Understanding diversity and disparities in a real-world (RW) locally advanced/metastatic urothelial carcinoma (LA/mUC) cohort: clinical characteristics, genomic landscape, and self-reported social determinants of health (SDOH)

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BACKGROUND

- **Fibroblast growth factor receptor (*FGFR*) alterations** are present in ~20% of advanced or metastatic urothelial carcinoma (LA/mUC) cases and are ***oncogenic drivers***.
- The pan-*FGFR* inhibitor, *erdafitinib,* has been approved for the treatment of patients with *LA/mUC harbouring FGFR2/3 alterations.* In the phase III THOR clinical trial (NCT03390504) *erdafitinib was associated with improved overall survival* in patients previously treated with systemic therapy including immune checkpoint inhibitors (ICI).
- The introduction of *FGFR*-inhibitor therapy has led to a rapidly changing treatment landscape, ***creating disparities in molecular testing and access to novel therapies***.
- In this multicenter prospective cohort study, we examined **treatment patterns, outcomes, genomic profile, diversity, and social determinants of health in patients with LA/mUC**.

STUDY DESIGN

- Patients with LA/mUC were **prospectively** enrolled from cancer centres in Alberta, Canada from April to September 2024.
- Baseline patient characteristics including self-reported SDOH were collected. Patients were followed to evaluate treatment patterns and outcomes.
- **Comprehensive genomic profiling (CGP)** of DNA and RNA on archived FFPE tissue was performed, including characterization of FGFR1-4.

This real-world analysis provides valuable insights into the genomic landscape, clinical characteristics, and SDOH of patients with advanced urothelial carcinoma.

- It is *feasible* to evaluate a diverse range of data to guide management in this patient population.
- 31% of patients had FGFR alterations, highlighting the necessity for *equitable access to precision oncology* to optimize patient outcomes.

RESULTS

42 patients were identified

Demographic & Clinical Characteristics

Table 1: Demographic & Clinical Characteristics (n=42)

Characteristic	n (%)
Median age at Diagnosis	68.5 years (IQR: 62 – 73 years)
Sex	
Male	33 (79)
Female	9 (21)
Primary Tumour Location	
Bladder	33 (79)
Upper Tract	9 (21)
Metastatic Disease upon Study Entry	
No	3 (7)
Yes	39 (93)
Visceral Metastases (n=39)	
No	31 (79)
Yes	8 (21) [93% liver involvement]

Social Determinants of Health

23 patients (62%) completed the survey questionnaire

- **4%** identified as Indigenous
- **96%** Caucasian
- **83%** Canadian-born

26% reside in a rural setting & commute > 60 minutes to their cancer care center

65% report tobacco use with a median 27 pack year history

47% report regular use of alcohol with a median 11 grams alcohol/day (one standard drink)

30% report a family history of Lynch Syndrome related malignancies

47% reported some level of financial stress
83% are retired
53% have extended health insurance

45% reported their highest level of education was high school
41% had vocational/technical training or a college diploma

Genomic Profile

35 patients have undergone CGP with 31% exhibiting *FGFR* alterations

Table 2: *FGFR* Alterations

Gene	Alteration(s) Identified	% of FGFR-mutation positive cases
FGFR3	• Point alteration • Fusion (FGFR1)	63%
FGFR2	• Fusion (USP11)	12%
FGFR1	• Fusion (TBC1D22A) • Amplification	25%

Treatment Sequence & Outcome

At the time of analysis, 88% of patients received systemic therapy for LA/mUC:

88% were alive, with a median follow-up of 14.6 months

Median overall survival is not yet reached

Table 3: Treatment received for unresectable LA/mUC and median progression-free survival by line of treatment

Palliative Treatment Line	Number	Therapy Type	Percent	mPFS (months) [95% confidence interval]
First line	37	CTx CTx + ICI ICI monotherapy ICI + ADC	81 3 13 3	8.33 [0.5 – 22.5]
Second line	26	ADC CTx ICI	7 12 81*	7.1 [0.5 – 31.7]
Third line	10	ADC CTx ICI Targeted	60 10 20 10	6.2 [2.1 – NR]
Fourth line	3	ADC CTx	33 67	1.7 [1.7 – NR]
Fifth line	1	ICI	100	NR

CTx: Chemotherapy; ICI: Immune checkpoint inhibitor; ADC: Antibody-drug conjugate; NR: not reached; * 50% maintenance avelumab

FUTURE DIRECTIONS

- The study is ongoing, with a **target enrollment of 200 patients over 24 months.**
- Genomic testing in patients with advanced urothelial carcinoma is currently not funded in Alberta. This project facilitates access to targeted therapy in eligible patients.
- This will be a comprehensive real-world analysis of treatment sequencing, outcomes, uptake, and safety of novel therapies in patients with advanced urothelial carcinoma. Serum and urine biomarkers are being evaluated to develop and validate minimally-invasive tests.

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