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IN CASE YOU MISSED... YEAR IN REVIEW

UNCONTROLLED GOUT

Comprehensive Updates on the Latest Management Strategies

This continuing education activity is provided by VINDICO medical education®

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This continuing education activity is provided by
This activity is supported by an educational grant from Horizon Therapeutics USA, Inc.
Beyond Simple Pain: Burden and Complications of Uncontrolled Gout
Suneet Grewal, MD

Early Detection: Evidence-Based Tools to Detect Uncontrolled Gout
Michael Pillinger, MD

Gout No More: Best Practices for Optimal Management of Uncontrolled Gout
Puja Khanna, MD

Panel Discussion: Multidisciplinary/Interprofessional Strategies to Improve Patient Outcomes
Beyond Simple Pain: Burden and Complications of Uncontrolled Gout

Suneet Grewal, MD
East Bay Rheumatology Medical Group
San Leandro, CA
Relevant Financial Disclosures

• No relevant financial relationships to disclose.
# Prevalence of Gout and Hyperuricemia in the US and Decadal Trends (NHANES 2007-2016)

<table>
<thead>
<tr>
<th>Prevalence of Gout in the US</th>
<th>~9.2 million people</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of adult population</td>
<td></td>
</tr>
<tr>
<td>• Overall</td>
<td>3.9%</td>
</tr>
<tr>
<td>– Men</td>
<td>5.2%</td>
</tr>
<tr>
<td>– Women</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prevalence of Hyperuricemia</th>
<th>~28 million people</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of adult population</td>
<td></td>
</tr>
<tr>
<td>• Overall</td>
<td>11.9%</td>
</tr>
<tr>
<td>– Men</td>
<td>20.2%</td>
</tr>
<tr>
<td>– Women</td>
<td>4.2%</td>
</tr>
</tbody>
</table>

NHANES = National Health and Nutrition Examination Survey.
Comorbidities Associated With Gout

CKD = chronic kidney disease.
Multiple Comorbidities in Gout Patients

The New York Gout Cohort

- Approximately 25% of patients in the New York Gout cohort had 4 comorbidities
- Nearly half the cohort had ≥4 comorbidities

Poor Serum Urate Control and Excess Cardiovascular Risk in Patients With Gout

Matched cohort study evaluating the associations between gout with major adverse cardiovascular events, heart failure (HF) hospitalization, and cardiovascular disease (CVD)-related death in US veterans

Risk of HF and Atherosclerotic CV Events in Gout vs Non-Gout Matched Controls

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Non-Gout (N=5,407,379)</th>
<th>Gout (N=559,243)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Rate per 1000 PY (95% CI)</td>
</tr>
<tr>
<td>Overall CVD</td>
<td>879,903</td>
<td>22.37 (22.32-22.42)</td>
</tr>
<tr>
<td>MACE</td>
<td>789,318</td>
<td>19.89 (19.84-19.93)</td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>64,856</td>
<td>1.62 (1.60-1.63)</td>
</tr>
<tr>
<td>CVD Death</td>
<td>98,735</td>
<td>23.23 (23.01-23.38)</td>
</tr>
<tr>
<td>CAD-death</td>
<td>310,903</td>
<td>7.71 (7.68-7.74)</td>
</tr>
<tr>
<td>HF-death</td>
<td>49,834</td>
<td>1.24 (1.23-1.25)</td>
</tr>
</tbody>
</table>

*Matched on age, sex, and year of VA enrollment
**In addition to matched factors, models adjusted for race, ethnicity, body mass index, smoking status, and comorbidities: myocardial infarction, stroke, hypertension, diabetes, lung disease, cancer, fracture, ulcer, and chronic kidney disease

- Gout was associated with a 68% increased risk of HF hospitalization, 25% increased risk of HF-related death, and a 22% increased risk of major adverse cardiovascular events
- Poorly controlled serum urate conferred a higher risk of CVD events independent of ULT

Impact of Uncontrolled Gout on Patient QoL

Patients with chronic gout have a lower QoL than age-matched controls.

PCS = Physical Component Score of the Short Form Health Survey (SF-36); QoL = quality of life.
Impact of Uncontrolled Gout on Patient QoL

Economic burden – gout patients lose workdays to flares

<table>
<thead>
<tr>
<th>Workdays Lost/Year</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td>1-5</td>
<td>20</td>
</tr>
<tr>
<td>6-30</td>
<td>30</td>
</tr>
<tr>
<td>30-60</td>
<td>18</td>
</tr>
<tr>
<td>60-90</td>
<td>5</td>
</tr>
<tr>
<td>90-120</td>
<td>3</td>
</tr>
<tr>
<td>&gt;120</td>
<td>3</td>
</tr>
</tbody>
</table>

In Case You Missed... Year in Review

Uncontrolled Gout

Comprehensive Updates on the Latest Management Strategies
Venous Thromboembolism in Patients With Gout in the US

Alka Mithal, Maanek Sehgal, Brian LaMoreaux, and Gurkirpal Singhors

Abstract # 0240
Presented at: ACR Convergence 2023
November 10-15, 2023
San Diego, CA

ACR = American College of Rheumatology.
Venous Thromboembolism in Patients With Gout in the US

Study Design and Findings:

- Examination of all 2020 inpatient hospitalizations with a primary or secondary diagnosis of gout and venous thromboembolism (VTE) from the National Inpatient Sample (NIS; stratified random sample of all US community hospitals designed to produce national estimates of inpatient utilization, cost, and outcomes)

- Of the 19.7 million all-cause US hospitalizations in persons aged ≥45 years, 785,905 occurred in people aged ≥45 years with a diagnosis of gout

- Of these hospitalizations, 79,260 (10.1%) also had a concomitant diagnosis of VTE

- Only 8.2% of hospitalizations in the general population aged ≥45 years had a concomitant diagnosis of VTE (P<.001 compared to persons with gout)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender</th>
<th>Hospitalizations with a Diagnosis of Gout N</th>
<th>Hospitalizations with VTE in Persons with Gout n (%)</th>
<th>All-cause Hospitalizations N</th>
<th>All-cause Hospitalizations with VTE n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-64</td>
<td>Male</td>
<td>165,325</td>
<td>16,710 (10.1%)</td>
<td>416,3365</td>
<td>323,625 (7.8%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>45,205</td>
<td>5150 (11.4%)</td>
<td>3,519,950</td>
<td>280,900 (8.0%)</td>
</tr>
<tr>
<td>≥65</td>
<td>Male</td>
<td>375,685</td>
<td>35,600 (9.5%)</td>
<td>5,756,550</td>
<td>473,905 (8.2%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>199,650</td>
<td>21,800 (10.9%)</td>
<td>6,300,300</td>
<td>547,550 (8.7%)</td>
</tr>
<tr>
<td>All patients ≥45</td>
<td></td>
<td>785,905</td>
<td>79,260 (10.1%)</td>
<td>19,741,255</td>
<td>1,626,055 (8.2%)</td>
</tr>
</tbody>
</table>

