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Clinical Photodynamics

In Dermatology

An International Newsletter for PDT and FD in Clinical Practice

Editorial

What's going on in PDT? Currently, there is no dermatological congress where PDT does not play a role. Recently, the 17th Congress of the European Academy of Dermatology and Venereology took place in Paris. This Congress, with the active presence of all European societies in the field, represents the dermatological Europe. In this issue of ***Clinical Photodynamics***, we present a report on this important Congress, which was attended by 11,000 participants – more than ever before.

Several talks, a workshop, a satellite symposium and several posters were dedicated to PDT. Not only innovations regarding photosensitisers for PDT, but also new indications and non-skin cancer applications, such as for acne or leg ulcers, were discussed. So, let us inform you on some new facets of PDT and inspire you to apply this therapy for the benefit of your patients.

In this issue, you will also find a report on the Australasian College's PDT session and the Calendar of Events will give you an overview on interesting events taking place in the near future. Special attention has to be drawn to the next Euro-PDT Annual Congress, which will take place in Noordwijk, The Netherlands, on March 13-14, 2009. Information about this Congress can be found at **www.euro-pdt.com**

We also want to cordially invite you to contribute to future editions of ***Clinical Photodynamics*** with an article on your personal experience of PDT or on a particular research area, a meeting report or meeting announcements.

Sigrid Karrer
Regensburg, Germany

The Australasian College of Dermatologists' Annual Scientific Meeting Photodynamic Therapy Report

17-21 May, 2008 Sydney, Australia

by: Assoc Prof Peter Foley
(*Melbourne, Australia*)

The world-famous Sydney Opera House.

THE AUSTRALASIAN COLLEGE OF DERMATOLOGISTS' ANNUAL SCIENTIFIC MEETING was held at Darling Harbour in Sydney. With a generous educational grant to the College from Galderma Australia, Prof Dr Rolf-Markus Szeimies, Associate Professor of Dermatology at Regensburg University, Germany, was able to share with us his expertise in PDT. In addition to his contribution to the Galderma-sponsored PDT breakfast, attended by over 200 delegates, Professor Szeimies also gave a plenary lecture on novel applications of PDT in dermatology.

Also in this Issue

Sydney Harbour Bridge.

PHOTODYNAMIC THERAPY BREAKFAST

PDT is still not reimbursed in Australia, but is now considered a mainstream therapy for non-melanoma skin cancer, no longer of an experimental nature. During the breakfast symposium, chaired by **Dr Robert Rosen** (Sydney), **Professor Szeimies** was joined by **Dr David Francis** (Consultant Dermatologist, Brisbane, Queensland) and **Associate Professor Peter Foley** (Melbourne, Victoria). After introductory comments from Dr Rosen, Professor Szeimies spoke on PDT for non-melanoma skin cancer: recurrence rates, patient satisfaction and management of side-effects. Topics covered by Professor Szeimies included what was new in the use of methyl aminolevulinate (MAL: Metvix®) PDT for superficial epithelial tumours since the release of the 2007 International Society for Photodynamic Therapy in Dermatology guidelines, patient satisfaction with PDT compared to other treatment modalities, and the management of side-effects – different options for different indications. Professor Szeimies commenced his presentation by reiterating the value of the international consensus guidelines, published in the *Journal of the American Academy of Dermatology* in January, 2007[1]. He covered field cancerisation and the use of MAL-PDT for actinic keratosis lesions not situated on the face and scalp. A multi-centre, controlled, randomised, open, intra-individual left right comparison of MAL-PDT and cryotherapy (with re-treatment at week 12 if there was a non-complete response) looked at lesion response, cosmetic outcome and patient preference at week 24. Efficacy for the two modalities was comparable, cosmetic outcome was superior for PDT and patient preference favoured PDT.

He then looked at the recently published five-year follow-up of nodular basal cell carcinoma (BCC) treated with MAL-PDT or surgery, commenting on short-term clinical clearance and recurrence over the five years of follow-up. A 12-month follow-up comparison of MAL-PDT with surgery in superficial BCC, currently 'In press', was also presented.

Patient satisfaction with PDT emphasised the superior cosmetic outcome with PDT compared with cryotherapy and the overall preference of both investigators and study subjects comparing MAL-PDT and cryotherapy. Professor Szeimies also commented on the patient preference for PDT over surgery, cryotherapy and 5-fluorouracil in the treatment of BCC.

SIDE-EFFECTS

The final part of the presentation concerned management of side-effects. Those he covered included the local discomfort and burning sensation, erythema, transient hyperpigmentation, bulla formation and infection. He emphasised the significant inter-individual variation, the more marked discomfort associated with AK than Bowen's disease, which in turn is more painful than BCC, the observation that pain tends to be greater in males than females, the site-related effect on pain, the difference between the two agents ALA and MAL, and how severely sun-damaged skin tends to be more likely to experience pain. A number of publications have now demonstrated that ALA is more painful than MAL-PDT. In a comparison between the pain associated with PDT and 5-fluorouracil, it was commented that more severe but short-lived pain is associated with PDT compared with weeks of a lower level of discomfort with 5-fluorouracil.

