EURO PDT

20TH ANNUAL CONGRESS

PARIS

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THE EUROPEAN SOCIETY FOR PHOTODYNAMIC THERAPY

Paris, France

Friday 17 and Saturday 18, June 2022

BEST OF SLIDES 2022

Plenary Session 4

How to optimize PDT efficacy?

Chairs: Thomas Dirschka, Colin A. Morton

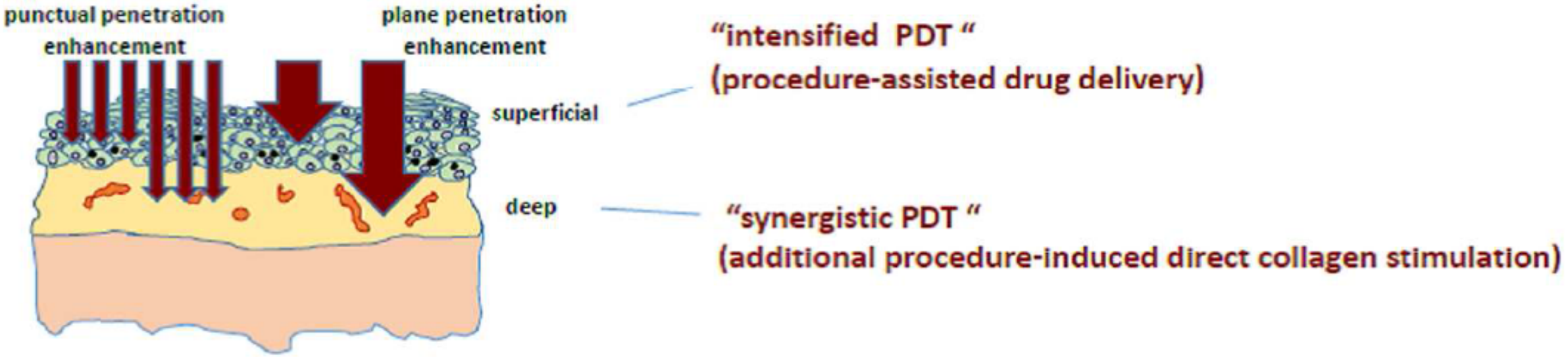
PDT combination therapies for aesthetic indications

Rolf-Markus Szeimies, Recklinghausen, Germany

Enhanced aesthetic efficacy of PDT by additive/synergistic effects

- Use of different light sources for PPIX excitation
  - Flash-lamp pumped, pulsed dye lasers
  - Intense pulsed light
- Physical/chemical Pretreatments to enhance drug penetration or deliver synergistic effects
  - drug (pre)treatment (Vit.D, urea, 5-FU, IMIQ)
  - Microdermabrasion, microneedling
  - Ablative fractional lasers

Optimization of clinical results by pre-treatments



From Philipp-Dormston W et al.: Daylight photodynamic therapy with MAL cream for large scale photodamaged skin based on the concept of 'actinic field damage': recommendations of an international expert group. JEADV 2016; 30:8-15

Lasers in Surgery and Medicine 42:150–159 (2010)

Photodynamic Photorejuvenation of the Face With a Combination of Microneedling, Red Light, and Broadband Pulsed Light

Matteo Tretti Clementoni, MD,[1] Marc B-Roscher, MD,[2] and Girish S. Munavalli, MD, MHS, FAAD[3,4]*
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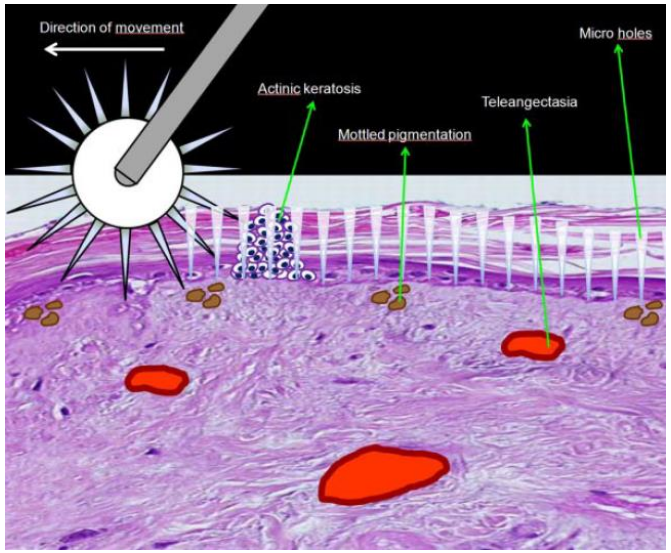
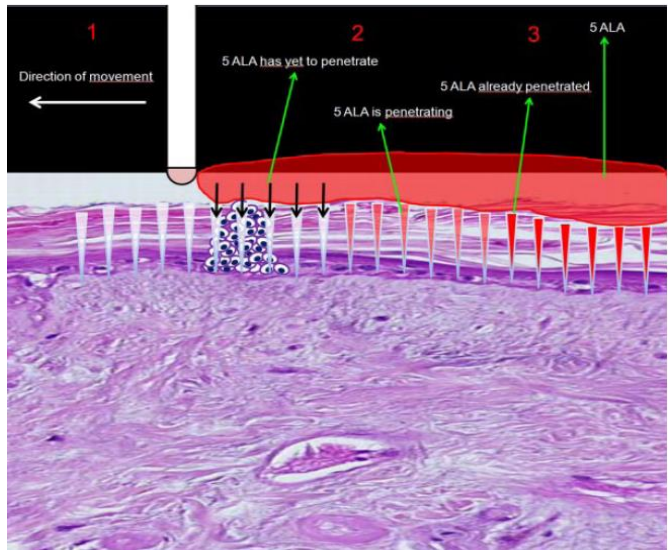
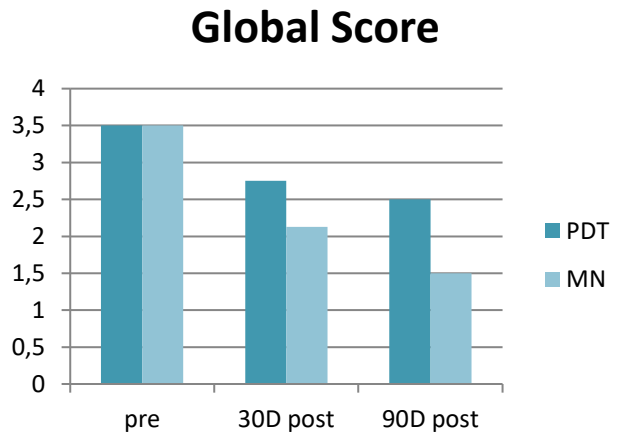
[2]*Nelson R Mandela School of Medicine, Department of Dermatology, Durban, South Africa*
[3]*Dermatology, Laser, and Vein Specialists of the Carolinas, Charlotte, North Carolina*
[4]*Johns Hopkins School of Medicine, Department of Dermatology, Baltimore, Maryland*

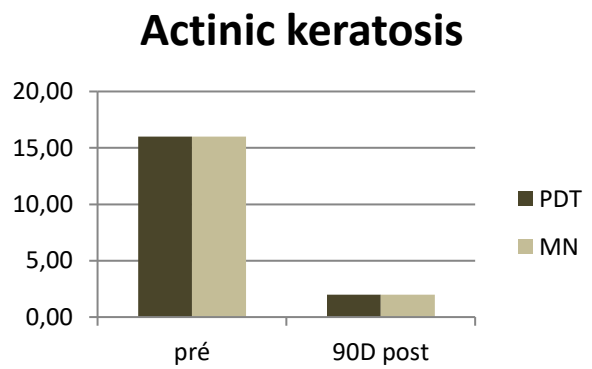


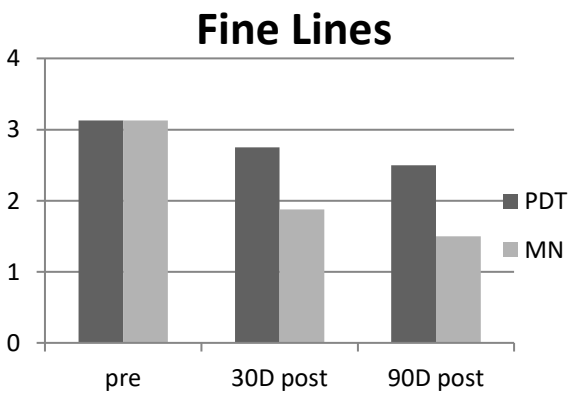


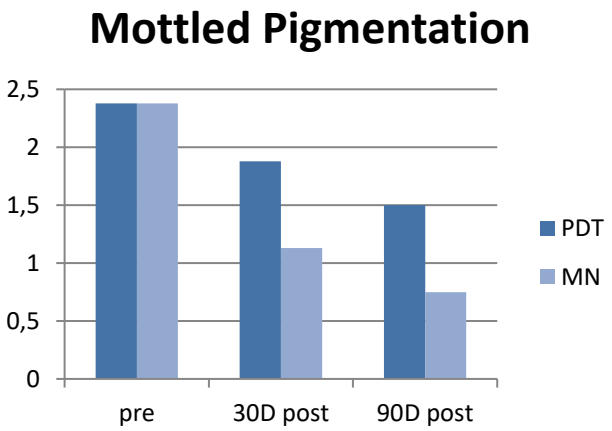
Microneedling & MAL-PDT for field cancerised areas

