

# PD-L1 Expression on Circulating Tumor Associated Macrophage Polyploids Predicts Patient Outcomes in Metastatic Breast Cancer

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## ABSTRACT

Many cancer types respond well to programmed cell death ligand-1 (PD-L1) immunotherapies (IMT) when tumor tissue expresses high levels of PD-L1; with the exception of metastatic breast cancer (mBC) that has relatively poor response rates to IMT. It has been suggested that this poor response is due to the dynamic nature of PD-L1 expression which can upregulate or downregulate expression following chemotherapy or radiation exposure, both common in mBC neoadjuvant treatments. Cancer associated macrophage-like cells (CAML), specific polyploid phagocytic stromal cells found in the peripheral blood of cancer patients (pts) has been described as upregulating PD-L1 expression after chemotherapy induction and correlative to IMT response rates in many cancer subtypes. We evaluated blood samples from n=120 mBC pts prior to start of chemotherapy alone or pts prior to IMT, to quantify the relationship between their CAML PD-L1 expression and pt responses by progression free survival (PFS) and overall survival (OS).

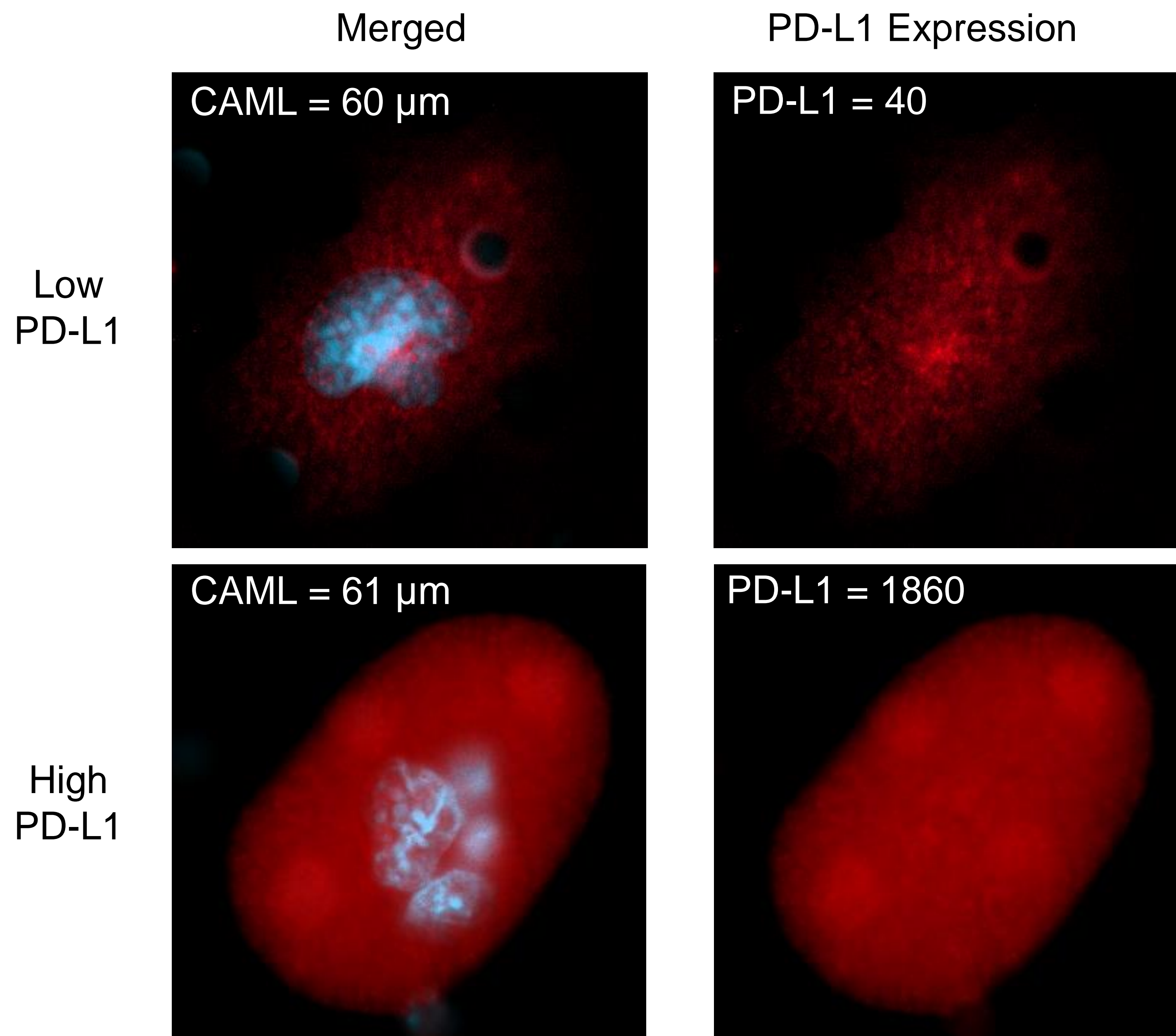
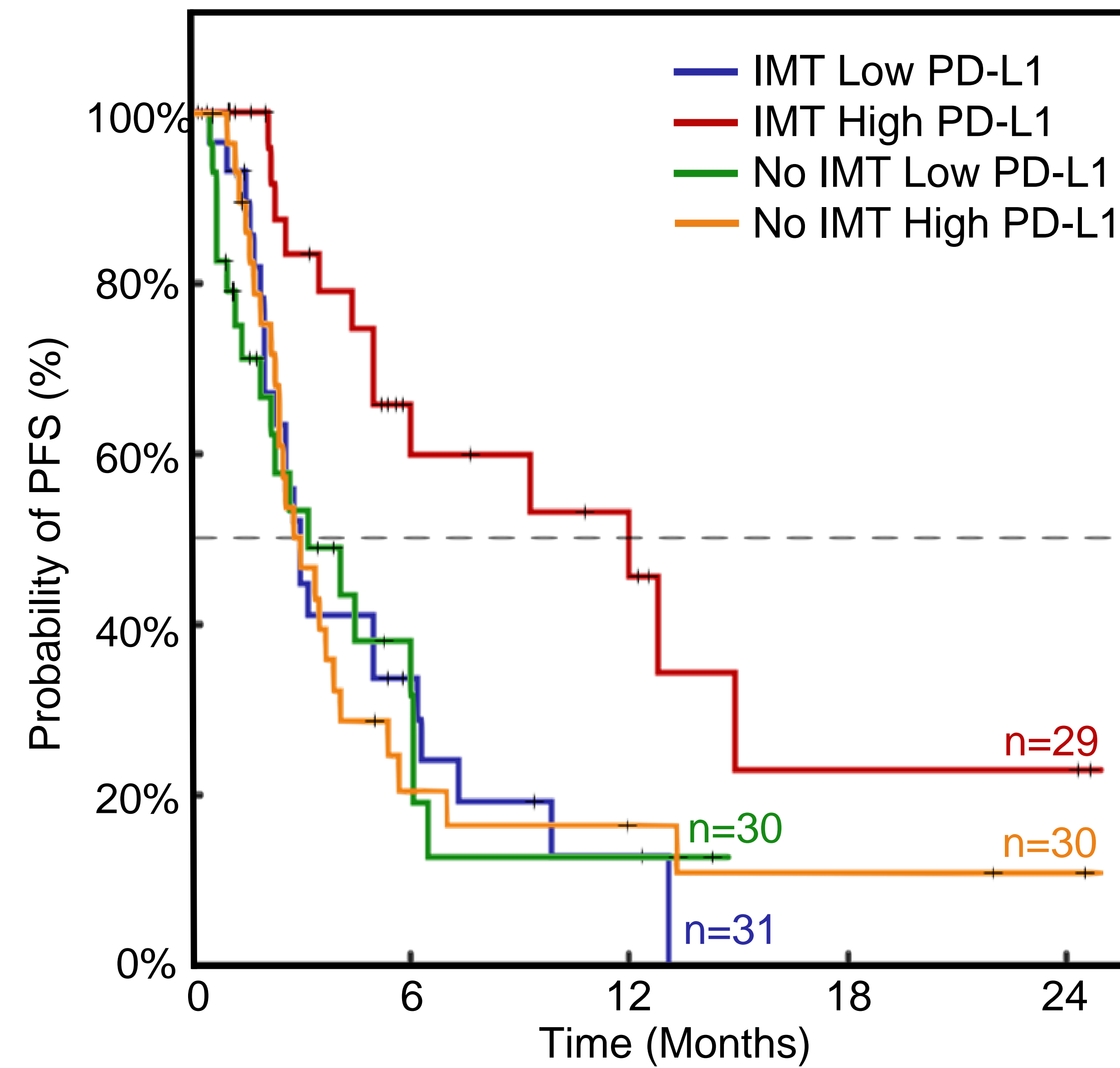


