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Enclosure:

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Reduction of Kidney Manifestations with Tolvaptan Through 6 Years of the C-MAJOR Registry

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INTRODUCTION

- Autosomal dominant polycystic kidney disease (ADPKD) is a hereditary disorder often leading to kidney failure, with a wide range of renal and extra-renal manifestations.
- Tolvaptan (Jinarc®) is efficacious in slowing progression of kidney enlargement and functional decline in people with ADPKD, however long-term real-world data with tolvaptan are limited.
- C-MAJOR (NCT02925221) was a Canadian, multicenter, observational study initiated as part of the Health Canada approval requirement for tolvaptan. Included were adults with ADPKD who initiated tolvaptan from 2015-2025 and volunteered to participate.

AIM

- To examine kidney manifestations through 6 years of tolvaptan in people with ADPKD enrolled in the C-MAJOR registry.

METHODS

- Routine care patient data were collected at baseline and 6-month intervals thereafter.
- Due to attrition over time, data were analyzed through 72 months from 2015-2023.
- Urinary tract infections (UTIs), hematuria, nephrolithiasis, albuminuria, and kidney pain were ADPKD manifestations of primary interest.
- Unadjusted and adjusted (early [G1-3a] vs late [G3b-5] chronic kidney disease [CKD]; Mayo Imaging Classification [MIC] 1B-E) general linear mixed models evaluated kidney manifestations, with time as a categorical variable.
- All p-values are nominal.

RESULTS

C-MAJOR Baseline Patient and Disease Characteristics

- Among 470 patients treated with tolvaptan, mean age at ADPKD diagnosis and tolvaptan initiation was 30 and 44 years, respectively.
- At tolvaptan initiation, patients had large kidneys (TKV=2010.8 mL) and 70% were at the early stages of CKD (CKD 1-3a).

Table 1. Baseline demographics and disease characteristics of the total population in C-MAJOR

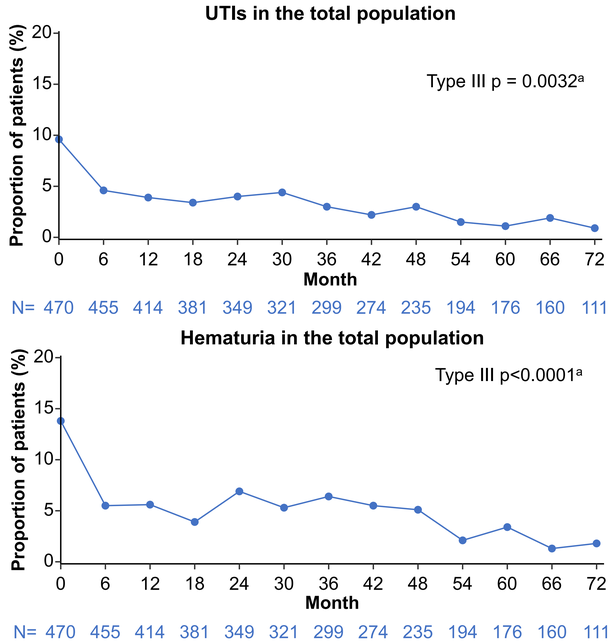
	Total Population (N=470)
Demographics	
Age at diagnosis, years	29.8 (13.6)
Female	239 (50.9%)
Race	
Caucasian	394 (83.8%)
Black	13 (2.8%)
Asian	26 (5.5%)
Hispanic	17 (3.6%)
Other	20 (4.3%)
Disease characteristics	
Duration of ADPKD disease, years	15.0 (10.7)
Age at tolvaptan initiation, years	44.4 (11.4)
TKV, mL	2010.8 (1559.1)[a]
ht-TKV, mL/m	1158.0 (890.6)[b]
Kidney length, cm	18.8 (4.0)[c]
eGFR, mL/min/1.73 m^2	63.5 (27.4)[d]
CKD category	
G1	91 (19.8%)[e]
G2	136 (29.6%)[e]
G3a	90 (19.6%)[e]
G3b	104 (22.7%)[e]
G4	38 (8.3%)[e]
G5	0 (0.0%)[e]

Data are mean (SD) or n (%) unless otherwise specified. [a]N=278. [b]N=215. [c]N=417. [d]N=464. [e]N=459. eGFR=estimated glomerular filtration rate; ht-TKV=height-adjusted total kidney volume; SD=standard deviation; TKV=total kidney volume.