Venous Thromboembolism in Patients With Gout in the US

Findings:

- Persons with gout and VTE had a mean age of 71.6 years and were mostly men (66%)
- The average cost of each hospitalization was $76,373 (95% confidence limit $73,343-$79,403), with a total annual national cost of over $6.1 billion

<table>
<thead>
<tr>
<th></th>
<th>Hospitalizations with a Diagnosis of Gout (N=785,905)</th>
<th>Gout Hospitalizations with a VTE (N=79,260)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (95% CI)</td>
<td>71.8 (71.7–71.9)</td>
<td>71.6 (71.4–71.8)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>541,010 (68.8%)</td>
<td>52,310 (66.0%)</td>
</tr>
<tr>
<td>Length of hospitalization, days, mean (95% CI)</td>
<td>5.8 (5.7–5.8)</td>
<td>6.4 (6.3–6.5)</td>
</tr>
<tr>
<td>Cost of hospitalization, USD, mean (95% CI)</td>
<td>72,533 (70,584–74,483)</td>
<td>76,373 (73,344–79,403)</td>
</tr>
<tr>
<td></td>
<td>Medicare</td>
<td>Medicare</td>
</tr>
<tr>
<td></td>
<td>572,575 (72.5%)</td>
<td>59,085 (70.5%)</td>
</tr>
<tr>
<td></td>
<td>Medicaid</td>
<td>Medicaid</td>
</tr>
<tr>
<td></td>
<td>48,495 (6.1%)</td>
<td>4975 (5.9%)</td>
</tr>
<tr>
<td></td>
<td>Private insurance</td>
<td>Private insurance</td>
</tr>
<tr>
<td></td>
<td>131,605 (16.7%)</td>
<td>12,305 (14.7%)</td>
</tr>
</tbody>
</table>

Key Takeaways

- One out of 10 hospitalizations in persons with gout have a concomitant diagnosis of VTE, with considerable clinical and economic consequences
- VTE occurred more frequently in hospitalized patients with gout aged ≥45 years (1/10 vs 1/12 patients); this has resulted in considerable economic burden

USD = United States dollar.
Identifying and Addressing Suboptimal Urate Lowering Therapy in Gout Patients With Chronic Kidney Disease

Lena Eder and David Leverenz

Abstract # 1909
Presented at: ACR Convergence 2023
November 10-15, 2023
San Diego, CA
Identifying and Addressing Suboptimal ULT in Gout Patients With CKD

Study Design and Goals:

- Mined electronic health record (EHR) data to identify patients seen within the academic medical center health system between 02/01/2022 and 02/01/2023
  - Charts of 121 patients reviewed who had an ICD-10 diagnosis code related to gout and CKD
  - Data points examined:
    - Glomerular filtration rate (GFR)
    - Stage of CKD
    - Serum uric acid (sUA), and whether it was checked in the past year
    - Type of ULT and dose, if applicable
    - Whether their gout was optimally managed according to the 2020 American College of Rheumatology Guideline for the Management of Gout

ICD-10 = International Classification of Diseases, 10th edition; ULT = urate-lowering therapy.
Identifying and Addressing Suboptimal ULT in Gout Patients With CKD

Findings:

- 40% had CKD 3, 35% had CKD 4, and 25% had CKD 5; average GFR was 28.5
- 52% (n=63) had a sUA checked within a year of their appointment, of which the mean sUA was 7.8
- 77% (n=93) had an active prescription for allopurinol or febuxostat
- 96% (n=116) were managed primarily by their PCP and had never seen a rheumatologist
- Overall, only 16% (n=19) of all the patients reviewed had optimal management of their gout according to ACR guidelines

Key Takeaways:

- Many of these patients were not being treated to goal—with suboptimal doses of ULT or no ULT at all
  - May be due to gaps in knowledge by PCP regarding ULT in patients with a diagnosis of CKD
- These findings suggest the need for an educational initiative or health systems-based intervention to address the care of these patients

Filling Gaps in Female Gout: A Cross-Sectional Study of 192,000 Patients Hospitalized With Gout From 2005 to 2015

E. Rodríguez-Sosa, E. De Miguel, F. Borrás, and M. Andrés

Abstract # OP0155
Presented at: EULAR 2023 Annual Meeting
May 31-June 3, 2023
Milan, Italy

EULAR = European Alliance of Associations for Rheumatology.
A Cross-Sectional Study of 192,000 Patients Hospitalized With Gout From 2005 to 2015

Study Design and Goals:

• Retrospective, nation-based cohort study of all Spanish hospitalizations, including gout as either primary or secondary diagnosis (ICD-9 coding) from 2005 to 2015

• Comorbidities of interest: obesity, dyslipidemia, CKD, diabetes mellitus, coronary heart disease, chronic heart failure, peripheral vascular disease, arrhythmia, VTE, cerebrovascular disease, dementia, urinary tract infection, pneumonia, sepsis, obstructive pulmonary disease, liver disease, and rheumatological disease

• A multiple logistic regression model was built to discern the strength of the association of comorbidities with each sex, for the entire population and stratifying by age (≤60 years and >60 years)

• 192,037 admissions were analyzed, 5.47% (n=10,512) with gout as primary diagnosis

• 158,646 cases occurred in men (82.6%) significantly younger than the women (64.0±14.4 vs 73.9±13.7 years; \( P<.001 \))

Rodríguez-Sosa E, et al. Presented at: EULAR 2023 Congress; May 31-June 3, 2023; Milan, Italy. Abstract POS0367.
• Differential comorbidity profile between men and women was confirmed:
  – Renal and rheumatic diseases were closely linked to women aged <60 years with gout; heart failure was most closely linked to women aged >60 years with gout
  – For men, coronary heart disease and obstructive pulmonary disease were the chief associations with gout

CHF = chronic heart failure; UTI = urinary tract infection; DM = diabetes mellitus; rheum = rheumatological disease; PVD = peripheral vascular disease; CHD = coronary heart disease; obes = obesity; OPD = obstructive pulmonary disease.
Rodríguez-Sosa E, et al. Presented at: EULAR 2023 Congress; May 31-June 3, 2023; Milan, Italy. Abstract POS0367.
A Cross-Sectional Study of 192,000 Patients Hospitalized With Gout From 2005 to 2015

Key Takeaways

- Nationwide analysis of 11 years of hospitalizations with gout confirm a different comorbidity profile between men and women.
- Women with gout were significantly older and more likely to suffer from heart failure, obesity, urinary infection, and diabetes.
- The association between sex and certain comorbidities is intense enough for sex prediction via an algorithm, with considerable accuracy.
- A different approach for female gout is thus needed to reduce gender blindness.

