

ABSTRACT

Studies have described the efficacy of immunotherapies (IMT) utilizing programmed death 1 receptor and its ligand (PD-L1) for treating solid tumors. However, many patients (pts) fail to respond to IMT, underscoring the need for better predictive biomarkers for improved pt identification and stratification. Poor IMT responses are often attributed to the dynamic nature of PD-L1 which may change after chemotherapy or radiation and is quantified by static immunostaining. Recently, studies have described PD-L1 upregulation in giant phagocytic stromal cells, i.e. Cancer associated macrophage-like cells (CAML), circulating macrophages that have engulfed tumors before entering circulation and may predict IMT responses. We conducted a pilot study to monitor the peripheral blood of n=46 metastatic cancer pts undergoing systemic treatment with IMT in combination with other therapies, to evaluate CAML PD-L1 prior to and post IMT induction with clinical correlation at 2 years.

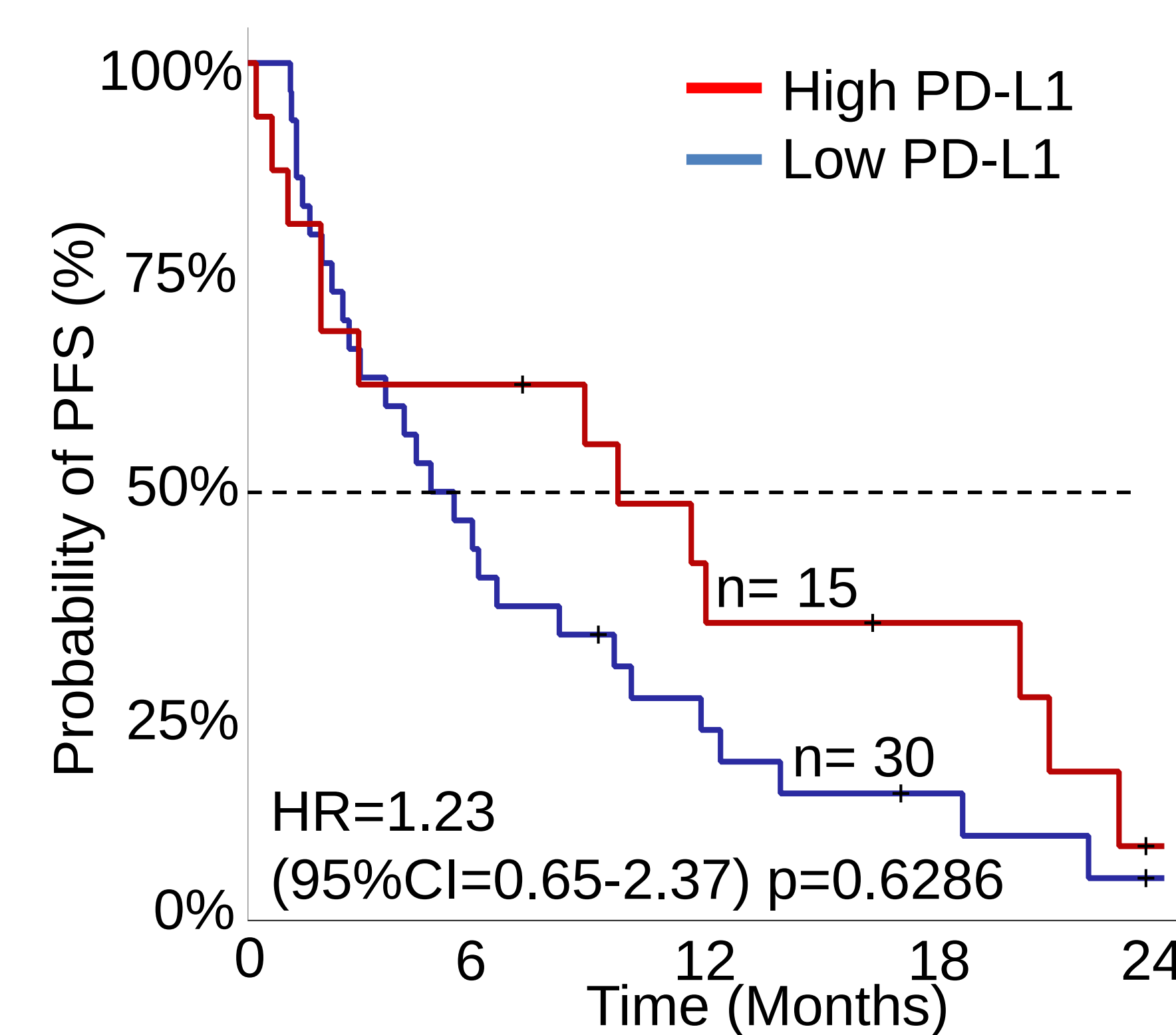
MATERIALS & METHODS

In a prospective pilot study of n=46 metastatic cancer pts, breast (n=14), non-small cell lung (n=24), and renal cell (n=8), all starting new lines of systemic chemotherapy in combination with IMT (pembrolizumab [n=30], nivolumab [n=13], Durva [n=1], or atezolizumab [n=3]) for newly diagnosed recurrent metastasis (n=24) or with previously treated progressive metastatic disease (n=22). We isolated CAMLs from 7.5 ml baseline (T0) blood using the LifeTracDx® PD-L1 test and scored PD-L1 as high or low (0=Neg, 1=Low, 2=High, 3=Very High). If possible, a follow-up sample (T1) was taken (~48 days) after IMT induction. Pts' progressive free survival (PFS) and overall survival (OS) hazard ratios (HRs) were analyzed by censored univariate analysis based on RECIST v1.1 over 2 years.

Table 1. Clinical Parameters

CAML Number at T0	0	1 (2%)
	≥1	45 (98%)
CAML size at T0	< 50	22 (48%)
	≥ 50	24 (52%)
CAML Number at T1	0	2 (6%)
	≥1	33 (94%)
CAML size at T1	< 50	8 (23%)
	≥ 50	26 (72%)
Cancer Type	Breast Cancer	14 (30%)
	Lung Cancer	24 (52%)
	Renal Cell Carcinoma	8 (17%)
Treatment Type	Pembrolizumab	30 (46%)
	Nivolumab	13 (28%)
	Atezolizumab	2 (4%)
	Durvalumab	1 (2%)

