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Clinical Photodynamics

In Dermatology

An International Newsletter for PDT and FD in Clinical Practice

Editorial

Photodynamic therapy (PDT) in dermatology is now a well-established treatment option for non-melanoma skin cancer throughout Europe, and it is also increasingly being used in other parts of the World.

In addition, PDT is increasingly being investigated for other indications, e.g. acne and rosacea, condylomata acuminata and common warts, lymphomas and bacterially infected ulcers and, last but not least, for photochemorejuvenation.

During the recent 21st World Congress of Dermatology in Buenos Aires, there were several sessions covering PDT. There was a World Photodermatology Day on Sunday, September 30th, an Ancillary Meeting of the International Society of Photodynamic Therapy (also on September 30th) and several other PDT lectures in the programme. These events were well-attended and the audience showed a keen interest in the treatment, demonstrated by the many interesting questions raised.

Taken as a whole, we feel that PDT was given appropriate attention at the World Congress. The next large international event will be the I-PDT/EURO-PDT meeting in Barcelona, Spain (March 6-8, 2008). We are looking forward to a successful Congress.

Professor Lasse R Braathen
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21st World Congress of Dermatology

30 September–5 October, 2007
Buenos Aires, Argentina

A combined report by:
Dr Sigrid Karrer
Regensburg, Germany

Dr Ann-Marie-Wennberg
Göteborg, Sweden

and Dr Colin Morton
Stirling, Scotland

Below are featured highlights from the recent World Congress of Dermatology.

The 'Casa Rosada' at the famous Plaza de Mayo in the heart of Buenos Aires.

PART 1: PHOTOBIOLOGY AND PDT INTERACTIVE SESSION

The 'Photobiology and PDT' interactive session was chaired by **Prof Rolf-Markus Szeimies**

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(Regensburg, Germany) and **Dr Pablo Gonzalez** (Buenos Aires, Argentina).

Prof Szeimies gave an introductory lecture on 'Photodynamic process in photodermatology – the spectrum is getting broader'. He pointed out that the spectrum of unapproved indications for PDT is continuously growing, while PDT already has become a routine treatment for AKs, basal cell carcinoma and Bowen's disease. Interesting new indications currently under investigation are acne vulgaris, skin rejuvenation and infectious diseases, such as warts or leishmaniasis.

Dr Sadick (New York, USA) presented a study to determine the effect of combination blue light and near infrared on moderate to severe acne vulgaris. For the treatment of moderate to severe facial acne, a combination therapy with blue light (Omnilux 415nm) and near infrared (830nm) was used. Fifteen patients were treated twice-weekly, alternating blue and near IR, for 4 weeks. Two patients did not experience an improvement; the other patients who completed the study showed an average decrease of acne lesions of 44.2%. Combination therapy showed promising results, was safe and well tolerated.

Dr Goukassian (Boston, USA) demonstrated that a single supplementation with telomere homolog oligonucleotides (T-oligos) induces a protective tanning response in human skin. His findings may predict that T-oligo treatment will increase melanogenesis, prolong epidermal arrest, and increase DNA repair rate after UV irradiation, thus decreasing the severity of acute and chronic photodamage in human skin.

Dr Wiegell (Copenhagen, Denmark) presented an interesting study on PDT of actinic keratoses, using red diode light versus sunlight. In her randomised, controlled, single-blinded study, 29 patients with actinic keratoses on the face and scalp received a split face treatment using Methyl Aminolevulinate (MAL: Metvix®) and irradiation with either red LED light or sunlight. After occlusive application of MAL for 30 minutes, one area of the face/scalp was exposed to daylight for about 2½ hours while light intensity was continuously measured. After 3 hours of incubation with MAL, the other area of the face/scalp was irradiated with red diode light with 37J/cm^2. After light treatment, remaining fluorescence was measured. Three months after treatment, 79% of AKs treated with daylight and 71% of AKs treated with red light had completely resolved. There was no statistically significant difference between the two groups. However, daylight was significantly better tolerated as compared to red light (maximum pain score during daylight: 2.0, pain score during red light: 6.7). Erythema and crusting after treatment were similar in the two treatment areas. Most patients preferred sunlight exposure to red light. The study showed that PDT with daylight was as effective and significantly less painful as compared to conventional PDT. This study was intensively discussed by the audience. Although sunlight is a cheap and easy way to apply light, as shown more than 100 years ago by Tappeiner and Jesionek when they treated the first patients with basal cell carcinomas using eosin and daylight, no adequate dosimetry is possible when using daylight. Some participants argued that daylight application is highly dependent upon several factors that cannot be influenced, e.g. time of day, season, weather, country, etc.

Dr Babilas from Germany giving his talk on the effect of variable pulsed light for PDT of AKs.

Dr Babilas (Regensburg, Germany) presented a randomised parallel-group study on the use of variable pulse light source (VPL™, Energist Ultra, UK) for PDT of actinic keratoses, with the aim of reducing irradiation-induced pain. 25 patients with 238 actinic keratoses on the head and scalp received a single treatment with MAL-PDT for three hours and irradiation with an LED light source (37 J/cm^2) on one side of the face. The contralateral side received 80J/cm^2 (double pulsed 40J/cm^2), with a pulse train of 15 impulses, each with a duration of 5 minutes, utilising a 610-950nm filtered handpiece. While treatment using the LED light source was significantly more painful as compared to the VPL™ treatment, no significant differences were found with regard to effectiveness and cosmetic results.

Dr Hapa (Ankara, Turkey) showed her results using narrowband UVB phototherapy for the treatment of pityriasis lichenoides chronica (n=25). Narrowband UVB was effective and well tolerated in this condition, with a complete response rate of 48%.

Dr Moloney (Sydney, Australia) performed a randomised, double-blind, prospective split-scalp study to compare the efficacy and adverse effects of topical MAL-PDT with topical ALA-PDT in 16 patients with extensive scalp actinic keratoses. After 3 hours of incubation with MAL vs. 5 hours of incubation with 20% ALA, irradiation was performed with red light (Waldmann lamp, 50J/cm^2). Evaluation of efficacy was documented 60 days after therapy. Reduction in AKs was not significantly different in both groups (87% in the ALA-PDT group and 71% in the MAL-PDT group). However, pain score was significantly higher in the ALA-PDT group at all timepoints (3 min, 12 min, 16 min) as compared to MAL-PDT. Discomfort after PDT also lasted longer after ALA-PDT (480 min) as compared to MAL-PDT (120 min). Therefore, all patients showed a preference for MAL-PDT.

The talks were actively discussed by the audience.

PART 2: WHAT DERMATOLOGISTS NEED TO KNOW ABOUT PDT

Dr Colin Morton (Stirling, UK) noted that guidelines have been published in *JAAD* (January 2007) concerning the use of PDT for non-melanoma skin cancer. There is strong evidence to support the use of PDT for Bowen's disease. With ALA-PDT, there are complete clearance rates of 86-93%. Red light is preferred, as it penetrates deeper than green light. Several studies have been performed comparing PDT with cryotherapy and 5-FU. PDT seems to work well for Bowen's disease on the penis, avoiding major surgery, but with the side-effect of pain.

Dr Peter Foley (Melbourne, Australia) presented several case reports for basal cell carcinoma (BCC) treatment and also referred the audience to the guidelines in *JAAD*. He advocated the use of PDT for superficial BCC and thin nodular BCC. He also emphasised that PDT does not induce squamous cell carcinomas (SCCs). Again, red light is important for penetration. Patient compliance with the treatment is important. The patient should be able to undergo 2 treatments and lie down without moving for 10 minutes. Thicker nodular BCCs should be debulked if treated. It is important to avoid treating micronodular or more free-form BCCs. Dr Foley offered some practical advice concerning treatment:

1. Prepare the lesion with a curette.
2. **Apply the cream in a 1mm thick layer.**
3. Use an occlusive dressing.
4. Pain management during illumination can be troublesome. Give paracetamol 1 hour before treatment and either give local

anaesthesia or use a fan to provide cool air during treatment.
5. Aftercare: keep the area clean.

