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Clinical Photodynamics

In Dermatology

An International Newsletter for PDT and FD in Clinical Practice

Editorial

This edition of ***Clinical Photodynamics*** reports on meetings both in Europe and the US, which saw ongoing and strong clinical interest in the dermatological applications of PDT. In addition to evidence-based updates on the current place of topical PDT, a symposium at the American Academy of Dermatology Congress debated the promises and limitations of topical PDT, as well as giving a detailed evaluation of the potential place of PDT in the treatment of acne. Also in this issue, we carry a report on the 9th Annual Meeting of Euro-PDT. Such was the interest in this year's meeting that several requests for oral presentations had to be declined, with attendance at full capacity. A well-organised one-day training course, hosted by the dermatology team in Leiden, preceded the annual meeting and achieved the intended balance of promoting training and education for those new to PDT, whilst also updating current PDT practitioners. Presentations on novel wearable light devices, patches containing topical photosensitiser, penetration enhancers and an assessment of the potential of daylight PDT all demonstrated continued activity to further develop PDT and promote an effective and easy-to-perform therapy.

A note for the diary: It has just been confirmed that the next meeting of Euro-PDT will be between 11th-13th March, 2010 in Monaco. Further details will be announced shortly and carried in ***Clinical Photodynamics***, as well as being available on the Euro-PDT website: www.euro-pdt.org.

Colin Morton
Stirling, Scotland

9th Euro-PDT Annual Congress

13-14 March, Noordwijk, The Netherlands

A combined report by:
Assoc Prof Peter Foley *(Melbourne, Australia)*
Dr Sigrid Karrer *(Regensburg, Germany)* and
Prof Ann-Marie Wennberg *(Göteborg, Sweden)*

FRIDAY 13TH MARCH

The Congress was opened by **Professor Lasse Braathen** (Bern, Switzerland), in his capacity as President of Euro-PDT, followed by the local Congress President, **Dr Rianne Gerritsen** (Nijmegen, The Netherlands) who gave the welcome address.

NEW DEVELOPMENTS

Prof Dr Rolf-Markus Szeimies (Regensburg, Germany) spoke about sensitisers and the latest developments. The advantage of topical administration is the low degree of invasiveness and good penetration properties of these small molecules. However, it is still possible to further optimise the therapeutic efficacy and handling of this procedure.

A seagull receiving red-light PDT on the beach at Noordwijk. *(Courtesy: Prof. Alexis Sidoroff)*

In this Issue

The skin can be pretreated to enhance the PDT effect[1]. There are a number of pretreatment options to aid photosensitiser penetration, which were discussed. Keratolytics can be applied 1-2 weeks before PDT, if practicable. Alternatives for reduction of lesion thickness include curettage, debulking, tape stripping, micro-dermabrasion or laser ablation. One can also use penetration enhancers[2] such as DMSO, azone, glycolic acid or oleic acid to increase penetration of ALA. There is also the option to use iontophoresis or ultrasound. Elevating the skin temperature during the PDT incubation phase can result in higher PpIX conversion rates. Microneedle pretreatment, in the form of microneedle arrays, can also enhance penetration. In nodular basal cell carcinomas (BCCs), EDTA and the iron chelator CP94 have been shown to enhance PDT[3].

Professor Axel Hauschild (Kiel, Germany) discussed a 5-ALA-impregnated patch for non-melanoma skin cancers[4]. This new ALA patch was compared against cryosurgery and placebo in 25 centres in Germany, with a total of 346 patients, who each had 4-8 AKs.

A future aim is to reduce the incubation time for ALA and MAL, down to as low as 1 hour. The use of a liposome formulation and microparticle technology might also be developments to be seen in coming years.

Dr Harry Moseley (Dundee, UK) considered the different light sources available. The emission spectrum of the light source must match the absorption characteristics of the drug. Additionally, the light penetration through tissue must be considered. Over the years, lasers and incoherent light sources have been employed to perform PDT. Recently, low-cost lamps and light-emitting diodes (LEDs) have been introduced in the PDT area. Another novel approach to delivering treatment is the so-called 'Ambulatory PDT', using a lightweight, portable, LED light source that is attached to the lesion following application of ALA or MAL. The most modern form of LED, organic LEDs (OLEDs), are used. Indeed, OLEDs are poised to make a huge impact in all forms of light-reliant technology in the future.

Hotels van Oranje, Noordwijk.

Dr Alison Curnow (Truro, UK) spoke about optimising PDT and further manipulation of the heme biosynthesis pathway using iron-chelating agents. Using CP94 that will increase PpIX accumulation by reducing the conversion to heme. Dr Curnow said that the combination of CP94 with fractionated light interruption to allow reoxygenation will substantially increase the cure rate of PDT[3].

