Circulating cellular biomarkers associated with delayed time to progression among bladder cancer patients treated with immune checkpoint inhibitors

Vadim S Koshkin1, Terence W. Friedlander1, Patricia Li1, Joseph Schonhoff2, Rachel Krupa2, Robin Richardson2, Priscilla Ontiveros2, Yipeng Wang2, Ryan Dittamore2, Pamela L Paris1

1. Division of Hematology-Oncology, Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA. 2. Epic Sciences, San Diego, CA

Twitter: @koshkin85 Email: vadim.koshkin@ucsf.edu

Background

- Circulating tumor cells (CTCs) are an important emerging biomarker in urothelial carcinoma
- CTCs and other serum-based biomarkers allow for a minimally invasive assessment of tumor activity and potential response to treatment
- Characterization of CTCs and other single cell populations can help guide treatment recommendations for patients with metastatic bladder cancer

Methods

- Patients with biopsy-confirmed metastatic bladder cancer who received treatment with anti-PD-1 and anti-PD-L1 agents were enrolled in this study
- Blood samples were prospectively collected from patients prior to the initiation of therapy and then while on treatment
- Samples were shipped to Epic Sciences and processed with the Epic CTC Platform as depicted in Figure 1 below

Patient Characteristics and Responses

<table>
<thead>
<tr>
<th>Patient Characteristics (N=27)</th>
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<tbody>
<tr>
<td>Median Age (range)</td>
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<tr>
<td>Male/Female</td>
</tr>
<tr>
<td>Treatment</td>
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<tr>
<td>Pembrolizumab</td>
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<tr>
<td>Atezolizumab</td>
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<tr>
<td>Nivolumab</td>
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</tbody>
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Figure 2: Consort diagram for study analysis

27 Patients with Bladder Cancer
15 treated with Pembrolizumab
11 treated with Atezolizumab
1 treated with Nivolumab

20 Evaluable Patients
9 treated with Pembrolizumab
10 treated with Atezolizumab
1 treated with Nivolumab

- Response to treatment was assessed by treating physicians according to RECIST v11
- Evaluable patients had ≥1 infusion and at least one follow-up scan
- Kaplan-Meier analysis was utilized to compare time to progression (TTP) of patients in the study

Patient Responses (N=20)

| Complete Response (CR) | 0 |
| Partial Response (PR) | 2 (1 atezolizumab, 1 pembrolizumab) |
| Stable Disease (SD) | 5 (2 atezolizumab, 3 pembrolizumab) |
| Progressive Disease (PD) | 13 |

Association of CTCs and Immune Cell Subsets with Immunotherapy Responses

A) CD4% and Time to Progression
B) Baseline CTCs and Time to Progression
C) CD4/CD8 Ratio and Time to Progression
D) CD8% and Time to Progression

- Among metastatic bladder cancer patients treated with immune checkpoint inhibitors, serum biomarkers including baseline CTCs and immune cell subsets can be predictive of clinical outcomes
- Patients with increased baseline CD4+ percentage had an association with delayed time to progression
- Patients with increased baseline CTCs had a statistically non-significant trend towards shorter time to progression
- This is a preliminary analysis in a limited sample of patients which should be further validated in larger patient cohorts