



Combining Circulating Tumor Cells and Cancer Associated Macrophage-Like Cells Enhances Risk Stratification Models in Pan-Cancer Metastatic Disease

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ABSTRACT

In metastatic cancer, Circulating Tumor cells (CTCs) are established prognostic indicators of patients (pts) less likely to respond to new lines of systemic therapy with poor outcomes, such as short progression free survival (PFS) and overall survival (OS). However, CTCs are typically found in specific malignancies (breast, prostate & colon), often in <20% of pts with metastatic disease, and pts without CTCs may also rapidly progress. Recently, an inflammatory pro-tumorigenic macrophage coming from tumor stroma (i.e. Cancer associated macrophage-like cell [CAML]) was found in >90% of metastatic cancer pts, and whose phagocytic engorgement appears to correlate with poor outcomes, independent of CTCs. As CTCs and CAMLs are isolated in conjunction from a single blood sample, and both are prognostic for outcomes, we evaluated their utilization prior to induction of new systemic therapy in 6 types of metastatic cancer to model pt risk stratification based on 2 year outcomes.

Figure 1. PFS and OS by Number of CTC in Patients Blood

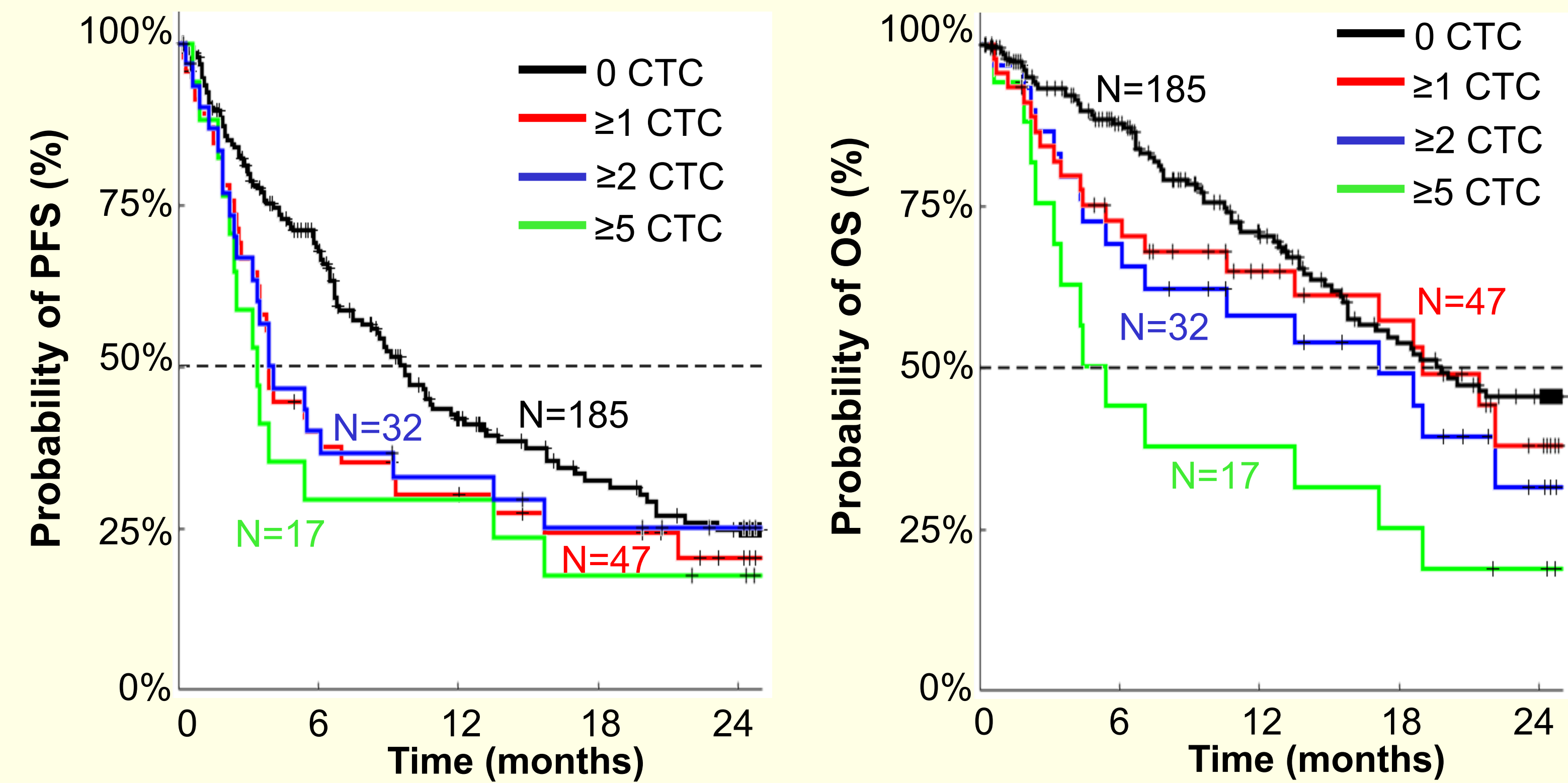


Figure 2. PFS and OS by CAMLs Sizes in Patient's Blood

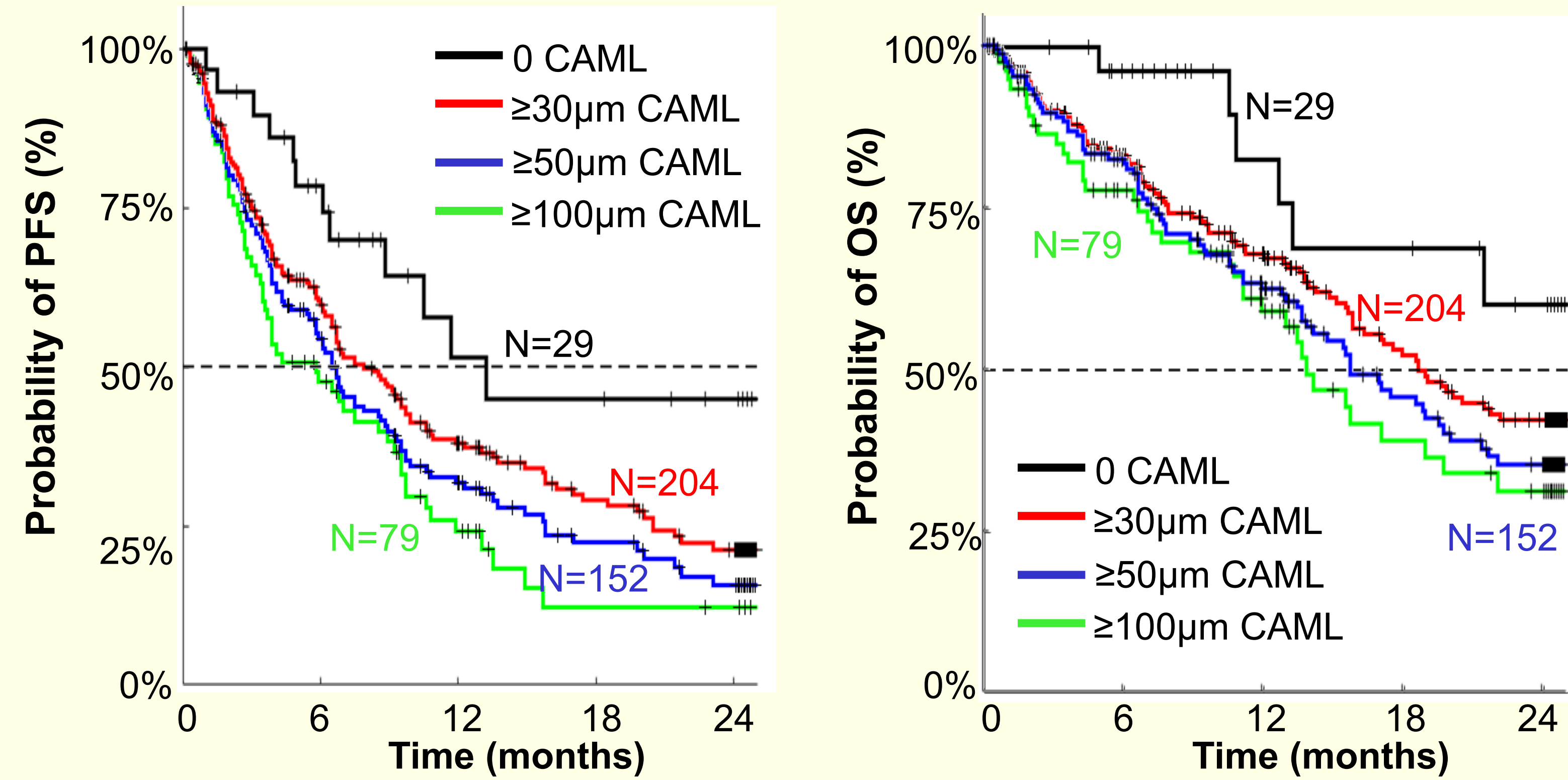
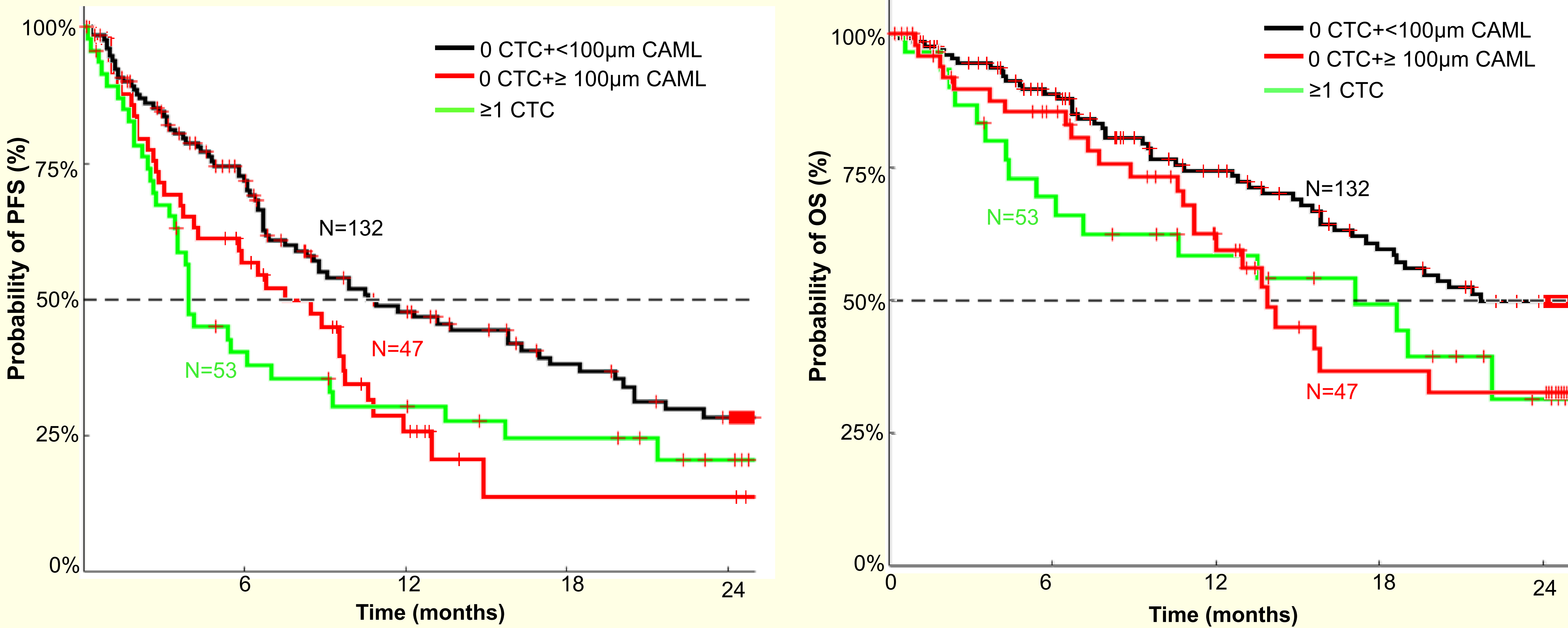