Dr Tim Smits (Nijmegen, The Netherlands) discussed fluorescence diagnosis (FD) in keratinocytic intraepidermal neoplasias and FD with ALA-induced porphyrins (FDAP). Porphyrin accumulation can be studied in vivo. Improved knowledge about porphyrin accumulation in different skin conditions may help us to understand the variable clinical results after PDT and to further increase clinical efficacy. His group has performed several studies on FDAP, where they studied, for example, lesional and non-lesional skin in psoriasis and actinic keratosis (AK), showing microscopic fluorescence and PpIX content to be well correlated. Heterogeneous fluorescence seen within most psoriatic plaques was studied, showing a negative correlation between the thickness of the stratum corneum and fluorescence intensity. Stratum corneum is an important barrier to penetration when performing FD. Therefore, performing tape stripping will increase the FDAP[4].

Dr Steve Keohane (Portsmouth, UK) talked about enhancing practice with fluorescence. His unit has conducted a study looking at FD of BCC with the resection margins left by Mohs' micrographic surgery after different applications of MAL (Metvix®). Three application times of Metvix® cream were studied: 90 minutes, 120 minutes and 150 minutes. Thirty patients with histologically proven BCCs requiring Mohs' surgery were randomised to one of the application groups. FD was performed using the Dyaderm® system. After one week, Mohs' surgery was performed. There was no statistically significant correlation between the extent of tumour by FD and microscopic extent of tumour by Mohs' surgery. The speaker concluded that the application time and threshold may need to be adjusted according to tumour subtype and site to optimise the predictive value of preoperative fluorescence.

PDT IN NMSC

Dr Colin Morton (Stirling, UK) presented the updated PDT guidelines[5]. There are now new data from long-term (>5 years) follow-up for PDT in NMSC. Also, good evidence for the use of PDT in routine clinical practice exists for AK, Bowen's disease (BD) and superficial BCC, with fair evidence for nodular BCC. There is sufficient evidence for the use of PDT in epidermal dysplasia in transplant recipients, but poor evidence for PDT in vulval intraepithelial neoplasia (VIN), extra-mammary Paget's disease and PDT as a therapy for prevention of skin cancer. There is fair evidence for the use of PDT in inflammatory acne, plantar and genital warts and for photorejuvenation.

Professor Peter Foley (Melbourne, Australia) gave an overview of PDT for AK and its place in clinical practice. AKs are the premalignant precursor of squamous cell carcinoma (SCC) and they are now often referred to as incipient SCC or even SCC in situ. It is not possible to predict which AK will progress to become invasive. Therefore, it is considered good clinical practice to treat all such lesions wherever possible.

Cryotherapy can only be a spot treatment for individual lesions. In comparison, PDT and various topical applications available can treat entire zones of field cancerisation, with a superior cosmetic outcome. PDT is clinician-controlled and often requires only a single treatment session, with a cure rate of more than 80% of the lesions.

The weather was not always as good as the presentations.

Professor P Calzavara-Pinton (Brescia, Italy) addressed the question: "What is the limit of PDT for SCC and SCC in situ?" He concluded that the use of PDT in nodular invasive and poorly differentiated SCC should be discouraged.

Professor Nicole Basset-Seguin (Paris, France) examined the use of PDT for BCC. She noted that two major long-term clinical randomised studies (60 months), using MAL-PDT, had been performed. One compared the use of MAL-PDT with cryotherapy for the treatment of superficial BCC. It showed that both treatments have the same efficacy (97% versus 95%) at 3 months and comparable recurrence rate (22% versus 20%) at 5 years. The cosmetic outcome was much superior

with PDT (87%) compared to cryotherapy (47%).

The other study compared MAL-PDT versus surgery for nodular BCC. The lesion response rate was 76% versus 96% which is considered to be acceptable.

Dr Fabrizio Fantini (Modena, Italy) considered the clinical and pathological factors influencing the therapeutic response of PDT in BCC. The author and co-workers have investigated which factors affect the response of BCC to PDT in 194 BCCs in 135 patients who were treated with MAL-PDT. Clinical parameters (sex, age, site, clinical type, diameter) and pathologic parameters (histological type, depth of invasion, ulceration) were recorded. The overall complete response (CR) rate was 62%, with superficial BCC responding better than nodular BCC (82% versus 33% CR). Univariate statistical analysis indicated nodular type, head/neck and limb location, tumour depth and ulceration as factors that negatively influenced prognosis. Analysis confirmed that limb versus trunk location and the tumour depth (<0.5mm versus >1mm) were independent determinants of treatment failure.

Professor Celeste Brito (Braga, Portugal) presented a critical review of 5 years of PDT use in NMSC therapy in Portugal. PDT is a relatively new treatment option in Portugal and she concluded that it works reasonably well in clinical settings.

EXTENDING THE SCOPE OF CANCER PDT

Dr Hans Christian Wulf (Copenhagen, Denmark) updated the audience on the subject of daylight PDT, which makes use of natural sunlight for the illumination source. Further results for this interesting option will shortly be published in the ***British Journal of Dermatology***.