Figure 1 T0 CAML PD-L1 PFS



T0 CAML PD-L1 OS

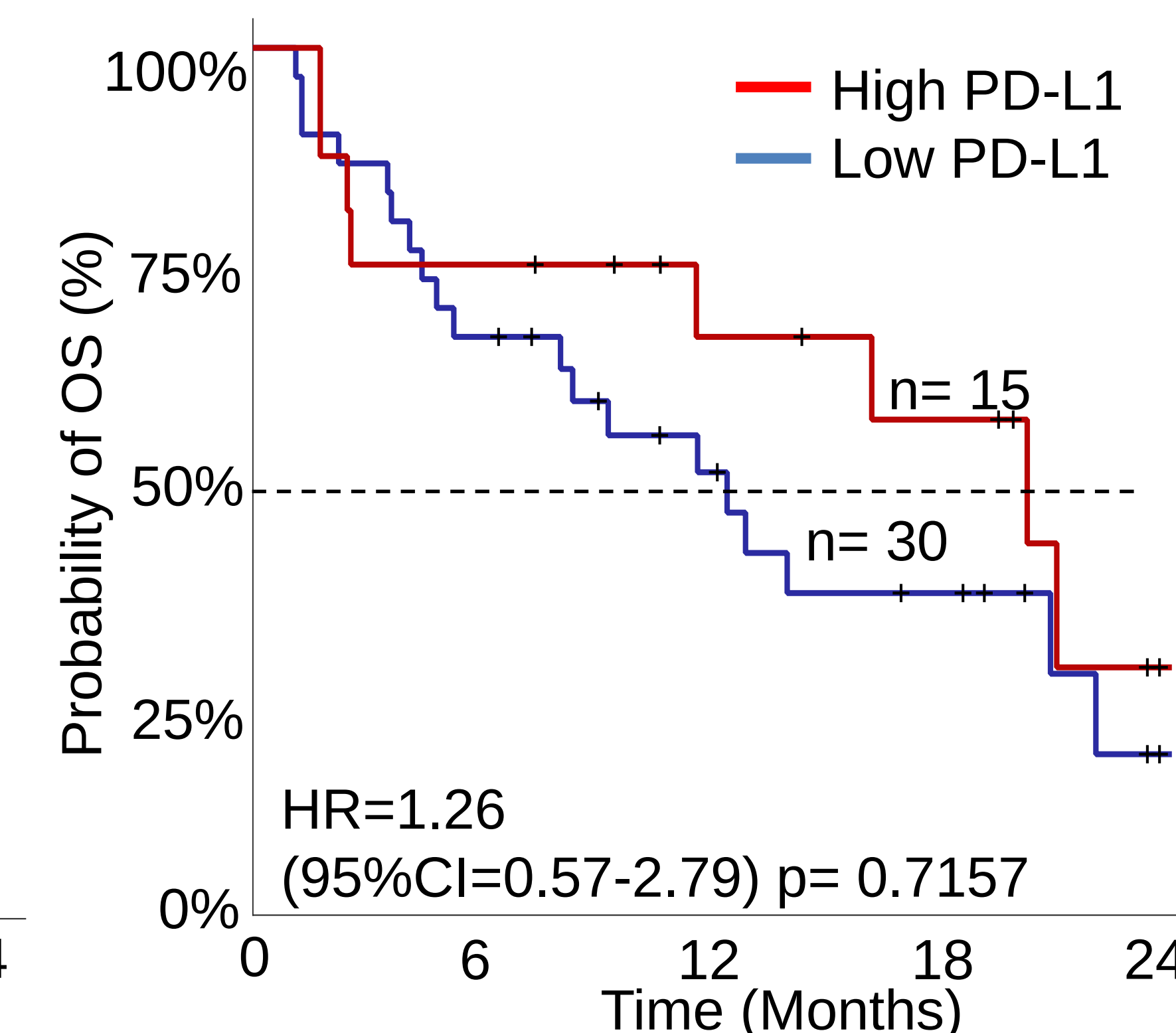
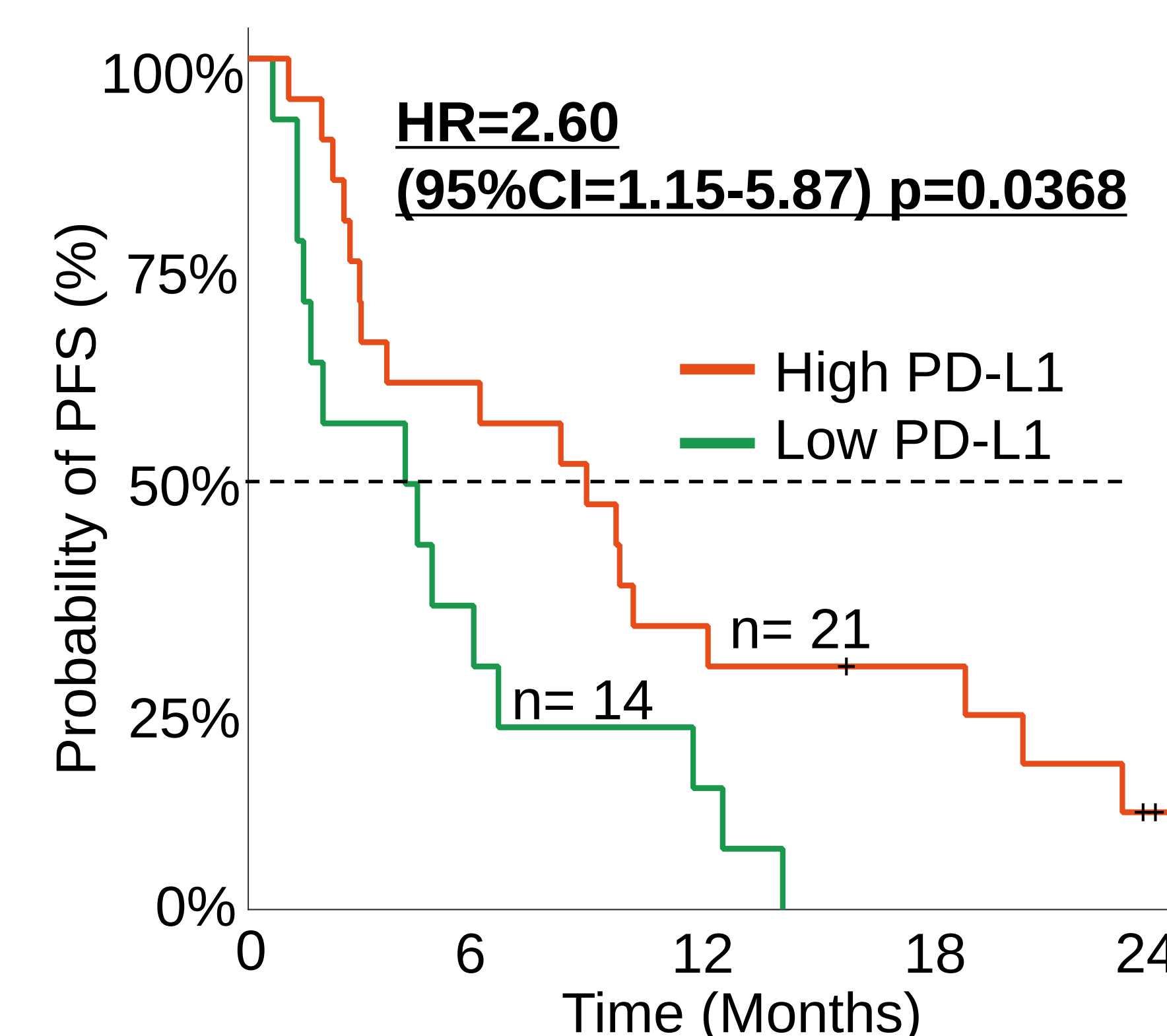
