

First International Photo-Dynamic Therapy (PDT) guidelines launched for the treatment of non-melanoma skin cancers (NMSC)

Practical, evidence-based recommendations highlight beneficial role of PDT with long term efficacy, improved cosmetic outcomes and patient satisfaction

Germany 12 January 2007: A group of leading dermatologists have concluded in the first international guidelines published today in the *Journal of the American Academy of Dermatology* that topical photodynamic therapy (PDT) is a highly effective treatment for non-melanoma skin cancers (NMSC) with benefits including superior cosmetic outcomes and patient satisfaction compared to standard treatment procedures.¹

“Skin cancer is the fastest growing cancer in the western world and it is important for clinicians, patients and health care systems that we evaluate new treatments and issue guidelines”, said Professor Lasse Braathen, chairman of the I-PDT, and from the Dermatological University Clinic, Bern, Switzerland. “There is very strong evidence and agreement now among specialists that photodynamic treatment of non-melanoma skin cancer is superior in some cases and just as effective and safe as the standard treatments used until now” continued Professor Braathen.

The recommendations were based on a review assessing quality of evidence for efficacy, safety/tolerability, cosmetic outcome and patient satisfaction. In light of recent data it was feasible to measure the relative efficacy and benefits of PDT compared to standard treatment procedures such as surgery, cryotherapy and 5-FU.

“The new evidence has confirmed that PDT is effective and well tolerated, with consistently favourable cosmetic outcome, particularly beneficial in sensitive areas such as the face, and can offer advantages for those patients with large, extensive and multiple lesions with the possibility of repeat use if required.” commented Professor Rolf-Markus Szeimies (I-PDT Founding Vice-President and from the Department of Dermatology, Regensburg University Hospital, Germany. “We hope that the new guidelines will provide physicians with an improved understanding of the role of PDT and support its wider use in the growing number of NMSC patients worldwide.”

PDT in the treatment of NMSC

A relative newcomer in the treatment and prevention of NMSCs, including actinic keratoses (AK), Bowen’s disease (BD), superficial and thin nodular basal cell carcinomas (sBCC and nBCC), PDT uses either a topical 5-aminolevulinic acid (ALA) solution or methyl aminolevulinate (MAL) cream.^{2,3} These photosensitisers are illuminated with an appropriate light source to ensure optimal photosensitiser excitation and skin penetration that is localised in diseased tissues. This ultimately leads to cell death of these targeted tumour cells. Certain variations between the two procedures result from the specific mode of action of the compounds ALA and MAL. For example there is evidence of greater selectivity for neoplastic tissue with MAL-PDT* compared to ALA-PDT**.¹

* Metvix® and Aktelite® are registered trademarks of PhotoCure ASA who developed Metvix® and are responsible for the marketing and sales of Metvix® in Nordic countries, while Galderma is responsible for the marketing and sales of Metvix® in the rest of the world.

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Guidelines recommendations¹

The new guidelines outline the criteria and practical recommendations for effective treatment or prevention of four forms of non melanoma skin cancer with support for topical PDT as first line therapy in actinic keratoses, Bowen’s disease and superficial basal cell carcinoma and MAL-PDT for nodular basal cell carcinoma lesions.

In particular, the I-PDT concluded that:

- with AK, the most common pre-malignant skin lesion, PDT should be offered as a first-line therapy with excellent cosmetic outcome for MAL-PDT versus cryotherapy
- in BD, PDT was considered as having an acceptable long-term efficacy, comparable with more established therapies, but with fewer adverse events.⁴
- PDT was also proven effective and reliable in the treatment of sBCC, with advantages in the treatment of large, extensive and multiple lesions.
- MAL-PDT demonstrated long-term efficacy in nBCC and sBCC.

Incidence of NMSC

NMSCs are the most common malignancies in Caucasian populations and have been increasing at a rate of 3-8% per year since 1964 with significantly higher rates in Australia. Despite wide geographical variation in incidence, the link between sun exposure, skin type and NMSC is well established. Although NMSCs have generally favourable prognosis they should be treated early as they can be locally invasive if left untreated. NMSCs occur most often on exposed and cosmetically sensitive areas of the body. Hence cosmetic outcomes and the possibility of multiple treatments with PDT offer advantages not currently feasible with some standard treatments and are integral to patient satisfaction.

Conclusion

Professor Colin Morton, Lead Consultant Dermatologist, Forth Valley Dermatology Centre, Stirling (Royal Infirmary), Scotland stated that “the I-PDT guidelines are in line with previous guidelines but for the first time provide a level of international support with new clinical evidence which will enable physicians to meet the needs of more NMSC patients, providing greater cosmetic benefits and a wider choice of reliable treatment options.”

