Aim: Cisplatin based neoadjuvant chemotherapy (NAC) improves survival in some patients with resectable muscle-invasive bladder cancer but carries significant toxicity. Development of predictive biomarkers to direct NAC is an urgent clinical need. Circulating tumor cells (CTC) are prognostic for survival in several metastatic epithelial cancers and for recurrence in patients undergoing cystectomy without NAC in muscle-invasive bladder cancer. Current CTC assays have poor sensitivity in non-metastatic disease. We hypothesized that CTC numbers before and after 1 cycle of chemotherapy could serve as potential biomarkers and investigated a novel microfluidic immunomagnetic CTC assay IsoFlux to detect CTCs in patients receiving NAC.

Methods: An IRB approved prospective pilot study at the University of Michigan Comprehensive Cancer Center to establish the feasibility of detecting CTCs in patients with locally advanced resectable bladder cancer (cT2-T4aNxM0) before and during cisplatin based neoadjuvant chemotherapy has enrolled 14 patients. Peripheral blood (7.5 mL) was drawn in EDTA tubes prior to NAC (baseline) and again after one cycle (3-4 weeks). We enumerated CTCs by the CellSearch and IsoFlux assays in parallel and by IsoFlux in duplicate samples in a subset of patients. We correlated CTC numbers with pathological stage at cystectomy. We also explored the feasibility of assessing EGFR and HER2 expression by RT-PCR in CTCs in 5 patients and assessed their baseline tumor HER2 gene status by Ion Torrent sequencing.

Results: Median age of patients (n = 14) was 63.5 yrs with 83% male. Clinical stage was 79% cT2Nx, 7% cT3Nx and 14% cT4aNx. NAC was cisplatin/gemcitabine in 6 patients and MVAC in 8 patients. The IsoFlux assay detected more CTCs per sample than CellSearch (median, 10 vs. 0) at baseline (n = 5) and after 1 cycle (5.5 vs. 0, n = 3). Exact concordance was 40% by IsoFlux assay in tubes drawn in parallel; a paired t-test showed no difference (p = 0.9). After 1 cycle, CTCs by IsoFlux declined from median of 10.5 to 3.75. Patients with <pT1N0 at surgery had declines greater than those with ≥ pT1N0 (median change= -1.75 vs. 2.5). CTC analysis for EGFR and HER2 expression was feasible.

Conclusions: CTC detection in patients undergoing NAC for bladder cancer is feasible, potentially more sensitive with the novel assay and a promising predictive biomarker.

Disclosure: C. Ionescu: Employee of Fluxion Biosciences Inc, CA; M. Schwartz: Employee of Fluxion Biosciences Inc, CA. All other authors have declared no conflicts of interest.