In Regensburg, it is emphasised that there is a need for the patient to be informed, prior to undergoing PDT, of the possibility of discomfort. Superficial cooling with ice pads, cold thermal water spray, liquid nitrogen spray and cooling devices, such as the Zimmer Cryo 5, are utilised. Analgesia, particularly with paracetamol, but also metamizol, are utilised. Local anaesthesia is occasionally required.

ANALGESIA

Professor Szeimies was followed on the stage by Associate Professor Foley, who discussed PDT and inhalation analgesia. Methoxyflurane (Penthrox) is an inhaled non-narcotic analgesic with rapid onset of action, gradual offset of relief, self-administered by the patient (under supervision) to control the level of relief intermittently during treatment. It is simple to use and requires minimal training. It has been demonstrated to be safe and efficacious and has been used in emergency departments and by ambulance officers in Australia for decades. At the doses used for analgesia, there are no significant side-effects, as compared to the large doses required when it is used as an anaesthetic agent. There is high patient compliance with this agent. A number of recent publications have emphasised its high patient acceptability, safety and efficacy, and the rapid relief experienced by patients. Clinical studies have included use in dentistry, burns patients, aesthetic surgery and emergency depart-

ments. There have been over two million administrations over the last 30 years, with no significant adverse events and no depression of the cardiopulmonary system. Occasionally, patients may experience drowsiness, dizziness or headaches, but these resolve spontaneously without medical intervention. There are no known drug interactions.

In addition to its analgesic properties, methoxyflurane acts as an anxiolytic and has some anaesthetic properties. The Australian experience to date has been a very positive one, and Professor Foley gave several case examples where PDT, which may have otherwise been required to be ceased due to the discomfort the patient was experiencing, was able to be tolerated. Patients remained conscious and alert during administration. Some may experience euphoria or a detached sensation. There is some mild retrograde amnesia.

PATIENT CONSENT

The final presentation was by Dr David Francis on practical consent for Metvix® (MAL) PDT. Dr Francis commenced by emphasising the need to choose the right lesions at the right site for PDT and the usage of this modality for the right reasons. He emphasised the need for a practitioner to know the limits associated with PDT. The role of consent for patients, in the view of Dr Francis, is that it gives an opportunity to educate the patient on his or her tumour and the technique to be used. It both instructs and prepares the patient for PDT and warns them, both in terms of the procedure and the outcomes both short- and long-term. The consent form, to a lesser extent, confirms that the patient has heard and understood both the procedure and cost. Other issues in the consent process include an emphasis to the patient of the need to consider how they will attend the practice, whether they need an escort and considerations for time off work. Specific practical issues used in Dr Francis's practice include information about PDT and what is going to happen, including the possibility of anaesthesia. Care of the treatment field before and after PDT is discussed, as are the usual, and less likely, side-effects. The likely outcome is also covered and a comparison is made with other modalities, including cost. The possibility of recurrent tumour and subsequent consequences are discussed with the patient, as is the emphasis placed on the need for long-term follow-up. He followed this up with a number of cases of successful therapy with PDT, as well as the less common potential complications such as pustular (sterile) inflammation, particularly on the upper lip and nose, the potential swelling that occurs – particularly periorbitally with tumours treated at this site, persistent erythema, and the potential for erosions.

Finally, Dr Francis gave a number of practical tips with regard to set-up for PDT, the consent process and local anaesthesia techniques, and he stressed the importance of the nurses involved in administering the illumination.

After the formal presentations, a highly interactive question and answer session ensued with excellent discussion.

Reference

1. Braathen L *et al* 2007 *J Am Acad Dermatol* **56** 125-143

Calendar of Events 2008-2009

December 12-14, Athens, Greece
13th COSMODERM – Joint Meeting of ESCAD/Hellenic Society of Dermatology and Venereology
Contact: Penelope Mitroyianni
Tel: +30 2 107 257 693 Fax: +30 2 107 257 532
e-mail: info@erasmus.gr

2009

February 18-20, Rio de Janeiro, Brazil
International Academy of Cosmetic Dermatology (IACD) Meeting
Contact: Meeting Secretariat
e-mail: iacd@dermato.med.br

March 6-10, San Francisco, USA
67th Annual Meeting of the American Academy of Dermatology (AAD)
Contact: AAD Secretariat
Tel: +1 202 842 3555 Fax: +1 202 842 4355

March 13-14, Noordwijk, The Netherlands
9th EURO-PDT Annual Congress
Contact: EURO-PDT 2009 Congress Secretariat
Tel: +33 (0)1 46 43 33 42 Fax: +33 (0)1 46 24 88 38
e-mail: europdt2009@vista-fr.com

April 23-26, Bucharest, Romania
6th Spring Meeting of the European Academy of Dermatology and Venereology (EADV)
Contact: Symposium Secretariat, Romania Travel Plus, 56 Tudor Stefan St. Sector 1, 011658 Bucharest, Romania
Tel: +40 21 230 42 82 Fax: +40 21 230 50 42
e-mail: info@eadvbucharest2009.com
Website: www.eadv.org/bucharest2009