There followed 4 different talks on the use of PDT in organ transplant recipients (OTRs). This will be discussed in greater depth in the next issue of ***Clinical Photodynamics***.

The first speaker of the session was **Dr Stefano Piaserico** (Padova, Italy) on the subject of cancer prevention with PDT. PDT control of skin cancer has been investigated both in animal models and in humans. In the laboratory, weekly PDT with MAL or ALA is able to delay the appearance of UV-induced skin cancer in hairless mice. Most of the clinical studies on prevention of skin cancer by repeated PDT have reported a significant reduction of the occurrence of new AKs. However, the mechanism by which PDT delays the onset of UV-induced skin cancer is unknown. PDT might induce a selective destruction of subclinical foci of atypical keratinocytes or modify the cytokine system with stimulation of tumour-specific immunity.

A nephrologist, **Dr Trond Jenssen** (Oslo, Norway), discussed his experience of NMSC in organ transplant recipients. The rate of renal transplantation is increasing in the Western World, ranging from 20-50 transplantations per million people in Europe in 2007. The intensity of immunosuppressive treatment has increased from dual-therapy prednisolone/azathioprine in the 1970s to the current potent quadruple medications (e.g. IL-II receptor antagonist/prednisolone/tacrolimus/mycophenolate mofetil). Due to this, the rate of rejections has decreased, but at the expense of an increase in viral infections and cancers, including NMSC.

The occurrence of NMSC in renal transplantation patients is increasing because of more aggressive immunosuppression, transplantation being available for more older patients, and longer survival in the transplanted population due to more aggressive cardiovascular prophylaxis. It is of great importance that there is a close collaboration between nephrologists and dermatologists, both in the transplantation process and follow-up of these patients.

Professor Ann-Marie Wennberg (Göteborg, Sweden) and **Dr Günther Hofbauer** (Zurich, Switzerland) gave separate presentations on PDT experience in the renal transplant community. After the medically necessary immunosuppressive regimen, he stated that sun damage is the second most important contributing factor. More than half of the renal transplant recipients who have survived 20 years post-transplantation are repeatedly affected by SCC. Field cancerisation of large areas of the face, ears, neck, hands and forearms and the trunk occurs. Early and non-invasive therapy should be more applicable in such a cancer-prone population, and PDT is one of the best-suited modalities for such interventions, helping to prevent new AK lesions.

PDT BEYOND NMSC

Dr Sandra Campbell (Truro, UK) examined the effects of ALA/MAL-PDT on hypertrophic scarring. Patients with localised scleroderma receiving ALA- or MAL-PDT have shown a reduction in skin tightness, suggesting that this therapy reduces skin sclerosis. In vitro studies suggest that it is due to an induction of collagen-degrading enzymes and reduction of collagen production following PDT.

The speaker and co-workers have studied PDT in patients with hypertrophic scarring to further investigate the antisclerotic effects of PDT. They looked at patients with severe hypertrophic scars and treated them with MAL-PDT. PpIX estimations were taken before and after treatment to check for a PDT effect. Biopsies were also taken before treatment and after 6 weeks to compare the collagen to elastin ratio in the skin samples. PpIX estimations were also studied in patients during treatment for keloid scars. Encouraging results were seen in the small observational study, but there is a need for further investigation in this area.

PDT works quite well in inflammatory acne, according to **Dr Stine Wiegell** (Copenhagen, Denmark), who referred to her two earlier studies presented in 2006 in the ***British Journal of Dermatology*** and the ***Journal of the American Academy of Dermatologists***.

The effect of MAL-PDT on acne vulgaris was also confirmed by **Dr Laura Eibenschutz** (Rome, Italy). ALA or MAL-PDT on acne has shown a good effect in a number of clinical studies. More recently, lasers and light-based therapies have been introduced as alternative treatments, including intense- pulsed light, pulsed dye lasers and PDT with photoactivation of ALA or MAL by continuous wave light sources, lasers and IPL systems.

Dr Carola Berking (Munich, Germany) discussed PDT for connective tissue diseases. Localised scleroderma, lichen sclerosus and keloids have been shown to improve after PDT with respect to rigidity and pruritus. In vitro studies indicate that these findings could partially be due to an increase in MMP-1 and MMP-3 production and a decrease in collagen type I synthesis in dermal fibroblasts, possibly via the paracrine effect by keratinocytes. PDT also may exert beneficial effects on granulomatous skin diseases. In anecdotal reports, granuloma annulare and necrobiosis lipoidica were cured by PDT, whereas case series showed CRs of only 57% and 39%, respectively, after repeated cycles of PDT. Randomised and placebo-controlled studies are needed to evaluate the further significance of PDT for connective tissue diseases.

PDT can be considered as a reasonable alternative to treat actinic cheilitis. Dr Berking referred to some case reports and case series of up to 19 patients published on the use of PDT for actinic cheilitis between 1996 and 2008. CRs from these studies varied from 47% to 100%.