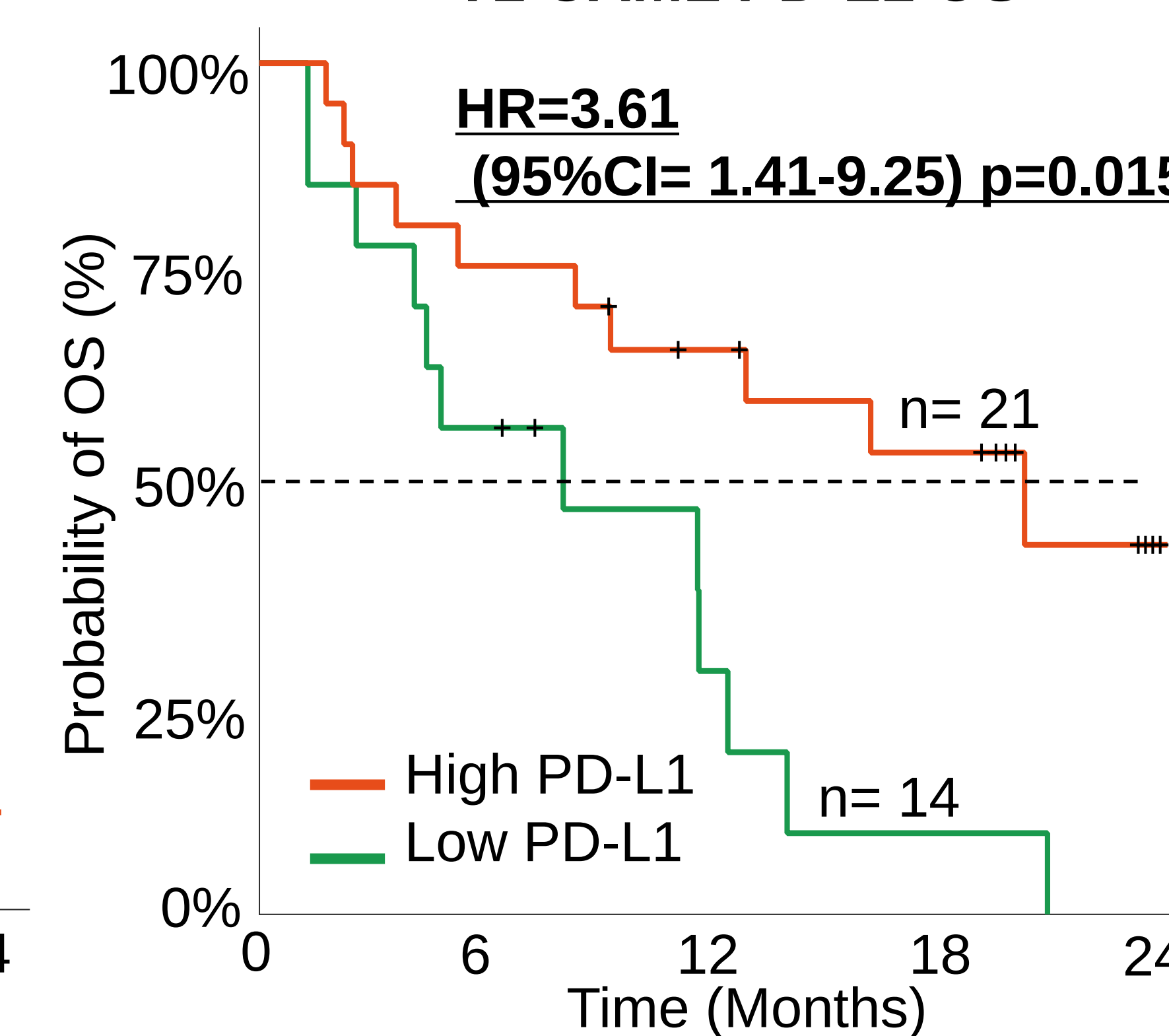