May 3-6, Tel Aviv, Israel
12th World Congress on Cancer of the Skin (WCCS)
Contact: WCCS Meeting Organiser
Tel: +41 229 080 488 Fax: +41 227 322 850
e-mail: wccs2009@kenes.com

May 12-16, Vienna, Austria
Joint Meeting: 7th World Congress on Melanoma / 5th Congress of the European Association of Dermato-Oncology
Contact: Annette Gleich
e-mail: Annette.Gleich@worldmelanoma2009.com
Website: www.worldmelanoma2009.com

May 20-24, Prague, Czech Republic
10th International Congress on Dermatology (ICD)
Contact: ICD 2009, Guarant International, Opletalova 22, 110 00 Prague 1, Czech Republic
Tel: +420 284 001 444 Fax: +420 284 001 448
e-mail: icd2009@icd2009.com
Website: www.icd2009.com

June 6-11, Seattle, USA
12th World Congress of the International Photodynamic Association (IPA)
Contact: David Kessel
Tel: +1 313 577 1766 Fax: +1 313 577 6739
e-mail: dhkessel@med.wayne.edu

June 18-23, Düsseldorf, Germany
15th International Congress on Photobiology
Contact: Katharina Beyen/Andrea Hardtke, Institut für Umweltmedizinische Forschung (IUF) an der Heinrich-Heine-Universität Düsseldorf gGmbH, Auf'm Hennekamp 50, D-40225 Düsseldorf, Germany
Tel: +49 (0)211 3389 216
Website: www.iuf.uni-duesseldorf.de/ICP2009

September 10-12, Budapest, Hungary
39th Annual Meeting of the European Society for Dermatological Research (ESDR)
Contact: ESDR Secretariat
Tel: +41 22 321 4890 Fax: +41 22 321 4892

17th Congress of the European Academy of Dermatology and Venereology (EADV)

17-21 September, 2008
Paris, France

A combined report by:
Assoc Prof Peter Foley (*Melbourne, Australia*)
Dr Colin Morton (*Stirling, UK*)
Mr Rod Robinson (*Barnham, UK*)
and
Prof Ann-Marie Wennberg (*Göteborg, Sweden*)

Palais des Congrès, Paris.

17TH SEPTEMBER

SUB-SPECIALITY SYMPOSIUM BY THE EUROPEAN SOCIETY OF PHOTODERMATOLOGY (ESPD) – 'WHAT IS NEW IN PHOTODERMATOLOGY?'

On Wednesday, the day prior to the main EADV Congress, the European Society of Photodermatology held an afternoon symposium, highlighted by the presentation by **Prof P Calzavara-Pinton** (Brescia, Italy), entitled 'Methyl aminolevulinate-based PDT of Bowen's Disease and Squamous Cell Carcinoma'. Methyl aminolevulinate-based PDT (MAL-PDT) is a well established therapy for actinic keratoses (AK), with high efficacy and excellent cosmetic outcome. A similarly high efficacy and cosmetic outcome is seen in squamous cell carcinoma in situ (Bowen's disease, BD) and, as a consequence, MAL-PDT is approved for both indications in the European Union. Previous publications of small series have reported response rates of squamous cell carcinoma (SCC) to PDT ranging from as low as 33% up to 100%. In a recent report from Xu *et al* from China (*Chinese Med J* 2002 **115** 1141-1145), in which 32 grade I and II lesions were treated with 3-6 sessions of ALA-PDT, all achieved complete remission. The recurrence rates were 22% (7/32) for SCC at follow-up 1-3 years after the therapy.

In Prof Calzavara-Pinton's study, 52 patients with 112 biopsy-proven lesions of BD and SCC were treated in an outpatient setting with MAL-PDT. The MAL cream (160mg/g) was applied 3 hours prior to illumination with a light-emitting diode source (wavelength range 635±18nm; total dose 37J/cm^2). The treatment was repeated 7 days later. The majority (71.4%) of lesions were located on the face and scalp. The overall complete response rates were 73.2% at 3 months and 53.6% at 24 months, with a recurrence rate of 19.6% during this time. Adverse effects were confined to mild to moderate erythema and oedema, more so than erosions or crusting. Pain was scored on a visual analogue scale with a mean of 4.1 ± 1.7 (range 2-6). Tumour variables examined as predictors of response showed no correlation for tumour diameter, but elevation (less than or greater than 2mm), Clark level (of microscopic invasion), and cytological atypia influenced outcome. Thin lesions (in situ or microinvasive – Clark levels I and II) were more responsive than nodular/invasive SCC. Well and moderately differentiated tumours (Broders' scores I and II) were more likely to respond than poorly differentiated lesions.

The speaker concluded that superficial, well differentiated SCC can be effectively treated with MAL-PDT, but the histological depth of invasion and clinical appearance were less relevant – hence, all lesions should be biopsied and appropriately reported before institution of this modality.

19TH SEPTEMBER

LUNCHTIME SATELLITE SYMPOSIUM

This satellite symposium was titled '5-ALA Patch-PDT of Actinic Keratosis: A Real Innovation'. The Chairman was **Prof Lasse**

Braathen (Bern, Switzerland). He noted that familiarity with the modality of PDT makes a large difference in outcome: a clinician who is inexperienced in PDT will only achieve a success rate of approximately 40%, compared to the near-100% successful outcomes being achieved by experienced PDT practitioners.

