Topically applied imiquimod 5% cream cleared actinic keratosis lesions

Lebwohl M, Dinehart S, Whiting D, *et al.* Imiquimod 5% cream for the treatment of actinic keratosis: results from two phase III, randomized, double-blind, parallel group, vehicle-controlled trials. *J Am Acad Dermatol* 2004;**50**:714–21.

Clinical impact ratings GP/FP/Primary care ★★★★★☆ Dermatology ★★★★★☆

Q In patients with actinic keratoses (AK), is a topically applied imiquimod 5% cream more effective than placebo for clearing lesions?

METHODS

Design: 2 concurrent randomised controlled trials subsequently merged into 1 trial for data analysis purposes.

Allocation: concealed.*

Blinding: blinded (patients, healthcare providers, data collectors, outcome assessors, data analysts, and the sponsor).*

Follow up period: 16 weeks of treatment followed by an 8 week observational period.

Setting: 24 centres in the US and Canada.

Patients: 436 otherwise healthy people >18 years of age (mean age 66 y, 87% men) who had 4–8 clinically diagnosed AK lesions within a contiguous 25 cm² treatment area on the face or balding scalp but not both. Exclusion criteria included previous treatment with imiquimod 5% cream in the treatment area, and allergies to any excipients in the cream.

Intervention: topical imiquimod 5% cream (n=215) or placebo (n=221) applied once per day, 2 days per week, for 16 weeks. The placebo was similar in appearance, and of identical composition to imiquimod 5% cream with the exception of the active ingredient.

Outcomes: complete clearance of AK lesions in the treatment area and adverse effects assessed at weeks 1, 2, 4, 6, 8, 10, 12, 16 (end of treatment), 20, and 24 (end of post-treatment).

Patient follow up: 95% (analysis was by intention to treat).

*See glossary.

MAIN RESULTS

At 8 weeks post-treatment, more patients in the imiquimod group than in the placebo group achieved complete clearance of AK lesions (table). More patients in the imiquimod group than in the placebo group had itching, burning, and bleeding at the target site (table).

CONCLUSION

In patients with actinic keratoses, a topically applied imiquimod 5% cream was more effective than placebo for clearing lesions.

Commentary

AK are rough scaly, premalignant skin lesions generally <1 cm in diameter. Cryosurgery with liquid nitrogen is the most widely used therapy and is the most appropriate therapy when lesions are few.¹

Field therapy is most useful for multiple lesions. Options include topical 5% 5-fluorouracil (5-FU), masoprocol, and photodynamic therapy. A meta-analysis by Pierre *et al* showed the overall efficacy of 5-FU used for 2–8 weeks to be 80%.² Efficacy is greatest on the face and scalp and least on the dorsum of the hands. Adverse effects include pain, inflammation, and erosions. Masoprocol use is supported by limited data; however in a head to head study against 5-FU, it caused substantially fewer and less severe side effects but was less efficacious.²

Currently available treatments for AK have limitations, particularly for patients with multiple AK on limbs and trunk. The study by Lebwohl *et al* examined the use of imiquimod 5% cream for the treatment of multiple AK on the head and scalp and confirmed the earlier findings of Stockfleth *et al*³ of superior efficacy to placebo. The reported complete clearance rate of 45.1% and partial clearance rate (>75% improvement) of 59.1% suggest that imiquimod is less effective than either cryosurgery or 5-FU; however, a direct comparative trial would be required to assess this observation. Cost, efficacy, ease of use, and morbidity all need to be considered when selecting the most appropriate therapy for AK.

Rodney Sinclair, MD
University of Melbourne
Melbourne, Australia

- 1 Thai KE, Fergin P, Freeman M, *et al.* A prospective study of the use of cryosurgery for the treatment of actinic keratoses. *Int J Dermatol* 2004;**43**:687–92.
- 2 Pierre P, Weil E, Chen S. Cryotherapy versus topical cryotherapy of actinic keratosis. A systematic review. *Allergologie* 2001;**24**:204–205.
- 3 Stockfleth E, Meyer T, Benninghoff B, *et al.* A randomized, double-blind, vehicle-controlled study to assess 5% imiquimod cream for the treatment of multiple actinic keratoses. *Arch Dermatol* 2002;**138**:1498–502.

For correspondence: Dr M Lebwohl, Mount Sinai School of Medicine, New York, NY, USA. Lebwohl@aol.com

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A topical imiquimod 5% cream v placebo in actinic keratoses (AK) at 8 weeks post-treatment*

Outcomes	Imiquimod	Placebo	RBI (95% CI)	NNT (CI)
Complete clearance of AK lesions	45.1%	3.2%	1324% (595 to 2864)	3 (2 to 3)
			RRI (CI)	NNH (CI)
Itching at target site	20.5%	6.8%	202% (75 to 424)	8 (5 to 14)
Burning at target site	5.6%	1.8%	208% (7 to 797)	27 (13 to 379)
Bleeding at target site	3.3%	0.5%	620% (170 to 4365)	36 (17 to 274)

*Abbreviations defined in glossary; RBI, RRI, NNT, NNH, and CI calculated from data in article.