Dr Sigrid Karrer (Regensburg, Germany) pondered the question: "Is PDT of use in viral infections?" Several clinical studies have shown efficacy of PDT for HPV-induced lesions. Placebo-controlled trials have demonstrated the superiority of repeated PDT treatments in clearing recalcitrant hand and foot warts. Larger trials have shown that anogenital warts respond well to PDT and also promising results have been published for intraepithelial neoplasia. Only a few case reports show efficacy for PDT in epidermodysplasia verruciformis and plain warts. Although several studies document

promising results for PDT on viral infections, treatment modalities are not yet standardised.

Dr Sally Ibbotson (Dundee, UK) gave a talk on ambulatory PDT: a novel approach involving 'wearable' light sources. The inconvenience of time-consuming hospital visits and discomfort in pain during the irradiation process can be significant drawbacks for PDT of an elderly patient group. A pain-free, home-based treatment would be a definite advantage. Ibbotson and co-workers have developed the use of a low irradiance and disposable lightweight organic light emitting diode (OLED) for ambulatory PDT. Twelve patients with BD or superficial BCC were treated with ALA-PDT using this wearable OLED source. Preliminary efficacy data are encouraging. This suggests that OLED-PDT could be a relatively painless alternative to conventional hospital-based treatment. Studies to explore this approach further are underway.

As the last speaker on this first day of Euro-PDT 2009 in Noordwijk, **Professor Alexis Sidoroff** (Innsbruck, Austria) summarised some recently reported novel indications for PDT. Dr Sidoroff stated that PDT not only works as a therapy of NMSC, but is also used for disorders of the pilosebaceous glands, as well as for inflammatory skin diseases, infectious diseases and hereditary disorders and for skin rejuvenation. Although PDT has an effect in a large number of these diseases, it currently does not work for all of them. New approaches, such as new sensitisers, improvement of the treatment procedure and larger sized trials might result in new indications in the future.

SATURDAY 14TH MARCH

View from the Congress Hotels Van Oranje in Noordwijk to the sea.

PHOTOREJUVENATION

The first session on Saturday morning was dedicated to the topic of photorejuvenation and was chaired by **Prof Dr Rolf-Markus Szeimies** (Regensburg, Germany) and **Dr Luis Torezan** (São Paolo, Brazil). Four experienced dermatologists gave their personal experience and reported on their studies on photorejuvenation.

Prof Szeimies and Dr Torezan.

Dr John Ashworth (Stockport, UK) treated 6 patients with MAL- (Metvix®) PDT with Aktilite® LED illumination specifically for photorejuvenation therapy. In his talk, he pointed out that the patient perspective in the case of photorejuvenation is completely different from the typical patient who attends for PDT for pre-cancerous or cancerous skin disease. The photorejuvenation patient is entirely concerned with cosmetic benefits and is less willing to accept a painful or embarrassing side-effect. He treated the patients once with MAL-PDT (incubation time of Metvix®: 1.5-3 hours). Patients were very satisfied with the treatment: side-effects were oedema post-PDT and sometimes pustules in the treatment area. Dr Ashworth recommended the use of a white eyeliner that has been stored in a freezer to mark the skin area that is to be treated.

Dr Christina Zane (Brescia, Italy) treated 20 patients with pronounced photodamage of the face and actinic keratoses with routine MAL-PDT, in whom photorejuvenation was a secondary goal of therapy. Two monthly treatments were performed with good therapeutic results. Echographic investigations showed that the subepidermal low-echogenic band (SLEB) after PDT was significantly reduced.

The mode of action of PDT for photorejuvenation was investigated by **Dr Luis Torezan**. Skin biopsies were performed after MAL-PDT of photodamaged skin and evaluated by histopathology and immunohistochemistry. After PDT, a decrease in both grade and amount of keratinocyte atypia, as well as an improvement of solar elastosis and an increased sub-epidermal collagen layer, could be demonstrated. Quantitative analyses of MMPs and collagen type I showed a trend towards new collagen deposition. Epidermal HP-53 expression was decreased in most of the patients after PDT. Such effects could be responsible for the excellent outcome of PDT with improvement of signs of photoageing.

Dr Niels Bech-Thomsen (Naestved, Denmark) performed a standard MAL-PDT procedure with two modifications (incubation time: 2 hours, no lesion preparation) for cosmetic purposes to rejuvenate the skin. The temples, under the eyes, around the mouth and on the chest were areas of particular interest, because these areas are usually difficult to rejuvenate with other procedures. He noticed more volume and less wrinkles after this procedure, with a high degree of satisfaction in the treated patients. His personal experience was that PDT can reduce the effect of botulinum toxin or fillers given previously, so he recommends that clinicians should not perform PDT directly after such treatments.

CANCER PDT IN THE NETHERLANDS

This session was chaired by **Dr Rianne Gerritsen** (Nijmegen, The Netherlands).