Torezan L et al., Dermatol Surg 2013; 39:1197-1201









p< 0.05 Wilcoxon´s Test

Non-ablative Fractional Thulium-Laser (TL) plus PDT for Skin Rejuvenation of the Sun-Damaged Chest – Split Sided RCT

Croix J et al. (2020) Lasers Surg Med 52:53-60

- Female pat. (n=11) with photodamage to the chest
- Division into 2 Tx-parts: one side non-ablative fractional TL, ALA-PDT on both sides
- TL with 5 mJ/mb, 5% coverage; thereafter immediate PDT with ALA 20% for 30 min under occlusion and heating pad, followed by illumination w. blue-light (417 nm) 10 J/cm²
- 3 treatments at week 0, 4, 8. Clinical assessment by blinded observers to week 20
- Improved scores for rhytides & skin texture in 11 or 10 pat. at wk 20
- **No significant difference in any efficacy outcome** between TL&PDT vs. PDT alone
- Severity of adverse events higher in combination group
- Problem: - laser parameters too low for PS enhanced penetration or synergistic anti-ageing effect
  - ALA incubation too short for induction of significant PDT effect

Fractional Thulium-Laser (TL) plus PDT for Skin Rejuvenation of the Sun-Damaged Décolleté – Split Sided RCT

Hendel K et al. (2020) Lasers Surg Med 52:44-52

- Female pat. (n=12) with mild-moderate sun damage at décolleté and cumulative AK (184, grade I Olsen)
- Division into 4 Tx: field-directed TL, PDT, TL plus PDT, lesion-directed curettage as control
- TL with 20 mJ/mb, 500 mJ/cm², 5 W, 8 or 16 passes (per 6 pat.); PDT with MAL for 3 h, followed by illumination w. LED 37 J/cm²
- Clinical assessment of sun damage and score items, OCT-imaging 3 mo follow-up
- TL alone & TL-PDT improve globally sun damage, mottled pigmentation and fine lines compared to curettage ($p<0.05$)
- Skin texture improved by additional PDT vs. TL alone ($p<0.05$)
- All 3 field-directed Tx led to complete remission of AK (TL 90%, PDT 82%, TL-PDT 100%), curettage (52%)
- Mild local AE, more pronounced by combination ($p<0.05$)

Summary – Aesthetic PDT

What can I expect?

- Significant Improvement:
  - Skin texture, roughness
  - Fine lines
  - Teleangiectasias
  - Dyspigmentation
- Remission and prevention of AK
- Tolerable and reversible AE

What shall I take care about?

- Realistic expectations!
  - Only mild improvement of deep wrinkles and sebaceous gland hyperplasia
  - Does not substitute surgical-aesthetic procedures
- Stay with recommended treatment protocols, especially when Aks/NMSC are in the target area

Optimizing treatment of acne with PDT to achieve long-term remission and reduce side effects

Ann-Marie Wennberg Larkö
Professor
Sahlgrenska University Hospital, Gothenburg, Sweden

MAL-PDT with an extended follow-up period in patients with mild to severe acne vulgaris

Wojewoda et al, *Journal of Photochemistry & Photobiology, B: Biology, 2021*

- Prospective, double-blinded, four-armed, split-face, randomized, placebo-controlled
- To achieve a reduction in pain, we shortened the incubation time to 1.5 h and reduced the light dose to 20 J/cm2
- 33 pat randomized, 2 or 4 tx
- MAL one cheek, placebo other cheek, 1–2 weeks apart
- 1.5-h pre-tx MAL, Illumination - red light (20 J/cm2)
- Assessments before tx and 4, 10, and 20 w last tx 2 or 4 tx

Material and Methods − challenges

124 patients assessed for eligibility

91 excluded (54 did not meet the inclusion criteria, 34 did not show up for inclusion, 3 not allocated for tx)

33 pat were allocated to tx, Aged 18–25 years (median: 21 years)

26 pat received all treatment with MAL on one side and placebo vehicle on the other side (two treatments: 14 patients, four treatments: 12 patients)

19 pat completed with all evaluations

Discontinuations: subjective lack of enough efficacy according to the patient's own assessment and to side effects

Results/Adverse Events

- MAL-PDT, 20 w - decreased number of inflammatory lesions
- 74% - 2 tx
- 85% - 4 tx

Pain

- Median VAS: 1.85
- Similar studies - VAS = 3.74
- Sign higher vs placebo-PDT, VAS = 0.0
- Improved quality of life, median DLQI = 7.5 to 2.0 at w20

