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Abstract 1025

Monitoring PD-L1 in Tumor Macrophage Fusion Cells in Blood Identifies High PD-L1 Checkpoint Inhibitor Responses in Metastatic Breast Cancer

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ABSTRACT

In metastatic breast cancer (mBC), anti-PD-L1/PD-1 immune checkpoint inhibitors (ICIs) (e.g. pembrolizumab) are approved for a sub-population of mBC patients (pts) with a ≥10 PD-L1 combined positive score (CPS) equating to a median progression-free survival (mPFS) of 9.7 months & median overall survival (mOS) of >24 months. However, 62% of pts have CPS <10 and may benefit from ICIs, as ≥ 1 CPS have mPFS of 7.6 months vs. 5.6 months for chemotherapy. One hypothesis as to why low PD-L1 pts respond to ICIs is dynamic PD-L1 upregulation after starting new therapies. Identifying this change requires the monitoring of PD-L1 and its subsequent ICI benefit. Recent studies have identified PD-L1-expressing myeloid cells that disseminate into the blood from primary tumors, tumor macrophage fusion cells (TMFCs), which may predict ICI response. However, changes in TMFC PD-L1 during ICI therapy and their relationship to patient response is unknown. In this study, we monitored PD-L1 expression in TMFCs during ICI treatment and compared it to tumor CPS in mBC pts to evaluate PFS and OS at 24 months.

MATERIALS & METHODS

We conducted a prospective pilot study of n=72 pts with pathologically confirmed mBC receiving anti-PD-L1 ICIs (n=28 Pembrolizumab, n=1 Nivolumab, n=5 Atezolizumab, n=38 Retifanlimab). CellSieve microfilters isolated TMFCs from 7.5ml peripheral blood samples prior to start of PD-L1 ICI (T0) and at monthly timepoints (T1-T3) for ~4 months after ICI induction. TMFCs were identified by enlarged cell size (>30 µm) and polyploid nucleus. Average PD-L1 expression in TMFCs were scored as negative or positive. Pearson's correlation compared average TMFC PD-L1 to CPS PD-L1 from tissue. TMFC PD-L1 and CPS were compared to pts' PFS & OS by Cox proportional univariate analysis at 24 months.

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Fig 1. Tumor vs. TMFC PD-L1

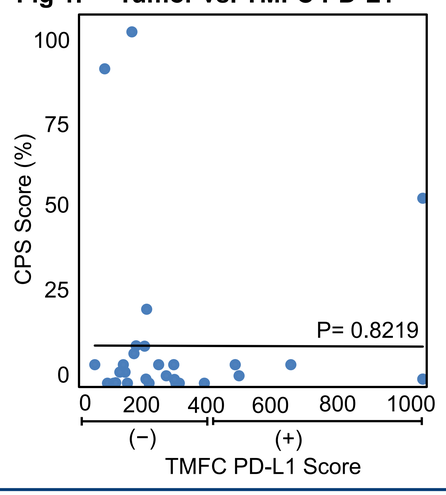


Table 1. Forest Plot For CPS and TMFC PD-L1

Study	PFS HR; p-value	PFS HR	OS HR; p-value	OS HR	
CPS ≥10	0.85; 0.9670		0.42; 0.3420		N=7 v 31
CPS 1-10	0.57; 0.2846		0.80; 0.8211		N=21 v 17
CPS <1	0.54; 0.2797		0.75; 0.8925		N=10 v 28
(+) TMFC PD-L1 T0	0.95; 0.9853		0.72; 0.6478		N=13 v 59
(+) TMFC PD-L1 T1	**0.37; 0.0107**		0.43; 0.1423		N=16 v 28
(+) TMFC PD-L1 T2	0.59; 0.2195		0.62; 0.4814		N=7 v 40
(+) TMFC PD-L1 T3	**0.31; 0.0458**		0.36; 0.1337		N=7 v 15
(+) TMFC PD-L1 at any timepoint	**0.52; 0.0201**		0.56; 0.1159		N=26 v 46