Dr Aimee Arits (Maastricht, The Netherlands) presented an ongoing single-blinded, randomised controlled multicentre trial comparing the efficacy, cosmetic result, compliance, side-effects, patient preference and cost-effectiveness of three non-invasive treatment options for superficial BCC. Patients are treated with PDT, imiquimod or 5-fluorouracil (5-FU). This is the first study comparing these non-invasive treatment modalities for superficial BCC. **Dr Verzijl** (Nijmegen, The Netherlands) discussed two treatment options for Bowen's disease: PDT versus surgery. Overall initial clearance rates for ALA-PDT are usually around 90%, with recurrence rates of about 0-10% after one year. Although surgery is widely used for the treatment of Bowen's disease, well-designed studies are not available: randomised controlled trials are needed to establish the best treatment option.

Dr Gertruud Krekels (Eindhoven, The Netherlands) gave an overview of the current studies for nodular BCC, which showed that surgical excision was more effective, compared to PDT. PDT combined with limited surgical excision or Mohs' micrographic surgery might reduce the number of large excisions or number of Mohs' stages.

PDT MASTERCLASS

Dr Rianne Gerritsen gave a talk on pretreatment options in PDT. Since limited uptake of ALA or MAL and suboptimal production of protoporphyrin IX may account for a variable treatment success of PDT, there is a need for optimisation. Hyperkeratosis is an important limiting factor for ALA uptake; thus pre-treatment of hyperkeratosis might be a prerequisite in PDT for improving treatment results. Keratolysis can be achieved with topical keratolytics, curettage/debulking, tape-stripping, microdermabrasion or laser ablation. Several studies have also shown that penetration of the photosensitiser can be improved by penetration enhancers, such as dimethylsulphoxide, azone, glycolic acid,

oleic acid or iontophoresis. Treatment results may also be improved by increasing skin temperature during ALA application and cooling down afterwards, as PpIX production is also dominated by temperature-dependent processes.

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 tetra-acetic acid, 3-hydroxypyridin-4-ones and desferrioxamine. Several iron chelators are able to significantly increase PpIX formation in ALA-treated skin. Thus, the clinical outcome of PDT might be improved by pre-treatment in addition to the regular practice of PDT.

Professor Rolf-Markus Szeimies gave the next talk on light sources: "Making the best of what we have in the office", since a crucial part of the PDT procedure is the appropriate light source. At the moment, the best devices are light-emitting diodes (LEDs) which perfectly match the last Q-band of the absorption spectrum of PpIX. Alternatives include the pulsed light sources, which are widely used for other indications like hair removal, vascular and pigmentary changes. A new Aktilite® CL512 LED lamp is soon to be on the market, which is suitable for the treatment of acne using VisonacTM-PDT.

Dr John Paoli (Göteborg, Sweden) showed how pain during PDT can be minimised. Nerve blocks using Mepivacaine or Bupivacaine are able to significantly reduce pain during PDT. Patients with field cancerisation of the forehead received unilateral supraorbital nerve blocks with Carbocain® adrenalin 5-10 minutes before irradiation began. Thus, pain could be significantly reduced in the anaesthetised side, compared to non-anaesthetised areas.

Professor Frank Hevert (Laupheim, Germany) summarised "What we know about pain in PDT" and explained his exciting theories about the origin of pain in PDT. Two kinds of pain can be distinguished: Type I pain has an onset shortly after commencing irradiation and is due to electrical depolarisations of polymodal receptors in C- and A-delta-nerve fibres within the epidermis; Type II pain has an onset of some minutes to some hours after illumination, which is caused by inflammatory and pain mediators such as prostaglandins and bradykinine. For Type I pain to be triggered, the photosensitiser must enter the epidermal nerve fibre: this is more easily achieved for the ALA molecule than for MAL. Therefore, MAL-PDT (Metvix®) is less painful than ALA-PDT. Since Type I pain is 'electrical' and not mediated by any substances, it cannot be influenced by prostaglandin antagonists or similar drugs, but rather by nerve blocks or by changing the receptor threshold via cooling.

Dr John Lear (Manchester, UK) talked about difficult cases for PDT, such as vulval intraepithelial neoplasia (VIN) and Gorlin's syndrome. He also presented data from a combination treatment where patients with VIN received a sequential treatment with imiquimod followed by two cycles of PDT. The overall response rate was 64% and the treatment was well tolerated.

Practical 'Pearls of Wisdom' from treating challenging cases were presented by **Professor Peter Foley** (Melbourne, Australia). Multiple clinical pictures were shown to illustrate the versatility of this therapeutic modality. **Dr Ann Haylett** (Manchester, UK) showed how laboratory observations can be converted into clinical practice. A wide range of variables may modify the therapeutic outcome and considerable research has been carried out to optimise treatment parameters.

The last talk of this Congress was given by **Dr Julian Lambert** (Wilrijk, Belgium) and dedicated to a very important topic: "Current coding and reimbursement status of PDT in Europe".

