Circulating tumor cell (CTC) enumeration in patients (pts) with metastatic genitourinary (mGU) tumors treated in a phase I study of cabozantinib and nivolumab (CaboNivo) +/- ipilimumab (CaboNivoIpi)

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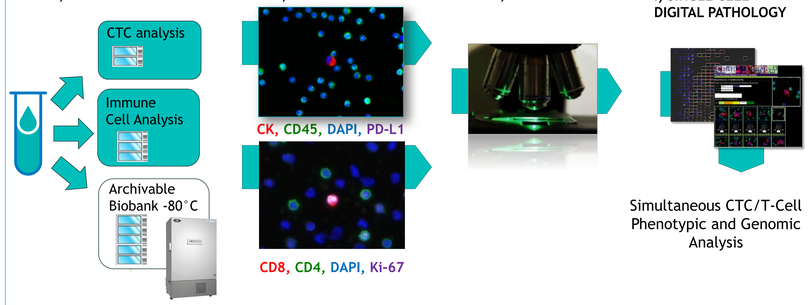
BACKGROUND

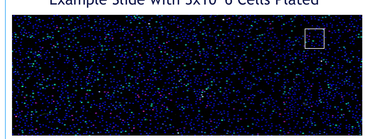
- Circulating Tumor Cells (CTCs) and circulating T-Cells may serve as biomarkers for clinical outcomes in GU tumor patients.
- Cabozantinib may have immunomodulatory properties that counteract tumor-induced immunosuppression, providing a rationale for combining cabozantinib with checkpoint inhibitors.
- We examined the association between CTCs and T-Cell populations at baseline and post-treatment at cycle 2 and 3, with progression free survival and overall survival (OS) and response to therapy with combination cabozantinib and nivolumab or cabozantinib, nivolumab, and ipilimumab.

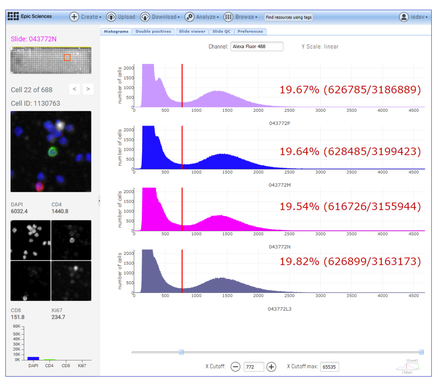
METHODS

Blood samples from mGU cancer patients undergoing CaboNivo or CaboNivoIpi therapy were collected at baseline and on-therapy and sent to Epic Sciences for processing. Slides were stained with pan-CK/CD45/PD-L1/DAPI for CTC detection or CD4/CD8/Ki-67/DAPI for T-Cell analysis. Approximately 3 million cells per slide were imaged through advanced digital pathology pipelines to detect and quantify changes in immune cell populations and to assess circulating tumor cells burden.



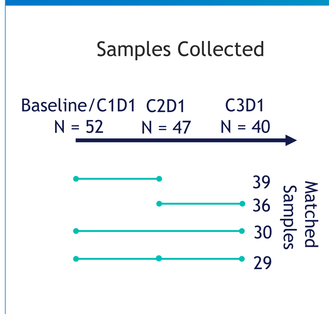
Example Slide with 3x10^6 Cells Plated





The Epic Functional Cell Profiling (FCP) platform enables characterization of CTC and immune cell populations from a single blood sample. Epic's software performs cloud-based image analysis to characterize 3 million cells per slide. Representative slide image (above) are shown for healthy donor samples that were stained with CD4, CD8, Ki-67, and DAPI. The histograms were used to determine mean fluorescent intensity (MFI) thresholds for each marker and to quantify leukocyte subpopulations.

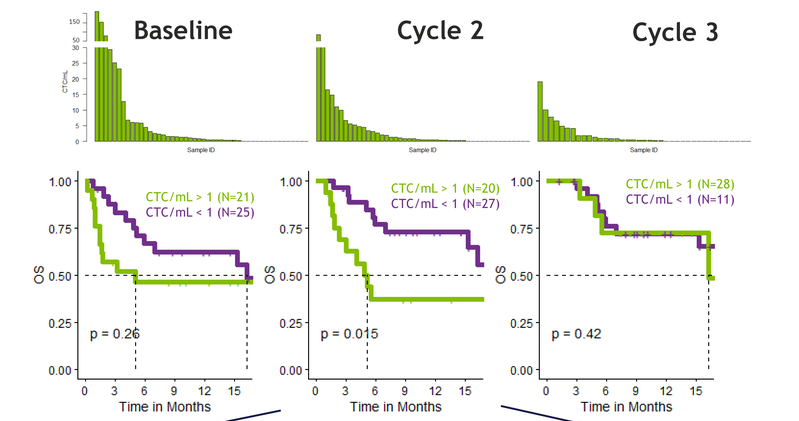
BLOOD SAMPLE AND PATIENT CHARACTERISTICS



