

Prostate Cancer - PSMA Detection in CTCs for improved Decision-Making Process

Prostate cancer (PC) is the 2nd most common cancer in men with worldwide around 1.3 million new cases per year. With a wide set of treatment options available, the stratification of patients likely to benefit from a specific therapy is crucial. The isolation and characterization of circulating tumor cells (CTCs) is a promising tool to enable this personalized approach.

The Role of PSMA in Prostate Cancer

PSMA (prostatespecific membrane antigen) plays a pivotal cancer-driving role. A strong PSMA expression has been associated to higher tumor stages, Gleason scores, preoperative PSA levels and to a higher risk of biochemical recurrence.

Therefore, PSMA is an interesting therapeutic target. Recently, different PSMA-based therapeutic approaches including antibody conjugates, antibody-based radiotherapy, or PSMA-based immunotherapy have been developed and tested in clinical studies.

PSMA Detection in CTCs

Investigation of PSMA on CTCs was performed in various clinical settings. A clear association of PSMA-positive CTCs to PSA progression-free survival, overall survival and predictive correlation to poorer treatment response was demonstrated.

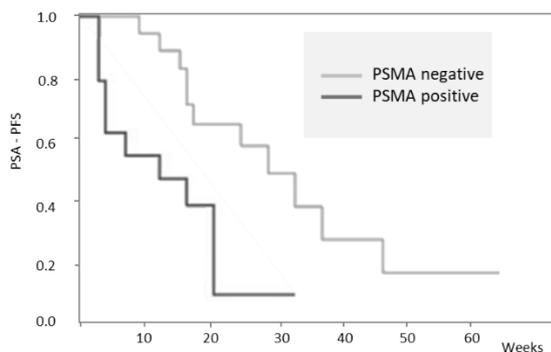


Figure 1 - adapted from Nagaya et.al. (2019): The Kaplan-Meier plot of PSA-PF survival was drawn according to the PSMA status in CTCs. The differences was compared with log-rank test (p=0.008).

CTC Profiling for Expression of PSMA, PAP, and PD-L1

A small pilot study (n=5) was initiated to test the possible utility of the GILUPI CellCollector® (Detektor CANCER01 - DC01) to detect CTCs in a planned first-in-man phase I study with a new therapeutic peptide vaccine (TENDU101®, EudraCT 2020-000918-15, NCT04701021).

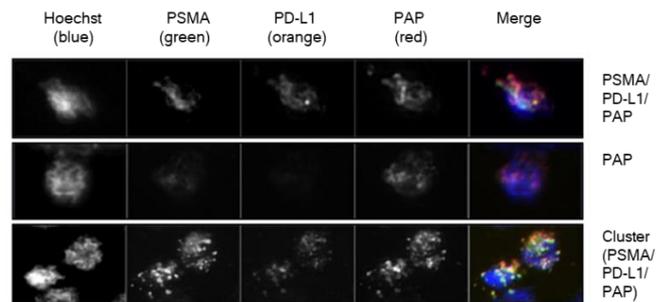


Figure 2: Immunofluorescence staining for PSMA, PD-L1, and PAP on captured CTCs in men with biochemical failure post-prostatectomy. Examples of stained CTCs captured in Gleason grade group 5.

All five patients had CTCs at recurrence (count range 18-31), and 4/5 had CTCs positive for PSMA, PAP, and PD-L1. The presence of CTCs was independent of PSA values or PSMA-PET findings.

A longitudinal observation of CTCs using the DC01 is performed in the ongoing phase I TENDU101® study (NCT04701021).

The implementation of CTC detection and profiling could improve the shared decision-making process addressing targeted therapy for men with de novo and relapsed PC after prostatectomy.