Rodríguez-Sosa E, et al. Presented at: EULAR 2023 Congress; May 31-June 3, 2023; Milan, Italy. Abstract POS0367.
Projected Benefits of Gout Control on the Health and Economic Burden of CKD Patients With Uncontrolled Gout in the US

J. Card-Gowers, L. Webber, L. Retat, M. Piotrowski, B. Lamoreaux, B. Marder, and A. Kumar

Abstract # POS-0509
Presented at:
EULAR 2023 Annual Meeting
May 31-June 3, 2023
Milan, Italy

Abstract # FR-PO921
Presented at:
ASN Kidney Week 2023
November 2-5, 2023
Philadelphia, PA

ASN = American Society of Nephrology.
Projected Health and Economic Burden of Controlled vs Uncontrolled Gout in Patients With CKD

Study Design and Goals:

• To quantify the 2023-2035 health and economic burden of controlled and uncontrolled gout in the US CKD population

• A validated microsimulation model was used to project gout burden in the US CKD population, which was reproduced virtually using United Nations data
  – Each individual was assigned estimated glomerular filtration rate (eGFR), albuminuria, and serum urate (SU) values, which were extracted through analysis of the US NHANES (2011 to 2018)
  – The prevalence of self-reported gout by age, sex, and CKD stage was also examined
  – Controlled and uncontrolled gout costs, eGFR decline rates, tophi and flare probabilities were drawn from the literature

• Uncontrolled gout was defined as SU >6 mg/dL and ≥2 flares/year or the presence of tophi

Projected Health and Economic Burden of Controlled vs Uncontrolled Gout in Patients With CKD

Findings:

- A predicted 9.2% growth in US in gout and CKD prevalence between 2023 and 2035 (7.6 → 8.3 million)
- By 2035: a projected 10.2% of CKD patients (5.5 million) with uncontrolled gout
- Between 2023 and 2035: a projected 9.4% growth in the number of people living with gout and advanced CKD (4.7 → 5.8 million)
Projected Health and Economic Burden of Controlled vs Uncontrolled Gout in Patients With CKD


Difference in Incident Complications in CKD Patients Between Treated (Intervention) and Untreated (Baseline) Uncontrolled Gout Scenarios

- **Baseline**: Modeled patients with gout were assigned complication risks for stroke, diabetes, and hypertension; also included: direct and indirect costs, oral ULT use/efficacy probability, and utility weight.

- **Intervention**: Modeled patients with uncontrolled gout (SU >6 mg/dL despite oral ULT, and ≥2 gout flares/year or ≥1 tophi) were “treated” with pegloticase, assuming a 71% SU-lowering efficacy rate (SU <6 mg/dL) through simulation end.
Projected Health and Economic Burden of Controlled vs Uncontrolled Gout in Patients With CKD

Key Takeaways

- In US CKD patients, gout prevalence and symptoms (tophi, flares) are projected to rise between 2023 and 2035
- Factors driving this increase are predominantly population growth and aging
- Uncontrolled gout is projected to contribute most to the health and economic burden of gout in CKD
  - Urate-lowering interventions may help reduce this burden by lowering the proportion of uncontrolled gout

Projected Annual Costs of Controlled and Uncontrolled Gout in CKD (2023 US$, Billions)

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost of controlled gout</th>
<th>Cost of uncontrolled gout</th>
</tr>
</thead>
<tbody>
<tr>
<td>2023</td>
<td>10.5</td>
<td>33.1</td>
</tr>
<tr>
<td>2029</td>
<td>11.1</td>
<td>34.8</td>
</tr>
<tr>
<td>2035</td>
<td>11.5</td>
<td>36.0</td>
</tr>
<tr>
<td>Cumulative (2023 – 2035)</td>
<td>143.7</td>
<td>450.7</td>
</tr>
</tbody>
</table>

- Predictions:
  - Combined direct and indirect costs of gout in CKD patients will increase from $43.5 to $47.5 billion from 2023 to 2035
  - **76% of cumulative costs are predicted to be due to uncontrolled gout**
  - US could save significantly (an estimated $169.9 billion) between 2023 and 2035 through good gout control in patients with CKD

Evidence-Based Tools to Detect and Assess Uncontrolled Gout

Michael H. Pillinger, MD, FACP
Professor of Medicine and Biochemistry and Molecular Pharmacology
New York University Grossman School of Medicine
New York, NY
Relevant Financial Disclosures

- **Consultant**: Horizon, Scilex, Sobi
- **Independent Research Contractor**: LG
When Is Gout “Controlled?”

- Serum urate ≤6.0 mg/dL
- No flares currently and no likelihood of future flares
  - How to assess “likelihood”?
- No tophi or urate deposition in tissues
  - How to assess tophi? What about the ones you can’t see?
- No bony damage, or no damage that is interfering with function
  - And no likelihood of future bony damage!
- Gout not adding to risk of incidence or progression of comorbidities in the future
  - eg, cardiovascular, renal disease
  - Data on role of gout in these remain controversial

When Is Gout “Uncontrolled?”

• Undiagnosed
• Treated only for flares
  – Will not keep future flares away!
  – Care by emergency department/urgent care with no long-term perspective
• Urate lowering started, but the patient is not being treated to target sUA <6.0 mg/dL
  – Physician is not recognizing the importance of the target
  – Patient is not complying, despite physician’s efforts
• Urate lowering therapy is maximized, but the patient still has sUA >6.0 and having flares
• sUA ≤6.0 is achieved, but the patient is still having flares
• sUA ≤6.0 is achieved and the patient is not having flares, but is still suffering the metabolic consequences of gout