Notes to editors:

For further information please also refer to the websites: www.i-pdt.org, www.metvix.com, www.levulanpdt.com

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Summary of I-PDT guidelines recommendations:

Actinic keratosis	
• PDT is a highly effective treatment for AK offering the advantage of excellent cosmetic outcome, and should therefore be considered as a first line therapy	AI
• MAL PDT has a superior cosmetic outcome compared with cryotherapy	AI
Bowen’s disease	
• Topical PDT is effective in Bowen’s disease, achieving good cosmesis, and is at least as effective as cryotherapy or 5-FU, but with fewer adverse events. Topical PDT should be considered as a first-line therapy for Bowen’s disease	AI
Superficial basal cell carcinoma	

• PDT is an effective and reliable treatment option for sBCC that offers excellent cosmetic outcomes	AI
• PDT offers an advantage in the treatment of large, extensive and multiple lesions	AI
• MAL PDT has demonstrated long term efficacy, with 5-year follow-up data	AI
Nodular basal cell carcinoma	
• MAL PDT is an effective and reliable treatment option for nBCC less than 2mm in depth with the advantage of good cosmetic outcome	AI
• MAL PDT has demonstrated long term efficacy, with 5-year follow-up data	AI

Strength of recommendations

- A. There is good evidence to support the use of the procedure
- B. There is fair evidence to support the use of the procedure
- C. There is poor evidence to support the use of the procedure
- D. There is fair evidence to support the rejection of the procedure
- E. There is good evidence to support the rejection of the procedure

Quality of evidence

- I. Evidence obtained from at least one properly designed, randomized controlled trial
- II-i Evidence obtained from well-designed controlled trials without randomization
- II-ii Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group
- II-iii Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
- III Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees
- IV Evidence inadequate due to problems of methodology (e.g. sample size, or length of comprehensiveness of follow-up or conflicts in evidence)

International Society for Photodynamic Therapy in Dermatology (I-PDT)

The International Society for Photodynamic Therapy (I-PDT) was founded in 2004 by Professor Lasse R. Braathen (Founding President [Switzerland]), Professor Rolf-Markus Szeimies (Founding Vice-President [Germany]), and Dr Colin Morton (Founding Secretary General [UK]). The aim of the Society is to promote the evidence-based use of PDT in dermatology and to be a forum for exchange of knowledge and scientific data, as well as clinical use/techniques.

The guidelines were developed as a joint collaboration of the I-PDT members. It is acknowledged that the guidelines are correct at the time of publication, but that subsequent studies and data may necessitate the revision of the current guidelines.

The new I-PDT guidelines reflect and are in accordance with previous guidelines published to date including:

- British Photodermatology Group Guidelines for Topical PDT (2002)
- UK NICE Guidance of the Use of PDT for Non-Melanoma Skin Tumours (Feb 2006) – prior to publication of 5 year Metvix data
- US Consensus Recommendations For Use of ALA-PDT in Dermatology (2006)

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Further information on the I-PDT can be found on the website: www.i-pdt.org

Actinic Keratosis (AK)

AK is the most common pre-malignant skin lesion, frequently found on the face, scalp, dorsum of the hands, forearms and other sun exposed areas. They are often multiple in these locations, resulting in areas of field cancerisation. AK develops into squamous cell carcinoma.

Non-melanoma skin cancers (NMSC)

Skin cancers are divided into two general types: non-melanoma and melanoma. Non-melanoma skin cancers are the most common cancers of the skin. They are called non-melanoma because this group of cancers includes all skin cancers except one – malignant melanoma. There are a number of different types of NMSC, the most common types being squamous cell carcinoma (SCC) and basal cell carcinomas (BCCs). NMSC is rarely life-threatening but if left untreated can cause extensive damage to surrounding organs and structures and increase the chances of developing new skin cancers in later years.

Basal Cell Carcinoma (BCC) is the most common human cancer and is locally destructive. Basal cell carcinoma is slow growing and accounts for about 70% to 80% of all skin cancers in men and 80% to 90% in women. They usually develop on sun-exposed areas, especially the head and neck. There are two main sub-types of BCC known as superficial and nodular BCCs.

Squamous cell Carcinoma (SCC) accounts for about 10% to 30% of all skin cancers and tends to be more aggressive than basal cell cancers. They commonly appear on sun-exposed areas of the body such as the face, ear, neck, lip, and back of the hands. They are more likely to invade tissues beneath the skin, and can spread to lymph nodes and/or distant parts of the body, although this is still uncommon.

Bowen's disease (BD)

BD is SCC in situ – an early stage of SCC where the tumour has not spread. It usually looks like a slow growing red and scaly patch. It needs to be removed, but elderly patients with lesions on their legs and face often find surgical treatment difficult.

References

1. Braathen L, Szeimies RM, Basset-Sequin N et al. Guidelines on the use of photodynamic therapy (PDT) for non-melanoma skin cancer – an international consensus. *J Am Acad Dermatol* 2007 Jan; **56**(1):125-43
2. www.metvix.com
3. www.levulanpdt.com
4. Leman JA, Mackie RM, Morton CA. Recurrence rates following aminolaevulinic acid- photodynamic therapy for intra-epidermal squamous cell carcinoma compare favourably with outcome following conventional modalities. *Br J Dermatol* 2002; **147** (Suppl 62):35.