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A Study to Investigate the Effect of Different Durations of Ameluz Application on Response to Treatment of Acral Actinic Keratoses

This research was a collaboration undertaken utilising the equipment, facilities and expertise of the Royal Cornwall Hospital NHS Trust and the University of Exeter Medical School. The Royal Cornwall Hospital NHS Trust Research and Development Charitable Fund kindly paid the MHRA application fees and the travel costs of the participants. Research Nurse support was funded by a British Skin Foundation Small Grants Award. There was no conflict of interest.

Actinic keratosis (AK) is a very prevalent form of pre-cancerous skin lesion that requires effective treatment. This can be achieved via photodynamic therapy; however, it has been observed that acrally located AKs respond less well to this treatment. Acral lesions were defined for this study as being located on the arms, hands, legs or feet.

This study was designed to determine whether applying Ameluz gel (Biofrontera, Germany) to acral AK lesions for longer (4 hours vs standard 3 hours control) would increase treatment effectiveness measured at 3 months. Participants were randomised to either have gel applied for 3 hours or 4 hours. When participants had multiple AKs (including on non-acral sites), these lesions were all treated in the same manner.

All 28 participants received their treatment as outpatients at the Dermatology Department of Royal Cornwall Hospital, Truro, Cornwall between November 2019 and August 2021. Once the gel was applied to the AK lesion(s), a light occluding dressing was applied for either 3 or 4 hours as determined by randomisation. Each treatment area was then exposed to red light, following standard photodynamic therapy treatment guidelines. Participants went home with all lesions covered with light occluding dressings with instructions to remove them 24-48 hours later.

Statistical analysis conducted in advance, indicated that 74 participants would need to be recruited to detect a significant difference in treatment outcome between the two application times being investigated (3 hours and 4 hours). The COVID-19 pandemic negatively impacted both participant recruitment and follow up. This resulted in a much longer than anticipated study duration, which could not be sustained due to the clinical pressures and staff attrition experienced within the Department post-pandemic. The difficult decision was therefore taken to stop recruiting participants to the study. This means it was not possible to achieve the original study objective. Of the 28 participants recruited, one was excluded as their lesion was subsequently found not to be AK. One participant withdrew from the study after treatment and prior to follow up taking place.

A further five participants were treated but were subsequently lost to follow up. This resulted in 21 participants in total with 50 acral AK lesions being treated and followed up.

The mean number of acral AK lesions per participant was 2.4 (range = 2 to 3). This was unexpected as the study team had anticipated that most participants would present with a single acrally located AK lesion. Fourteen participants (32 acral AK lesions) were followed up on schedule at 3 months after treatment. Seven participants (18 acral AK lesions) had (COVID) delayed follow up ranging from 5 to 8 months after treatment. This resulted in a mean study follow up time of 4.5 months.

All treatments proceeded safely without incident, with only two adverse events being recorded throughout the study. One participant experienced redness and pain in the treatment area, which is a known side effect of photodynamic therapy. Another participant experienced sore eyes in the four days following treatment, which was concluded by the clinical team to be unlikely to be related to the photodynamic therapy treatment.

The mean age of the study participants was 71 years, with 48% being female. Predominantly the acral AK lesions were located on the hands (38 lesions/19 participants), with 6 lesions on the arms (4 participants), 5 on the legs (3 participants) and only 1 AK lesion (1 participant) located on a foot.

Although not enough participants were recruited to be able compare the effectiveness of different gel application times, some limited global analysis was possible. This indicated that 55% of the acral AK lesions treated were completed resolved, 38% were partially resolved and 7% of the acrally located AK lesions did not respond to the photodynamic therapy treatment. These results are comparable with our previous findings in this respect (61% complete response observed in 31 acral AK lesions).

Digital photographic images (using a Dyaderm fluorescence imaging system, Biocam, Germany) were also taken of all lesions i) prior to treatment, ii) following the 3 or 4 hour Ameluz gel application period, and iii) immediately after the light treatment completed. The level of active drug present in the lesion can be determined from these images. Previous research indicates that the reduction of active drug levels during the period of light treatment is related positively to the effectiveness of the treatment.

The images taken of the 38 acral AK lesions treated on the hands of 19 of the participants will therefore be analysed in more detail, with a view to publishing the findings. How much active drug accumulated during each Ameluz gel application period will be determined, as well as any effect this may have had on the subsequent reduction observed during the light treatment. As pain scores were recorded using a visual analogue scale, we will also be able to determine if there was any relationship between active drug levels and any pain experienced by participants during light treatment.

We would like to thank all the participants who took part in this study.