Dr Colin Morton (Stirling, UK) reviewed the key studies and current status of PDT modalities for the treatment of AK. A number of studies have established a firm evidence base for the efficacy of topical PDT in the treatment of thin and intermediate AKs, particularly on the face and scalp, although AKs on other body areas can benefit from PDT.

Two photosensitising agents for topical PDT have been developed. In North America, the US FDA have approved the use of 5-aminolevulinic acid (ALA: Levulan®) plus blue light, whereas in Europe and other countries, the methyl ester of ALA, methyl aminolevulinate (MAL: Metvix®), has been widely approved, in conjunction with red light illumination, which penetrates more deeply into tissue and thus offers the chance of treating thicker skin lesions.

Direct comparison trials have shown that topical PDT is at least as effective against AK as the main treatment option, cryotherapy, but with superior cosmetic results. As a larger area can be treated in a single session, PDT also offers the opportunity of treating sites with widespread multiple AKs. Moreover, emerging evidence indicates that topical PDT offers the benefit of treatment of co-existing sub-clinical lesions and early non-melanoma skin cancers (NMSC), opening further possibilities for pre-emptive treatment in long-term immunosuppressed patients such as organ transplant recipients, who are at greater risk of developing NMSC. Some cosmetic clinicians are also exploring the use of topical PDT in skin rejuvenation.

The duration of skin exposure to the chosen photosensitiser, prior to illumination, varies: non-formulary solutions of ALA are usually applied for 4-6 hours, which is considered to be sufficient, although the US FDA licence requires a 14-18 hour application time. However, a number of US practitioners now use even shorter application times of 0.5–3 hours. MAL-PDT is licensed for a 3-hour application prior to illumination. Both photosensitisers require the treatment area to be covered with an occlusive dressing during the application time. Over the years, a wide variety of light sources have been used with topical PDT, with the general trend being towards more efficient and easier to use devices.

Pain during light exposure remains a significant barrier to wider use of topical PDT: however, considerable effort is being directed towards new methods of pain control and improved treatment protocols. It is expected that pain will become less of a problem in the future.

Dr Peter Mohr (Buxtehude, Germany) explained the combination of ALA with an adhesive patch, which can be applied to the skin and acts as its own occlusive dressing during the application time. Each patch is square, with an area of 4cm^2, and contains 8mg of ALA.

Initial studies indicated that 4 hours was the optimum application time for uptake of ALA into the lesions.

Two Phase III clinical trials have been performed, using the 4-hour application time. **Prof Axel Hauschild** (Kiel, Germany) described the first of these, which compared the ALA patch with a placebo patch. The observer-blinded trial recruited 103 patients with mild to moderate AK lesions. Larger areas of AK lesions were treated by applying the patches in a tile-like manner, up to a maximum of 32cm^2. Patients were randomised to receive either ALA-patch PDT or placebo (single treatment only) and the results were assessed 12 weeks later. There was a statistically significant difference in AK clearance rates between the two groups (82% for ALA versus 19% for placebo: $P<0.0001$). There were no serious adverse events, and the pigmentation status of treated lesions was not different between the two groups. The patients gave their opinions of the cosmetic outcome: 86% of those who received ALA-patch PDT declared themselves to be satisfied, compared to 24% of those who received placebo ($P<0.001$).

Prof Dr Rolf-Markus Szeimies (Regensburg, Germany) presented the other Phase III trial, which compared ALA-patch PDT to cryotherapy and a placebo patch. The 346 patients were randomised to receive a single-patch treatment with either ALA or placebo, or to undergo standard cryotherapy. The patients were assessed at 12 weeks. Patients who received ALA-patch PDT showed 89% clearance of lesions, compared to 77% for those who underwent cryotherapy and 29% for the placebo group. Pigmentation of the cleared lesions was also assessed: 33% of cryotherapy patients showed hypopigmentation, compared to 3% of ALA-patch PDT patients ($P<0.001$).

Conversely, 9% of the ALA-treated lesions were assessed as hyperpigmented, compared to 2% of the cryotherapy-treated lesions. Patients in both the cryotherapy and ALA-patch PDT groups experienced local reactions on study sites: however, the patients who received ALA-patch PDT were more satisfied overall with their outcome than those who received either cryotherapy or placebo (both $P<0.0001$).

A lively question session followed the presentations, the most interesting of which could be separated into two groups: cost/availability; and practicality of use.

COST/AVAILABILITY

Naturally, the question of cost of therapy was raised, but apparently this has not been finalised and therefore comparative costs cannot be extrapolated. With regard to availability, the ALA patch has not yet been licensed anywhere.

One delegate asked whether the patches could be cut to treat smaller areas: Prof Szeimies replied that they could be cut into two pieces, but any smaller sub-divisions were likely to lead to undesirable loss of ALA on the scissors and from handling. Another frugally-minded delegate asked whether the patches could be re-used: although this has not been tested, Prof Szeimies thought that very little ALA would remain for a second application.