Figure 1. Example of Low and High PD-L1 expressing CAMLs. Giant polyploid CAMLs with large atypical nucleus (blue) can have various PD-L1 expressions (red). Box is 80 μm.

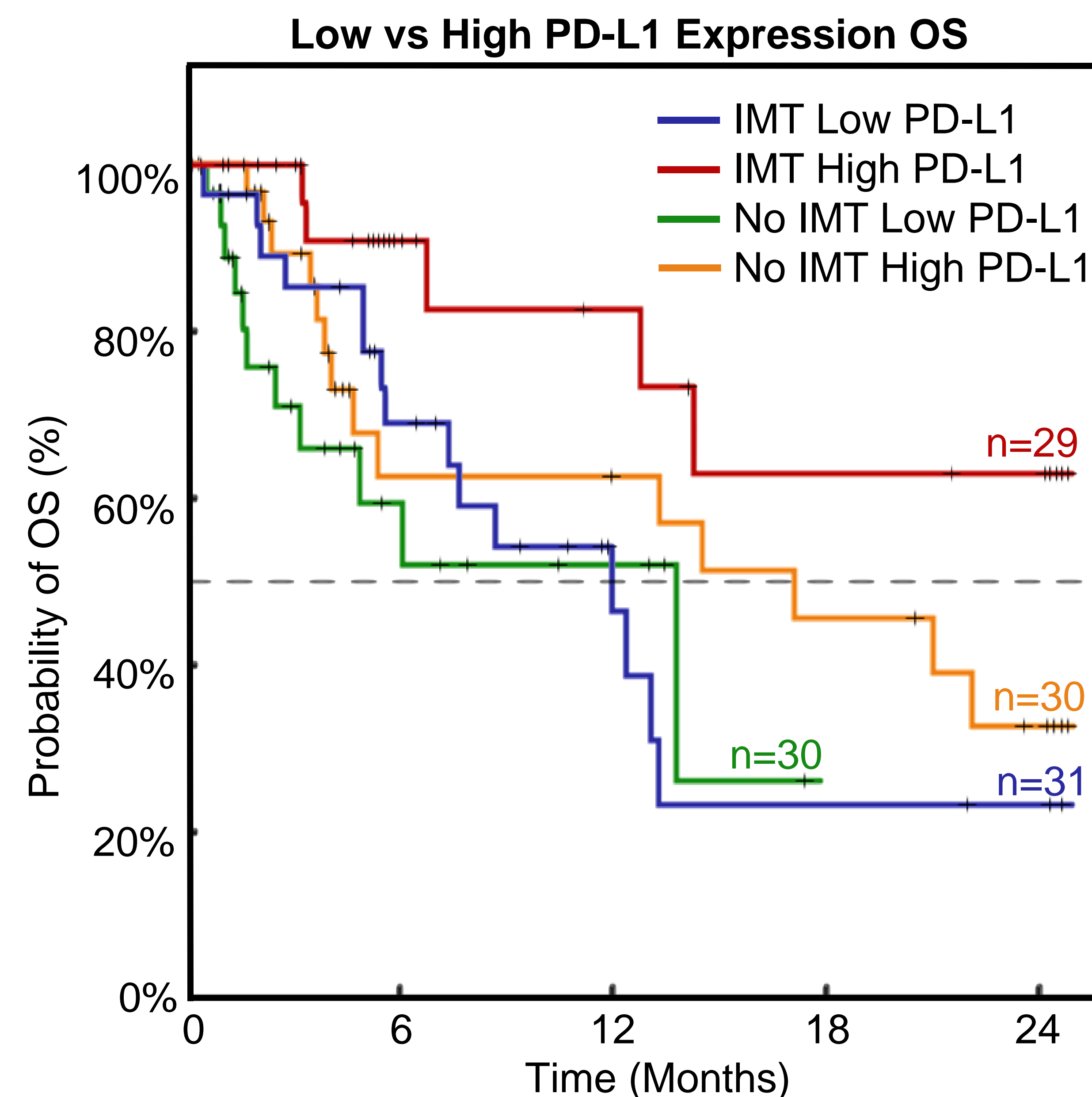
## FUNDING SOURCES

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Figure 2. Low vs High PD-L1 Expression PFS



IMT: HR=3.116, 95%CI=1.555-6.244, p= 0.0025  
No IMT: HR=1.00, 95%CI= 0.544-1.845, p=0.8802



IMT: HR=2.967 95%CI=1.217-7.232, p= 0.0309  
No IMT: HR=1.674, 95%CI=0.702-3.995, p=0.3469

## MATERIALS & METHODS

In a prospective pilot study in patients previously treated with chemotherapy/radiation, we recruited n=60 mBC patients beginning new lines of IMT or n=60 patients starting new lines of only chemotherapy. We isolated CAMLs from patient blood samples using CellSieve™ microfiltration. Peripheral blood (7.5mL) was procured and filtered for CAMLs, then stained for PD-L1, which was then measured for expression using Zen2011 Blue software. If possible, PD-L1 expression was then monitored in CAMLs from follow-up samples, post new therapy induction. Patient PFS and OS hazard ratios (HRs) were analyzed by censored univariate analysis based on RECIST v1.1 over two years.