Dr Foley noted that patients prefer PDT over other treatments because of the superior cosmetic results.

Dr P Calzavara-Pinton (Brescia, Italy) examined the data on PDT for lymphomas. Isolated forms of cutaneous T-cell lymphoma may be treated. There are also case reports of good results for PDT for cutaneous leichmaniasis and *Mycobacterium marinum* infection.

Dr Michael Gold (Nashville, USA) reported on the use of PDT in photochemorejuvenation. In the USA, only treatment with blue light is approved. Photorejuvenation is increasingly common in the USA, but of course there is no reimbursement for this. Small studies have shown a beneficial effect. ALA appears to boost collagen increase when used together with intense pulsed light (IPL).

Prof Ann-Marie Wennberg (Göteborg, Sweden) discussed cancer prevention in immunosuppressed patients (e.g. organ transplant recipients). Immunosuppressed patients have a hundred-fold increased risk of SCC, and malignancy is a major cause of morbidity for organ transplant recipients. Prof Wennberg presented a study from her group, demonstrating the good effect of PDT in these patients. It might be that this patient group should be regularly treated in order to avoid precancerous skin lesions.

Dr Sigrid Karrer (Regensburg, Germany) gave a resumé of the data for PDT treatment of warts and other infectious skin disorders. Case studies have shown a good effect for PDT against warts. Additionally, Wang *et al* showed some beneficial results for PDT in urethral condylomata, and there are a few studies on PDT for the treatment of mycoses.

Dr Robert Bissonnette (Montreal, Canada) observed that several groups have reported that PDT is beneficial for acne. PDT for rosacea is not an approved indication and the mechanism of action is unclear. In acne, there seems to be an accumulation of porphyrins in the sebaceous glands following ALA- or MAL-PDT application. Holgcharu demonstrated that ALA-PDT decreases both lesion counts and sebum production.

PART 3: POSTERS

Over 3000 posters were available for viewing at the World Congress, with 47 focused on PDT. Interest in the use of PDT for **non-melanoma skin cancer** now extends worldwide, with considerable enthusiasm from countries new to approved products for PDT. **Torezan *et al*** (6991) reported on their experience of the use of MAL-PDT in **superficial BCC** and **Bowen's disease**, with cure rates at six months of 98.4% and 94.7%, respectively. **Issa *et al*** reported two cases (6988 and 6989) using MAL-PDT successfully to treat a thin nodular BCC in the facial H-zone and multiple BCC in a second patient who had failed surgery. **Lucas *et al*** (5717) reported a case of extensive **Bowen's disease** (plaque diameter 8cm) on the neck of an elderly patient that cleared following one cycle of MAL-PDT. **Orlandi *et al*** (5686) noted clearance of 25/27 AK following a single PDT treatment. **Pierard *et al*** (5679) used MAL-PDT (6 treatments at weekly intervals) to clear **cutaneous verrucous carcinoma**.


Posters from WCD.

Vinciullo *et al* (6935) reported international experience of patient satisfaction after treatment of **AK** and **BCC** with MAL-PDT compared to previous therapies. Analysis indicated preference of patients to PDT compared with surgery, cryotherapy and topical 5-fluorouracil. In a further multicentre study reported by **Rhodes *et al*** (6933), MAL-PDT was used to treat AK on the extremities, comparing PDT with cryotherapy. Cryotherapy produced a superior reduction in lesion count of 88% vs. 78% with PDT at week 24, but cosmesis was superior following PDT. Patient assessment also indicated a preference for PDT, based on lower discomfort, shorter healing time and similarity of perceived effectiveness.

Szeimies *et al* presented a poster (5678) of interim results from a multicentre international study comparing MAL-PDT with simple excision in patients with **superficial BCC**. Lesion clearance three months after MAL-PDT was 87.4% against 89.4% with surgery. PDT produced a superior cosmetic outcome. A separate poster indicated the benefits in considering PDT for large superficial BCC, with **Brito** (5700) reporting three cases of the use of MAL-PDT using a standard dosage regimen, with sustained clearance for at least six months.

Gyulai (6976) reported on topical PDT in different anatomical regions in 49 patients with AK or sBCC. Both MAL and ALA were used, applied for 4 hours, with illumination from a red Actilite LED source 37J/cm^2), with the agents of similar efficacy, but with MAL-PDT associated with significantly less pain.

Molenberg and Lorentzen (6632) observed a patient with a long history of NMSC lesions who was treated with topical MAL-PDT and, following a second treatment at seven days, presented with a pruritic erythematous papular rash on the treated areas of the shoulders and back. Histology showed focal acantholysis with lymphocytic infiltrate consistent with **Grover's disease**. It is known that UV light may be a trigger, and this case suggests that red light ALA-PDT might have been a factor, although it is also known that heat and sweating can be capable of eliciting latent disease.

Gontijo *et al* (6956) reported on MAL-PDT for **BCC** as an adjuvant before Mohs' surgery. In their case report, the extent of disease area was reduced following PDT, facilitating surgery to a site close to the inner canthus. A further study by the same authors (6957) used MAL-PDT in recurrent, extensive, digital **squamous cell carcinoma** as an adjuvant before Mohs' in a patient unwilling to contemplate amputation as it would have risked his livelihood. MAL-PDT reduced the extent of disease, with biopsies taken after the procedures showing evidence of in situ change only. **Kint and Roseeuw** (6936) reported a case of the use of MAL-PDT as adjuvant in **extramammary Paget's disease**. MAL was applied pre-op for margin delineation. The patient underwent surgical excision and post-op PDT was performed to remaining foci with clearance after four sessions. The patient remains disease-free 14 months after treatment.

James and Richmond (6944) reported on the use of PDT to treat **lentigo maligna**. A preparation containing 5% hydroquinone was applied daily for two months to remove pigmentation pre-PDT. ALA- or MAL-PDT resulted in histological clearance, maintained for 12 or more months in only 4/12 patients. Whilst not recommended as a primary treatment for LM, the authors suggest that this case series should stimulate interest in this indication in complex cases and suggest that initial use of a depigmenting agent might also facilitate PDT in other pigmented skin cancers.

Monti and Motta (4091) provided a poster on **acne**, suggesting that the use of micropeeling followed by ALA-PDT was complementary with micropeeling clearing comedones and PDT clearing inflammatory lesions. **Kuzmin and colleagues** (4120) demonstrated that the effectiveness of PDT in acne was directly dependent on the level of endogenous porphyrins, with the better

clinical results being achieved with highest photosensitiser levels, allowing for clinical remission in 85% of patients. A case report by **Godoy** (4026) demonstrated the impressive therapeutic effect of ALA-PDT in acne, using a 5% preparation in an occlusive cream applied overnight and a 635nm red LED light source. Another poster by **Godoy** (6975) reported the same protocol for **sebaceous gland hyperplasia**, with the clinical pictures in the case presented showing a marked response to PDT, lasting for more than six months.

Campbell (6937) reported on the use of PDT in a patient with painful lesions on the helix of an ear of **granuloma annulare**. MAL-PDT performed by a standard regimen and repeated at one week, with assessment after six weeks, showed complete clearance, with settling of associated pain and improvement maintained over the six months of review.

