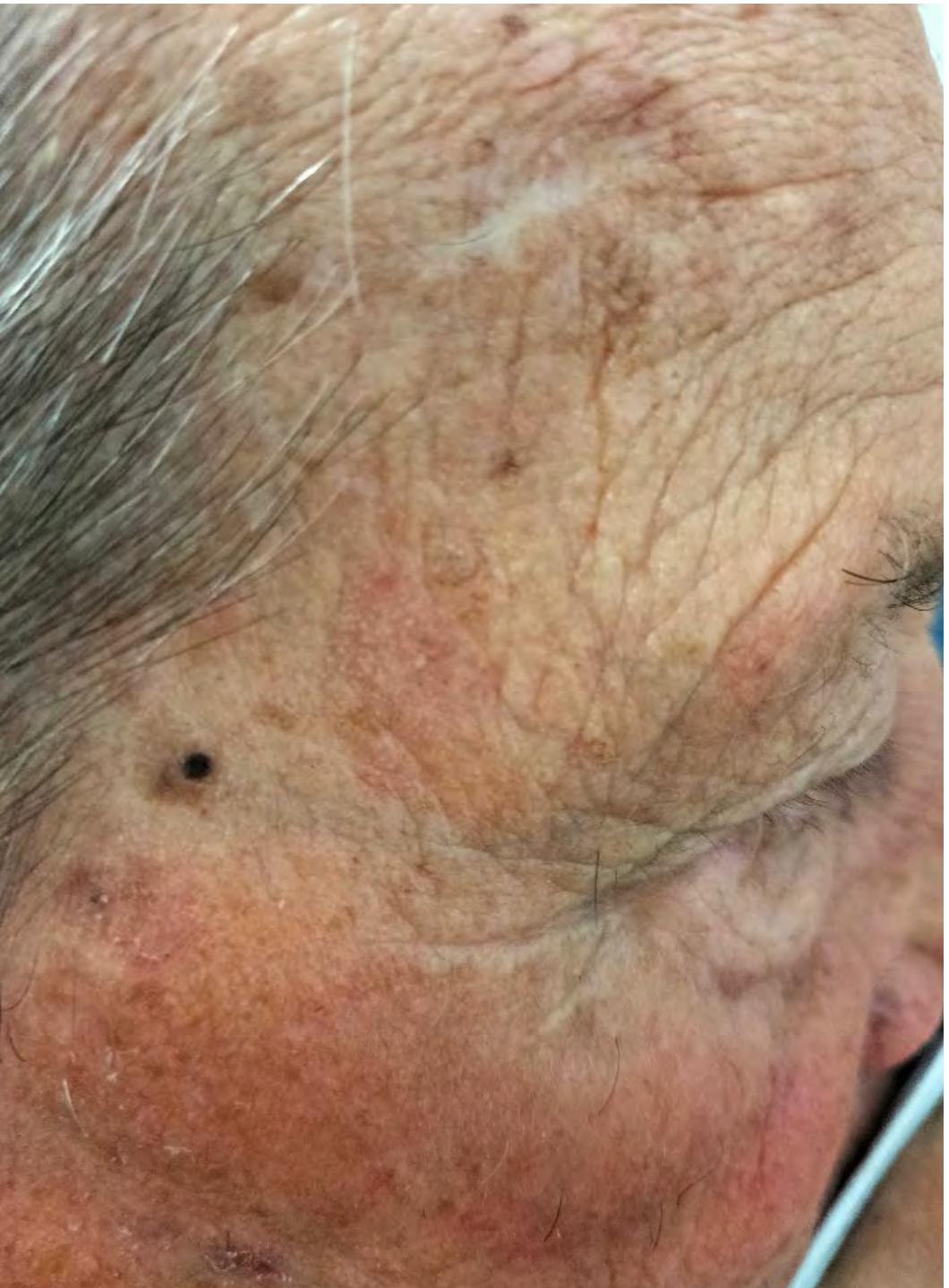
Department of Community Health Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia

Journal of Wound Care, VOL. 27, NO. 12 | Practice

Photodynamic therapy in infected venous and mixed leg ulcers: a pilot experience

Giovanni Mosti, Pietro Picerni, Manuel Licau, Vincenzo Mattaliano





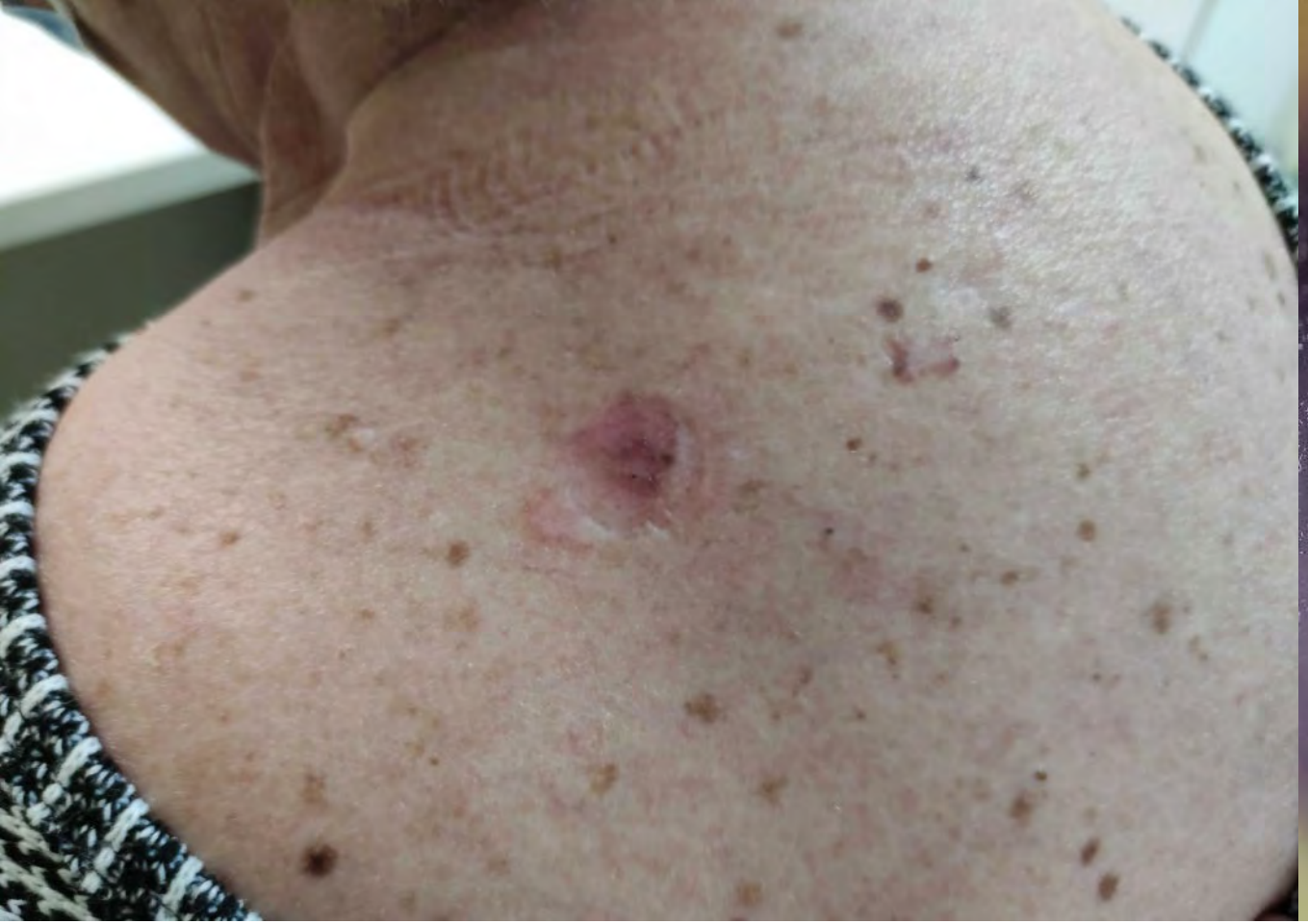
TD
86 yr
Male

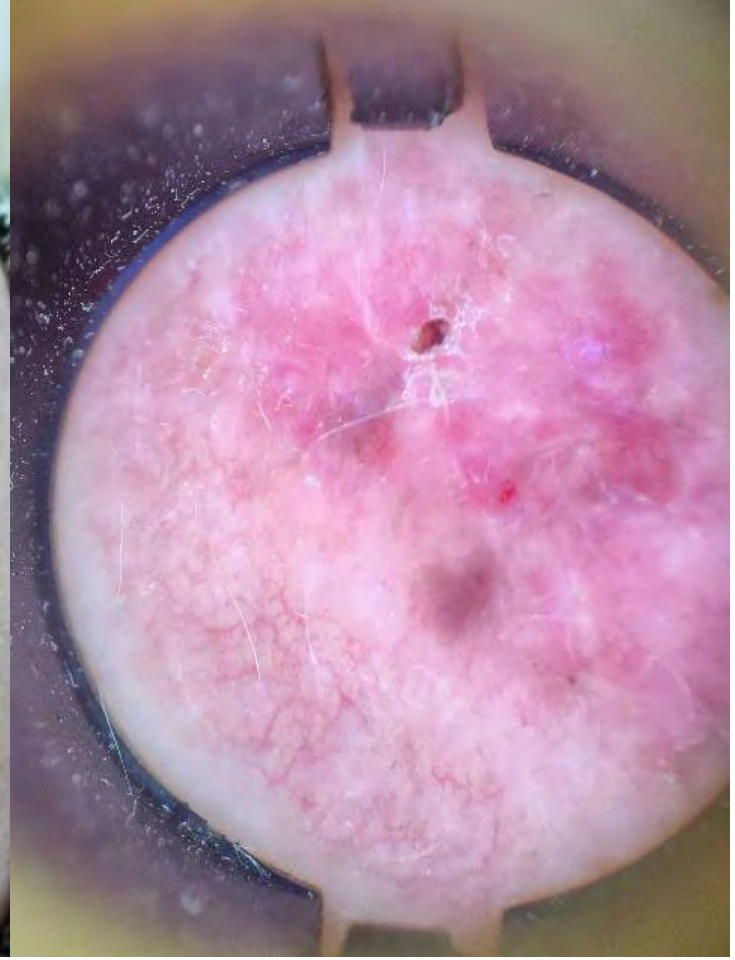
Skin cancerization

2 sessions

1st consultation: lesion in neck
Shave bx
SCCin situ

2 sessions



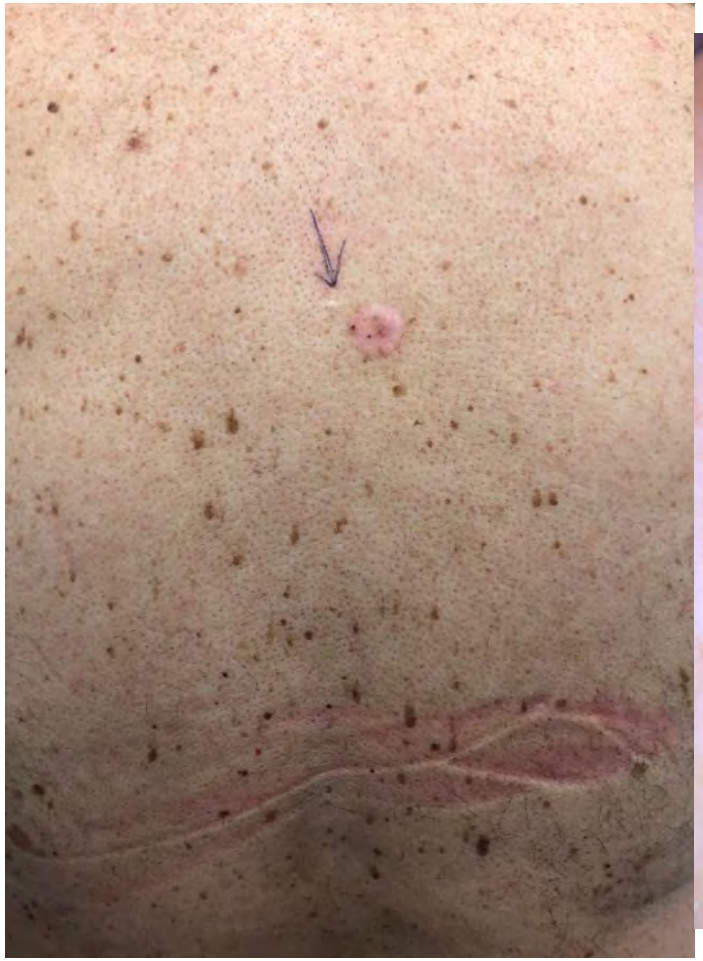


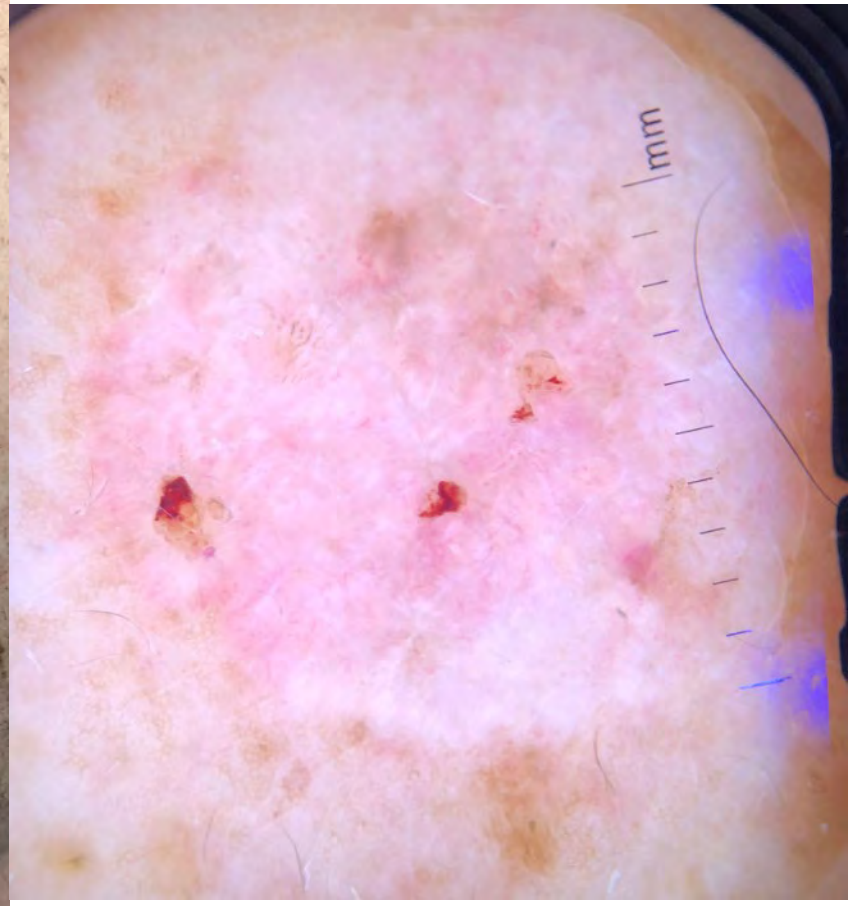
TD
76 yrs
female

Shave biopsy
Family Physician

TD: Superficial BCC

2 PDT





TD
79 yrs
Male

Shave biopsy
Family Physician

TD: Superficial BCC

2 PDT

NURSES AND dPDT

- Initial contact
- Instruct the patient
- Monitor
- Re-schedule

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Daylight-PDT in general practice in the Netherlands

Maartje Spit
Son, Netherlands

Read the abstract

The role of the NP

General practitioner (GP), nurse practitioner (NP) and physician assistant (PA)

- NP and PA are master educated and both provide medical care
- Independent treatment relationship to patient
- Authorised by law to indicate and perform reserved procedures (art. 47 BIG act)
- Authorised to prescribe medications

Added value NP

- NP combines care and cure*
- More time per patiënt
- Medical speciality
- Independence (no supervision by GP)
- Research, education en innovation
- Case

* V&VN VS Working together with the nurse practitioner. Utrecht, 2009

Actinic keratosis in the Netherlands

- People > 45 year are affected;
- Prevalence 28% women and 49% men*
- Number of new AK patients appr. 160.000 /year**
- GP’s are the gatekeepers of care
- Appr. 67 GP’s / 100.000
- Appr. 3 dermatologists / 100.000***
- > 40.000 AK referrals / year ****

* Flohil S. et al, J Invest Dermatol. 2013 Aug;133(8):1971-8.
** Zon MW
*** *Open DIS data 2021: appr. 100.000 AK/y by dermatologist
**** Noels et al. Br J Dermatol 2019;181:96-104.

Agreement: treat AK in general practice

Dutch Guideline for suspected skin lesions (NHG, 2017)*

- Cryotherapy < 5 lesions
- Topical therapy > 5 lesions
- 5-fluoracil (Efudix ®)

- GP’s increased AK treatments since the introduction with 32%**
- Cryotherapy is most used (78%) ***
- Topical agents (<2%)

* Baaten et al, Huisarts Wet 2017;60:276-90. Utrecht, 2017.
** GP scan 2021
*** Noels et al. BR J Derm. 2019:181:96-104

MAL-DL- PDT

- Methylaminolevulinate – cream (Metvix ®)
- Was only available for dermatologists until 2020
- Since 2022 this treatment is enabled for general practice (reimbursed care)
- Pilot in spring/summer 2022
- Appr. 30 PT with AK grade 1-2

Pilot

- Training in our practice
- Teamwork
  - NP: screening, diagnosis and PT education
  - Doctor’s assistance : performed treatment
    - Sunscreen was appplied
    - Keratin was removed
    - Mal was applied
    - After 30 minutes the PT went outside for 2 hours
    - PT removed cream afterwards at home
  - NP: Follow-up after 3 months

Experiences

- involvement local pharmacy
- DA: considered it an appropriate task
- NP: patients were satisfied , barely any side effects
- Patience adherence was no issue
- 3-5 patients responded moderately, therefore a second treatment was proposed

Future

- Implementation DL-PDT in general practice
- Appr. 90% (n=100) GP's finds DL-PDT an interesting option (Lisa Chamberland, 2021)
- This was supported by the study of Charlotte Verhoeven (2022)
- DL-PDT with supervision
- Homebased DL PDT

* Chamberland, L. The feasibility of realizing photodynamic therapy by general practitioners in the primary care for actinic keratosis in the Netherlands. Thesis, Leuven, 2021.
** Verhoeven, C. Optimization of the needs and challenges of general practitioners towards the management of actinic keratosis in primary care. Thesis, Leuven, 2022.

Plenary session 4
PDT outside AK

Chairs: Sally Ibbotson, Colin A. Morton

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Barcelona, Spain
Friday 9 and Saturday 10, June 2023

The Solid Organ Transplant Clinic in Padova: Our 25-Year Experience

Stefano Piaserico
Padova, Italy

Read the abstract

Transplant clinic-Padova

- open every morning, without need to book the visit
- 250 patients visited every month
- more than 4000 OTRs under follow-up

Circulation. 2000 Nov 7;102(19 Suppl 3):III222-7.
Transplantation. 2000 Nov 27;70(10):1479-84.
J Am Acad Dermatol. 2003 Dec;49(6):1020-2.
Arch Dermatol. 2004 Sep;140(9):1079-85.

Skin cancer incidence in OTR compared with the general population

Skin cancer	Increased risk[1-3]
SCC	65–100
SCC of lip	20
BCC	10
Melanoma	2–4
Kaposi's sarcoma	80

[1]Caforio ALP, Belloni Fortina A, Piaserico S, et al. Skin Cancer in Heart Transplant Recipients: Risk Factor Analysis and Relevance of Immunosuppressive Therapy. Circulation 2000; 102: 222-227.
[2]Tessari et al. Incidence and clinical predictors of Kaposi's sarcoma among 1721 Italian solid organ transplant recipients: a multicenter study. *Eur J Dermatol.* 2006;16:1-6.
[3]Belloni-Fortina A, Piaserico S, Tonin E, Alaibac M. Melanoma and immunosuppression. *Dermatology*. 2009;218(1):88

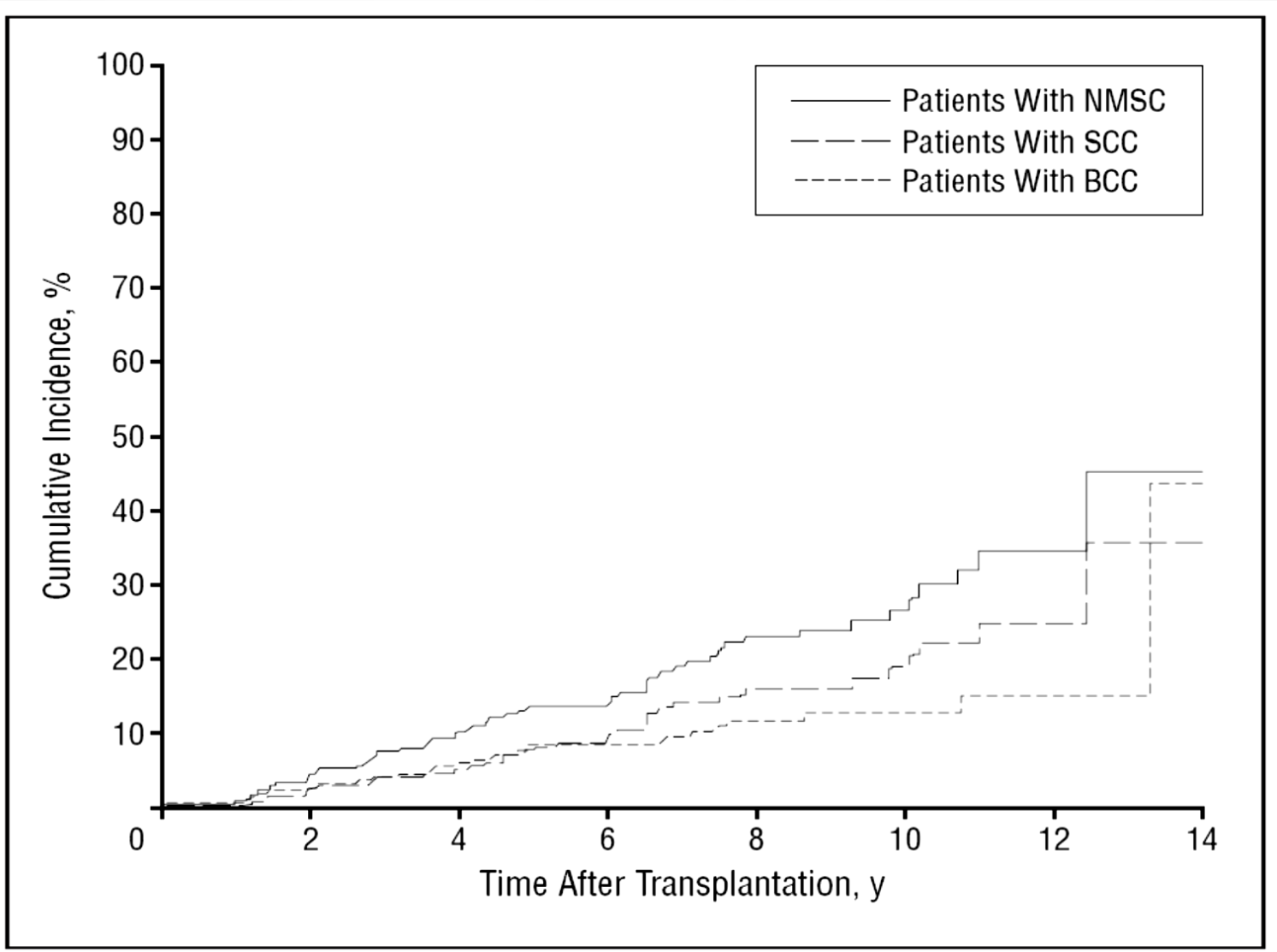


Figure 1. Kaplan-Meier analysis of risk of skin cancer in heart transplant recipients after transplantation. BCC indicates basal cell carcinoma; NMSC, nonmelanoma skin cancer; and SCC, squamous cell carcinoma.

Belloni Fortina A, Piaserico S, Caforio ALP et al. Arch Dermatol. 2004 Sep;140(9):1079-85.

Characteristics of SCC In OTR

- Increased incidence
- Younger age at onset
- Increased aggressiveness:
  - may have more rapid rate of growth
  - increased risk of local recurrences, regional and distant metastasis (up to 8%)
  - increased mortality (27% deaths 4 yrs post-HT in Australia)*

* Ong CS et al. *J Am Acad Dermatol* 1999;30: 27-34.

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Skin Cancer in Heart Transplant Recipients : Risk Factor Analysis and Relevance of Immunosuppressive Therapy

Alida L. P. Caforio, Anna Belloni Fortina, Stefano Piaserico, Mauro Alaibac, Francesco Tona, Giuseppe Feltrin, Esmeralda Pompei, Luca Testolin, Antonio Gambino, Sergio Dalla Volta, Gaetano Thiene, Dino Casarotto and Andrea Peserico

Circulation. 2000;102:Iii-222-Iii-227
doi: 10.1161/01.CIR.102.suppl_3.III-222
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

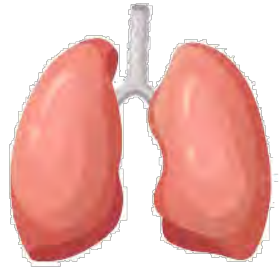
Received: 11 October 2020 | Revised: 24 December 2020 | Accepted: 30 December 2020
DOI: 10.1111/dth.14749

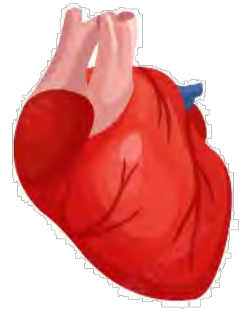
ORIGINAL ARTICLE

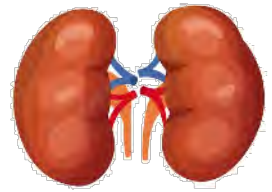
DERMATOLOGIC THERAPY WILEY

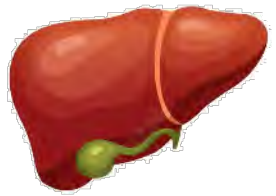
Skin cancers in Italian lung transplant recipients: Incidence and risk factors analysis

Marco Vecchiato[1] | Stefano Piaserico[2] | Giulia Biolo[2] | Anna Chiara Frigo[3] | Monica Loy[4] | Federico Rea[4] | Irene Russo[2] | Mauro Alaibac[2]









HIGHER RISK

STUDY

Immunosuppressive Level and Other Risk Factors for Basal Cell Carcinoma and Squamous Cell Carcinoma in Heart Transplant Recipients

Anna Belloni Fortina, MD; Stefano Piaserico, MD; Alida L. P. Caforio, MD, PhD; Damiano Abeni, MD, MPH; Mauro Alaibac, MD, PhD; Annalisa Angelini, MD; Sabino Iliceto, MD; Andrea Peserico, MD

Arch Dermatol 2004

Skin Cancer in Heart Transplant Recipients: Frequency and Risk Factor Analysis

Anna Belloni Fortina[a], MD, Alida L.P. Caforio, MD, PhD[b], Stefano Piaserico, MD[a], Mauro Alaibac, MD, PhD[a], Francesco Tona, MD[b], Giuseppe Feltrin, MD[c], Ugolino Livi, MD[c], and Andrea Peserico, MD[a]

J Heart Lung Transplant 2000

0041-1337/00/7010-1479/0
TRANSPLANTATION

Vol. 70, 1479–1484, No. 10, November 27, 2000
Printed in U.S.A.

