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Contact: dan@creatvmicrotech.com
301-983-1650

Sequential Monitoring of PD-L1 on Circulating Stromal Cells in Blood Predicts PFS in NSCLC Patients Undergoing Immunotherapy after Definitive Chemoradiation

Daniel L Adams[1], Alexander Augustyn[2], Jianzhong He[2], Yawei Qiao[2], Ting Xu[2], Zhongxing Liao[2], Kirby P. Gardner[1,4], Jillian A. Moran[1,3], Cha-Mei Tang[5], Steven H. Lin[2]

[1] Creatv MicroTech, Inc., Monmouth Junction, NJ 08852, [2]MD Anderson Cancer Center, Houston, TX 77030, [3]Rutgers, the State University of New Jersey, New Brunswick, NJ 08901, [4]Rutgers University Graduate School of Biomedical Sciences, [5]Creatv MicroTech, Inc., Potomac, MD 20854

ABSTRACT

Cancer Associated Macrophage Like cells (CAMLs) are circulating stromal cells in the blood of patients (pts) with solid tumors that are phagocytic giant macrophages that may represent the inflammatory state of the tumor microenvironment. Previously, we demonstrated in non-small cell lung carcinoma (NSCLC), CAMLs ≥50µm after chemo-radiation therapy (CRT) is associated with worse progression free (PFS) and overall survival (OS). We have also shown that PD-L1 expression on CAMLs is dynamic and can change with CRT, which is difficult to assess with repeat biopsies but possible with liquid biopsies. For this study, we evaluated if the CAML parameters can predict response to CRT with or without immunotherapy (IMT) agents in unresectable NSCLC.

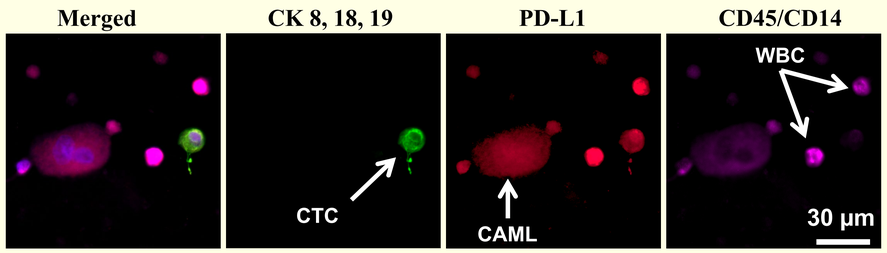

Figure 1. Example of CTC isolated with a CAML. CTCs are Cytokeratin positive (green) & CD45/CD14 negative. CAMLs are CD45/CD14 positive (purple) & may be weakly positive for Cytokeratin (green). White blood cells (WBCs) are normal sized CD45/CD14 positive cells.

MATERIALS & METHODS

A single blind multi-year prospective study was undertaken to test the relationship of PD-L1 expression & ≥50µm CAMLs to PFS/OS in NSCLC, pre & post CRT, with (n=96) & without (n=72) anti-PD-L1/PD-1 IMT. This included atezolizumab (prospective single arm NCT02525757) n=39, durvalumab n=52 or pembrolizumab n=5 both after 2018 FDA approval. We recruited 168 pts with pathologically confirmed unresectable NSCLC prior to CRT. Blood samples (15 mL) were taken at Baseline (BL), CRT completion (T1), & ~1 month after (T2) CRT (with n=96 or without n=72 IMT). Blood was filtered by CellSieve filtration & CAMLs quantified for size (<49 µm or ≥50 µm) & PD-L1 expression, to evaluate PFS & OS hazard ratios (HRs) by censored univariate/multivariate analysis at 24 months.

CONCLUSIONS

- In unresectable NSCLC, ≥50 µm CAMLs after CRT is prognostic regardless of IMT use.
- PD-L1 in CAMLs appears to predict for response to consolidated IMT after CRT.
- CAML size after completion of CRT appeared to predict for long term patient benefit
- Monitoring dynamic changes of PD-L1 in CAMLs appears to predict immunotherapy effectiveness in NSCLC after CRT
- Follow up patient subtyping and analysis is ongoing to evaluate OS & PD-L1 in CAML populations

References

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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)

Funding Sources

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RESULTS

- CAMLs were found in 90% of all samples, average 5.8 CAMLs/15mL (**Fig 1**).
- ≥50µm CAMLs did not predict PFS in CRT pts or CRT with IMT at BL (**Fig 2**)
- ≥50µm CAMLs did predict PFS in patient treated with or without IMT, after completion of CRT (T1)
- PD-L1 in primary tumor biopsies (>1%) did not predict IMT response (HR 1.8, p=0.262)
- High PD-L1 in CAMLs did not predict PFS in pts receiving CRT alone nor CRT with IMT at either the BL nor T1 time points
- Pts with high PD-L1 CAMLs after CRT and start of IMT had significantly better PFS when treated with IMT (**Fig 3**)

Figure 2. PFS of ≥50µm vs < 50µm CAMLs with or without IMT

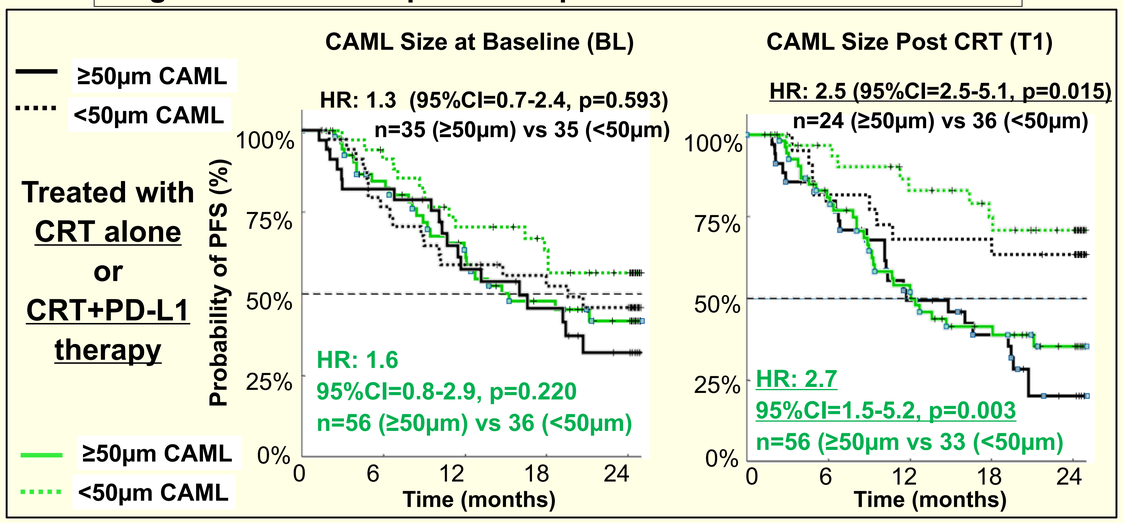

Figure 3. PFS of PD-L1 expression in CAMLs in patients treated with or without IMT