Can a pill prevent skin cancer?
An update on chemoprevention strategies

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Overview

• Why chemoprevention?
• A brief word on topicals
• Oral agents
  • By evidence
  • Future directions

The Skin Cancer Burden

• Lifetime risk 1:5
  • 3 million US adults annually
  • $8 billion spent annually
• Keratinocyte carcinoma (KC):
  • 5 million cases annually
  • 4.3 million basal cell carcinomas (BCCs)
  • 1 million squamous cell carcinomas (SCCs)
• Melanoma:
  • 5th most common cancer
  • 178,560 cases annually
  • 9,320 deaths annually

Chemoprevention Targets

Disclosures

I have no relevant financial disclosures.
I will discuss off-label medication use.
**Topicals**

- Fluorouracil (5%)
  - RCT to face and ears bid x 2-4 weeks in those with a history of 2 KC in past 5 years
    - 75% risk reduction in SCC at 1 year
    - No effect at study end (4 years)
- RCT of 5-FU mixed in 0.005% calcipotriol ointment x 4 days in those with AKs on the face, scalp, or upper extremities
  - 78% reduction in face and scalp SCCs at 3 years
  - Similar non-significant trend at 1 and 2 years
  - No effect on upper extremities

**Oral Agents**

- Clinic ready:
  - Nicotinamide
  - Acitretin
- We are using in select situations:
  - Nicotinamide

**Nicotinamide**

- Water-soluble form of vitamin B3
- Mechanism: Protects against cellular energy loss from UV radiation
  - Enables immune response and DNA repair
- Evidence for reduction in:
  - KC
  - Actinic keratoses (AKs)
  - Lacking for melanoma

**Nicotinamide: The Evidence**

- **ONTRAC RCT**
  - 500 mg nicotinamide bid x 12 months in patients with 2 KC in the past 5 years
  - No differences in adverse events

**Nicotinamide: The Evidence**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Nicotinamide</th>
</tr>
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<tbody>
<tr>
<td>Reduction of actinic keratoses</td>
<td>12/12</td>
<td>19/19</td>
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**Nicotinamide**

- When: multiple KCs
- Dose: 500 mg bid
- Side effects: Minimal
  - Lacks vasodilatory side effects of niacin
Acitretin

- Vitamin A derivative
- Mechanism: Anti-proliferative, modifies growth factors and proto-oncogene expression
- Evidence for reduction in:
  - KC
    - In organ transplant recipients (OTRs)
      - RCT 30 mg/day: 11% vs 47% of patients developed at least one KC at 6 mo (acitretin vs placebo)
      - Cross-over study: 25 mg/day: Decreased severity of KC by 50% (acitretin vs drug free)
      - RCT 0.2 or 0.4 mg/kg/day: Decreased AKs by 50% but no effect on KCs
  - Cross-over study 25 mg/day: Decrease in average number of SCC (2.8 vs 2)
  - RCT 0.2 or 0.4 mg/kg/day: Decreased AKs by 50% but no effect on KCs
- 15 to 30% withdrew due to side effects
- Lacking for melanoma


Acitretin

- When: 3-5 KC a year (especially SCC)
- Dose:
  - 10 mg every other day
  - Increase by 10mg each month to a goal dose of 20 to 25 mg daily
- Monitoring:
  - CBC, LFTs, lipids
  - At baseline
  - Monthly after dose adjustment
  - Q3 months once dose is stable
- Adverse effects: Xerosis, teratogenicity, hyperlipidemia, hepatitis

Capecitabine

- Mechanism: oral chemotherapeutic agent
- Prodrug of fluorouracil
- Low evidence for reduction in:
  - KC
    - In OTRs
      - Case-series: 10 patients dosed 0.5 – 1.5 g/m2 for 14/21 days for 12-24 months
        - Decreased severity of KC by 50-80%
      - 70% required dose adjustment
      - 20% discontinued due to side effects
      - Side effects: fatigue, hand foot syndrome, GI disturbance, renal impairment
  - SCCs
    - 68% reduction in mean SCCs/month at 12 months
    - 70% required dose adjustment
    - 20% discontinued due to side effects
- Side effects: fatigue, gout, hand foot syndrome, GI disturbance, renal impairment

B Endrizzi et al, Capecitabine to reduce nonmelanoma skin carcinoma burden in solid organ transplant recipients, Derm Surg, 2013

Capecitabine

- When: High rates of new KC despite other efforts
- Dose:
  - 500 mg BID for 1 week on/1 week off
    - Depending on tolerability, may escalate up to 1 g BID 1 week on/1 week off
    - Dosed by body size (m2)
    - Dose adjust for renal impairment
    - Contraindicated if GFR < 20 mL/min
    - Continuous if GFR = 20 mL/min
- Monitoring:
  - CBC and CMP at baseline, after 4 weeks and with any dose adjustment, then Q3 months
- Duration: 6 months
  - May have sustained effect

Mixed Evidence

- NSAIDs
- Vitamin D
- Statins

Future Directions

- Polypodium leucotomas extract
- Resveratrol
- Sulforaphane
- Silibinin
Thank you!

Drs. Emily Ruiz and Abigail Waldman