Evaluating the Clinical Utility of Circulating Tumor Cells (CTC) Profiling to Predict Selection of Preferred Therapeutic Regimens in Newly Diagnosed or Pretreated Refractory Renal Cell Carcinomas (RCC)

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DATAR CANCER GENETICS

INTRODUCTION

- Current unmet need for biomarkers enabling therapeutic selection and prediction of clinical outcomes in kidney cancer .
- We evaluated the feasibility and utility of profiling of circulating tumor cells (CTCs) via multiplexed fluorescence immunocytochemistry (ICC) to identify liquid biopsy biomarkers linked to treatment response (or resistance) in advanced RCC patients.
- Transcriptome analysis for 20802 genes from exosomal RNA is planned to evaluate novel prognostic and predictive signatures.

OBJECTIVES

Primary Endpoint

- To detect the proportion of patients with RCC in whom CTCs can be detected and profiled

Secondary Objective

- To evaluate the response rate, progression free survival and overall survival in the patient cohort tested and compare the outcomes in biomarker positive and negative patients.

METHODS

- The study will meet its primary endpoint if for at least 12 patients the assay detects CTC and profiling is feasible.
- With an overall sample size of 50 the width of a 95% confidence interval for the rate of providing a therapeutic intervention is guaranteed to be less than 26%.

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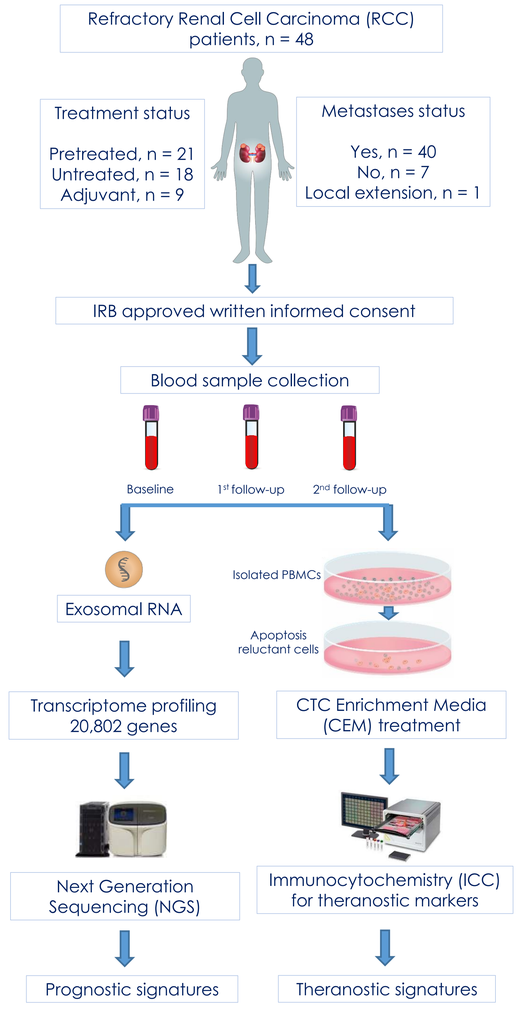
STUDY SCHEMA

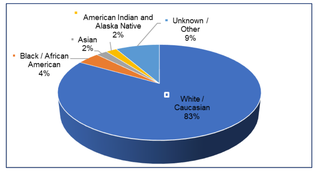


STUDY POPULATION

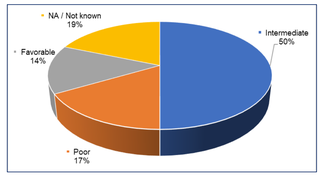
A) Age Distribution

Gender	Age – Range (Median)
Female (n=10)	46 - 85 (66)
Male (n=39)	41 - 80 (64)

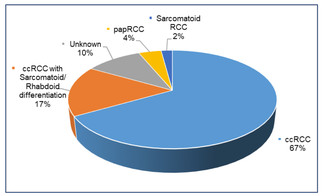
B) Race/Ethnicity Distribution



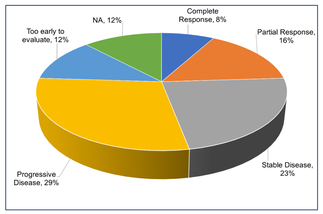
C) IMDC Risk Category



D) Histology Distribution



E) Response Rates



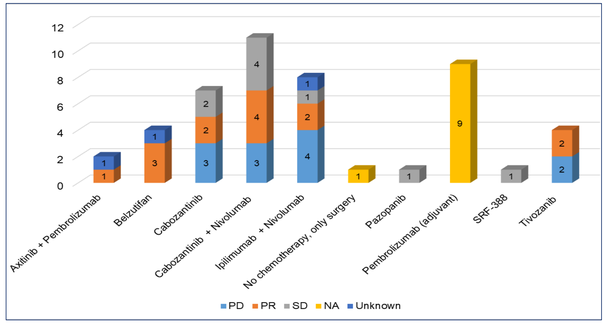
CONCLUSIONS

- The primary endpoint was met, and feasibility of the test was demonstrated with 38 out of 48 (80%) of the baseline samples showed CTC detection
- 43 out of 48 samples (90%) showed biomarker expression.
- VEGFA (39.6%) was the most detected biomarker on CTC-ICC profiling
- The study defined a transcriptome analysis that may be promising for predicting novel prognostic and predictive signatures for immunotherapy and targeted therapy response.

RESULTS

- 48 evaluable patients have been enrolled 10 females, 38 males.
- Median age was 64 years (range 40-85 years). 40 white patients, 2 black patients and 6 of other races/ethnicities have been enrolled.
- 18 patients were untreated, 21 were pretreated and 9 were undergoing adjuvant therapy post nephrectomy. 41 patients had clear cell histology, 4 non clear cell, 2 papillary, and 2 unclassified histology.
- CTCs positivity rate with CK+EPCAM was observed in 38 out of 48 (80%) patients.
- Positivity for ≥ one theranostic marker was observed in 43 out of 48 (90%) patients.
- Out of 10 individuals with negative CK+EPCAM CTCs, 4 were in adjuvant setting and all had Intermediate IMDC score and were negative for rhabdoid/sarcomatoid transformation (except one case showing focal rhabdoid transformation).

A) Therapy Outcome



B) Differentially expressed genes identified in Progressive Disease (PD, n = 12) cohort Vs Response (PR + SD, n = 23) cohort

Gene	Upregulated in PD cohort	Downregulated in PD cohort	Upregulated in PR + SD cohort	Downregulated in PR + SD cohort
HS6ST1	1	8	0	11
TREML1	0	10	0	11
APOL3	7	0	11	0
OR2T12	0	7	0	11
RRAS	0	7	0	11
CCT6P1	0	8	0	11
MFSD2B	0	8	0	9
SMG1P1	6	1	10	1
ARIH2OS	0	7	0	10
LOC284023	0	7	0	11
PHACTR3	0	7	0	8
PPL	0	7	0	11
HGD	1	6	0	10
RAB1A	0	8	0	11
ANPEP	0	7	0	11
TMEM41B	7	0	7	3
ZNF335	7	0	9	2
INO80E	8	0	7	1
SURF1	7	0	7	1
FCGR2C	10	0	12	1

CONCLUDING REMARKS

- Correlation of longitudinal CTC with clinical outcomes is ongoing.
- This blood-based, non-invasive liquid biopsy demonstrated high sensitivity for detection of cancer cells and presents a potential opportunity for biomarker profiling to predict therapeutic efficacy of conventional RCC therapeutic agents.