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**THE EUROPEAN
SOCIETY
FOR PHOTODYNAMIC
THERAPY**

**PDT Annual Congress
7th- 8th March 2008
Hotel AC Barcelona,
Barcelona, Spain**

With the participation
of the Euro-PDT
board members

Barcelona



Dear Colleagues,

It is a pleasure and an honour to welcome you to Barcelona to the 8th Euro-PDT Congress.

The meeting will focus on current and future developments of photodynamic therapy (PDT).

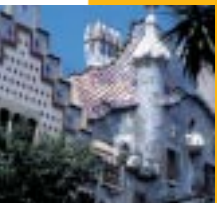
We hope this Congress will offer everyone the opportunity to learn how PDT can enrich our medical, as well as cosmetic treatment strategies in dermatology.

The meeting aims are to promote interactive discussions on PDT use in Europe.

We will make every effort to ensure the success of the meeting, hoping many practitioners and researchers will participate in this scientific program. The exchange of knowledge is a key factor for innovative development in medicine, including PDT.

Welcome to Barcelona !

Dr Alex Camps-Fresneda
Centro Médico Teknon, Barcelona, Spain



BARCELONA

Meeting organization



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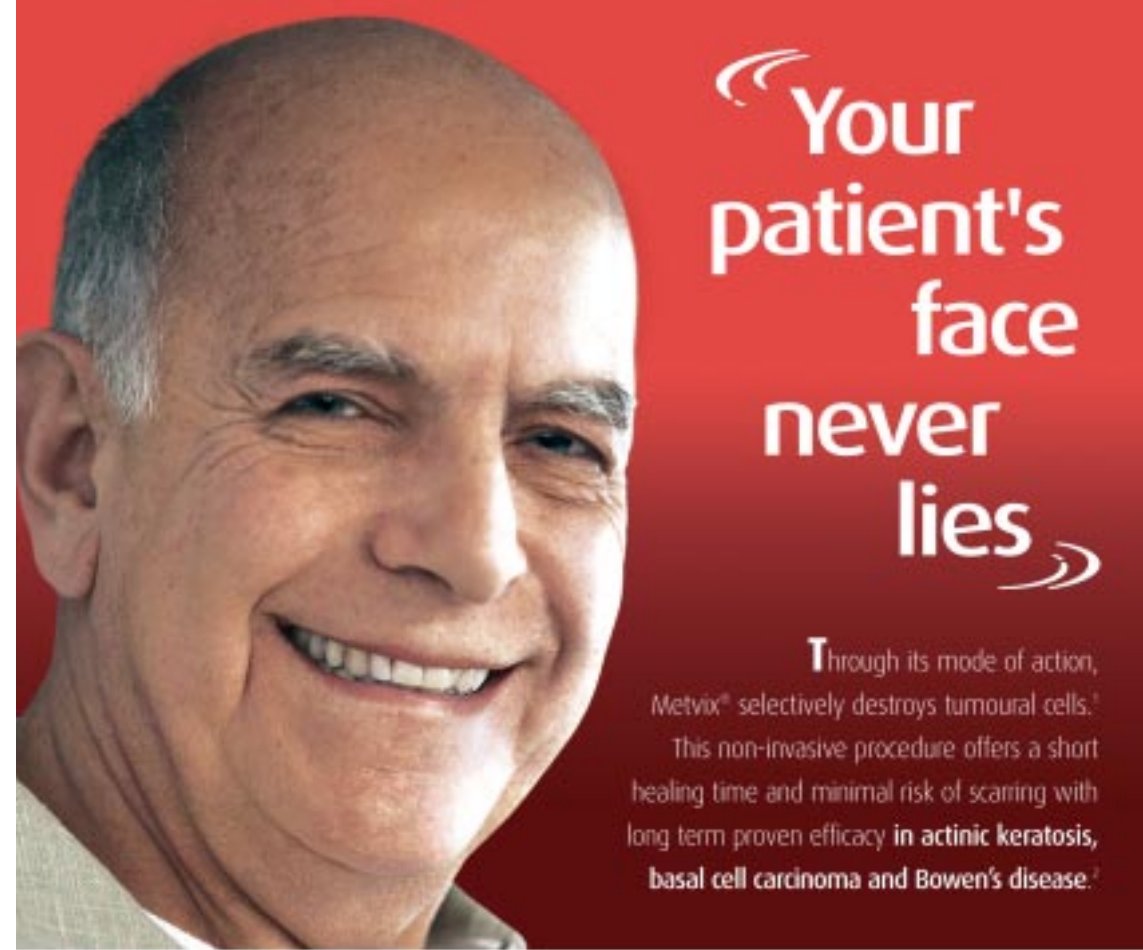
VISTA

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NAME OF THE MEDICINE PRODUCT: Metvix 100 mg/g cream. **CLINICAL INDICATIONS:** Treatment of thin or non-hyperkeratotic and non-infiltrated actinic keratoses on the face and scalp, when other therapies are considered less appropriate. Only for treatment of superficial and/or shallow basal cell carcinoma available for other available therapies due to possible treatment-related morbidity and poor cosmetic outcome, such as lesions on the eyelids or ears, lesions on severely sun-damaged skin, large lesions, or recurrent lesions. Treatment of squamous cell carcinoma in situ (Bowen's disease) when surgical resection is considered less appropriate. **POSIBILITY AND METHOD OF ADMINISTRATION:** Adults (including the elderly). **For the treatment of actinic keratosis (AK):** one session of photodynamic therapy should be administered. Treated lesions should be evaluated after three months and if needed, treatment should be repeated with a second therapy session. **For treatment of basal cell carcinoma (BCC) and Bowen's disease:** two sessions should be administered with an interval of one week between sessions. Before applying Metvix cream, the lesion surface should be prepared to remove scales and crusts and roughen the surface of the lesion. Remove the dressing and clean the area with saline and immediately expose the lesion to red light with a continuous spectrum of 630-670 nm and a total light dose of 75 J/cm² at the lesion surface. Lesion response should be assessed after three months, and at this response evaluation, lesion sites showing no complete response may be retreated if desired. It is recommended that the response of BCC and Bowen's disease lesions be confirmed by histological examination of biopsy material. Subsequently, close long term clinical monitoring of BCC and Bowen's disease is recommended, with biopsy if necessary. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients which includes alcohol. Alcoholism (based on oral intake). Pregnancy. **PRECAUTIONS:** Metvix is not recommended during pregnancy. **CAUTIONS:** In the absence of clinical experience, breast feeding should be discontinued for 48 hours after application of Metvix cream. **UNDESIRABLE EFFECTS:** Approximately 60% of patients experience reactions related to the treatment site. The incidence of adverse reactions in a clinical trial population of 512 patients receiving the standard treatment regimen, in the following very common: Pain of skin, skin burning sensation, scalp erythema - common; Paresthesia, headache, skin infection, skin ulcer, skin redness, skin swelling, itching, skin hemorrhage, pruritus, skin oedema, skin warts, application site discharge, itching hot - uncommon; eye swelling, eye pain, second hemorrhage, nausea, urticaria, tooth skin irritation, photosensitivity reaction, skin hyperpigmentation, skin hypopigmentation, heat rash, skin discoloration, herpes. Application site crusting and allergic contact dermatitis have been described in post-marketing reports (frequency not known). **PHARMACOLOGICAL PROPERTIES:** Anticancer agent, AK (late I/II). **DOSE:** After topical application of methyl aminolevulinate.



1. Summary of Product Characteristics Metvix® 2. Lermano P. et al. JAMA Dermatol. 2001; 137(10):1481-1485. 3. Braathen L. et al. J Am Acad Dermatol. 2002; 46(5):625-631.

Program

Friday, 07 March 2008

Welcome L. R. Braathen, A. Camps-Fresneda

- 9:00 am Welcome Address President EURO-PDT
Lasse R. Braathen, Bern, Switzerland
- 9:05 am Welcome Address Local Congress President
Alejandro Camps-Fresneda, Barcelona, Spain

New developments

- 9:10 am C1 Sensitizers 2008
Rolf-Markus Szeimies, Regensburg, Germany
- 9:30 am C2 Light sources in current use
Alexis Sidoroff, Innsbruck, Austria
- 9:50 am C3 Mechanism of action / PDT as biological response
modifier
Lesley Rhodes, Manchester, UK
- 10:10 am C4 Worldwide introduction of MAL-PDT
to respond to the patients needs
Janusz Czernielewski, Paris, France
- 10:30 am Coffee Break and Poster Viewing

PDT in NMSC C.A. Morton, A.-M. Wennberg

- 11:00 am C5 Guideline recommendations
Lasse R. Braathen, Bern, Switzerland
- 11:20 am C6 Treating cutaneous lymphoma
Piergiacomo Calzavara-Pinton, Brescia, Italy
- 11:40 am C7 Enhancing PDT in NMSC via Chelation
Sandra Campbell, Cornwall, UK
- 12:00 am C8 PDT in view of other treatment options (Moh's etc.)
Julián Conejo-Mir, Sevilla, Spain
- 12:20 am C9 Learning the hard way – different protocols
with PDT in NMSC
Allan Oseroff, Buffalo, USA
- 12:40 am C10 NMSC-PDT - What do we learn from the 5-yr
follow-up data?
Nicole Basset-Seguín, Paris, France

1:00 pm Lunch Break and Poster Viewing

New Horizons R.-M. Szeimies, H.-C. Wulf

- 2:00 pm C11 Guidelines for emerging indications
Colin A. Morton, Falkirk, UK
- 2:20 pm C12 Concepts for cooperation – fighting NMSC in OTR –
view of the dermatologist
Ann-Marie Wennberg, Gothenburg, Sweden
- 2:40 pm C13 Fluorescence diagnosis - useful in the office or not?
Wolfgang Bäuml, Regensburg, Germany
- 3:00 pm C14 Back to the roots of PDT - Sunlight as a potential light
source?
Stine R. Wiegell, Copenhagen, Denmark
- 3:15 pm C15 Dose response study with MAL-PDT in AK:
comparison between 1h and 3h incubation
Lasse R. Braathen, Bern, Switzerland
- 3:30 pm Coffee Break and Poster Viewing

PDT beyond NMSC P. Lehmann, A. Camps-Fresneda

- 4:00 pm C16 Photorejuvenation - how PDT is used in the Americas
Luis Torezan, Sao Paulo, Brazil
- 4:15 pm C17 Photorejuvenation by PDT in the EU
Ricardo Ruiz-Rodriguez, Madrid, Spain
- 4:30 pm C18 HPV-induced lesions - is PDT of use?
Sigrid Karrer, Regensburg, Germany
- 4:45 pm C19 Rosacea - is PDT of benefit?
Lars Erik Bryld, Roskilde, Denmark
- 5:00 pm C20 New indications
Pedro Jaén, Madrid, Spain
- 5:15 pm C21 Paget's Disease
Christophe Bédane, Limoges, France
- 5:30 pm Discussion

