

Meeting News

4th Annual Meeting of European Society of Photodynamic Therapy – Stirling, Scotland, March 26–27, 2004

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The Euro-PDT meeting was held in the ancient town of Stirling located 56 km northwest of Edinburgh. An impressive castle dominates Stirling. "The battle of Bannockburn" a memorable battle in which Scotland gained its independence, took place in Stirling in 1314.

The meeting was excellently organised by the secretary of Euro-PDT, Dr Colin A Morton (Falkirk Royal Infirmary, UK). It was the largest meeting to date of the European Society for photodynamic therapy with about 255 delegates with 37 lectures and 22 posters presentations.

The aims of the meeting was

1. to present the current evidence-base for topical photodynamic therapy applications in dermatology.
2. to inform of recent advances in the field of topical photodynamic therapy

Systemic versus topical PDT

Systemic photosensitizers may be advantageous for treatment of extensive skin diseases such as psoriasis and basal cell naevus syndrome. Verteporfin, approved for treatment of macular degeneration, has in a multi center phase II study shown high complete response after a single injection followed by irradiation 1–3 h later of basal cell carcinomas. Oral ALA (up to 10 mg/kg) followed by red light can induce apoptosis in lesional T cells of patients with psoriasis and in a pilot study improvements in plaque severity of psoriasis was reported by *R Bissonnette*.

New photosensitizers under development may have useful dermatological applications, not only for non melanoma skin cancer but also for treatment of microbial infections. As professor *S Brown* expresses "it may be beneficial because there is no mechanism by which microorganisms can become resistant to singlet oxygen".

The encouraging possibilities for PDT for internal premalignant and malignant states were reported by *James Ferguson* with use of an impressive slide-and videoshow.

Encouraging results in Barrett oesophagus, airways obstruction due to primary and secondary malignancy, hepatobiliary carcinoma, brain cancer and head, neck malignancies were presented.

PDT in the Clinic

The therapeutic effect as well as post-treatment prediction of outcome of topical ALA-PDT for basal cell carcinoma syndrome (Gorlin) by measuring lesion thickness before and after ALA-PDT by ultrasound analysis. BCC < 1.5 mm were more likely to have no ultrasound evidence of disease 4–6 weeks post treatment than those of >1.5 mm (*J. V Moore*)

R Groves summarized PDT for patients with multiple actinic keratoses as a validated therapeutic alternative. Two large multi centre randomised studies with MAL PDT in comparison with cryo therapy have shown equivalent efficacy with a superior cosmetic outcome. In addition ALA-PDT has shown to be beneficial in immunosuppression-associated actinic keratoses.

Preparation of lesions weeks before PDT with salicylic acid and urea containing emollients was suggested.

C Morton suggested the off-label use of MAL PDT as the first line therapy option for Bowen's disease (complete cure rate 90–100%). Squamous cell carcinomas are not yet advisable to treat.

A Sidoroff reported the experience with the use of PDT for multiple (e.g. Gorlin), large superficial as well as smaller BCC in problematic locations. Compliance of patients are better when using PDT than imigimod or 5-FU. Morphea carcinomas and thick BCC should not be treated with PDT.

Malignant and premalignant cells absorb derivatives (esters) of aminolevulinic acid much more effectively than ALA. Clinical results with (methylesteraminolevulinic acid (Metvix) show less normal cell phototoxicity and pain.

Efficacy of Metvix acid in clinical well designed studies has been shown in actinic keratoses, superficial and nodular BCC (H Morris).

Repeated PDT may be useful in early patch and plaque stage CTCL supported by selective accumulation of photosensitisers in lymphocytic cell lines with T and B cell toxicity and induction of lymphoblast mutations (JA Leman).

PDT for non-oncological diseases

Promising results for cutaneous sarcoidosis (1 patient) and localized sclerodermia (10 patients) using multiple (20-30) treatments with low dose ALA (3%) applied for 6 h followed by irradiation with low light doses (10-20 J/cm²) (S Karrer).

Repetitive treatments with Metvix followed by Curelight showed promising effect in healing of especially

the central part of necrobiosis lipoidica (HC Wulf).

Sally Ibbotson reviewed the literature relating to the use of topical PDT in skin conditions other than non melanoma skin cancer. A potential use of PDT for warts and acne vulgaris. The use of PDT for psoriasis have shown unpredictable results. Cases treated with PDT are reported for keratoacanthoma, erythroplakia of Querat, lichen sclerosis, extramammary Mb Paget, condylomata, scleroderma, hirsutism, Leismaniasis, naevus sebaceous, penile lichen planus, sarcoid, tinea pedis, chondrodermatitis, alopecia areata, porokeratosis, breast metastases.

Preliminary findings demonstrated that superficial skin mycoses as dermatophytes and yeasts effectively metabolise ALA to PpIX why PDT was suggested to have a potential role in the treatment off various mycoses (PG Calzavara-Pinton)

Topical ALA PDT for acne vulgaris facilitate destruction of *propionibacterium acnes* and inactivates intracellular viruses as herpes simplex and HIV (M McKenna)

Anti microbial PDT may be able to treat localised infections. Eradication of bacteria by PDT in cell culture and in animal models give encouraging results.

