Rilonacept For Gout Flare Prophylaxis During Urate Lowering Therapy Initiation

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Interest
Objectives

1. Define gout and the consequences of untreated gout.
2. Describe typical agents used for urate lowering therapy and for treatment or prophylaxis of acute gout flares.
3. Know the limitations of current gout prophylaxis agents.
4. Evaluate the risks and benefits of using rilonacept during urate lowering therapy initiation after analyzing rilonacept studies.
5. Formulate a conclusion about the use of rilonacept during urate lowering therapy initiation to prevent gout flares.

Abbreviations

- ACR = American College of Rheumatology
- AE = Adverse event
- BMI = Body mass index
- CKD = Chronic kidney disease
- GF = Gout flare
- IL-1β = Interleukin-1 Beta
- ISR = Injection site reaction
- MSU = Monosodium urate
- NSAID = Nonsteroidal anti-inflammatory drug
- SUA = Serum uric acid
- ULT = Urate lowering therapy
- URTI = Upper respiratory tract infection
- XOI = Xanthine oxidase inhibitor
**Gout Background**

- Monosodium urate crystals deposit in joints resulting in a painful, inflammatory condition
- Impacts around 8 million adults in the US
- Gout flares typically last 7 to 10 days
- Untreated gout may cause limited mobility, structural joint damage, chronic pain, frequent flares, reduced work productivity, and high health care costs

**Pathophysiology of Gout**

- Gout can be described by different pathophysiologic stages
  1. Hyperuricemia
  2. Crystal deposition without symptomatic gout
  3. Crystal deposition with acute gout flares
  4. Advanced gout with tophi, chronic gouty arthritis, and radiographic erosions
- Monosodium urate crystals may induce release of active IL-1B
Common Gout Flare Locations

- Gout can present in different locations

![Body diagram with highlighted Gout flare locations: Elbow, Hands, Knees, Ankle, Mid-foot, Big toe]


Risk Factors For Gout

**Non-modifiable**
- Male
- Older age
- Genetics
- Chronic disease states
- Renal insufficiency/failure

**Modifiable**
- Diet
  - Purine-rich meat, alcohol, high-fructose corn syrup drinks
- Weight
- Medications
  - Thiazides, loop diuretics, niacin, etc.


**Acute Gout Flare Treatment**

- Start treatment within 24 hours of the onset of a gout flare

  - **Mild-moderate pain, 1 or a few small joints, or 1-2 large joints**
    - NSAID
    - Colchicine
    - Systemic corticosteroid

  - **Severe pain, polyarticular attack, multiple large joints**
    - Combination therapy

- Inadequate Response (< 20% improvement in pain score within 24 hours or < 50% at ≥ 24 hours)
  - Switch monotherapy
  - Combination therapy

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**Urate Lowering Therapy**

- Pharmacologic treatment with ULT to reach a SUA level < 6 mg/dl should be started if certain criteria is met along with a diagnosis of gout
  - Tophus or tophi present
  - Frequent attacks (≥ 2 years)
  - CKD stage 2 or worse
  - Past urolithiasis

- Urate lowering therapies strategies
  - Allopurinol
  - Febuxostat
  - Contraindication to XOIs: Probenecid

- Last line: Pegloticase, Lesinurad

**AND**

- Acute gout prophylaxis for 3-6 months
- Possible off-label option?

  - NSAID
  - Colchicine
  - Systemic corticosteroid
  - Interleukin-1 Inhibitors

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• Up to 90% of patients with gout have a contraindication to NSAIDS and up to 40% have a relative contraindication to colchicine

Cardiovascular disease
Renal impairment
Higher bleeding risk
GI upset

Severe GI upset
Myopathy
Blood dyscrasias
Numerous interactions

CUSHINGOID
Uncontrolled diabetes

Problems with Acute Gout Prophylaxis

• Current indication: Cryopyrin-associated periodic syndromes

• Mechanism of Action: IL-1α and IL-1β inhibitor that prevents this pro-inflammatory cytokine from interacting with its receptor.

