INTRODUCTION: A relatively novel application for dermoscopy and reflectance confocal microscopy (RCM) is their use in the monitoring of topical treatment response for non-melanoma skin cancer. Actinic keratosis (AK) is the early phase of a multistep biologic continuum leading to invasive squamous cell carcinoma. A number of topical therapies are now available for the treatment of AK but their disadvantages include long treatment duration and prolonged local reactions. Ingenol mebutate is a newer therapy for AK which is only applied for 2 or 3 days. CASE REPORT: Dermoscopy and RCM findings in two patients with AK treated with ingenol mebutate confirm that it induces rapid lesion necrosis and specific neutrophil-mediated, antibody-dependent cellular cytotoxicity. Necrosis occurs via mitochondrial membrane disruption, with subsequent eradication of residual tumor cells via transient inflammation. Local skin reactions to ingenol mebutate should be considered part of the drug’s mechanism of action rather than an adverse effect. CONCLUSION: Ingenol mebutate is a valuable therapy for the treatment of AK. This case report adds further evidence to the usefulness of dermoscopy and RCM in the assessment and monitoring of treatment outcome. KEYWORDS: Actinic keratosis; Dermoscopy; Field cancerization; Ingenol mebutate; Reflectance confocal microscopy