PDT Research N. Basset-Seguín, M. Sánchez-Viera

- 5:45 pm C22 PDT in cutaneous mycological infections
Stan Pavel, Leiden, The Netherlands
- 5:55 pm C23 Prevention of photocancerization with MAL-PDT
Angeles Juaranz, Madrid, Spain
- 6:05 pm C24 Changes in the histology and tumor suppressor proteins
expression in AK and BCC after MAL-PDT
Lorea Bagazgoitia, Madrid, Spain
- 6:15 pm C25 Detection of tumor margins by fluorescence diagnosis
Mirem Marquina, Navarra, Spain
- 6:25 pm Discussion
- 6:30 pm End of Session
- 8:30 pm Tapas evening

Program

Saturday, 08 March 2008

ALA vs. MAL - Comparative studies A. Sidoroff, M.-J. P. Gerritsen

- 9:00 amC26 ALA vs. MAL in initial SCC and sBCC
Paul Collins, Dublin, Ireland
- 9:20 amC27 Enhance NMSC-PDT via fractionation
(comparison of MAL and ALA)
Ellen R. M. de Haas, Rotterdam, The Netherlands
- 9:40 amC28 Acne and beyond
Hans-Christian Wulf, Kopenhagen, Denmark

Difficult to treat patient

- 10:00 amC29 MAL and Imiquimod in treating VIN
John Lear, Manchester, UK
- 10:10 amC30 Combination CO₂ laser with PDT for nBCC
William James, Swansea, UK
- 10:20 amC31 Hard areas to manage with PDT
Roman Miñano, Miguel Sánchez-Viera, Madrid, Spain
- 10:30 amCoffee Break and Poster Viewing

Expert's forum - Treatment Management C. Bedane, L. Rhodes

- 11:00 amC32 Mechanisms of PDT-induced pain
Paul Bigliardi, Lausanne, Switzerland
- 11:15 amC33 How to manage pain - UK perspective
Sally Ibbotson, Dundee, UK
- 11:30 amC34 Pretreatment options in PDT
MJP Gerritsen, Nijmegen, The Netherlands
- 11:45 amC35 Pain Management in field cancerisation areas
Carlos Guillen Barona, Valencia, Spain

Expert's forum - How to set up a PDT unit

- 12:00 amC36 PDT business in Denmark (office based)
Birgitte Hansted, Copenhagen, Denmark
- 12:15 amC37 PDT business in Germany (hospital based)
Percy Lehmann, Wuppertal, Germany
- 12:30 amC38 PDT business in Italy
Stefano Piaserico, Padova, Italy
- 12:45 amC39 French experience with PDT
Nicolas Meyer, Toulouse, France
- 13:00 pmC40 Fluorescence diagnosis - Clinical applications
Bibiana Perez, Madrid, Spain
- 13:15 pmPoster & best presentation prizes
- 14:00 pmClosure of the meeting

LEXIQUE

NMSC : Non-melanoma skin cancer

PDT : Photodynamic therapy

BCC : Basal cell carcinoma

MAL : Methyl aminolevulinate

Abstracts





Sensitizers 2008

R.-M. Szeimies

Klinik und Poliklinik für Dermatologie, Klinikum der Universität Regensburg, Regensburg, Germany

Meanwhile methyl aminolevulinate is a well established photosensitizer in Europe and registered for the treatment of actinic keratoses, Bowen's disease and both nodular and superficial basal cell carcinoma. The vast majority of well-designed clinical trials in the field of topical PDT following GCP-guidelines are available for this drug.

Since extratemporaneous formulations with ALA for topical PDT are of concern regarding medicolegal aspects and stability, there is a strong interest in other registered photosensitizers for dermatologic PDT which may not face the afore mentioned problems. A couple of ALA-based formulations are currently under investigation in phase II/III clinical trials (some of them recently published) for PDT of non-melanoma skin cancer.

In the moment, drug development focuses on actinic keratoses as potential indications, since follow-up periods in clinical studies are reasonably shorter than for BCC. This probably will result in registration of different ALA-formulations (ALA-containing patch, ALA nanocolloid formulation) in the next years.

Key Words: methyl aminolevulinate (MAL), aminolevulinic acid (ALA), nanocolloid ALA formulation, ALA patch



PDT in Dermatology: Light Sources In Current Use

A. Sidoroff

Innsbruck, Austria

W. Bäumler

Department of Dermatology, University of Regensburg, Germany

During the last years a vast range of specialized light sources for PDT has been developed and many innovative ideas are still being explored. The current types of light sources deliver coherent (lasers) or incoherent light. In the latter group one can find high pressure mercury / xenon lamps (HPL), the now widely used light emitting diodes (LED), and increasingly intense pulsed light sources (IPL). Wavelength clearly has to fit the absorption spectrum of the sensitizer and an adequate penetration is desirable (red > blue) for the treatment of non-melanoma skin cancer. This is why most light sources used in Europe emit in the red spectrum. But not only light sources, also the method of application of light ("ambulatory PDT", light emitting textile fibres) are being explored. In addition combination devices of treatment and fluorescence-diagnosis light sources are of practical interest and introduced into the market.

Key Words: fluorescence diagnosis, intense pulse light sources, lasers, light emitting diodes, penetration depth, photodynamic therapy

3

Mechanism of Action PDT as a biological response modifier

A. Haylett, L. Rhodes

*Photobiology Unit, Dermatology Centre, University of Manchester,
Salford Royal Foundation Hospital, Manchester, UK*

Topical PDT is effective in types of skin malignancy and also achieves a therapeutic response in non-malignant conditions. Selective uptake of prodrug followed by its conversion to photoactive porphyrins, results, after light exposure, in the release of reactive oxygen species which cause target cell death and/or modification. Host responses may contribute to therapeutic efficacy, but these are as yet poorly defined in humans. Experimental models show a brisk inflammatory reaction with neutrophilic, lymphocytic and monocytic infiltrates, followed by an immune response that may help eradicate residual target cells. Immunosuppressive effects of PDT are also seen. Biological responses modified by PDT may have both beneficial and deleterious effects on treatment efficacy. We report on host responses to topical PDT in humans and discuss their potential role.

Key Words: *host responses, mediators*

4

Worldwide introduction of MAL-PDT to respond to the patients needs

J. Czernielewski

Paris, France

Non melanoma skin cancer and actinic keratosis can be multiple, extensive and at risk of leaving unwanted scars with surgery or cryotherapy. Photodynamic Therapy (PDT) with Metvix® offers a tissue sparing and well tolerated alternative. The level of medical evidence provided for its use in actinic keratosis, superficial basal cell carcinoma (BCC), nodular BCC and Bowen's Disease is rated highest (A1) by the International Society for PDT and various guidelines are now available. Patient satisfaction was consistently high across all studies. Metvix® is approved in 29 countries worldwide. Workshops are organised not only to familiarise physicians with the treatment but also to address patient management and logistical constraints. Economic models and an observational study showed that Metvix® is cost-effective in actinic keratosis versus cryotherapy and in BCC versus surgery, supporting reimbursement in most European countries. Phase IV studies and physician initiated studies show promising new perspectives.

Key Words: *methyl-aminolevulinate, Metvix, photodynamic therapy, review*

5

PDT guidelines recommendations

L. R. Braathen
Berne, Switzerland

In a special article, guidelines on the use of Photodynamic Therapy (PDT), published in the Journal of the American Academy of Dermatology (JAAD 2007, 56:125-43), recommendations were made on the basis of the quality of evidence for efficacy, safety/tolerability, cosmetic outcome, and patient satisfaction/ preference.

Topical PDT is highly effective in the treatment of actinic keratosis, Bowen's disease, and superficial and thin nodular basal cell carcinomas. The cosmetic outcome is superior to that achieved with existing standard therapies. PDT may also be a means of preventing certain non-melanoma skin cancers in immunosuppressed patients.

Key Words: *PDT, efficacy, actinic keratosis, basal cell carcinoma, Bowen's disease*

6

Unilesional cutaneous T cell lymphoma treated with PDT

P. Calzavara-Pinton,
C. Zane
Department of Dermatology, University of Brescia, Brescia, Italy

Unilesional mycosis fungoides (MF) is a primary Cutaneous T cell Lymphoma (CTCL) characterized by a limited involvement of the skin and a indolent course. Standard therapies have several side-effects and toxicity. We have treated 5 patients affected by unilesional MF with photodynamic therapy (PDT) with topical methyl-aminolevulinate ((Metvix cream®, Galderma, F) to assess the efficacy of this therapy. PDT was repeated once weekly until complete clearing of the lesions or the therapy was interrupted when 3 successive treatments provided no further improvement. A complete remission was observed in 4 patients and a partial improvement in 1, without recurrences at follow-up (12-34 months).

Key Words: *cutaneous T cell lymphoma, methyl-aminolevulinate, photodynamic therapy, unilesional mycosis fungoides*

7

Enhancing PDT in NMSC using iron chelating agents

S. Campbell, A. Pye and A. Curnow
Cornwall, UK

Introduction: The enhancement of PDT is investigated using an iron chelating agent to temporarily increase PpIX accumulation.

Materials and Methods: PpIX fluorescence and cell kill was quantified in cultured human cells of dermatological origin incubated with ALA/MAL +/- the novel iron chelator, CP94 or the established iron chelator, desferrioxamine. Additionally the effect of CP94 on PpIX accumulation and PDT damage following the topical application of ALA+/- CP94 in normal rat skin was considered before conducting a small clinical study in patients with biopsy proven nBCC.

Results and Conclusions: Experimentally, CP94 has been found to produce greater PpIX fluorescence when administered with ALA or MAL. CP94 has also been found to be superior to DFO in the enhancement of PpIX fluorescence. Increased PpIX fluorescence was associated with increased PDT damage both in vitro and in vivo. Clinically there was a significant trend of improvement in histological clearance observed with increasing doses of CP94.

Key words: CP94, desferrioxamine, fluorescence, iron chelation, nBCC, PpIX

8

PDT in view of other treatment options (Moh's etc.)

J. Conejo-Mir
Sevilla, Spain

NC

9

Learning the hard way – different protocols with PDT in NMSC

A. R. Oseroff

Roswell Park Cancer Inst, Buffalo, NY, USA

Multiple approaches have been employed for topical PDT, often without clear bases for treatment parameters. We examined effects of ALA application time and light dose on initial response and recurrence rates for sBCC and nBCC. We also studied effects of irradiance on PDT efficiency, and on pain. For sBCC, single treatments with 4-6 or 18-24 h ALA and light doses of 200 or 300 J/cm² at 150 mW/cm² (633 nm) all gave initial CR rates ~93%. Skin reactions were stronger with 4-6 h ALA and durability significantly better, particularly with 300 J/cm², with 3% recurrences at 3 yrs and 8% at 7 yrs. For nBCC, initial responses were comparable, but 4-6 h ALA also gave more durable responses than overnight applications. PDT efficiency measured by photobleaching kinetics improved at lower irradiances, and pain was minimal at ≤ 50 mW/cm². Varying irradiance during PDT maintained pain-free efficiency.