Kidney Manifestations in the Total Population

- Rates of UTIs and hematuria decreased significantly from baseline (9.6% and 13.8%, respectively) to month 72 (0.9% and 1.8%).
- Numerical reductions were observed from baseline to 72 months in rates of nephrolithiasis (14.3% to 7.2%) and kidney pain (24.0% to 9.9%) (data not shown).

Figure 1. UTI and hematuria rates in the total population

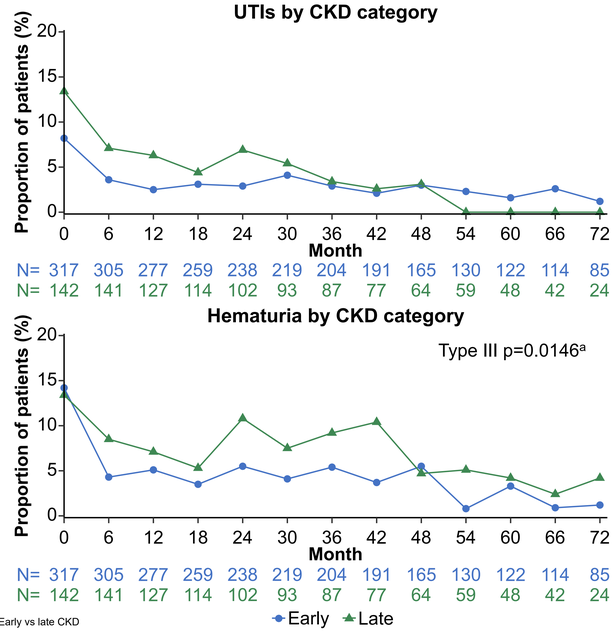


[a]72 months vs baseline

Kidney Manifestations by CKD Category

- Rates of UTIs from baseline to month 72 were similar for early and late CKD.
- The rates of hematuria decline from baseline to month 72 were significantly different between early (14.2% to 1.2%) vs late CKD (13.4% to 4.2%).
- Nephrolithiasis (early CKD: 12.6% to 9.4%; late CKD: 18.3% to 0%) and kidney pain (early CKD: 24.3% to 8.2%, late CKD: 23.9% to 12.5%) were generally similar for early vs late CKD (data not shown).

Figure 2. UTI and hematuria rates in early and late CKD

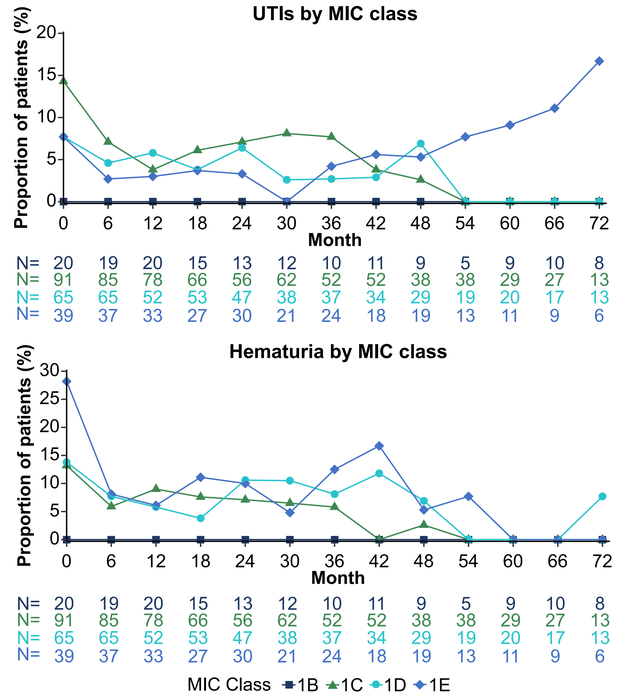


[a]Early vs late CKD

Kidney Manifestations by MIC Classification

- Rates of kidney manifestations through month 72 were similar across MIC classes and consistent with the overall population.
- Small sample sizes may limit interpretation.

Figure 3. UTI and hematuria rates by MIC classification



CONCLUSION

- Long-term follow-up in the real-world C-MAJOR study confirms the benefits of tolvaptan in treating clinical ADPKD progression.
- Marked improvements in kidney manifestations including hematuria, nephrolithiasis, and kidney pain and significant reductions in rates of UTIs were observed through 72 months.
- Findings were consistent for early and late CKD stages and MIC classes.

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