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Monitoring prostate specific membrane antigen and androgen receptor expression on Circulating Stromal Cells in advanced prostate cancer patients and their correlation with patient response

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ABSTRACT

Metastatic Prostate cancer (mPCa) mortality rates are high despite numerous treatment options against various mechanisms of action, including targeted therapies like prostate-specific membrane antigen (PSMA)-targeted therapy (Pluvicto) or anti-androgen receptor (AR) (Enzulamide, Biculamide, etc.). Further, tumor biomarkers (i.e. PSMA and AR) can change over time and with resistance mechanisms that develop after treatments. This suggests that primary biopsies may not represent later stage PCa tumors necessitating a way to identify patients that may respond to later line therapies. Blood based biopsies can be used to monitor PCa treatment, which can include circulating tumor cells (CTCs) and the newly discovered cancer associated macrophage like cells (CAMLs), which are cancer specific circulating phagocytic stromal cells. Interestingly, while PSMA & AR have been identified in CTCs, these targets have not been evaluated in CAMLs, nor have PSMA and AR expressions in CTCs & CAMLs been evaluated in an anti-AR therapy setting. We measured CAMLs & CTCs in mPCa to evaluate their PSMA & AR expression, as well as patients treated with anti-AR therapies.

MATERIALS & METHODS

We evaluated CAMLs & CTCs in a multi-institutional prospective pilot study using n=30 mPCa patients with progressive disease, prior to starting a new line of therapy (T0). Whole peripheral blood (7.5mL) was filtered for CAMLs & CTCs and stained for PSMA (n=15) & AR (n=15). In addition, 15 patients were treated with anti-AR therapy as standard of care and responses by PET/CT were compared against AR expression. When possible, follow up samples (T1) were also procured.

Table 1. Clinical Parameters

CAML number present at BL (n=30)	0	1 (3%)
	≥1	29 (97%)
CTC number present at BL (n=30)	0	25 (83%)
	≥1	5 (16%)
CAML size at BL (n=30)	< 50µm	14 (46%)
	≥ 50µm	16 (54%)
PSMA in CTCs or CAMLs (n=15)	Positive	9 (60%)
	Negative	6 (40%)
AR in CTCs or CAMLs (n=15)	Positive	8 (53%)
	Negative	7 (47%)
AR Therapy Type (n=15)	Enzalutamide	5 (33%)
	Bicalutamide	3 (20%)
	Abiraterone	1 (7%)
	Other	6 (40%)

Fig 1.

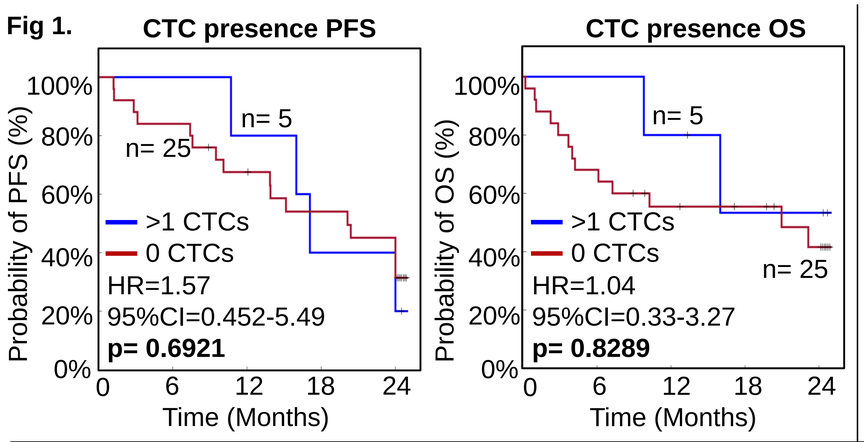


Fig 2.

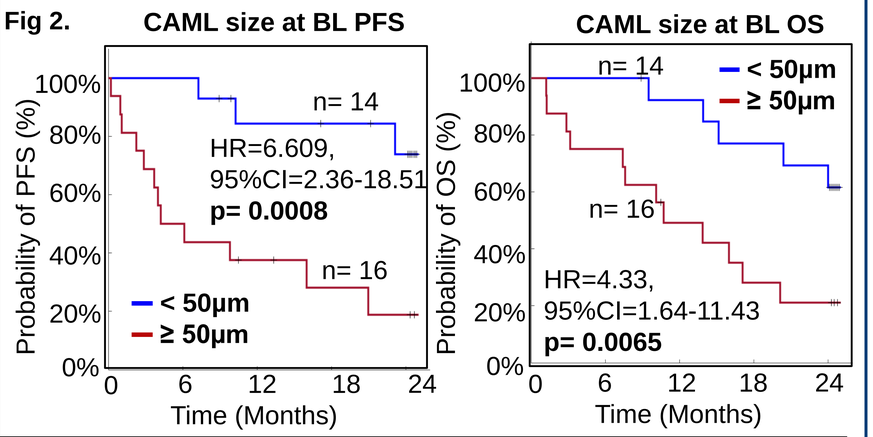


Fig 3.