Key words: ALA-PDT, fluence, irradiance, NMSC, recurrences, response rate

10

PDT for basal cell carcinoma

N. Basset-Séguin

Hôpital Saint-Louis, Paris, France

Basal cell carcinoma (BCC) represent slow growing tumors with no or little metastatic potential.

According to their local aggressivity they can be divided in good, intermediary or low prognostic groups.

Superficial basal cell carcinomas (sBCC) belong to the good prognosis group. These tumors are often multiple, locate on the back on which surgery often leaves dystrophic scarring and affect young patients. PDT is an attractive option for such patients as with one or 2 cycles of treatment they are cleared with no or little scarring. Several studies have looked at response rate and long term follow up of PDT for sBCC. Response rate at 3 months was $>90\%$ in most studies. A randomized study comparing PDT and cryotherapy showed identical CR rate (93 vs 95 % respectively) and recurrence rate (23 vs 20 %) at 5 years of follow up but the quality of the healing process was always superior with PDT. Nodular BCC (nBCC) have also been treated with PDT. Several studies have looked at the efficacy of MAL PDT for the treatment of nBCC. Several randomized placebo controlled studies have shown a clear efficacy of MAL-PDT compared to placebo. A more recent study has compared efficacy of MAL PDT versus surgery for nBCC. At 3 months complete response rate was 91% for PDT versus 98% for surgery. At 36 months of follow up recurrence rate was 10 % for MAL PDT versus 2% for surgery. At 60 months follow up recurrence rate was 14% with PDT compared to 4 % with surgery. All patients treated with MAL PDT had a better cosmetic outcome. The main side effect observed in these studies was the pain which upon control is generally tolerable. PDT is an attractive option for the treatment of BCC. Its indication should be restricted to good or intermediary prognosis forms. Patients treated by PDT should be followed as it is the cases for all tumor patients. PDT offers them a chance to be treated with little or no scarring and in case of failure does not complicate any further surgical procedure.

11

Guidelines for Emerging Indications

C.A. Morton

Stirling Royal Infirmary, Scotland, UK

The efficacy, tolerance, cosmesis and long-term outcome of topical PDT for non-hyperkeratotic AK, Bowen's disease, superficial and thin nodular BCC are now well-established. A substantial number of studies now exist assessing the potential of PDT beyond these current indications. In the absence of current licensed approvals, the quality of evidence is considered for the use of PDT in other cancers and infectious/inflammatory dermatoses.

PDT may prevent as well as treat NMSC in patients at increase cancer risk, although the response of OTR is reduced compared with immunocompetent controls. Small patient numbers in individual reports continue to limit the evidence for PDT in localized CTCL, VIN and extra-mammary Pagets, although available data is encouraging.

The development of PDT in infective and inflammatory dermatoses requires revised protocols with lower dose, less intense multiple treatment regimens, to deliver tolerable yet efficacious treatment. A substantial evidence base is already available for its use in acne, viral warts, cutaneous leishmaniasis, and photo-rejuvenation. We need to consider which of these indications have potential for use either in routine clinical practice, or for patients resistant to conventional therapies.

Key Words: *acne, warts, leishmaniasis, photo-rejuvenation, photodynamic therapy*

12

Concepts for cooperation – fighting NMSC in OTR* – view of the dermatologist

A.-M. Wennberg

Gothenburg, Sweden

Patients who receive immunosuppressive therapy after organ transplantation are at an increased risk of developing non-melanoma skin cancer (NMSC). These patients have a higher occurrence of actinic keratosis (AK) than an untreated population and the AKs are highly associated with development of squamous cell carcinomas (SCC). The risk increases with the duration of immunosuppressive therapy and is also associated with sun exposure before and after transplantation. Photodynamic therapy (PDT) is a convenient and effective therapy for non-melanoma skin cancer as well as for premalignant lesions.

Animal studies indicate that UV-induced AK, SCC and basal cell carcinoma (BCC) formation may be delayed by using PDT. These findings suggest that PDT might have a potential for treatment of non-melanoma skin cancer in organ transplant patients.

Recent clinical studies indicate a role for PDT as a preventive treatment for new skin lesions in immunocompromised organ transplant recipients.

Key Words: *actinic keratosis, clinical studies, immunosuppressive therapy, organ transplant recipients, photodynamic therapy*

*OTR: Organ transplant recipients

13

Fluorescence diagnosis - useful in the office or not?

W. Bäumlér

Department of Dermatology, University of Regensburg, Germany

Fluorescence diagnosis (FD) in dermatology represents a promising procedure for the in vivo diagnosis of dysplastic or neoplastic tissue. For FD a fluorescent chromophore (e.g. 5-ALA induced protoporphyrin IX) is applied topically or systemically, which accumulates thereafter rather selectively in the target tissue. Due to the irradiation with light matching the absorption spectrum of the chromophore, the emitted red fluorescence allows the detection of the diseased skin. The fluorescence can be excited by high power Light Emitting Diodes (LED) with emission in the spectral range of 380 to 450 nm. The area of interest is directly exposed to the excitation light and the fluorescence of the lesion is monitored by a CCD-camera triggered by the flash lamp. Using the pulsed fluorescence excitation, the system enables fluorescence diagnosis in dermatology in an ambient light situation. FD is a powerful tool to assist diagnosing of neoplastic or dysplastic lesions in the skin. Meanwhile, there are complete FD systems available that can be easily used in private office.

Key Words: fluorescence diagnosis, chromophore, blue-light excitation, 5-ALA

14

Back to the roots of PDT – sunlight as a potential light source

S. R. Wiegell, M. Hædersdal, P. Philipsen,
P. Eriksen, C. Enk and H. C. Wulf
Copenhagen, Denmark

Photodynamic therapy (PDT) is a highly effective treatment of actinic keratoses (AK) but is however time consuming and often painful for the patient. Instead of fast activation of large amounts of PpIX accumulated after occlusive treatment with MAL, continuous activation of PpIX during its development might be just as efficient. The continuous activation of small amounts of PpIX could possibly reduce treatment-related pain, which is the only acute severe adverse effect of PDT. Red and blue light required to activate porphyrins are part of the daylight spectrum. Daylight-PDT would make the treatment much easier since illumination would be independent of the clinic.

We will report two studies of daylight mediated MAL-PDT. In both studies 29 patients with AK in face and scalp were treated with MAL-PDT in two symmetrical areas. In the first study one area was treated with conventional MAL-PDT using red LED light after 3 hours occlusion. The other area was treated with daylight for 2? hours after MAL had been under occlusion for ? hour. In the second study the two areas were treated with 8% and 16% MAL cream and exposed to daylight at home.

Daylight mediated PDT was as effective as conventional PDT with a reduction of AK lesions at the 3-months follow-up of 79% in both studies. No difference was found between 8% and 16% MAL cream. Treatment response in the daylight area did not depend on the intensity of the light. Illumination with LED was more painful than daylight with a mean pain score of 6.7 compared to 2.0 ($p < 0.0001$). Erythema and crusting were similar after daylight- and conventional-PDT.

PDT of AK by continuous activation of porphyrins by daylight proved to be as effective as conventional PDT. PDT using daylight activation will make the treatment of these extremely common pre-malignant tumors more time and cost effective, and more convenient for the patient.

Key words: Actinic keratosis, daylight, methyl aminolevulinate, pain, photodynamic therapy

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Dose response study with MAL-PDT in AK : comparison between 1h and 3h incubation

L. R. Braathen
Berne, Switzerland

The standard operation procedure (SOP) for Methyl-ALA (MAL) Photodynamic Therapy (PDT) includes 3 hours incubation time for the 16 mg/g MAL cream (Metvix®) followed by illumination with red light.

In order to compare the therapeutic efficacy of PDT for actinic keratosis (AK), AK in 28 patients were incubated with MAL for 1 hour and in 30 patients for 3 hours.

The patient mean response rate 3 months after one or two treatments was 74% in the 1 hour group and 85% in the 3 hour group. The difference is not statistically significant.

In conclusion the lack of significant difference between the therapeutic efficacy of 1 hour and 3 hours MAL incubation time indicate that 1 hour incubation time is sufficient for MAL-PDT. The SOP can therefore be shortened accordingly giving a considerable gain of time for the patient and easier practice management.

Key Words: *Incubation time PDT, dose response*

16

Photorejuvenation: how PDT is used in the Americas

L. Torezan
Hospital das Clinicas, Sao Paulo, Brazil

Photodynamic therapy with 5-ALA or MAL is a well established modality for the treatment of actinic keratoses (AK) and basal cell carcinoma. Recent guidelines have shown the optimal indications as well as the best parameters to be used.

PDT may be used with different light sources, especially intense pulsed light (IPL) devices and pulsed lasers to induce an improvement in the signs of photoaging.

PDT for photorejuvenation remains still off-label. Up to now, many studies have shown its efficacy on the treatment of AKs and also on the improvement of fine lines, skin texture, solar lentigos and telangiectasias of the face. Some recent studies have shown that ALA-IPL-PDT offers more advantages when compared with IPL alone. Once PDT effect, namely erythema, edema, crusting and desquamation, may be considered a draw-back, short-contact ALA-PDT has become very popular, decreasing side effects and offering excellent final cosmesis, as well as being more tolerable.

In Brazil, PDT for photorejuvenation is becoming very common in the last 2 years, once both MAL and ALA have been approved for oncologic purposes. Undoubtedly, the combination of ALA or MAL with these pulsed light sources play a role in decreasing AKs and improving photorejuvenation. However, within the context of short-contact IPL-PDT, there is very little PpIX production even in AKs. Besides, there is no IPL standard parameter that allows us to treat AKs with great efficacy, especially in long term follow-up clearance. Thus, ALA or MAL – PDT for photorejuvenation may be considered for patients with photodamage associated with AKs, ensuring that the guidelines are being followed.

Key Words: *ALA, MAL, Photorejuvenation, photoaging, PDT*

17

Photodynamic Rejuvenation

R. Ruiz-Rodriguez

Department of dermatology, Clinica Ruber, Maldona 50, Madrid, Spain

Objective. To evaluate the clinical efficacy, tolerability and side effects of topical 5-methyl aminolevulinic photodynamic therapy in photorejuvenation.

Design. Randomized, prospective, controlled, split-face comparison study.