RISK OF NONMELANOMA SKIN CANCER IN ITALIAN ORGAN TRANSPLANT RECIPIENTS. A REGISTRY-BASED STUDY

LUIGI NALDI,[1,8] ANNA BELLONI FORTINA,[2] SILVIA LOVATI,[1] ANNALISA BARBA,[3] ELIANA GOTTI,[4] GIANPAOLO TESSARI,[3] DONATELLA SCHENA,[3] ANDREA DIOCIAIUTI,[5] GIUSEPPE NANNI,[6] ILARIA LESNONI LA PAROLA,[7] CINZIA MASINI,[5] STEFANO PIASERICO,[2] ANDREA PESERICO,[2] TULLIO CAINELLI,[1] GIUSEPPE REMUZZI[4]

Acta Derm Venereol 2012; 92: 411–415

CLINICAL REPORT

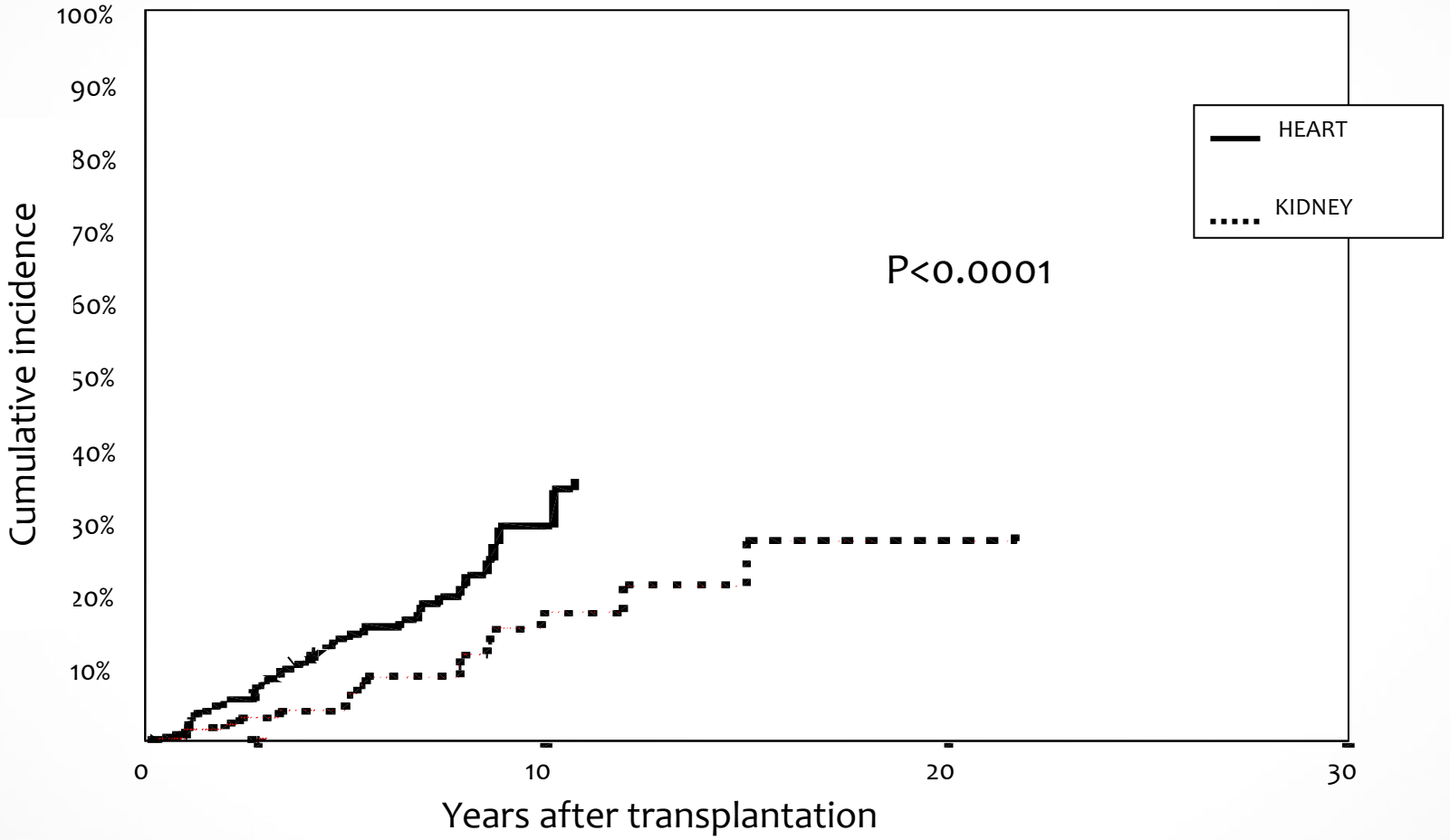
Skin Cancer and Other Cutaneous Disorders in Liver Transplant Recipients

Anna BELLONI-FORTINA[1], Stefano PIASERICO[1], Matteo BORDIGNON[1], Martina GAMBATO[2], Marco SENZOLO[2], Francesco Paolo RUSSO[2], Andrea PESERICO[1], Giuseppe DE MATTEIS[1], Egle PERISSINOTTO[3], Umberto CILLO[4], Alessandro VITALE[5], Mauro ALAIBAC[1] and Patrizia BURRA[2]
[1]Unit of Dermatology, [2]Unit of Gastroenterology, [3]Environmental Medicine and Public Health Department, Biostatistics Unit, and [4]Hepatobiliary and Liver Transplant Unit, University of Padua, and [5]Unità di Chirurgia Oncologica, Istituto Oncologico Veneto, IRCCS, Padova, Italy

SHARED WITH THE GENERAL POPULATION		SPECIFIC FOR ORGAN TRANSPLANT PATIENTS
Enviromental	*Genetic*	
Age	Ethnicity	Length and level of immunosuppression
Latitude	Skin type	Pre-transplant history of SCC
Chronic sunlight exposure	Eyes color	Polycystic kidney disease
(HPV infection)	Hairs color	Primary sclerosing cholangitis
(Smoking)	(Male sex)	Voriconazole
	(HLA-A11)	
	(p53 gene polymorphism)	
	(IL-10 gene promoter polymorphism)	
	(GST gene polymorphism)	

Caforio AL, Fortina AB, Piaserico S, et al. Circulation. 2000
Belloni Fortina A, Caforio ALP, Piaserico S. J Heart Lung Transplant 2000
Belloni Fortina A, Piaserico S, Caforio ADL et al. Arch Dermatol. 2004

Cumulative incidence of non-melanoma skin cancer



Belloni Fortina A, Caforio ALP, Piaserico S, Alaibac M. *J Heart Lung Transplant* 2000;19:249-255

TREATMENT

- Treat AKs aggressively
  - LN2, topicals, PDT
- Treat SCC with usual methods more aggressively applied
- Special issues:
  - Reduction of Immunosuppression
  - Swith to mTOR inhibitors
  - Retinoid Chemoprevention

- Multidisciplinary approach
- Dedicated transplant dermatology clinics
- Trained transplant dermatologists
- Patients need to be educated on self-examination and counseled on sun protection (remember UVA)

Recommended follow-up intervals for OTR (personal opinion)

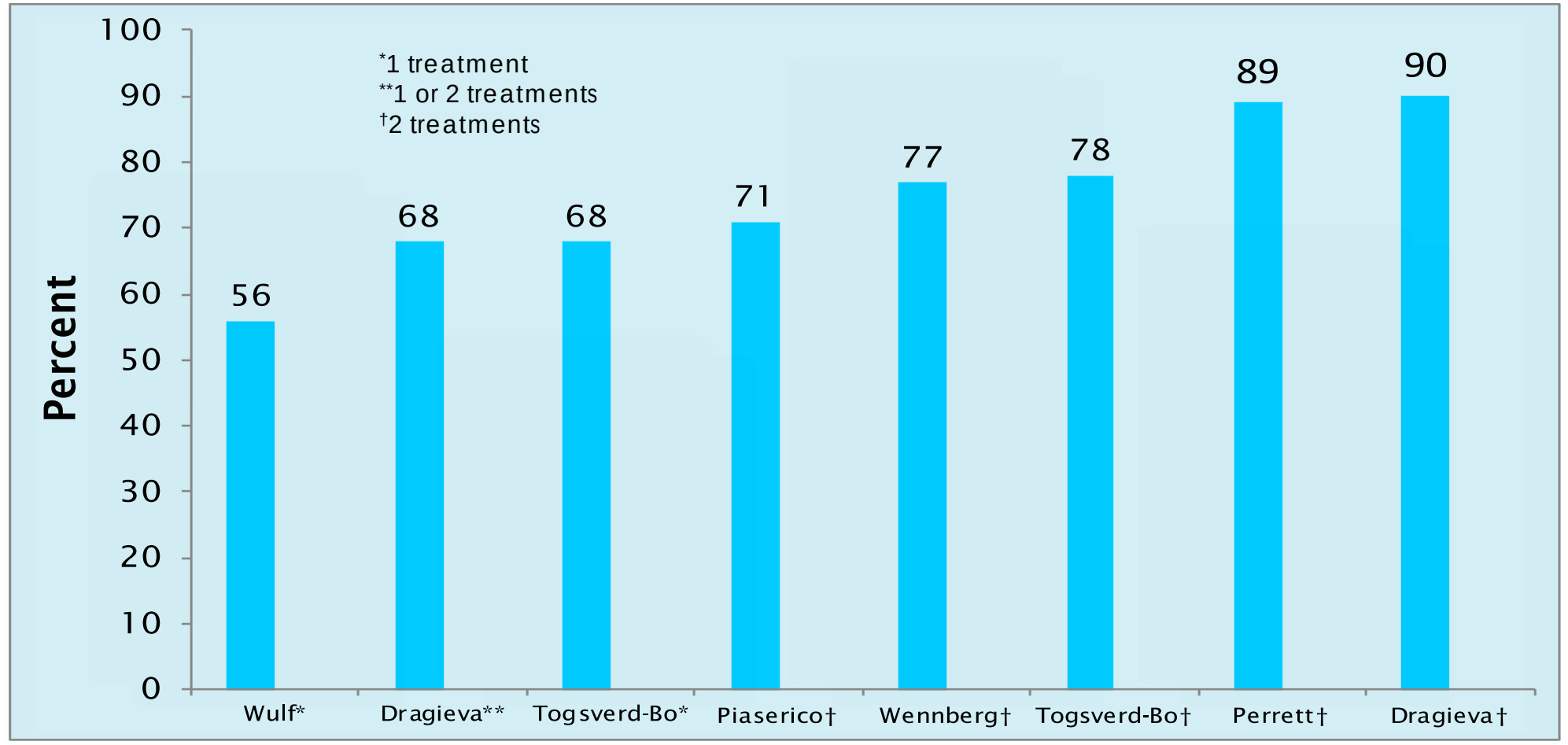
Type of patient	Interval for dermatological examination (months)
No skin cancer/field disease	12
Field disease OR 1 skin cancer	3-6
Multiple skin cancers	1-2

Clinical trials with acitretin in OTR

Study	Design and dose	Length of study	Results
Bavinck et al[23]	RCT (n =38); 30 mg/day	6 months	Statistically significant fewer patients with new SCCs
McKenna et al[26]	NCG (n = 16); 0.3 mg/kg/day	5 years	Statistically significant reduction of new SCCs after 5 years compared to pretreatment period
George et al[27]	RCT (n = 23); 25 mg/day	2 years	No. of SCCs significantly lower on acitretin compared to drug-free period
Harwood et al[24]	Retrospective study; 0.2-0.4 mg/kg/day	1-16 years	Significant reduction in SCCs sustained for at least 8 years

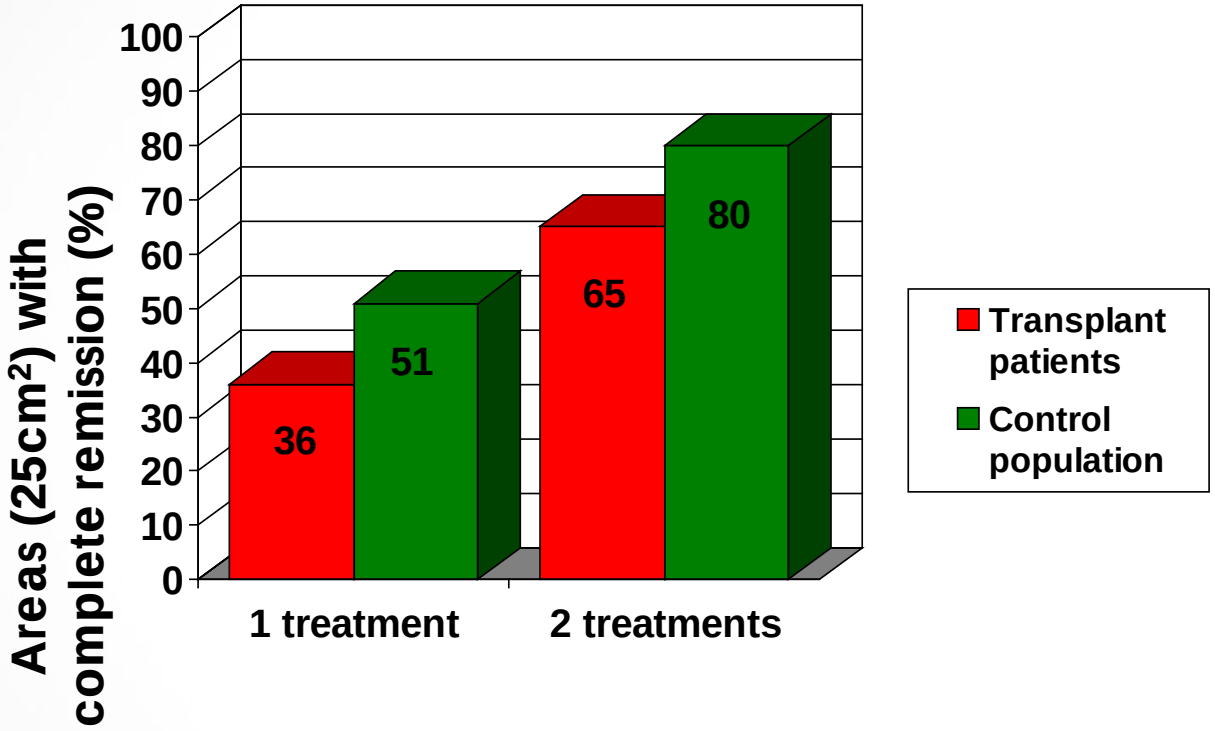
O'Really et al. *J Am Acad Dermatol.* 2011;65: 263.

PDT in OTRs:
Complete response rate at 3–6 months



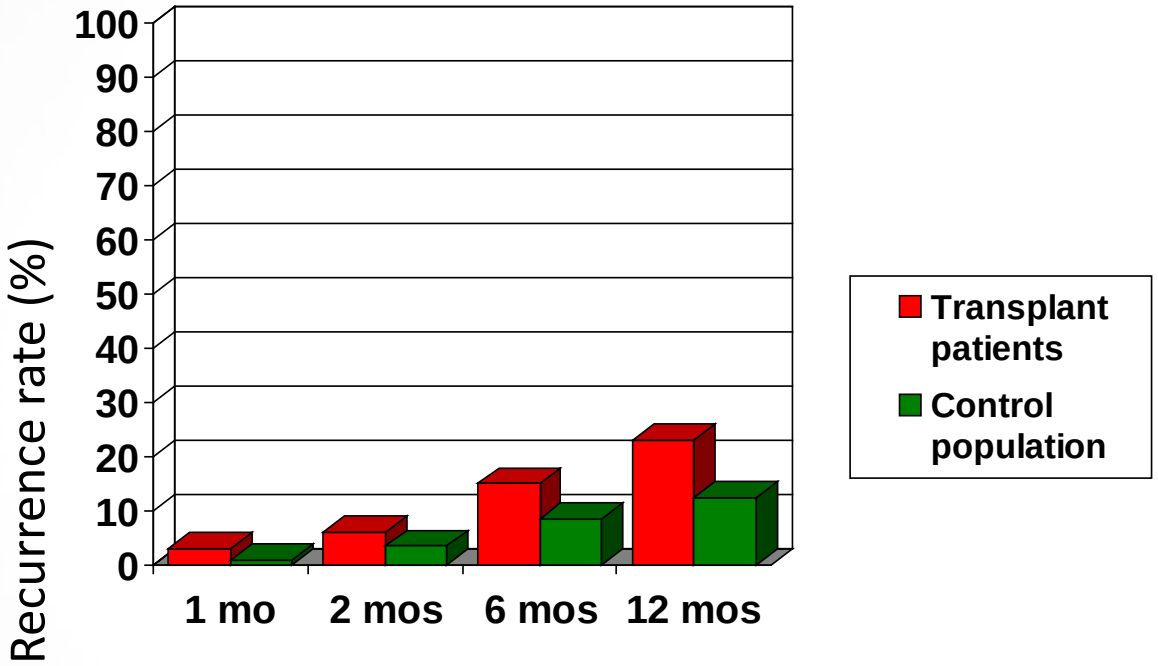
Wulf H. Acta Derm Venereol 2006;86:25-8. Dragieva G.Transplantation 2004;77:115-21. Piaserico S. Transplant Proc 2007;39:1847-50. Wennberg AM. Transplantation 2008;86:423-9. Perret CM. Br J Dermatol 2007;156:320-8. Dragieva G. Br J Dermatol 2004;151:196-200 Togsverd-Bo Br J Dermatol 2018

Efficacy compared with immunocompetent patients



Piaserico S. Transplant Proc 2007;39:1847-50

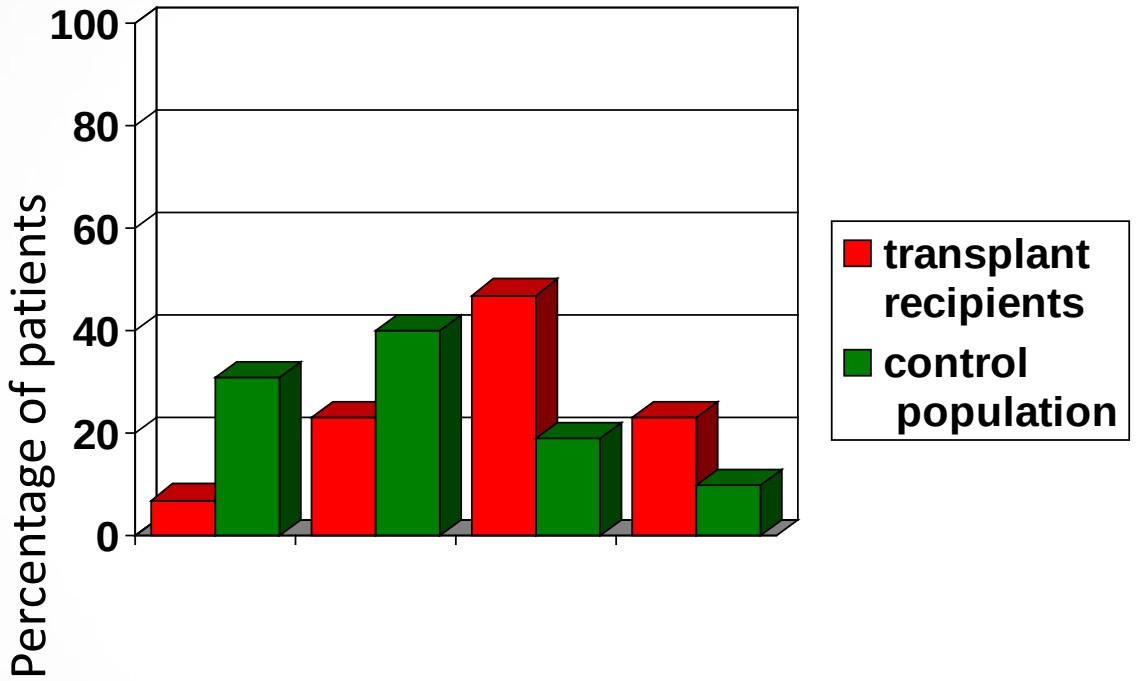
Relapses in the treated areas



p <0.05

Follow-up

Reported pain-AK



p <0.01

Mild (0-3)

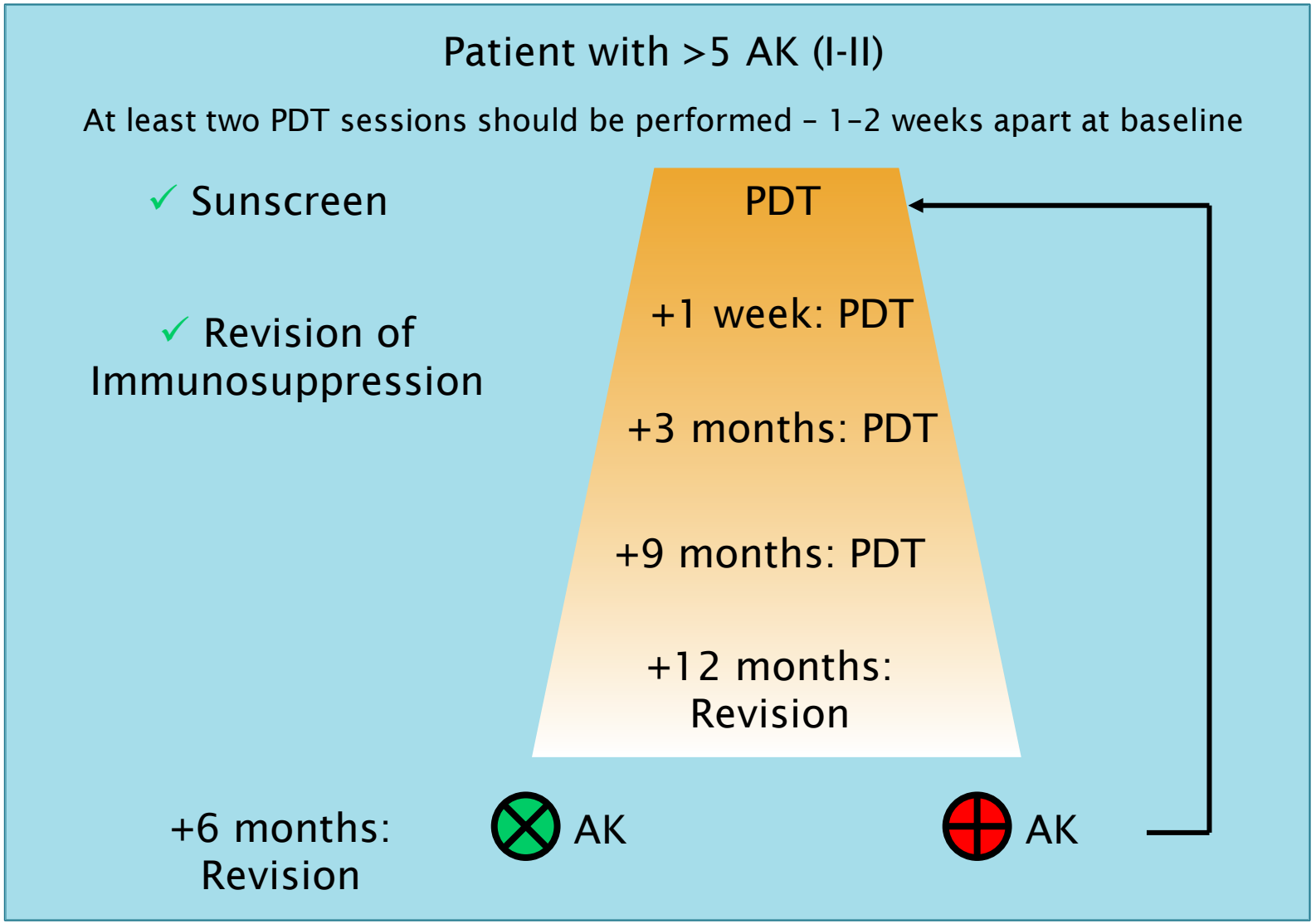
Moderate (4-5)

Severe (6-8)

Intoler. (9-10)

VAS

Suggested treatment protocol



Photodynamic therapy for actinic keratosis in organ transplant patients.
Basset-Seguin N, Baumann Conzett K, Gerritsen MJ, Gonzalez H, Haedersdal M, Hofbauer GF, Aguado L, Kerob D, Lear JT, Piaserico S, Ulrich C. J Eur Acad Dermatol Venereol. 2013 Jan;27(1):57-66.