PDT-side effects and safety

The most troublesome side effect of PDT is pain during and after treatment irradiation.

Patients reported mild degree of pain when treated for AK, BCC, Bowen, squamous cell carcinoma, mycosis treated with Metvix followed by irradiation with Waldmann PDT 1200 and a fan. The pain was independent of lesion type but dependent on site (head and hands more painful than body). No difference between PDT pain analgesia using tramadol or paracetamol (N Kapur).

Treatment of large areas results in more pain. Men seem, as expected, to have more pain than women. The use of methylester (Metvix) is less painful than ALA (Ann-Marie Wennberg).

Recurrence rates after PDT increase with longer periods of observation, whereas cosmetic out come use to improve. The possible genotoxic, mutagenic and carcinogenic effects in cells affected by sub lethal doses of PDT were discussed.

Irradiation in PDT

In animal studies, topical applied ALA followed by fractionated illumination, splitting the illumination into two fractions with a 2 h dark interval, rather than following a single light fraction, leads to significantly more PDT damage (ERM de Haas).

Fluorescence diagnostic with use of CCD camera and digital imaging system may be useful for a directed biopsy or for preoperative planning of surgery. 5-aminolevulinic acid (ALA) and -5-amino-4 oxopentanoate

(MAOP) have a unique feature, which can be exploited for diagnostic purposes after topical or systemic administration because these photosensitizers show a high tumour to surrounding tissue ratio. Fluorescence diagnostic is a helpful tool to prove the efficacy of PDT (*R-M Szeimies*).

J Moan reflected on cream based on ALA derivatives as attractive candidates for sun protectors due to pigment induction and the anti-photocarcinogenic effect in ALA PDT.

Photorejuvenation

PDT seems to be a potential treatment for skin rejuvenation.

ALA-PDT improves skin surface quality as well as the actinic keratoses using ALA followed by intense pulsed light (*R Ruiz-Rodrigues*). Reduction of fine lines and wrinkles using low concentrations of ALA (5% ALA for 30 minutes) followed by Omnilux LED 633 nm gave safe and reproducible data (*Nick Lowe*).

Posters

The effect of topical photodynamic therapy with MAL or ALA followed by red light (PDT) for actinic keratoses (AK), nodular and superficial BCC (n/sBCC) are briefly summarized.

In a minor study PDT with 5% ALA was as effective as 20% ALA in the treatment of scalp actinic keratoses (*Monti et al*).

MAL PDT in phase III trials was significantly more effective than cryotherapy ($p < 0.02$) and placebo PDT ($p < 0.0001$) of thin and moderate AK. The cosmetic outcome was better with MAL PDT than with cryotherapy (*Foley et al*).

MAL PDT is as effective as cryotherapy for treatment of sBCC but has significantly better cosmetic outcome both at 3 and 12 months follow up (*Basset-Sequin et al*).

MAL PDT is not better than excision surgery according to cure rate of nBCC, and a higher recurrence was observed with MAL PDT, however better cosmetic results were reported with MAL PDT (*Rhodes et al*).

MAL PDT is superior to placebo PDT ($p < 0.001$) with a higher response rate on the face (100%) than on the trunk (73%) or on the extremities (60%) (*Foley et al*).

MAL PDT for "difficult to treat" BCC were compared with conventional therapies. Response rate at 3 months was 89% and at 12 months recurrence was confirmed in 7% of the lesions. Cosmetic outcome was excellent (*Viniciullo et al*).

MAL PDT was superior to placebo PDT ($p < 0.001$) of nBCC. Complete response rate was 80% for MAL PDT versus 51% for placebo PDT (*Tope et al*).

Preliminary results deal with increasing ALA penetration depth in nBCC with increasing application times and not with increasing ALA

concentrations. The depth of penetration is about 2 mm (*McLoone et al*).

In a pilot study the addition of the iron chelator CP94 in a standard 20% ALA PDT seems to enhance the clearance rates of nBCC (*Morton et al*).

Comparison of light doses (70, 100, 140 J/cm²) show that an irradiation dose of 70 J/cm² is sufficient for ALA PDT of AK (*Radakovic-Fijan et al*).

PDT for non-oncological applications

A randomised study with ALA PDT twice weekly for a maximum of 12 treatments showed unsatisfactory clinical response for psoriasis (*Radakovic-Fijan et al*).

In a pilot study Levulan plus blue light in four weekly sessions appear to be effective in a small group of patients that have failed blue light monotherapy in inflammatory acne (*Russell et al*).

Preliminary reports on photodynamic peeling in photo-aged skin with a single treatment with 5% ALA PDT gave a good cosmetic outcome in terms of smoothness, fine texture, bleaching and clearing of solar melanosis (*Monti et al*).

Pain induced by topical applied PDT was reported to be reduced by a "LaserAid" pad during and after PDT (*Strasser et al*) and by a cold air device to reduce pain during PDT (*Fraser et al*).