Interventions. Three treatments using topical methyl aminolevulinate cream, 160 mg/g, applied for 1 hour on one half of the face and 3 hours on the other half before illumination (37 J/cm² of red light at 570 to 670 nm) with a 3-week interval.

Results. An improvement in fine lines was observed by blinded investigators mainly in the 3-hour incubation time side after treatment in all subjects. There were no changes in mottled pigmentation and tactile roughness. Side effects were observed in all subjects (erythema, edema, scaling) mainly in the 3-hour incubation time side.

Conclusion. 5-methyl aminolevulinic-photodynamic therapy with red light can improve fine lines and maintain the response in a long term.

Key Words: MAL, non-ablative, rejuvenation, photodynamic therapy, red light, side effects

18

HPV-induced lesions- is PDT of use?

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PDT has been approved only for actinic keratoses, basal cell carcinomas and Bowen's disease. Nevertheless, also human papilloma virus (HPV)-induced lesions are possible targets for PDT, since rapidly proliferating cells in viral acanthomas selectively accumulate ALA-induced PpIX as compared to surrounding non-infected cells. Thus, PDT can destroy HPV-infected cells without harming adjacent normal tissue and can also target subclinically infected cells that are not clinically evident.

Several studies have shown the efficacy of PDT for HPV-induced lesions. Placebo-controlled trials demonstrated the superiority of repeated PDT series in clearing recalcitrant hand and foot warts. Larger trials have shown that anogenital warts respond well to PDT and also for intraepithelial neoplasia promising results have been published. Only few case reports document the efficacy of PDT in epidermodysplasia verruciformis and plane warts.

Although several studies document promising results for PDT of different kinds of warts, treatment modalities are not yet standardized.

Key Words: condylomata acuminata, warts, intraepithelial neoplasia, human papilloma virus, ALA, MAL

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Rosacea - is PDT of benefit?

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Photodynamic therapy has shown promise in the treatment of several skin diseases besides actinic keratoses (AK) and skin cancer (NMSC). Especially, the effect of PDT on acne seems increasingly well-documented; because of the many similarities in the appearance and hypothesised pathogenesis of acne and rosacea respectively, we have for some years offered PDT as a treatment option for rosacea patients referred to our department. It has been offered as an experimental treatment only, after having achieved unsatisfying results through conventional therapy. We have in a number of cases experienced longer remission times after PDT than under previous therapy. Caution must be warranted and careful information must be given to the patient, when obtaining consent to the treatment, as local reaction after PDT for rosacea seems to be more profound than when treating AK and NMSC. Results will be presented and hypothesised mechanisms of action will be discussed.

Key Words: *PDT, photodynamic, rosacea, treatment*

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PDT in non-approved indications

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We report our results in patients with cutaneous T cell lymphoma (CTCL), psoriasis, lichen sclerosus et atrophicus, follicular mucinosis, lupus erythematosus, pityriasis lichenoides chronica, Paget disease, scleroderma, alopecia areata, Hailey-Hailey disease, cheloides, lipoid necrobiosis, actinic porokeratosis, vitiligo, hidrosadenitis suppurativa and viral warts.

We used metilaminolaevulinic acid (Metvix®) as fotosensitizer and either red light or pulsed dye laser as light sources, depending on the dermatosis or the localization of the affected area.

We believe PDT is in an exploratory stage with promising results in some inflammatory or infectious cutaneous diseases. Only short series or isolated cases report, apart from psoriasis, viral warts and CTCL, have been published in the literature. Further studies are necessary to optimize PDT new applications.

Key Words: *fluorescence diagnosis, methyl aminolevulinic acid, red light, non-approved indications*

21

PDT and extramammary Paget disease

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Extramammary Paget disease is an uncommon cutaneous neoplasm presenting with erythematous plaques most frequently located in the anogenital region. Management of patients needs to evaluate the occurrence of a visceral malignancy or a secondary carcinoma in the underlying dermis. Several modalities can be used to treat the cutaneous component of the disease, electrodesiccation and curettage, laser surgery, radiotherapy, topical chemotherapy or wide surgical excision. Among them topical ALA PDT offers a reliable treatment of extramammary paget disease. To date only small series of ALA PDT treated patients have been published. Complete response needs at least three to four runs of treatment with an interval of one to two weeks due to local irritation. PDT in ano genital region is usually very painful and needs strong local or regional anesthesia before illumination which can limit the feasibility of the treatment. Small and circumscribed lesions offer a better control than larger and widespread Paget disease. Therefore ALA PDT remains a good therapeutic option in elderly patients with a good cosmetic outcome.

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PDT of superficial skin mycoses: In vitro and ex vivo experience with *T. rubrum*

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Superficial skin mycoses belong to the most frequently occurring human infections. Current antimycotic treatment is largely based on the inhibition of ergosterol synthesis in growing hyphae. The sensitivity of spores to this treatment is, however, of limited value.

In order to develop effective therapy for dermatophytoses based on the photodynamic principles we first investigated the susceptibility of *Trichophyton rubrum* to PDT with the use of synthetic porphyrin photosensitizers. From the examined photosensitizers, Sylsens B showed the highest efficiency. The PDT effectiveness was dependant on pH and molarity of the Sylsens B solution. These results were confirmed on our newly developed ex-vivo model that made use of *T. rubrum* grown on isolated human stratum corneum. The susceptibility of *T. rubrum* could be examined in different fungal growth stages. Our experiments allow us conclude that the development of an efficient single PDT of skin mycoses caused by *T. rubrum* is feasible.

Key Words: *Photodynamic therapy, porphyrin, mycosis, photosensitizer, T. rubrum, dermatophyte*

23

Prevention of photocancerization with MAL and red light in hairless mice

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We have designed a preventive-PDT protocol based in the use of methyl-aminolevulinate (MAL) and red light on hairless mice SKH-1 chronically exposed to UVB radiation. During the 30 weeks of UVB-exposure mice were treated 4 times with 16% topical MAL (Metvix®) for 2 h and then exposed to light from a LED source ($\lambda = 635 \text{ nm}$, 6 J/cm^2). A significant delay in the time of appearance ($P < 0.005$) and in the number of tumors per animal ($P < 0.01$) was observed in mice subjected to the preventive-PDT protocol, when compared to those exposed only to UVB. Fluorescence detection showed that PpIX was preferentially accumulated in UVB-exposed skin lesions as compared to normal skin. In addition, after PDT, changes in the expression of tumor suppressor proteins such as: p53, p14 and p19 in the UVB-exposed skin, were detected. The results obtained showed that MAL with red light prevents the formation of UVB-induced skin lesions.

Key words: Photodynamic therapy, hairless mice, UVB, skin lesions, prevention

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Changes in the histology and tumor suppressor proteins expression in AK and BCC after MAL-PDT

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Photodynamic therapy (PDT) has shown to be effective for the treatment of both, actinic keratosis (AK) and basal cell carcinoma (BCC). Four patients with AK and field cancerization and four patients with BCC were treated with PDT using Methyl aminolevulinate (MAL) and red light. A skin biopsy was performed before and six weeks after PDT for histological analysis. Hematoxiline-eosin, PAS, orcein, giemsa and Masson's trichrom staining were performed in order to assess the histological changes. Immunohistochemistry (IHC) was also carried out, not only for several tumor suppressor proteins, such as p53, p63 and p16, but also for Ki-67 which is a proliferation marker. Improvement of histological signs of photoaging, including: reduction of elastosis and dysplasia of the basal layer of the epidermis were observed. In addition, IHC showed significant changes in the expression and redistribution of the studied proteins in preneoplastic and neoplastic tissues after PDT.

Key words: Photodynamic therapy, actinic keratosis, basal cell carcinoma, prevention

25

Detection of tumor margins by fluorescence diagnosis

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Basal cell carcinomas (BCC) tend to occur in sun-exposed areas, such as the face, where complete removal with satisfactory cosmetic results can be difficult. There is a need of preoperative tools so as to allow and improve accurate demarcation of BCC, which would simplify surgery. We have investigated the concordance between MAL-induced fluorescence images and the clinical and histopathological tumour in 45 BCCs bounded to face. Based on fluorescence images, initially foreseen surgical lateral margins had to be modified in 16 patients: 7 out of 20 treated by Mohs surgery and 9 of 25 treated with conventional surgery. With this technique the number of Mohs excisions practised was at least one less, and only in a patient treated with conventional surgery the margin was affected. We think that MAL-induced fluorescence prior to surgery allows us to define lateral surgical margins of BCC with a high degree of accuracy.

Key Words: basal cell carcinoma, diagnosis, MAL, surgery

26

Randomized, double-blind, prospective study to compare MAL¹ with ALA² PDT for squamous cell carcinoma in situ

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The aim of this study was to compare the efficacy and adverse effects of MAL with ALA-PDT for the treatment of biopsy proven SCC in-situ.

Methods Patients were randomised for 20% ALA >50mgcm² Porphin[®] or MAL >50mgcm² Metvix[®] for a 5 h or 3 h period respectively and treated with 50 J cm² at 50 mW cm² using a Waldmann PDT lamp MSR 1200 (580–740 nm). Irradiance was measured using a calibrated hand-held meter (International light 1400A with Selo33 /F /W /QND52 detector with filters). A second treatment was performed six weeks later. Pain was assessed using a visual analogue scale (VAS) (1–100 mm) at 3, 6, 12 and 16 min. Patients were assessed for clinical response 1 month after their second treatment.

Results 41 patients (mean age 69.9yrs range 43-87yrs), 31 female, who had 54 SCC in-situ ; 40 lower limb, 8 head and neck, 4 upper limb and 2 on the trunk were recruited. Twenty five patients with SCC in-situ at 26 sites had MAL PDT and 15 cleared, 4 had partial clearance and 7 failed. Twenty six patients with SCC in-situ at 28 sites had ALA PDT and 24 cleared and 4 failed. The Chi-square test was significant at the 5% level (p=0.04) for clearance. Nine patients had paired SCC in-situ on lower limbs treated with MAL and ALA PDT and Mc Nemars test was not significant at the 5% level (p=0.41).

Adverse events Patients treated with MAL PDT had lower median pain scores at all time points but the only significant difference at the 5% level was at 12 minutes p=0.015 (Mann-Whitney U test using Minitab software). There was no discernible relationship between tumour size (area in cm²) and pain at all time points using scatter plots.

Conclusion Both ALA and MAL PDT were effective and well tolerated. ALA is as effective as MAL PDT for SCC in situ in this study and much less expensive.