Figure 2. T1 CAML PD-L1 PFS



T1 CAML PD-L1 OS



RESULTS

- T0 samples were available for 98% (n=45/46) of patients and T1 samples were available for 76% (n=35/46) of patients
- At T0, high CAML PD-L1 was not correlated with improved PFS (HR=1.23, p=0.6286) or OS (HR=1.26, p=0.7157)
- At T1, high CAML PD-L1 was significantly correlated with improved PFS (**HR=2.60, p=0.0368**) and OS (**HR=3.61, p=0.0150**).
- Pts with consistently low PD-L1 at T0 & T1 had the poorest responses (mPFS=2.0 mons, mOS=6.8 mons),
- Pts with consistently high PD-L1 had the best responses (**mPFS=10.1 mons and mOS=20.9 mons**)

FUNDING SOURCES

This work was supported the U.S. Army Research Office (ARO) and Defense Advanced Research Projects Agency (DARPA) (W911NF-14-C-0098). The content of the information does not necessarily reflect the position or the policy of the US Government. This work was supported by a NIH grant R43CA206840

Figure 3. CAML PD-L1 Changes Between T0 and T1

	mPFS	mOS
Low to Low N=12	2.0 (1.5-5.0)	6.8 (4.3-12.1)
High to Low N=2	0.7 (0.67-12.0)	2.7 (2.7-12.2)
<u>Low to High</u> <u>N=11</u>	<u>5.0</u> <u>(2.8-10.5)</u>	<u>11.4</u> <u>(5.5->24.0)</u>
<u>High to High</u> <u>N=10</u>	<u>10.1</u> <u>(3.1-23.8)</u>	<u>20.9</u> <u>(16.8->24.0)</u>

CONCLUSIONS

- We describe a cancer agnostic blood-based biopsy to monitor dynamic PD-L1 changes in circulating tumor immune cells (i.e. CAMLs)
- Monitoring the PD-L1 in CAMLs appears to offer a dynamic perspective on immune response modulation over time
- In mBC, mNSCLC, and mRCC, high PD-L1 expression in CAMLs after starting IMT appeared prognostic for increased IMT benefit
- While this initial pilot study appears to stratify pts with better IMT responses, larger validation studies are needed.

REFERENCES

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