• Dosing Schedule: Once-weekly subcutaneous injection after an initial loading dose

• Cost: $6,000 for a 220 mg vial that needs to be reconstituted

Rilonacept

• Current indication: Cryopyrin-associated periodic syndromes

• Mechanism of Action: IL-1α and IL-1β inhibitor that prevents this pro-inflammatory cytokine from interacting with its receptor.

• Dosing Schedule: Once-weekly subcutaneous injection after an initial loading dose

• Cost: $6,000 for a 220 mg vial that needs to be reconstituted
Controversy

- Acute gout prophylaxis is recommended because ULT can cause gout flares during initiation
  - Many patients have a contraindication or intolerance to typical acute gout flare prophylaxis agents
  - ≈ 50% stop ULT within three months because of gout flares

- Interleukin-1 inhibitors have been studied for acute GF prophylaxis

- The FDA denied approval for rilonacept for prophylaxis of gout flares during ULT initiation in 2012 because they wanted more data

Rilonacept (IL-1 Trap) for Prevention of Gout Flares During Initiation of Uric Acid–Lowering Therapy: Results From a Phase III Randomized, Double-Blind, Placebo-Controlled, Confirmatory Efficacy Study

Schumacher HR. *Arthritis Care Res* (Hoboken). 2012; 64(10): 1462-1470
Schumacher et al - Objective & Study Design

- **Objective**: To determine the safety and efficacy of once-weekly subcutaneous rilonacept versus a matched placebo for prevention of gout flares in patients initiating ULT

- **Study Design**: 16-week, phase III, randomized, double-blind, placebo-controlled, multicenter trial with a 4-week follow-up

- **Intervention**: Rilonacept 180 mg or 320 mg subcutaneously on day 1 followed by 80 mg or 160 mg, respectively, of rilonacept once weekly

- **Comparator**: Matched placebo

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Schumacher et al - Methods

- **Outcomes**:
  - **Primary** – Efficacy over 16 weeks
    - Mean number of gout flares per patient
  - **Secondary** – More efficacy and safety over 16-20 weeks
    - Proportion of patients with ≥ 1 and ≥ 2 gout flares
    - Mean number of flare days
    - Mean number of days with a pain severity score ≥ 5
    - Number of flares using an alternate gout flare definition
    - Safety in terms of clinical assessments and incidence of adverse events
Schumacher et al - Methods

• Population: 241 patients from 64 centers in the US and Canada

<table>
<thead>
<tr>
<th>INCLUSION CRITERIA</th>
<th>EXCLUSION CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-80 years old with gout involving at least 6/13 of the ACR criteria or MSU crystals in the joint fluid</td>
<td>Acute gout flare within 2 weeks</td>
</tr>
<tr>
<td>Initiating ULT</td>
<td>Use of allopurinol, probenecid, or a sulfinpyrazone within 3 months</td>
</tr>
<tr>
<td>Serum uric acid ≥ 7.5 mg/dl</td>
<td>Chronic active gouty arthritis</td>
</tr>
<tr>
<td>Self-reported history of ≥ 2 gout flares within the last year</td>
<td>Use of glucocorticoids within 4 weeks</td>
</tr>
</tbody>
</table>

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>241 - Randomized</td>
<td>241 - Randomized</td>
</tr>
<tr>
<td>80 - Placebo</td>
<td>81 - Rilonacept 160 mg</td>
</tr>
<tr>
<td>80 - Rilonacept 80 mg</td>
<td></td>
</tr>
<tr>
<td>27.5% - Drop-outs</td>
<td>20.0% - Drop-outs</td>
</tr>
<tr>
<td>5% - AE Drop-out</td>
<td></td>
</tr>
<tr>
<td>13.6% - Drop-outs</td>
<td>3.7% - AE Drop-out</td>
</tr>
</tbody>
</table>
Schumacher et al – Statistical Analysis

- Power: An explanation of the power calculation is not provided
- A full analysis set was used
- Wilcoxon rank sum test or Student t-test – ordinal or continuous endpoints
- Fisher’s exact test – proportional assessments
- Sequential testing procedure
- LOCF was used in sensitivity analyses to impute missing pain severity scores