Motta and Monti also provided a poster (6759) on ALA-PDT to enhance **ulcer closure** in patients with SLE and symmetrical paramalleolar ulcers. They reported on an experience where half the ulcers were treated with light alone and the other half with ALA-PDT and indicated that multi-session ALA-PDT, rather than light alone, appeared capable of stimulating re-epithelialisation of the ulcers, with a reduction in healing time by 50% in comparison with standard dressing use. There was no change in bacterial isolation and density before and after PDT, suggesting that immunomodulatory and/or anti-inflammatory activity was responsible for the observed effects.

Macedo *et al* (6987) reported the case of a series of patients where they had used PDT both to treat AK and promote **photorejuvenation**. The authors reported not only AK clearing, but improvement in mottled pigmentation, fine lines, roughness and sallowness in all patients treated.

KEY POINTS

The 3 principal learning points from perusal of the posters were:

1. The opportunity to further expand the beneficial use of PDT, with novel presentations on lentigo maligna, granuloma annulare, and wound healing.
2. As PDT use becomes more widespread, reports of rare possible side-effects are likely: the report of apparent induction of Grover's disease was of interest.
3. The adjuvant role for PDT in extensive cutaneous malignancy, either pre- and/or post-surgery, needs consideration for certain complex cases.

Scanning the large number of posters on PDT and the – often dramatic – clinical responses, it was satisfying to see that the potential of this exciting therapy is receiving exposure at major international Congresses.

11th World Congress of the International Photodynamic Association (IPA)

28-31 March, 2007
Shanghai, China

by: Dr Alison Curnow[1] and Professor Qian Peng[2]
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Over 450 participants from more than 30 different countries travelled to Shanghai in March to attend the 11th IPA World Congress. This was organised locally by the Congress President, **Professor Jing Zhu** (China), and Secretary General, **Professor Yuanlong Yang** (China), in association with **Professor Qian Peng** (Norway), as the Scientific Committee Chair. This Congress followed in the great tradition of these biennial conferences which routinely attract leading clinical and scientific researchers in the fields of photodynamic therapy (PDT) and photodiagnosis (PD) alike.

The opening ceremony.

The IPA is an academic society whose membership consists of the most prominent international clinicians and scientists involved in performing and researching PDT and PD. It aims to promote the study of diagnosis and treatment using light and photosensitisers, to disseminate such information to the members of the IPA, the medical community and to the general public. The biennial World Congress therefore plays an important role in the activity of the society, and attendance is an excellent way to keep abreast of new developments in this rapidly evolving field.

28th March

Following the formal IPA Board meeting, the Congress opened in the evening with a Welcome Ceremony, including two guest lectures delivered by **Johan Moan** (Norway) and **Jun-Heng Li** (China), respectively detailing the history of PDT in general and in China. The Welcome Reception was a traditional Chinese banquet, accompanied by numerous forms of traditional Chinese entertainment.

Shanghai skyline.

29th March

The first whole day of the scientific meeting was predominantly set aside for a series of highly informative plenary sessions delivered by some of the World's leading authorities. **Kevin Smith** (USA), **David Kessel** (USA) and **Brian Wilson** (Canada) commenced proceedings by considering photosensitising agents, mechanisms of cellular death and light administration, respectively. A series of application reviews then followed, summarising the current state of the art in dermatology (**Lasse Braathen**, Switzerland), gastroenterology (**Stephen Bown**, UK), pneumology (**Harubumi Kato**, Japan), head and neck surgery (**Colin Hopper**, UK), neurosurgery

(**Herwig Kostron**, Austria), urology (**Raphaela Waidelich**, Germany) and gynaecology (**Peter Hillemans**, Germany). This list quickly demonstrates the wide range of clinical areas where PDT and PD are currently being applied.

Lunchtime symposia considered photodynamic cell purging (Chair: **Qian Peng**, Norway) and the new directions of PDT (Chair: **Bjorn Klem**, Norway). The plenary sessions then concluded with interesting talks on photodetection (**Stephan Lam**, Canada), antimicrobial PDT (**Stanley Brown**, UK), photodynamic drug delivery (**Hubert van den Bergh**, Switzerland) and PDT technology transfer to developing countries (**Thierry Patrice**, France).

The parallel sessions commenced after tea and ran in triplicate, starting with sessions on photosensitisers (Chairs: **Ravindra Pandey** [USA] and **Johan van Lier** [Canada]), light sources & dosimetry (Chairs: **Timothy Zhu** [USA] and **Dominic Robinson** [The Netherlands]) and mechanisms of action (Chairs: **Johan Moan** [Norway] and **Heinrich Walt** [Switzerland]). A dinner cruise on the Huangpu River (sponsored by PhotoCure ASA) then followed. This was the highlight of the social programme and, as dusk fell, the lights of the city came alive.

30th March

The parallel sessions continued on Friday morning, with the first part on dermatology (Chairs: **Trond Warloe** [Norway] and **Georges Wagnieres** [Switzerland]), gastroenterology (concentrating on the use of porfimer sodium) (Chairs: **Herbert Wolfson** [USA] and **Drew Schembre** [USA]) and photodetection (Chairs: **Sune Svanberg** [Sweden] and **Brian Pogue** [USA]). Organisers received so many abstract submissions in these areas that it was necessary to split the topics over two separate sessions.

Chairs of dermatology.

The first dermatology parallel session opened with a presentation of a collaboration (**Oseroff** *et al*) between Roswell Park and the University of Rochester (USA), investigating the optimisation of ALA-PDT dosimetry for the treatment of superficial basal cell carcinoma (BCC), nodular BCC and Bowen's disease (BD). Over 800 lesions had been recruited to receive a variety of ALA-PDT protocols. They concluded that an application time of 4-6 hours was slightly better than 18-24 hours and that there was no advantage in increasing the light dose from 200J/cm^2 to 300J/cm^2. The best complete response (CR) rates observed at 6 months were 92%, 75% and 83% for superficial BCC, nodular BCC and BD, respectively. They noted that if nBCC of <2cm were only considered, the CR rate increased to >80%, and sBCC recurrence rates were 7% at two years follow-up. This was followed by a study from Belarus and Russia (**Petrov** *et al*) which employed the photosensitiser, Photolon® (Fotolon) to treat disseminated skin melanoma (n=30) which had previously been excised and treated with chemotherapy, radiotherapy or immunotherapy. They observed a "pronounced therapeutic effect" in 54% of their patients with skin metastases with a regimen that comprised 1-2mg/kg Fotolon i.v. plus 600-900J/cm^2 irradiation with a 600nm diode laser at 3 hours. This effect was maintained throughout the follow-up period of 18 months.

Sukhin *et al* (Russia) presented a novel PDT regimen described as prolonged PDT. This involved a single i.v. injection of 0.3-0.5mg/kg sulfonated aluminium phthalocyanine (Photosens), followed by 5-10 periods of irradiation with a 670nm diode laser (single light dose = 30-50J/cm^2; total light dose delivered = 300-500J/cm^2). They found this approach to be useful when initially treating an incurable patient with local spread or skin metastases (complete/partial response rates for melanoma metastases or breast cancer metastases were ~70%). Another novel treatment approach was presented by the University of Shanghai (**Jing** *et al*). In this case, topical ALA (8%) was combined with a small systemic dose of HpD (1.5mg/kg i.v.) to visualise and treat (250mW/cm^2 for 20 minutes at 630nm) a variety of skin cancers. All but one of the 21 patients considered achieved a CR to this treatment regimen, with cutaneous photosensitivity of 10-14 days being reported.