PRACTICALITY OF USE

Several delegates asked how big an area could be treated at once: although areas of up to 32cm^2 were treated safely in the trials, no further data are currently available.

Coincidental treatment of sub-clinical lesions is seen as an advantage of the existing ALA and MAL cream formulations, and it was queried whether the patch concept might reduce the area of skin being treated: however, Prof Hauschild observed that the trials were only aimed at demonstrating the efficacy of the ALA patch, rather than making any attempt to perform field therapy.

One delegate asked about the use of blue light and other light sources with the ALA patch: again, the use of a red LED light source was for standardisation of the trial procedure, and the possibility of using blue light remains to be examined. The option of giving patients a prescription for the patches and having them apply them at home was discussed: although home application was an interesting idea and could save valuable clinic time, there were doubts about the ability of all patients to apply the patches appropriately.

20TH SEPTEMBER

PDT SESSION

SKIN CANCERS AND PDT

Dr A Sidoroff (Innsbruck, Austria) spoke about the lifetime risk of getting a non-melanoma skin cancer (NMSC): for AK, this is 28-33%, and for SCC it is 7-11%. He then raised the very hot topic of 'Why treat AKs?' In approximately 20% of cases, AKs regress

spontaneously and rate of progression of one AK into an invasive SCC is between 1 and 2.5 per 1000. Often, however, the patient has several AKs at once, hence the increased risk for SCC. Also, there is no way of predicting the outcome of the individual AKs – i.e. which particular ones might turn into SCCs.

There are about 20 different treatment modalities for AK. PDT is the first-line treatment for large and multiple AKs. PDT also shows a good efficacy rate for SCC in situ (Bowen's disease). With regard to basal cell carcinoma (BCC), PDT is less effective than surgery, but works as well as cryosurgery.

PAIN AND PDT

Dr S Ibbotson (Dundee, UK) discussed pain during PDT, where the mechanisms are unclear and the possibility of predicting the pain experience is small. It is important to take the issue of pain seriously, because it is a limitation for successful treatment. According to Dr Ibbotson, 16% of patients have severe pain during PDT, as shown by a study by her unit in Dundee, in which 4717 PDT sessions were performed.

When trying to predict pain, the following criteria have to be taken into consideration: lesion size and site; type of disease (e.g. AK, BCC, BD and acne); redness and pre-treatment fluorescence; type of photosensitiser to be used (i.e MAL or ALA); and type of irradiation.

Higher pain scores are reported in PDT of AKs, face and scalp sites, large lesions and those with strongest fluorescence. There are indications that MAL may be less painful than ALA, but this has to be investigated further.

Studies on topical local anaesthetics such as EMLA or tetracaine do not seem to show significant benefit for pain relief in PDT. A recent study from Paoli and co-workers showed that nerve block before treatment reduced the pain significantly when performing PDT on the face and scalp.

FLUORESCENCE TUMOUR DETECTION

Dr A-M Wennberg (Göteborg, Sweden) reviewed the use of fluorescence for tumour detection. There is a need for improved means to detect cancerous tissue to allow early diagnosis and therapy. Fluorescence imaging is an attractive diagnostic technique for localising skin cancer. The method can also be used to demarcate tumours and has the potential to move into clinical use. Topically applied porphyrins are excited with blue wavelength light and the emitted light is then monitored. Bispectral fluorescence imaging combines skin autofluorescence with delta-ALA-induced fluorescence. To evaluate the technique, fluorescence data can be compared with the histopathological extent of the tumour defined during Mohs surgery.

An aggressively growing BCC of the morphea type which is localised on the face would be an example of the need for FD. Results in the literature imply that the technique can be applied as a useful tool for indicating the tumour boundary of these aggressive BCCs.

The iconic Eiffel Tower, Paris.

PROMOTION OF WOUND HEALING BY PDT: A PHASE II, RANDOMISED, PLACEBO-CONTROLLED TRIAL IN CHRONIC LEG AND DIABETIC FOOT ULCERS

Prof S Brown (Leeds, UK) referred to a study on leg ulcers treated by PDT. There is a need for non-antibiotic treatments for leg ulcers, and there is laboratory evidence that PDT may promote wound healing by causing a reduction in bacterial load and also by stimulation of growth factors.

In the study, 32 patients were enrolled in order to see if PDT can reduce bacterial load and accelerate wound healing. Pre- and post-PDT swabbing for bacteria was performed and the wound area was also measured. The results showed that PDT resulted in a significant reduction in bacterial load and a trend towards wound healing. The treatment was also well tolerated by the patients. As the results were so encouraging, further trials are planned.

Dr H Wulf (Copenhagen, Denmark) considered the use of MAL-PDT (Metvix®) in the treatment of AKs, with the sun as an illuminating light source, and presented results from his unit at Bispebjerg University Hospital. In one study, MAL and red LED-PDT was compared to sunlight-PDT in 29 patients in a split face trial. The two regimens showed almost the same cure rate, but pain was significantly reduced in the sunlight group. Additionally, 62% of the patients preferred the sunlight to LED-PDT.

