Evaluation of Gout Management with Urate-Lowering Therapy in a Kidney Clinic

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Background

- Gout is common in chronic kidney disease (CKD) patients and significantly impacts quality of life
- Urate-lowering therapy (ULT) is recommended for patients with ≥ 2 gout attacks per year
  - The most widely used urate-lowering agent is allopurinol
  - Febuxostat is a reasonable but more costly alternative for patients with an allopurinol allergy or intolerance
  - The usual serum uric acid (SUA) target is < 360 µmol/L
- Patients enrolled in the Vancouver General Hospital Kidney Care Clinic (VGH KCC) have primarily stage 3-5 CKD
  - Stages 3, 4, and 5 refer to estimated glomerular filtration rates (eGFRs) of 30-59,15-29 and <15 mL/min/1.73 m^2, respectively
- Gout management for KCC patients typically occurs in primary care
- KCC providers have observed that many patients receive suboptimal ULT, possibly as a result of safety concerns about allopurinol in CKD
  - KCC patients commonly continue to have frequent gout attacks due to inadequate allopurinol dosing
  - Febuxostat is at times prescribed in KCC patients without a known allopurinol allergy or intolerance
- KCC pharmacists and nephrologists may intervene to optimize ULT
  - ULT-related medication changes may be implemented during KCC visits or recommended to the patient's GP

Objectives

Primary:

Among patients enrolled in the VGH KCC:

- Evaluate gout management with ULT in the overall population and across CKD stages 3-5 by assessing urate-lowering agent doses used and the achievement of SUA < 360 µmol/L
- Determine the proportion of febuxostat users who do not have a documented allopurinol allergy or intolerance

Secondary:

Among VGH KCC pharmacists and nephrologists:

- Describe ULT-related interventions
- Evaluate GPs' uptake of ULT-related recommendations

Methods

Part 1 (primary objectives): Cross-sectional study using PROMIS

- Inclusion criteria: Patients enrolled in the VGH KCC for ≥ 1 year; current medication list includes allopurinol or febuxostat
- Exclusion criterion: Most recent SUA level was drawn prior to the last documented allopurinol or febuxostat dose change

Part 2 (secondary objectives): Retrospective chart review of 100 patients randomly selected from Part 1

- Additional exclusion criterion: Documented indication for allopurinol or febuxostat is not gout
- Assumptions when evaluating GPs' uptake of ULT-related recommendations:
  - ULT changes made between KCC visits were done by GPs
  - GPs had the opportunity to implement ULT-related recommendations between KCC visits

Analysis: Descriptive statistics; Mann-Whitney U test

Results

Table 1: Part 1 and 2 – Patient characteristics

	Part 1 (N = 230)	Part 2 (N = 100)
Age (years), mean ± SD	74 ± 12	73 ± 13
Male, n (%)	152 (66)	68 (68)
Ethnicity, n (%)		
Caucasian	88 (38)	35 (35)
Asian	135 (59)	59 (59)
Body mass index (kg/m^2), mean ± SD	28 ± 5	28 ± 5
eGFR (mL/min/1.73 m^2), mean ± SD	25 ± 11	25 ± 12
Comorbidities, n (%)		
Hypertension	NA	93 (93)
Diabetes	NA	52 (52)
Dyslipidemia	NA	43 (43)
Cardiovascular disease*	NA	32 (32)
Thiazide and/or loop diuretic, n (%)	109 (47)	46 (46)
Allopurinol, n (%)	203 (88)	89 (89)
Most recent SUA (µmol/L), mean ± SD	315 ± 110	353 ± 98
Febuxostat, n (%)	27 (12)	11 (11)
Most recent SUA (µmol/L), mean ± SD	259 ± 99	267 ± 88

*Includes coronary artery disease, ischemic cerebrovascular disease, and/or peripheral artery disease
NA = Not available

Figure 1: Part 1 – Percentage of allopurinol and febuxostat users with most recent SUA < 360 µmol/L, stratified by CKD stage (N = 230)