Other AE, mild = 15 patients

- Moderate erythema, Hyperpigmentation,Minor ulceration,Mild scarring

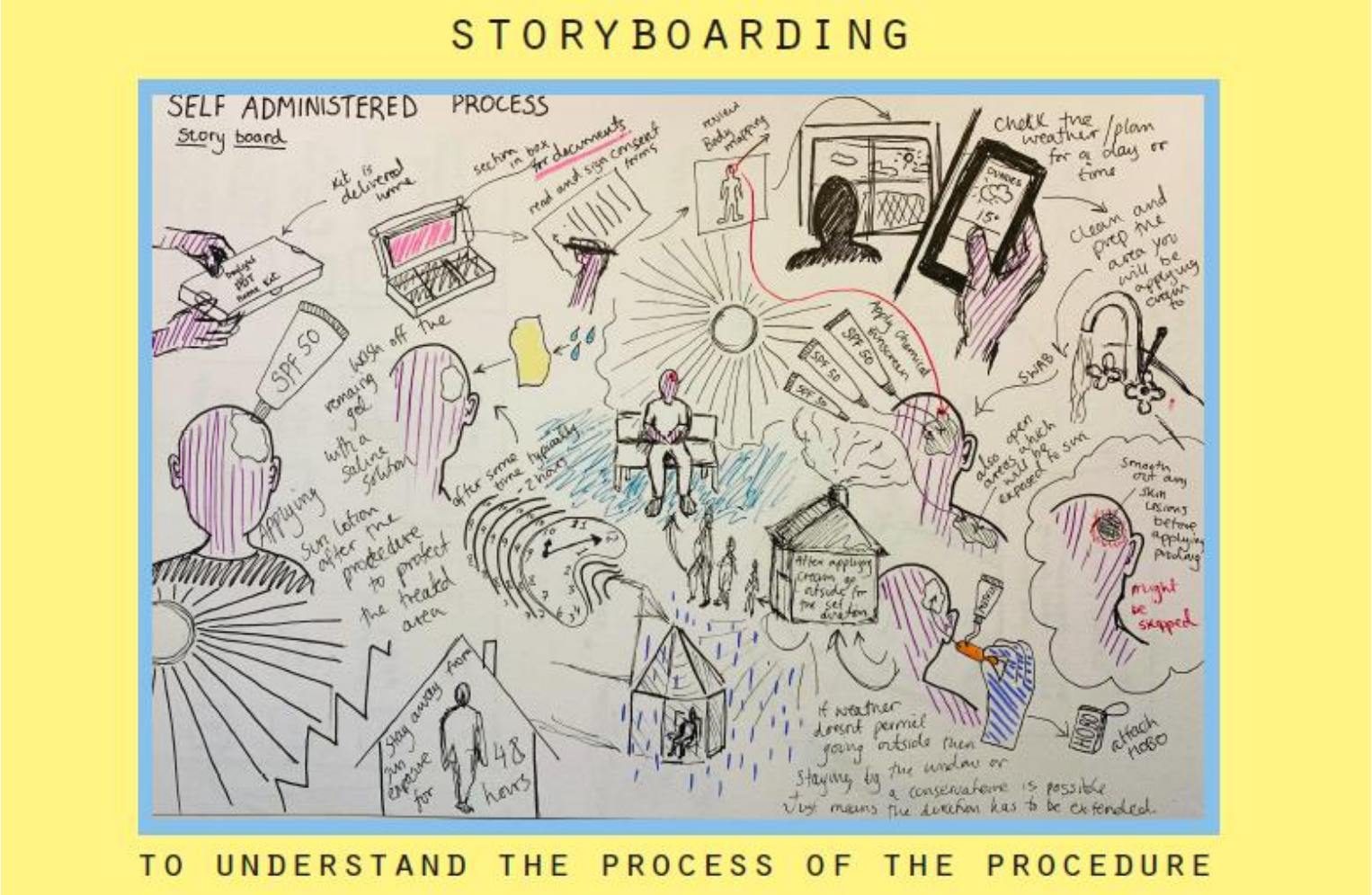
Conclusions

- Change in inflammatory and non-inflammatory lesions seemed to differ between MAL-PDT and placebo-PDT after 4, 10, and 20 weeks, but not significant
- Best effect after 20 w
- Earlier studies – PDT an effective treatment for acne lesions
- This new treatment regimen for both MAL-PDT and red-light-only PDT, with shortened pre-treatment (1.5 h) and reduced light dose (20 J/cm2) can be an effective modality
- Tolerable side effects
- We observed improved quality of life in patients
- Future research investigating the use of red light alone or combination with other topical treatments is needed

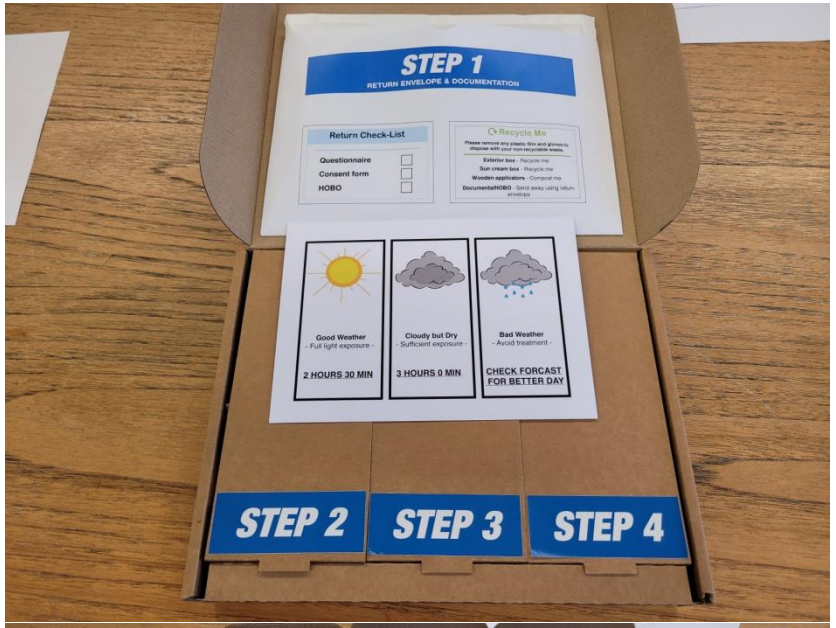
Product design in the development of a home-based daylight PDT service

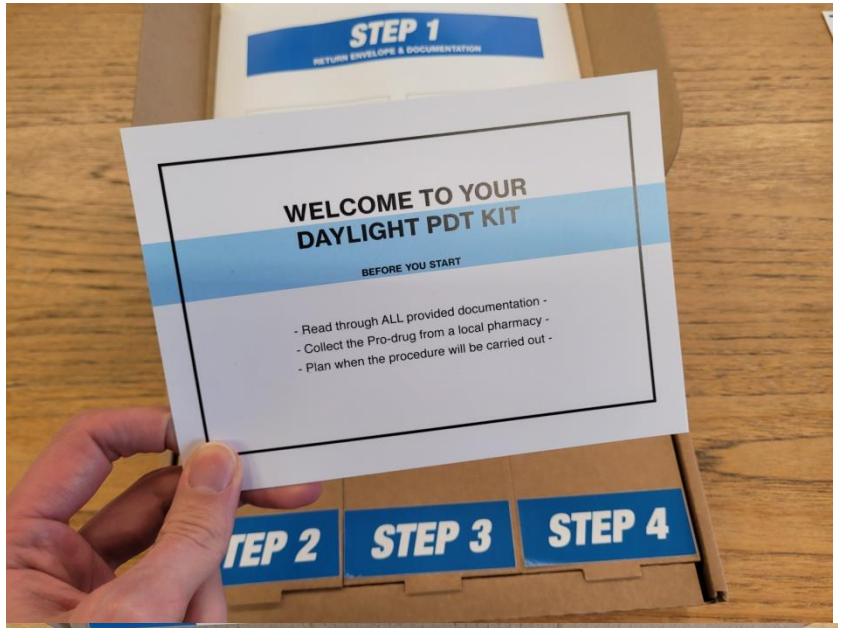
Dr Paul O'Mahoney
University of Dundee

Proof of concept home kit to permit home-based daylight PDT service



Daniella Levins
University of Dundee
Product Design


STEP 1
RETURN ENVELOPE & DOCUMENTATION
Return Check-List
Questionnaire
Consent form
HOBO
Recycle Me
Good Weather
- Full light exposure -
2 HOURS 30 MIN
Cloudy but Dry
- Sufficient exposure -
3 HOURS 0 MIN
Bad Weather
- Avoid treatment -
CHECK FORCAST FOR BETTER DAY
STEP 2
STEP 3
STEP 4


STEP 1
RETURN ENVELOPE & DOCUMENTATION
WELCOME TO YOUR
DAYLIGHT PDT KIT
BEFORE YOU START
- Read through ALL provided documentation -
- Collect the Pro-drug from a local pharmacy -
- Plan when the procedure will be carried out -
STEP 3
STEP 4


1. Review treatment area
2. Clean skin
3. Exfoliate skin (if necessary)
4. Apply sun cream SPF50 to all exposed areas
5. Wash hands and dry thoroughly
6. Put on gloves
7. Remove lid from pro-drug
8. Apply pro-drug from the tube onto the applicator
9. Apply to area
10. After taking off gloves wash hands and dry thoroughly
11. Apply sun cream SPF50 to hands before going outside
12. Attach HOBO device (if supplied)
13. Go outside for instructed time
14. Wipe off any remaining pro-drug using warm water
15. Apply sun cream to treatment/ exposed areas daily
Metvix® 160mg/g Cream
methyl aminolevulinate
CREAM
cutaneous use
GALDERMA
ANTHELIOS
LA ROCHE-POSAY
GAUZE SWABS
PEEL OPEN HERE


DRY SCRUB BRUSH
Metvix® 160mg/g Cream
Received 26/01/22
methyl aminolevulinate
CREAM
cutaneous use
2g
GALDERMA
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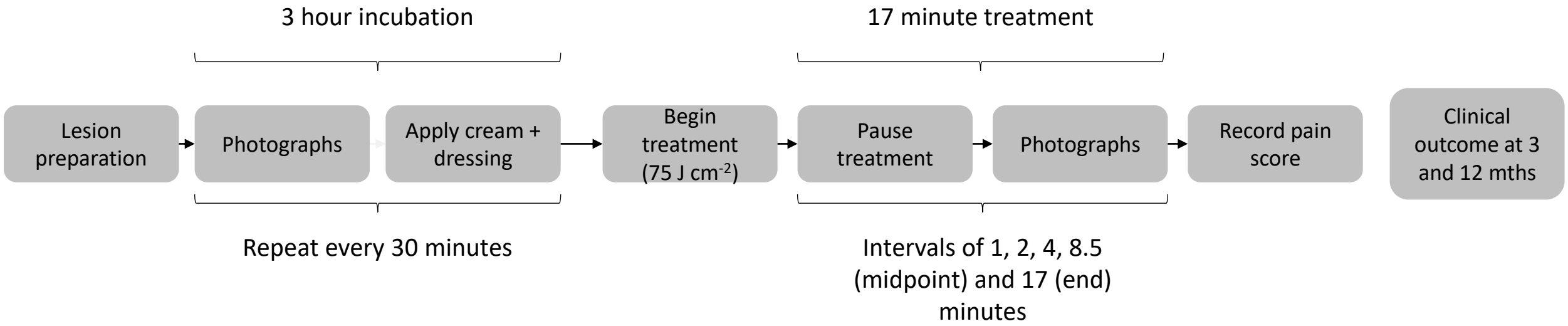
HOBO
ANTHELIOS
LA ROCHE-POSAY
PEEL OPEN HERE
GAUZE SWABS