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THE EUROPEAN SOCIETY FOR PHOTODYNAMIC THERAPY

Barcelona, Spain
Friday 9 and Saturday 10, June 2023

PDT as Treatment Option for Cutaneous Lymphoma

Stefano Caccavale
Naples, Italy

Read the abstract

PRIMARY CUTANEOUS T-CELL LYMPHOMAS

(INDOLENT clinical behavior)

WHO-EORTC CLASSIFICATION	FREQUENCY (%)	5-YEAR SURVIVAL RATE (%)
MYCOSIS FUNGOIDES (MF)	54	88
- FOLLICULOTROPIC MF	6	80
- PAGETOID RETICULOSIS	1	100
- GRANULOMATOUS SLACK SKIN	<1	100
PRIMARY CUTANEOUS CD30+ LYMPHOPROLIFERATIVE DISORDERS		
- PRIMARY CUTANEOUS ANAPLASTIC LARGE CELL LYMPHOMA (C-ALCL)	10	95
- LYMPHOMATOID PAPULOSIS (LyP)	16	100
SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA (SPTCL)	1	82
PRIMARY CUTANEOUS CD-4 POSITIVE SMALL/MEDIUM PLEOMORPHIC T-CELL LYMPHOMA	3	75

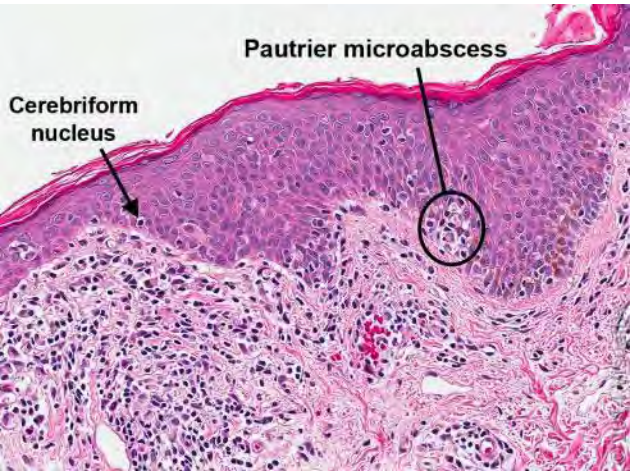
PRIMARY CUTANEOUS T-CELL LYMPHOMAS

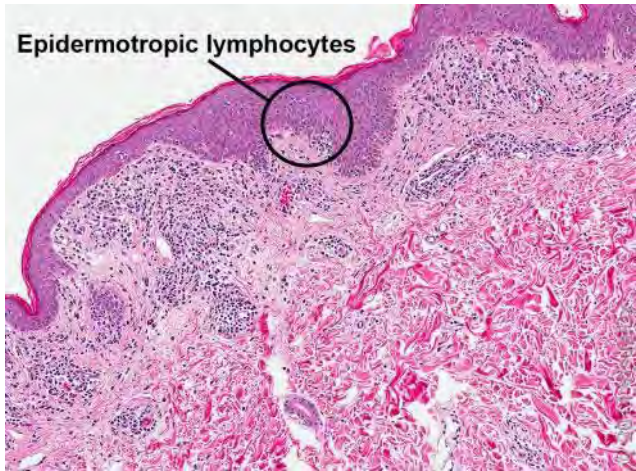
(AGGRESSIVE clinical behavior)

WHO-EORTC CLASSIFICATION	FREQUENCY (%)	5-YEAR SURVIVAL RATE (%)
SEZARY SYNDROME (SS)	4	24
ADULT T-CELL LEUKEMIA/LYMPHOMA (ATLL)	NDA	NDA
EXTRANODAL NK/T-CELL LYMPHOMA, NASAL TYPE	1	<5
PRIMARY CUTANEOUS CD8-POSITIVE AGGRESSIVE EPIDERMOTROPIC CYTOTOXIC T-CELL LYMPHOMA	<1	18
PRIMARY CUTANEOUS GAMMA/DELTA T-CELL LYMPHOMA (PCGD-TCL)	1	<5
PRIMARY CUTANEOUS PERIPHERAL T-CELL LYMPHOMA (PTCL), UNSPECIFIED	3	16

MYCOSIS FUNGOIDES (MF)

- annual incidence of 0.3–0.5 new cases per 100,000 inhabitants
- more predominant in males and in the elderly, even though patients of all ages (children and adolescents too) may be affected
- originates from skin-homing CD4+ T cells
- its etiology is still unknown, and the identification of genetic mutations and environmental factors requires further studies





- CTCL are usually treated with a **multimodal approach**
- All treatments may lead to **acute or chronic adverse effects** and **long-term toxicities** that may be particularly relevant if repeated or protracted treatment schemes would be necessary
- The selection of appropriate treatments for MF is fundamental and is based on the **clinical stage** at diagnosis and patient **prognosis** and **comorbidities**

SKIN DIRECTED

- Topical corticosteroids
- Topical chemotherapy
  - Nitrogen mustard (*Mustargen*)
  - Carmustine (*BCNU*)
- Topical retinoids
  - Bexarotene gel (*Targretin gel*)
- Phototherapy
  - Narrow-band UVB (NBUVB)
  - Psoralen with UVA (PUVA)
- Radiation therapy
  - Total-skin electron beam therapy (TSEBT)
  - Site-directed radiation

SYSTEMIC

- Vorinostat (ZOLINZA™)
- Bexarotene capsules (*Targretin*)
- Denileukin diftitox (*Ontak*)
- Alemtuzumab (*Campath*)
- Interferon-α

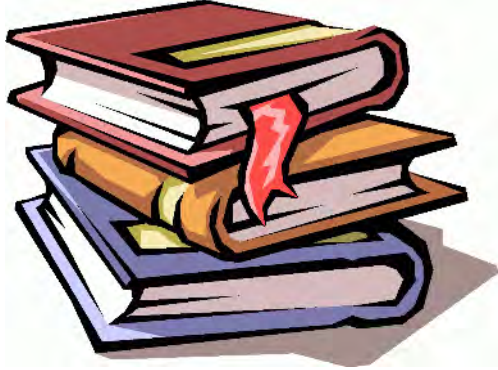
- Extracorporeal photochemotherapy

Chemotherapy_single agent

- Chlorambucil (*Leukeran*)
- Cladribine
- Fludarabine (*Fludara*)
- Methotrexate
- Gemcitabine (*Gemzar*)
- Pegylated doxorubicin (*Doxil*)
- Pentostatin (*Nipent*)

Combination chemotherapies

- CHOP
- ESHAP
- EPOCH



- Among all these therapies, clinical success was reported in the last decades using **PDT** to treat MF, in particular for its efficacy and its tolerability

- The first case using ALA-PDT for the treatment of MF lesions was reported in **1994**

- Many case reports of successful PDT for MF have been published

Wolf, P.; Fink-Puches, R.; Cerroni, L.; Kerl, H. Photodynamic therapy for mycosis fungoides after topical photosensitization with 5-aminolevulinic acid. J. Am. Acad. Dermatol. 1994, 31, 678–680.

Investigator	Type of MF	Number of patients/lesions	Lesion type	Previous treatments	Photosensitizer/occlusion time (h)	Light (nm)/ light doses (J/cm^2)	Number of PDT sessions	Complete Response (%)	Follow-up (mo)
Dairi et al	MF, FMF	4/4	Plaque	Clobetasol	16% MAL/3	630/37	4-12 AFL-PDT	4/4 (100%)	6-18
Debu et al	FMF	3/8	Plaque/1Patch	NM	16.8% MAL/3	630/37	1-7	7/8 (88%)	12-28
Pileri et al	MF	4/4	Patch	PUVA and acitretin, topical and systemic steroids, nbUVB	16% MAL/3	630/37	4-9	2/4 (50%) and 2/4 PR (50%)	6-120
Jung et al	Localized pagetoid reticulosis	1/1	Plaque	Eight treatment sessions with a 308-nm excimer laser	16% MAL/1.5	630/37	8 AFL-PDT	1/1 (100)	NM
Jang et al	MF	1/1	Patch	Topical steroids	MAL cream/4	570-670/37	2	1/1 (100%)	NM
Calzavara-Pinton et al	MF	19/19	Plaque	NM	16% MAL/3-4	635±18/37	1-7	5/19 (26%); 2 patients relapsed at follow-up	10.0±10.5
Quereux et al	MF	12/29	Patch, Plaque	HN2, BCNU, nbUVB, Rx, imiquimod, PUVA, systemic bexarotene, interferon	20% MAL/3	630/37	2-6	6/12 (50%) and 3/12 PR (25%)	6-35
Han et al	MF	3/3	Plaque	PUVA, interferon	20% ALA solution/4	635/60nw/cm^2	2-3	2/3 (66.7%) and 1/3 PR (33.3%)	8-17
Kim et al	MF	10/10	Plaque, Patch	UVA1, acitretin, PUVA, topical steroids	16.8% MAL/3	630/37.5	2-6	5/10 (50%) and 2/10 PR (20%)	8-31
Kaufmann et al	MF	1/1	Patch	Topical steroids and topical immunomodulators	20% ALA/	Cooled LED-based PDT device	8	1/1 (100%)	48
Hasson et al	MF	1/1	Tumor	PUVA, bexarotene, TSEBI	16% MAL/3	Incoherent light, 570-670 nm/37J/cm^2/ 70 Mw/cm^2	3	1/1 (100%)	60
Juan-Carpena et al	MF	1/1	Plaque	Topical corticosteroids, oral acitretin, PUVA, oral methotrexate and interferon, imiquimod, HN2	16% MAL/NM	630/37 (c-PDT on palms) and DL-PDT (soles)	6 c-PDT (palms) and 8 DL-PDT (soles)	4/4 (100%)	12

PDT EFFECTIVENESS ON MF

- In a systematic review, the effectiveness of PDT on MF across 24 eligible studies, published between 1994 and 2017, was estimated as an **overall pooled response of 69.5%**

Seyed Jafari, S.M.; Cazzaniga, S.; Hunger, R.E. Photodynamic therapy as an alternative treatment for mycosis fungoides: A systemic review and meta-analysis. G. Ital. Dermatol. Venereol. 2018, 153, 827–832.

- Another systematic review obtained an **overall complete response (CR) rate of the lesions of 63.2%** (60.9% in plaques, 72.2% in patches, and 71.4% in tumors)

Xue, J.; Liu, C.; Liu, Y. Photodynamic therapy as an alternative treatment for relapsed or refractory mycosis fungoides: A systemic review. Photodiagn. Photodyn. Ther. 2017, 17, 87–91.

- A recent systematic review that selectively focused on stage IA MF reported a **CR in 67.3%, a partial response (PR) in 13.5%, and no response** (NR, defined as <50% clinical response) in 3.8% of patients. Stable disease (SD) was reported in 3.8% of cases and non-available (NA) clinical response data in 11.5%

Hooper, M.; Hatch, L.; Seminario-Vidal, L. Photodynamic therapy of mycosis fungoides: A systematic review of case studies. Photodermatol. Photoimmunol. Photomed. 2021, 37, 549–552.

MECHANISMS OF PDT EFFICACY ON MF

- How PDT works in treating MF is **poorly understood** because the contribution to neoplastic cell death and the role of inflammatory cells in the response has not been elucidated. Proliferating tumor cells are certainly more susceptible to photosensitizers
- PpIX production is probably increased in highly proliferating tissues, such as CTCL, by **changes in the cellular enzyme activity**, leading to a strong reduction in the malignant cells number and the suppression of proliferation
- PDT seems to have a direct potential for the induction of toxicity in T cells. In 2001, Gad et al. demonstrated an **increase in caspase-3-like activities and an increase in the DNA fragmentation** in malignant T cells following PDT

Xue, J.; Liu, C.; Liu, Y. Photodynamic therapy as an alternative treatment for relapsed or refractory mycosis fungoides: A systemic review. Photodiagn. Photodyn. Ther. 2017, 17, 87–91.
Rittenhouse-Diakun, K.; Van Leengoed, H.; Morgan, J.; Hryhorenko, E.; Paszkiewicz, G.; Whitaker, J.E.; Oseroff, A.R. The role of transferrin receptor (CD71) in photodynamic therapy of activated and malignant lymphocytes using the heme precursor delta-aminolevulinic acid (ALA). Photochem. Photobiol. 1995, 61, 523–528.
Gad, F.; Viau, G.; Boushira, M.; Bertrand, R.; Bissonnette, R. Photodynamic therapy with 5-aminolevulinic acid induces apoptosis and caspase activation in malignant T cells. J. Cutan. Med. Surg. 2001, 5, 8–13. [

TOTAL NUMBER OF PDT SESSIONS AND THE TIME INTERVAL

- Certainly, PDT needs more sessions to be successful in treating MF
- The total number of PDT sessions and the time interval between two treatment sessions in the literature is very variable for MF (**1 to 14 treatments**), because established treatment protocols have not yet been optimized
- A mean number of **9.5** was reported in a recent systematic review (**range 1–46**)
- The frequency of sessions is about every **1 to 8 weeks** in the literature

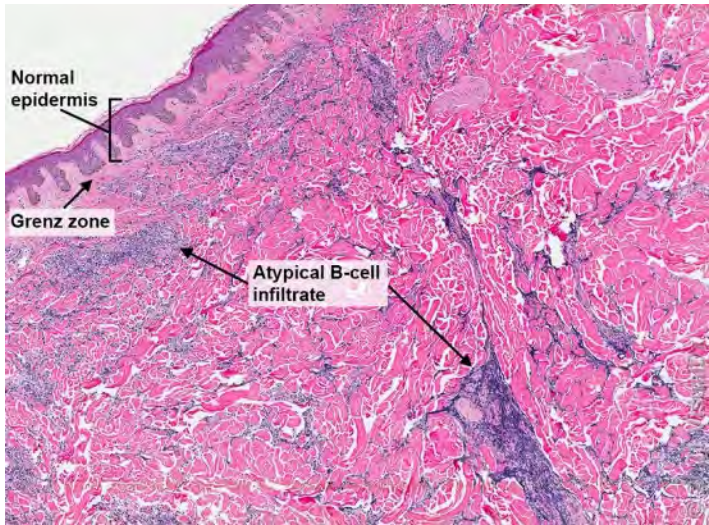
Hooper, M.; Hatch, L.; Seminario-Vidal, L. Photodynamic therapy of mycosis fungoides: A systematic review of case studies. Photodermatol. Photoimmunol. Photomed. 2021, 37, 549–552.

Seyed Jafari, S.M.; Cazzaniga, S.; Hunger, R.E. Photodynamic therapy as an alternative treatment for mycosis fungoides: A systemic review and meta-analysis. G. Ital. Dermatol. Venereol. 2018, 153, 827–832.

- PRIMARY CUTANEOUS T-CELL LYMPHOMAS
- **PRIMARY CUTANEOUS B-CELL LYMPHOMAS**
- CUTANEOUS PSEUDOLYMPHOMAS

PRIMARY CUTANEOUS B-CELL LYMPHOMAS

- heterogeneous group of extranodal B-cell non-Hodgkin lymphomas, which primarily involve the skin without evidence of extracutaneous disease at the onset
- their incidence has increased in the last years and currently is about four cases for one million people
- middle age of onset >50 years



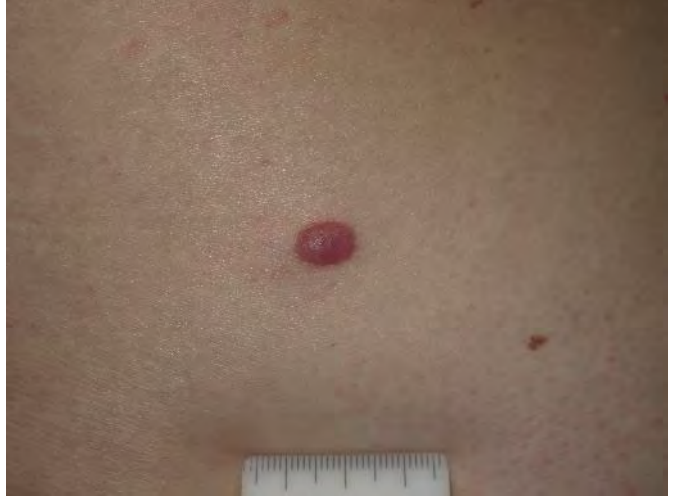
Vitiello, P.; Sica, A.; Ronchi, A.; Caccavale, S.; Franco, R.; Argenziano, G. Primary Cutaneous B-Cell Lymphomas: An Update. Front. Oncol. **2020**, 10, 651

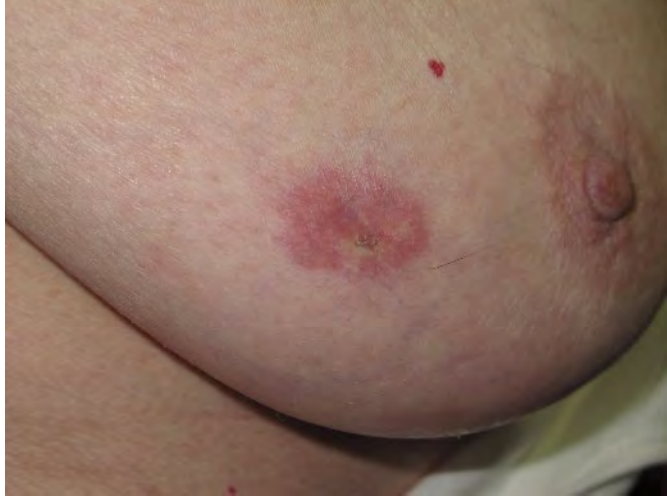
- The three major subtypes are (WHO 2017):

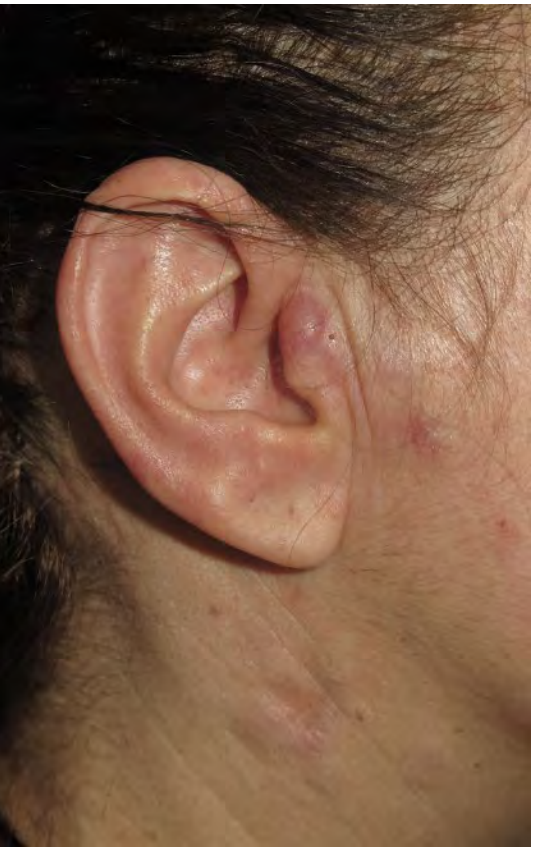
1. primary cutaneous marginal zone lymphoma (PCMZL)
2. primary cutaneous follicle center lymphoma (PCFCL)
3. diffuse large B-cell lymphoma, leg type (PCDLBCL, LT)

Goyal, A.; LeBlanc, R.E.; Carter, J.B. Cutaneous B-Cell Lymphoma. Hematol. Oncol. Clin. N. Am. **2019**, 33, 149–161.

PCFCL and PCMZL



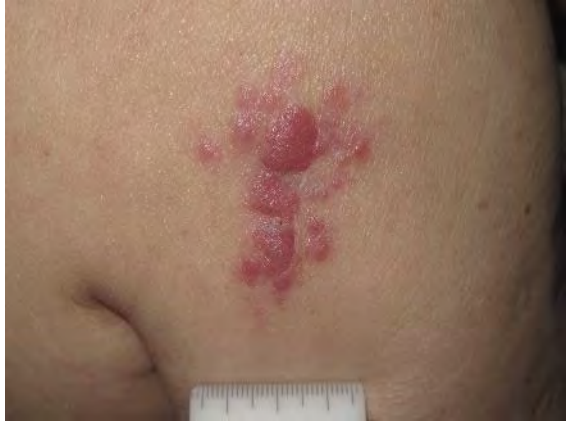




- For both PCFCL and PCMZL, an extracutaneous involvement is very rare, and the **overall prognosis is excellent** (5-year survival rate > 95%)
- The therapeutic approaches are similar for these two variants of CBCL and depend on the number of lesions, the age and compliance of each patient, the presence of a systemic lymphoma or negative prognostic factors, comorbidities, and so on
- Usually, **surgical excision**, when the number of lesions is limited, and **radiotherapy** (RT) represent the gold standard, with a high rate of response
- Despite effective treatments, **about 25% of cases have relapses**
- Many therapies have been proposed, including imiquimod, cryotherapy, topical and intralesional steroids, the antiCD20 monoclonal antibody, chemotherapy

Wilcox, R.A. Cutaneous B-cell lymphomas: 2019 update on diagnosis, risk stratification, and management. Am. J. Hematol. **2018**, 93, 1427–1430.

PDT AND CBCL



- **Rarely, off-label PDT has been used for low-grade CBCL treatment**
- Within all the literature currently available on Pubmed, there is only a pilot study published in 2006

Mori, M.; Campolmi, P.; Mavilia, L.; Rossi, R.; Cappugi, P.; Pimpinelli, N. Topical photodynamic therapy for primary cutaneous B-cell lymphoma: A pilot study. J. Am. Acad. Dermatol. 2006, 54, 524–526.

Patient no.	Age (y)/sex	Disease/stage	Previous tx	PDT sessions	Photosensitizer	Results	Follow-up (mo)
1	62/F	CBCL (FCL)	None	1	ALA	CR	17
2	38/F	CBCL (MZL)	None	1	Metvix	CR	8
3	56/M	CBCL (MZL)	RT	2	ALA	CR	24

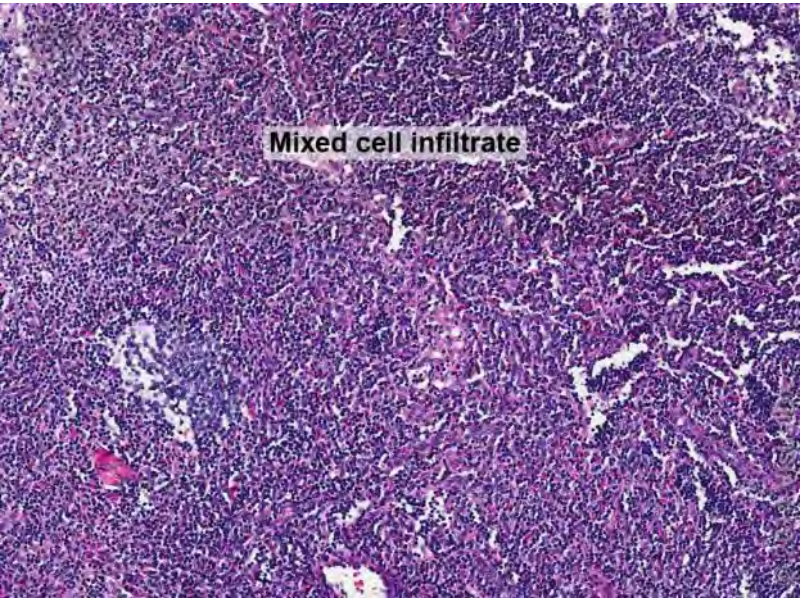
ALA, Aminolevulinic acid 20%, oil-in-water emulsion; *CBCL*, cutaneous B-cell lymphoma; *CR*, complete response; *FCL*, follicle center lymphoma; *Metvix*, methyl ester of ALA; *MZL*, marginal zone lymphoma; *PDT*, photodynamic therapy; *RT*, orthovolt radiotherapy (20 Gy); *tx*, therapy.

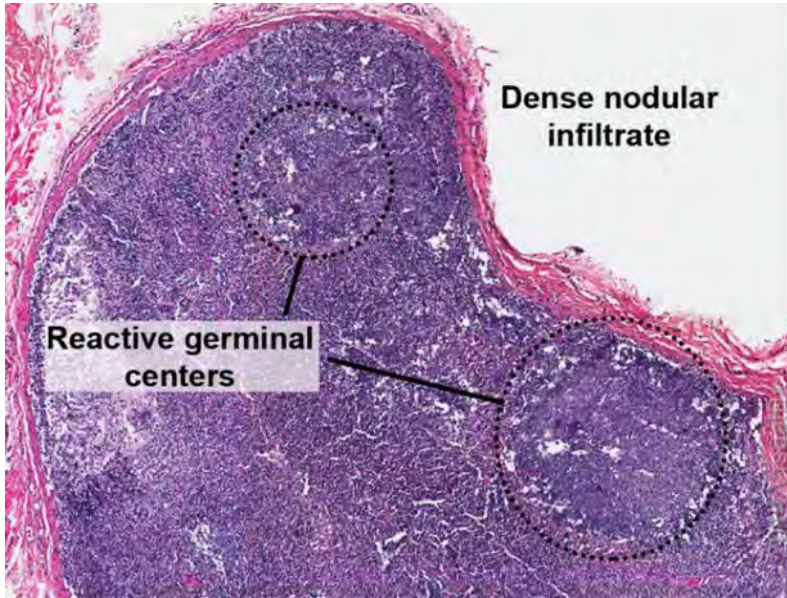
- 4-h occlusion time; 630 nm wavelength light, emitted by a diode lamp; fluence of 37 J/cm2
- All patients had complete remission after a maximum of two PDT sessions at a 1-week interval
- No patient experienced particular side effects, and the pain was easily managed after the PDT sessions

- PRIMARY CUTANEOUS T-CELL LYMPHOMAS
- PRIMARY CUTANEOUS B-CELL LYMPHOMAS
- **CUTANEOUS PSEUDOLYMPHOMAS**

CUTANEOUS PSEUDOLYMPHOMAS (CPL)

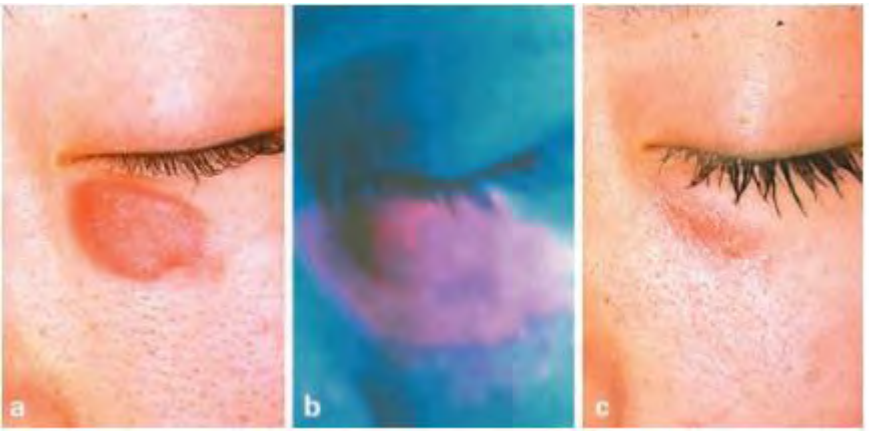
- cutaneous benign entities characterized by a diffuse lymphocytic proliferation that histologically and often clinically resembles a real cutaneous lymphoma
- divided into B-cell CPL and T-cell CPL, if they resemble, respectively, a B or T lymphoma

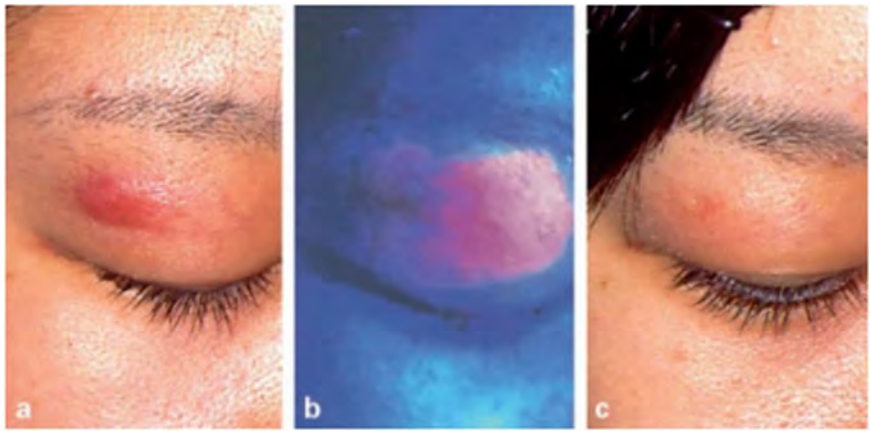




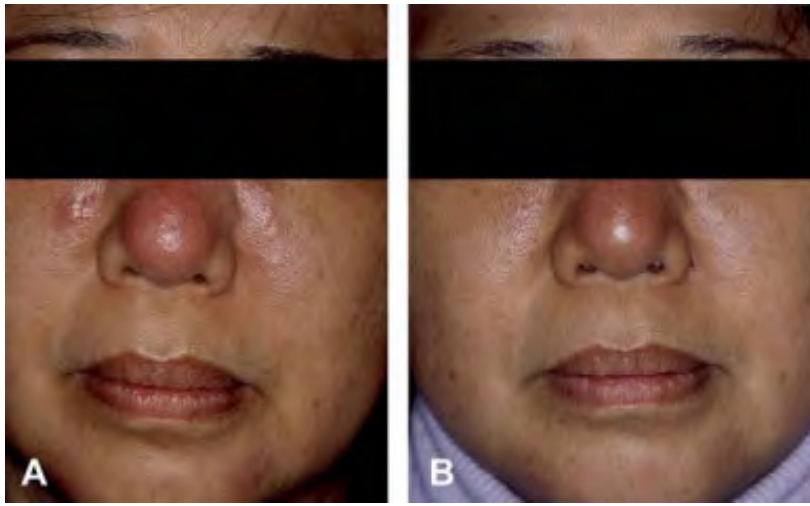
- Takeda et al., in 2005, treated two patients affected by lymphadenosis benigna cutis of the face with PDT (ALA 20%, oil–water emulsion, applied with an occlusion medication protected by the light for 4–6 h, irradiated with visible light, peak 630 nm, for 15–20 min, 120 J/cm2, repeated for five sessions, every two weeks)

Takeda H, Kaneko T, Harada K, Matsuzaki Y, Nakano H, Hanada K. Successful treatment of lymphadenosis benigna cutis with topical photodynamic therapy with delta-aminolevulinic acid. Dermatology. 2005;211(3):264-6.