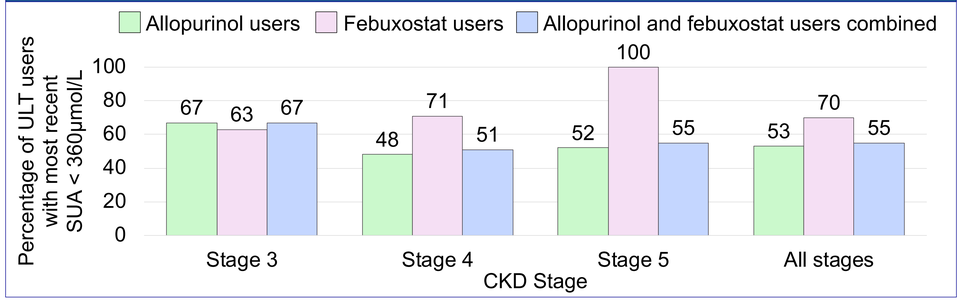
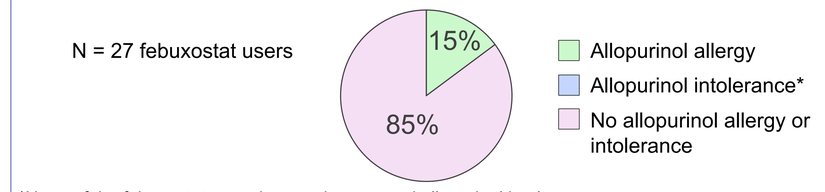


Table 2: Part 1 – Current urate-lowering agent doses and comparison of doses in patients with most recent SUA < 360 µmol/L vs. ≥ 360 µmol/L, stratified by CKD stage

	Overall	Comparison by most recent SUA		
		< 360 µmol/L	≥ 360 µmol/L	p-value
Allopurinol dose (mg/day), median (IQR)				
CKD stage 3 (n=49)	200 (100-300)	200 (200-300)	100 (100-150)	0.001
CKD stage 4 (n=119)	200 (100-200)	200 (150-200)	100 (100-200)	< 0.0001
CKD stage 5 (n=29)	200 (100-200)	200 (200-250)	200 (100-200)	0.03
All CKD stages (n=203)	200 (100-200)	200 (200-300)	100 (100-200)	< 0.0001
Febuxostat dose (mg/day), median (IQR)				
CKD stage 3 (n=8)	40 (40-80)	40 (40-40)	80 (60-80)	0.30
CKD stage 4 (n=17)	80 (40-80)	80 (40-80)	80 (40-80)	0.83
CKD stage 5 (n=2)	40 (40-40)	40 (40-40)	N/A (n=0)	N/A
All CKD stages (n=27)	80 (40-80)	40 (40-80)	80 (40-80)	0.54

Figure 2: Part 1 – Allopurinol allergy or intolerance in febuxostat users



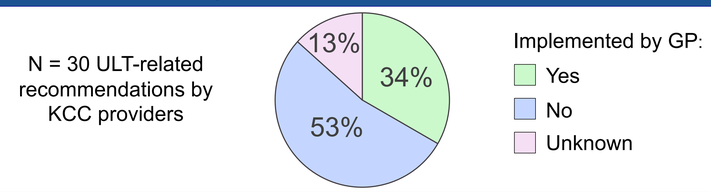
*None of the febuxostat users have a documented allopurinol intolerance

Table 3: Part 2 – ULT-related interventions by KCC providers

ULT-related Intervention	By pharmacist	By nephrologist
Start allopurinol	12	30
Increase allopurinol dose	8	19
Decrease allopurinol dose	3	3
Discontinue allopurinol (and all ULT)	0	2
Start febuxostat	0	5
Increase febuxostat dose	1	1
Decrease febuxostat dose	1	2
Discontinue febuxostat (and all ULT)	0	1
Change allopurinol to febuxostat	0	0
Change febuxostat to allopurinol	2	0
Total*	**27**†	**63**§

*40 of 100 patients received ≥ 1 ULT-related intervention
†24 recommended to nephrologist, 3 recommended to GP
§36 implemented by nephrologist, 27 recommended to GP

Figure 3: Part 2 – GPs' uptake of ULT-related recommendations



Limitations

- Single-center study that did not capture patients with gout who are not receiving ULT
- Achievement of the SUA target is only a surrogate marker of gout control
- Possibly inaccurate data in PROMIS medication lists and in charts reviewed
- Few febuxostat users, CKD stage 3 & 5 patients, and recommendations made to GPs

Conclusions

- 55% of VGH KCC patients receiving ULT achieved a most recent SUA < 360 µmol/L
  - 53% of allopurinol users; 70% of febuxostat users
- Allopurinol doses used are similar across CKD stages 3-5 and are consistently higher in patients with a most recent SUA < 360 µmol/L vs. ≥ 360 µmol/L
  - Above trends not seen with febuxostat; larger studies needed to explore this further
- Gout management is often suboptimal in patients seen at the VGH KCC
  - 85% of KCC patients receiving febuxostat do not have a documented allopurinol allergy or intolerance that warrants febuxostat use
  - KCC pharmacists and nephrologists commonly recommended or implemented allopurinol initiations and allopurinol dose increases for suboptimal gout control
  - GPs appeared to implement only 34% of ULT-related recommendations
- The next step will be to examine barriers to prescribing optimal ULT for this population