Why Is Gout Uncontrolled?
Adherence to Gout Treatment Is Poor

Table 1. Studies measuring adherence to urate lowering therapy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Site</th>
<th>Source</th>
<th>Size of gout population</th>
<th>Adherence at 1 year (%)</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>[13]</td>
<td>Italy</td>
<td>Research database</td>
<td>3727</td>
<td>3.2</td>
<td>Mantarro et al.</td>
</tr>
<tr>
<td>[14]</td>
<td>Ireland</td>
<td>Pharmacy claims-based records</td>
<td>15,908</td>
<td>35.3</td>
<td>McGowan et al.</td>
</tr>
<tr>
<td>[15]</td>
<td>Netherlands</td>
<td>MEMS</td>
<td>29</td>
<td>84**</td>
<td>de Klerk et al.</td>
</tr>
<tr>
<td>[16]</td>
<td>South Korea</td>
<td>Pill counts</td>
<td>132</td>
<td>71.2</td>
<td>Lee et al.</td>
</tr>
<tr>
<td>[22]</td>
<td>United Kingdom</td>
<td>Medical record database</td>
<td>49,359</td>
<td>39.7</td>
<td>Kuo et al.</td>
</tr>
<tr>
<td>[28]</td>
<td>New Zealand</td>
<td>Pharmacy records</td>
<td>953</td>
<td>78</td>
<td>Horsburg et al.</td>
</tr>
</tbody>
</table>

MEMS, Medication Event Monitoring Systems.
*(Compliance rate measured as: days’ supply from 1st prescription filled / fill date of 2nd prescription filled – fill date of 1st prescription filled) for each fill and for up to 24 months of fill history.
*(Average ‘taking compliance’ across all patients measured as (total number of recorded medication events / total number of prescribed doses) × 100%.

ACR/EULAR vs ACP Gout Treatment Guidelines

ACR—Initiate urate lowering if\(^1\):
• \(\geq 1\) tophi
• Radiographic damage
• \(\geq 2\) flares per year
• \(>1\) flare lifetime (conditional)
• First flare and CKD \(\geq 3\), sUA >9, urolithiasis (conditional)

Treat to sUA <6.0 mg/dL

EULAR—Very similar to ACR, but also treat at time of first flare if\(^2\):
• <40 years of age
• sUA >8.0 mg/dL
• Comorbidities

Treat to sUA <6.0 mg/dL
Accelerate to <5.0 mg/dL if tophi or severe gout present

ACP—Treat to avoid symptoms\(^3\)
• Urate lowering not necessarily mandated

DON’T treat to target

---

The TRUST Study: Comparing Treat to Target vs Treat to Avoid Symptoms in Gout Patients

(But rheumatologists are right!)

TTASx = treat to avoid symptoms; TTT-SU = treat-to-target serum urate.
Gout Treatment in the US Is Woefully Inadequate

- Total gout population in the US (8.3 million)
- Gout patients receiving some form of ULT (5.0 million)*
  - Gout patients “adequately treated” (0.5 million)*
  - Gout patients “inadequately treated” (4.5 million)*

Only about 6% of gout patients may be adequately treated!

- Poor patient compliance
- Poor physician performance
- Incorrect diagnosis
- Treatment intolerance
- True treatment failure

How Can We Identify and Characterize Uncontrolled Gout?

Easy
- sUA > 6.0
- Ongoing flares
- With or without adequate medical treatment

Appropriate for the ascertainment of compliance, acceleration of therapy and, if already on maximal oral therapy, advancement to pegloticase

Hard
Despite sUA < 6.0 and no current flares, how can we tell that:
- Flares will not recur in the near or intermediate future?
  - Since flares are intermittent and even 1 flare per year would indicate noncontrol
- The urate burden is resolved?
- Comorbidities of gout will not progress (due to gout?)
- Bone damage is over?

A need exists for better assessment tools to identify and guide treatment for this kind of uncontrolled gout
- Imaging?
- New or better used biochemical markers?

Answering these questions may help reinforce the need to meet the “easy” part of gout control

The following abstracts may help address these issues
In Case You Missed... Year in Review
Uncontrolled Gout
Comprehensive Updates on the Latest Management Strategies
Target Serum Urate Levels, Recurrent Gout Flare Rates, and Gout-Primary Hospitalizations: Nationwide Prospective Cohort Study of 3613 Gout Patients

Natalie McCormick, Chio Yokose, Gregory Challener, Amit Joshi, Sruthi Tanikella, and Hyon K. Choi

Abstract # 1120
Presented at: ACR Convergence 2023
November 10-15, 2023
San Diego, CA
Study Design and Findings:

- Prospective cohort study of 3613 prevalent gout patients (86% male, mean age, 60 years); recruited 2006-2010
- At 1 year:
  - Going from a SU of 6 to 7 increases flare risk almost 6-fold
  - In patients whose urate is the up at 10, flare risk increases 32-fold

| Table 1. Rate and Rate Ratio (RR) for Recurrent Gout Flares According to Serum Urate Level and Follow-Up Time from Baseline |
|---------------------------------|-----------------|------------------|-----------------|-----------------|-----------------|
|                                | No of Gout Patients | Follow-up, Person years (PY) | No of Flares | Flares per 1000 PY | Crude RR (95% CI) | Age, Sex, and Race Adjusted RR (95% CI) |
|                                |                  |                             |               |                  |                  |                                   |
| 1 Year                          |                  |                             |               |                  |                  |                                   |
| <6 mg/dL                        | 1057             | 1057                        | 10            | 9.5              | 1.0 (ref)        | 1.0 (ref)                        |
| 6 to 7                          | 781              | 780                         | 42            | 53.9             | 5.69 (2.86 to 11.34) | 5.03 (2.52 to 10.07) |
| 7 to 8                          | 872              | 870                         | 109           | 125.3            | 13.24 (6.93 to 25.29) | 11.64 (6.06 to 22.35) |
| 8 to 9                          | 609              | 609                         | 77            | 126.4            | 13.36 (6.91 to 25.81) | 11.81 (6.08 to 22.92) |
| 9 to 10                         | 212              | 212                         | 41            | 193.8            | 20.47 (10.26 to 40.87) | 18.95 (9.46 to 37.97) |
| >10 mg/dL                       | 82               | 82                          | 25            | 306.7            | 32.40 (15.57 to 67.46) | 29.13 (13.94 to 60.87) |
| Per mg/dL                       | 3613             | 3608                        | 304           | 84.3             | 1.60 (1.49 to 1.71)  | 1.59 (1.48 to 1.71)  |

Key Takeaways

• 95% and 98% of flares occurred in baseline SU ≥6 and ≥5 mg/dL groups, respectively
• Higher SU levels are strongly associated with frequency of recurrent flares in a graded manner
• Associations were more prominent for hospitalized flares, with no cases among those with SU <5 mg/dL
• These findings support the utility of target urate levels for gout patient care, consistent with a treat-to-target approach recommended by ACR and EULAR
Clinical Impact of Cardiovascular Monosodium Urate Deposits Measured by DECT: A Retrospective Evaluation