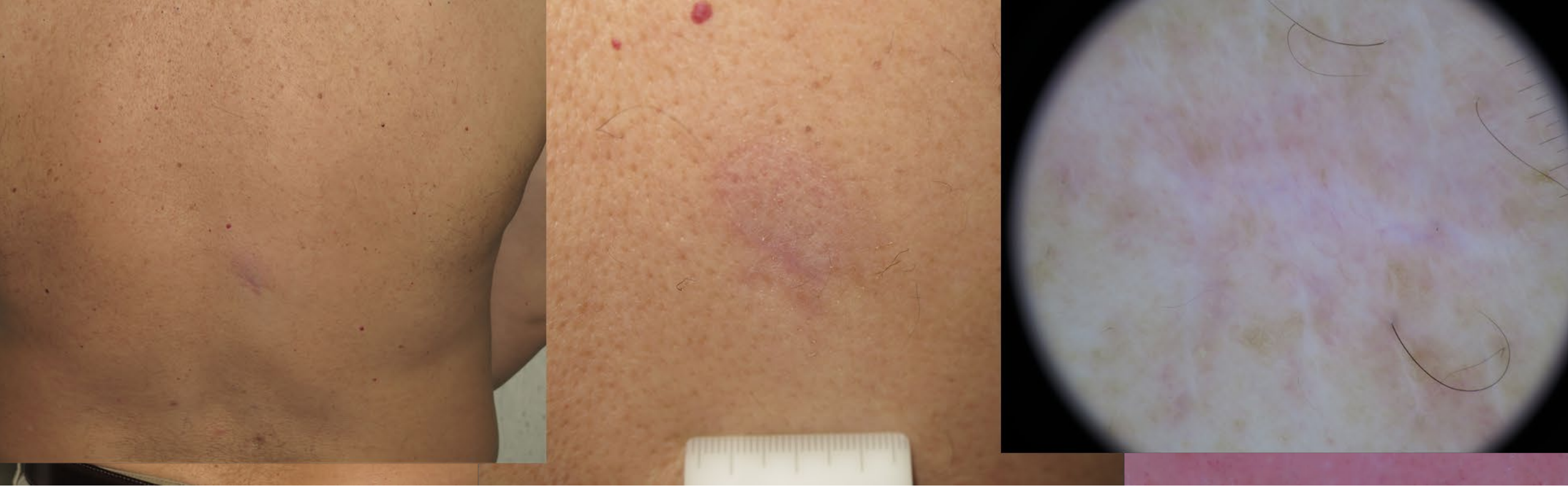




- Mikasa et al., in 2005, published a case report on the use of 20%-ALA-PDT in a 51-year-old female patient with two B-cell CPLs localized on her right cheek and nose
- 4–6 h of an occlusion medication; irradiated by using an excimer dye laser, pulsed 630 nm artificial visible light, 100 J/cm2
- irradiated 3 times (cheek) and 5 times (nose)
- the clinical results were remarkable
- the patient refused a control punch biopsy



Mikasa K, Watanabe D, Kondo C, Tamada Y, Matsumoto Y. Topical 5-aminolevulinic acid-based photodynamic therapy for the treatment of a patient with cutaneous pseudolymphoma. J Am Acad Dermatol. 2005 Nov;53(5):911-2.



- In 2020, our group published a case of CPL in a 50-year-old patient treated with MAL-PDT
- 3 h of occlusion without light exposition; artificial red light of 630 nm was administrated, 100 J/cm2
- The treatment was repeated every 3 weeks for three sessions
- A complete response was obtained, and our patient was disease free after 24 months of follow-up

CONCLUSIONS

- **PDT confirms itself as a safe and effective treatment for CL and CPL**
- identifying the stage of the disease and the type of lesions is of crucial importance to decide which patients can benefit from PDT
- **PDT use should not be preferred in the case of thick, multiple and widespread lesions**, especially when it could be difficult or impossible to include all of them in a few illumination fields
- **further RCT involving a greater number of patients and centers with a long follow-up are necessary** to assess the efficacy of PDT and establish a unique standardized treatment protocol

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Barcelona, Spain
Friday 9 and Saturday 10, June 2023

PDT for Acne & Rosacea

Elena Sotiriou
Thessaloniki, Greece

Read the abstract

PDT: mechanism of action in acne

PDT inhibits multiple acne pathogenetic factors

PDT action modes include:

Transient antimicrobial & antiinflammatory effects

Atrophy/destruction of sebaceous glands

Reduction of follicular obstruction & hyperkeratosis

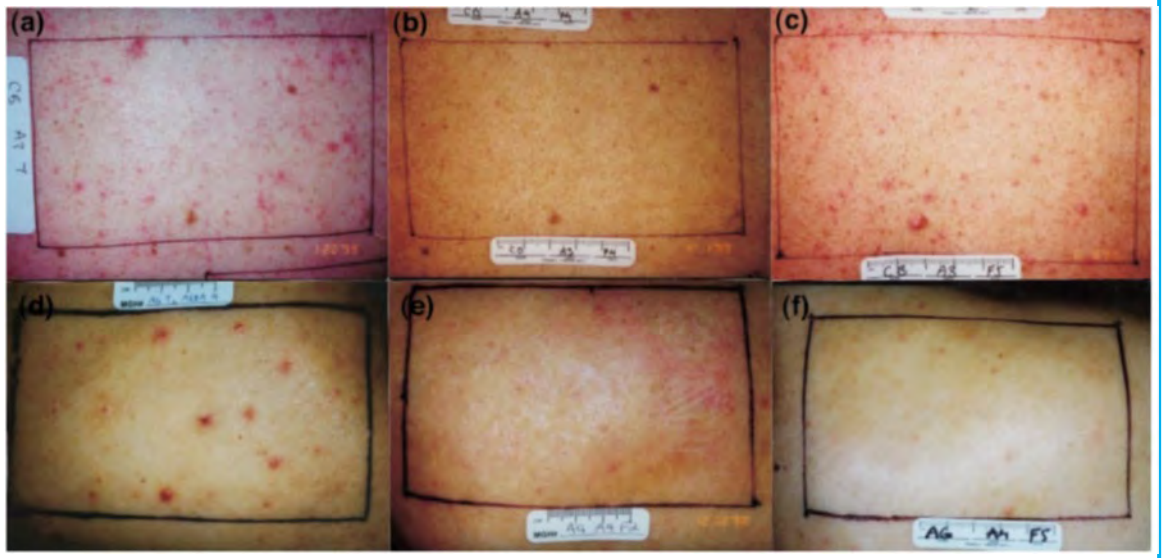
Topical ALA-Photodynamic Therapy for the Treatment of Acne Vulgaris

Wichai Hongcharu, Charles R. Taylor, Yuchiao Chang,* David Aghassi, Kittisak Suthamjariya, and R. Rox Anderson

Massachusetts General Hospital, Wellman Laboratories of Photomedicine, Departments of Dermatology and *Medicine, Harvard Medical School, Boston, Massachusetts, U.S.A.

THE JOURNAL OF INVESTIGATIVE DERMATOLOGY

- Broad-band red light, 150 J/cm²
- 20% ALA, 3 hours occlusion
- One vs multiple treatments



➢Significant clearance of inflammatory acne for 20 weeks after multiple sessions & for 10 weeks after a single session.

➢Sebum excretion was abruptly inhibited, then slowly & partially recovered by week 20

Systematic reviews

- Photodynamic therapy for the treatment of different severity of acne: A systematic review Photodiagnosis Photodyn Therapy 2016
- The Role of Photodynamic Therapy in Acne: An Evidence-Based Review Am J Clin Dermatol 2017
- Light therapies for acne: abridged Cochrane systematic review including GRADE assessments Br J Dermatol 2018
- Efficacy of photodynamic therapy for the treatment of inflammatory acne vulgaris: A systematic review and meta-analysis J Cosmet Dermatol 2020

Systematic reviews

- PDT can improve inflammatory acne
- Can be used for mild to severe acne, in various skin types, for facial & truncal lesions
- It is not considered appropriate for the noninflammatory type of acne
- ALA & MAL: the most commonly used photosensitizers
- Similar effects in high dose conditions (long incubation period & high fluence red light exposure)
- Longer incubation periods are associated with long term remission
- Trend towards shorter incubation times & lower strength photosensitizer preparations
- Red light is the most widely used light source
- Red light sources have deeper penetration & demonstrate better long-term results
- Optimal dosimetry & light source have not been established
- More treatment sessions improve clearance & control acne flares
- Number of sessions needed depend on patient’s response

Adverse effects?

➢Pain during illumination

- Erythema & oedema (3-5 days after treatment)
- Desquamation
- Hyperpigmentation (in darker skin types, usually reversible)
- Acneiform eruption
- Blistering

Severity of adverse events is influenced by:

- Strength of photosensitizer
- Light source
- Incubation period

Daylight PDT

Daylight photodynamic therapy with 5-aminolevulinic acid 5% gel for the treatment of mild-to-moderate inflammatory acne

Ital J Dermatol Venerol 2021

- 20 patients with mild to moderate inflammatory facial acne vulgaris
- 5% ALA gel, 4 times at 14-day intervals
- Mean decrease of inflammatory lesions: 16.7±4.4 to 5.2±3.3
- No adverse events were reported, and no patients were lost to follow-up
- DL-PDT seems to be an effective and tolerable therapy for the treatment of mild-to-severe inflammatory acne

Conventional PDT vs DL PDT ?

Conventional versus daylight photodynamic therapy for acne vulgaris: A randomized and prospective clinical study in China

Photodiagnosis and Photodynamic Therapy 2020

- 40 patients CPDT: 5% ALA cr., 2 hours application period, LED red light 40J/cm²
- 40 patients DLPDT: 5% ALA cr., 30’ incubation, daylight exposure for 2 hours
- 3 treatment sessions at 2-weeks intervals

➢No statistically significant difference in response rate at weeks 2,4 & 6

➢Mean VAS pain scores: DL PDT 1.8 ± 0.19, range: 1-2

C PDT 5.8 ± 0.26, range: 2-8

DLPDT is effective & less painful for acne treatment

PDT vs Conventional Treatments ?

Comparison of efficacy of aminolaevulinic acid photodynamic therapy vs. adapalene gel plus oral doxycycline for treatment of moderate acne vulgaris-A simple, blind, randomized, and controlled trial

Photodermatol Photoimmunol Photomed 2019

- 23 patients: 2 PDT sessions at 2 weeks interval, 20% ALA, 1,5 h incubation, red light at 37J/cm²
- 23 patients: doxycycline 100mg/day & adapalene gel 0.1% for 6 weeks

➢ inflammatory lesion reduction at week 12: PDT 84% , DC & AP 74%

PDT has a higher effectiveness than the combination of doxycycline and adapalene gel in reducing inflammatory lesions

PDT has been studied & found to be an effective treatment modality for acne

Acne (Strength of Recommendation B, Quality of Evidence I)

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]

Key questions:

What is the optimal PDT treatment protocol?

How does PDT compare with conventional therapies?

What is the evidence for its efficacy in the long term?

- RCTs are needed to establish standard guidelines

Till then

PDT remains a useful second line option for acne treatment!

The mechanism of PDT in rosacea is not clear

- PDT regulates number & function of multiple immune cells
- Exhibits antimicrobial action
- Reduces collagen type I & III synthesis
- Leads to a series of vasculotoxic effects
- Suppresses lipid secretion of sebocytes
- Induces atrophy of sebaceous glands

Review

Photodynamic therapy in the treatment of rosacea: A systematic review

Photodiagnosis and Photodynamic Therapy 38 (2022)

Databases searched: Pubmed, Embase, Cohrane library

Keywords: “Photodynamic therapy” & “rosacea”

137 identified articles

9 studies included (published between 2004 & 2019): 4 prospective

2 retrospective

3 case studies

Total no of patients: 95 (range 1-30)

Different rosacea subtypes (ET, PP, phymatous, granulomatous)

Follow-up period: 1-25 months

PDT parameters

Author, year	Photosensitizer	Concentration of PS	Light source	Wavelength (nm)	Power density (mW/cm2)	Energy fluence (J/cm2)	Duration of irradiation	Frequency	Sessions
Amari N, 2004 [24]	ALA	20%	Red light	575 –725	Not reported	100	Not reported	Not reported	2
Nybaek H, 2005 [25]	MAL cream	160 mg/g	Red light	632	Not reported	37	8 min	Not reported	2–3
Katz B, 2006 [26]	ALA	Not reported	PDL	595	Not reported	3.4 to 7.5	Not reported	2 weeks	6
Bryld LE, 2007 [27]	MAL cream	Not reported	Red light	Not reported	Not reported	37	Not reported	1 week	1–4
Togsverd-Bo K, 2009 [28]	MAL cream	Not reported	LPDL	595	Not reported	7.5	10 ms (2 passes)	2 weeks	3
Baglieri F, 2011 [29]	ALA	20%	Tungsten lamp	630 (400–700)	Not reported	40	Not reported	2 weeks	6
Friedmann DP, 2016 [30]	ALA	20%	Red light Blue light PDL IPL	Red light: 630 Blue light: 417 PDL: not reported IPL: not reported	Not reported	Red light: 37 Blue light: 10 PDL: 5–12 IPL: 15–22	Red light: 8 min Blue light: 15 min PDL: 0.5–40 ms (2–3 passes) IPL: 3.5–4 ms	Not reported	Not reported
Fan L, 2018 [31]	ALA	5%	Red light	635 ± 15	100	80–90	15 min	10 days	4
Sun Y, 2019 [32]	ALA	5%	Red light	633 ± 10	80–100	Not reported	20 min	7–10 days	3–6

Efficacy of PDT in rosacea?

- Different outcome measurements (descriptive, qualitative & quantitative)
- Satisfactory clinical response for most of the patients
- PDT was more effective in PP rosacea
- Most studies reported recurrences during follow-up period
- Extra PDT sessions were required in some patients to achieve better results
- Follow-up periods were not long enough to assess long-term safety & efficacy

Adverse effects

- Tolerant, temporary, self-limited
- Pain, itching, burning sensation, swelling, erythema, edema, desquamation,erosions, pustules, acne outbreaks

Rosacea Flare - Up after Photodynamic Therapy (PDT) for Field Cancerization and a Review on Adverse Events with PDT in General

Open Access Maced J Med Sci. 2019 Sep 30; 7(18):2998-3001.

Current studies provide evidence that PDT is safe & effective in rosacea treatment

However studies lack:

- Big sample sizes
- Comparative control groups
- Long follow-up time
- Scale methods of outcome measurements

➢RCTs are needed to explore appropriate treatment protocols

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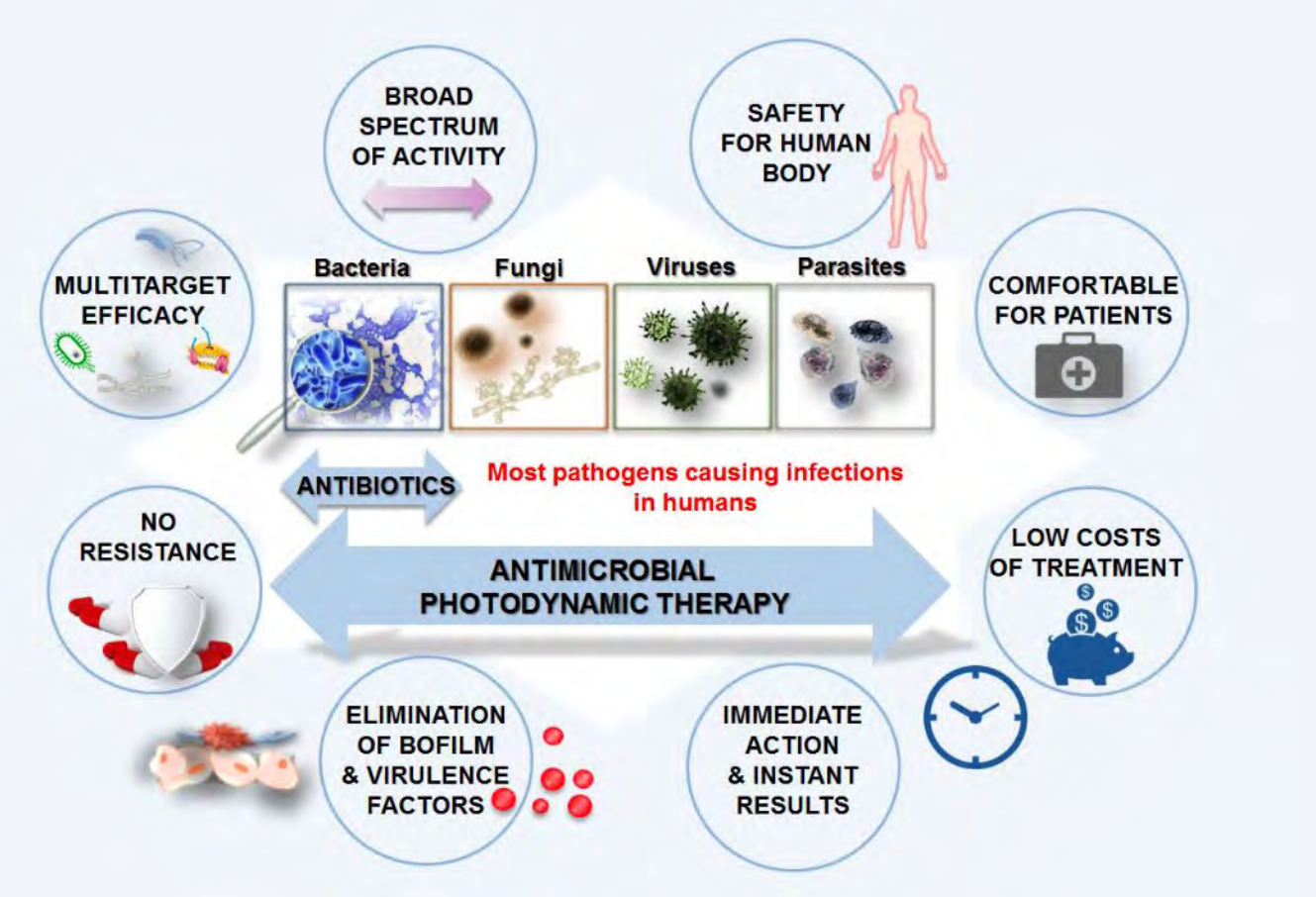
PDT on microorganisms - still too far away from routine use?

Yolanda Gilaberte
Zaragoza, Spain

Read the abstract

Advantages of aPDT



Kawczyk-Krupka A, et al. Photodyagnosis Photodyn Ther 2018;23:132-143

OUR EXPERIENCE

aPDT Clinical Uses

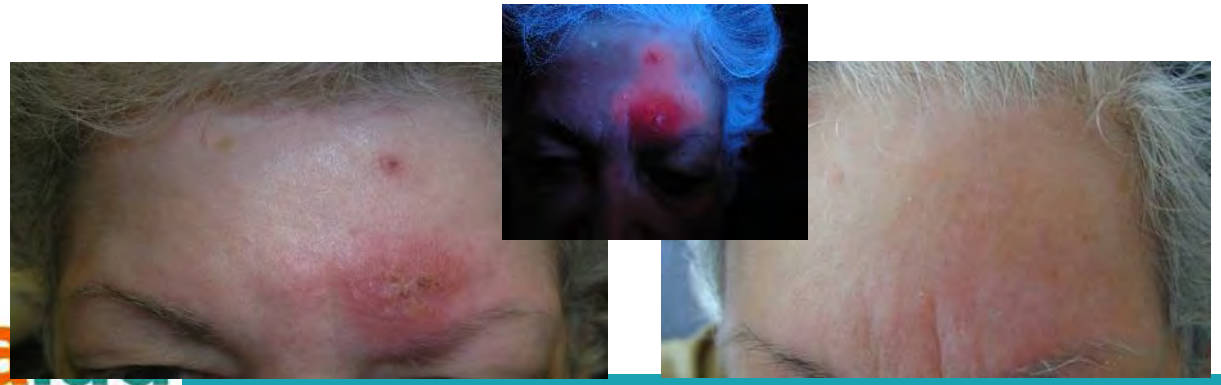
- Fungal infections:
  - Onychomycoses
  - Deep fungal infections
  - Tinea capitis/Granuloma de Majocchi
- Atypical mycobacteria
- Leishmaniasis
- Recalcitrant warts also genital
- Acne
- Hidradenitis suppurativa
- Chronic wounds

J Eur Acad Dermatol Venereol. 2020 Jan;34(1):17-29. doi: 10.1111/jdv.16044. Epub 2019 Dec 5.

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 Haedersdal [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]

- Rates of CR 96-100%
- ALA topical or intralesional
- MAL (3 h incubation)
- Sessions every 1-2 weeks
- Aktilite or Daylight
- Number of sessions: 1-8



Cortesy Dr. B. Pérez-García

Table 1 Summary of recommendations (including indications reviewed in Part 17)

Indication	Strength of recommendation	Quality of evidence
• Actinic keratosis*	A	I
• Squamous cell carcinoma in situ*		
• Superficial Basal cell carcinoma*		
• Nodular Basal cell carcinoma*		
• Photorejuvenation		
• Treatment of NMSC in organ transplant recipients	B	I
• Prevention of NMSC in organ transplant recipients		
• Field cancerization*		
• Acne		
• Refractory warts, plane and genital warts		
• Cutaneous leishmaniasis		
• Onychomycosis		
• Superficial fungal infections	C	II-III
• Deep cutaneous mycoses		
• Hypertrophic and Keloid Scars		
• Sebaceous gland hyperplasia		
• Cutaneous T-cell lymphoma (CTCL)		
• Extramammary Paget's disease		

PDT for atypical mycobacteria

- *M. abscesus* only sentitive to amikacin and clarithromycin
- Doxicicline + clarithromycin was not effective
- **Protocol:**
  - Start with 1 h incubation until 3 h
  - 74 J/cm2
  - 8 sessions were needed

Received: 30 April 2022 | Revised: 16 July 2022 | Accepted: 2 August 2022
DOI: 10.1111/dth.15756

LETTER

DERMATOLOGIC THERAPY WILEY

Multiresistant *Mycobacterium abscessus* ulcer treated with photodynamic therapy with methyl-aminolevulinate

Dear Editor,

Mycobacterium abscessus is a rapidly growing mycobacterium.[1] They are a rare cause of infections with an incidence of 0.2 per 100,000.[2]

The lungs are the most frequent site of infection. However, in the last few years, an increase of cases affecting the skin and soft tissues have been reported.

Outbreaks of furunculosis caused by this atypical mycobacteriosis (AM) have been linked to baths in nail salons. The cutaneous involvement can occur via hematological dissemination in immunocompromised patients or by direct inoculation into the skin.[3,4]

The treatment of AM has become a challenge for clinicians, due to the increasing drug resistance of mycobacteria and the locations in which it appears.

A 36-year-old woman, was referred to our service for evaluation of a persistent erythematous abscessed nodule on the third finger of the right hand after getting a piercing in that area 3 months earlier (Figure 1A). The patient had received multiple systemic and topical antibiotic treatments without any improvement. A skin biopsy and a culture test revealed an AM due to *M. abscessus* subs. *massiliense* (Figure 2), in addition the antibiogram showed multiresistance, being sensitive only to amikacin and clarithromycin. Treatment with clarithromycin 250 mg and doxycycline 100 mg twice/day for 7 days associated with surgical debridement was ineffective, so treatment using photodynamic therapy with methyl-aminolevulinate (MAL-PDT) was initiated with 1 h of incubation progressively increasing the incubation time to 3 h and subsequent illumination with Aktilite® increasing dosages from 37 to 74 J/cm². MAL-PDT was performed once a week. After eight sessions, the lesion showed partial improvement, but since the culture of the lesion evidenced persistent infection, the photosensitizer was switched to methylene blue (MB) with

FIGURE 2 Direct microscopic examination of cultures following Kinyoung staining was positive for acid-fast bacilli magnification ×1000

(A) (B)

FIGURE 1 (A) Clinical image. *Mycobacterium abscessus* ulcer resistant to systemic antibiotic therapy in the third finger of the right hand. (B) Clinical image. Resolution of ulcer with residual hyperpigmented scar after treatment with photodynamic therapy

Paulina Cerro-Muñoz and Alba Navarro-Bielsa contributed equally as first authors.

PDT for mycoses

Indication	Strength of recommendation	Quality of evidence
• Actinic keratosis* • Squamous cell carcinoma in situ* • Superficial Basal cell carcinoma* • Nodular Basal cell carcinoma* • Photorejuvenation	A	I
• Treatment of NMSC in organ transplant recipients • Prevention of NMSC in organ transplant recipients • Field cancerization* • Acne • Refractory warts, plane and genital warts • Cutaneous leishmaniasis • Onychomycosis	B	I
• Superficial fungal infections • Deep cutaneous mycoses • Hypertrophic and Keloid Scars • Sebaceous gland hyperplasia • Cutaneous T-cell lymphoma (CTCL) • Extramammary Paget's disease	C	II-III

J Eur Acad Dermatol Venereol. 2020 Jan;34(1):17-29. doi: 10.1111/jdv.16044. Epub 2019 Dec 5.

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ALA 20% + red LED (nail abraded) (*T. rubrum*):
CR 34.3% (follow-up 12m)

MB 2%, session every 2 weeks, nail abraded:
CR 90% vs 45% fluconazole (follow-up 12 months)

MB 1%-PDT vs IPL (*T.rubrum)*
MB-PDT 70% clinical improvement)
IPL 80% clinical improvement
Limitations: follow-up 3 months, no microbiological study

Aluminium-phthalocyanine cloride nanoemulsion + red LED (urea 40%), sessions every 2 weeks:
CR 40%

> Pharmaceuticals (Basel). 2022 Jun 7;15(6):722. doi: 10.3390/ph15060722.

Combination of Photodynamic Therapy and Oral Antifungals for the Treatment of Onychomycosis

Alba Navarro-Bielsa [1], Tamara Gracia-Cazaña [1], Pilar Robres [2], Concepción Lopez [1], María Dolores Calvo-Priego [1], Carmen Aspiroz [3], Yolanda Gilaberte [1]

> Pharmaceuticals (Basel). 2022 Jun 7;15(6):722. doi: 10.3390/ph15060722.

