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PD-L1 Expression on Circulating Antigen Presenting Macrophages in Blood Predicts PFS & OS in an Array of Metastatic Cancer Types Treated with PD-L1/PD-1 Immunotherapies

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ABSTRACT

Cancer Associated Macrophage-Like cells (CAMLs) are a specific type of antigen presenting circulating stromal cells found in the blood of cancer patients (**Figure 1**). Recently, PD-L1 expression on CAMLs was described in a variety of cancers, appearing to parallel the inflammatory PD-L1 state of the tumor microenvironment, and acting as a possible predictive biomarker for PD-L1/PD-1 immunotherapeutics (IMTs). To determine if the predictive value of CAMLs, we monitored CAML PD-L1 from n=54 patients in an array of solid tumor subtypes, prior to induction of a new line of systemic PD-L1/PD-1 immunotherapy, to evaluate CAML's ability to predict response by progression free survival (PFS) and overall survival (OS).

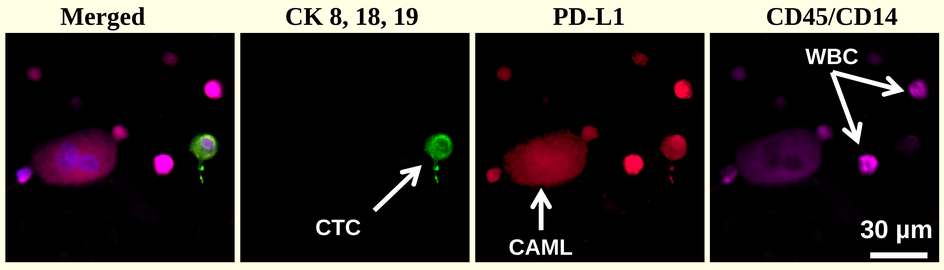

Figure 1. Example of CTC isolated with a CAML. CTCs are Cytokeratin pos. (green) & CD45/CD14 neg. CAMLs are CD45/CD14 pos. (purple) & maybe pos. for Cytokeratin. White blood cells are smaller CD45/CD14 pos.