POSTER SESSION

Over 20 posters were displayed during the Euro-PDT Congress. Nations represented included the Congress hosts, The Netherlands, other EU countries such as Switzerland, Germany, Portugal, Spain, the United Kingdom, France and Italy, and Eastern Europe (represented by Russia). There were also posters from non-European centres in South Korea and the United States of America.

The range of topics varied from case reports of conventional PDT indications with approved agents (eg. BCC treated with Metvix® cream and Aktilite® illumination) through to treatment of non-listed indications such as cutaneous T-cell lymphoma, pseudoepitheliomatous hyperplasia, disseminated superficial actinic porakeratosis and pigmented purpuric eruption. One poster provided details on the website of the European Society for Photodynamic Therapy in Dermatology (www.euro-pdt.org). Back copies of ***Clinical Photodynamics*** are now available as low-resolution PDFs for downloading from this website and also from the International Society for PDT (I-PDT) website (www.i-pdt.org).

Treatment of psoriasis with PDT was also detailed. An evaluation of PDT regarding pain, phototoxic reaction and patient satisfaction was portrayed, and PDT as part of field cancerisation therapy was described. Other, more research-focused, posters included a look at PpIX-induced fluorescence at different sites and time intervals, while a new photosensitiser, Radachlorin, had posters on in vitro work as well as response rates in BCC.

A great deal of interest was displayed in the posters by delegates at the meeting. All authors are to be congratulated on the quality of the work and the effort put into their presentations.

The poster presentation was well visited by congress participants.

PRIZES

At the end of the meeting, Prof Alexis Sidoroff presented the best poster and oral presentation awards. The prize for the best poster was awarded to **Dr Mark Tanner** and colleagues from Germany, who described a method to decrease the size of excisional defects in NMSC by safety margin PDT. The second poster prize went to **Dr Denny Siem** and **Dr Gertruud Krekels** from The Netherlands for their study on PDT of disseminated superficial actinic porokeratosis. The third poster prize was given to **Dr You Chan Kim** and colleagues from Korea, who were the first to describe PDT for the treatment of pigmented purpuric dermatosis. **Dr Tim Smits** from The Netherlands won the award for the best oral presentation for his excellent talk on fluorescence diagnosis in keratinocytic intraepidermal neoplasias. **Dr Günther Hofbauer** from Switzerland received the second prize for his oral presentation on his experience with PDT in a renal transplant community. The third prize went to **Dr Celeste Brito** from Portugal for her critical review of 5-year NMSC therapy in Portugal.

Last but not least, the Congress President, Dr Rianne Gerritsen, was thanked for organising this very successful Congress at this very beautiful site beside the beach at Noordwijk.

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67th Annual Meeting of the American Academy of Dermatology (AAD)

6-11 March, 2009 San Francisco, USA

by: Dr Colin Morton
(*Stirling, UK*)

This year's AAD saw a continued interest in PDT, despite its current limited use in North America, with licensed approval only for use in actinic keratosis (AK) in immunocompetent patients.

METVIXIA® LAUNCH

Although Metvix® (Methyl Animolevulinate [MAL]) has been available across Europe and beyond for a few years now, it was commercially launched under the name Metvixia® in the USA at the AAD this year. This was the first exposure of American dermatologists to an approved cream-based PDT drug, with activiation by red light from the Aktilite®. Galderma report considerable interest in the product, despite the sole current US label of AK, unlike the wider licence of AK, Bowens disease and BCC in many other countries.

PDT POSSIBILITIES

Professor R Rox Anderson (Harvard, USA) provided an appropriate theme for the symposium he directed, contemplating the 'Promises and Limitations of Photodynamic Therapy'. He noted that PDT offers a versatile concept in photomedicine with the availability of the porphyrin precursors aminolevulinic acid (ALA) and MAL affording us the opportunity to explore a variety of applications and giving us the chance to achieve a limited control of endogenous porphyrin metabolism. Furthermore, PDT can provide cell killing and offer efficacy against certain infections: also discussed was the potential of photochemical tissue bonding (PTB), where Rose Bengal applied to wound edges and illuminated with green light can promote tissue bonding and improve scarring. However, the current limits of PDT and hence the challenges of the therapy are to achieve adequate depth of therapeutic effect as well as target specificity of the topical agents used.

PDT IN ACNE

During Professor Anderson's symposium, **Dr M Haedersdal** (currently working at the Wellman Centre for Photomedicine in Boston, USA, but based in Copenhagen, Denmark) presented an overview of PDT's potential in the treatment of acne. Even the pursuit of limited specific areas of the acne therapy spectrum could offer additional help to many people, given that acne affects more than 80% of people at some time in their life. Moreover, antibiotic resistance continues to increase and concern over the side-effects of retinoids is continuing to drive an enthusiasm towards new alternative treatments. Suggested mechanisms for the observed improvement in acne following PDT includes direct antibacterial activity, selective damage to sebaceous glands, reduction in follicular obstruction by keratinocyte shedding and secondary host responses. The subject is covered in detail by an evidence-based review of PDT in acne[1]. There certainly is an accumulating evidence base to support the use of PDT in acne but, despite 16 randomised comparison trials and 3 control trials, we yet have to define the optimum protocol that will be both acceptable to patients and yield sufficient response. A common theme of studies is the significant improvement in inflammatory lesions but much more limited response of non-inflamed lesions, suggesting that optimising protocols in acne will probably require adjunctive therapy.