Schumacher et al – Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N = 79)</th>
<th>Rilonacept 80 mg (N = 80)</th>
<th>Rilonacept 160 mg (N = 81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.2 (13.6 SD)</td>
<td>52.9 (11.6 SD)</td>
<td>51.9 (11.6 SD)</td>
</tr>
<tr>
<td>Sex, male</td>
<td>76 (96.2%)</td>
<td>71 (88.8%)</td>
<td>76 (93.8%)</td>
</tr>
<tr>
<td>White</td>
<td>64 (81.0%)</td>
<td>60 (75.0%)</td>
<td>69 (85.2%)</td>
</tr>
<tr>
<td>BMI</td>
<td>33.1 (7.6 SD)</td>
<td>33.3 (6.3 SD)</td>
<td>33.3 (6.7 SD)</td>
</tr>
<tr>
<td>Visible tophi</td>
<td>8 (10.1%)</td>
<td>10 (12.5%)</td>
<td>8 (9.9%)</td>
</tr>
<tr>
<td>SUA (mg/dl)</td>
<td>9.42 (1.35 SD)</td>
<td>9.03 (1.24 SD)</td>
<td>9.07 (1.23 SD)</td>
</tr>
<tr>
<td>Polyarticular Gout</td>
<td>63 (79.7%)</td>
<td>55 (68.8%)</td>
<td>53 (65.4%)</td>
</tr>
<tr>
<td>GF/year</td>
<td>4.6 (3.6 SD)</td>
<td>4.6 (2.9 SD)</td>
<td>4.5 (3.6 SD)</td>
</tr>
<tr>
<td>Duration of GF (days)</td>
<td>6.7 (4.6 SD)</td>
<td>6.1 (4.1 SD)</td>
<td>7.7 (8.4 SD)</td>
</tr>
</tbody>
</table>
### Schumacher et al – Efficacy Results

- **Primary:** Mean number of GF per person for rilonacept 160 mg versus placebo

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Rilonacept 80 mg</th>
<th>Rilonacept 160 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total # of GF</strong></td>
<td>88</td>
<td>23</td>
<td>17</td>
</tr>
<tr>
<td><strong>Mean # of GF/person</strong></td>
<td>1.06 (95% CI, 0.71-1.42)</td>
<td>0.29 (95% CI, 0.12-0.46)</td>
<td>0.21 (95% CI, 0.09-0.33)</td>
</tr>
<tr>
<td><strong>RRR vs. placebo</strong></td>
<td>-</td>
<td>73% (95% CI, 57.1%-83.0%), p &lt; 0.001</td>
<td>80% (95% CI, 66.3%-88.1%), p &lt; 0.001</td>
</tr>
</tbody>
</table>

- **Secondary:**
  - RR of a having at least ≥ 1 GF relative to placebo
    - **Rilonacept 160 mg:** 0.35 (95% CI, 0.24-0.67), p < 0.001 (RRR = 65.3%, NNT = 2)
    - **Rilonacept 80 mg:** 0.4 (95% CI, 0.20-0.60), p < 0.001 (RRR = 60.0%, NNT = 2)
  - Data for those with ≥ 2 GFs relative to placebo had over 80% RRRs