Fluorescence and skin temperature: their relationship in photodynamic therapy

Dr Paul O'Mahoney
University of Dundee

Methods

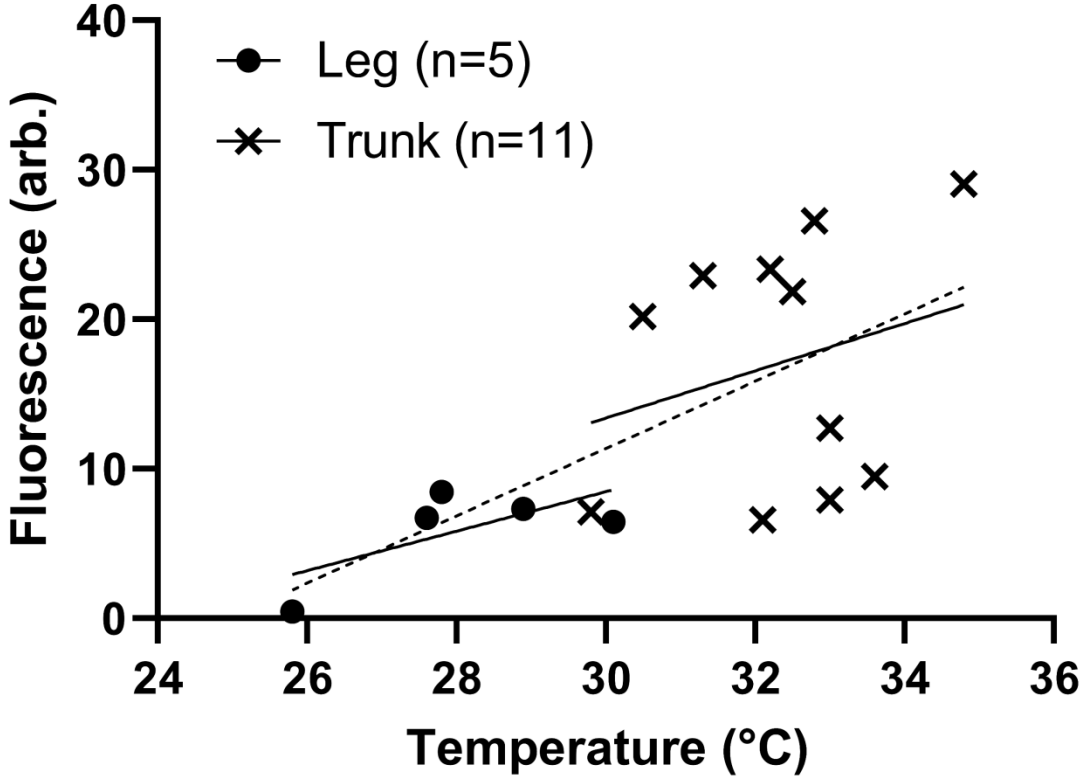


Recruited:
18 participants
(BD or BCC)

→ 16 datasets
→ 11 lesions on trunk
→ 5 lesions on lower leg
→ 2 datasets unusable

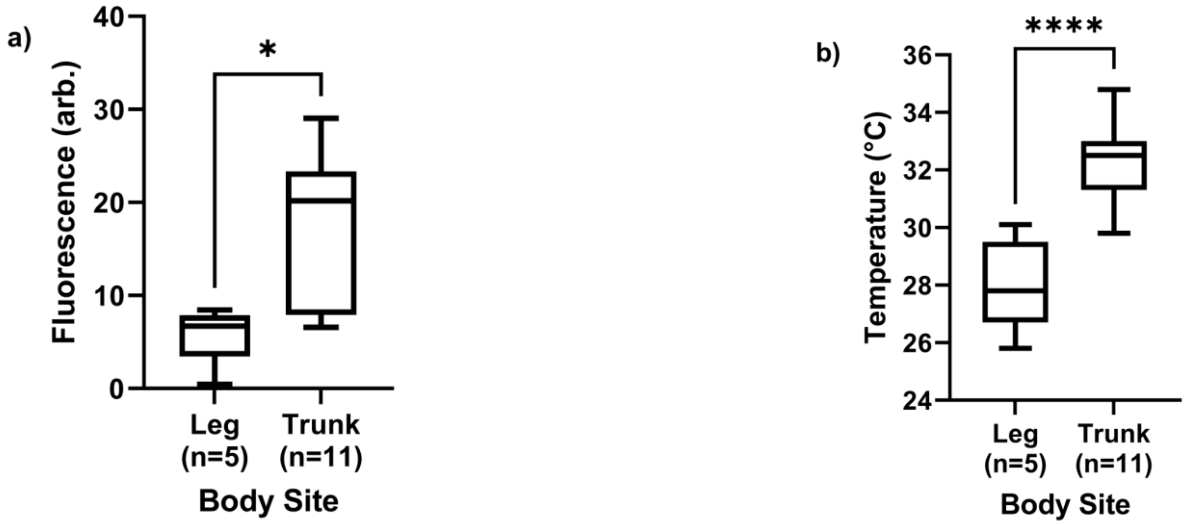
Results

- Temperature and fluorescence are positively correlated at t=180 mins ($p<0.01$)
- Not correlated within body site



Results

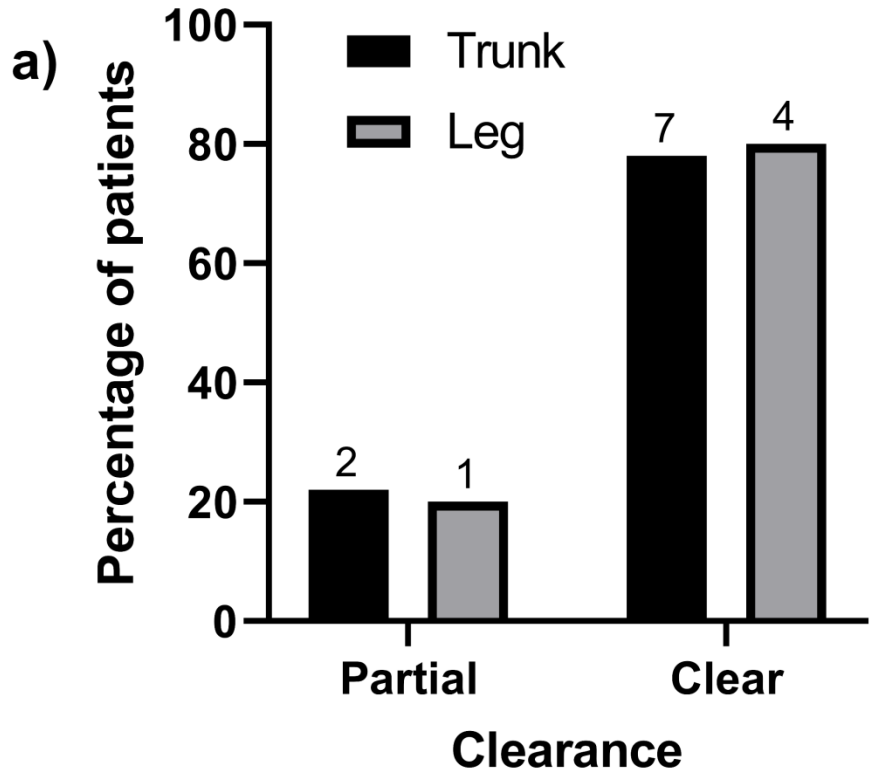
- Lower peak fluorescence (at 180 minutes) on the lower leg than the trunk ($p<0.05$)



- Lower temperature (at 180 minutes) on the lower leg than the trunk ($p<0.001$)

Results

- No correlation between body site (or fluorescence or temperature) and outcome at 12 months



Conclusions

- Evidence that fluorescence and temperature are correlated
- Physiological differences in PpIX accumulation between body sites
- Did not find any correlations with fluorescence or temperature and clearance at 12 months
- No difference in efficacy between body site found – contradicts accepted literature
- Higher reported pain on the lower leg