Combination of Photodynamic Therapy and Oral Antifungals for the Treatment of Onychomycosis

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- 20 patients with recalcitrant onychomycoses
- *55% T. rubrum*
- 90% toenail
- 50% associated *tinea pedis*
- *10 cases combined with oral terbinafine (8 only 1 month) 3 topical*
- ***RESULTS:***
  - *80% complete clinical response*
  - *60% microbiological response*

	N (%)
T. rubrum	11 (55)
A. terreus	3 (15)
T. mentagrophytes	2 (10)
A. sydowii	2 (10)
A. fumigatus	1 (5)
F. oxysporum	1 (5)

PDT for chronic ulcers

Photodiagnosis and Photodynamic Therapy 21 (2018) 294–305

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

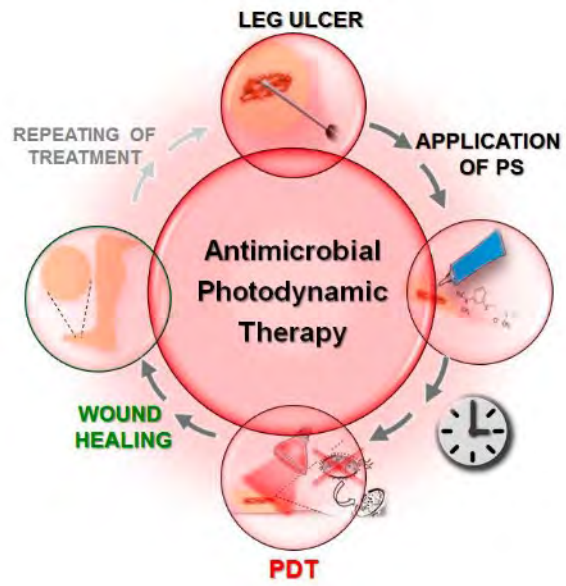
Contribution of photodynamic therapy in wound healing: A systematic review

Vanessa Nesi-Reis[a,*], Daniele Stéfanie Sara Lopes Lera-Nonose[a], Jully Oyama[b], Marielle Priscila Paula Silva-Lalucci[b], Izabel Galhardo Demarchi[c], Sandra Mara Alessi Aristides[c], Jorge Juarez Vieira Teixeira[c], Thaís Gomes Verzignassi Silveira[c], Maria Valdrinez Campana Lonardoni[c]

Photodiagnosis Photodyn Ther. 2018 Sep;23:132-143. doi: 10.1016/j.pdpdt.2018.05.001. Epub 2018 May 3.

Photodynamic therapy as an alternative to antibiotic therapy for the treatment of infected leg ulcers.

Kawczyk-Krupka A[1], Pucelik B[2], Międzybrodzka A[3], Sieroń AR[1], Dąbrowski JM[4].



- PDT accelerates the closure of the wound
- PDT reduces significantly the germ load
- No significant side effects
- No systemic absorption

Review > Photodiagnosis Photodyn Ther. 2022 Sep 13;40:103118.
doi: 10.1016/j.pdpdt.2022.103118. Online ahead of print.

Photodynamic therapy for treating infected skin wounds: A systematic review and meta-analysis from randomized clinical trials

Analú Barros de Oliveira [1], Túlio Morandin Ferrisse [2], Carla Raquel Fontana [3], Fernanda Gonçalves Basso [4], Fernanda Lourenção Brighenti [5]

- **Objective:** PDT efficacy for treating infected wounds based on randomized clinical trials (RCTs).
- **Results:** Only **4** out of 573 articles were selected
- All studies used red LED light.
- Patients treated with PDT showed:
  - Lower microbial cell viability in the wound (15% to 17% ($p = 0.0003$/ $I^2=0\%$)
  - Significantly smaller wound size (0.72 cm^2/$p = 0.0187$/$I^2=0\%$)

  than patients treated with placebo or red-light exposure.
- **Conclusion:** PDT can be an excellent alternative treatment for infected skin wounds, though larger trials are needed.

PDT for chronic ulcers: Clinical Trials

Br J Dermatol. 2013 Mar;168(3):617-24. doi: 10.1111/bjd.12098. Epub 2013 Jan 18.

Phase IIa randomized, placebo-controlled study of antimicrobial photodynamic therapy in bacterially colonized, chronic leg ulcers and diabetic foot ulcers: a new approach to antimicrobial therapy.

Morley S[1], Griffiths J, Philips G, Moseley H, O'Grady C, Mellish K, Lankester CL, Faris B, Young RJ, Brown SB, Rhodes LE.

- Photosensitizer PPA904 [3,7-bis(N,N-dibutylamino) phenothiazin-5-ium bromide]

Photomed Laser Surg. 2018 Jan;36(1):44-50. doi: 10.1089/pho.2017.4305. Epub 2017 Oct 9.

A Study on the Macroscopic Morphometry of the Lesion Area on Diabetic Ulcers in Humans Treated with Photodynamic Therapy Using Two Methods of Measurement.

Carrinho PM[1], Andreani DIK[1], Morete VA[2], Iseri S[2], Navarro RS[3], Villaverde AB[4,5].

- Methylene Blue dye (0.01%)

Photodiagnosis Photodyn Ther. 2018 Mar;21:252-256. doi: 10.1016/j.pdpdt.2017.12.012. Epub 2017 Dec 22.

ALA-PDT exerts beneficial effects on chronic venous ulcers by inducing changes in inflammatory microenvironment, especially through increased TGF-beta release: A pilot clinical and translational study.

Grandi V[1], Bacci S[2], Corsi A[3], Sessa M[4], Puliti E[2], Murciano N[2], Scavone F[2], Cappugi P[5], Pimpinelli N[5].

- ALA 20% gel

Acta Diabetol. 2014;51(3):435-40. doi: 10.1007/s00592-013-0533-3. Epub 2013 Dec 19.

Photodynamic topical antimicrobial therapy for infected foot ulcers in patients with diabetes: a randomized, double-blind, placebo-controlled study--the D.A.N.T.E (Diabetic ulcer Antimicrobial New Topical treatment Evaluation) study.

Mannucci E[1], Genovese S, Monami M, Navalesi G, Dotta F, Anichini R, Romagnoli F, Gensini G.

- RLP068 is a novel cationic zinc phthalocyanine derivative

Drugs Context. 2019 Aug 20;8:212610. doi: 10.7573/dic.212610. eCollection 2019.

The benefits of antimicrobial photodynamic therapy with RLP068 in the management of diabetic foot ulcers.

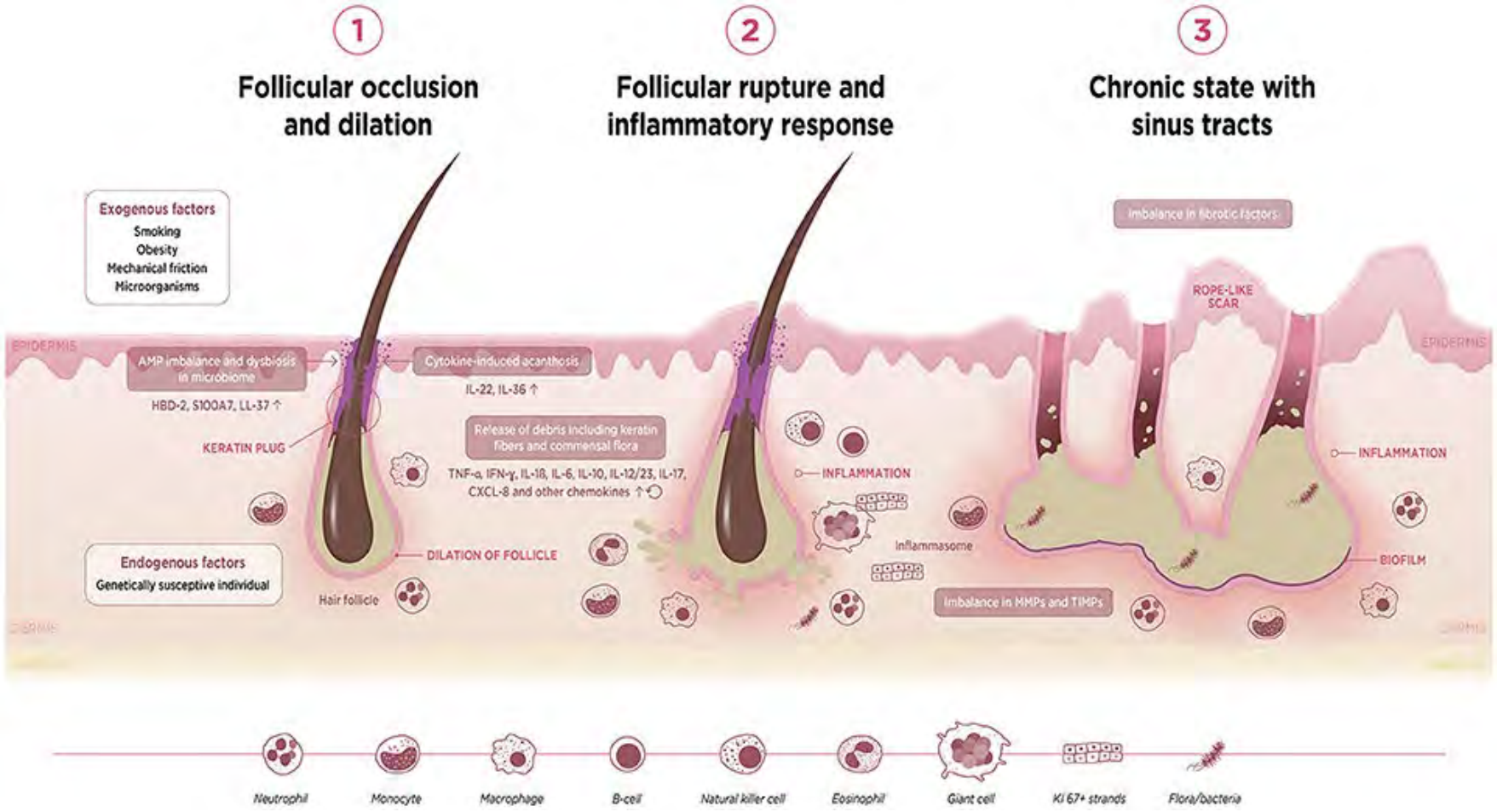
Martinelli N[1], Curci V[2], Quarantiello A[2], Saldalamacchia G[3].

- Cationic zinc phthalocyanine derivative,
- **VULNOFAST plus** (Molteni Therapeutics S.R.L., Italy)
- **PROTOCOL:**
  - RLP068 (Tegaderm and nontransparent bandage)
  - 30 minutes incubation
  - LED light device (**VULNOLIGHT,** Molteni Therapeutics S.R.L., Italy)
    - 630 nm λ, fluence 60 J/cm2.
  - Ulcer washed with saline solution
  - Twice a week

VULNOFAST® gel 0.3%

VULNOFAST® plus

Hidradenitis supurativa



Received: 7 February 2021 | Revised: 4 May 2021 | Accepted: 19 June 2021
DOI: 10.1111/php.12709

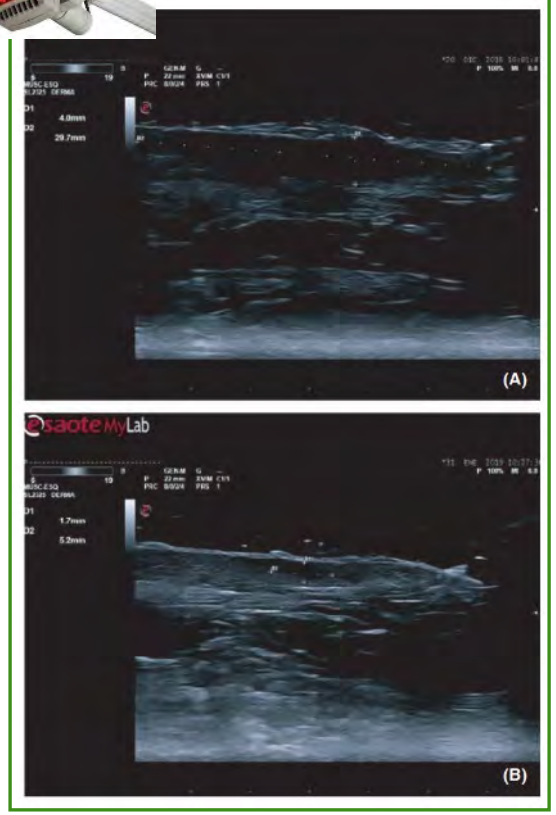
ORIGINAL ARTICLE

Photodermatology, Photoimmunology & Photomedicine WILEY

Ultrasound-guided photodynamic therapy with intralesional methylene blue and a 635 nm light-emitting diode lamp in hidradenitis suppurativa: A retrospective study of 41 patients

Marta Gamissans[1] | Núria Riera-Martí[1] | Jorge Romaní[1] | Yolanda Gilaberte[2]

41 patients



Treated location	
Groins	39% (n = 16)
Armpit	29.3% (n = 12)
Intermammary	2.4% (n = 1)
Gluteal	9.8% (n = 4)
Abdomen	2.4% (n = 1)
Scrotum	2.4% (n = 1)
Vulvar	14.6% (n = 6)
Type of lesion	
Abscess	26.8% (n = 11)
Fistula	73.2% (n = 30)

Percentage of improvement[3]	Main diameter (mm) before / after treatment (mean ± SD)	% (n)
≥75%	8.5 ± 2 / 2.1 ± 0.7	58.5% (n = 24)
50%-75%	8.3 ± 1.75 / 3.9 ± 0.2	22% (n = 9)
<50%	9.1 ± 1.9 / 7.5 ± 1.4	19.5% (n = 8)

Intralesional PDT with 2% ALA gel or solution

- 10 patients
  - Age (mean) 56,4 (rango:23, 66)
  - 6 men and 4 women
  - (6 treatment with biologics)
  - Follow-up: 3-18 months
  - Pain: mean 7 (VAS 0-10)
- Complete response (50%):
  - 2 patients armpit (1 and 2 sessions)
  - 2 patients groins (2 sessions)
  - 1 patient gluteal (1 sesión)
- Partial response (40%):
  - 1 patient armpits and groins (3 sessions) (1very severe patient with ustekinumab)
  - 1 patient armpits (3 sessions) (PASH very severe with adalimumab)
  - 1 patient armpits (1 session)
  - 1 patient groin (1 session)
- No response (10):
  - **1 patient armpit (1 session)**
- Side effects: inflammation, infection (1 case)

Antimicrobial PDT

Advantages

- No side effects
- No interactions
- No resistances
- Effective against resistant microorganism
- Different light sources
- Sinergy in combination
- Less expensive than new antimicrobials

Limitations

- Time consuming for doctors/nurses
- Several sessions are needed
- Lamps are useful only for localized lesions
- Antimicrobial effect last only during illumination

Conclusions

- aPDT could be useful to manage especially challenging cases in our clinics (**especially recalcitrant infections and immunosuppresed patients**)
- **Onychomycosis, leishmaniasis, HPV infections, wound healing and HS** are the most promising applications
- **Combination** with conventional antimicrobials can be **synergistic and help to shorten the treatment**
- **New light devices and adapted photosensitizers** are needed to perfom PDT in shorter times and at home
- Clinical trials and interest of industries are needed **for routine use of PDT in clinical dermatology**

Giornale Italiano di Dermatologia e Venereologia 2018 mese;153(0):000-000
DOI: 10.23736/S0392-0488.18.06007-8

REVIEW

PDT FOR NON-MELANOMA SKIN CANCER

Antimicrobial effects of photodynamic therapy

Vanesa PÉREZ-LAGUNA [1, 2], Ana J. GARCÍA-MALINIS [3], Carmen ASPIROZ [4], Antonio REZUSTA [1, 5], Yolanda GILABERTE [1, 6] *

[1]IIS Aragón, Zaragoza, Spain; [2]University of Zaragoza, Zaragoza, Spain; [3]Unit of Dermatology, Hospital San Jorge, Huesca, Spain; [4]Unit of Microbiology, Hospital Royo Villanova, Zaragoza, Spain; [5]Department of Microbiology, Hospital Universitario Miguel Servet, Zaragoza, Spain; [6]Department of Dermatology, Hospital Universitario Miguel Servet, Zaragoza, Spain

*Correspondence author: Yolanda Gilaberte, Hospital Universitario Miguel Servet, Av. Isabel la Católica 14, 50009 Zaragoza, Spain.
E-mail: ygilaberte@salud.aragon.es

pharmaceuticals *Pharmaceuticals* **2021**, *14*, 603. https://doi.org/10.3390/ph14070603 MDPI

Review

Photodynamic Therapy Combined with Antibiotics or Antifungals against Microorganisms That Cause Skin and Soft Tissue Infections: A Planktonic and Biofilm Approach to Overcome Resistances

Vanesa Pérez-Laguna [1,*], Isabel García-Luque [2], Sofía Ballesta [2], Antonio Rezusta [3,4,5,†] and Yolanda Gilaberte [3,6,†]

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Barcelona, Spain
Friday 9 and Saturday 10, June 2023

PDT for aesthetic indications

Ruben Del Rio Gil
Barcelona, Spain

Read the abstract

MY PROTOCOL

Application of the photosensitizer

1:30-3 hours incubation time (according to degree of photodamage)

Red light (LEDs) or IPL (according to the presence of pigmented or vascular lesions)

PDT. "PHOTODYNAMIC PHOTOREJUVENATION"

- Ruiz-Rodriguez et al
- 17 p
- IPL-PDT 5-ALA (4h) 2 sessions
- Improvement of 87% AK, fine wrinkles, texture, dyschromia and telangiectasias
- AE: erythema, edema, scabs

IPL-PDT

- Alster et al. 10p. Split-face IPL-PDT was superior to IPL (2ses)
- Dover at al. IPL-PDT was superior to IPL (3 ses) in global photorejuvenation, pigmentation and superficial wrinkles
- Gold et al IPL-PDT vs IPL was superior in periocular wrinkles, roughness, mottled hyperpigmentation and erythema

PDT. HISTOLOGY

- Marmur et al. IPL-PDT vs IPL.
  - Increase of type I collagen, improvement of elastosis and superficial densification of superior dermal collagen I in IPL-PDT side
- Park et al. ALA Red light-PDT.
  - Increase of procollagen I and III, TGF-R. Decrease of metalloproteinases MMP 1, 3 and 12

PDT AND PHOTOTYPES

- Xi et al. 26p. IPL-PDT vs IPL. Phototypes III-IV. 3 ses
- Global improvement global and fine wrinkles
- AE: erythtema, edema and **more postinflammatory hyperpigmentation in the IPL-PDT side**

MAL-PDT

- Ruiz-Rodriguez et al.
  - More incubation leads to better results in roughness and fine wrinkles but more AE
- Bazagoitia et al.
  - Decreased elastosis, dysplasia and Ki-67 expression (proliferation marker) and p53 (early epidermal carcinogenesis marker).
  - PDT can reverse the process of carcinogenesis in photodamaged skin.
- Szeimies et al.
  - Reduction of the degree of keratinocyte atypia and elastosis. Increase of procollagen and decrease of p53

DAYLIGHT PDT

- Sanclemente et al. Randomized, controlled, double-blind, placebo-controlled study
- MAL-Daylight PDT, 2h, 3 ses
- Improvement of all signs of photodamage
- Safe procedure

LIGHT SOURCES

Blue light: poor penetration

IPL & PDL: The benefits of the light source itself are added in photoaging, lentigos and telangiectasias

Red light is very useful in cases of severe photoaging with actinic keratoses and field cancerization

PHOTOSENSITIZER

- Any drug ALA or M-ALA can be used
- Phototoxicity increases with:
  - Incubation time
  - Photosensitizer concentration
  - Light dose

LOCAL SKIN REACTIONS

- Laser-assisted PDT: more pain, erythema, scabs and pigmented changes.
- In the long term, better results in photorejuvenation.

CONCLUSIONS

- PDT is very effective in photorejuvenation through the increase of neocollagenesis and decrease of solar elastosis
- Global improvement of the skin quality
- Smoother texture
- Wrinkle reduction
- Scar Improvement
- Less evidence in mottled pigmentation

CONCLUSIONS

PDT is a great resource in Dermatology at the same time that it treats precancerous lesions

Several protocols have been described

The ideal pacient has a fair phototype with severe photodamage and actinic keratoses.

CONCLUSIONS

PDT has a high safety profile

The association with fractional ablative laser as a photosensitizer carrier improves the results, but increases adverse effects.

Round table discussion:
ADL- vs. DL- vs. cPDT for AKs: freedom of choice or clear recommendations?

Moderator: Rolf-Markus Szeimies
Participants: Colin A. Morton, Yolanda Gilaberte, Thomas Dirschka, Stine Regin Wiegell

Key points of discussion

Take home message: The choice of PDT modality for a particular patient can depend on several factors

Disease factors

- There remains an indication for conventional (c)PDT for AK lesions that are highly localized or clustered, and for cheilitis, as well as for BCC and Bowen's disease
- Standard or artificial daylight (DL)-PDT is widely favoured for more widespread AK to reduce pain

Patient factors and preferences

- Mobility issues may limit the choice to modalities that can be performed in the clinic room
- Some patients prefer the hospital setting and for all aspects of the protocol to be performed by HCPs; others prefer home-delivered treatment
- Although many patients tolerate cPDT well, those with experience of DL-PDT typically prefer it (as less pain)
- It is important to accommodate patient/family preferences wherever possible and appropriate for the disease type

Resources

- Some clinics lack access to artificial DL (ADL)-PDT equipment or reimbursement
- Patient volume, staffing (nurses, doctors) and space remain challenges to PDT delivery
- Weather may limit DL-PDT provision in some countries/seasons
- DL-PDT and ADL-PDT can require less staff time (convenient for busy clinics); However, DL-PDT is typically the most cost effective

Treatment factors

- Efficacy – striving for a modality with highest efficacy may not always be necessary, given AK chronicity and need for further treatment, provided good disease control is achieved and patients are alert to non-responding lesions e.g. lower efficacy may be observed with home-based PDT, but it might still be appropriate for some patients, with suitable reviews
- Control of treatment variables – greater for cPDT and ADL-PDT
- Pain – lower for DL-PDT
- Non-PDT options, as well as pre-/post-treatment and combination options, may also be appropriate

AK, actinic keratosis; HCP healthcare professional; PDT, photodynamic therapy.

Free communications and case reports

Chairs: Elena Sotiriou, Rolf-Markus Szeimies

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Kaposi Disease treated with PDT

Lasse R. Braathen
Bern, Switzerland

Read the abstract

Patient.

73 year old healthy caucasian male presented with a 4 weeks old red tumorous lesion at his right heel.

HIV negative.

Biopsy result.

HHV-8 pos. immunohistochemical analysis

No atypical melanocytic proliferation

Diagnosis: Kaposi Sarcoma

Braathen 2023

Kaposi sarcoma

Whole–exome sequensing.

Indolent=Kaposi Disease:

Tumour mutational burden; one or no deleterious mutations.

Aggressive Kaposi sarcoma:

At least 3 deleterious mutations

Malouf et al. Genetic landscape of indolent and aggressive Kaposi sarcomas. JEADV 2022, 36, 2343-2351

Treatment

Conventional photodynamic therapy 5 times with weekly intervals.

3 hours incubation with the drug followed by red light illumination for approx. 10’

Painful.

After 2 months a small recurrence was followed by 3 courses of PDT. Lesion free since then, 6 months.

Braathen 2023

Photodynamic Therapy of Kaposi sarcoma.

Shiryaev et al. Photodiagnosis Photodyn Ther.
2021 Sep, 35.

79 year old man
- Case reports
- No studies

- Aggressive Kaposi sarcoma is a tumour/cancer.
- Indolent Kaposi sarcoma is an opportunistic skin disease, caused by HHV-8 induced endothelial cell-proliferation.
- The two entities should be separated into the
  A: (Tumour/cancer) Kaposi sarcoma
  and
  B: (Indolent) Kaposi Disease.