Key words: aminolevulinic acid, aminolevulinic acid methylester, photodynamic therapy, randomised controlled trial, squamous cell carcinoma in-situ

¹Topical 5-aminolevulinic acid methylester

²Topical 5-aminolevulinic acid photodynamic therapy

C27

Different response to fractionated ALA & MAL-PDT

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In Rotterdam we investigated the response to fractionated ALA-PDT. Importantly, the use of two fractions separated by a dark interval of 2h, enhanced the clinical efficacy of ALA-PDT in sBCC, Bowens disease and AK. Considering the increasing clinical use of MAL and the expected gain in efficacy by light fractionation we investigated the response to MAL-PDT using a single and a two-fold illumination scheme and compared that with ALA-PDT. In mice skin fractionated illumination does not enhance the efficacy of PDT using MAL as it does using ALA despite comparable fluorescence intensities at the end of the first light fraction and at the start of the second light fraction. Only the initial rate of photobleaching was greater during ALA-PDT although the difference was small. Our data suggest that the distribution of MAL and ALA in tissues, and therefore the site of PDT induced damage, is important. The clinical relevance of these results will be discussed.

C28

Acne and beyond

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Copenhagen, Denmark

NC

29 Clinical and Immunological Results of a Phase II Trial of Sequential Imiquimod and PDT for Vulval Intraepithelial Neoplasia

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High risk human papillomavirus (HPV) associated vulval intraepithelial neoplasia (VIN) is difficult to treat. Small studies of photodynamic therapy (PDT) and imiquimod treatments have shown some success. 20 women with high grade VIN were treated with topical imiquimod and PDT sequentially. The women were followed up for 1 year. Clinical response was assessed by measuring lesion size.

The treatment was well tolerated. An overall response rate of 55% by intention treat and 64 % per protocol is clinically relevant to this condition. The 52 week symptom response was 65% asymptomatic, compared with 5% at baseline. The non responders showed a significantly higher level of T regulatory cells in the lesions after imiquimod treatment. Overall the initial non-responders to imiquimod appear to be relatively refractory. The potential benefit of this treatment is its ability to treat multi focal disease. Further randomised trials are required to compare with other experimental therapies and against standard treatment.

Key Words: VIN, PDT, Aldara

30 Combined CO₂ Laser with PDT for the Treatment of Nodular BCC

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Basal cell carcinomas (BCCs) are often seen by plastic surgeons, treatment usually necessitates surgical excision with an appropriate margin, often resulting in less than ideal cosmetic outcomes, especially if local flaps or skin grafts are required for reconstruction. Photodynamic therapy (PDT) and CO₂ laser when used as monotherapy have been successfully used to treat BCCs with greatest success in the superficial histologic subtype. These modalities when used alone have a number of limitations when compared with surgical excision, which potentially limits the efficacy of treatment of nodular BCCs which are deeply invasive. We describe our positive experiences of combination therapy with both modalities in 12 patients, with the aim of improving treatment efficacy.

Methods: Twelve patients with 13 biopsy-proven nodular BCCs on the head and neck were treated with combined therapy using an Ultra Pulse CO₂ laser and PDT using Methyl Aminolevulinate (METVIX). The mean follow-up period was 18.1 months, with a range of 7 to 26 months. All lesions responded to treatment as assessed by clinical evaluation. There were no recurrences during this time period.

Key words: BCC, PDT, CO₂ laser, Combined therapy, Future of activation

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Difficult to manage locations

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Lip, ear and periorbital area are not rare places to develop actinic premalignant lesions, as well as Basal (BCC) and Squamous Cell Carcinoma (SCC). Photodynamic Therapy (PDT) treated BCC located on the eyelid, periorbital area and deep in the helix of the ear will be shown, as well as Actinic Cheilitis on the lower lip. In these cases, final results are highly dependent on the operator ability to provide enough light energy all along the lesion surface. Otherwise, untreated areas will remain and recurrences will happen more often than expected. We discuss different tips to manage such hard areas with PDT using as light source both, LEDs lamp or laser devices. Special attention will be paid on protection measures when treating the periorbital region to avoid ocular damage.

Key Words: *Actinic cheilitis, basal cell carcinoma, eyelids, helix, Lower lip*

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Mechanisms of PDT-induced pain

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The main adverse effect of PDT treatment is an intense burning pain during and after illumination and this is the most important therapy-limiting factor. There exist several theories why PDT induces these burning pain sensations, but none of these theories are substantiated or proven. The presentation will discuss and evaluate the different existing approaches to reduce pain during PDT treatment. In addition the different mechanisms behind this burning pain will be reviewed from the point of view of a Neurodermatologist. Especially new knowledge in cutaneous innervation can add new insights to the effects of the PDT on peripheral nerve endings. New ideas and basic research is needed to fully understand the origin of these burning pains. The results of this research can lead to new and more efficient therapeutic approaches to master the burning pain during and after PDT and increase compliance and acceptance of this treatment.

Key Words: *burning pain, cutaneous nerve endings, cold activated receptor, opioids, heat*

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How to manage pain The UK perspective

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The pain of photodynamic therapy (PDT) is unpredictable and mechanisms are unclear. Keeping the patient relaxed and use of a fan or a cold air spray can be helpful but about 20% of patients experience severe pain. Larger lesions, male sex, head and face sites and actinic keratosis seem to be associated with more pain. Methyl ester ALA may be associated with less pain than ALA for superficial lesions, but this needs to be substantiated. The irradiation method is a significant factor, with low irradiance delivery, with low output LEDs being less painful. The emission spectrum also seems to be a factor. Topical local anaesthetics such as EMLA or Ametop do not seem to be of significant benefit for pain relief in PDT, although injectable local anaesthetic can be of help. Other forms of pain relief need investigation. Common practices for pain relief during PDT will be discussed.

Key Words: ALA, MAL, pain, PDT, anaesthetic, irradiance

34

Pre-treatment options in PDT

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The response rates of PDT vary widely. Limited uptake of topically applied 5-ALA or its methyl ester and suboptimal production of protoporphyrin-IX (PpIX) may account for these differences. In Europe these precursors of the photosensitizer PpIX are commonly used in PDT. The skin distribution of these drugs depends on drug permeability through the stratum corneum and diffusion through the epidermis and dermis. Factors like drug structure, formulation, the release from the vehicle, local drug clearance, de-esterification of ALA-esters, and the capability to convert ALA into PpIX eventually determine total PpIX content and are important for treatment success. The presentation will focus on pre-treatment of the skin, in order to improve the clinical outcome of ALA/MAL- PDT.

In the past we have demonstrated a negative correlation between thickness of the stratum corneum and fluorescence intensity in fluorescence diagnosis (FDAP), indicating hyperkeratosis to be an important factor in intra- and interpatient differences in ALA uptake. Pre-treatment of hyperkeratosis is an important prerequisite for improving treatment results. This can be achieved with keratolytics, curettage/debulking, tape-stripping, microdermabrasion, or laser ablation. Penetration enhancers may alter the composition or organization of the intercellular lipids of the stratum corneum. Several studies have been performed on the use of DMSO, azone, glycolic acid, oleic acid or iontophoresis to increase the penetration of ALA. As PpIX production is also dominated by temperature-dependent processes, elevating skin temperature during ALA application may also improve treatment results. Another approach to increase PpIX formation is the use of additives that interact with the heme-biosynthetic pathway, e.g. by removing ferrous iron with iron-chelating substances, e.g. ethylene diamine tetraacetic acid (EDTA), 3-hydroxypyridin-4-ones (HPOs) and desferrioxamine (DFO). It has been demonstrated that several iron-chelators are able to significantly increase PpIX formation in ALA treated skin.

In conclusion, simple pre-treatments or additions to the regular practice of PDT, aimed to optimize intralesional PpIX content, may improve the clinical outcome in PDT.

Key words: hyperkeratosis, PDT, penetration, PpIX formation, pre-treatment

35

Pain in photodynamic therapy

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Pain during the illumination, referred as burning, itching and intense pain, is the main secondary effect in PDT. It often leads to treatment interruption.

Exact mechanism is unclear; local heat and nerves endings stimulation are involved.

Intensity varies among patients, and depends on type, extension, location of lesions and PDT procedure: actinic keratosis is more painful than basal cell carcinoma or Bowen's; ulcerated lesions and lesions on face and scalp are more painful; as extensive is the area the more intense pain; methyl aminolevulinate (MAL) is less painful than aminolevulinic acid (ALA).

For pain management, topical anaesthetics are not effective; being the best procedures cooling procedures and anaesthetics infiltrations.

Results of a trial in the frontoparietal area in 20 patients, comparing cold (Cynosure Cryo-5) vs. 3% mepivacaine hydrochloride truncal supraorbital/supratrochlea nerves block, are shown.

Key Words: *Pain, PDT, methyl aminolevulinate, actinic keratosis, anaesthetics, cold*

36

PDT business in Denmark (office based)

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Birgitte Hansted is a dermatologist with a one-man practice in the center of Copenhagen. Photodynamic therapy (PDT) was introduced in the clinic in march 2003. Today I am sharing with you, my experience on start up, practical execution of the PDT treatment, making agreement with Danish National Health Insurance. Selection of patients to be offered the treatment, the PDT treatment from the patients perspective. Information to patients with emphasis on the differences between actinic keratosis and basal cell carcinoma and D-vitamin deficiency. Summary of 5 years work with PDT.

Key Words: *Photodynamic therapy (PDT), execution in practice, patients comments*

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Hospital based PDT Business in Germany

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Wuppertal, Germany

89 Clinics were approached to answer a questionnaire concerning the clinical use of PDT.

43 answered the questions:

The majority of the clinics use PDT as an outpatient as well as an inpatient procedure depending on various factors, e.g., extension of the treatment areas. Various light sources are used and the majority have several sources available: 30 clinics use Actilite (Galderma), 14 Waldmann Red Light, 9 Saalman Green Light and 7 Hydrosun. As photosensitizer most clinics use Metvix as well as special prescriptions, depending on the patient's insurance situation. The main indications are: Actinic keratosis/field cancerisation, followed by Bowen's disease and superficial basalioma. Only 4 clinics treat nodular basalioma, 3 cutaneous Leishmaniasis, and 3 HPV-infections with PDT as a routine procedure.

The range of treated patients per year reaches from 20 to 1000, the majority treat about 80-120 patients/year.

Key words: PDT, clinics, light sources, photosensitizer

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PDT business in Italy

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As an experimental therapy for NMSC, photodynamic therapy has been in use more than 10 years ago in Italy. The centres of Brescia, Padova, Florence and Naples were among the first to employ this technique. The drug has been finally licensed for therapy of AK and BCC in 2004.

For a while, methylaminolevulinic acid has been made available only to private and public hospitals and very recently it has been made available also to privately practising dermatologists. The price of one tube Metvix has been now considerably reduced, from initially more than 400 Euros to roughly 220 Euros for private practising dermatologists and about 170 Euros to public health institutions.