Abstract # OP0155
Presented at: EULAR 2023 Annual Meeting
May 31-June 3, 2023
Milan, Italy

DECT = Dual-energy computed tomography.
Clinical Impact of Cardiovascular Monosodium Urate Deposits Measured by DECT

Study Design and Findings:

- Retrospective analysis of 189 patients with clinical suspicion of gout examining:
  - 1) possible correlations of CV MSU deposits with clinical gout diagnosis
  - 2) the impact of CV MSU deposits on MACE in gout patients
- Of the 189, 69.3% revealed a clinical diagnosis of gout, and 38.2% of these were tophaceous
- MACE were observed in 35 patients (18.5%) with a higher prevalence in patients with CV MSU deposits (compared to those without CV MSU (25.9% vs 12.5%; \( P=0.022 \))
  - All 22 patients with MACE and CV MSU had gout or hyperuricemia
- MACE were increased when there was urate deposition, and urate deposition was increased when the patients had gout

Key Takeaways

- First evaluation of clinical features of patients revealing CV MSU deposits detected by DECT
- The higher prevalence of MACE in patients with CV MSU deposits may help for risk stratification of gout patients
- Definitions of controlled gout should include some evidence of whether the vasculature is being appropriately treated

A Transversal Study of 826 Untreated Gout Patients Shows that Echogenicity of the Renal Medulla Increases With Gout Duration/Severity and Steroid Use

T. Bardin, Q. Nguyen, K. Tran, C. Tran, D. Huynh, D. M. Do, P. Richette, J. M. Correias, M. Resche-Rigon

Abstract #POS0086
Presented at: EULAR 2023 Annual Meeting
May 31-June 3, 2023
Milan, Italy
Echogenicity of the Renal Medulla Increases With Gout Duration/Severity and Steroid Use

• Confirm the finding of gouty microcrystalline nephropathy and examine its progression with gout duration
• Patients who had more severe gout seemed to have urate deposition within the kidney
  – They also had evidence of being on higher doses of steroids for gout

### Study Goals and Findings:

<table>
<thead>
<tr>
<th>Study Goals</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirm the finding of gouty microcrystalline nephropathy and examine its progression with gout duration.</td>
<td>Patients who had more severe gout seemed to have urate deposition within the kidney. They also had evidence of being on higher doses of steroids for gout.</td>
</tr>
</tbody>
</table>

### Multivariate analysis

#### Table 1: Summary of Multivariate Analysis

<table>
<thead>
<tr>
<th></th>
<th>Grade 0n = 541</th>
<th>Grade 1n = 147</th>
<th>Grade 2n = 138</th>
<th>p.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) median [IQR]</td>
<td>47 [38, 56]</td>
<td>51 [44, 59]</td>
<td>54 [45, 62]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Males n (%)</td>
<td>441 (81.7)</td>
<td>147 (100.0)</td>
<td>138 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension n (%)</td>
<td>145 (26.8)</td>
<td>64 (36.7)</td>
<td>88 (63.8)</td>
<td>0.006</td>
</tr>
<tr>
<td>CHD n (%)</td>
<td>6 (1.1)</td>
<td>7 (4.8)</td>
<td>7 (5.1)</td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes n (%)</td>
<td>62 (11.5)</td>
<td>17 (11.6)</td>
<td>27 (19.6)</td>
<td></td>
</tr>
<tr>
<td>Tophi n (%)</td>
<td>298 (55.1)</td>
<td>14 (95.9)</td>
<td>137 (99.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urinary stone n (%)</td>
<td>23 (4.3)</td>
<td>18 (12.2)</td>
<td>13 (9.4)</td>
<td></td>
</tr>
<tr>
<td>SUA (umol/l) median [IQR]</td>
<td>437 [322, 548]</td>
<td>533 [432, 602]</td>
<td>558 [493, 618]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR &gt; 60 ml/min n (%)</td>
<td>506 (93.5)</td>
<td>128 (87.1)</td>
<td>112 (81.2)</td>
<td></td>
</tr>
<tr>
<td>Maximum double contours</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0 n (%)</td>
<td>17 (34.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Thin n (%)</td>
<td>86 (20.7)</td>
<td>8 (5.4)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Medium n (%)</td>
<td>306 (73.6)</td>
<td>114 (77.8)</td>
<td>66 (47.8)</td>
<td></td>
</tr>
<tr>
<td>Thick n (%)</td>
<td>7 (1.7)</td>
<td>25 (17.0)</td>
<td>71 (51.4)</td>
<td></td>
</tr>
<tr>
<td>8 am cortisol median [IQR]</td>
<td>7.55 [3.58, 10.33]</td>
<td>6.60 [1.96, 10.72]</td>
<td>1.91 [0.59, 8.06]</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Y = years; IQR = interquartile range; BMI = body mass index.
Echogenicity of the Renal Medulla Increases With Gout Duration/Severity and Steroid Use

Key Takeaways

- Hyperechogenicity of the renal medullas progressively increased with gout duration, MSU deposition and steroid treatment, and is associated with decrease of renal function and hypertension.
- Gout may involve the kidneys, and these observations reinforce the early indication of ULDs in gout patients.

ULDs = urate-lowering drugs.
Bone Erosion Remodeling After Depletion of MSU Deposition With Intensive Urate Lowering With Pegloticase in Patients With Uncontrolled Gout: MIRROR RCT DECT Findings

N. Dalbeth, J. Botson, K. Saag, A. Kumar, L. Padnick-Silver, B. Lamoreaux, F. Becce

Abstract # POS0514
Presented at: EULAR 2023 Annual Meeting
May 31-June 3, 2023
Milan, Italy

RCT = randomized controlled trial.
MIRROR RCT DECT Findings: Bone Erosion Remodeling With Pegloticase

Study Design and Goals:

• To examine $V_{\text{MSU}}$ and bone erosion imaging findings in MIRROR RCT participants who underwent serial DECT imaging
• Analysis included 6 patients receiving pegloticase + MTX co-therapy and 2 patients receiving pegloticase + PBO
• $V_{\text{MSU}}$ markedly decreased during therapy in both treatment groups at week 52:
  - Peg + MTX: -94% ±9% [9 imaging regions of 6 patients]
  - Peg + PBO: -96% ±3% [4 imaging regions of 2 patients]

MTX = methotrexate; PBO = placebo; $V_{\text{MSU}}$ = MSU deposition volume.
Evidence of concomitant bone erosion remodeling was observed in 69% of evaluated erosions (75% of imaged regions; 75% of patients).