Braathen 2023

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High Frequency Ultrasound – Its use in informing the suitability and effectiveness of PDT at the Christie Hospital, Manchester

Colin Swift
Manchester, United Kingdom

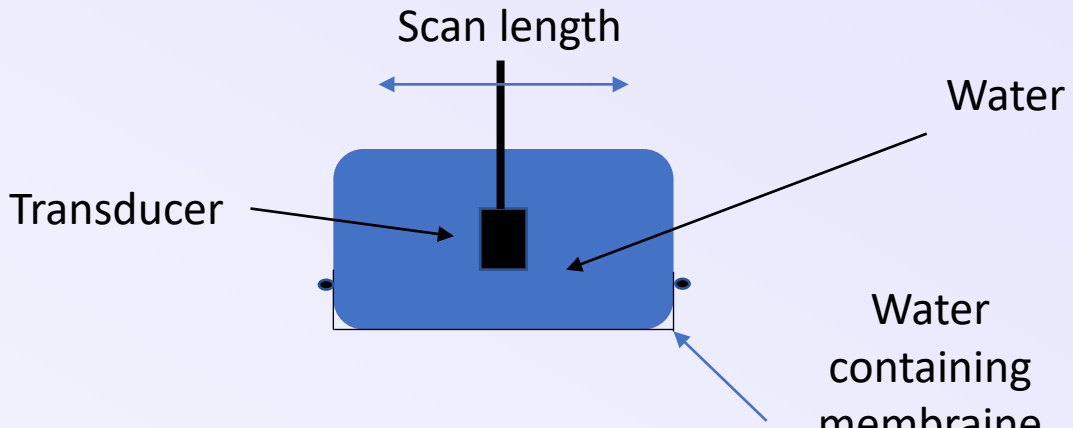
Read the abstract

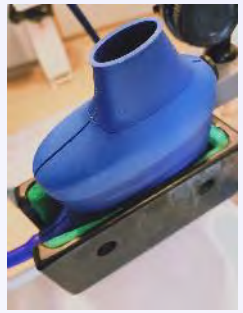
High frequency ultrasound

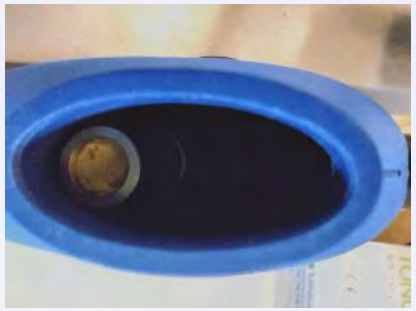
- Considered to be ultrasound waves >10MHz
- Improved spatial resolution of the scan
    - Increased attenuation by tissue leading to reduction in the depth which can provide useful information

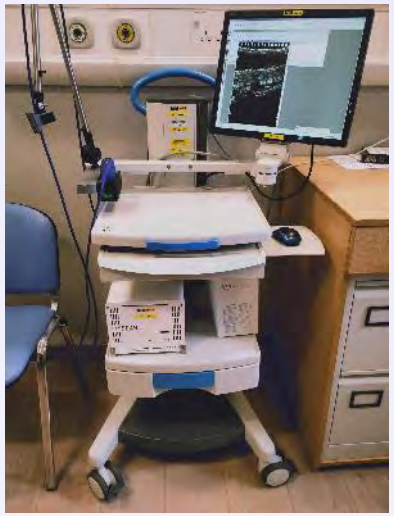
Unit at the Christie

- Longport Episcan I-200 High frequency ultrasound system
  - 35Mhz Probe used at the Christie
  - Mechanically scanned single element transducer
  - 15mm scan length



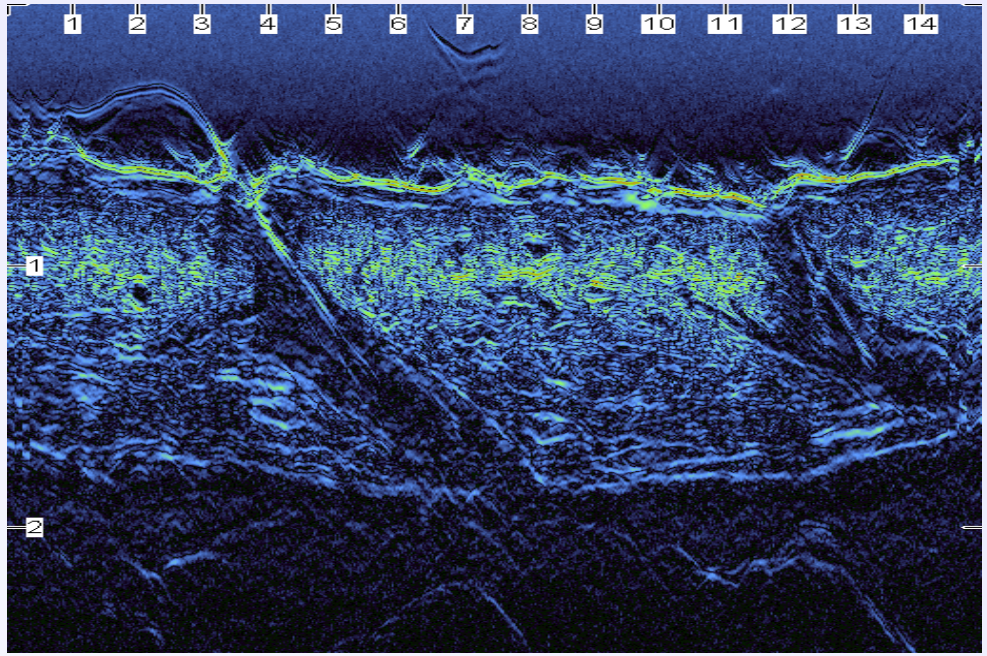






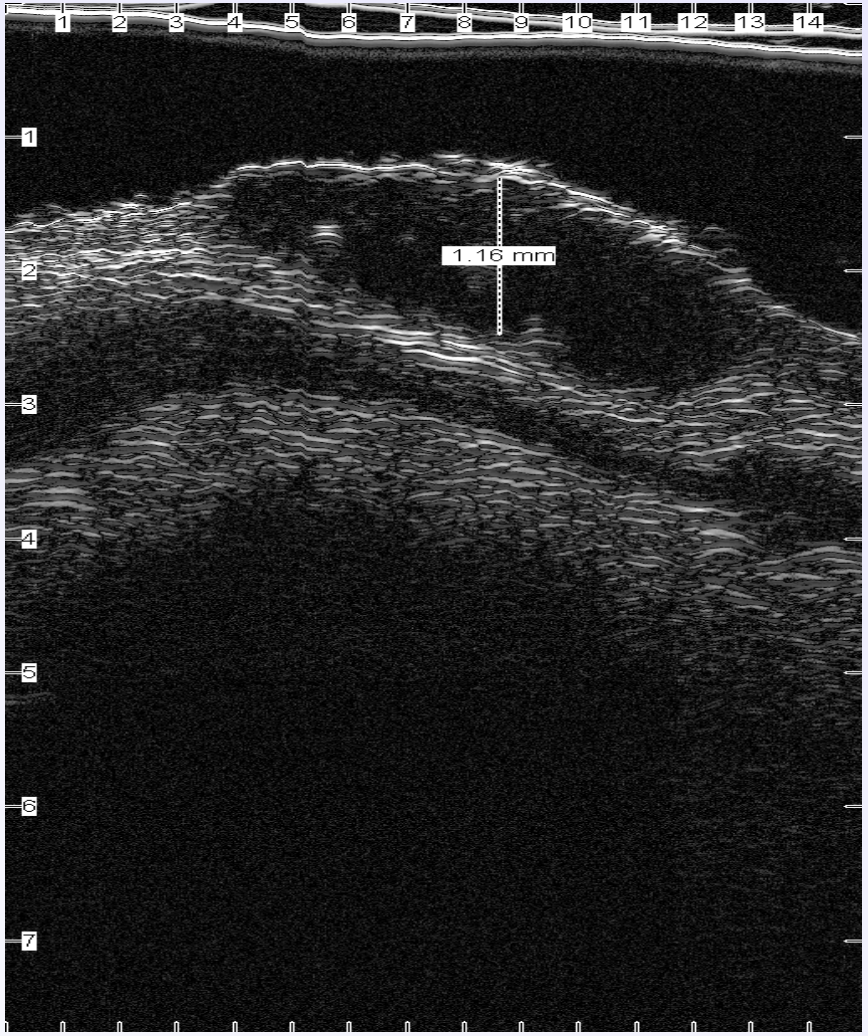
High frequency ultrasound – normal skin

- Epidermis – Hyperechoic due to presence of Keratin
- Dermis – Hyperechoic due to presence of collagen
- Subcutis – Hypoechoic fat allows ultrasound to travel relatively unimpeded



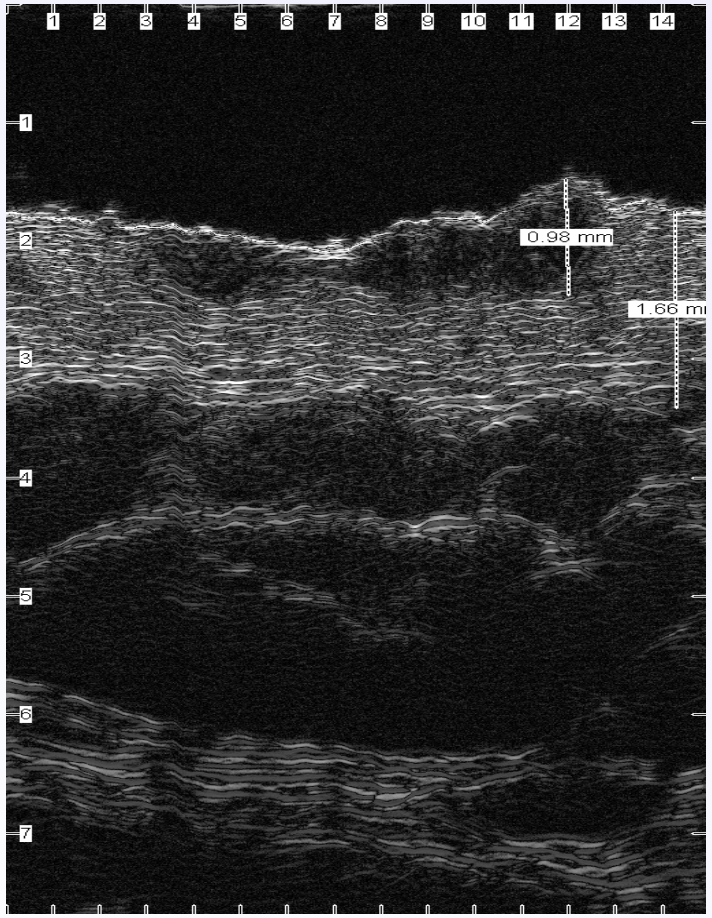
Basal cell carcinomas - Echogenicity

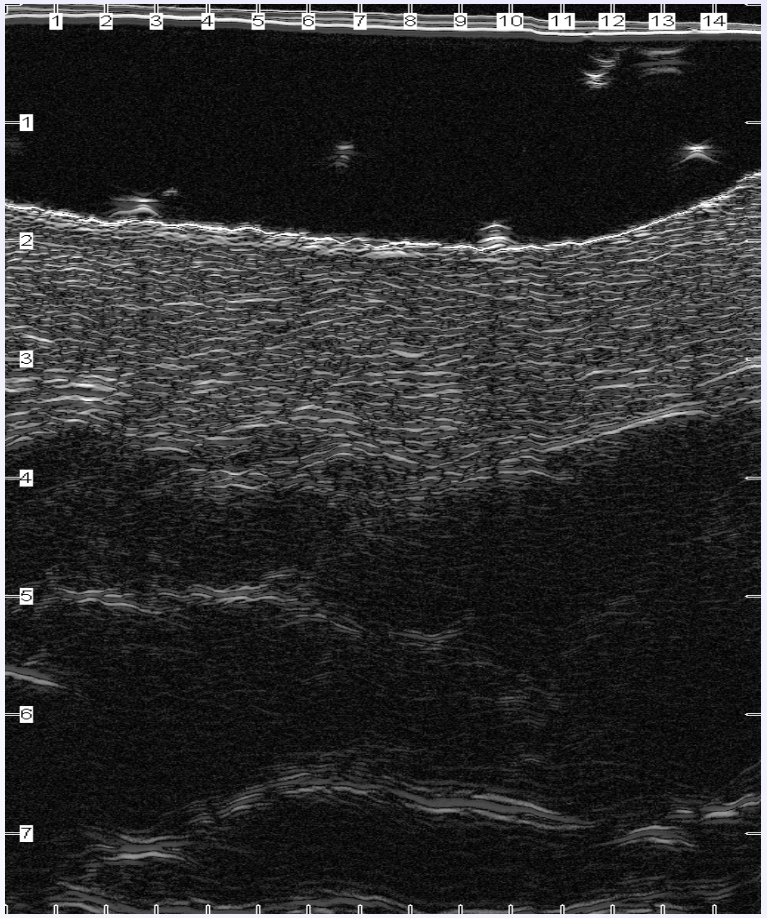
- Dermis is hyperechoic due to its fibular nature resulting in the strong reflection of the ultrasound waves
- Basal cell carcinomas reveal themselves as hypoechoic circular or oval like structures



The Christie NHS
NHS Foundation Trust

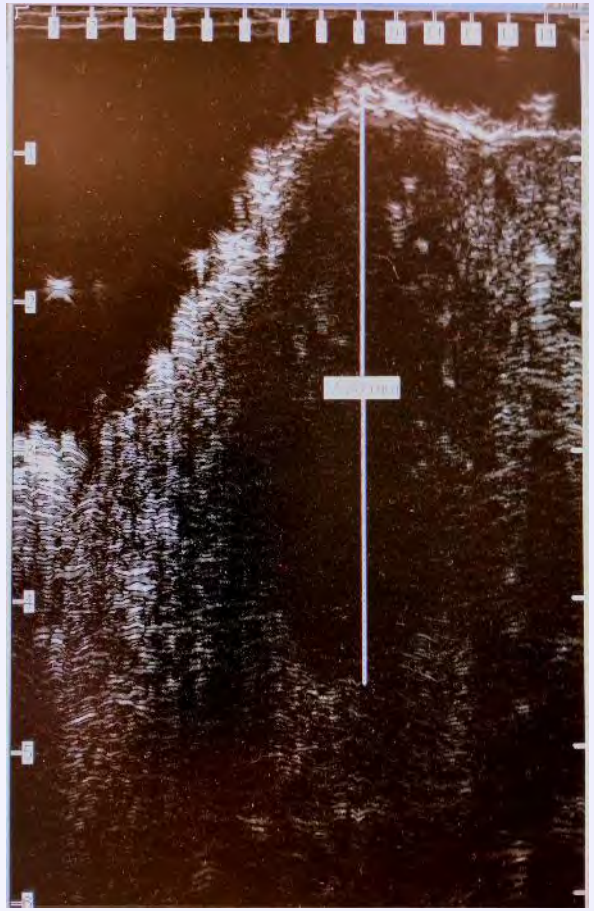
Some examples – before and after treatment





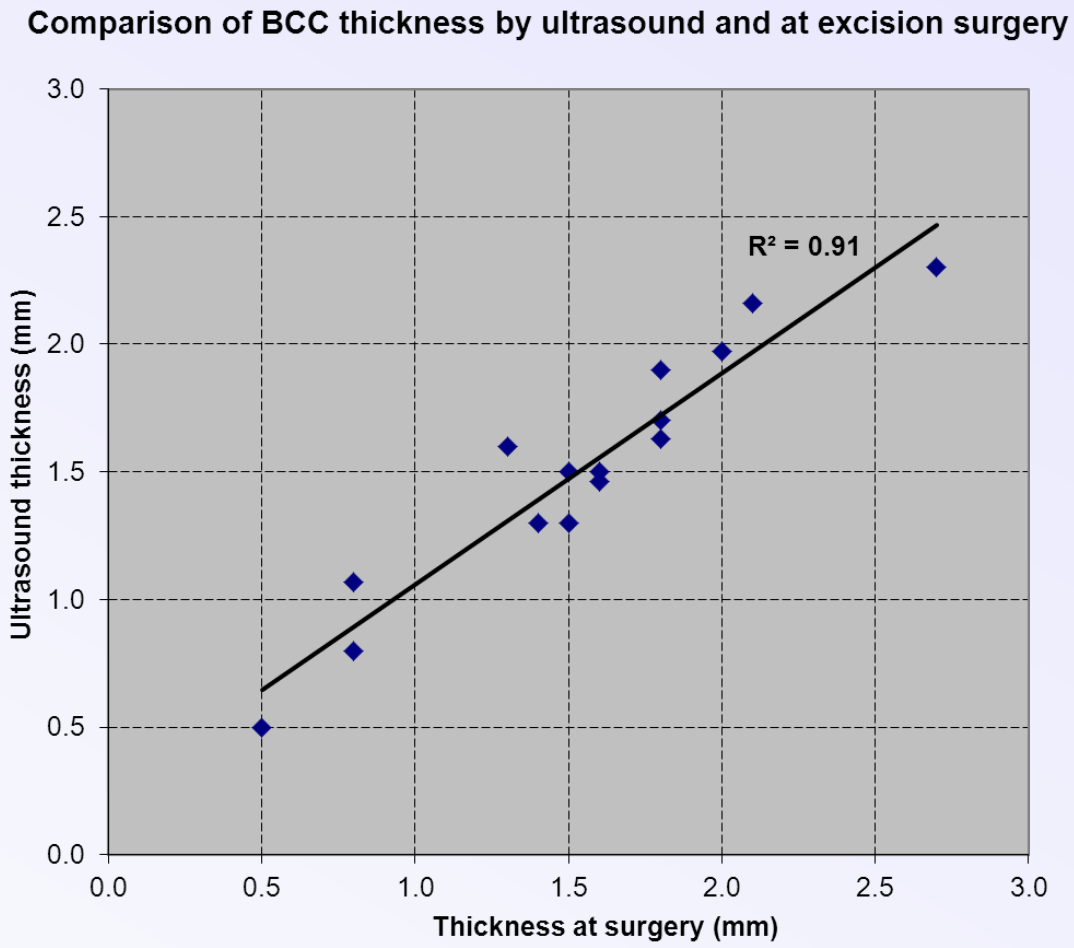
Some examples

- Scan shows depth of BCC 3.98mm
- Too deep for PDT
- Other options explored in this case



An Informed decision?

- Study of BCC thickness using ultrasound and excision surgery
  - Allows an informed decision on the treatment pathway for the BCC



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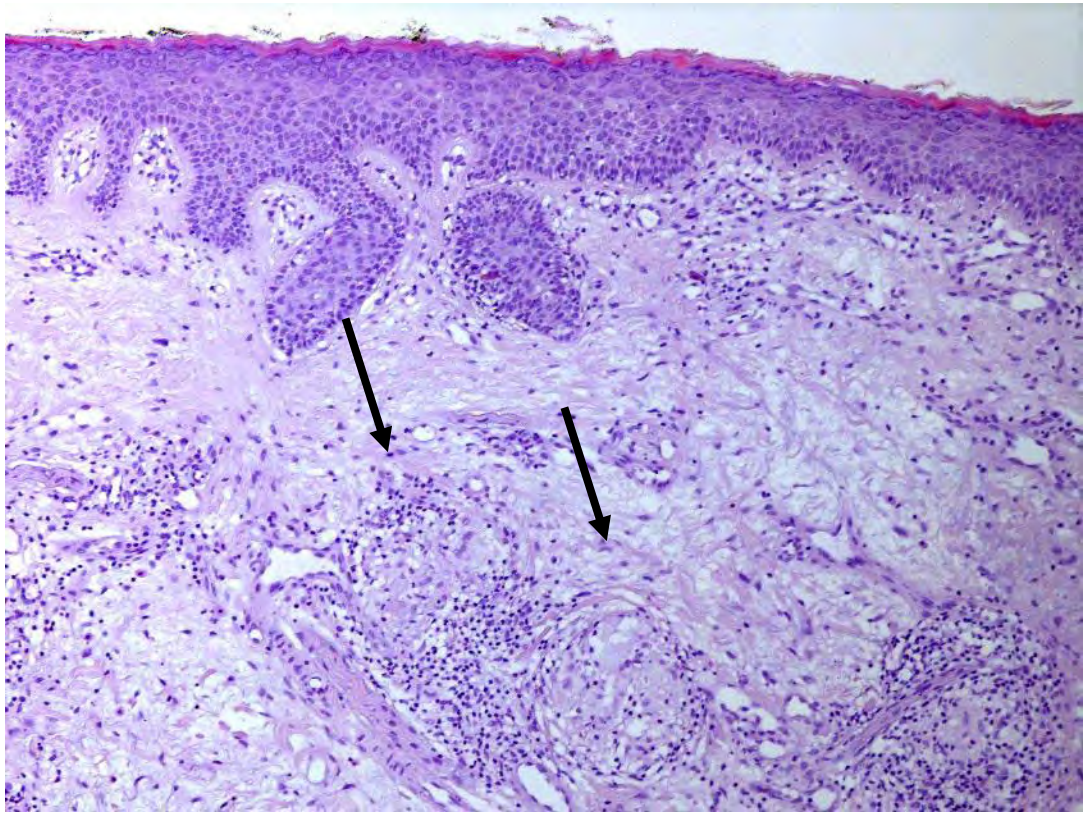
Miescher granulomatous macrocheilitis

Muriel Creusot
Lasne, Belgium

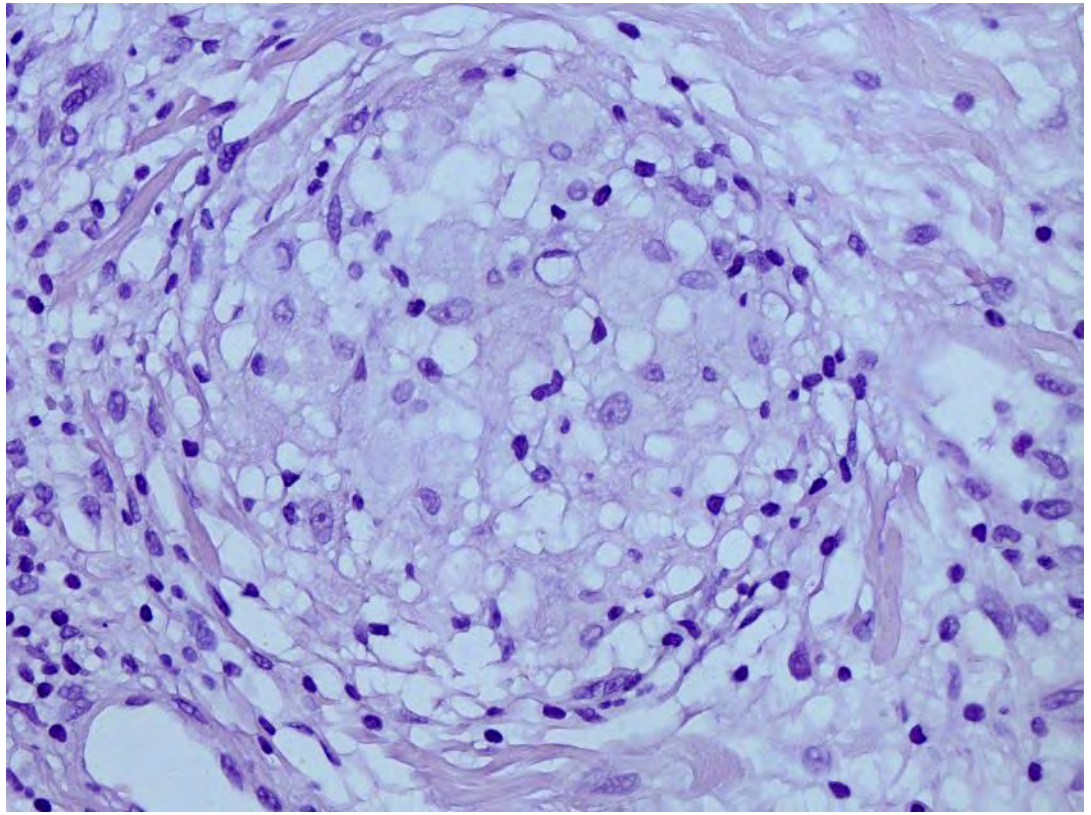
Read the abstract

Biopsy

Anatomopathology Pr Josette André



At higher magnification: presence of two small epithelioid granulomas within the infiltrate (arrows)



Focus on an epithelioid granuloma

Biopsy

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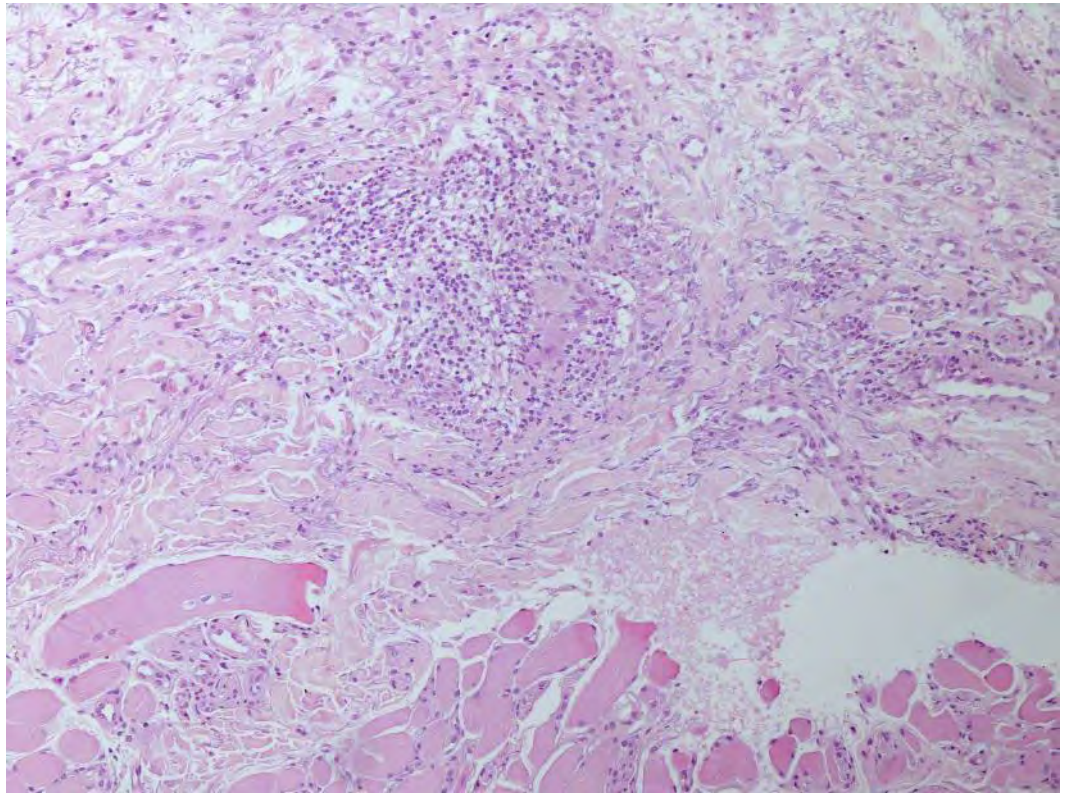
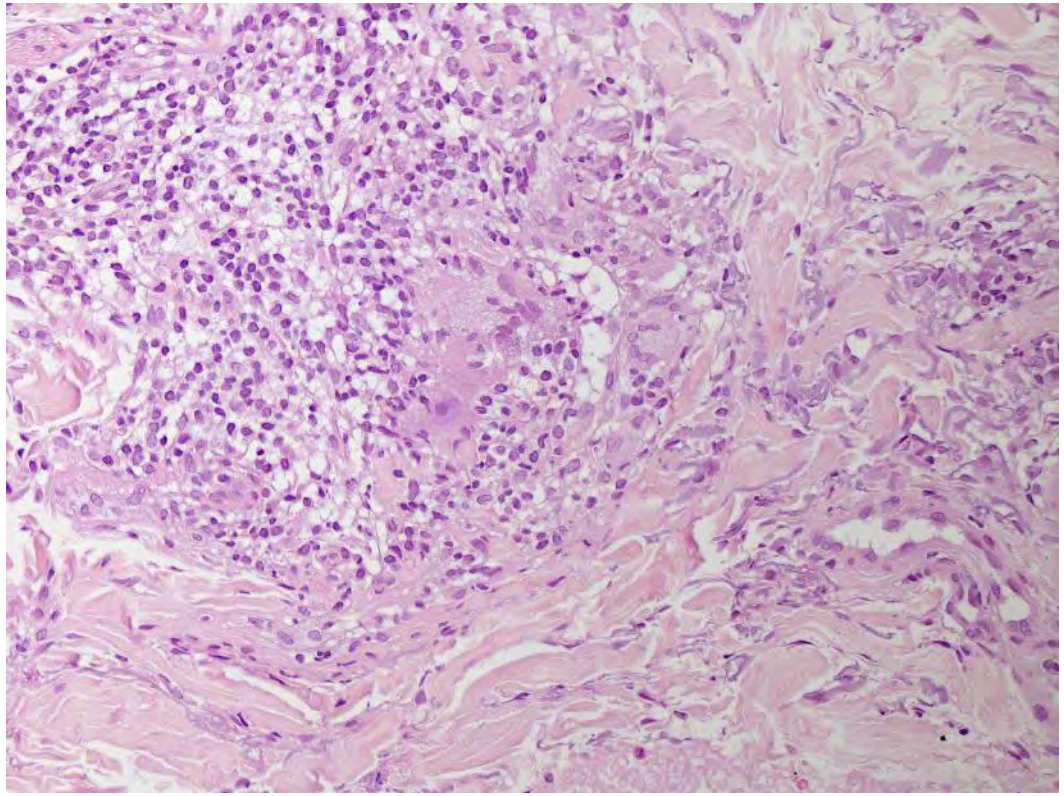


Other deeper area (near skin muscles) with granulomas protruding into the vascular lumen (arrow)



Same as previously, at higher magnification.

