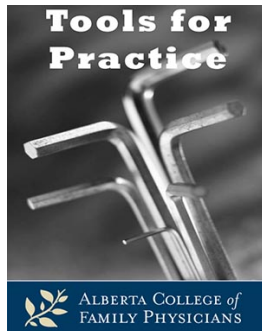


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Actinic Keratosis: Out Damned Spot!

Clinical Question: Which commonly used topical therapies (cryotherapy, 5-Fluorouracil, imiquimod, or ingenol) are preferred for actinic keratosis?

Bottom Line: Topical treatments have similar efficacy to each other and will result in complete clearance of lesions beyond placebo for every 3-4 patients treated. Clearance rates may reach ~90% depending on strength of cream (5% 5-fluorouracil [5FU] greater than 0.5%), longer duration of therapy, and complexity of lesion. The effects on cancer incidence have not been studied.

Evidence:

Five systematic reviews.¹⁻⁵ Most complete: 83 Randomized Controlled Trials (RCTs), 10,036 participants, >350 comparisons of all interventions:¹

- Versus placebo (complete clearance):
 - 0.5% 5-FU (three RCTs, 522 patients):
 - 30% versus 1.5% after 1-4 weeks of treatment with four weeks follow-up. Number Needed to Treat (NNT)=4.
 - 5% imiquimod (11 RCTs, 2,880 patients): 42% versus 5%, NNT=3.
 - Decreased roughness, scaliness/dryness: 55% versus 18%, NNT~3.
 - Ingenol mebutate (two RCTs, 456 patients): 38% versus 7%, NNT=4.
 - Pigmentation changes: No difference.
- Versus cryotherapy (complete clearance; one RCT, 51 patients):
 - 5% 5-FU: 96% versus 68%, NNT=4.
 - "Excellent" cosmetic outcomes: No difference.
 - 5% imiquimod: 84% versus 68%, no statistical difference.
 - "Excellent" cosmetic outcomes 81% versus 4%, NNT=2.
- Versus 5% 5-FU (complete clearance):
 - 5% imiquimod (two RCTs, 89 patients): Larger study, 85% versus 88%, no statistical difference.
 - "Excellent" cosmetic outcome (one RCT, 50 patients): 81% versus 4%, NNT=2. Results unreliable.

Context:

- Large, extensive, or atypical lesions often excluded from RCTs.

- No RCTs have investigated effects of treatments on cancer incidence.
- Rate of progression to squamous cell carcinoma (individual lesions) varies: 0-0.53%/year depending on sun exposure, age, and number/size of lesions.⁶
 - Hypertrophic, painful, atypically broad lesions may progress faster.⁵
- Guidelines suggest cryotherapy for smaller, isolated lesions, and topical creams (field-directed treatment) for ≥ 4 clustered lesions.⁷
- Whether creams after cryotherapy improve effectiveness over creams alone is unclear.⁷
- Adverse effects include (all): Localized pain, erythema, swelling, vesicles/bullae, pigmentation changes.
 - Cryotherapy: Rarely scars/hair loss.
 - Creams: Burning/itching, erosions.
 - 5-FU: Ulcers, toxic agranulocytosis (very rare).
 - Imiquimod: Photosensitivity, systemic effects if applied on larger areas (joint/muscle pain, fever, headache).
 - Ingenol: Hypersensitivity.

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Disclosure:

Authors do not have any conflicts of interest to declare.

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