Conference Abstracts

Prognostic value of Nectin-4 and Trop2 extracellular vesicles for plasma and urine samples collected from patients with bladder cancer just prior to cystectomy

Albert Jang, MD[1a], Yohan Kim, PhD[1], Emily Bauer, BS[1], Prabin Thapa, MS[1], Igor Frank, MD[1], Paras Shah, MD[1], John Cheville, MD[1], Jacob Orme, MD, PhD[1], Fabrice Lucien, PhD[1]

[1] Mayo Clinic, 200 First Street SW, Rochester, MN, United States

Corresponding author

[a] Albert Jang, MD, Mayo Clinic, 200 First Street SW, Rochester, MN, United States, Email: Jang.Albert@mayo.edu

Keywords: extracellular vesicle, Nectin-4, Trop2

https://doi.org/10.53876/001aa.129600

International Journal of Cancer Care and Delivery

Vol. 5, Issue Supplement 1, 2025

Background

Extracellular vesicles (EVs) hold promise as non-invasive cancer biomarkers, but their clinical utility in bladder cancer remains to be investigated. Nectin-4 and Trop2 are cell surface proteins overexpressed in bladder cancer and therapeutic targets of FDA-approved antibody-drug conjugates. Here, we analyzed the levels of EVs positive for Nectin-4 and Trop2 and their association with clinicopathological features in a cohort of patients diagnosed with bladder cancer and treated with radical cystectomy.

Methods

Blood and urine samples were collected within 48 hours pre-cystectomy from 107 patients diagnosed with locally or locally advanced bladder cancer between 2006 and 2013 at Mayo Clinic. Samples from 20 healthy donors (HD) collected between 2019-2022 were included as controls. They were stored at –70°C and then thawed in spring 2025 for analysis. EVs were stained with fluorescent antibodies against Nectin-4 (enfortumab) and Trop2 (sacituzumab) and quantified by nanoscale flow cytometry. Immunohistochemistry was used to measure protein expression in matched surgical tissue specimens.

Results

For 107 patients, there were 83% men, 93% Caucasian, 25% variant histology, 13% received neoadjuvant chemotherapy, and 20% received adjuvant chemotherapy. Median time to recurrence was 0.8 years. Median overall survival (mOS) after cystectomy was 2.9 years. Median Nectin-4 H-score was 90 (83% cases had H-score>5). Median Trop2 H-score was 300 (95%; H-score>5). No correlation was found between EV levels and tissue expression. Higher urine Trop2 EV concentrations were found in bladder cancer patients compared to healthy donors ($p<0.0001$). Thirty-five (33%) patients had pTa/Tis/T1/T2pN0, while 37 patients (35%) had pT1-4pN1-3, with mOS 13.8 vs 1.3 years (HR 0.22, $p<0.0001$), respectively. The pT1-4pN1-3 cohort had significantly higher plasma levels of Nectin-4 and Trop2 EVs over the pTa/Tis/T1/T2pN0 cohort (3.5x107 vs 1.4x107, $p=0.0024$; and 7.2x106 vs 4.1x106, $p=0.0056$; respectively). No significant differences in EVs/mL were seen for these cohorts when comparing total plasma ($p=0.603$), urine nectin-4 ($p=0.276$), urine trop2 ($p=0.071$), and total urine ($p=0.588$).

Conclusion

Pre-cystectomy Nectin-4 and Trop2 plasma EVs may be potential non-invasive biomarkers for

bladder cancer. These are exploratory findings limited by sample size, timing of collection, and specimen quality. Validation in larger sample sizes and prospective cohorts is underway.