Granuloma: Patho-mechanism of PDT

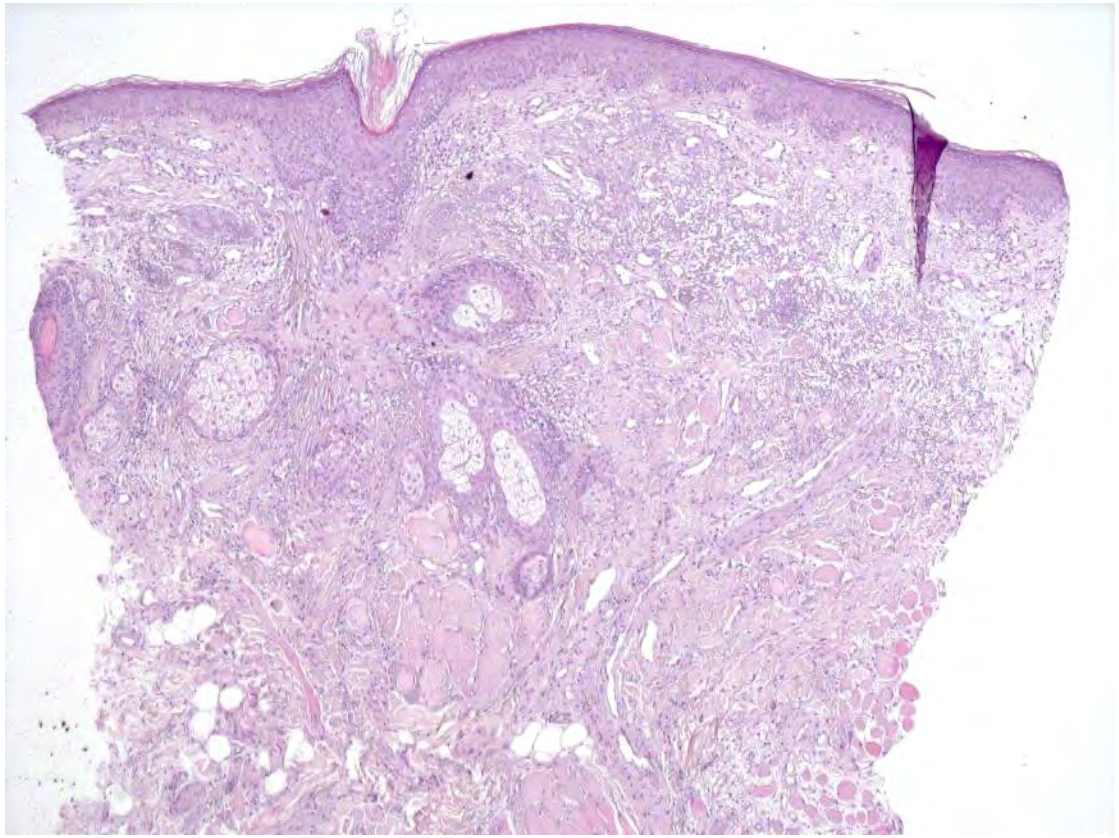
Anti-inflammatory and immunomodulatory effects	• New approaches for management of inflammatory dermatologic diseases
Protoporphyrin 9 levels are **higher in active immune cells** after application of 5-ALA cream	• **Photo-apoptosis** • Inactivation during illumination by red light without damage on skin cells
PDT may reduce	• **MHC I and** II on dendritic cells • Immune cells surface receptor expression
PDT increases	• **Anti-inflammatory IL-10 levels**
PDT decreases	• **Pro-inflammatory IL-6 levels**

Treatment

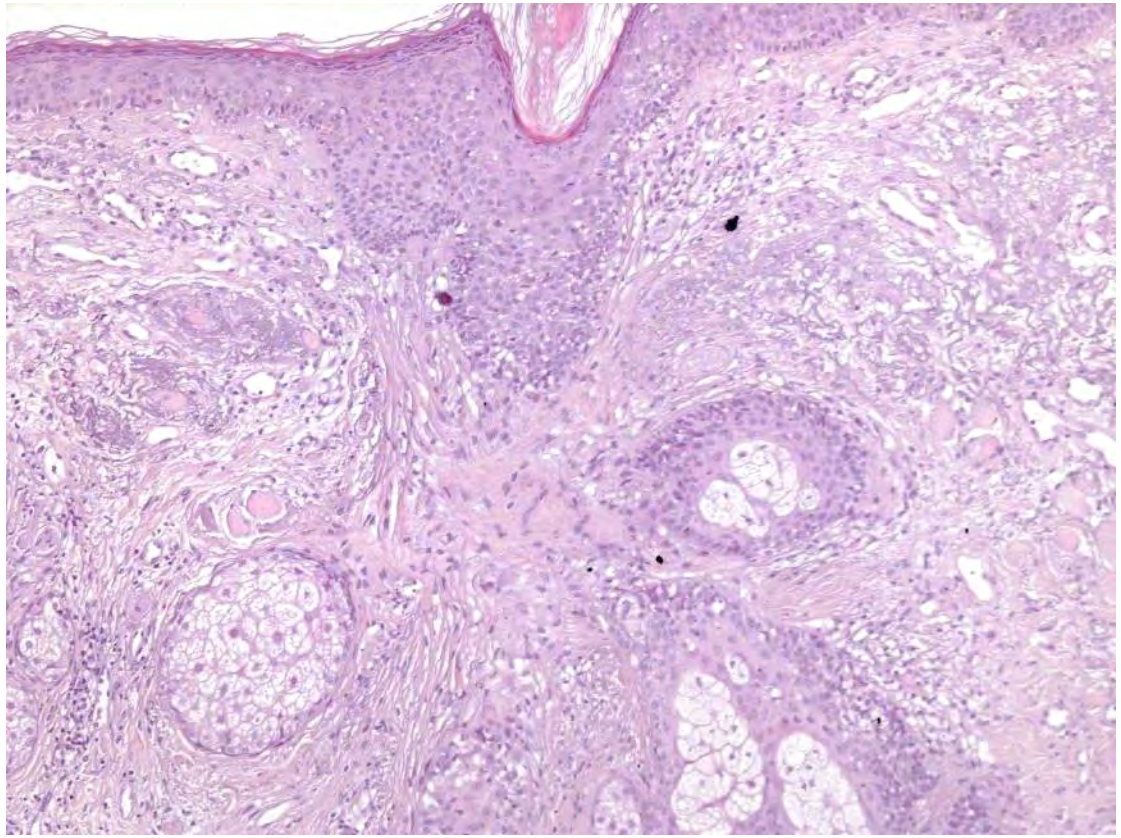
- Considering **the major aesthetic and functional discomfort** caused, the patient was offered treatment with conventional photodynamic therapy:
  - **3 monthly sessions** of conventional photodynamic therapy
  - Methyl-aminolevulinic acid cream (Metvix) to the entire lip and perioral area
  - A 3-hour session with application under an opaque dressing
  - Session of illumination under a red LED lamp 632nm and 37J/cm2

Post Treatment Biopsy

Anatomopathology Pr Josette André



Clear regression of the infiltrate. Only a discrete granuloma-free infiltrate around a pilar infundibulum remains.



At higher magnification, discrete, superficial, perifollicular lymphocytic infiltrate (arrow)

PDT: results

- **1st session:**
  - improvement in the frequency of flare-ups right from the first session, going from **daily oedema to 1 or 2 flare-ups per week.**
- **2nd session:**
  - frequency of flare-ups was reduced from **daily to monthly** and she reported a clear improvement in her quality of life with regard to aesthetic and functional discomfort.
- **3rd session:**
  - **no further relapses.**
  - **complete regression** of the labial hypertrophy with a return to basal status
- **Follow up after 2 years : no relapse !!!**

EUROPDT

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21ST ANNUAL CONGRESS

THE EUROPEAN SOCIETY FOR PHOTODYNAMIC THERAPY

Barcelona, Spain
Friday 9 and Saturday 10, June 2023

N-acetyl cysteine and Raloxifene in the response of squamous cell carcinoma cells to photodynamic therapy

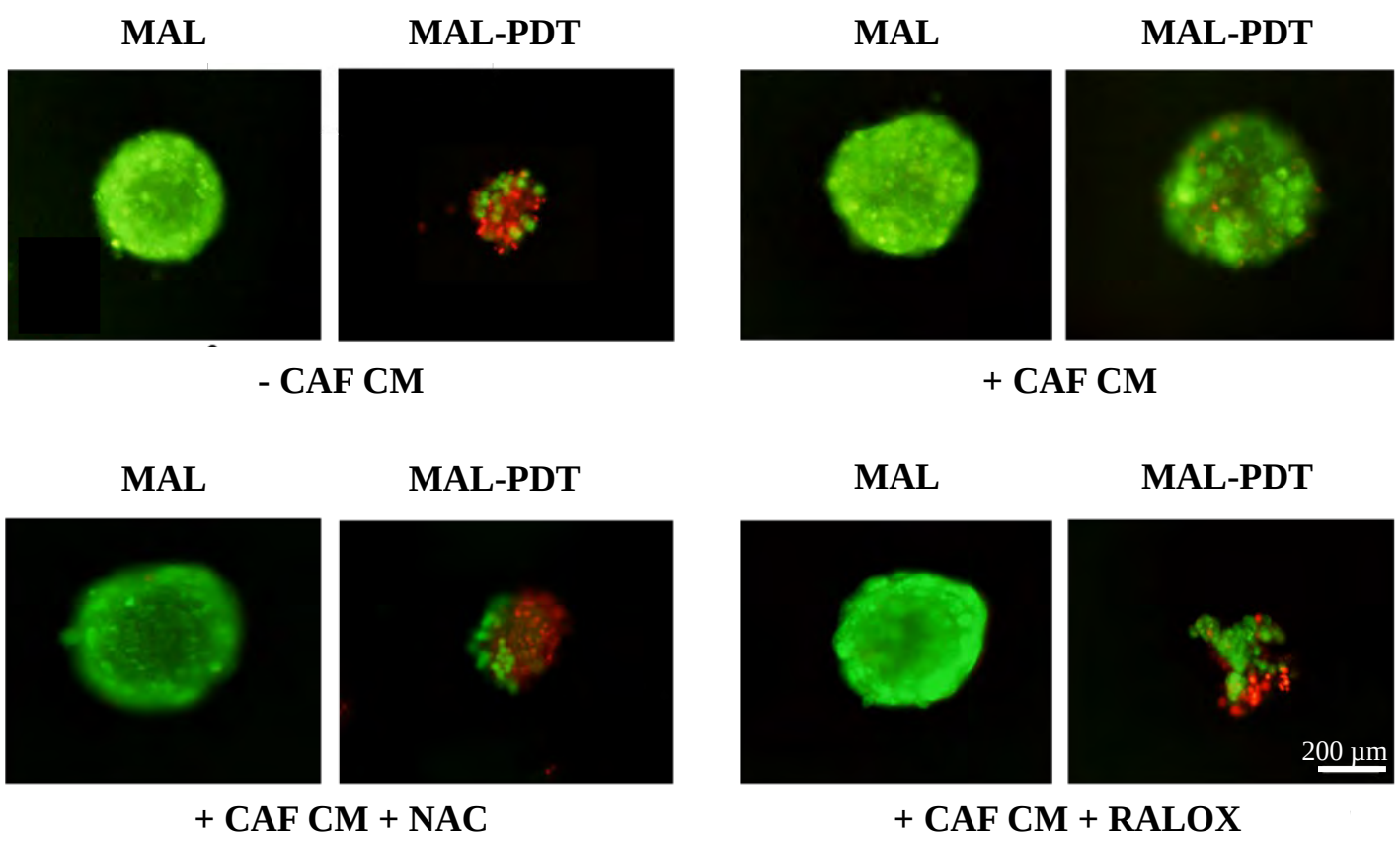
María Gallego Rentero
Madrid, Spain

Read the abstract

VIABILITY AND SIZE OF A431 SPHEROIDS IN RESPONSE TO COMBINED TREATMENTS

Acridine orange: all cells

Propidium Iodide: dead cells



MAL 0.5 mM

MAL + CM

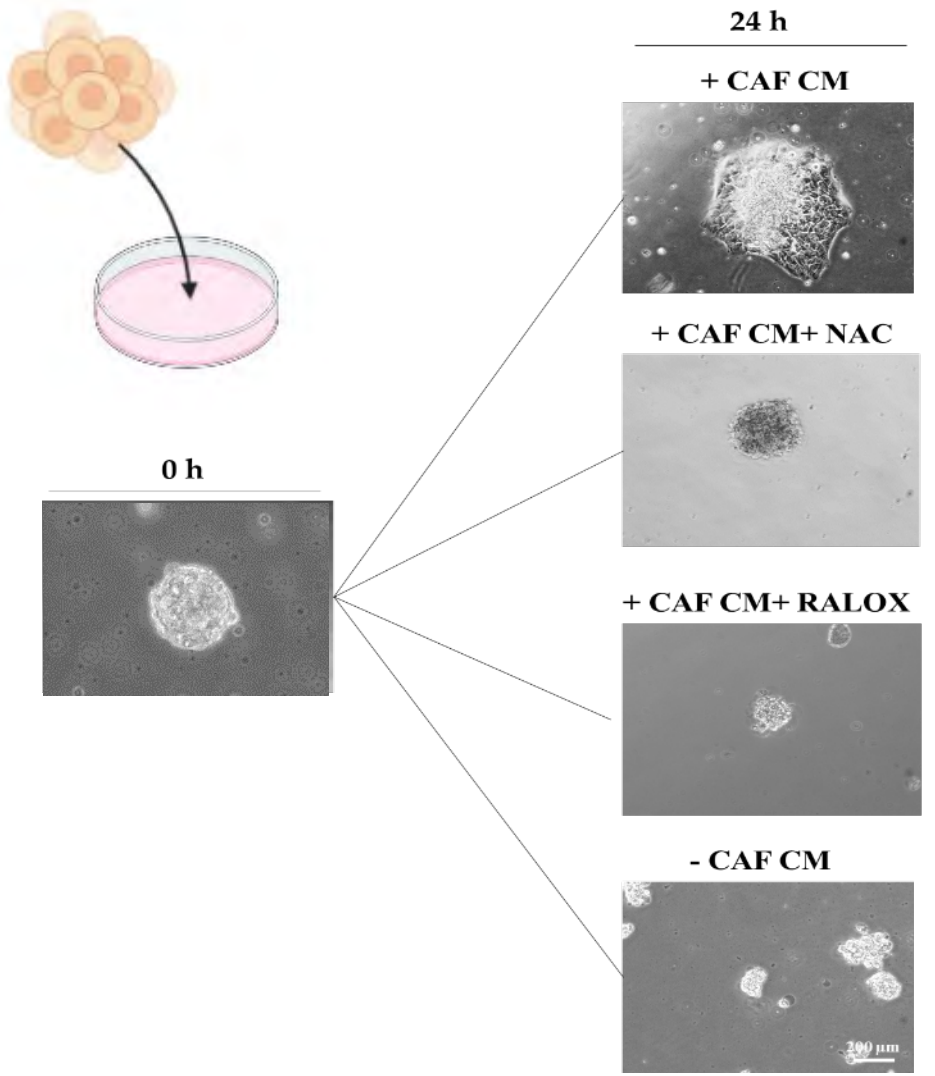
MAL + CM + NAC 100 µM

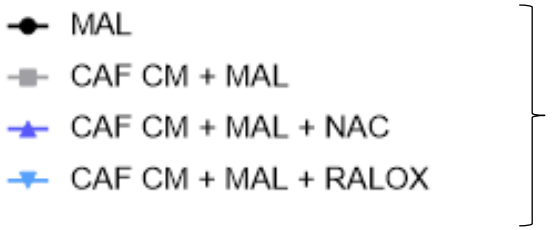
MAL + CM + RALOX 0.2 nM

NAC and raloxifene reverse PDT resistance induced by CAF CM in A431 spheroids

Gallego-Rentero *et al*. Cancers. 2021

EXPLANT SIZE OF A431 SPHEROIDS



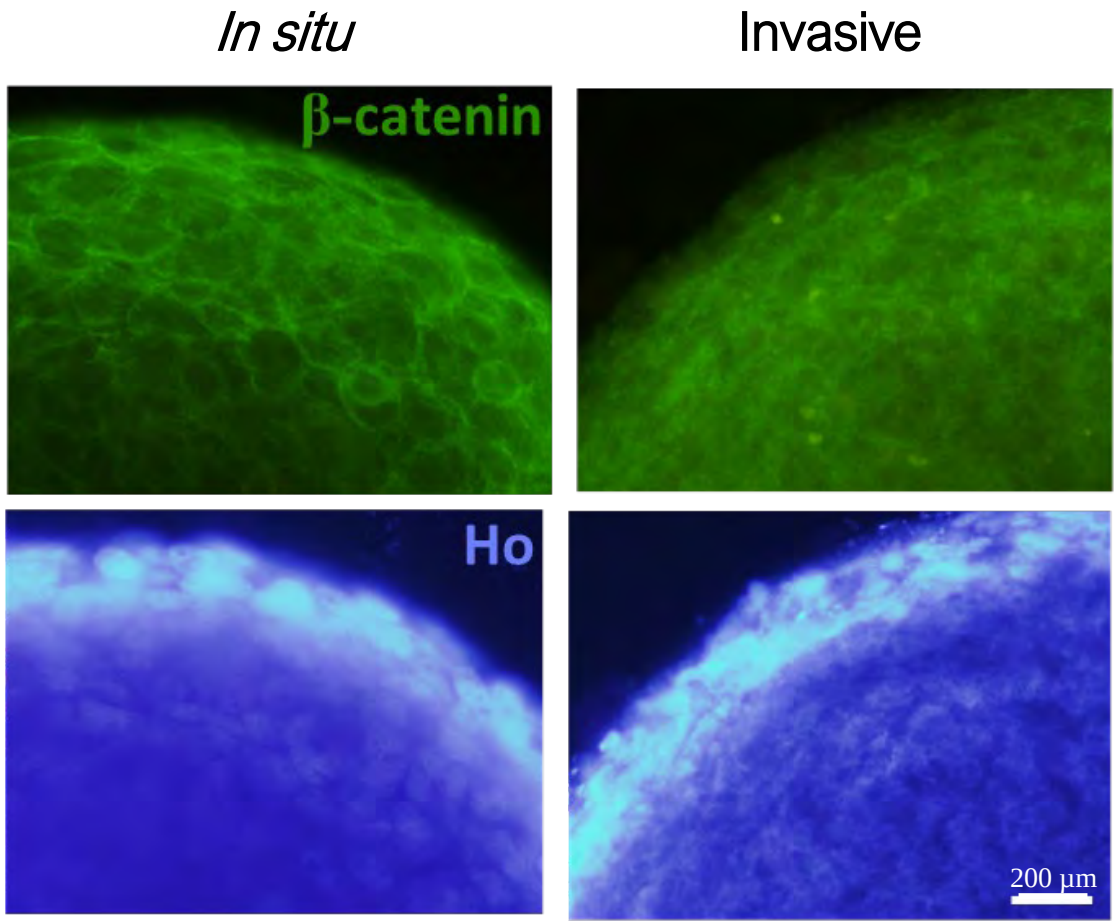


+ RED LIGHT

NAC and raloxifene reverse the migratory capacity induced by CAF CM in A431 spheroids

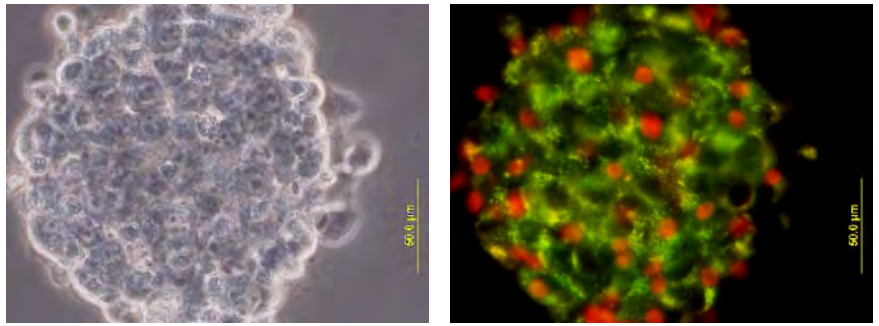
Gallego-Rentero *et al*. Cancers. 2021

MIXED SPHEROIDS: SCC CELLS + CAFs



CONCLUDING REMARKS

- CAF CM induces resistance to PDT in A431 spheroids.
- NAC and Raloxifene reverse PDT resistance in A431 spheroids.
- Mixed spheroids formed with SCC cells and CAFs constitute a promising model for the study of resistance to PDT.



Meeting summary

Summary 1/3

Current landscape in PDT for AK/NMSC

- The priority is to **prevent AK progression to SCC** (with basal proliferation a risk factor for progression)
- New recommendations and tools exist for the **personalized management** of AK
- The evidence base for PDT in AK/skin cancer care is strong – including new 5-year data for PDT for BCC, and confirmed effectiveness for actinic cheilitis
- Patient populations of high therapeutic need include people with **occupational sun exposure** and **solid organ transplant recipients**
- PDT is a 'booming business', with ongoing global research

Remaining unmet needs in PDT for AK/NMSC

- Clinical trials – if number of AKs/area size are the most relevant factors, why keep these parameters low in clinical trials?
- Inequity of access – it is important to provide every patient with appropriate, efficient, sustainable treatment – encourage patient access to PDT
- Wider programme – need for AK treatment strategies to be embedded as part of optimized primary prevention and early diagnosis/surveillance

AK, actinic keratosis; BCC, basal cell carcinoma; NMSC; non-melanoma skin cancer; PDT, photodynamic therapy.

Summary 2/3

Optimizing delivery of PDT

- Evolution in PDT application: Conventional, daylight, simulated daylight, home treatment and more
- **Daylight-PDT** is effective, well tolerated and feasible (even in countries not known for sunny weather!)
  - Careful selection of patients and lesions is critical; particularly effective for thin field change AK
  - Nurses can have a major role in the delivery and monitoring of daylight PDT
- **Home daylight-PDT** offers greater convenience, but needs further study to identify the most appropriate patients
- Increasing published data on the efficacy of **artificial daylight PDT** in the treatment of AK
- **Combination therapies** show promise
- Expert recommendations have been recently published **for pre- and post-PDT-procedure skin care**, and for use of **laser-assisted PDT**

AK, actinic keratosis; PDT, photodynamic therapy.

Summary 3/3

PDT beyond AK/NMSC: Emerging indications

- PDT has been used in certain presentations of **cutaneous lymphoma** and **pseudolymphomas**
  - Early disease stage and lesion type are key to patient selection
  - Further studies are needed
- PDT is effective for **acne** in clinical studies
  - Optimized protocols and guidelines, evidence for long-term efficacy, and licensing approval are awaited
- Antimicrobial PDT can assist the treatment of challenging **infections**, although more clinical trials are needed
- PDT is effective for **photorejuvenation**, by increasing neocollagenesis with several protocols described
- Case reports suggest a potential role for PDT in **Kaposi sarcoma** and **Miescher granulomatous macrocheilitis**
- The EDF guidelines on PDT capture the current strength of evidence for emerging indications

AK, actinic keratosis; EDF, European Derrmatology Forum; NMSC; non-melanoma skin cancer; PDT, photodynamic therapy.

Abstracts

New Insights in Pathology of AK

Thomas Dirschka
Wuppertal, Germany

Actinic keratoses (AK) represent early in-situ squamous cell carcinomas of the skin. Without appropriate therapy there is a risk of progression into invasive cancer. In view of the increasing number of patients suffering from AK and more and more extensive cases of field cancerization in impercetibly strained heath systems, it is almost impossible to treat all lesions completely. It is therefore becoming increasingly important to separate aggressive growth forms of AK at an early stage to avoid invasive tumour growth. Clinically, it is bearly impossible to distinguish between AK of different pathological abilities as they resemble each other. However, field cancerization represented by high AKASI, proliferative basal growth pattern, acantholysis and treatment refractory lesions are indicators of high aggressivity. Recently developed new technologies as line-field confocal optical coherence tomography open up new ways to assess AK lesions non-invasively.

Global Trends and Guidelines in PDT for skin cancer

Colin Morton
Stirling, UK

Publications around PDT for skin cancer have been mapped to 79 countries in a bibliometric analysis from 1988-2022, with the largest number of studies from US, China, UK and Germany. From the business perspective, a market report indicates that the global PDT market size is expected to grow from $4.58 billion in 2022 to $9.35 billion in 2027. Evaluation of availability of PDT for the US Medicare population 2012-17 showed inequity of access - offered by 41.6% of dermatologists in metropolitan regions compared with only 5.4% of nonmetropolitan counties.

Evidence-based guidelines identify the indications and presentations where we can expect best response to the use of topical PDT although most commercialisation has been around the approved indications of AK, Bowens and BCC (JEADV 2019;33:2225-38). Emerging indications including acne have also been extensively assessed but still lack optimization of protocols (JEADV 2020;34:17-29). Evolution of protocol for PDT use to treat AK via daylight or simulated daylight, to minimize discomfort, and an increasing number of studies around treatment at home, are likely to improve patient access to PDT. Clearer direction on efficacious combination therapy with PDT will also likely see growth in therapy use.

MAL-PDT for the treatment strategy of actinic keratosis: Broader clinical perspectives beyond the data and guideline recommendations

Piergiacomo Calzavara-Pinton, Chiara Arisi Maria, Sara Rovaris
Brescia, Italy

Recently, a growing number of drugs and physical techniques became available for the treatment of multiple actinic keratoses and field of cancerization.
All treatments are presented in term of clearance rate after a single treatment cycle.
Therefore, the efficacy of these drugs is presented in terms of ability to obtain an oncological eradication.
However, a definitive eradication is hardly obtained in the case of multiple actinic keratoses and field of cancerization.
We have reviewed the medical files of our patients with multiple Aks who were treated at least 10 years ago and were followed up at 6-12 months intervals.
No patient cleared permanently and forever but they needed more treatment cycles.
Some patients developed BCC and SCC in the treatment area but they were superficial and the surgical removal was enough to heal.
Therefore, tumor eradication is an unrealistic goal for these patients who should be treated in the perspective of a chronic palliation and a prolonged follow-up.
In this perspective, patients' adherence to treatments, acceptance of treatments and willingness to repeat the treatments play a very important role.

The Personalising Actinic Keratosis Treatment (PAKT) project - final outcome

Colin Morton, Samira Baharlou, Nicole Basset-Seguin, Piergiacomo Calzavara-Pinton, Thomas Dirschka, Yolanda Gilaberte, Merete Haedersdal, Günther Hofbauer, Sheetal Sapra, Rick Waalboer-Spuij, Leona Yip, Rolf-Markus Szeimies
Recklinghausen, Germany

Actinic keratoses are pre-malignant skin lesions that require personalised care, a lack of which may result in poor treatment adherence and suboptimal outcomes. Current guidance on personalising care is limited. The aim of the Personalising Actinic Keratosis Treatment panel, comprised of 12 dermatologists, was to identify unmet needs in care and, using a modified Delphi approach, develop recommendations to support personalised, long-term management of actinic keratoses. Panellists generated recommendations by voting on consensus statements. Voting was blinded and consensus was defined as ≥75% voting 'agree' or 'strongly agree'. Consented statements were used to develop a clinical tool, of which, the goal was to improve understanding of disease chronicity, and the need for long-term, repeated treatment cycles. The expert recommendations and the clinical tool can be used to facilitate patient-centric actinic keratoses management in daily practice, encompassing patient priorities and goals to set realistic treatment expectations and improve care outcomes.