A large and long-term study presented by **Dr Warloe's group** (Norway) considered the response of over 3,700 non-melanoma skin lesions treated with Metvix-PDT (MAL-PDT). Median follow-up was 5 years (range 2-10 years). They found CR rates (including retreatments) to be as follows: sBCC = 93%, nBCC = 88%, BD = 95% and AK = 82%. The relatively small numbers of infiltrating BCC and SCC lesions considered responded less well, however (77% and 40%, respectively). An investigation of light dose fractionation of sBCC was presented by **de Haas** *et al* (The Netherlands). This experimentally successful technique was applied clinically (two light fractions of 20 and 80J/cm^2, 4 and 6 hours after a single dose of 20% ALA) and was found to significantly increase ($p<0.002$) CR rates when compared with a single light fraction. The sBCC CR rate at one year for the fractionated regimen was 97% compared with 89% in the non-fractionated control group. Another study presented by Dr Xu summarised the efficacy of ALA-PDT in China. It was found to be a useful technique when treating BCC, SCC, AK or BD, particularly in patients not suitable for application of other more conventional treatment modalities, e.g. infirm, elderly patients.

Dr Campbell (UK) presented a pilot study (n=30) investigating the use of a jet of oxygen (from an Oxyjet® machine) to improve the application/penetration of topical MAL-PDT to nBCC lesions. Fluorescence microscopy was employed to assess the production and localisation of PpIX in specimens excised at various timepoints (0, 30, 60, 120 and 180 minutes) following the pro-drug application. Although tumour heterogeneity prevented quantitative analysis, a trend of increase in relative tumour concentration of the active photosensitiser was observed in the nBCC lesions treated with the Oxyjet device, and this also occurred at earlier timepoints. It was demonstrated that with some treatment parameters it is also possible to produce PpIX fluorescence throughout the complete depth of these thick lesions. The final presentation in this session (**Barge** *et al*, Switzerland) investigated the pain associated with PDT. Five normal volunteers participated, and 3cm spots of normal leg skin were treated with various doses of topical ALA (10-100%, 6mg/cm^2) and a 635nm diode laser (50-200mW/cm^2; 10-200J/cm^2; at 1-6 hours). A clear correlation between increased irradiance and increased pain was observed. Pain also increased with increasing length of the drug-light interval.

Subsequent parallel sessions considered otorhinolaryngology and pneumology (Chairs: **Merrill Biel** [USA] and **Eric Edell** [USA]), neurosurgery (Chairs: **Katherine Drummond** [Australia] and **Samuel Eljamel** [UK]) and molecular targets (Chairs: **Tayyaba Hasan** [USA] and **Kristian Berg** [Norway]).

At lunchtime, the General Assembly of the IPA Membership was chaired by the IPA Secretary General, **Professor Patrick Barron** (Japan). It was announced that the IPA Board Directors had decided that the 2011 IPA World Congress would be hosted by **Professor Herwig Kostron** in Austria. It was already known that the next IPA World Congress will be held in Seattle, USA (11-15 June 2009) and is being organised by **Professor David Kessel**. Further details

(as they become available) about the forthcoming IPA Congresses can be found on the IPA website (www.pms.ac.uk/ipa). Members were also requested to check and update their website entry as required. Researchers interested in joining the IPA can also find membership application details on this website.

Time was then allocated in the programme for viewing of the numerous scientific posters being presented by delegates and to visit the interesting collection of stands provided by exhibitors.

Parallel sessions continued with: new techniques (Chairs: **Yoram Salomon** [Israel] and **Guo-Giang Yu** [USA]); PD & PDT with porphryrin precursors (Chairs: **Alcira Batlle** [Argentina] and **Zvi Malik** [Israel]); urology & gynaecology (Chairs: **Patrice Jichlinski** [Switzerland] and **Tetsuya Muroya** [Japan]); vascular targets (Chairs: **Zheng Huang** [USA] and **Malini Olivo** [Singapore]); dermatology II (Chairs: **Rolf-Markus Szeimies** [Germany] and **Xiuli Wang** [China]); gastroenterology II (Chairs: **Alex Hsi** [USA] and **Peter Mlkvy** [Slovakia]). In fact, there were so many interesting sessions available that it was sometimes difficult to decide which parallel session/presentations to attend, and some proved so popular that only standing room remained.

The second dermatology parallel session was opened by **Professor Szeimies** (Germany), with a presentation which considered the use of topical ALA-PDT to treat inflammatory dermatoses. Although the exact mechanism of how PDT exerts anti-inflammatory effects is not yet fully understood, it was clear that repeatedly performed topical ALA-PDT was a useful treatment strategy for patients with sarcoidosis or localised scleroderma (where other treatment modalities such as PUVA had failed) and warranted further detailed study. **Dr Wang** *et al* (China) then considered the pharmacokinetics of topical ALA-PDT in urethral condylomata acuminate lesions. Investigating ALA solutions of varying concentrations (0.5-10%) for various periods of time (1-7 hours), biopsy specimens from 65 patients were analysed using fluorescence microscopy. Results indicated that an ALA solution of 5-10% for a period of 3-5 hours

Prof Lasse Braathen.

represented the best parameters to be employed when treating this type of lesion.

Huang *et al* (China) used mathematical (Monte Carlo) modelling to determine the best treatment parameters for port wine stains. They then conducted a clinical study (n=83) to test these recommended parameters (using a domestic photosensitiser; 3.5-5.0mg/kg PSD-007 and a 532nm laser; 80-100mW/cm^2) and found the clinical results to be consistent with the findings of the modelling studies. A second study of port wine stains from **Zhou** *et al* (China) also found PDT to be useful in this condition. They presented their findings from over 300 cases collated over a number years of clinical practice and found a Krypton laser at 413nm to be the best light source for the photosensitiser they employed. **Wang** *et al* (China) investigated using topical ALA-PDT to treat severe acne vulgaris. They found that a complete response was produced in all but one of their patients (n=11) when using 3% ALA and 60-80J/cm^2 (630nm; 200mW/cm^2) once a week for a total of three weeks. Three of their complete responses recurred during the three month follow-up period, but the treatment approach was found to be simple, safe and effective.

A study of photorejuvenation was presented by **Dr Smadar** (Israel). Topical ALA cream (5-10%) and a 630nm LED light source (~150J/cm^2; 100mW/cm^2) was employed at 4 hours to treat 42 individuals with a variety of sun damage and signs of ageing (either once or twice). Some beneficial effects began to be observed 2 weeks following treatment, and good or very good effects were observed in approximately half the subjects (n=20). A number of local, transient adverse effects were noted, however, and included pain during irradiation, and blistering or pseudofolliculitis, erythema and crusting post-irradiation. The final presentation in the session was from **Xu** *et al* (China) who had treated (up to three times) 60 patients with plantar warts with either semiconductor laser evaporation or ALA-PDT. They found that patients who received ALA-PDT had a statistically significant increase in complete responses, which was well maintained throughout the follow-up period (CR = 93% and recurrence rate = 7% at 6-24 months follow-up). This brought to a close the diverse dermatology parallel sessions, which had been well attended throughout the Congress and produced lively discussion amongst delegates in this field.

In the evening, a Gala Banquet (sponsored by Biolitec AG) was held at the Yu-Yuan Garden, with further traditional entertainment being provided by the organising committee.

31st March

The final day of the Congress closed at lunchtime, following the final parallel sessions: infectious diseases and immunology (Chairs: **Michael Hamblin** [USA] and **Mladen Korbelik** [Canada]), combined photodynamic therapy (Chairs: **Woong-Shick Ahn** [Korea] and **Kai Wang** [China]) and the second part of photodetection (Chairs: **Andrea Leunig** [Germany] and **Hidetoshi Honda** [Japan]). The closing plenary session (Chair: **Stanley Brown** [UK]) considered the new horizons of PD and PDT, specifically diagnostics and treatment of tumours using laser techniques (**Katarina Svanberg** [Sweden]) and photochemical internalisation: a technology for site-specific drug delivery (**Kristian Berg** [Norway]).