Artificial Daylight-PDT with the Multilite system – office based experience

Sven Quist, Helix Medical Excellence Center Mainz

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

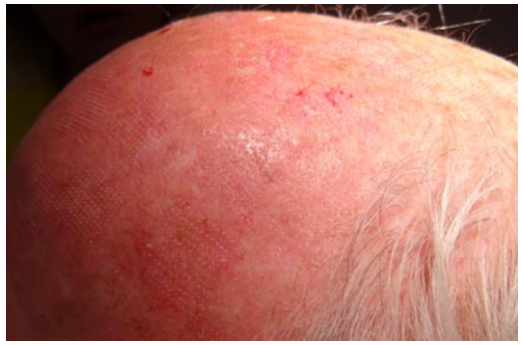
- Short protocol (60 min incubation followed by 35 min irradiation)
- Low pain
- Area of 500 cm2 (or 2x500 cm2 or 2 parallel treatments with 500 cm2)
- Easy to use
- Flexible (easy movable)
- small

Indications

- Actinic keratoses (head, arms, legs, back)
- Initial SCCs
- BCCs (superifical, thin nodular)
- Folliculitis decalvans
- Skin rejuvination
- Acne
- Hand eczema (only 585 nm)

Protocol

removal of crusts



FX-CO2 Laser abl.

MAL/ALA 60 min

aPDT multilite 35 min

post-treatment Care

Results

- **566 patients treated**
  556 with 35 min protocol,
  10 patients with 80 min protocol

- **pain level 3/10 with 35 min protocol**
- **pain level 1/10 with the 80 min protcol**

- **good result (almost clear/complete clearance in 91%)**

Light textile PDT in other indications

Henry Abi-Rached, M.D
CHU de Lille

Phoslstos®

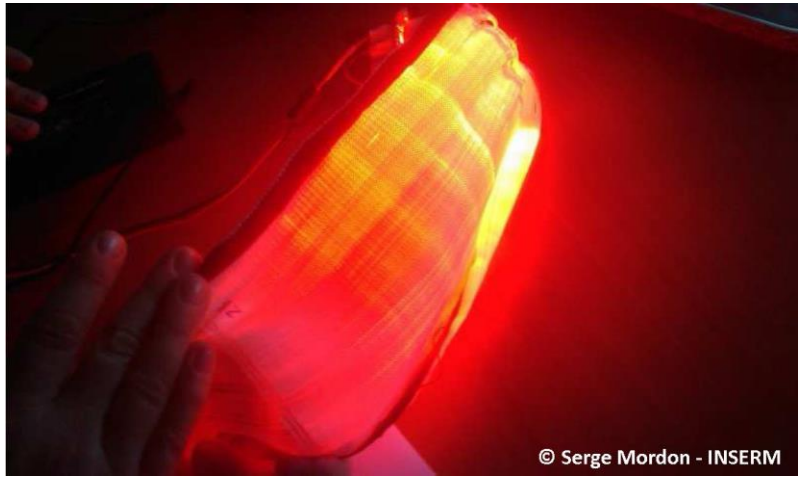
BJD British Journal of Dermatology
IMPROVING PATIENT OUTCOMES IN SKIN DISEASE WORLDWIDE

Clinical Trial

The conventional protocol vs. a protocol including illumination with a fabric-based biophotonic device (the Phosistos protocol) in photodynamic therapy for actinic keratosis: a randomized, controlled, noninferiority clinical study†

S. Mordon, A.S. Vignion-Dewalle, H. Abi-Rached, E. Thecua, F. Lecomte, C. Vicentini, P. Deleporte
... See all authors

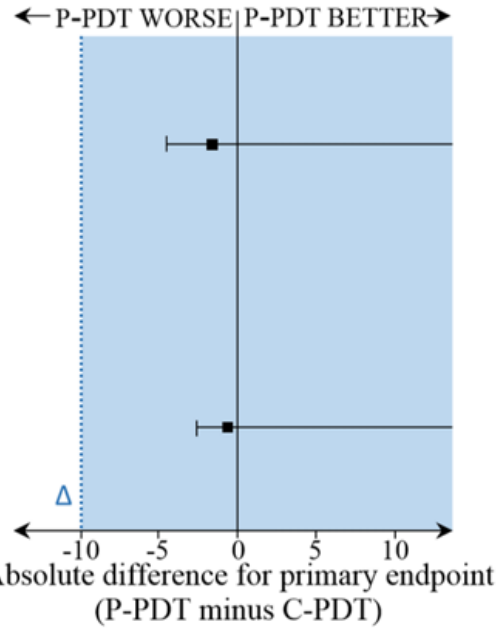
First published: 25 April 2019 | https://doi.org/10.1111/bjd.18048 | Citations: 14



PhosIstos®

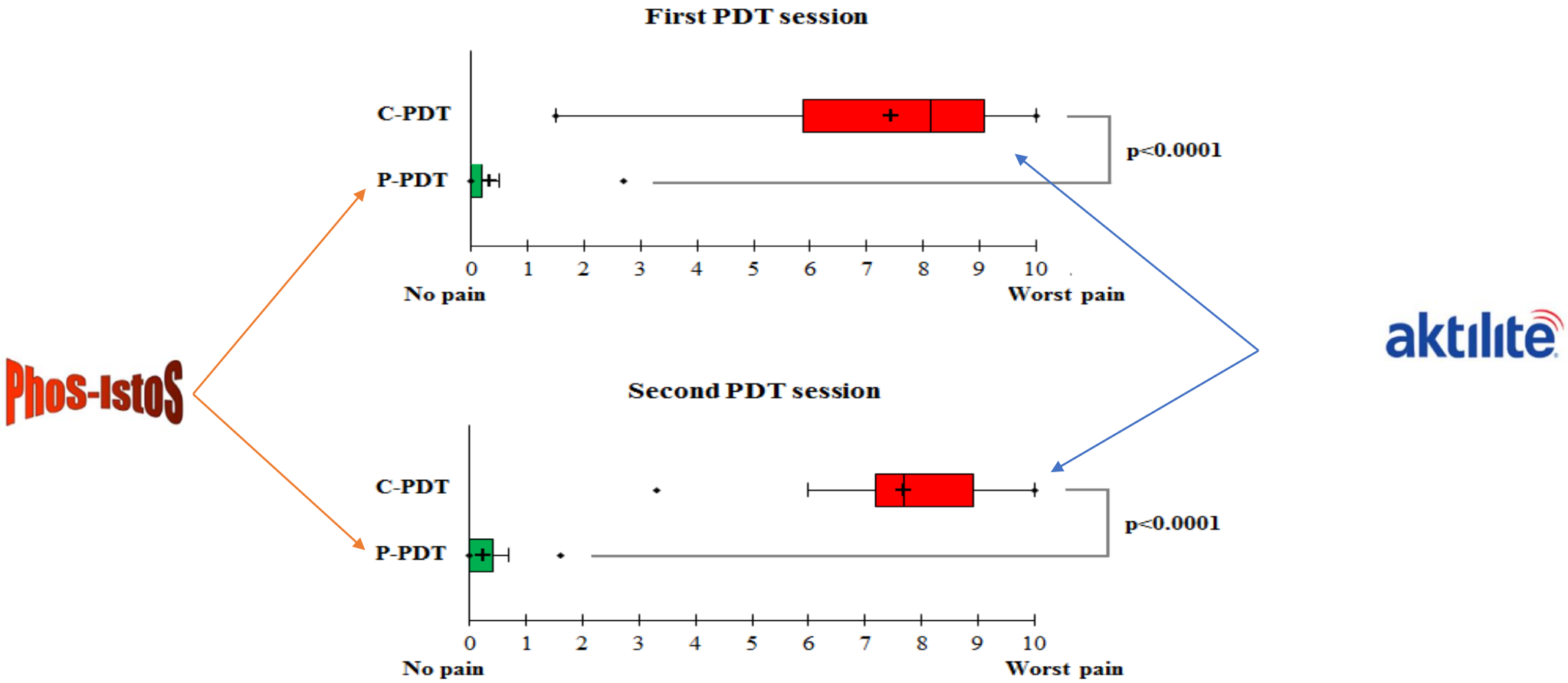
- **Primary end point : clinical response at 3 months**

AK in complete response (%)	C-PDT	P-PDT	P-PDT minus C-PDT (95% CI)	P-PDT minus C-PDT (95% CI)	p-value for superiority
At 3-month follow-up (after one PDT session)	226/280 (80.7)	222/280 (79.3)	-1.6 (-4.5 to ∞)		0.34
At 6-month follow-up (after one or two PDT sessions)	261/275 (94.9)	259/275 (94.2)	-0.6 (-2.6 to ∞)		0.66



Abbreviations: C-PDT, conventional photodynamic therapy; P-PDT, Phosistos photodynamic therapy; CI, confidence interval.