In this light, **Stefania Motta *et al*** (Milan, Italy) presented a poster demonstrating the benefits of micropeeling before ALA-PDT, with sessions repeated every 15 days until clearance. The percentage reduction in inflammatory lesions after 1, 3 and 6 months were 62%, 84% and 96%, respectively. However, the level of contribution that PDT itself made to this treatment effect is unknown. Evidence to date suggests that ALA-PDT promotes more severe adverse effects than MAL-PDT in acne, but that MAL-PDT can still promote severe phototoxic skin reaction and might require patients to stay at home for between 1 day and 1 week following treatment.

MEDICAL APPLICATIONS

A forum titled 'Medical Applications of Topical Photodynamic Therapy' looked in detail at the current approved uses of topical PDT across the world as well as the evidence base for supporting its wider use in inflammatory and infectious dermatosis. The audience was

Welcome to the Conference.

reminded that updated guidelines by the British Photodermatology Group and consensus guidelines from the International Society of Photodynamic Therapy in Dermatology both concur that there is good evidence to support the use of topical PDT in the treatment of thin and moderate thickness AK, squamous cell carcinoma (SCC) in situ, and superficial and thin nodular basal cell carcinomas (BCC). Although current approvals in the USA are for the use of PDT for non-hyperkeratotic AK of the face and scalp, a study in 2008 confirmed that, whilst MAL-PDT achieved a lesion reduction at 24 weeks of 78% against 88% for cryotherapy, excellent cosmesis was demonstrated for 79% of PDT patients against 56% of cryotherapy patients. It is certainly my experience that PDT can offer a good initial treatment for patients with very widespread acral AK, with the opportunity to subsequently clear residual lesions with a more locally destructive therapy. A further study published in 2008 compared MAL-PDT against surgery with a 3mm margin for superficial BCCs. The lesion clearance rates at 3 months was 92% for PDT, compared with 99% for surgery. Nine per cent

San Francisco skyline: Fisherman's Wharf in right foreground; Telegraph Hill beyond; Transamerica Pyramid Building is the tallest of the high-rise buildings.

of PDT lesions recurred by 12 months, versus no recurrences in the surgery group. Again, the initial efficacy superiority of surgery is contrasted with superiority of cosmetic outcome, with a good or excellent outcome in 94% of PDT-treated patients at 12 months against 59% in the surgery group. Although there remains sensible debate over which nodular BCC lesions may be appropriate for topical PDT, the study emphasises the potential value of PDT at least for superficial lesions, where acceptable sustained clearance rates can be achieved for this slow-growing lesion.

Dr Robert Bissonnette (Montreal, Canada) also provided a focus session on PDT, covering the basic principles, advantages and limitations of PDT, focusing on increasing awareness of the potential of PDT in clinical practice.

Each of the scientific sessions at which PDT was presented drew good – indeed, impressive – attendances, given the multitude of choice for delegates at the AAD meeting.

POSTERS

Posters were available for electronic access. **Je-Ho Yeon *et al*** (Seoul, South Korea) described a concerning case where topical MAL-PDT applied to treat a keratoacanthoma resulted in marked enlargement of the tumour over a period of 3 weeks following treatment. This resulted in a requirement for surgical removal of the lesion. This experience contrasts with a previous publication of four patients with keratoacanthoma where the lesions cleared completely following two treatments with ALA PDT. The authors questioned whether insufficient light or photosensitiser penetration had led to the stimulation of cell growth, instead of choosing a cell-kill effect. Of course, the observation could be simple coincidence and that PDT had simply failed to achieve adequate response in a growing lesion, but any experience of this phenomenon by readers of ***Clinical Photodynamics*** would be welcome – please contact the Editorial Office.

Robert Sayre, from the Rapid Precision Testing Labs in Cordova, Tennessee, presented a multi-site study on the emission spectra of a number of light sources used in topical PDT. As expected, the results predict sizeable differences in the protoporphyrin IX activation effectiveness between sources. The highest protoporphyrin IX indices were demonstrated for red light with the Aktilite® and Omnilux® sources and for blue light for the Omnilux® blue and the Blue-U® light sources.

Marcello Monti and colleagues (Milan, Italy) observed that multi-session ALA-PDT using red light is effective in promoting skin ulcer closure. The authors report a study comparing weekly PDT (24-hour application under occlusion of 10% ALA, then red light) with standard ulcer dressings in 13 chronic venous ulcers. A 50% reduction in the time required for ulcer healing was observed, although the ALA-PDT was not shown to have specific antibacterial activity. The underlying biologic mechanisms remain unclear.