### Schumacher et al – Safety Results

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Rilonacept 80 mg</th>
<th>Rilonacept 160 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any AE</strong></td>
<td>48 (60.8%)</td>
<td>49 (61.3%)</td>
<td>53 (65.4)</td>
</tr>
<tr>
<td><strong>Treatment-related AE</strong></td>
<td>6 (7.6%)</td>
<td>14 (17.5%)</td>
<td>26 (32.1%)</td>
</tr>
<tr>
<td><strong>Serious AE</strong></td>
<td>3 (3.8%)</td>
<td>3 (3.8%)</td>
<td>3 (3.7%)</td>
</tr>
<tr>
<td>- <strong>Death</strong></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Treatment-related serious AE</strong></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Infections/Infestations</strong></td>
<td>28 (22.8%)</td>
<td>15 (18.8%)</td>
<td>14 (17.3%)</td>
</tr>
<tr>
<td><strong>Most common AE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Injection site reaction</td>
<td>1 (1.3%)</td>
<td>7 (8.8%)</td>
<td>16 (19.8%)</td>
</tr>
<tr>
<td>- URTI</td>
<td>2 (2.5%)</td>
<td>4 (5.0%)</td>
<td>5 (6.2%)</td>
</tr>
<tr>
<td>- Bronchitis</td>
<td>1 (1.3%)</td>
<td>4 (5.0%)</td>
<td>5 (6.2%)</td>
</tr>
<tr>
<td>- Pain in extremity</td>
<td>4 (5.1%)</td>
<td>2 (2.5%)</td>
<td>3 (3.7%)</td>
</tr>
<tr>
<td>- Headache</td>
<td>1 (1.3%)</td>
<td>5 (6.3%)</td>
<td>2 (2.5%)</td>
</tr>
</tbody>
</table>

- No increased risk of rebound flares after therapy cessation versus placebo
Schumacher et al – Strengths & Limitations

Strengths
• Caucasian, middle-aged, males
• High RRRs, low NNTs
• Rebound phenomenon is unlikely

Limitations
• Short study duration
• Small study population to assess safety
• Power calculation not described
• More polyarticular gout in placebo group
• Missing baseline information about medication use and disease states that impact gout
• Blinding possibly compromised

Schumacher et al – Conclusions

Investigators’:
• Rilonacept is a new and efficacious option for preventing GFs during ULT initiation
• Rilonacept significantly reduces GFs relative to placebo
• Rilonacept has a favorable safety and tolerability profile
• Rilonacept may improve ULT adherence and ultimately improve disease control

Seminarian’s:
• Rilonacept 160 mg is more efficacious for preventing GFs during ULT initiation than 80 mg
• Rilonacept can cause URTI, bronchitis, and injection site reactions
• Longer study durations of at least 6 months are needed to further assess the usefulness of rilonacept
Rilonacept for Gout Flare Prevention in Patients Receiving Uric Acid-lowering Therapy: Results of RESURGE, a Phase III, International Safety Study

Sundy JS. *J Rheumatol.* 2014; 41(8): 1703-1711

**Sundy et al - Objective & Study Design**

- **Objective:** To determine the efficacy and safety of once-weekly subcutaneous rilonacept 160 mg versus a matched placebo for prevention of gout flares in patients initiating or continuing ULT

- **Study Design:** 16-week, phase III, randomized, double-blind, placebo-controlled, multiregional trial with a 4-week follow-up.

- **Intervention:** Rilonacept 360 mg subcutaneously on day 1 followed by 160 mg weekly

- **Comparator:** Matched placebo
Sundy et al - Methods

• Outcomes:
  • Primary – Safety over 20 weeks
    • Incidence and types of treatment-emergent adverse events, including serious adverse events and clinically significant abnormal clinical laboratory variables
  • Secondary – Efficacy over 16 weeks
    • Mean number of gout flares per patient
    • Proportion of patients with ≥ 1 and ≥ 2 flares
    • Number of flares days
    • Time to first flare

Sundy et al - Methods

• Population: 1315 patients from the US, UK, Germany, South Africa, India, Indonesia, and Taiwan were randomized in a 3:1 ratio

<table>
<thead>
<tr>
<th>INCLUSION CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-80 years old with gout involving at least 6/13 of the ACR criteria</td>
</tr>
<tr>
<td>Initiating or continuing ULT</td>
</tr>
<tr>
<td>Serum uric acid ≥ 7.0 mg/dl or visible tophi for those with ≥ 2 months of ULT at baseline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EXCLUSION CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute gout flare &lt; 2 weeks before screening</td>
</tr>
<tr>
<td>Intolerance/inadequate response to allopurinol</td>
</tr>
<tr>
<td>Glucocorticoid use within 4 weeks</td>
</tr>
<tr>
<td>NSAID or colchicine use within 2 weeks</td>
</tr>
<tr>
<td>EGFR &lt; 30 ml/min/1.73 m²</td>
</tr>
<tr>
<td>Increased risk of infection (e.g. chronic or active infections, recent anti-infective treatment, current/previous TB)</td>
</tr>
<tr>
<td>Pregnant, lactating, or men/women unwilling to use adequate contraception</td>
</tr>
</tbody>
</table>
Sundy et al - Methods