So, another international World Congress of the IPA concluded. It was both a scientifically rigorous and clinically relevant meeting. The programme was packed full of high quality content, delivered by both eminent and up-and-coming researchers. Discussions were interesting and thought-provoking, demonstrating that this is an area of medical research where there is still much to learn and to apply to further improve patient care. For many Western participants, this was their very first trip to China and although Shanghai is only a small portion of this vast and diverse country, it was unforgettable.

11th World Congress on Cancers of the Skin

Amsterdam, The Netherlands

An Adaptable Modality: Topical PDT for Detection, Treatment and Prevention of Non-Melanoma Skin Cancer

Galderma Satellite Symposium

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The use of PDT in dermatology, especially in the diagnosis and treatment of non-melanoma skin cancer (NMSC), is increasing worldwide. This satellite symposium, sponsored by Galderma, brought together an impressive international line-up of PDT experts to present the latest opinions and recommendations for best practice and to form a discussion panel to address questions from the audience of dermato-oncologists.

The Co-Chairmen, **Prof Lasse R Braathen** (Bern, Switzerland) and **Prof Hendrik M Neumann** (Rotterdam, The Netherlands), welcomed the audience. Prof Braathen noted that the global incidence of NMSC, including actinic keratosis (AK), squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and Bowen's disease, has been rising in recent years. Accordingly, greater numbers of dermatologists have turned to PDT as an effective treatment modality with excellent cosmesis. In particular, the increased use of PDT has been driven by the introduction of Methyl Aminolevulinate (MAL: Metvix®), a versatile molecule which can be used equally for treatment and for fluorescence detection (FD) and evaluation of results. He drew the audience's attention to the publication, in January 2007, of comprehensive guidelines for the use of topical PDT in NMSC[1].

EARLY DETECTION OF NMSC: IN WHICH PATIENTS AND WITH WHICH DIAGNOSTIC TOOLS?

Prof Brigitte Dréno (Nantes, France) observed that the definition of an AK is an initiated skin lesion, which may or may not progress to an SCC. From this statement, dermatologists need to answer three questions: what type of AK will undergo transformation to a cancer? What is the profile of the high-risk population? And how can the lesions be detected?

AK is one of the most common conditions treated by dermatologists. Four types are recognised: Types I and II occur singly and are variable in colour; Type III consists of multiple similar flat lesions; and Type IV is the crusted, hyperkeratotic form. Type IV lesions and, to a lesser extent, Type III lesions have the highest risk of transformation to skin cancer. A qualitative review of existing studies on AK[2] concluded that the transformation rate for an individual AK lesion to SCC varied between 0.025% and 20% per year. Risk factors for types of AK associated with progression to SCC are shown in **Figure 1**. The authors concluded that the risk of malignancy rose with the number of major criteria present in each patient.

Major criteria	Minor criteria
● Induration/Inflammation	● Pigmentation
● Diameter >1cm	● Palpability
● Rapid enlargement	● Pain
● Bleeding	● Pruritus
● Erythema	● Hyperkeratosis
● Ulceration	

Figure 1: Risk factors for progression of AK.

Patient types

Patients who have a higher risk of developing AKs and subsequent skin cancers are, not surprisingly, of Caucasian race with skin phototypes I and II, light coloured eyes, red or blond hair and freckles. Older age and male sex are also associated with higher risk, as is higher cumulative sun exposure (i.e. a combination of several factors, including the total amount of outdoor exposure through work/recreation, duration/intensity/intermittency of exposure and geographical location). This can also include migration to a land with higher sun exposure (e.g. from Northern Europe to Australia). Again not surprisingly, a previous history of SCCs is a strong indicator of likely progression of lesions in the future.

The immunosuppressive status of the individual is significant: as well as the development of highly immunosuppressive chemotherapy regimens to treat cancer patients, the need to prevent rejection in transplant recipients has created a sub-population of people receiving immunosuppressive drugs over many years. Some of these drugs have been found to show carcinogenic properties with extended use[3], whilst the cumulative impact of long-term immunosuppression manifests in earlier and more aggressive development of skin cancers[4].

Other factors that may predispose to high risk are genetic abnormalities (e.g. albinism, xeroderma pigmentosum) and exposure to ionising radiation or hazardous chemicals (e.g. arsenic, hydrocarbons and tars).

Diagnostic tools

Dermoscopy offers a simple and non-invasive method of diagnosis of possible AKs. However, despite the publication of aids to visual recognition of AKs[5], diagnosis is not foolproof. Confocal laser microscopy may offer diagnostic advantages over conventional microscopy, but is of limited use in hyperkeratotic AK.

Macroscopic FD for visualisation of skin lesions was first developed using aminolevulinic acid. More recently, the availability of MAL has allowed very selective and accurate visualisation of the precise foci of hyperplasia within the skin[6].

Cutaneous biopsies are used to check diagnoses of invasive carcinoma, and should be considered when there is irritation or pain, or thickening, bleeding or ulceration of the area. A recently published redefinition of AK as early in situ SCC[7] proposes a three-stage histological continuum from AK to SCC.

Biomarkers of cell proliferation offer the latest option for diagnosis. Mutations in tumour suppressor genes occur early in the initiation of cell hyperplasia. Research interest has focused upon the biomarker, Ki67, which in AK is generally limited to the basal/suprabasal layers or is extended to the mid-zones of the epidermis, whereas it extends throughout the full thickness of the epidermis in carcinoma in situ[8]. Increasing expression of the tumour suppressor genes p16, p53 and Bcl2, correlating with the

histological extent of the clinical lesions, has been demonstrated in AKs and carcinomas in situ[9,10].

Conclusions

Prof Dréno concluded that, by examination of their genetic predisposition and history of sun exposure, it is feasible to identify the subpopulation of people at high risk of developing skin cancer. A number of diagnostic tools exist or are in the clinical research stage, which can help to further define this group and thus allow the development of effective management strategies to treat AKs before they progress to SCCs.

QUESTIONS

Delegate: What about p53?

Prof Dréno: Yes, I think it's an easy to use and interesting marker for confirmation of diagnosis of progression.

WHAT'S NEW IN NMSC TREATMENT GUIDELINES?

With the rapid expansion of the use of PDT in dermatology, **Prof Rolf-Markus Szeimies** (Regensburg, Germany) noted that there are many recent publications showing evidence for the long-term efficacy of PDT[11], its use in nodular basal cell carcinoma (nBCC)[12,13] and its expanding role in the prevention of NMSC[14]. Therefore, an international group of acknowledged PDT experts considered that it was timely to undertake a comprehensive review of the best randomised clinical studies of the use of PDT in NMSC, and from this to publish a set of guidelines[1] that would represent both an international consensus and the 'state of the art' for PDT in NMSC. These evidence-based guidelines were then examined in more detail by Prof Szeimies.

Actinic keratoses

The use of topical PDT in the treatment of AKs was established in four papers using aminolevulinic acid (ALA) and five papers using MAL (**Figure 2**).

The results of these trials enabled the authors to conclude that PDT is a highly effective treatment for AKs, offering the advantage of excellent cosmesis. Furthermore, MAL-PDT has demonstrated a superior cosmetic outcome to cryotherapy, especially for cosmetically sensitive areas. The ability to use PDT over a large area is particularly advantageous for patients showing field cancerisation. Therefore, topical PDT should be considered as a first-line therapy for AKs.

Bowen's disease

The authors evaluated a total of four papers for ALA-PDT and MAL-PDT (**Figure 3**).