Drs Patterson and **George**, from Amersham, UK, reported a case of a woman with a slowly enlarging plaque of sarcoid treated successfully with ALA-PDT using a red light source. She received 5 treatments with significant improvement and good cosmetic outcome. The authors propose that possible mechanisms include ALA uptake by infiltrating lymphocytes producing cytokines that kill the granuloma cells, or that the ALA could be directly taken up by the granuloma cells. **Dr Fai *et al*** (Lecce, Italy) reported the successful use of PDT in treating a resistant plaque of scalp discoid lupus erythematosus following 2 sessions with MAL-PDT.

Although the number of posters reporting experience with PDT was reduced from previous years, it is encouraging to see the interest in PDT maintained at the AAD, given the many subjects competing for presentation.

Reference

1. Haedersdal M *et al* 2008 *JEADV* **22** 267-278

Prime Time PDT

An international roundup of
PDT-related papers and publications

Short Incubation Time with Methyl Aminolevulinate for PDT of Actinic Keratoses

Braathen L, Paredes B, Saksela O *et al* 2009 *J Eur Acad Dermatol Venereol* **23** 550-555

Although PDT has several advantages over other therapies for the treatment of actinic keratosis (AK), one clinical drawback is the length of incubation time following application of the sensitiser and prior to irradiation. For MAL-PDT, this is usually 3 hours – but does it have to be so long? This open randomised study compared 2 MAL-PDT variables: 1-hour versus 3-hour incubation times; and 160mg/g versus 80mg/g MAL concentration. A patient population of 112 patients with 384 previously untreated AK received debridement and MAL-PDT. The majority of lesions were thin (55%) or moderately thick (34%) and located on the face or scalp (87%). At 12 months post-treatment, face/scalp lesion complete response rates for 160mg/g MAL-PDT and 1-hour incubation were 78% (thin AKs) and 74% (moderately thick AKs) versus 96% and 87% for 3-hour incubation times, respectively (p = not significant).

A subset of 60 patients received 2 MAL-PDT sessions: as might be expected, the lesion recurrence rates were higher in the 80mg/g MAL-PDT group and for those receiving 1-hour incubation times. The authors concluded that a 1-hour incubation period may be sufficient for successful treatment of selected AKs.

An Economic Evaluation of Topical Treatments for Actinic Keratosis

Muston D, Downs A, Rives V 2009 *J Dermatolog Treat* **Jan 1** (E-Pub ahead of print)

The authors compared MAL-PDT with other topical treatments (5-FU, imiquimod) over two lines of treatment for actinic keratosis (AK). Outcomes for efficacy were taken from two investigator-led studies and limited to 'complete clinical response' and 'excellent cosmetic outcome'. The greatest probability of achieving complete clinical response was found to be the use of MAL-PDT first-line, followed by other second-line treatments (91.7%). However, the greatest probability for achieving excellent cosmetic outcome was MAL-PDT for first- and second-line treatment (73.6%). The costs (at 2007 prices) were £437 for two lines of MAL-PDT, or £418 for first-line MAL-PDT followed by another therapy as second-line treatment. The authors concluded that MAL-PDT for AK compares well with other treatments for both costs and effectiveness.

Calendar of Events 2009-10

June 25-28, Munich, Germany
American Academy of Dermatology and European Academy of Dermatology and Venereology 'State of the Art' in Dermatology
Contact: AAD/EADV Meeting Organiser
Tel: +847 240 1485 Fax: +847 330 1135
e-mail: mstein@aad.org

June 27, Destin, USA
Optimizing Management of Non-Melanoma Skin Cancers: Current Data and Future Treatment Options
Contact: Meeting Organiser
Tel: +609 921 6622 Fax: +609 921 6428
e-mail: kwetzel@academycme.org

July 1-5, Vancouver, Canada
Canadian Dermatology Association 84th Meeting
Contact: CDA Meeting Organiser
Tel: +613 738 1748 Fax: +613 738 4695
e-mail: contact.cda@dermatology.ca

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

October 7-11, Berlin, Germany
18th Congress of the European Academy of Dermatology and Venereology (EADV)
Contact: EADV 2009 Secretariat, MCI-Berlin Office, Markgrafenstr. 56, D-10117 Berlin, Germany
Tel: +49 (0)30 20 45 90 Fax: +49 (0)30 20 45 950
e-mail: registration@EADVBerlin2009.com
Website: www.EADVBerlin2009.com

November 19-21, Dubai, UAE
International Congress in Aesthetic Anti-Aging Medicine
Contact: Omair Khan
Tel: +97 143 365 161 Fax: +97 143 364 021
e-mail: omair.khan@iirme.com

2010

January 21-23, Bangkok, Thailand
International Congress of Aesthetic Dermatology
Contact: Catherine Decuyper
Tel: +33 0 1 568 637 805
e-mail: emc@euromedicom.com

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