While 20 – 30 public hospitals and clinics use PDT, this procedure is only at its beginning in private offices. As a matter of fact the drug has been only recently available for private practices, and the awareness of the advantages of the technique is not yet as widespread as it deserves. However, setting up a PDT treatment in a private practice could mean entering a market with a considerable chance of further growth, especially if one considers the not yet fully explored properties of PDT in the field of skin rejuvenation.

Key Words: PDT, Italy, public use, private use

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How to set-up a PDT unit: doing it the French way!

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The Toulouse medical teaching-Hospital's oncodermatology unit is aimed at the management of melanomas, non-melanoma skin cancers, and cutaneous lymphomas. This unit comprises dermatologists and nurses, and is equipped with a 630nm wave length photodynamic therapy (PDT) lamp. Our experience of PDT is based on a 2 year-cohort of 350 patients treated with PDT. The most prominent indications were actinic keratosis and superficial basal-cell carcinomas. Our experience is also based on the treatment of non approved indications of PDT. This concerns patients for whom conventional treatments were ineffective or inappropriate such as nodular basal cell carcinomas, vulvar Paget's disease. In addition the therapeutic role of PDT for non melanoma skin cancers arising in patients with genetic predisposing skin diseases such as Xeroderma Pigmentosum and Gorlin's syndrome appears to be promising. The optimal use of PDT requires a multidisciplinary team working in close connection including : a specialized nurse, a dermatologist, a pain control specialist for difficult cases.

Key Words: *Photodynamic therapy, Gorlin's syndrome, Xeroderma pigmentosum, actinic keratosis, basal-cell carcinoma*

40

Fluorescence diagnosis Clinical applications

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Fluorescence diagnosis (FD) in photodynamic therapy is based on the selective accumulation of porphyrines in diseased tissue after application of an exogenous photosensitizer, usually topical 5-aminolevulinic acid (ALA) or ALA methyl ester. These porphyrines show a characteristic red fluorescence when the skin is illuminated with Wood's light (370-405nm), delineating the lesion from the surrounding skin. This is specially useful for cutaneous cancer diagnosis and management, because this method can help to chose a proper place for a cutaneous biopsy, define the borders of clinically ill defined tumours, differentiate a cancer relapse from a scar, or guide the preoperative planning in Mohs surgery. Moreover, FD is a helpful tool to evaluate the efficacy of PDT, and it is part of the routinized procedure in PDT treatments. The fluorescence images can be captured with adapted camera systems and processed with image analysis computerized systems to better define the colour differences. Anyway, some limitations in the FD related to the diffuse fluorescence emission in some cutaneous areas or the lack of fluorescence in some kinds of tumours, make the FD a useful tool for cancer management but yet not a substitute for histological study.

Key Words: *Fluorescence diagnosis, photodynamic therapy, porphyrines, 5-aminolevulinic acid, ALA methyl ester, Wood's light*



Posters

P1

A clinical study comparing MAL-PDT and Surgery sBCC, with a 12-month follow-up

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on behalf of the Excilight Study Group

Objective: To compare the efficacy and cosmetic outcome of MAL-PDT with surgery for sBCC over a 1 year period.

Methods: Prospective, multicentre, randomised, controlled, open study. Patients were treated at baseline either with MAL-PDT (2 sessions 7 days apart, repeated 3 months later if incomplete clinical response) or elliptical simple excision surgery.

Results: A total of 196 patients were randomised with 1.4 lesions on average. Mean percentage of sBCC that had cleared at 3 months was 92.2% with MAL-PDT versus 99.2% with surgery confirming the non inferiority of MAL-PDT vs. surgery (95%CI [-12.1;-1.9]). At 12 months, 9.3% lesions recurred with MAL-PDT and none with surgery. Cosmetic outcome, assessed by the investigator and by the patient, was statistically superior with MAL-PDT at all time points, and improved with time contrary to surgery.

Conclusion: MAL-PDT offers the advantage of a high efficacy and a much better cosmetic outcome than surgery in sBCC.

Key Words: *cosmetic outcome, methyl aminolevulinate, photodynamic therapy, recurrence, superficial basal cell carcinoma, surgery*

P2

MAL/PDT: a useful adjunct therapy for a recalcitrant ulceration in pemphigus vulgaris

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We report the case of persistent neck ulceration in a patient with PV, recalcitrant to systemic immunosuppressant therapy and intralesional corticosteroids, which cleared only when photodynamic therapy was added.

A 30-year-old, phototype III, Brazilian woman, presented blisters and erosions on her mouth for the last 7 months, followed by numerous bullous lesions on the scalp, chest, neck, and genital region. Histology and direct immunofluorescence confirmed pemphigus vulgaris. Re-epitelization of most erosion was achieved by combining prednisone, mycophenolate, and dapsone. Azathioprine proved to be ineffective. Most lesions cleared with this regime, excepting one ulceration located on the neck, which was more resistant to therapy, including to intralesional triamcinolone. Two weekly sessions of MAL-PDT (Metvix® and Aktelite®) – three hours of occlusion of MAL and 10 minutes illumination, 37J/cm² - healed the lesion completely. The ulceration did not recur, even after the tapering of steroid and mycophenolate mofetil.

Key Words: *methylaminolevulinate, MAL/PDT, pemphigus vulgaris, photodynamic therapy, ulcers*

P³

MAL-PDT in necrobiosis lipoidica

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One case of necrobiosis lipoidica (NL) treated with 6 sessions of MAL/PDT, with good results, is reported in the literature. The promising results obtained in a personal case, stimulated to expand the number of patients treated with this regime.

Four patients with NL (1 with diabetes) were treated with 6 weekly sessions of MAL ointment (Metvix®), under occlusion for 3 hours, followed by illumination with Aktilite®, 10 minutes, at 37J/cm².

Necrotic ulcerations appeared after the third/fourth treatment session in all cases, followed by gradual scarring. In one patient the ulcerations lasted for 2 months after completing the treatment. The diabetic patient showed the best results, her control biopsy showing superficial fibrosis and disappearance of the granuloma

Key Words: Photodynamic therapy, necrobiosis lipoidica, methilaminolevulinate, MAL/PDT

P⁴

Enhanced PDT

L. C. Cowell, M. Cowell

Current PDT application methods have no control of the area or uniformity of photosensitizer thickness nor secure containment during incubation. A technique for precise quantitative application of topical chemotherapy, such as PDT photosensitizer, was developed. Using a transparent device to rapidly assess a lesion's size, a known volume pliable blank is selected and with a guide mark system applied to the skin. A silicon molding is then created which is tared with the required weight of topical medication before snug relocation to the desired site. Consistent application to curved surfaces ensues. Study of the technique assessed outcomes using fluorescent imaging at application and punch sample histology both prior and at 3 months of follow up for selected basal cell carcinomas and Bowens disease. Recommended PDT method was otherwise employed. Results for 129 biopsies of the 132 follow up assessments obtained are presented. In 127 cases no residual tumour was found.

Key Words: photodynamic therapy (PDT), basal cell carcinoma (BCC), squamous cell carcinoma in situ (SCCIS), topical chemotherapy

References

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P 5

MAL-PDT in Patients with sBCC

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The objective of this multicentre, prospective, non-comparative study with 12-month follow-up was to assess the efficacy and safety of MAL-PDT in patients with sBCC and who were at risks of surgical complications. Patients were treated at baseline with MAL-PDT (2 sessions 7 days apart, repeated 3 months later if incomplete clinical response). A total of 30 patients with 1.2 lesions on average were included. The complete lesion response rate at 3 months was 97.1%. At 12 months, 5 of the 35 evaluated lesions (14.3%) had recurred. According to the investigators and the patients, 100% of the treated lesions had a good to excellent cosmetic result at 3 and 12 months. The tolerability of MAL-PDT using a visual analogue scale was recorded 'good' immediately after and 15 minutes after illumination. This study results confirm the therapeutic efficacy and the good tolerability of MAL-PDT in patients with sBCC at risks of surgical complications.

Key Words: methyl aminolevulinate, photodynamic therapy, superficial basal cell carcinoma, surgical risk patients

P 6

PDT of basal cell carcinoma of the eyelid

J. Kotimäki

Eyelid is the most demanding area what comes to the diagnostics and management of basal cell carcinomas (BCCs). In this area, BCCs may easily progress to the deeper layers of the skin and even to orbita. A risk of residual tumor after the treatment is high.

A proper function of the eyelid is important. Surgery and cryotherapy have been traditionally used in this area. However, cosmetical and functional disorders may follow and plastic reconstructions may be needed.

In recent years, photodynamic therapy (PDT) has been introduced in the treatment of nonmelanoma skin cancers. It is also applicable on tumors of eyelid area. We demonstrate the use of PDT in the lower eye lid BCC with five consecutive patient cases. The follow-up after treatment is 17 to 29 months. According to our experiences, PDT has led to excellent cosmetic and functional results and is well tolerated by the patients.

Key Words: Photodynamic therapy, basal cell carcinoma, eyelid

P7

MAL-PDT in squamous cell carcinoma

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Report case. An 81-year-old man was referred to our department for a ulcero-vegetant lesion measuring to 1,8 X 2,5 cm on the left cheek. Histological examination showed an invasive SCC. We discussed his file in multidisciplinary dermatooncology meeting and we decided to perform a treatment by MAL-PDT after the shave excision of the lesion. One week after shaving of the lesion, we accomplished two photodynamic therapy sessions administered at weekly intervals. 8 weeks after last treatment clinical and histological lesion evaluation was a complete response. Histological examination showed only a scaring dermis without neoplastic cells. The cosmetic response is good. No recurrence was observed during a 4-months follow-up.

Discussion Three open-label studies have described the use of ALA-PDT in cutaneous SCC, with initial complete response rates of 54% to 100% for superficial cutaneous SCC(1,3). There are only one published report of use of MAL-PDT for verrucosa SCC (6 seances weekly) with good clinical and histological response (4). New studies with histological and clinical features are necessary to define what will be the place of MAL-PDT in the SCC treatment.

Key Words: MAL-PDT, squamous cell carcinoma, shaving excision

P8

Treatment of multiple AK with MAL and red light: results in 57 patients and correlation with fluorescence diagnosis

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Objective: evaluate the results of PDT in multiple actinic keratosis (AK) by locations and the correlation with fluorescence diagnosis.

Material and methods: we carried out a retrospective, descriptive and observational study in 57 patients treated for multiple AK with PDT in our Hospital. All were treated using methylaminolaevulinic acid (Metvix®) occluded 3 hours and red light (Aktilite®, 7.5 minutes, 37 J/cm²). We evaluated the differences between locations and the correlation with fluorescence image with the Chi-cuadrado statistical test.

Results: a best response, less number of sessions and longer time of remissions is obtained in the face. A high correlation exists between the fluorescence area and response to treatment.