PhosIstos®


First PDT session
C-PDT
P-PDT
p<0.0001
0 1 2 3 4 5 6 7 8 9 10
No pain
Worst pain
Second PDT session
C-PDT
P-PDT
p<0.0001
0 1 2 3 4 5 6 7 8 9 10
No pain
Worst pain

Fluxmedicare®

ELSEVIER

Photodiagnosis and Photodynamic Therapy

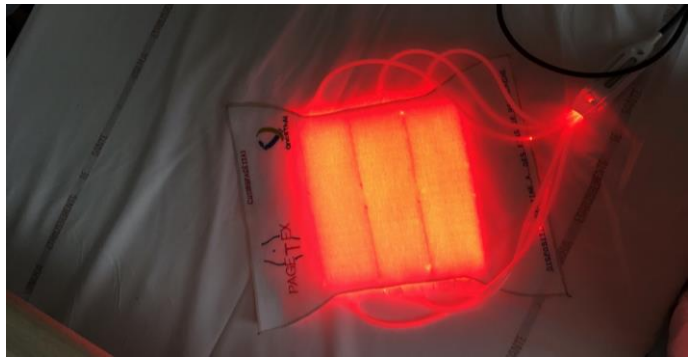
Volume 34, June 2021, 102213

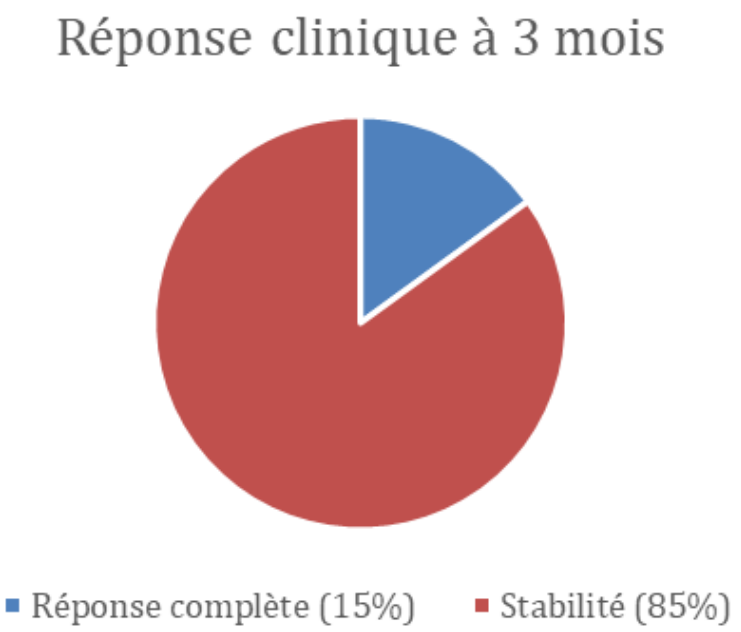
Real-life evaluation of the treatment of actinic keratoses by textile photodynamic therapy (FLUXMEDICARE® device)

M. Dubois [a] ✉, H. Abi Rached [a, b], F. Dezoteux [a, c], C. Maire [a, b], C. Vicentini [a, b], H. Behal [d], E. Thecua [b], F. Lecomte [b, e], S. Mordon [b], L. Mortier [a, b]

Extramamary Paget Disease

- ~ 400 cm^2 light emitting fabric
- <u>Treatment parameters:</u>
  - 1,3 mW/cm^2
  - 2h30
    → 12 J/cm^2





- **VAS scores** = 0.11/10
- Better quality of life and less disease related symptoms
- Good **functional and aesthetic** outcome
- **Noninvasive** treatment

Clinical versus punch biopsy assessment of BCC subtype and thickness within a PDT-setting

Erik Mørk, MD
Trondheim, Norway

Study – Aims and materials and methodS

- Is clinical assessment of BCC subtype and thickness reliable in selecting lesions for PDT?
- 7-centre study in Norway.
- 2-4 mm punch biopsy, taken from the area clinically regarded as thickest for verification of BCC-diagnosis.
- Experienced dermatologist for clinical assessment, blinded histological subtype and thickness.

Results

- 343 BCCs with clinical and histological data.
- 108 men, 93 women. Average: 66 years.
- Clinical subtypes: 258 sBCC (75%), 85 nBCC (25%).
- Histological subtypes: 217 sBCC (63%), 83 nBCC (24%), 43 aBCC (13%).
  - aBCC: 35 infiltrative, 6 morphea and 2 micronodular.
- Localization: trunk (240), extremities (67), head/neck (36).

Subtype and thickness assessment

	Clinically correct diagnosed BCCs among histologically verified BCCs, ratio (%)	Ratio of histologically aggressiv subtypes among clinical subtype (%)	Mean thickness difference* (mm)
Superficial	201/217 (93)	19/258 (7)	0,39
Nodular	45/83 (54)	24/85 (28)	-0.38

* Thickness difference: clinical – histological thickness

Clinical assessments of BCC subtypes and thicknesses within PDT-recommendations

Subtype and thickness	Histologically within PDT-recommendations, ratio (%)
sBCC ≤ 2 mm	235/258 (91%)
nBCC ≤ 2 mm	46/85 (54%)

Summary

- Agreement between clinical and histological assessment of BCC-subtype and thickness was to unreliable for clinical use alone, which supports the use of pre-PDT biopsy.

- However, when a BCC-diagnosis is verified and clinically considered to be superficial $\leq$ 2 mm thick, clinical diagnosis of subtype and thickness pre-PDT might be sufficient in selected cases.

The biphasic activation protocol for BCC.

Red light followed by IPL delivered with mechanical pressure

Dr Robert Stephens MB BS FACD
North West Sydney Dermatology & Laser

Flushing and Blanching

Flushing

- Represents a loss of luminance in the dermis
- The loss is **throughout the visible spectrum**
- Skin appears as red because the attenuation of light is most profound in the blue-green-yellow spectrum

Blanching

- Creates a positive luminance effect on account of less incident light being absorbed
- The additional luminance is of **scattered light** from dermal tissue/stroma

Scattered light can overcome shadows created by small structures in tumour, stroma and epidermis. Is it therefore of “higher quality” for photodynamic activation??

2 treatments same day

5 mins Aktilite, 3 passes using 560nm cut-off filter (15J/ 200ms/ 20º)

→ Reapply Metvix

→ wait 90 mins

→ 5 passes using 560nm filter (no Aktilite)

Red light activation

1. Initially
   - Oxygen is consumed
   - OxyHb → deoxyHb
   - Light attenuation starts
2. Later, due to hyperaemia +/- flushing, heat
   - ↑↑ chromophore (Hb)
   - OxyHb → deoxyHb
   - ++ Light attenuation
   - Oxygen is **generated**

Lesion compression following a period of red light activation

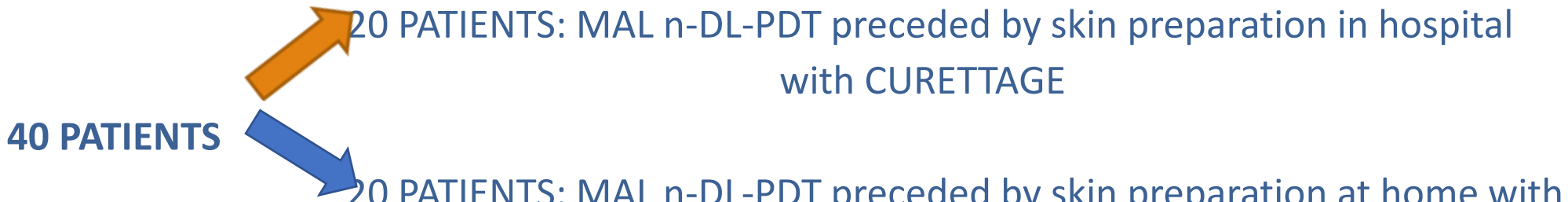
- Removes the chromophore (Hb)
- Does not remove O2 (not immediately)
- Facilitates penetration and scattering of **stronger photodynamic wavelengths** when using an IPL device with appropriate filter