1,315 - Randomized
330 - Placebo
16.4% - Placebo drop-outs
3.0% - AE
3.9% - Lost to follow-up
6.6% - Other
985 - Rilonacept
16.3% - Rilonacept drop-outs
4.7% - AE
4.0% - Lost to follow-up
5.5% - Other
1,100 Completed the study

Sundy et al – Statistical Analysis

- Power: A sample size of ≥ 900 rilonacept patients was desired to identify safety concerns associated with rilonacept
- A full analysis set was used
- No formal statistical tests were used for safety assessments
- Wilcoxon rank sum test with exact method using Monte Carlo Estimation – continuous endpoints
- Fisher’s exact test – proportional assessments
- Kaplan-Meier curve – time to first gout flare
Sundy et al – Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N = 330)</th>
<th>Riloncept (N = 985)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.4 (10.6 SD)</td>
<td>52.8 (11.5 SD)</td>
</tr>
<tr>
<td>Sex, male</td>
<td>297 (90.0%)</td>
<td>857 (87.0%)</td>
</tr>
<tr>
<td>White</td>
<td>210 (64.6%)</td>
<td>658 (66.8%)</td>
</tr>
<tr>
<td>BMI</td>
<td>31.6 (6.0 SD)</td>
<td>32.2 (6.9 SD)</td>
</tr>
<tr>
<td>SUA (mg/dl)</td>
<td>8.2 (2.0 SD)</td>
<td>8.0 (1.9 SD)</td>
</tr>
<tr>
<td>Presence of tophi</td>
<td>102 (30.9%)</td>
<td>279 (28.3%)</td>
</tr>
<tr>
<td>Renal/urinary disorder</td>
<td>12 (3.6%)</td>
<td>44 (4.5%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>172 (52.7%)</td>
<td>521 (52.9%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>52 (15.8%)</td>
<td>269 (17.2%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>40 (12.1%)</td>
<td>133 (13.5%)</td>
</tr>
<tr>
<td>Initiating ULT</td>
<td>212 (64.2%)</td>
<td>614 (62.3%)</td>
</tr>
<tr>
<td>Continuing ULT</td>
<td>118 (35.8%)</td>
<td>371 (37.7%)</td>
</tr>
</tbody>
</table>

Sundy et al – Safety Results

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Riloncept 160 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>59.1%</td>
<td>66.6%</td>
</tr>
<tr>
<td>Treatment-related AEs</td>
<td>13.0%</td>
<td>27.5%</td>
</tr>
<tr>
<td>Serious AE</td>
<td>3.9%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Death</td>
<td>0.9%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Treatment-related serious AE</td>
<td>0.6%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Injection site reactions or erythema</td>
<td>8.2%</td>
<td>19.2%</td>
</tr>
<tr>
<td>Infections/Infestations</td>
<td>19.1%</td>
<td>20.1%</td>
</tr>
<tr>
<td>URTI</td>
<td>10.5%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Neutrophil values &lt; 1500 cells/ul</td>
<td>3 (1.0%)</td>
<td>30 (3.3%)</td>
</tr>
<tr>
<td>Headache</td>
<td>7.9%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Musculoskeletal pain/discomfort</td>
<td>9.7%</td>
<td>11.2%</td>
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</table>
Sundy et al – Efficacy Results