Conclusions: The results of the treatment of multiple AK with PDT are better in the face, than in the scalp or in the hands. Fluorescence diagnosis seems to be a useful tool in the prediction of treatment response.

Key Words: actinic keratosis, fluorescence diagnosis, methylaminolaevulinic acid, red light, retrospective study

P 9

MAL-PDT and red light in non-approved indications

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Objective: evaluate the results of PDT in non-approved indications.

Material and methods: we carried out a prospective, descriptive and observational study in a variety of dermatosis. All were treated using methylaminolaevulinic acid (Metvix®) occluded 3 hours and red light (Aktilite®, 7.5 minutes, 37 J/cm²). We applied a monthly or biweekly session.

Results: We report our results in patients with cutaneous T cell lymphoma, psoriasis, lichen sclerosus et atrophicus, follicular mucinosis, lupus erythematosus, pitiriasis lichenoides chronica, Paget disease, scleroderma, alopecia areata, Hailey-Hailey disease, cheloides, lipoid necrobiosis, actinic porokeratosis, vitiligo, hidrosadenitis suppurativa and viral warts.

Conclusions: PDT is in an exploratory stage with promising results in some inflammatory or infectious cutaneous diseases.

Key Words: *fluorescence diagnosis, methylaminolaevulinic acid, red light, non-approved indications*

P 10

MAL-PDT, a non-surgical alternative for the treatment of precancerous lesions and skin cancer in OTRs

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Advances in immunosuppressive therapy have lead to a long graft survival and to a marked increase in the number of organ transplantations performed worldwide.

Topical photodynamic therapy with methyl aminolevulinate (MAL-PDT) is a non-surgical alternative for the treatment of precancerous lesions and skin cancer in OTRs. We have treated 23 caucasian OTRs with MAL-PDT with multiple pre-malignant and malignant skin lesions for the last 2 years. A target lesion, either Actinic keratosis, Bowen's disease or Basal Cell Carcinoma, was selected in each patient and evaluated prospectively for response and cosmesis at week 16 and 1 year.

The results in this study confirmed the usefulness of MAL-PDT in OTRs. MAL-PDT is a valuable therapeutic alternative for the treatment of multifocal tumors in OTRs.

Assessment of long term efficacy in large clinical trials using MAL-PDT in OTRs and real life effectiveness are needed in the future.

Key Words: *actinic keratosis, Basal Cell Carcinoma, Bowen's disease, MAL-PDT, organ transplant recipients*

OTR: Organ Transplant Recipient

P 11 Squamous Cell Carcinoma on the Scalp Treated with MAL-PDT in a 102-Year Old Man

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MAL-PDT is better indicated for Superficial Basal Cell Carcinoma (sBCC), Actinic Keratosis (AK) and Bowen's Disease (BD), i.e. in situ squamous cells carcinoma. Due to its tendency for metastasis, squamous cells carcinomas (SCC) should not be treated with Mal-PDT as first choice treatment. The authors present a particular 102-year old patient who developed a fast growing SCC on the scalp. He had presented before MAL PDT was available with several skin tumors and underwent excisions or 5 FU cream. Due to his age, tumor site and surgical conditions, and considering histological type of this SCC (well differentiated type) we indicated MAL-PDT. We performed three sessions, the first and the second seven days apart and the third one was performed one month after the second one. Debulking of tumor as well as lidocaine anesthetic was performed before procedure. Ten months follow up (February 2008) did not showed tendency to recurrence.

Key Words: Anesthetic, Elderly, MAL-PDT, Off-lable indication, Scalp, Squamous Cell Carcinoma

P 12 Application duration of a novel self adhesive 5-ALA patch determines not only PPIX fluorescence but also clinical efficacy

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In a fluorescence diagnosis study with the novel self-adhesive patch AlaCare it was demonstrated that PPIX contents in mild to moderate AK lesions depends on the application interval of the patch. 4h application proved being the optimum application duration. A randomised, blinded-observer dose finding study was conducted where varying application intervals of AlaCare (0.5h, 1h, 2h, 4h) were followed by standardised illumination protocol (Aktilite, 37 J/cm²; 630 +/- 3 nm). PDT was performed once without prior debulking of the lesions. For the primary aim, efficacy was evaluated in 140 patients (520 lesions). Results show that clinical efficacy increases with extended application duration (4h: 86% cleared lesions, 2h: 73%, 1h: 72%, 0.5h: 51%). 4h application again proved statistical superiority over the other treatments (generalised estimating equations (GEE) model). All treatments were well tolerated but patients with clearance seemed to experience local reactions to a greater extent than patients without clearance.

Key Words: Aminolevulinic acid, actinic keratosis, clinical trial, photodynamic therapy

P 13 Photodynamic activity of Pheophorbide from *Scutellaria barbata* as a free molecule and conjugated to polyethylene glycol

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Various studies have established that photodynamic therapy (PDT) is a valuable therapeutic method for some cancers and viruses. PDT involves the application of a photosensitizer and light which catalyze the production of cytotoxic reactive oxygen species. An ideal photosensitizer must absorb at wavelengths longer than 700 nm to treat more deep-seated or larger tumors. We focused on pheophorbide a (Pba), an active compound isolated from *Scutellaria barbata*. We have evaluated by standard resazurin and trypan blue assays the PDT effect mediated by Pba on two cell lines: HeLa and HepG2. Following 30-60 min irradiation in the presence of Pba, the cells exhibited membrane blebbing and DNA fragmentation. Moreover, preliminary experiments demonstrated high malondialdehyde (MDA) levels indicating lipid peroxidation. To improve the photosensitizer pharmacokinetic behaviour, we have conjugated Pba to polyethylene glycol (PEG) and now we are evaluating the mechanism of action of the free and conjugated porphyrins.

Key Words: Pheophorbide, polyethylene glycol, PDT, proliferation assay, MDA

P 14 Are Cutaneous vessels one of the targets of resurfacing with PDT?

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Introduction

Nonablative skin rejuvenation is a relatively new concept in facial rejuvenation, which aims to induce dermal remodeling without visible epidermal disruption. It can be acquired after treatments using laser devices, intense pulsed light, radiofrequency devices, fractional resurfacing, plasma skin rejuvenation, and photodynamic therapy (PDT).¹ Among the conditions that can be treated with this novel approach are erythema, telangiectasia, lentigines, and textural imperfections such as fine and moderate rhytides.

Material and methods

We present three patients with numerous actinic keratoses in the face treated with MAL-PDT. In addition to the disappearance of the tumors, the treated areas underwent an intense cutaneous rejuvenation marked by a decrease or disappearance of previous telangiectasias.

Discussion

PDT has been shown to induce vascular damage in both normal and tumor tissue. Supported by our clinical outcomes we suggest that one of the MAL-PDT targets which explains resurfacing results could be the vascular tissue.

Key Words: methyl-aminolevulinic, photodynamic therapy, rejuvenation, resurfacing, telangiectasia

P 15 Management of Multiple AK with MAL-PDT in Real-Life Practice in the Belgian Population

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MAL-PDT allows treating AK lesions with a high level of compliance. However, few real life data exist today in the use of MAL-PDT in patients with multiple AK.

In a prospective, observational, one arm study in Belgium, 64 patients with more than 10 AK lesions (mean: 11.2) located on the face or scalp, were followed 6 months after MAL-PDT. The mean number of visits to a dermatologist was 3.7 per patient. The mean number of MAL-PDT sessions was 1.98. The average cumulative amount of MAL-PDT used was 2.35 grams for the total treatment. Adverse events at the application-site were reported in seven patients, none serious; all completely resolved. Only 1 patient had to stop treatment during illumination. Clinical complete lesion response rate was 74% at the end of the study. Cosmetic outcome was "Excellent" or "Good" in 79% patients.

MAL-PDT offers a convenient non-invasive therapy option with high efficacy and notable cosmesis.

We would like to thank the patients and investigators who were involved in this study. In particular: Doctors R. Roelandts, H. Boonen, C. Leys, A. Nikkels, V. Van Den Haute, L. Van Quickenbome, E. Verhaeghe and B. Leroy, as well as Doctor L. Annemans and K. Caekelbergh.

Key Words: actinic keratosis, MAL-PDT, observational study

P 16 Management of sBCC with MAL-PDT in Real Life Practice in the Belgian Population

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MAL-PDT is a well standardized physician-controlled treatment for sBCC. However, few real life data are available in the management of patients with sBCC.

In a prospective, observational, one arm study in Belgium, patients with sBCC or actinic keratosis were followed 6 months after MAL-PDT. A subset analysis of 99 patients with sBCC only (mean number: 1.85; 89% primary lesions; mean diameter: 17.8 mm) showed that patients visited their dermatologist 4.3 times on average, and received a mean number of 2.28 MAL-PDT sessions. The average cumulative amount of MAL-PDT used for the complete treatment was 1.32 grams. Adverse events at the application-site were noted for two patients only; they were not serious and completely resolved. Clinical complete response rate was 84% at the end of the study. Cosmetic outcome was "Excellent" or "Good" in 93% of the patients.

This real-life MAL-DPT study confirms the efficacy found in prior randomized trials.

We would like to thank the patients and investigators who were involved in this study. In particular: Doctors R. Roelandts, H. Boonen, C. Leys, A. Nikkels, V. Van Den Haute, L. Van Quickenbome, E. Verhaeghe and B. Leroy, as well as Doctor L. Annemans and K. Caekelbergh.

Key Words: MAL-PDT, observational study, superficial basal cell carcinoma

P 17 Side by side comparison between MAL-PDT and imiquimod in “field treatment” of forehead solar keratoses

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In two patients with diffuse forehead solar keratoses treated on one side with imiquimod and on the other with a solitary MAL-PDT session, we compared the benefit, complications and patient satisfaction observed with each treatment.

MAL-PDT induced pain and swelling, and erythema which settled within 2 weeks. Imiquimod provoked crusts, tenderness and swelling by week 2. Patient 1 developed more extensive lesions than the initial site of treatment and remained erythematous and swollen for 3 months. Patient 2 developed lethargy, malaise and “flu like symptoms” within 3 to 4 weeks. He then developed secondary infection and discontinued imiquimod treatment. Both patients claimed that they would prefer to use MAL-PDT for field treatment in the future.

Both modalities were effective in clearing solar keratoses from a wide area of damaged skin. MAL-PDT was shown to be more convenient and resulted in fewer side effects than imiquimod.