Randomised Clinical Studies	No. lesions treated with PDT	Response: % clearance rate: PDT (control)	Response: Time-point
1 x MAL-PDT vs. 2 x freeze-thaw cryo[1]	367	**69** (75)	3 months
2 x MAL-PDT vs. placebo-PDT[2]	260	**89** (38)	3 months
2 x MAL-PDT vs. 1 x freeze-thaw cryo vs. placebo-PDT[3]	295	**91** (68 / 30)	3 months
2 x MAL-PDT vs. placebo in transplant patients[4]	17 patients	**13/17** (0) clear	4 months
1 x MAL-PDT repeated if necessary after 3 mo vs. 2 MAL-PDT 7 days apart[5]	400	**92** vs. **87**	3 months

1. Szeimies et al. *J Am Acad Dermatol* 2002a;47:258-62.
2. Pariser et al. *J Am Acad Dermatol* 2003;48:227-32.
3. Freeman et al. *J Dermatol Treat* 2003;14:99-106.
4. Dragieva et al. *Transplantation* 2004; 77:115-21.
5. Tarstedt et al. *Acta Derm Venereol* 2005;85:424-8.

Figure 2: PDT in AK: supporting evidence for MAL-PDT.

They concluded that topical PDT is effective in the treatment of Bowen's disease, achieving good cosmesis, and is at least as effective as cryotherapy or 5-fluorouracil (5-FU), but with fewer adverse events. Therefore, it should be considered as a first-line therapy for Bowen's disease.

Basal cell carcinoma

Early trials using ALA-PDT in superficial BCC (sBCC) provided inconclusive results, due to the lack of reliable follow-up data. However, more recent trials using MAL-PDT (**Figure 4**) allowed the authors to conclude that PDT is effective and reliable in treating sBCC, again offering excellent cosmetic outcomes. Furthermore, PDT offers an advantage in the treatment of large (>2cm diameter), extensive and multiple lesions.

Existing data on the use of MAL-PDT in nBCC show that, although it is still slightly inferior to surgery, MAL-PDT can offer an effective and reliable treatment option for nBCCs <2mm deep (after debulking), with the advantage of good cosmetic outcome. Therefore, MAL-PDT can be considered for areas where surgery would present an unacceptable risk to the patient or result in undesirable scarring. MAL-PDT has also now shown long-term efficacy, with 5-year follow-up data available in both sBCC and nBCC.

Conclusions

Topical PDT, and in particular MAL-PDT, is a highly effective addition to the armamentarium of treatments for AKs, Bowen's disease and BCCs. PDT offers excellent cosmetic outcomes and high patient satisfaction rates compared to other standard therapeutic modalities, such as 5-FU, cryotherapy and surgery. Follow-up data, especially for MAL-PDT, shows a proven long-term efficacy, and the authors agreed that PDT could be recommended as a first-line treatment in most forms of NMSC.

Randomised Clinical Studies	No. lesions treated with PDT (all treatments)	Response: % clearance rate: PDT (control)	Response: Time-point
MAL-PDT			
PDT vs. cryo and 5-FU[1]	111 (275)	**93** (86 / 83)	3 months
ALA-PDT			
1 x PDT vs. 1 x cryotherapy[2] repeated every 2 mths if necessary	20 (40)	**75 after 1 treatment** (50 after 1 treatment) **100 after 2 treatments** (100 after 3 treatments)	variable
1 x PDT (red light) vs. PDT (green)[3]	61	**88** vs. **48**	12 months
1 x PDT (extemporaneous ALA) vs. 5-FU[4] Repeated after 6 wks if necessary	33 (66)	**88** (67)	6 weeks

1. Morton et al. *JEADV* 2005;19(Suppl 2): 237-238.
2. Morton et al. *BJD* 1996;135:768-71.
3. Morton et al. *BJD* 2000;143:767-72.
4. Salim et al. *BJD* 2003;148:539-43.

Figure 3: PDT in Bowen's disease: supporting evidence.

Study Design/Comparison	No. lesions treated with PDT (all treatments)	Response: % clearance rate: PDT (control)	Response: Time-point
Randomised Clinical Study			
1 x PDT*† vs. 2 x cryotherapy[1,2]			
Where necessary treatment repeated with 2 x PDT 7 days apart and 2 x cryotherapy	102 (219)	97 (95)	3 months
Open-label study in 'difficult to treat' or 'high-risk' sBCC			
2 x PDT*†[3]	38	80	3 months
2 x PDT*†[4]	80	93	3 months
Retrospective study			
1 x PDT*[5]	147	91	3 months

*lesion preparation; † re-treated after 3 months where necessary

1. Basset-Seguin et al. JEADV 2004;18 (Suppl 2):412.
2. Basset-Seguin et al, JEADV 2005;19 (Suppl 2):237.
3. Horn et al, BJD 2003;149:1242-9.
4. Vinciullo et al, Poster at ISCC, Zurich, July 2004.
5. Soler et al, BJD 2001;145:467-71.

Randomised Clinical Studies			
2 x MAL-PDT* vs. surgery[3]	56 (110)	91 (98)	3 months
2 x MAL-PDT*† vs. placebo-PDT[4]	41 (80)	82 (49) (clinical) 79 (35) (histological)	6 months
2 x MAL-PDT*† vs. placebo-PDT[5]	34 (70)	73 (21) (histological)	6 months
Open label in 'difficult to treat' or 'high-risk' nBCC			
2 x PDT*†1	40	87	3 months
2 x PDT*†2	49	94	3 months

*lesion preparation; † re-treated after 3 months where necessary

1. Horn et al., BJD 2003;149:1242-9.
2. Vinciullo et al, Poster at ISCC, Zurich, July 2004
3. Rhodes et al, Arch Dermatol 2004;140:17-23.
4. Tope et al, JEADV 2004;18 (Suppl 2):413-4.
5. Foley et al, Poster at ISC Conference, Zurich, July 2004.

Figure 4: PDT in sBCC and nBCC: supporting evidence.

QUESTIONS

Delegate: You didn't mention SCC, so can you recommend PDT for SCC?

Prof Szeimies: There are some data from small-scale studies on the use of PDT in SCC but, due to time constraints, I decided to leave them out of this presentation. As far as the consensus guidelines are concerned, these data show a high recurrence rate, so the consensus was that PDT cannot currently be recommended for a disease such as SCC, because of the high metastatic potential.

Delegate: Have you had any experience with actinic cheilitis? In particular, do you have any comments about the post-treatment oedema that is seen?

Prof Szeimies: Yes, and I would say that PDT is an easy, exciting and effective option for treatment that is within the MAL licence, as actinic cheilitis is very similar to AK. As for the oedema, I don't think that it's any worse than what is seen with CO_2 laser therapy or the tissue damage with surgery. The cosmetic outcome is excellent, and we've also performed re-treatment after a couple of years with no problems. The only drawback is the pain during treatment, but that can be overcome with a nerve block injection similar to that which dentists administer.

Delegate: How about the use of PDT in xeroderma pigmentosum?

Prof Szeimies: Yes, the first paper describing the successful use of PDT in xeroderma pigmentosum and multiple NMSCs was published in 1992. The photodynamic process is different from that involved in the xeroderma pigmentosum repair mechanisms: there is no DNA damage. However, it doesn't stop the development of melanoma in these patients.

Delegate: Cost-effectiveness is a very important topic for health authorities these days: can you say anything about the cost-effectiveness of PDT?

Prof Szeimies: Any cost-effectiveness analysis also needs to consider the side-effects of treatments and any costs that might result from their subsequent treatment. There are several published studies that show that, when all costs are taken into account, PDT is not dramatically different in cost from other therapies, with the added bonus of extremely good cosmetic outcomes.