Fig 2. CPS Score PFS / CPS Score OS

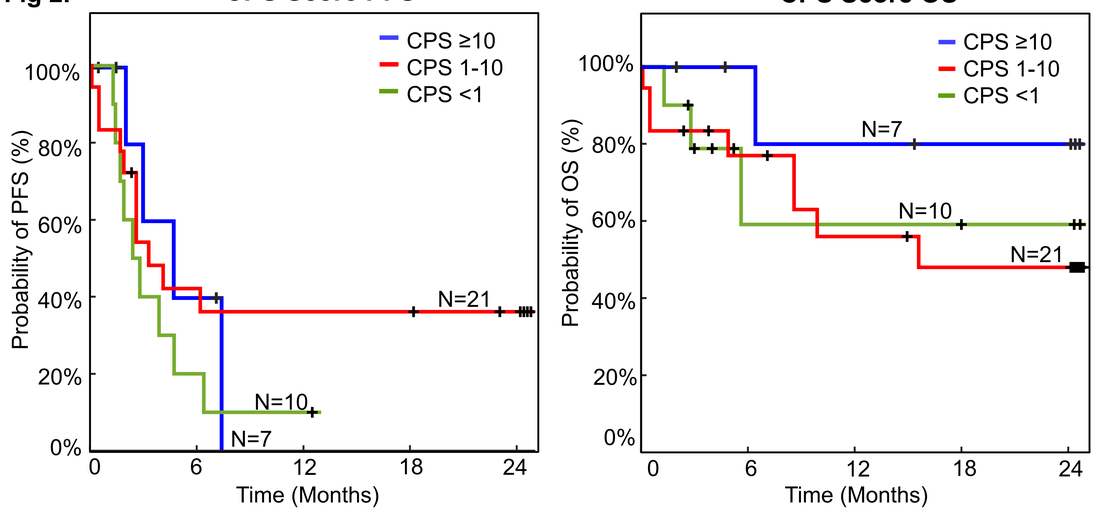


Fig 3. Positive vs. Negative TMFC PD-L1 PFS / Positive vs. Negative TMFC PD-L1 OS

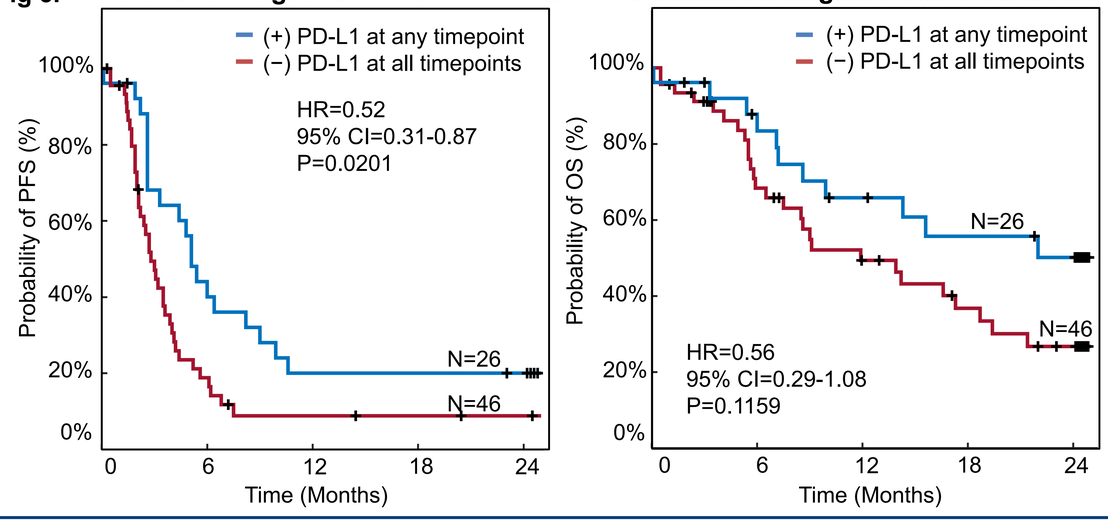
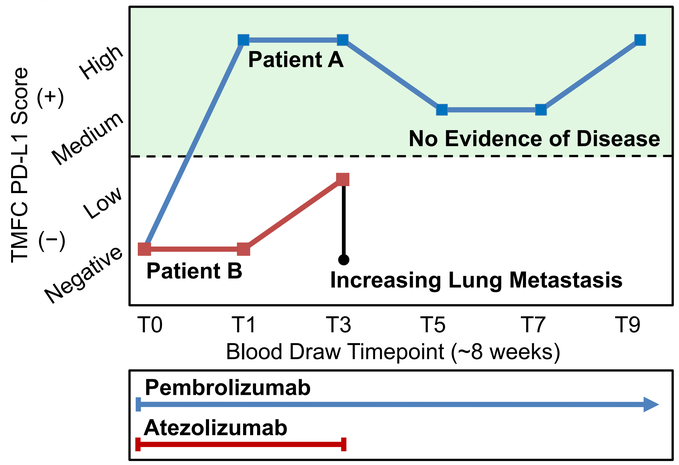


Fig 4. Case Study In Monitoring TMFC PD-L1



RESULTS

- 99% (n=71/72) of pts provided a T0 sample. 83% (n=60/72) provided T1 (~22 days after ICI), 50% (n=36/72) provided T2 (~62 days), and 40% (n=29/72) provided T3 (~113 days).
- CPS was not significant for PFS or OS. (**Table 1 & Fig. 2**)
- CPS vs. T0 TMFC PD-L1 were not correlated. (**Fig. 1**)
- Patients with PD-L1 positive TMFCs had improved PFS at T1 (HR=0.37, p=0.0107) and T3 (HR=0.31, p=0.0458). No TMFC timepoints were significant for OS. (**Table 1**)
- Patients with PD-L1 positive TMFCs at any timepoint had significantly improved PFS (HR=0.52, p=0.0201), but not OS. (**Fig. 3**)

CONCLUSIONS

- Tumor PD-L1 CPS was not found to be correlated with clinical outcomes. However, monitoring PD-L1 in TMFCs throughout therapy correlated with improved PFS and trends toward improved OS.
- Monitoring PD-L1 in TMFCs may serve as a real-time biomarker to better indicate ICI response. (**Fig. 4**)
- Further studies into the role of TMFC PD-L1 in predicting therapeutic response are ongoing.

REFERENCES

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