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Rilonacept 160 mg</th>
<th>RRR</th>
<th>NNT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean # of GF/patient</td>
<td>1.73</td>
<td>0.51</td>
<td>70.3%</td>
<td>-</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(95% CI, 1.44-2.02)</td>
<td>(95% CI, 0.44-0.59)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ≥ 1 GF</td>
<td>51.1%</td>
<td>25.7%</td>
<td>49.6%</td>
<td>4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(95% CI, 0.44-0.59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ≥ 2 GFs</td>
<td>34.7%</td>
<td>11.7%</td>
<td>66.4%</td>
<td>5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(95% CI, 0.44-0.59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total # of GF days/patient</td>
<td>7.7</td>
<td>2.7</td>
<td>64.9%</td>
<td>-</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(95% CI, 6.4-9.0)</td>
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</tr>
</tbody>
</table>

- There was no difference between those who initiated versus continued allopurinol therapy.

Sundy et al – Strengths & Limitations

**Strengths**
- Large study population
- Includes patients who were initiating or continuing ULT
- Describes concomitant disease states
- No increased risk of infection was found with rilonacept

**Limitations**
- Short duration
- No safety statistics
- No information about baseline use of medications that may increase gout risk
- Blinding possibly compromised
Sundy et al – Conclusions

**Investigators’:**
- Rilonacept 160 mg has an acceptable safety profile
- The AEs identified were consistent with previous trials
- Rilonacept can be used for patients starting or continuing ULT who have a variety of comorbidities
- Rilonacept 160 mg efficacy results confirmed a benefit in terms of reducing gout flares

**Seminarian’s:**
- Rilonacept may be more useful for continuing ULT situations
- Rilonacept-associated infections seem less concerning over 16 weeks
- It remains difficult to draw conclusions about the use of rilonacept for longer durations or about the cost-effectiveness of the therapy

Other Research

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>N</th>
<th>Duration</th>
<th>Conclusions/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitha, 2013</td>
<td>Rilonacept vs placebo</td>
<td>248</td>
<td>16 weeks</td>
<td>• Rilonacept 160 mg provided a statistically significant 72.6% RRR compared to placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Most common AEs were ISR and URTI</td>
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<td>• An increase in rilonacept-associated infections was not identified</td>
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<td>Schlesinger, 2011</td>
<td>Canakinumab vs colchicine</td>
<td>432</td>
<td>16 weeks</td>
<td>• Canakinumab significantly reduced the number of flares compared to colchicine 0.5 mg</td>
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<td>• Mean number of GF/person was 0.75 with colchicine</td>
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<td>• Canakinumab’s results ranged from 0.23 to 0.51 depending on the dose</td>
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<td>• Infections occurred in 18% of canakinumab patients and in 12% of colchicine patients</td>
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</tbody>
</table>

Risks and Benefits of Rilonacept

**Risks**
- Expensive
- No efficacy data beyond 16 weeks
- No safety data beyond 20 weeks
- Injection site reactions
- URTIs

**Benefits**
- May prevent gout flares during ULT
- May improve adherence to ULT
- Provides an alternative to NSAIDs, colchicine, and steroids
- NNTs are small and RRRs are high

Evidence-Based Conclusions

Use colchicine, NSAIDS, or possibly corticosteroids for GF prophylaxis during ULT initiation

Contraindication to first line agents

Assess gout disease burden, ULT use, and patient preference

Severe gout burden with ULT-precipitated GFs

Mild gout burden and/or no previous ULT trial

Consider rilonacept x 16 weeks if affordable

Avoid rilonacept

*Future Research:* Studies with longer durations and more studies of interleukin-1 inhibitors for acute gout flare treatment
Role of the Pharmacist

- Educate patients about modifiable risk factors such as diet and weight loss
- Adjust medications (e.g. thiazides, loop diuretics)
- Encourage adherence to ULT
- Evaluate candidacy for regimens such as NSAIDS, colchicine, or steroids
- Be aware of future IL-1 inhibitor research for gout and possible FDA approvals
- Consider rilonacept for patients with severe gout burden, ULT precipitated GFs, and with an absolute contraindication to NSAIDS, colchicine, and steroids

Rilonacept For Gout Flare Prophylaxis During Urate Lowering Therapy Initiation

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November 7, 2017
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University of Utah College of Pharmacy