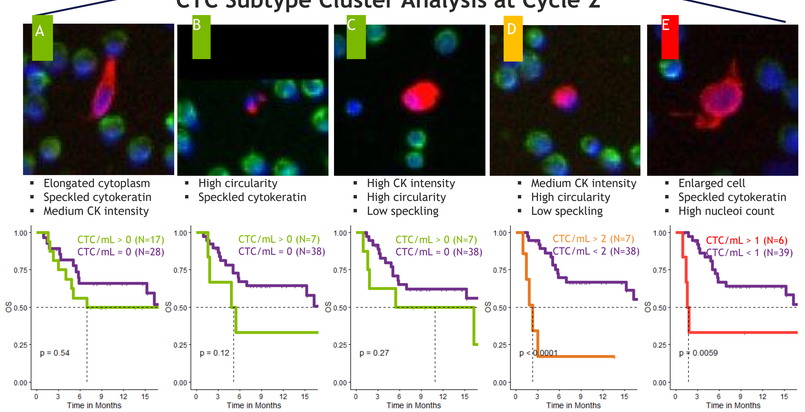
Patient Characteristics		N=52
Age in years (range)		61.5 (20,82)
Cancer Type - (%)		
Urothelial		21 (40)
Urothelial renal pelvis		14 (27)
Bladder Adenocarcinoma		7 (13)
Bladder Squamous cell carcinoma		3 (6)
Bladder small cell		2 (4)
Urothelial carcinoma plasmacytoid		1 (2)
Penile		2 (4)
Renal medullary		1 (2)
Renal clear cell		1 (2)
Visceral Mets - (%)		39 (75)
Liver Mets - (%)		16 (31)
Bone Mets - (%)		11 (21)
CTC Incidence	Percentage	Median(range)
Baseline	69% (36/52)	0.75 (0,211)
Cycle 2	70% (33/47)	0.5 (0,86)
Cycle 3	60% (24/40)	0.4 (0,19)

Patients with metastatic genitourinary tumors including: urothelial carcinoma of the bladder/urethra/ureter/renal pelvis, clear cell renal cell carcinoma, adenocarcinoma of the bladder, nonresectable squamous cell carcinoma of the penis or squamous cell carcinoma of the bladder.

HIGH ON-THERAPY CTC COUNT AND PRESENCE OF SPECIFIC CTC SUBTYPES AT CYCLE 2 ASSOCIATE WITH POOR OS

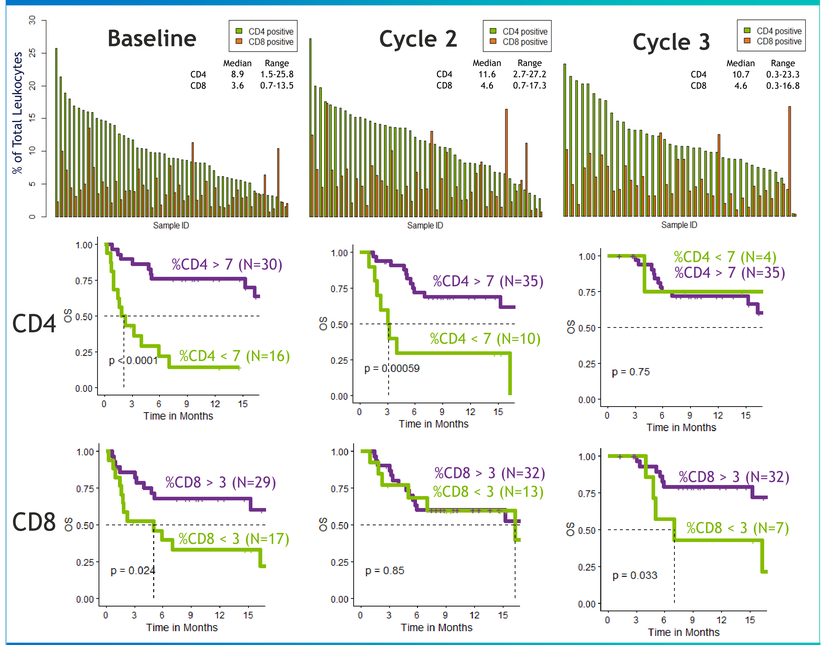


CTC Subtype Cluster Analysis at Cycle 2

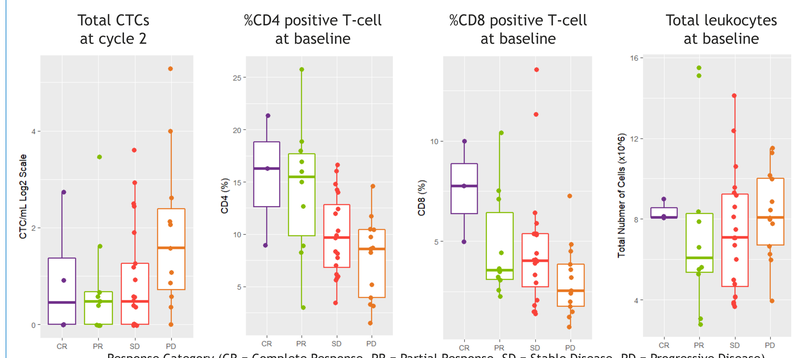


Similar trends were observed with Progression Free Survival

LOW CD4 AND CD8 AT BASELINE ASSOCIATE WITH POOR OS



LOW CD4 AND CD8 AT BASELINE AND HIGH CTC AT CYCLE 2 ASSOCIATE WITH RESISTANCE TO THERAPY



CONCLUSIONS

- The Epic Sciences Functional Cell Profiling (FCP) platform is able to detect and characterize CTC and T-cell at the single cell level with a sensitivity of 10^{-6} - 10^{-7} from a single tube of blood
- High CTC counts at Cycle 2, and low %CD4 in GU-cancer patients is associated with lower response to therapy and shorter survival
- Ongoing efforts include morphology analysis of T-cell populations and single cell sequencing of CTC subtypes associations with response