Introduction

Objective

Methods

Clinical Protocol

- Patients diagnosed with locally advanced muscle invasive bladder cancer (MIBC) and scheduled for chemotherapy were prospectively recruited between 2013 and 2017.
- All patients were treated with neoadjuvant or first line chemotherapy before cystectomy (CX) and had up to 2 years of follow-up.

Plasma Sequencing QC

- In the sequencing QC with preferred across-5 HEGF, FC 360x600, average target depth of reads and background error rates are shown in Figure 2.

Molecular Protocol (Signatera RUO)

- Patient-specific nucleic acid sequences were identified by whole exome sequencing (WES) of tumor and matched normal tissue.
- Targeted multiplex PCR assays were used to detect patient-specific tumor DNA in plasma using Signatera from tumor exomes.

For each patient, sequencing of 16 tumor-specific targets were performed and data were analyzed in a dichotomized fashion in the presence or absence of detectable tumor DNA in the plasma.

Samples were considered OncoPanel positive if at least two positive patient-specific targets were called and met the quality control score requirements.

Concordance (electronic imaging and histopathological review) was unblinded and compared directly to the Signatera plasma call results.

Results

- A total of 50 patients were included in the study (Table 1).

Table 1. Patient Characteristics and Demographics (N=50)

<table>
<thead>
<tr>
<th>Gender, n (%)</th>
<th>10 (20)</th>
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</thead>
<tbody>
<tr>
<td>Age, years, median (range)</td>
<td>71 (24-90)</td>
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<tr>
<td>Disease stage at diagnosis, n (%)</td>
<td>24 (48)</td>
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<tr>
<td>Clinical relapse, n (%)</td>
<td>12 (24)</td>
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<tr>
<td>Distant metastases (bone, lung, liver, skin)</td>
<td>36 (72)</td>
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- Median time from clinical relapse to molecular recurrence was 256 days (range 4-4096). Median time from molecular recurrence to clinical relapse was 245 days (range 0-245).

- Median tumor burden (TMB) at clinical relapse was 75,000 copies/mL plasma (log2).

- Early signs of metastatic disease were detected at variant allele frequencies (VAFs) as low as 0.02% at the time of molecular recurrence, which had a lead time of up to 265 days.

- Plasma sequencing detected lead time to molecular recurrence with a sensitivity of 100% and a specificity of 98%.

Conclusions

- These data demonstrate that ctDNA analyses (eg, via Signatera) can help clinicians in clinical relapse detection, provide real-time tumor burden monitoring, and help identify metastatic disease up to 265 days before radiographic imaging.
- ctDNA analysis could be incorporated into routine care for early detection of bladder cancer recurrence, which could potentially offer earlier initiation of alternative treatment such as immunotherapy.

- The lead time overall survival gain by ctDNA signal detection should be assessed in randomized clinical trials.