In another study from 2007, with 30 patients, LED-PDT was compared to sunlight-PDT using MAL in two different concentrations of 8% and 16%. In this study, the patients applied a sunscreen before PDT. The results showed no difference between the different concentrations, indicating that half as much MAL has a similar efficacy to full strength MAL. Sunlight as a light source was as good as LED illumination, with much less pain. Further studies are ongoing.

GUIDELINES FOR PDT

Prof L Braathen (Bern, Switzerland) presented the guidelines on the use of PDT, published in the *Journal of the American Academy of Dermatology* in 2007 (see page 2). The group of international PDT specialists considered the recommendations for PDT, based on the quality of evidence for efficacy, safety/tolerability, cosmetic outcome, and patient satisfaction/preference. From this, topical PDT was rated as highly effective in the treatment of AK, Bowen's disease and superficial BCC. PDT may also prevent certain NMSCs in immunosuppressed patients. Certain studies have indicated this, but the area requires further study. The major benefit of PDT is the excellent cosmetic result. Also, the fact that the procedure is in the hands of the dermatologist ensures good compliance by the patient.

POSTERS

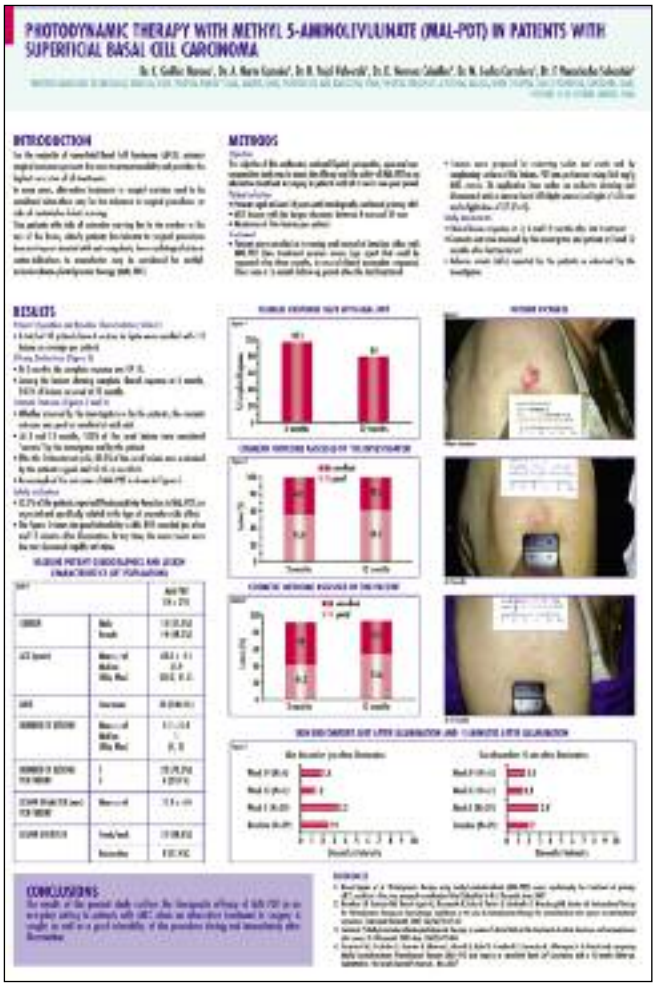
This year's EADV saw 1736 posters offered for presentation. Amongst the many rows, several interesting studies/reports concerning PDT could be found. Below, I have summarised a few of them that caught my eye.

Dr A Soler and colleagues (P0304) from The Norwegian Radium Hospital (Oslo, Norway) presented a randomised double-blinded study to investigate the potential of MAL-PDT to cause irritant and allergic contact

dermatitis. In 21 patients who had previously received MAL-PDT on at least four occasions, MAL cream (Metvix®) or placebo cream was applied to the left and the right side of the back, then occluded for 48 hours. Skin reactions were assessed after 48, 72 and 96 hours. A positive reaction to MAL cream was noted on initial testing in 3 (14%) patients. These 3 patients were retested with 3 patches of MAL cream, with an application time of 3 hours with and without illumination after removing the patches (2 patches) and 48 hours (1 patch). One patient had a positive patch test on all test sites, 1 patient had a sharply demarcated erythematous plaque without blistering and spreading outside the test area on the 48 hours test site (indicating an irritant contact dermatitis) and the 2 other test sites were negative. The third patient had completely negative results at all 3 test sites. The findings echo clinical experience that, with over 300,000 patients now treated with MAL-PDT worldwide, the incidence of allergic and irritant contact dermatitis is low.

Prof Dr R-M Szeimies and co-investigators (Regensburg, Germany) reported on 12-month follow-up of a multi-centre randomised controlled study, involving 196 patients, comparing MAL-PDT with surgery in superficial BCC (P1105). Following double-treatment PDT, repeated 3 months later, if required, lesion count reduced by 92% at 3 months, whereas surgery showed clearing of 99% of lesions. At 12 months, 9% of lesions recurred in the PDT group, with no recurrences following surgery. As dermatologists, we are unlikely to be surprised by this result profile, which demonstrated PDT performing well, but surgery, carefully undertaken, showing a slightly higher efficacy. The message to be taken from this type of study is the reassurance of another study showing respectable clearance rates following PDT for those of our patients where we are keen to avoid surgery, with the knowledge that cosmetic superiority can be achieved, as also demonstrated in this study.