Of the 29 erosions with remodeling, 100% had a decrease in size (mean: -7% change at week 52), with recortication (4 erosions [14%]) and new bone formation also observed in 10% of erosions.

Key Takeaways

- In agreement with a prior serial DECT study, rapid and near complete $V_{\text{MSU}}$ depletion was observed within 1 year of initiating pegloticase therapy.
- Concomitant bone erosion remodeling was also observed after 52 weeks of pegloticase.
- These analyses suggest that bone remodeling is possible following MSU crystal depletion.

Gout No More: Best Practices for Optimal Management of Uncontrolled Gout

Puja Khanna, MD, MPH, FACR
Professor of Medicine
Department of Medicine – Rheumatology
University of Michigan
Ann Arbor, MI
Relevant Financial Disclosures

• *Advisor:* Arthrosi, Horizon, Sobi
1. About 90% of the patients with hyperuricemia underexcrete urate
2. Urate anion transporter 1 (URAT1) is the major transporter in renal reabsorption of urate
Urate-Lowering Drugs

Uricostatic Drugs
- XO inhibitors decrease UA synthesis in both overproduction and renal underexcretion
  - Allopurinol
  - Febuxostat

Uricosuric Drugs
- Inhibit UA reabsorption in proximal tubule
  - Potent (probenecid)
  - Moderate (fenofibrate)\(^a\)
  - Weak (losartan, atorvastatin)\(^a\)

Uricolytic Drugs
- Uricases catalyze ultimate degradation of UA to allantoin
  - Pegloticase

IV pegloticase is the mainstay of therapy for uncontrolled gout

\(^a\) Off-label use.

UA = uric acid.


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Background on Pegloticase

- Only current FDA-approved IV uricase for treating patients with suboptimally controlled gout
- Significant tophus-debulking effect seen within months in responders
- Limitations include:
  - Infusion reactions, PEG – antibodies that affect pharmacokinetics and pharmacodynamics
  - High titer antibody formation (>1:2430) associated with a loss of efficacy manifested by a rapid increase in the urate levels
- Emerging data since 2018 that combining pegloticase with immunomodulators (e.g., azathioprine, MTX, and leflunomide) may reduce ADA production
- Reduces blood pressure in patients with CKD
- Recent label change in 2022 with proof-of-concept trials – RECIPE and MIRROR

ADA = antidrug antibody; PEG = polyethylene glycol.
RECIPE Trial: Pegloticase + MMF

Proof-of-concept study: evaluate the ability of MMF to mitigate ADA production and improve efficacy of pegloticase

At 12 weeks, a serum urate level of 6 mg/dL was achieved in 19 (86%) of 22 participants in the MMF arm compared with 4 (40%) of 10 in the placebo arm ($P = .01$)

MMF therapy with pegloticase was well tolerated and showed clinically meaningful improvement in targeted serum urate level of 6 mg/dL at 12 and 24 weeks

ADA = antidrug antibody; MMF = mycophenolate mofetil.
MIRROR RCT: Pegloticase + Methotrexate

Urate-Lowering Response Rate

+ MTX 15-mg oral dose/week

<table>
<thead>
<tr>
<th>Month</th>
<th>Pegloticase+MTX (N=100)</th>
<th>Pegloticase+PBO (N=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 3</td>
<td>79.0%</td>
<td>40.4%</td>
</tr>
<tr>
<td>Month 6</td>
<td>*71.0%</td>
<td>38.5%</td>
</tr>
<tr>
<td>Month 9</td>
<td>*68.0%</td>
<td>36.5%</td>
</tr>
<tr>
<td>Month 12</td>
<td>*60.0%</td>
<td>30.8%</td>
</tr>
</tbody>
</table>

*Significant Cochran-Mantel-Haenszel treatment response difference (95% CI), p<0.0003

- Safety and efficacy findings further support 15 mg MTX weekly as co-therapy to pegloticase and showed no IRs after treatment at month 6.
- The proportion of patients with tophus resolution was higher at week 52 than week 24, suggesting continued therapeutic benefit beyond month 6 in some patients.

Response rates were nearly 2X higher among patients receiving pegloticase plus MTX versus pegloticase plus placebo through 12 months.

IRs = incidence rates.
**Management Approach Has Evolved Further**

- **RESOLVE Acute Flare**
  - Treat the acute flare rapidly with an anti-inflammatory agent

- **INITIATE Urate-Lowering Therapy**
  - Initiate urate-lowering therapy to achieve serum urate level <6 mg/dL
  - Use concomitant anti-inflammatory prophylaxis for up to 6 months to prevent mobilization flares

- **MAINTAIN Treatment to Control sUA**
  - Continue urate-lowering therapy to control flares and avoid continual crystal deposits
  - Used for at least 3–6 months while serum urate levels normalize

---

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Drugs in the Pipeline: Focus on Targeted Therapies

ULT

• AR882: selective URAT1 inhibition
• SEL-212: pegadricase – PEGylated version of the therapeutic enzyme uricase – in combination with SVP rapamycin to mitigate ADA production

Acute

• NLRP3 inhibitor – oral therapy for acute flares
• SGLT2 inhibitors – oral therapy for acute flares

IN CASE YOU MISSED... YEAR IN REVIEW
UNCONTROLLED GOUT
Comprehensive Updates on the Latest Management Strategies
AR882, an Efficacious and Selective URAT1 Inhibitor for Patients With Chronic Gouty Arthritis and Subcutaneous Tophi: Results From a Global, Prospective, Proof-of-Concept Trial Using DECT

Robert Keenan, James Cheng-Chung Wei, Sarah Morris, Pamella Mundell, Wen Wei, Ke Shi, Zancong Shen, Vijay Hingorani, Shunqi Yan, Bahram Kiani, and Litain Yeh

Abstract # L15
Presented at: ACR Convergence 2023
November 10-15, 2023
San Diego, CA
Phase 2B Study of AR882 in Patients With Gout

Study Design and Findings:

- Patients were randomized to receive:
  - AR882 75 mg, once daily
  - AR882 50 mg + allopurinol, once daily
  - Allopurinol up to 300 mg, once daily

- **Primary endpoint:**
  sUA change at month 3

- **Secondary endpoints:**
  Resolution of target tophus area and change from baseline in target tophus crystal volume at month 6

- **Safety assessments:**
  Vital signs and electrocardiograms

---

![Percent of Patients with sUA at Targets at 12 Weeks](image)

Findings:

