Isotretinoin Guidelines*

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Indications
- Prescribing Information
- Recalcitrant Nodulocystic Acne
- Consensus
  - Severe Nodular/Nodulocystic Acne 165-167
  - Moderate Acne: 134-138
  - Treatment Resistant
  - Physically scarring
  - Psychosocial Distress

Isotretinoin Dosing – Background
- Some efficacy seen at 0.1 mg/kg/d – 1.0 mg/kg/d
  - Reduction in Sebum was dose-dependent
- Similar efficacy 0.5 mg/kg/d and 1.0 mg/kg/d
- 1.0 mg/kg/d – Lower relapse & retreatment
  - NOT in Guidelines
  - Maximum Dose is 2 mg/kg/day
Isotretinoin Daily Dosing

- Consensus
  - Severe Acne
    - 0.5mg/kg QD for 1st Month
    - 1.0mg/kg QD after 1st Month
  - Extremely Severe Acne: Lower starting dose + steroids

Isotretinoin Cumulative Dosing

- Consensus
  - To Reduce Chance of Relapse
    - 120mg/kg minimum
    - Up to 150mg/kg
  - Potential New Evidence
    - 220mg/kg
    - Recent Paper: 116 Pts., Lower Relapse Rate
      - 47.4% vs. 26.9%
      - Further Study

Low Dose Isotretinoin

- Moderate AV
  - Treatment-resistant
  - Quick-relapsing
- Dose: 0.25 – 0.4mg/kg/day
- Better Tolerated Than Higher Doses
- Fewer Side Effects
- Higher Pt. Satisfaction
- Comparable to high/standard dose regimens
- Relapse Rate
- Intermittent Dosing NOT RECOMMENDED
Isotretinoin Absorption

- Retinoid Absorption: 25-50% of single dose
- Isotretinoin is highly lipophilic
  - Best absorbed with food
- Take with meals
- Amount of fat required for optimal absorption - Unhealthy
- Proprietary formulation encases isotretinoin in lipid
  - Increased absorption in fasting state

Isotretinoin – Side Effects

- “Routine”
- Inflammatory Bowel Disease (IBD)
- Depression/Mood Changes/Anxiety
- Bone Mineralization
- CV Risk Factors/Lipids
- LFTs/CBC
- Scarring
- Staph Aureus Colonization
- Teratogenicity

Isotretinoin – “Routine” Side Effects

- Mimic Hypervitaminosis A
  - Mucocutaneous
  - Musculoskeletal
  - Ophthalmic
- Temporary
- Resolve with Cessation of Therapy
Isotretinoin - IBD

- Evaluated Literature 122-126,281,282,283
  - Ulcerative Colitis (UC)
  - Crohn Disease (CD)
- Controversial Issue
- Medicolegal Issues
- No evidence of a relationship between isotretinoin and CD
- 2 Studies suggest potential relationship to UC
- More recent analyses: NO relationship to UC
- Later analysis of same database finding an association

Isotretinoin – IBD

CONSENSUS

- Agreement with Position Statement of AAD 284

  “Current Evidence is insufficient to prove either an association or causal relationship between isotretinoin use and IBD.”

Isotretinoin – Mood Changes

- Sporadic Reports 127-131,137,285-288
  - Depression
  - Anxiety
  - Suicidal Ideation
  - Suicide
- No studies suggest evidence-based link
- Multiple studies – Population Level
  - Isotretinoin improves or has no effect on mood, memory, attention/executive function
Isotretinoin – Mood Changes

- Despite objective population-based studies
  - Depression, anxiety, suicidal ideation/suicide are prevalent
    - General Population
    - Adolescents
- CONSENSUS:
  - “Prescribing physician should continue to monitor for these symptoms and make therapeutic decisions within the context of each individual patient”

Isotretinoin – Bone Issues

- Early Concerns following approval in 1980’s
- No reported cases of bone demineralization
- 2 reported cases of premature epiphyseal closure: 290,296
  - ST Isotretinoin Rx
- No other reported issues
- Consensus:
  - Routine Screening NOT REQUIRED for ST Isotretinoin Rx

Isotretinoin – Lipids/LFTs/CBC

- Hyperlipidemia: 140-142
  - Increases in Serum Cholesterol and TGs seen with ST Isotretinoin
  - Consensus: MONITOR
  - No Proof of LE Cardiovascular Risk
- Liver Function: 139,291-292
  - Increases in ALT/AST/GGT seen
  - Consensus: MONITOR
- CBC
  - No evidence to suggest alterations in CBC by ST Isotretinoin
  - Consensus: DO NOT MONITOR
Update: Isotretinoin Monitoring Frequency

- NOT part of Guidelines
- Isotretinoin
  - Assoc. with changes in CBC, LFTs & Lipids (statistically significant)
  - Changes DID NOT meet criteria for high risk
  - Monthly Monitoring NOT recommended
- Monitor LFTs and Lipids
  - Baseline
  - After 2 months of therapy
  - If Abnormalities found/persist


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Update: Isotretinoin Labs

Alternative Thoughts

- Frequency (Weiss)
  - Baseline
  - After every dosage increase
  - Monthly if risk factors present or abnormalities arise/persist
- Labs to check (Baldwin)
  - Lipid Profile
  - LFTs
    - GGT instead of AST/ALT
  - CK

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Isotretinoin - Scarring

- Concerns based on a few early case reports
- Previous Guideline
  - Delay procedures 6-12 months (Resurfacing, Dermabrasion, etc)
- Recent prospective studies/case reports
  - No atypical scarring with chemical peels/dermabrasion/resurfacing
  - CONSENSUS
  - Delay elective procedures 6-12 months when possible
  - Careful consideration on case-by-case basis for earlier procedures OK
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**Isotretinoin – Staph Aureus Colonization**

- Colonization with Staph Aureus does occur with ST Isotretinoin 300, 301
- Folliculitis and furunculosis
  - Treat appropriately
- Colonization in setting of cheilitis can cause:
  - Lip abscess
  - Perioral abscess
  - Prompt attention required

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**Isotretinoin - Teratogenicity**

- Embryopathy 302
- iPledge
  - 3rd Risk Management Program for pregnancy prevention
  - Still approx. 150 pregnancies per year 143, 144
  - 33% admit non-compliance 144
  - 29% don’t use condoms
  - 39% missed ≥ 1 contraceptive pill
  - CONSENSUS: Patient-independent/long-acting contraceptives whenever possible/appropriate

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**Isotretinoin – Research/Knowledge Gaps**

- Studies Needed:
  - Link to Depression
  - Link to IBD
  - Preventing Pregnancy
  - Optimal Cumulative Dosing
Isotretinoin Guidelines 2016
High Level "Take Aways"

- Expand Usage to Moderate Acne in Appropriate Patients
- No proven link to IBD
  - More study
- Mood NOT negatively affected in vast majority of individuals
  - More study
  - Monitoring still necessary
- iPledge
  - Imperfect
  - Protective