Key Words: *imiquimod, MAL-PDT, patient satisfaction, solar keratoses*

P 18 ALA-PDT treatment for dermatophytic tinea pedis of interdigital type: a small clinical study

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Our aim was to assess the efficacy of ALA-PDT in the treatment of interdigital dermatophytic tinea pedis. Ten patients with dermatophytic interdigital tinea pedis were enrolled in the study. Treatment consisted of 50J/cm² of red light 4 hours after ALA application. Endpoint was either clinical and mycological cure or a total of 3 treatments at 2-week intervals. Clinical and mycological evaluations were performed at baseline, 1 week following each treatment and 2 months after the last treatment. After 7 days direct microscopic examination was negative in one patient. The rest of the patients received 2 additional treatments that lead to the clinical and mycological recovery in 5 of them. At the last follow-up visit 3 patients had a negative direct microscopic examination. ALA-PDT had in our study an unsatisfactory therapeutic effect in interdigital tinea pedis. More studies are needed to determine the beneficial effect of PDT in mycotic infection.

Key Words: *ALA-PDT, dermatophytosis, tinea pedis*

P 19

PDT with MAL and HAL equally delays UV-photocarcinogenesis in hairless mice

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Hexyl aminolevulinate (HAL) is a aminolevulinic acid ester derivative which has been proposed in topical photodynamic therapy (PDT) because of its more lipophilic properties, that may penetrate deeper into skin. The purpose of this study was to determine whether HAL-PDT can prevent photocarcinogenesis in hairless mice in comparison with methyl aminolevulinate-PDT. 405 mice were irradiated with solar UV three times a week until tumour development. At day 45 and 90 selected groups were treated with PDT using HAL or MAL in cream concentrations according to group: Group 1: 20% MAL, group 2: 20% HAL, group 3: 6% HAL and group 4: 2 % HAL. The time to first tumor was significant longer for groups 1-4 than in mice only exposed to solar UV or solar UV/placebo PDT ($p < 0,0001$). In conclusion, 2%, 6% and 20% HAL-PDT and 20% MAL-PDT are equally effective in preventing UV-induced tumors in hairless mice.

Key Words: hairless mice, hexyl aminolevulinate, methyl aminolevulinate, photodynamic therapy, UV solar irradiation

P 20

PDT for facial acne vulgaris using six month follow up MAL

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Introduction: Acne is a very common disorder of great cosmetic concern and topical photodynamic therapy (PDT) using methyl aminolaevulinate (MAL), a lipophilic derivative of 5-aminolaevulinic acid (ALA), has shown efficacy in the treatment of inflammatory acne.

Objective: to evaluate the efficacy and tolerability of MAL-PDT in 5 patients with moderate to severe facial acne vulgaris.

Methods: 5 patients, aged 15-30 years, received 3 treatments sessions, 4 weeks apart. Inflammatory acne lesions were counted at baseline, after each treatment session and at 12 and 24 weeks follow-up.

Results: a medium reduction of 60.4% of total inflammatory acne lesions was observed at 4 weeks after last treatment. A direct effect between number of sessions and greater clinical improvement was observed. The medium maximal pain score was 7 (range 5-10). Post inflammatory hyperpigmentation was temporarily observed in one patient skin type IV. The clinical results lasts up to 6 months follow up.

Key Words: photodynamic therapy, acne, methyl aminolevulinate

P 21

MAL-PDT of in situ, microinvasive and invasive squamous cell carcinoma

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PDT with methyl-MAL is an approved non-invasive treatment option for AK, a precursor of squamous cell carcinoma (SCC). In this study a total of 112 SCC were treated with MAL-PDT. The cream (160 mg/g) was applied for 3 hours prior to illumination from a LED source (wavelength range: 635 ± 18 nm; light dose 37 J/cm²). A second MAL PDT session was given 7 days later.

Results: The overall complete response rates were 73.2 % at 3 months and 53.6 % at two years. The time (mean \pm SD) to recurrence was 6.55 ± 4.10 months.

Local adverse effects consisted of strong erythema followed by erosion or ulceration. Pain was mild to moderate and treatment discontinuation was never required.

Conclusion: MAL-PDT may represent a valuable, effective and well tolerated treatment option with a good cosmetic outcome for superficial, well-differentiated (Broders' scores I and II), in situ SCCs.

Key Words: *squamous cell carcinoma, methyl-aminolevulinic acid, photodynamic therapy, PDT, cosmetic outcome*

P 22

Comparison of five different red light sources for topical PDT of AK in controlled split-face studies regarding efficacy, painfulness, patient satisfaction, and cosmesis

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For the treatment of actinic keratosis (AK) photodynamic therapy (PDT) with 5-aminolevulinic acid (ALA) or with methylaminolevulinic acid (MAL) is an effective and safe treatment option but sometimes painful. Incoherent lamps, light emitting diodes (LED), and variable pulsed light (VPL) as potential red light sources were compared regarding efficacy, painfulness, patient satisfaction and cosmesis in controlled split-face studies.

Patients (n=82) with overall 953 actinic keratoses in a symmetrical dissemination suitable split-face studies were included. The first group received topical ALA-PDT using the incoherent lamp (160 mW cm⁻²; 100 J cm⁻², PDT 1200L, Waldmann Medizintechnik, Villingen-Schwenningen, Germany) vs. a LED-system (80 mW cm⁻²; 40 J cm⁻², Omnilux®, Photo Therapeutics Ltd, Altrincham, U.K.). The second group received topical MAL-PDT using the same incoherent lamp (160 mW cm⁻²; 100 J cm⁻²) vs. another LED-system (120 mW cm⁻²; 40 J cm⁻², LEDA, WaveLight AG, Erlangen, Germany). The third group received topical MAL-PDT using a LED-system (50 mW cm⁻²; 37 J cm⁻², ActiLite®, Galderma, France) vs. VPL (80 J cm⁻², Energist Ultra VPL™, Energist Ltd, Swansea, U.K.). A re-evaluation up to 3 months was performed.

In all groups 3 months following treatment there was no significant difference between the compared light sources regarding the infiltration and keratoses scores. In group 1 and 2 there was no significant difference regarding pain during light treatment and patient satisfaction as well as cosmesis following therapy. In group 3 the painfulness was significantly lower during and after VPL irradiation [$t(df=24)=4.42$, $p<0.001$].

These results prove the efficacy of three different LED-systems and VPL for topical PDT of AK. The yielded remission rates and cosmetic results are not inferior as compared to standard treatment regimes. Interestingly, VPL causes significantly less pain during treatment.

Keywords: *photodynamic therapy, protoporphyrin IX, 5-aminolevulinic acid, LED-system, actinic keratoses, intense pulsed light (IPL)*

P 23

Topical PDT for extramammary paget's disease: clinical and histological study of 4 cases

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Introduction: Standard surgical treatment and other ablative modalities for extramammary Paget's disease (EMPD) are associated with high recurrence rates and morbidity.

Objective: to evaluate clinical effectiveness and tolerability of methyl aminolaevulinate photodynamic therapy (MAL-PDT) as an adjuvant treatment for in situ EMPD.

Methods: four patients, aged 67-76 years, with vulvar⁽²⁾, axillary⁽¹⁾, and scrotal⁽¹⁾ EMPD received 3 to 8 treatment sessions, 4 weeks apart. The lesion's extension ranged from 4.5 to 20 cm, and the axillary lesion had failed previous imiquimod. Histopathological exams were performed before and one month after last treatment. Local anesthetic infiltration was sufficient for the pain control, except for the most extensive vulvar lesion, that required intravenous morphine boluses.

Results: one patient, with EMPD of 4.5 cm located on the scrotum, had a complete clinical response, confirmed by histopathological exam performed one month after 3 sessions. All patients presented a medium extension reduction of at least 50% after last treatment session, in addition to symptomatic improvement. Except for transitory edema, no adverse event was observed.

Conclusion: MAL-PDT may be considered as an adjuvant treatment for in situ EMPD, reducing the extent of subsequent surgical excision. The role of topical PDT remains to be established.

Key Words: Extramammary Paget's disease, topical photodynamic therapy, methyl aminolaevulinate

P 24

Bioavailability of ALA and MAL in BCC – A perfusion study using microdialysis in vivo

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Background: Photodynamic therapy has reported varying cure rates and the transdermal penetration of drugs has been discussed as a limiting factor.

Objectives: Our objective was to investigate the transdermal penetration of aminolaevulinic acid (ALA) and methyl-aminolaevulinate (MAL) in BCC in vivo using a microdialysis-technique.

Patients and Methods: Twenty patients with 27 BCCs were randomly treated with MAL and ALA and curettage was performed at random. Microdialysiscatheters were inserted into the tumours at depths 0.4 to 1.9 mm. Dialysates were collected for 4 h and the interstitial concentrations of MAL and ALA were determined using HPLC.

Statistics: Student's two-sample t-test, Fischer's test.

Results: No significant difference in interstitial drug concentration was observed between lesions treated with ALA or MAL. Detectable levels of drug were not obtained in almost 50% of the lesions where catheters were situated 1 to 1.9 mm in the lesion. Curettage was not found to affect the interstitial concentration.

Key Words: aminolaevulinic acid, basal cell carcinoma methyl-aminolaevulinic acid, microdialysis, penetration

P 25

PDT with a light-source from underneath the lesion: “Subluminescence”

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In addition to my presentation in Bern 2006 I will present the method to apply pdt, with a light source placed underneath the skin lesion to be treated. Since then the technique has been improved.

Technique: The tumor is pre-treated with 20% ALA in typical manner. The light is brought to the area to be treated by means of a fibre which is to be positioned into a cannula. In local anaesthesia the skin is punctured with the cannula, which contains a trokar. Exactly underneath the the tumor in about 2-3mm depth the light fibre is fixed. The radiation takes 30 minutes. I have not seen adverse side effects. The results of the few patients are very encouraging.

A short video-clip and slides show the procedure.

Key Words: *Ligth-cannula, PDT in BCC and hyperkeratotic actinic keratoses, PDT from underneath the lesion, Subluminescence – PDT, thick lesions*

P 26

5-ALA PDT in decreasing the size of excisional defects: reflections on bladeless surgery in NMSC

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Non-melanoma skin cancer can spread out over large fields by superficial peripheral growth, while the central, invasive portion remains relatively small. Our principle is to remove the solid, invasive, exophytic tumor utilizing micrographic surgery preliminary to treating the infiltrative borders non-invasively with PDT.

An 89 year old female exhibited an amelanotic melanoma adjacent to a colliding squamous cell carcinoma (SCC) of the right temple region. The melanoma was removed with a sufficient safety margin after the third excisional level, while the neoplastic cells of the SCC continued detectable. The final surgical defect measured 3,7 x 4,2 cm. After due consideration, we discontinued further excision and implemented three photodynamic therapeutic applications at two-week intervals, thereby attempting removal of all remaining atypical cells.

We review our own and other experiences, with special regard on PDT's pain-free administration by facial nerve blocks and surgical tumescent anesthesia (Field).

Key Words: *Excision margins, non-invasive surgery, bilevel anaesthesia, pain therapy*