Supporting this view, Poster 1096, presented by **Prof C Guillén Barona** *et al* (from multiple Spanish departments), reported on a multicentre, prospective, non-comparative study with 12-month follow-up to assess the efficacy and safety of MAL-PDT in 30 patients with superficial basal cell carcinoma (BCC), with all recruits at risk of surgical complications. Patients were treated at baseline with MAL-PDT (2 sessions) repeated 3 months later if required. The complete lesion response rate at 3 months was 97%, with a recurrence of 14% by 12 months. All treated lesions had a good to excellent cosmetic result at 12 months.


PHOTODYNAMIC THERAPY WITH METHYL 5-AMINOLEVULINATE (MAL-PDT) IN PATIENTS WITH SUPERFICIAL BASAL CELL CARCINOMA

INTRODUCTION

METHODS

RESULTS

CONCLUSIONS

Drs C Mork and **P Helsing** (Oslo, Norway) added to the clinical experience of MAL-PDT for the treatment of lesions in organ transplant recipients (P1050). MAL-PDT achieved clearance of 9/10 AKs, 3/4 Bowen's plaques, and 7/9 BCCs in 23 patients at four months.

Poster 1095 by **Dr R Rosen** (Kogarah, Australia) had a high visual impact, contrasting the appearance of the skin in a side-by-side comparison of MAL-PDT (single treatment) and imiquimod (3 times weekly for 16 weeks) in field treatment of forehead AKs. Although both therapies were effective in the 2 patients demonstrated, PDT resulted in much less inflammation, with erythema settled by 2 weeks, compared with pronounced inflammation on the imiquimod side at 3 and 6 weeks, settling by 16 weeks. In another comparison by **Dr A Webber** *et al* (Porto Allegre, Brazil) (P1221), MAL-PDT was shown to be as efficacious as imiquimod in treating AKs, but patients preferred PDT, due to the prolonged inflammation associated with imiquimod use.

Posters 0029 and 1723 were presented by **Dr S Motta** and colleagues (Milan, Italy). In the first poster, micropeeling using two peeling agents (2% salicylic acid and 2% glycolic acid) was applied to acne patients nightly for 2 weeks to promote comedone removal prior to ALA-PDT. PDT was delivered using a non-formulary 10% ALA preparation applied for 2 hours, with the treatment field illuminated with red light. Patients resumed peel treatment 1 week later. PDT was repeated fortnightly for recalcitrant lesions. The mean reduction in inflammatory lesions after the first PDT treatment was 62% with a 32% reduction in comedones. At 6 months, with repeat treatments where required, resolution of acne was seen in 95% of the 50 patients enrolled. This confirms the suspicion that PDT has good potential for inflammatory acne lesions, but requires a complementary therapy to achieve comedone lesion clearance. In the group's second poster, ALA-PDT was used to promote skin ulcer healing, reducing heal times by 50%, although the mechanism of action is unclear. Red light alone was not effective, and a direct antibacterial action of PDT was not demonstrated. In a patient with ulcers at both ankles, repeated PDT was applied once weekly to 1 ulcer only, with reduced healing time, although the picture suggests this was the slightly smaller ulcer. The observations are certainly of interest, given the great therapeutic challenge and health care costs around ulcer healing.