Mean (SE) change in DECT crystal volumes at month 6

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Visit</th>
<th>N</th>
<th>Crystal volume, cm$^3$</th>
<th>Absolute change, cm$^3$</th>
<th>Percent change</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR882 75 mg</td>
<td>Baseline</td>
<td>12</td>
<td>15.6 (9.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Month 6</td>
<td>11</td>
<td>8.7 (5.0)</td>
<td>-8.3 (5.8)</td>
<td>-30.7 (17.7)</td>
</tr>
<tr>
<td>AR882 50 mg + allopurinol</td>
<td>Baseline</td>
<td>12</td>
<td>4.7 (2.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Month 6</td>
<td>9</td>
<td>3.2 (1.8)</td>
<td>-0.9 (0.5)</td>
<td>-31.5 (13.9)</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>Baseline</td>
<td>13</td>
<td>11.5 (5.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Month 6</td>
<td>13</td>
<td>10.3 (4.3)</td>
<td>-1.2 (3.8)</td>
<td>-16.8 (25.5)</td>
</tr>
</tbody>
</table>

DECT image of gouty arthritis showing 68% reduction in total urate crystal volume from baseline (left) to month 6 after taking AR882 75 mg once daily.

Phase 2B Study of AR882 in Patients With Gout

Key Takeaways

• 6-month treatment of AR882 demonstrated safe and efficacious sUA lowering, tophus resolution, and total crystal volume dissolution in gout patients
  – Majority of patients receiving AR882 had achieved sUA levels below 5 or 4 mg/dL
• AR882 was well tolerated over the 12-week treatment period and patients with comorbidities did not require any adjustments in management of the diseases while being treated with AR882
• AR882 may offer improved efficacy with acceptable safety compared to existing therapies and may have utility in the treatment of patients across the spectrum of gout

Safety & Efficacy of SEL-212 in Patients With Gout Refractory to Conventional Treatment: Primary Outcomes From 2 Randomized, Double Blind, Placebo-Controlled, Multicenter Phase 3 Studies

Herbert Baraf, Alan Kivitz, Sheri Rhodes, Sheldon Leung, Olu Folarin, Tania Gonzalez-Rivera, Joanna Sobierska, Jacquie Christie, Anand Patel, Wesley DeHaan, Rehan Azeem and Peter Traber

Abstract # 0246
Presented at: ACR Convergence 2023
November 10-15, 2023
San Diego, CA
Safety & Efficacy of SEL-212 in Patients With Gout Refractory to Conventional Treatment

Study Design and Goals:

- SEL-212: infusion of tolerogenic nanoparticles containing rapamycin followed by pegadricase (uricase modified with PEG)
- DISSOLVE I & II enrollment criteria:
  - ≥3 gout flares within 18 months prior to screening or ≥1 tophus or a current diagnosis of gouty arthritis
  - Failure to normalize sUA and control symptoms with any XOI
  - No previous exposure to a pegylated uricase-based therapy

Findings:

• Response rates in all treatment groups were significantly different from placebo ($P ≤ .0008$)

• The safety profile of SEL-212 was favorable, with 3.4% and 4.5% of participants experiencing infusion reactions in the high and low-dose groups, respectively

• Reports of gout flares were comparable between treatment groups and placebo

• Six participants (3.4%) in the pooled active treatment groups experienced treatment-related serious AEs (n=4 anaphylaxis, n=2 gout flares)

AEs = adverse events.
Key Takeaways

- Once-monthly treatment with SEL-212 demonstrated statistically significant response rates and reductions in sUA versus placebo.
- The safety profile of SEL-212 was consistent with that of uricase therapies.
- Targeted immunomodulation with SEL-212 has the potential to provide a new uricase-based treatment option for patients with gout refractory to conventional therapies.

Summary of Select ACR Presentations on Pegloticase ± MTX for Treating Gout

0236: Orrin Troum, Mai Duong, Katie Obermeyer, Lissa Padnick-Silver and Brian LaMoreaux
1103: Emily Holladay, Amy S. Mudano, Fenglong Xie, Jingyi Zhang, Ted R Mikuls, Brian LaMoreaux, Lissa Padnick-Silver and Jeffrey Curtis
1107: James Mossell, Mai Duong, Katie Obermeyer, Lissa Padnick-Silver, Brian LaMoreaux and Sanjay Chabra
1123: John Botson, Qianhong Fu, Kaiding Zhu, Lissa Padnick-Silver and Brian LaMoreaux

Abstracts # 0236, 1103, 1107, 1123
Presented at: ACR Convergence 2023
November 10-15, 2023
San Diego, CA
Pooled post-hoc analysis of clinical trials to examine CV/VTE events after initiation of pegloticase

- Including participants of the phase 3 registration trial, MIRROR RCT, and MIRROR open-label trial

- 1.5% (5/328) beginning pegloticase had ≥1 CV/VTE event
- 1.2% (3/244) had CV/VTE events during biweekly pegloticase
- CV/VTE incidence (35.4/1000 PY) was similar to the general gout population (20.99-44.7/1000 PY) and lower than with XOI initiation (51.8-99.3/1000 PY)

PY = patient years.
Evaluation of Outcomes Following Discontinuation of Pegloticase Therapy

Study Design and Findings:

- Pegloticase discontinuation (d/c) was defined as a gap ≥12 weeks after an infusion
- Lab changes in patients who d/c pegloticase with median differences compared to pre-d/c values:
  - SU: 2.4 mg/dL (0.0 to 6.3)
  - eGFR: -1.9 mL/min (-8.7 to 3.7)
  - CRP: -0.8 mg/L (-12.8 to 0.0)
  - ESR: -4.0 mm/hr (-13.0 to 0.0)
- 83% of those who d/c pegloticase started other ULTs and 8% restarted pegloticase
  - After starting a new oral ULT, median SU values were 5.8 (4.7 to 7.0) and 5.8 (4.5 to 7.9) mg/dL for users of allopurinol and febuxostat, respectively
  - Patients who restarted pegloticase achieved a median SU of 0.9 mg/dL (0.2 to 9.7) after a median of 156 days since prior d/c

CRP = c-reactive protein; ESR = erythrocyte sedimentation rate.
Predictors of Pegloticase Urate-lowering Response in the Presence and Absence of Methotrexate Co-Therapy

Study Design and Findings:

- Analyses included uncontrolled gout patients who received biweekly pegloticase (8 mg) in the Phase 3 pegloticase registration and MIRROR RCTs.
- Treatment response = SU <6 mg/dL for at least 80% of month 6.
- MTX co-therapy led to increased response rate during month 6 in both age groups.
- Younger patient age and higher body weight were predictors of treatment failure, in agreement with PK studies showing an influence of ADAs and body surface area on serum pegloticase concentrations.
- Support the importance of MTX co-administration with pegloticase to maximize the number of patients who may benefit from this often last-line therapy.

