Intralesional Methotrexate & 5-Fluorouracil for Keratoacanthomas Therapeutic Cheat Sheet

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FDA APPROVAL

- *Intralesional administration of 5-FU is* **not** *FDA-approved*
- *Intralesional administration of MTX* **is FDA-approved** *for keratoacanthoma treatment*

EFFICACY

- *MTX & 5-FU demonstrate high clearance rates from 92-100%*
  - *No significant difference between treatments demonstrated [Seger]*
- *5-FU → faster resolution compared to MTX*
  - *3.7 vs. 4.6 weeks, respectively [Seger]*
- *MTX → Reduction in mean size of tumor by 50-80% prior to surgical extirpation → less aggressive surgery required [Martorell]*

MECHANISM OF ACTION

- *Methotrexate (MTX)*
  - *Inhibition of dihydrofolate reductase & folate metabolism → inhibition of DNA synthesis*
- *5-fluorouracil (5-FU)*
  - *Inhibits synthesis of thymidine via binding of major anabolic enzyme (thymidylate synthetase) → disruption in DNA synthesis*
- *Preoperative Considerations*

PREOPERATIVE CONSIDERATIONS

- *Patient Indications*
  - *Advanced age*
  - *Debilitation*
  - *Comorbid medical conditions*
  - *Social contraindications*
  - *Underserved populations (lack of access to specialist)*
- *Tumor Indications*
  - *Difficult anatomical location*
  - *Tumor recurrence secondary to koebnerization*
  - *Pre-surgical extirpation adjuvant therapy (to reduce size)*
- *Dosing*
  - *Methotrexate*
    - *Concentration: 12.5-25 mg*
    - *Total dose: avg. of 22 mg/treatment (range of 5-87 mg)*
    - *Injection aliquots: 0.1-2 mL (per tumor)*
  - *5-fluorouracil*
    - *Concentration: 50 mg/ml*
    - *Total dose: avg. of 37.5 mg/treatment*
    - *Injection aliquots: 0.1-0.5 mL (per tumor)*
- *Laboratory Evaluation*
  - *Blood work*
    - *Baseline: CBC*
    - *Follow-up: Weekly CBCs recommended*
    - *MTX: CMP w/ liver function testing*
  - *Biopsy*
    - *Hematoxylin & eosin staining*
    - *Histopathological examination to ensure appropriate diagnosis*

SIDE EFFECTS

- *Methotrexate*
  - **Mild** *injection discomfort*
  - *Pancytopenia (esp. anemia)*
- *5-fluorouracil*
  - **Severe** *injection discomfort*
    - *Counsel patients preoperatively*
  - *Leukopenia, thrombocytopenia*
- *Intraoperative Technique*
  1. *Divide the tumor into four quadrants* **(Figure 1)**
  2. *Debulk tumor with shave or curettage*
  3. *Administer local anesthetic*
     a. *Over dilution with local anesthetic may result in less efficacy with each treatment*
  4. *Administer aliquot doses* **(described above)** *into each quadrant*
- *Post-operative Considerations*
  - *Weekly or biweekly dosing (weekly is performed in majority of cases)*
    - *Average duration of treatments is 4 weeks (5-FU) and 5.7 weeks (MTX)*
  - **Clinical endpoint:** *tumor necrosis*
- *Follow-up: q2-4 weeks → monitor response, readminister PRN*
  - **STOP:** *consider alternative therapies following* **two** *administrations without improvement*
    - *Mohs micrographic surgery vs. wide local excision*

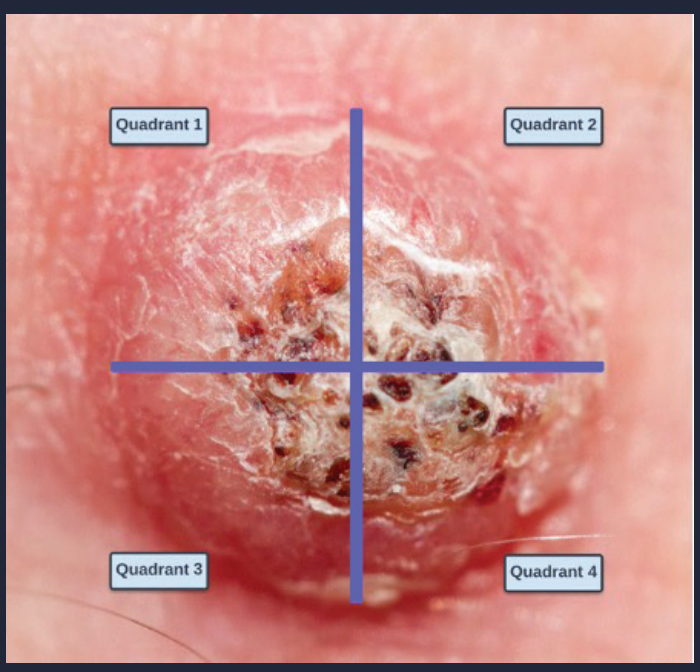

Figure 1