MAL DL-PDT FOR AK ON FACE, SCALP & RELATED FIELD CANCERIZATION WITH DIFFERENT PRE-TREATMENTS (CURETTAGE VS. KERATOLYTICS) – AN INTERVENTIONAL STUDY CONDUCTED IN ITALY

Stefano Caccavale,
Napoli, Italy

Methods

- **40 patients** with at least three grade I and/or grade II AKs on the face/scalp areas were included in this study and randomized in two groups
- **Randomization** was casual (odd or even number); the randomization ratio was 1:1
- All treatments were performed by the same investigator (SC)
- Evaluation of treatment efficacy was performed by other investigators collegially



Results

- **40 patients (38 males, 2 females) aged between 57 and 89 years** were included in the study
- 421 AKs at V1 in keratolytics group (mean number/patient: 21.05 AKs)
- 337 AKs at V1 in curettage group (mean number/patient: 16.85 AKs)
- **39 participants completed the study**
- 1 patient in the keratolytics group dropped out of the protocol after V1 because he refused to be exposed to daylight for two consecutive hours in our hospital garden

Results

V1-V4 MEAN REDUCTION OF AK NUMBER: **- 57.82%**

	V1-V4 MEAN REDUCTION OF AK NUMBER	V1-V4 MEAN % REDUCTION OF AK NUMBER
UREA	10.73 AK	54.73 %
CURETTAGE	10.35 AK	58.65%

(Mann-Whitney U test, two-tailed, significance level 0.05, p value 0.254, U value 149)
The difference in reduction of actinic keratosis from V1 to V4 between the two groups was not statistically significant

Conclusions

- No difference was found in **efficacy** (based on clinical, dermoscopic and confocal assessments) and **patient satisfaction** comparing the 2 treatment regimens
- The **pain score** reported during and after daylight exposure was similar and low in the two groups
- No unexpected **adverse events** occurred during the trial period
- DL-PDT without curettage preceded by skin preparation at home by keratolytics maintained the same treatment effect as DL-PDT with curettage
- Curettage could be not necessary to obtain full treatment effect of DL-PDT

MOLECULAR MARKERS OF RESPONSE IN THE TREATMENT OF ACTINIC KERATOSES WITH DAYLIGHT PHOTODYNAMIC THERAPY

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MATERIAL AND METHODS

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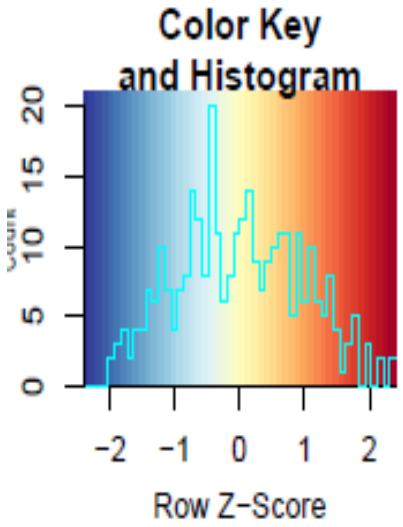
- **Prospective study** in patients with at least 5 AK I-II on the head.

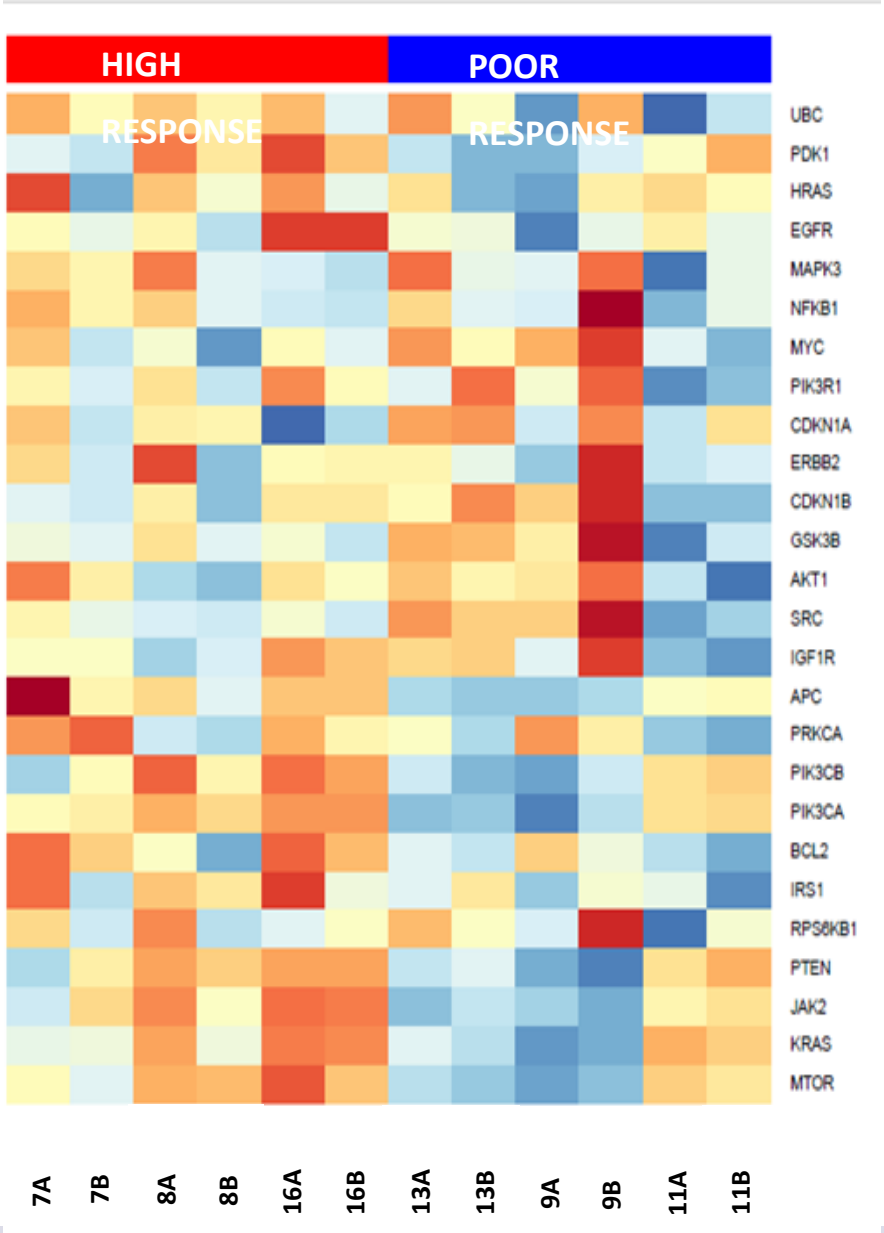
- **Skin biopsies** after and before Daylight-PDT.

- **Statistical analysis**: T test for appeared averages, Chi-square with Fisher correction

- Treatment with **topic MALA** (methyl-amino-levulinic acid, Metvix®)
- Following visit at **3 months** and at **6 months.**

Expression gene analysis





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Differences in the expression of the genes analyzed before and after DL-PDT.
To the left we had high responders, and to the right poor responders. The genes are shown colored according to expression, with overexpressed genes in red and underexpressed genes in blue.
Patients with high clinical response showed under-expression of most of the genes after the treatment, as we can see in patient 8.
On the contrary, poor responders showed overexpression of most genes, as we can see in patient 9.