PK = pharmacokinetic.
Pegloticase ± MTX: Post-hoc Analyses of Clinical Trial Data and Real-World Trends

Key Takeaways

- In clinical trials:
  - CV/VTE events with pegloticase therapy occurred at a similar incidence to the general gout population and at a lower incidence than with XOI initiation.
  - Younger patient age and higher body weight were predictors of treatment failure with pegloticase monotherapy. However, with MTX-co-therapy, neither patient age nor body weight predicted response.
- Development of ADAs may require pegloticase d/c. However, patients who were able to restart pegloticase after a prolonged gap in therapy achieved the expected SU-lowering effect.
- Wide-spread awareness and adoption of IMM co-administration with pegloticase in real-world setting.

Real-World Trends in the Use of Immunomodulation as Co-Therapy to Pegloticase

Oral Urate-Lowering Therapy Use and Efficacy Following Pegloticase Treatment: Findings From a Rheumatology Network Database

Lissa Padnick-Silver, Andrew Concoff, Hong-Ye Gao, Qianhong Fu, Brian LaMoreaux and N. Lawrence Edwards

Abstract # 0237
Presented at: ACR Convergence 2023
November 10-15, 2023
San Diego, CA
Oral Urate-Lowering Therapy Use and Efficacy Following Pegloticase Treatment

Study Design and Goals:

- 211 patients from the UR-NICE data repository
  - 77% male; mean age: 62.7, BMI: 32.9 kg/m², eGFR: 66.0±24.7 mL/min/1.73 m² [46% eGFR <60]
- 74% had tophaceous gout and pre-pegloticase SU was 7.9 mg/dL (n=148), available inflammatory biomarkers were moderately elevated
- 141 patients (67%) had pre-pegloticase oral ULT use
- Patients received a mean of 12 pegloticase infusions with a 2-week dosing interval
- Following the last infusion, 115 patients (55%) began oral ULT
  - 67% allopurinol, 44% febuxostat, and/or 17% probenecid), most (67%) within 30 days of last pegloticase infusion
- More patients who received ≥12 infusions had an SU <6 mg/dL when treated with post-pegloticase oral ULT than those who received <12 infusions
  - First post-ULT SU <6 mg/dL: 78% vs 36%; mean SU: 4.7±3.0 [n=37] vs 7.4±2.9 mg/dL [n=47]

Oral Urate-Lowering Therapy Use and Efficacy Following Pegloticase Treatment

Key Takeaways

- Two-third of patients began oral ULT after pegloticase, most within 30 days of last infusion.
- Patients who had a longer pegloticase course (≥12 infusions) were more likely to have post-treatment oral ULT efficacy, perhaps because of a greater urate burden depletion.

Comparative Effectiveness of Sodium-Glucose Cotransporter-2 Inhibitors for Recurrent Gout Flares and Gout-primary Emergency Department Visits and Hospitalizations: A General Population Cohort Study

Natalie McCormick, Chio Yokose, Jie Wei, Na Lu, Deborah Wexler, Mary De Vera, J. Antonio Avina-Zubieta, Yuqing Zhang, and Hyon K. Choi
Comparative Effectiveness of Sodium-Glucose Cotransporter-2 Inhibitors for Gout

Study Design and Goals:

- Active comparator cohort study enrolling 8150 gout patients with type 2 diabetes (T2D) from British Columbia (2014 to 2022)
- Flare rate was lower among SGLT2i than DPP-4i initiators:

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>SGLT2i</th>
<th>DPP-4i</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gout Flare Counts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR, per 1000 person-years</td>
<td>52.4</td>
<td>79.7</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>0.66 (0.57, 0.75)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>RD (95% CI)</td>
<td>-27.4 (-36.0, -18.7)</td>
<td>Ref</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensitivity Analyses</th>
<th>SGLT2i</th>
<th>DPP-4i</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flares Requiring ED Visits or Hospitalizations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR, per 1000 person-years</td>
<td>3.6</td>
<td>7.0</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>0.52 (0.32, 0.84)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>RD (95% CI)</td>
<td>-3.4 (-5.8, -0.9)</td>
<td>Ref</td>
</tr>
<tr>
<td>Up to 1 Year of Follow-Up, No Prior ULT Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR, per 1000 person-years</td>
<td>73.1</td>
<td>103.8</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>0.70 (0.59, 0.84)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>RD (95% CI)</td>
<td>-30.1 (-46.3, -15.1)</td>
<td>Ref</td>
</tr>
</tbody>
</table>

RD = risk difference; DPP-4i = dipeptidyl peptidase 4 inhibitors.

- Cardiovascular and control outcomes among patients with gout and T2D initiating SGLT2i vs DPP-4i
  - HR and RD for myocardial infarction: 0.69 (0.54 to 0.88) and -7.6 (-12.4 to -2.8) per 1000 PY
  - HR for stroke: 0.81 (0.62 to 1.05)
  - For control outcomes, SGLT2i initiators showed higher risk of genital infection, as expected, and no altered risk of osteoarthritis encounter
Key Takeaways

• Among gout patients, SGLT2i may reduce recurrent flares and gout-primary ED visits/hospitalizations, along with cardiovascular benefits, without apparent paradoxical flares

ED = emergency department.
Blood Pressure Changes With Intensive Urate Lowering in Uncontrolled Gout Patients With and Without CKD

Brad Marder, Richard J. Johnson, Hyon Choi, Katie L. Obermeyer, Brian LaMoreaux, Peter E. Lipsky

Abstract # SA-PO505
Presented at: ASN Kidney Week 2023
November 2-5, 2023
Philadelphia, PA
Study Design and Findings:

- BP changes during pegloticase use were examined in 152 patients from MIRROR RCT.
- Uncontrolled gout was defined as SU ≥7mg/dL, oral ULT failure/intolerance, and ≥1 gout symptom.

MIRROR RCT: Blood Pressure Changes With Intensive Urate Lowering in Uncontrolled Gout

Key Takeaways

- BP decreased during pegloticase therapy in CKD and non-CKD patients
- After 6 months, patients cotreated with MTX and without CKD had more pronounced BP changes
- These data support a possible role of urate (and potentially MTX) in regulating BP, but further study is needed
Educational Tools for Your Clinical Practice

For downloadable handouts, patient education tools, and online resources, please visit: VindicoCME.com/EducationalTools