PDT for prevention

Claas Ulrich
Berlin, Germany

Cutaneous squamous cell carcinoma (cSCC) represents one of the most common cancers among Caucasians worldwide and is dramatically increasing in terms of overall prevalaence but also critical cases and even fatalities. Relevant factors beyond chronic UV-exposure are the increasing lifespans and the improvements in survival for conditions that impair local cutaneous- or overall immunosurveillance. In the USA the absolute mortality of cSCC exceeds melanoma in and approaches that of melanoma worldwide. cSCC could arise de novo or be the result of a progression of the actinic keratosis, an in situ carcinoma. PDT represents one of the most established and effective therapy which shows its immanent benefits especially if used in wider areas of actinic field damage representing the typical areas of origin for subsequent invasive cSCC. With persistent remission rates exceeding 70% of AK lesions treated in the 12 months follow-up, PDT represents not only an attractive management for the short term but provides a certain preventive effect against new AK lesions developing in the field treated. However, strong evidence for a preventive impact of PDT (and other topical AK therapies) against invasive cutaneous squamous cell carcinoma is still missing in this high risk groups (outdoor workers, organ transplant recipients and others). Similar to other treatment approaches aiming for AK, but nowadays representing an essential pillar in the comprehensive and sustainable management of patients at high risk for invasive cSCC, new studies evaluating secondary preventive effects against invasive skin cancers are much needed.

5-FU pretreatment for PDT

Stine Regin Wiegell, Gabriella Fredman, Flemming Andersen, Peter Bjerring, Uwe Paasch and Merete Haedersdal
Copenhagen, Denmark

Daylight photodynamic therapy (dPDT) and topical 5-fluorouracil (5-FU) are effective treatments of actinic keratosis (AKs). However, efficacy is significantly reduced when treating moderate or thick AKs and topical treatments can be associated with severe local skin reactions. The aim of this study was to compare the efficacy of sequential 4% 5-FU and dPDT with dPDT monotherapy in the treatment of multiple actinic keratoses in the face and scalp. Sixty patients were treated in two symmetrical areas of the face or scalp which were randomized to 4% 5-FU creme twice daily for 7 days before a single dPDT procedure and dPDT monotherapy. Twelve weeks after treatment 87% of all AKs cleared after 5-FU+dPDT compared to 75% after dPDT alone ($p<0.0001$). For moderate thick AKs, the lesion response rate increased from 56% with dPDT monotherapy to 78% after 5-FU+dPDT ($p<0.0014$). 5-FU pre-treatment resulted in moderate to severe erythema before dPDT in 50% of the patients. Moderate/severe erythema was seen in 88% 5-FU+dPDT areas compared to 41% of dPDT areas. Twelve weeks after treatment 75% of the patients were equally very satisfied with both treatments. Sequential 5-FU and dPDT was more effective than dPDT monotherapy in the treatment of AKs in the face and scalp, especially for moderate thick AKs. Local skin reactions were more pronounced after combination treatment, but no patients discontinued the treatment. The combination of 5-FU and dPDT is a convenient and effective treatment with high compliance.

PDT for Occupational Diseases

Berenice Lang
Mainz, Germany

AK and SCC caused by natural UV radiation have been listed as occupational diseases in Germany recently. With this legal anchoring, employees who have worked predominantly outdoors are entitled to have their treatment costs covered by the employers' liability insurance association.

Patients with a recognized occupational disease have usually suffered a high degree of chronic UV damage in the course of their working lives, and the late effects will continue to appear gradually. Thus, this patient group has a regular need for treatment in the sense of a chronic disease.

PDT is ideally suited for the treatment of AK in an occupational context: on the one hand, it can be performed quickly, is easy to reproduce and a combination with other procedures such as laser is possible. On the other hand, not only acute tumors but also preclinical lesions are already treated in terms of secondary prevention.

European Consensus on the Consistent Use of the Term “Keratinocyte Cancer”

Wolfgang Philipp-Dormston
Cologne, Germany

Rationale: Scientific progress, a better understanding of the pathophysiological mechanisms, new findings and treatment options, and finally the growing acknowledgment for the medical field of keratinocyte derived cancer as paramount part within dermato-oncology have led to an increasing number of terms and definitions in that field. Some of these with historical background, some based on more or less reasonable assumptions and yet others being unprecise due to the exponentially forwarding scientific progress. At the head the unfavorable term "non melanoma skin cancer (NMSC)".

Taking into consideration, that a medical diagnose, respectively group of diagnoses is defined be what "it is not", in terms of “anything but Melanoma” does not give the right consideration and appreciation to that important group of malignancies and their precursors. Furthermore, the term NMSC reveals a lack of precision, at least in the way it is commonly used, referring to alterations and cancer in keratinocytes. Other malignancies, e.g. Merkel cell carcinoma are also subsumed within NMSC. A more precise and reasonable terminology, valuing the relevance of keratinocyte derived cancer, appears therefore consequent to meet its clinical and scientific significance. The hereby proposed sporadically used term "keratinocyte cancer (KC)", would be far more precise and applicable.

Consensus procedure: The consistent use of the term "keratinocyte cancer" will be proposed, based on a questionnaire-voting amongst the faculty and members of the Euro-PDT 2023 to obtain a European consensus carried by the expertise of the leading dermato-oncologist in that field. The results of the consensus will be evaluated and discussed, with the aim to publish a letter together with the board of the Euro-PDT proposing the consistent use of this new terminology.

Daylight-PDT and Weather - always an easy one?

Sally Ibbotson, O'Reilly M, Goodman C, Yule S, Lesar A, Eadie E.
Dundee, UK

Daylight-PDT (DPDT) is an effective and well-tolerated approach for actinic keratoses (AK) on the face and scalp, although relying on the weather is risky in Northern Europe. We commenced DPDT in Dundee in 2013 and found it effective and well-tolerated, despite Scottish weather. A patient engagement event highlighted that convenience was as important as efficacy and adverse effects for those receiving DPDT. In conjunction with an Art & Design student, we therefore developed a recyclable home-DPDT-kit to enable patients to take control of their treatment, and to select treatment days based on the weather. We piloted this in 2021, showing low pain scores (median 1.5/10) and excellent/good outcomes in 66% (n=6). Patients were highly satisfied with treatment, found it convenient and would have home-DPDT-kit again, indicating as proof-of-concept that this approach merits further research and development as a convenient home-based treatment for patients with superficial AK on the face and scalp.

Multilite-PDT for AK - a single center observational study

Sven Quist, Jennifer Quist
Mainz, Germany

Skin cancer is continuously increasing in the western hemisphere. One of the most efficient ways to treat skin cancer such as actinic keratosis, Bowen's Disease or superficial basal cell carcinoma is photodynamic therapy. The Multilite light artificial daylight PDT system starts with blue (415 nm), followed by yellow (585 nm) and red light (635 nm) light allowing a penetration dependent layer-by-layer activation of PpIX. In this observational study, we analyzed around 600 treatments for actinic keratosis, using a 35 min protocol and an 80 min protocol. Patient were examined around 3, 6, and 12 months following the Multilite treatment. Results: Remission was observed in 91% of patients. The remission rate did not differ significantly between the two protocols. The 80 minutes protocol was much less painful than with the 35 minutes protocol. Conclusion: the Multilite artificial indoor gentle, photodynamic therapy is officious flexible, easy to apply and space-saving treatment option.

PDT for Actinic Cheilitis

Ana Julia Garcia Malinis, Dolores Planas Linares, Yolanda Gilaberte
Huesca, Spain

Introduction: Actinic cheilitis is a premalignant condition that may progress to squamous cell carcinoma. This disorder of the lips is associated with higher propensity for metastasis. Optimal treatment for actinic cheilitis has not been well established. In systematic reviews, multiple treatments have been described, from the most invasive such as surgery to less invasive treatments such as laser or imiquimod.. We present our experience with PDT and actinic cheilitis.

Material and methods: A retrospective observational study was performed including all patients diagnosed with Actinic cheilitis and treated with PDT between 2008 and 2019. Continuous variables were described using means and standard deviations. Statistical analyses were carried out using SPSS software (version 20.0, Armonk, NY: IBM Corp).

Results: Twelve patients were included in the study. Ten patients (80%) were men and 2 women (20%), with an average of 80 years old. All patiens responded to PDT treatment. The mean follow-up was 30 months.

Discussion: The efficacy of PDT in the Actinic cheilitis is high. Conventional photodynamic therapy (PDT) and daylight PDT may offer a noninvasive effective treatment option for actinic cheilitis.

What’s new with PDT Light, a painless and effective Treatment of Light Skin Cancer?

Martin Braun, Anna Wölling
Überlingen, Germany

Following experiences of 546 patients discontinuing PDT-treatment between 2003- 2014 because of intolerable pain, showed the necessity for milder therapies. Therefore, a less-respectively-no-pain-PDT-method should be implemented as primary goal of patient-centered health care.
Meanwhile, we audited all cases. To overview the longer-term-effectiveness, an obligatory-follow-up-examination was implemented. Average-follow-up examination time: 8,14 months. Thus, from primarily 178 patients, 49 who had not appeared within 6 months after last treatment, were excluded from the study.
Our single-centre-retrospective-study reports 152 cases (129 patients) with AK 1-AK 2, BCC (thickness < 1 mm).
We refined the evaluation of our study, subdividing the results observed at followup-examination, into 5 different classes: A-Clearance (80-100%=excellent) was achieved at 78,1%, B-Clearance (60-79%=good-very good) at 11,6%, severe-sideeffectsat 5,6% of cases. Main results:

1. Significant pain-reduction with achievement of lowest VAS-Score (1,33).
2. Similar efficacy, compared to classical PDT-methods.
3. For the cold period, a 2-step-illumination-protocol, with advantages to Artificial-DL-PDT, is presented.

Artificial daylight: IndoorLux experience

Wim Venema
Assen, Netherlands

Daylight-PDT is a proven simple yet effective treatment for mild to moderate AK. Temperature and illumination are limiting factors leading to increased interest in artificial light sources.` In the Wilhelmina Hospital Assen we installed a light room using the IndoorLux system producing a light spectrum between 570 and 630nm mimicking part of daylight. We performed a small prospective study in 28 patients with mild to moderate AK. Results were compared with a recent daylight study using the AKASI score. Comparing mean improvement of AKASI score no clear difference in outcome was observed. Due to the limited sample size no statistics where performed. VAS score for pain was very low and the treatment had a high convenience. PDT using artificial daylight with the IndoorLux system offers results comparable to regular daylight PDT yet offering increased usability.

Simulated Daylight-PDTwith BF-200 ALA for AK: assessment of the efficacy and tolerability in a retrospective study

Christina Haut, C. Kellner, S. Bauriedl, S. Hollstein, U. Reinhold
Rheda-Wiedenbrueck, Germany

Background: Photodynamic therapy (PDT) is a highly effective treatment for patients with actinic keratosis (AK). It is, however, often painful and may even lead to acute postoperative hypertension. Natural daylight-mediated PDT (NDL-PDT) has recently been suggested as a more tolerable treatment procedure for PDT. While offering some advantages, NDL-PDT is a non-standardized approach that is influenced by several factors such as geographic location, weather conditions and time of the year.

Objectives: The objective of this retrospective study was to evaluate the efficacy and safety of a simulated daylight PDT (SDL-PDT) performed in a treatment room of a dermatological praxis.

Homebased Photodynamic Daylight Therapy, My daily practice approach at the UZ Brussels

Samira Baharlou
Brussels, Belgium

Daylight Photodynamic therapy is a convenient and long-established option to treat large areas of field-cancerisation. This method is usually painless, with significantly less side effects and a shorter recovery time than classic PDT. However specific weather conditions are necessary for a successful treatment outcome and can challenge both doctors and patients in the daily practice.

Homebased photodynamic daylight treatment opens up a new possibility for patients to plan their treatment when weather conditions are optimal and personal timing is suitable. Avoiding postponing and re-planning these necessary treatments as well as enabling patients to self-manage their treatment procedure in the comfort of their own home.

Patients that are already familiar with classic- or daylight photodynamic therapy are most suitable to transition smoothly to a homebased treatment option since procedure steps as well as post treatment care are already known.

Since introducing homebased daylight photodynamic therapy into my daily practice at the UZ Brussel Dermatology Department, I was able to conduct more successful photodynamic daylight treatments as well as improve significantly my patient’s satisfaction.

Galderma provides well thought thru patient treatment kits and a new mobile phone application which helps patients to navigate safely thru their treatment cycle.

Is it still necessary to use dedicated red LED sources for PDT of deep lesions?

Serge Mordon
Ascain, France

Conventional-PDT protocol (C-PDT) involves 8 to 10 min of illumination with red light (Galderma, Aktilite CL128® 37 J/cm²) three hours after MAL application. C-PDT is associated with high pain during illumination that often lead to premature end of treatment. To address the pain, Artificial Daylight-PDT protocol (AD-PDT) induces continuous activation of PpIX with low-intensity light exposure with white light during two hours and thirty minutes after MAL application (Surgiris, Dermaris®)
To date, the treatment of squamous cell carcinoma in situ and superficial basal cell carcinoma with C-PDT is based on the claim that only red light penetrates deep enough into the epidermis to reach deep lesions However, most AD-PDT light sources deliver white light with continuous spectrum, a significant amount of red light is provided.
Thus, the illumination time required with AD-PDT light sources to obtain the same PpIX effective fluence in depth as the C-PDT light sources can be calculated. On the one hand, PpIX effective fluence obtained with C-PDT have been determined considering spectral irradiance of Aktilite CL128®, fluence rate at 1 mm depth, PpIX absorption spectrum and 8 minutes of illumination. On the other hand, illumination time of AD-PDT light source required to achieve same PpIX effective fluence obtained with C-PDT have been determined considering spectral irradiances of Dermaris®.
Finally, same PpIX effective fluence obtained with C-PDT at 1 mm depth can be performed with AD-PDT light source after 3 hours with Dermaris®. This illumination time can be as short as 30 minutes by reducing the size of the light field (Surgiris, Dermaris +®).
Moreover, recent clinical results have indicated that PDT of actinic keratoses can be performed successfully with reduced illumination time. This finding suggests that illumination time with AD-PDT light sources could be even reduced and would better fit the organization of private practice.

ADL-PDT revisited: My experience with the Medisun device

Wolfgang Philipp-Dormston
Cologne, Germany

The artificial daylight PDT system Medisun® (Schulze & Böhm GmbH, Germany) has been specifically developed for the treatment of actinic keratosis and field cancerization. The computer-controlled LED daylight spectrum consists of wavelengths between approx. 400 nm and approx. 750 nm and thus acts simultaneously on all absorption peaks of the photosensitizer. Different protocols have shown to be safe and effective: 120 min. illumination beginning within 0-30 min after MAL application (on-label protocol), 60 min. incubation with MAL or ALA followed by 60 min. illumination.

Pre-treatment procedures in terms of fractionated laser assisted drug delivery to enhance the efficacy of the Medisun®-ADL-PDT have also been investigated with remarkable results and contribute to improved treatment outcomes in daily practice.

Due to the individual programmability of the high-performance multicolor LEDs by means of digital touch control, mono-color treatments with red light, blue light or red/blue light are also feasible for special indications.

Pre- and Post-treatment procedures for PDT

Jens Malte Baron, Yvonne Marquardt, Sebastian Huth
Aachen, Germany

Recently various national and international expert recommendations and guidelines have been published on the pretreatment before and the supportive skin care after photodynamic therapy (PDT) of the skin. These recommendations will be presented in this talk.

In addition pre- and post-treatment after PDT was recently studied in vitro by our research group utilizing a human 3D skin model of actinic keratosis (AK-3D). These models were first irradiated with a fractional ablative laser (Er:YAG or CO2 Laser) directly followed by topical treatment with a cream containing 5-methyl-aminolevulinic acid. This was followed by irradiation with an artificial daylight lamp or red LED lamps with or without topical aftercare-treatment for a total of 24 hours. After this treatments, histological examination was performed using haematoxylin-eosin staining and gene expression profile was detected using NGS- or microarray analysis.

Nurses for Daylight-PDT

Pasquali Paola
Valls, Spain

Nurses will participate more in the management of the elderly population and their sun related morbidities. Daylight PDT and classical PDT are procedures that can and should be managed by trained nurses. The following presentation will deal on the experience of PDT in nursing homes and the supporting role of Teledermatology in reducing unnecessary transfer, reduce morbidity, and improve on early diagnoses in the geriatric population

Daylight-PDT in general practice in the Netherlands

Maartje Spit
Son, Netherlands

The prevalence of actinic keratosis (AK) in the Netherlands is high and causes a burden on the healthcare system. Since GP's are the gatekeepers of healthcare, many patients with AK are treated in general practice. Patients with AK are treated by GPs, nurse practitioners (NPs) and physician assistants (PAs). In the Dutch guideline for suspected skin lesions (2017) it is advised to treat AK in primary care. Most lesions are treated by cryotherapy or topical agents. Treating field AK can be challenging. Since 2022 DL-PDT can be used in general practice, attention for this treatment is increasing. The goal of this presentation is to share experiences from a Dutch general practice with DL-PDT performed by a nurse practitioner.

Counteracting side effects of PDT

Hans Christian Wulf
Copenhagen, Denmark

Classic PDT consists of superficial curettage, application of 5-aminolevulinic acid (ALA) or methyl aminolevulinate (MAL), occlusion for 3 hours, followed by illumination with red LED 37 J/cm2. Side effects include unpleasant, possibly painful, pretreatment, severe pain during illumination, and long waiting time in the clinic, which can be prevented by using daylight PDT.

To counteract side effects and simplify the procedure we propose to: (i) reduce pre-treatment pain, bleeding, and oozing by omitting curettage which is of particular concern in patients treated with anticoagulants; (ii) shorten the MAL incubation time from 3 hours to 30 minutes (pulse PDT) to minimize pain and risk of post-treatment inflammation; (iii) use topical corticosteroids combined with different PDT modalities to further reduce inflammation without loss of effect. In addition, options of timing, incubation, and illumination indoors and outdoors are discussed, focusing on advantages and disadvantages for the patients and clinics.

The Solid Organ Transplant Clinic in Padova: Our 25-Year Experience

Stefano Piaserico
Padova, Italy

An increased frequency of neoplastic disorders is a recognized complication of solid organ transplantation1. Skin cancers are the most common malignancies that occur in transplant recipients; their frequency increases with time after transplantation1. A reversed squamous cell carcinoma (SCC)/basal cell carcinoma (BCC) ratio has been observed in transplant recipients compared with the general population as a result of an excess incidence of SCC. Moreover, SCC is believed to be more aggressive, with a higher risk of metastasis in transplant recipients than in the general population2. In 1996, a dedicated Organ Transplant Recipients (OTR) Clinic was started in Padova. Since then, we've been offering this service every morning without the need of booking the appointment. Currently, we are following more than 3000 transplant patients. Conventional therapies for AK, using curettage, cryotherapy, surgical excision, topical therapies and photodynamic therapy (PDT), are often less effective, and may be inappropriate, for treating the greater numbers and extent of lesions in OTR. Against this backdrop, Topical PDT could represent a useful therapeutic alternative for AKs in OTR because large lesions can be repeatedly treated with excellent cosmetic outcome.

Laser-assisted PDT – here to stay?

Merete Haedersdal
Copenhagen, Denmark

Ablative fractional lasers have emerged as powerful tools to enhance delivery of photosensitizers and drugs into the skin. Laser-assisted PDT has reached maturity as a standard treatment technique, leading to improved therapeutic outcomes for patients with a high burden of actinic keratosis and severe photodamage. The enhanced efficacy compared to PDT-monotherapy has been confirmed in RCTs and systematic reviews.
It is now the time to call for intelligent application of laser-assisted PDT, combining the highly customizable laser-pretreatment with different photoactivation approaches such as conventional PDT, natural and artificial daylight-PDT.
It is the goal is to tailor PDT treatments to individual patient needs.

PDT as Treatment Option for Cutaneous Lymphoma

Stefano Caccavale
Naples, Italy

Photodynamic therapy (PDT) is a non-invasive treatment frequently used in dermatology to treat superficial skin cancers and some inflammatory or infectious dermatoses. PDT appears a promising therapeutic option also for cutaneous lymphomas, either of T- or B-cell origin. PDT has given promising results in many reports published in the literature so far. It is a well-tolerated and safe treatment; it has excellent cosmetic outcomes, less side effects compared to other therapies (steroids, radiotherapy, surgery), few contraindications, and it is easily repeatable in case of relapses. However, the peculiar mechanisms involved in the treatment of cutaneous lymphoproliferative diseases with PDT are poorly understood. The literature data are still controversial; thus, further randomized, controlled clinical trials involving a greater number of centers and patients with a long follow-up are necessary to establish a standardized treatment protocol for each type of cutaneous lymphoma, depending on the type, thickness, and location of cutaneous lesions.

PDT for Acne and Rosacea

Elena Sotiriou
Thessaloniki, Greece

Acne vulgaris is a very common follicular disorder affecting a very high percentage of adolescents and young adults. The physical, psychosocial and economic burden of the disease is significant. First line treatment for acne are conventional topical and oral medications. However, due to limitations of these treatments many light based interventions have been used as alternative options and among them PDT is the most studied one.

Rosacea is a chronic inflammatory disease. Given its chronic, intermittent course it leads to substantial burden. Conventional treatments may display limited therapeutic efficacy. It remains thus challenging to cure or prevent recurrences of rosacea. Several trials reported improvement of rosacea with PDT treatment, suggesting that PDT could serve as an alternative treatment option.

An overview of trials assessing the efficacy and safety of PDT in acne and rosacea as well as of the treatment protocols that were used and evaluated will be presented.

PDT on microorganisms - still too far away from routine use?

Yolanda Gilaberte, Tamara Gracia-Cazaña, Alba Navarro-Bielsa, Manuel Almenara
Zaragoza, Spain

Antimicrobial photodynamic therapy (aPDT) has the advantages of killing all types of microorganisms in minutes, in planktonic or biofilm, being effective against resistant strains and with a low capacity of inducing resistance due to its multitarget action.
However, those microbes that survive after illumination can regrowth and maintain the infection; therefore, several PDT sessions and combination with conventional antimicrobials are needed to cure infections.
Even though, several photosensitizers have been shown to effectively photoinactivate different types of microbes, their use in clinical practice is off-label. However, there are some photodesinfection systems already commercialized to decolonize nares (based on methylene blue) and to treat infected chronic ulcers (a tetracationic Zn(II)phthalocyanine derivative).
The availability of specific photosensitizers to treat infections, protocols to combine with conventional antimicrobials and portable light systems to perform the treatment at home might help to establish aPDT as a routine therapy for cutaneous infections.

PDT for aesthetic indications

Ruben del Rio Gil
Barcelona, Spain

Photodynamic Therapy has its main indication in the treatment of actinic keratosis but also has high efficacy in photorejuvenation in photoaging skin.
Many publications have demonstrated this effect clinically and histologically. Several protocols have been proposed with different photosensitizers, incubation times and light sources

Indications for PDT in children

Francesco Borgia
Messina, Italy

Although Photodynamic Therapy (PDT) is proven as a safe and effective therapeutic option in adults, its use is not well standardized in the pediatric population. On this topic, clinical applications, mechanisms of action, protocols, and adverse events in children and adolescents will be reviewed. Most of pediatric experiences concerned treatment of skin cancers in Gorlin syndrome and xeroderma pigmentosum, acne vulgaris, and viral warts, but other applications emerged, such as cutaneous lymphoma and pseudo-lymphomas, necrobiosis lipoidica, hidradenitis suppurativa, dissecting cellulitis, leishmaniasis, angiofibromas, verrucous epidermal nevus, and linear porokeratosis. A deeper knowledge of its mechanisms of action is required to better define its spectrum of action and safety in pediatric patients.

Successful PDT for Kaposi Disease

Lasse R. Braathen
Berne, Switzerland

A 73-years old healthy Caucasian HIV-negative male presented with a 4x5 mm four weeks old tumorous lesion at his right heel.
A punch biopsy showed Kaposi Sarcoma with positivity for HHV-8.
He was treated with conventional photodynamic therapy with weekly intervals a total of 8 times resulting in complete healing of the lesion. No recurrence after 6 months.
Genetic studies demonstrate few or none deleterious mutations in indolent Kaposi Sarcomas and three or more in aggressive forms.
The question arises if we should rename the cutaneous non-aggressive indolent form to be called Kaposi Disease, being a HHV-8 induced proliferation of endothelial cells, in contrast to the genuine aggressive Kaposi sarcoma.

High Frequency Ultrasound – Its use in informing the suitability and effectiveness of PDT at the Christie Hospital, Manchester

Colin Swift, Laura Foster, Andrew Sykes, Agata Rembielak
Manchester, United Kingdom

The Photodynamic Therapy (PDT) clinic within the Christie Hospital (Manchester, UK) has for a number of years routinely used high frequency ultrasound (HFUS) within the clinic. This serves two main purposes – firstly to determine whether PDT is the optimal treatment modality by determining the depth of the lesion. The lesion should ideally be 3mm or less to ensure sufficient penetration of the activating light and absorption of the photosensitizing cream. Secondly HFUS is used monitor the effectiveness of the treatment and tumor shrinkage should follow up treatments be required.

Within the last year scans have been performed on 213 patients over multiple sites and has proven very effective in determining whether PDT will be the optimal treatment. This presentation outlines the technology of HFUS and its use within the PDT clinic at the Christie Hospital.

Miescher's macrocheilitis successfully treated by Conventional PDT

Muriel Creusot, Evylou Hector, Josette André
Brussels, Belgium

Miescher's macrocheilitis is a rare granulomatous disease whose pathophysiology is still poorly understood and whose treatments are often unsatisfactory. Patients with this condition experience flare-ups of labial oedema that can eventually lead to chronic lip hypertrophy. This article describes the case of a 68-year-old female patient whose diagnosis of Miescher's macrocheilitis , evolving for the last 6 years, was confirmed after biopsy and exclusion of other granulomatous pathologies. Systemic treatments introduced over the years, such as oral corticosteroids, minocycline, hydroxychloroquine, had not been effective. The flare-ups became more and more frequent, several times a day, representing a physical, but also aesthetic and social inconvenience.

Conventional photodynamic therapy with 5 methylaminolevulinate application and illumination under a red LED lamp 632nm and 37J/cm2 at a rate of 1 session per month was performed. After the third session, clinical and anatomopathological remission was achieved.

Role of TGFβ1 secreted by CAFs in combination with N-acetyl cysteine or Raloxifene in the response of SCC cells to PDT

Author(s)
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Transforming growth factor β1 (TGFβ1) produced by cancer-associated fibroblasts (CAFs) has been implicated in cancer resistance to therapies, although its role in the resistance of cSCC to photodynamic therapy (PDT) has not been fully addressed yet.

N-acetyl cysteine (NAC), approved for the treatment of pulmonary fibrosis, and Raloxifene, a drug approved for hereditary haemorrhagic telangiectasia, are known to reduce TGFβ1 levels. Thus, NAC or Raloxifene in combination with PDT could improve the treatment of cSCC by counteracting the effects of CAF-derived TGFβ1.

We investigated the impact of CAF-derived conditioned medium on the response of cSCC cells to PDT. An induction of resistance to PDT was observed in A431 cells in both 2D and 3D models. Pre-treatment of CAFs with NAC or Raloxifene prevented this effect. Overall, our results highlight TGFβ1 as a potential target for the optimization of PDT and point to NAC and Raloxifene as promising adjuvant agents.

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