Figure 2. PFS of CAML PD-L1

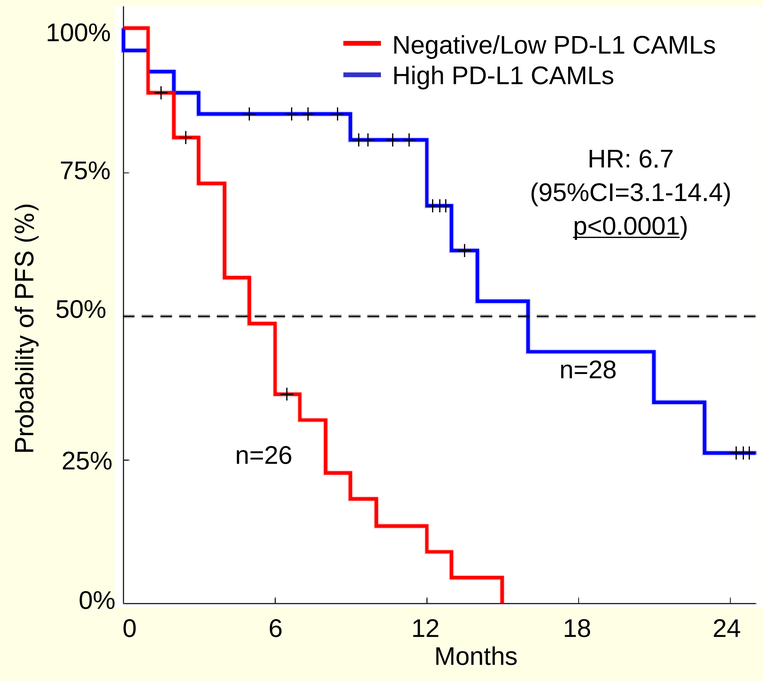

Figure 3. OS of CAML PD-L1

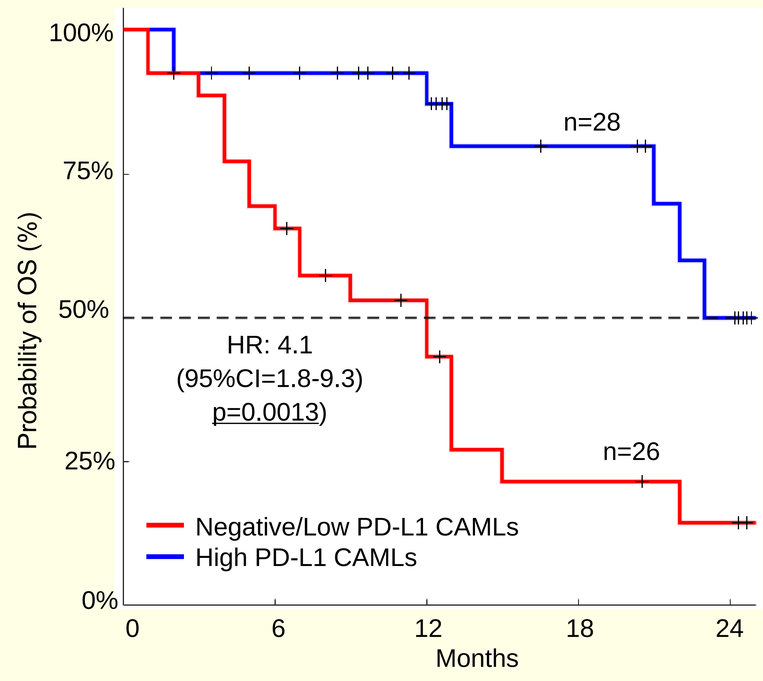

Table 1. Demographic Table

Median Age (Range)	**66 (34-81)**
Gender	
Male	**23 (43%)**
Female	**31 (57%)**
Race	
Caucasian	**47 (87%)**
AA	**3 (6%)**
Other	**3 (6%)**
ECOG	
0	**39 (72%)**
≥1	**15 (28%)**
Node positive	
0	**16 (30%)**
≥1	**33 (61%)**
unknown	**5 (9%)**
Number Prior Lines of Therapies	
1	**24 (44%)**
2	**11 (20%)**
≥3	**19 (35%)**
Cancer Types	
Lung	**24 (44%)**
Breast	**20 (37%)**
RCC	**10 (19%)**
Immunotherapy Type	
Pembrolizumab	**35 (65%)**
Nivolumab	**14 (26%)**
Atezolizumab	**5 (9%)**
Number of Metastatic Sites	
1	**36 (67%)**
≥2	**18 (33%)**

MATERIALS & METHODS

Three single blind multi-year prospective studies were run to evaluate PD-L1 CAML expression prior to induction of PD-L1 or PD-1 based immunotherapy in metastatic Lung Cancer (LC) (n=24), metastatic Breast Cancer (BC) (n=20) or metastatic Renal Cell Carcinoma (RCC) (n=10) to evaluate patient's PFS and OS (**Table 1**). We recruited patients with pathologically confirmed disease, progressing by PET/CT after at least one failed prior line of therapy (**Table 1**). Blood samples (7.5 mL) were taken prior to start of new PD-L1/PD-1 therapeutic regimes, i.e. pembrolizumab (n=35), or nivolumab (n=14), or atezolizumab (n=5). Whole blood was filtered by CellSieve microfilters to collect CAMLs. CAMLs were identified by CD45/CD14 positivity and stained for PD-L1. CAML's PD-L1 was scored as a binary, high or low/negative. PFS & OS hazard ratios (HRs) were evaluated by censored univariate and multivariate analysis at 24 months (**Table 2**).

RESULTS

- CAMLs were found in 98% of all tested samples.
- Pts with high CAML PD-L1 expression treated with IMT had significantly better PFS (HR=6.7, p<0.0001) independent of other clinical parameters (**Figure 2**)
- Pts with high CAML PD-L1 expression treated with IMT had significantly better OS (HR=4.1, p=0.0013) independent of other clinical parameters (**Figure 3**)

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Table 2. Univariate and Multivariate Table

Variable	Uni PFS (p value)	Multi PFS (p value)	Uni OS (p value)	Multi OS (p value)
CAML PD-L1 high vs Low	**<0.0001**	**<0.0001**	**0.0013**	**0.0025**
Race	**0.2005**		**0.6736**	
Male vs Female	**0.4395**		**0.1464**	
Age <65 vs ≥65	**0.4966**		**0.0128**	**0.0158**
ECOG 0 vs ≥1	**0.6089**		**0.6861**	
Cancer Type	**0.7356**		**0.9013**	
Node Negative vs Positive	**0.8945**		**0.7565**	
# Prior Lines of Therapy 1 vs ≥2	**0.7098**		**0.9895**	
# of Metastatic sites 1 vs ≥2	**0.2601**		**0.5507**	
Immunotherapy type	**0.7795**		**0.4566**	

CONCLUSIONS

- These data suggests that PD-L1 expression in circulating CAMLs appears to independently predict pts with increased benefit to PD-L1/PD-1 IMTs in an array of tumor types (**Table 2**)
- Larger and more refined studies are needed to validate these findings.

REFERENCES

1. Adams DL, et al "Circulating giant macrophages as a potential biomarker of solid tumors." PNAS, 111(9):3514-3519. (2014)
2. Cristofanilli M, "Liquid Biopsies in Solid Tumors" *Springer Intl Publish.* (2017)
3. Adams DL, et al. "Sequential tracking of PD-L1 expression and RAD50 induction in circulating tumor and stromal cells of lung cancer patients undergoing radiotherapy" Clin Can Res, 23(19): 5948-5958. (2017)