ABSTRACT

BACKGROUND: To date, studies with ingenol mebutate gel have used clinical clearance, not histological clearance, as a primary efficacy endpoint. OBJECTIVES: This phase 1, multicentre, single-arm, open-label study sought to histologically confirm clinical clearance of actinic keratoses (AKs) to support a treatment effect deep in the epidermis. METHODS: Patients (n = 108) aged ≥18 years with histologically confirmed AK within a 25-cm² contiguous treatment area on the trunk and extremities received ingenol mebutate 0.05% gel for 2 consecutive days and were followed up on day 3 and week 8. One AK was randomly pre-selected at day 1 for clinical and histological evaluation at week 8; and for reflectance confocal microscopy (RCM) in a subset of patients. Primary endpoint was clinical and histological clearance of AKs at week 8. RESULTS: The observed agreement rate between clinical and histological assessments of clearance of a single AK was 81.9% and the positive predictive value of a clinical assessment of clearance was 87%. Agreement between the two pathologists was 88%. The common composite 8-week complete clearance rate was 41% (95% confidence interval 32%, 50%). Observed agreement rates between RCM and pathologist I and II assessments of clearance were 72.9% and 81.4%, respectively. Thirty patients (27.8%) experienced 38 adverse events (AEs). Application-site pain (four patients, 3.7%) was the most common treatment-related AE inside the treatment area.

CONCLUSION: Ingenol mebutate achieves histopathological clearance of AKs that correlates with observed clinical clearance. Clinical clearance is a good predictor for histological clearance. This article is protected by copyright. All rights reserved. KEYWORDS: Actinic keratoses; histology; ingenol mebutate 0.05% gel; reflectance confocal microscopy; safety PMID:27518593 DOI:10.1111/bjd.14968