## RESULTS

- ▶ CAMLs were found in 90% (n=54/60) of IMT treated patients and 100% (n=60/60) of chemotherapy treated patients.
- ▶ PD-L1 expression in polyploid CAMLs was high in 52% (n=31/60) of patients receiving IMT and high in 50% (n=30/60) of chemotherapy patients.
- ▶ Patients with high PD-L1 expressing CAMLs treated with IMT (red) had significantly better PFS (HR=3.1, p=0.0025) and significantly better OS (HR=2.9, p=0.0309) compared to low PD-L1 expressing CAMLs (blue).
- ▶ Patients with high PD-L1 expressing CAMLs treated with IMT (red) had significantly better PFS (HR=2.67, p=0.0062) but not OS (HR=2.47, p=0.0741) compared to patients with high PD-L1 expressing CAMLs in the no IMT group (orange).
- ▶ Patients with high PD-L1 expressing CAMLs treated with no IMT (orange) did not have significantly better PFS (HR=1.00, p=0.8802) nor OS (HR=1.6, p=0.3469) compared to low PD-L1 expressing CAMLs (green).

## CONCLUSIONS

- ▶ Circulating giant polyploid cells found in patients with mBC can express high levels of PD-L1.
- ▶ High levels of PD-L1 in CAMLs appears to predict patient response to PD-L1/PD-1 IMTs.
- ▶ Studies monitoring dynamic changes to evaluate PD-L1 expression in mBC CAMLs after induction of new therapies is ongoing.

## REFERENCES

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