The use of topical 5-aminolevulinic acid–photodynamic therapy (ALA-PDT) for the treatment of Bowen disease (squamous cell carcinoma in situ) is gaining acceptance.1 However, there is limited evidence for the most appropriate treatment regimen, and clinical follow-up remains limited. The treatment of choice for Bowen disease is surgery. Five-year response rates have shown a recurrence rate of 19.0% after conventional surgery and 6.3% after Mohs micrographic surgery.2 In a comparison of ALA-PDT and cryotherapy, results significantly favored ALA-PDT.3 In a comparative study of ALA-PDT vs topical flououracil, recurrence rates at 12 months were 7% and 27%, respectively.4

In a review of 11 PDT studies5 using broadly similar protocols, response rates of 90% to 100% were found after 1 to 3 treatment sessions, and an average recurrence rate of 12% was calculated. Importantly, however, follow-up periods varied widely (3-36 months), and therapy was often repeated.

Our research group has investigated the role of light fractionation in the response of tissues to ALA-PDT in animal6,7 and clinical studies.8,9 In a randomized comparative study of the response of superficial basal cell carcinoma (sBCC) to ALA-PDT, our group showed a significantly higher complete response rate at 1 year (n=476) (P= .002) using a 2-fold illumination scheme (20 and 80 J/cm²) with a 2-hour dark interval compared with a single illumination (75 J/cm²).9

Methods. Fifty biopsy-proven patches of Bowen disease were randomly assigned to 2 equal treatment groups. The local ethics committee approved the study. Forty patients (17 men and 23 women) attending the department were recruited sequentially after providing written informed consent. The mean patient age was 74 years (age range, 49-91 years). The mean lesion diameter was 14.5 mm (range, 5-40 mm) (Table). The ALA ointment was prepared by our university pharmacy using 20% ALA (FLUKA, Zwijndrecht, the Netherlands) in Instilagel (Medeco, Oud Beijerland, the Netherlands).8 Surface scale or crusts were removed and the ALA was applied topically and left in place for 4 hours, with a margin of 1 cm.

In the single illumination scheme, Bowen patches were light treated 4 hours after ALA application with 75 J/cm². Lidocaine, 2%, without epinephrine (field block) was used if patients required it. In the 2-fold illumination group,
patches were light treated 4 and 6 hours after ALA application with 20 and 80 J/cm², respectively, separated by a 2-hour dark interval. Each illumination was delivered at 50 mW/cm². A diode laser (Carl Zeiss, Oberkochen, Denmark) and light-emitting diode (Omnilux, Tiel, the Netherlands) provided illumination at a wavelength of 630 nm. Our group has shown that there is no difference in response of sBCC to ALA-PDT using these sources and light fractionation. The rationale for choosing these illumination schemes—in particular the reason we used unequal total light fluences—is based on extensive work in preclinical models and our group’s demonstrated results in the treatment of sBCC. These factors are discussed at length by de Haas et al.9

Patients were examined after 4 weeks and then at 3-month intervals. Complete response was defined as no clinical evidence of disease, with macroscopically normal skin at the treated site. Patients with patches that responded partially were considered nonresponders. Cosmesis was scored as good, fair, or poor at 12 months.

The primary response and recurrence rates of patients treated with different illumination schemes were compared using the Fisher exact test. A Kaplan-Meier-type analysis was performed on relative complete response rates after therapy, and the log-rank test was used to compare treatment groups. Statistical significance was set at P<.05. Patients with recurring lesions were retreated with fractionated ALA-PDT but were not considered responders in the statistical analysis.

Results. The relative complete response rate is shown in the Figure. In the single illumination group, a complete response was achieved in 20 patches (80%) at 12 months. In the 2-fold illumination group, complete response was achieved in 22 patches (88%). We found a higher response rate in patches treated with the 2-fold illumination, but this increase in response did not reach statistical significance (P=.41 log-rank test). The average complete response for all patches was 84% at 12 months.

The progression of the clinical response of all lesions after 12 months is shown in the Figure. Overall, the complete response was 80%, with a mean and median follow-up of 24 months. All patients experienced some discomfort during treatment, but all finished therapy. No serious adverse effects were seen.

Patients reported a 3-week maximum healing time, which was not different between treatment schemes. In the single illumination group, none of the patients complained of pain during therapy. In the 2-fold illumination group, 5 patients complained about pain in the treatment of 6 patches. Lidocaine without epinephrine was used in 4 patches (Table).

Comment. Two-year response rates to ALA-PDT and conventional surgery are comparable, and in our view, ALA-PDT may offer the best treatment option for Bowen disease. Surgery may be contraindicated for general health reasons. Also, Bowen disease is often located on difficult-to-treat areas such as the lower limbs and face. For patches in these areas, and in particular for the larger ones, there is a significant need for an alternative to surgery. The present pilot study shows the potential of light fractionation for enhancing the response of Bowen disease following ALA-PDT by the same order of magnitude as our group has achieved in sBCC and illustrates the need for a larger suitably powered study involving approximately 200 patches in each illumination group to determine if this effect is statistically significant.

Ellen R. M. de Haas, MD, LLM
Henricus J. C. M. Sterenborg, PhD
H. A. Martino Neumann, MD, PhD
Dominic J. Robinson, PhD

Correspondence: Dr de Haas, Erasmus MC, PO Box 2040, 3000 GA Rotterdam, the Netherlands (e.m.dehaas@erasusmc.nl).

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