PDT TREATMENT OF NMSC IN ORGAN TRANSPLANT RECIPIENTS

Dr Tobias Forschner (Berlin, Germany) reported that of the 20,000 patient visits annually to his hospital's dedicated skin cancer centre, approximately 25% involve organ transplant recipients. As mentioned previously, organ transplant recipients receive long-term immunosuppressive therapy to prevent graft rejection and, as a result, are at a much higher relative risk of skin cancer development[15] (**Figure 5**). The incidence of some other non-skin cancers is also elevated (e.g. lymphomas, lung, colorectal and kidney cancers).

	Relative Risk (RR)
Actinic keratosis	>250
Squamous cell carcinoma	>100
Basal cell carcinoma	10
Kaposi's sarcoma	500
Anogenital tumours	100
Melanoma	5

Figure 5: Relative risk of skin tumour development in organ transplant recipients.

The majority of skin cancers seen are in sun-exposed areas and, due to the dramatically accelerated rate of development and increased numbers of skin cancers seen, organ transplant recipients constitute a clinically useful model for trials of skin cancer therapies.

Field cancerisation

Topical PDT is particularly well suited to treating field cancerisation, where large areas of skin are riddled with a range of UV-damaged cells, warts, multiple AKs and developing skin cancers. An ongoing multicentre trial of MAL-PDT in stable (>3 years out from transplantation) organ transplant recipients with field cancerisation[16] recently reported that patients treated with MAL-PDT showed higher rates of complete clearance than a control group (patients treated with cryosurgery, excision or laser therapy), and the number of new lesions was significantly lower in the MAL-PDT group, compared to the controls. Moreover, MAL-PDT was well tolerated and the rate of hypopigmentation seen more than two years after therapy was much lower in the MAL-PDT group.

Conclusions

Dr Forschner emphasised that, because organ transplant recipients are at particularly high risk of developing NMSC, it is important that they should be referred to a dermatologist as soon as possible after transplantation. A precise treatment strategy should be adopted, and PDT can play a

valuable role in this strategy. MAL-PDT has been demonstrated to be effective in treating patients with severe field cancerisation and appears to offer a preventive role in the development of new NMSC in these patients.

QUESTIONS

Delegate: Have you any data on patient satisfaction between the MAL-PDT patients and those who received other therapies?

Dr Forschner: This hasn't been recorded in this trial, but we are looking to develop a preventive trial, and patient opinions about their treatments would be an important aspect to record.

PREVENTION OF NMSC WITH PDT

Dr Robert Bissonnette (Montreal, Canada) examined the other experimental and clinical data for PDT having a preventive role in NMSC development. As well as organ transplant recipients, the population of people with fair skins and a high degree of sun exposure are candidates for prevention of NMSC through PDT, as are patients with basal cell naevus syndrome and those who have received extensive PUVA therapy or radiotherapy.

Pre-clinical studies

The first report of prevention of AK in a hairless mouse model exposed to UV light was published 10 years ago[17], and showed a delay in AK appearance with weekly or bi-weekly ALA-PDT. Similar results for AK and SCC were reported by Liu and colleagues[18]. MAL-PDT has also been shown to delay AK and SCC appearance[19]. With regard to BCC, a study using PTCH heterozygous mice exposed to UV light[20] found that weekly MAL-PDT completely prevented the development of BCCs, a result that was statistically significant ($p=0.015$).

Clinical studies

In addition to the ongoing study by Wennberg *et al*[16] already discussed by Dr Forschner, Dr Bissonnette described a study of 27 renal transplant recipients with 2 contralateral areas on the dorsal side of the hands with at least 2 AKs and a maximum of 10 other skin lesions, who were randomised to receive MAL-PDT on one hand and observation only on the other[21]. The authors found a statistically significant increase in the time taken for new AKs to develop in the MAL-PDT areas ($p=0.03$).

Dr Bissonnette emphasised that it was necessary for clinicians to treat aggressively and use multiple PDT treatments. He described a case study of a renal transplant recipient who presented with multiple AKs and was treated with four courses of PDT over a three-month period in order to achieve an improvement (**Figure 6**).

Figure 6: Renal transplant recipient, treated with 4 courses of PDT.

Although no clinical trials have yet been published, ALA-PDT has been used with success in case studies[22] of three children with diffuse BCCs (Gorlin's syndrome). Recurrence of BCCs was apparently prevented in the treated areas.

Conclusions

Dr Bissonnette concluded that pre-clinical evidence exists for the prevention of AK, SCC and BCC by PDT in mouse models, and small-scale clinical studies have indicated that PDT can prevent AKs in transplant recipients. Case reports also suggest that PDT can successfully prevent recurrence of BCCs. However, more research is needed to determine the appropriate PDT regimens in these at-risk patients. The situation is complicated by the widespread use of non-standard procedures with ALA-PDT, especially in North America.

QUESTIONS

Delegate: The epidermis renews itself every two weeks or so, and malignant cells will develop even faster, so how frequently should PDT be repeated in any clinical trial?

Dr Bissonnette: If the trial population consists of transplant patients, a treatment every 3-4 months is probably required, but some transplant patients will require more frequent treatments. In the case study I described, the patient has widespread lesions all over her body, so different areas of the body are treated every 2 weeks, so that each area is treated on average every 2 months. For non-immunocompromised, fair-skinned patients with AKs, treatment every 6 months, or even annually, may be sufficient, if I was designing such a trial.

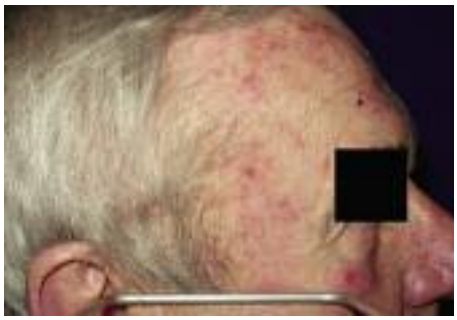
CASE STUDIES

A series of case studies were presented, with the panel members and audience invited to comment at intervals throughout.

CASE STUDY 1: AK

Presented by Prof Szeimies:

- 63 year-old man
- Long history of itchy scales on face and scalp
- Hobbies: sailing, mountain climbing
- Working in his own business (souvenir sales, requiring his presence daily in his premises) – appearance important, downtime not possible



Prof Braathen: This type of patient is becoming more common in my practice: someone who has 'no time to spare' for treatment, but who also expects to be cured with no side-effects. What did you do?

Prof Szeimies: I offered the patient a range of options: a prescription treatment, such as 5-FU, diclofenac or imiquimod; or an office-based therapy, such as cryotherapy, topical podophyllin (still available in Germany), curettage and electrodessication, laser therapy or PDT.

Prof Braathen: When you offered these options to the patient, you explained the

implications and side-effects of each therapy. What was his response?

Prof Szeimies: He wanted a treatment that could be given on the few days that he could spare from his business and which would have the least visible side-effects.

Prof Braathen: I'd like to ask the audience what they would use:

5-FU: 9 delegates
Diclofenac: 1 delegate
Imiquimod: 3 delegates

Remember that this patient didn't want unsightly side-effects. With 5-FU, you need to treat for 3 weeks, the lesions are erosive, and it's another 6 weeks or so before the patient's appearance is back to normal. With imiquimod, the time period is about 3 months, and the patient will be red-skinned for most of the time.

Cryotherapy: 10 delegates

This patient would require multiple cryotherapy sessions. The technique is quick and simple: however, hypopigmentation and depletion of the skin would be possible side-effects.

