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#### **Abstract**

Actinic keratoses progress more quickly to squamous cell carcinoma than basal cell carcinoma

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Actinic keratoses (AK) are common, costly, and may evolve to keratinocyte carcinoma (KC): basal cell (BCC) and squamous cell carcinoma (SCC) of the skin. Time to malignant transformation is controversial. We used data from the placebo arm (n=166) of a randomized trial of veterans with multiple prior KCs. Study dermatologists examined participants' faces/ears at enrollment and semiannual visits. Clinically diagnosed AKs were marked, photographed, and treated with cryotherapy (starting at 6 months). Lesions suspicious for KC were marked, photographed, and biopsied. AKs were tracked using these photographs. For each AK that progressed to KC (n=23), the time between the first appearance of the AK and the biopsy resulting in a KC diagnosis was measured. Among all 4,231 tracked AKs, the difference in time to progression of AKs that progressed to BCC (12/4,231) vs. SCC (11/4,231) was not statistically detectable (Cox proportional hazards analysis). However, among the 23 AKs that progressed to KC, AKs progressed more quickly to SCC compared to BCC (two-sided Wilcoxon test; p=0.01) with respective mean progression times of 13 and 25 months. This may be due to clinical misdiagnosis of early BCCs as AKs, as BCCs are known to grow slowly; or perhaps SCCs become more rapidly clinically distinguishable. Differences in progression could also indicate differences in sensitivity to cryotherapy, as lesions progressed despite this treatment. Alternatively, if these were true AKs, then certain events—with different likelihoods and timing—may be needed for AKs to progress to BCC vs. SCC.