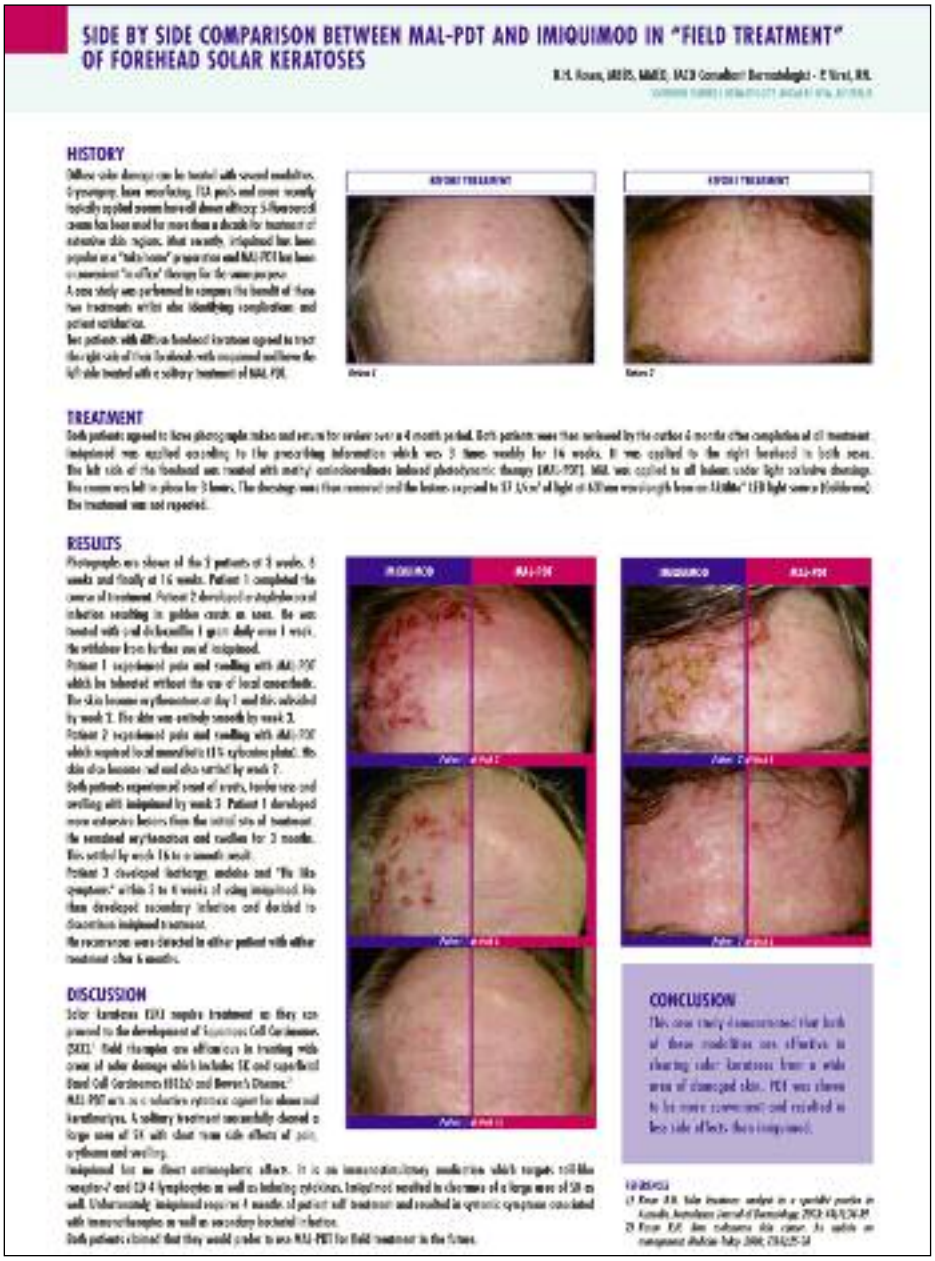
Drs M Taylor and **M Gonzalez** (UK) (P0749) presented a review of evidence to date concerning PDT for acne. Of note, they observed that, whilst ALA-PDT is effective, MAL is more folliculotropic, associated with less phototoxicity within normal tissue and possibly achieves greater depths of penetration, with less severe side-effects. Another ALA ester, hexyl 5-aminolevulinate, may cause even less erythema and pigmentation than MAL without a drop in efficacy and could be a useful agent to evaluate further. The authors also commented about application times of the current photosensitising agents in acne. To achieve prolonged reduction in sebum excretion, incubation times of approximately 3 hours would be desirable to ensure a penetration depth of 2-3mm, but improvement in skin texture and pore size probably can be achieved with shorter contact times.

Dr S Segura *et al* (Barcelona, Spain)

(P0748) successfully employed MAL-PDT to treat BCC in 4 patients with Gorlin syndrome (GS) and 2 siblings with xeroderma pigmentosum (XP). Lesions received 1-3 double treatments of MAL-PDT. Every cycle comprised 2 sessions of PDT, 7 days apart. In XP patients, clearance was obtained in one third of the tumours only. In GS patients, clearance was obtained in 55-75% of the lesions in 3 of the patients, but only 20% of over 200 lesions in a 4th patient.

Other posters observed the potential for topical PDT in photorejuvenation with MAL-PDT and red light in a standard protocol, employed both by **Dr C Zane** and colleagues (Brescia, Italy) (P1220), and **Dr O Macedo** and team (Sao Paulo, Brazil) (P0740). In Poster P0741, the same team noted the enhanced effect of PDT after fraxel non-ablative resurfacing in a group of 10 patients treated in the peri-oral skin area. **Dr E Gimeno Carpio** (Valencia, Spain) (P1194) reported clearance of a BCC arising in an area of chronic radiation dermatitis following MAL-PDT. The team from Brescia (P1217) also assessed the potential for topical MAL-PDT in SCC. They concluded that it was a safe and effective option for superficial well-differentiated in-situ lesions, but was inferior to surgery for invasive lesions.

The EADV organisers are to be praised for keeping with the physical presentation of posters, in comparison with the American Academy's use of electronic posters. A good pair of shoes and a strong coffee remain essential, however, before commencing 'The Poster Walk'. The pleasure of poster viewing is to meet some authors and colleagues amongst the aisles. I have yet to leave a poster hall without considering that I had gained some fresh insight into the World of Dermatology!


SIDE BY SIDE COMPARISON BETWEEN MAL-PDT AND IMIQUIMOD IN "FIELD TREATMENT" OF FOREHEAD SOLAR KERATOSES

HISTORY

TREATMENT

RESULTS

DISCUSSION

CONCLUSION

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