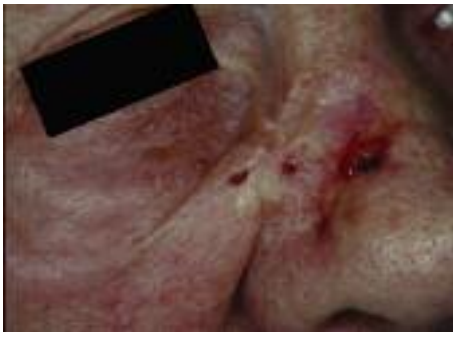
Prof Szeimies: Initially, we were favouring cryotherapy, but the patient had a history of unsuccessful cryotherapy treatments, so we decided to use topical PDT. The cosmetic outcome was very good, the patient was pleased with the results, and side-effects were limited to a little scaling, oedema and pain during illumination, the latter being controlled by anaesthetic.

Prof Braathen: PDT is a physician-controlled treatment, so patient compliance is not a problem, unlike with home treatment using creams that give skin reddening and other unpleasant side-effects. In my experience, patients are often put off by these adverse events and don't use the home treatments properly.

CASE STUDY 2: BCC

Presented by Prof Szeimies:

- 73 year-old woman
- One week of persistent bleeding after towelling in the bathroom
- Daughter (doctor's assistant) assumes it is skin cancer



- Refuses surgery, since she read in the newspaper that there are other therapeutic options

Panel Member: This looks like a morphaic BCC to me: what was the outcome of the biopsy?

Prof Szeimies: You are correct: it was a morphaic BCC.

Panel Member: I'll ask the audience: is PDT an option for this condition? No, the audience agrees that it is clearly not an option.

Prof Szeimies: We were able to persuade her to undergo Moh's surgery, and it took 4 sessions to clear the whole of the BCC.

Panel Member: What other options are available?

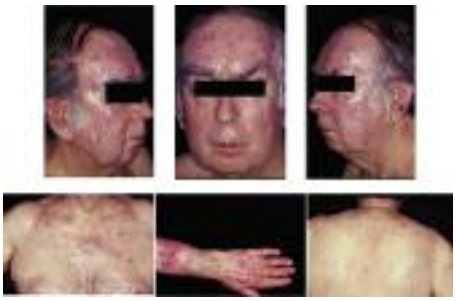
Radiotherapy: 2 delegates

OK, we appear to be agreed that Moh's surgery is the best option for this patient.

CASE STUDY 3: NMSC IN AN ORGAN TRANSPLANT RECIPIENT

Presented by Dr Forschner:

- 70 year-old male
- Polycystic kidney disease
- 1992: kidney transplantation
- Immunosuppression with ciclosporin, methylprednisolone, azathioprine
- 1992-2007: more than 200 surgical treatments for NMSC: multiple BCCs, AKs and Bowen's disease; later, also SCCs
- After 1998, also treated with 5-FU, retinoids, cryotherapy, laser, PDT
- Field cancerisation on scalp and forehead, numerous lesions elsewhere
- First presented at Dr Forschner's clinic in 2002



Panel Member: Was this patient under dermatological surveillance from the time he was transplanted?

Dr Forschner: No. He had been seen by a plastic surgeon on occasions, and some lesions were excised. 'Pre-malignant lesions' were ignored. We first saw him 10 years after transplantation, in the state you see in the photos.

Panel Member: I would have to say that this is a case of negligence. He should never have been allowed to get so bad. Dermatologists should be involved in post-transplant clinics from the start. How did you treat this patient?

Dr Forschner: We used a combination of large-field topical MAL-PDT and excision. We used FD to visualise the extent of the tumours, then used 2 sessions of MAL-PDT where possible, with cryotherapy of any remaining AKs, and surgical excision of other tumours thought unsuitable for PDT.

I have to say that this type of patient presents a huge challenge: this patient also had an ear amputated and a nucleation of an eye, due to a metastatic SCC. We have seen him every 2-3 weeks and have performed MAL-PDT over 40 times, plus other therapeutic interventions.

Prof Dréno: Did you suggest to the nephrologist that his immunosuppressive regimen should be altered?

Dr Forschner: Yes, and the immunosuppression was reduced by removal of azathioprine and substitution with sirolimus, which is thought to have an antiproliferative impact. However, this patient is really beyond the point of no return.

Prof Dréno: Do you give systemic retinoids to organ transplant patients?

Dr Forschner: No: we do give them in less advanced cases to control lesion development, in conjunction with 5-FU, but we see no clear benefit in such advanced-disease patients.

CASE STUDY 4: OPTION FOR PDT OR NOT?

Presented by Prof Neumann:

- 75 year-old male
- Bald head, widespread lesions: field cancerisation
- Previously treated with 5-FU and cryotherapy

Dr Neumann: We have treated younger patients like this with laser resurfacing, but

this may not be the best option in the elderly. PDT may offer an alternative to laser resurfacing.

For BCCs, especially nBCCs, I believe that Moh's surgery offers the safest option. What do the audience think about the use of PDT in BCCs?

Delegate: I would not use PDT for BCCs in high-risk areas, such as the temple, because if the tumour recurs, the surgery thereafter could be very dangerous.

Prof Szeimies: I think that each tumour has to be assessed for the risk versus the benefit of PDT. There is no simple answer.

FINAL QUESTION SESSION

Delegate: For under-developed countries, with low levels of resources, what would be the best combination of photosensitiser and light source?

Prof Braathen: Firstly, red light penetrates deepest, so you need a good source of red light. Secondly, ALA is licensed in the USA, and MAL is licensed in Europe: as you've heard today, MAL-PDT has been shown to be particularly effective in NMSCs.

Delegate: With these large areas of field cancerisation, how large an area can you treat with one tube of MAL-PDT?

Dr Forschner: The area is not the limiting factor, really. MAL remains where it is applied and doesn't get transported elsewhere in the body. The pain is more of a problem, so I treat, say, one arm in a single session.

Delegate: What I mean is, is it necessary to have the cream so deep, so that it only covers a 25cm^2 region from one tube, and no more?

Prof Szeimies: Personally, I reckon that a 2g tube of Metvix is enough to treat half a face. If you try to do a larger area, then it's difficult to get the required amount of Metvix evenly spread.

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Calendar of Events 2008

February 1-5, San Antonio, USA
66th Annual Meeting of the American Academy of Dermatology (AAD)
Contact: AAD Secretariat
Tel: +1 202 842 3555 Fax: +1 202 842 4355

March 6-8, Barcelona, Spain
EURO-PDT 8th Annual Congress
Contact: Claudia Zange, Department of Dermatology
University of Regensburg, Franz-Josef-Strauss-Allee 11
93053 Regensburg, Germany
Fax: +49 941 944 9662
e-mail: claudia.zange@euro-pdt.org URL: www.euro-pdt.org

March 27, London, UK
Medical Dermatology
Contact: Conference and Event Services
The British Association of Dermatologists, 4 Fitzroy Square
London W1T 5HQ
Tel: +44 (0)20 7391 6358 Fax: +44 (0)20 7388 0487
e-mail: conference@bad.org.uk
URL: www.bad.org.uk

May 15-17, Athens, Greece
9th Congress of the European Society for Pediatric Dermatology (ESPD)
Contact: Penelope Mitroyianni
Tel: +30 2 107 257 693 Fax: +30 2 107 257 532
e-mail: info@espd2008.com URL: www.espd2008.com

June 5-7, Athens, Greece
12th 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

July 1-4, Liverpool, UK
88th Annual Meeting of the British Association of Dermatologists
Contact: Conference and Event Services
The British Association of Dermatologists, 4 Fitzroy Square
London W1T 5HQ
Tel: +44 (0)20 7391 6358 Fax: +44 (0)20 7388 0487
e-mail: conference@bad.org.uk URL: www.bad.org.uk

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