RESULTS

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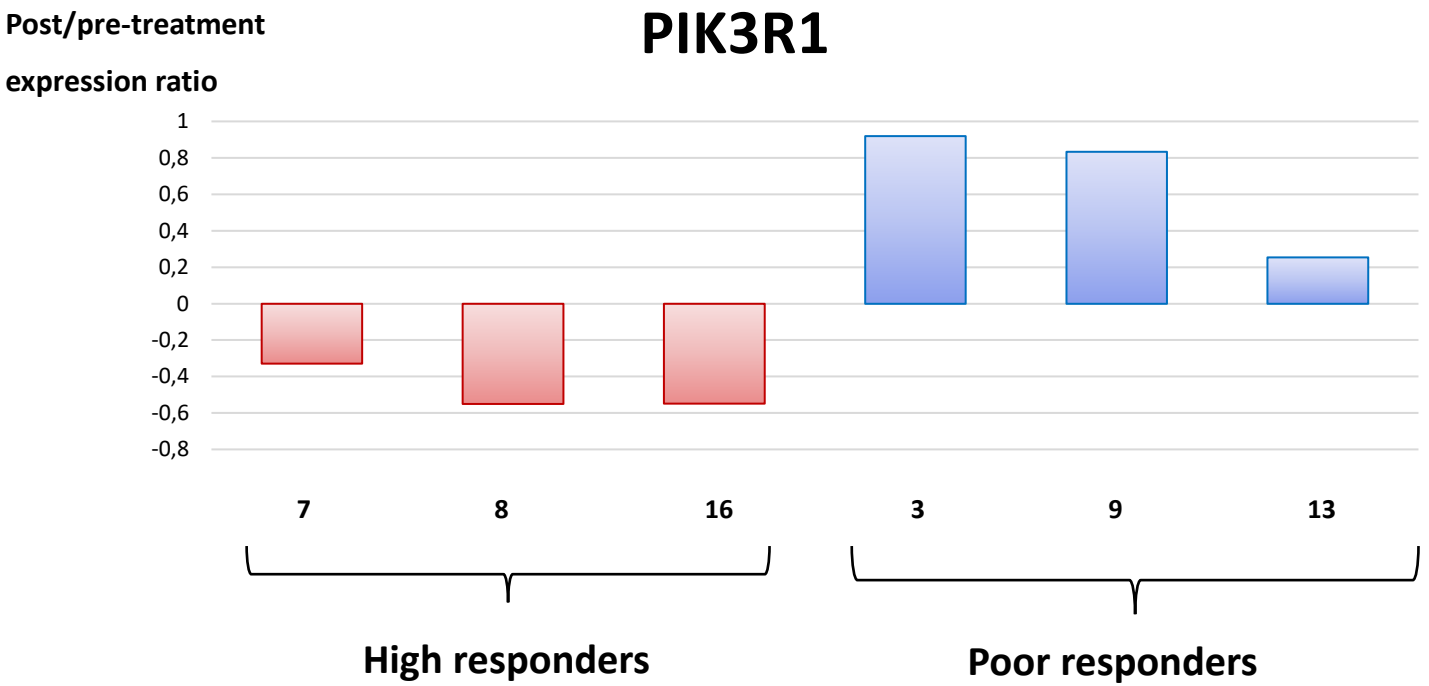
RNA Arrays

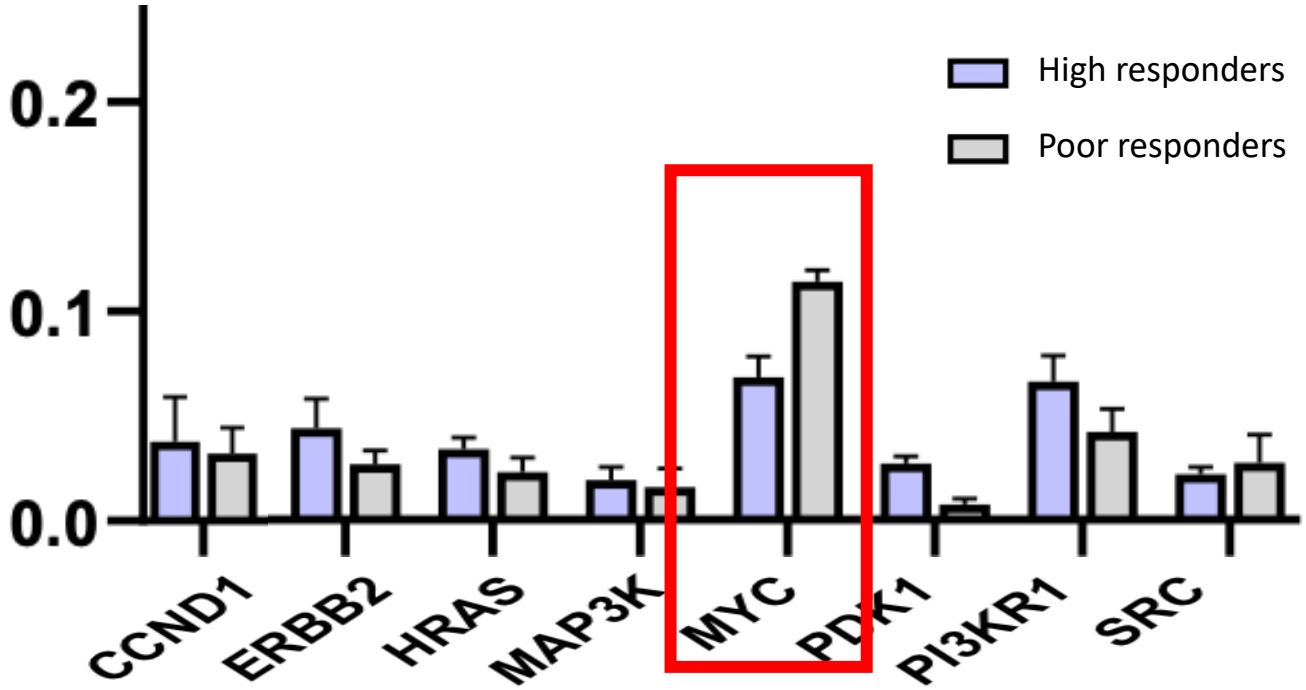


The most striking differences between high and poor responders is PIK 3 R 1 gene

RESULTS

Oncogene expression: differences in pre-treatment expression

We proceeded to analyze the expression of genes before treatment to detect possible predictive markers of response. Poor responders showed a significant overexpression of the Myc oncogene prior to treatment



	P value
AKT	0,775383
ERBB2	0,393621
HRAS	0,581158
MAP3K	0,866561
MYC	**0,048265**
PDK1	0,384456
PI3KR1	0,231739
SRC	0,786424

RESULTS

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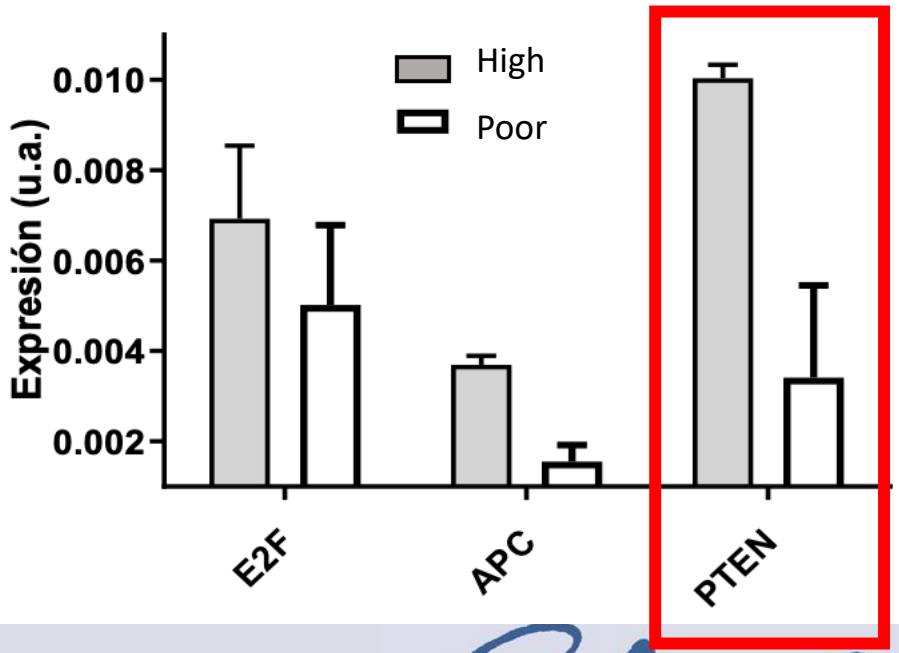
Expression of tumor suppressor genes: differences in pre-treatment expression

Regarding tumor suppressor genes, PTEN was significantly overexpresed in good responders prior to treatment, being a marker of good response



	P value
E2F	0,319069
APC	0,315176
PTEN	**0,015011**

CONCLUSIONS

- **Daylight PDT is effective** in AK patients by reducing the number of lesions, AKASI index and histological dysplasia. However, there are cases of poor response and even worsening.

- Overactivity in the **PI3K/Akt pathway** is probably related to poor response to DL-PDT, since we found an overexpression of PIK3R1 and other related genes in poor responders.

- Overexpression of **Myc oncogene** could represent a marker of poor response to DL-PDT, and overexpression of **PTEN**, a marker of good response. These results are promising but need to be confirmed in more statistically powered studies.

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