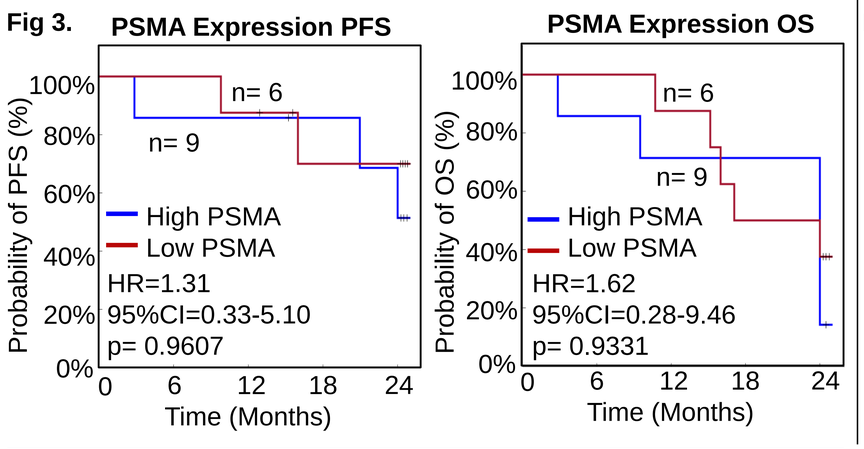
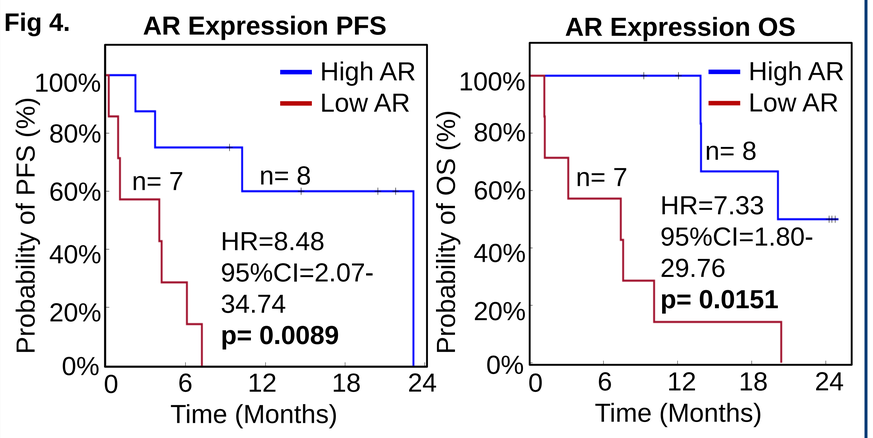


Fig 4.



RESULTS

- CTCs were found in 17% of patients and CAMLs identified in 96%, with 54% having hyper-engorged CAMLs ≥50 µm (**Table 1**)
- CTCs in patients were not associated with worse PFS HR=0.18, p=0.546 nor OS (HR=1.30, p=0.865) (**Fig 1**)
- Patients with ≥50 µm CAMLs had significantly worse PFS (**HR=6.6, p=0.0008**) and worse OS (**HR=3.5, p=0.0074**) (**Fig 2**)
- PSMA CAML/CTC expression was high in 60% of patients but was not associated with improved PFS nor OS (**Fig 3**)
- Those patients with high AR CAML/CTC expression (53%) were associated with significantly improved PFS and OS when treated with AR therapies (**Fig 4**)

CONCLUSIONS

- We utilized liquid biopsies to monitor the expression of two common cell surface receptors (PSMA and AR) in CAMLs and CTCs in patients with mPCa.
- Patients with hyper-engorged ≥50 µm CAMLs appeared to have poor prognosis evaluated over 24 months
- In a small subset of patients treated with AR therapy, high AR CTC/CAML expression appeared to correlate with better response PFS and OS outcomes evaluated over 24 months.
- Larger prospective studies analyzing the PSMA and AR surface receptors in the context of AR therapy are needed.

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