Figure 3. PFS and OS by Presence of CTCs and Subtyped by CAML's Size in Patients Blood



MATERIALS & METHODS

A prospective 2 year blind multi-institutional study was undertaken to model CTCs and CAMLs in prognosticating outcomes prior to induction of a new line of systemic therapy (n=233) in metastatic: Breast (n=60), Prostate (n=40), Pancreas (n=25), Colon (n=28), Renal Cell Carcinoma (RCC) (n=39), and Lung (n=40). Blood was filtered by CellSieve™ filters with subtypes of CTCs and hyper-enlarged CAMLs (≥100µm) enumerated. A machine learning algorithm was trained on this initial data set to develop predictive models which could stratify pt populations by risk for likelihood of PFS & OS over 2 years, including known clinical variables.

RESULTS

- CTCs were absent in 80% (n=185/233) of pts, and CTC absence was prognostic for better PFS (HR=1.6, p=0.046), but not OS (HR=1.3, p=0.2045), **Fig. 1**.
- Enlarged CAMLs (≥100µm) were found in 34% (n=79/233) of pts and were prognostic for worse PFS (HR=2.0, p=0.0082) and OS (HR=1.9, p=0.0412), **Fig 2**.
- CTCs were found in 55% (n=34) breast, 20% (n=8) prostate, 12% (n=3) pancreas, 11% (n=3) colon, 0% (n=0) RCC, and 0% (n=0) Lung pts.
- ≥100µm CAMLs were found in 45% (n=27) breast, 20% (n=8) prostate, 44% (n=11) pancreas, 44% (n=17) colon, 18% (n=7) RCC and 20% (n=8) Lung pts.
- Overall, models indicated that:
 - Pts with ≥1 CTC (n=47) had the worst mPFS=3.9 & mOS=16.5 (**Fig. 3**).
 - Pts with 0 CTCs & ≥100µm CAMLs (n=51) had better mPFS=6.9 but similar mOS=13.8 as ≥1 CTC (**Fig. 3**).
 - Pts with 0 CTCs & <100µm CAMLs (n=134) had a better mPFS=10.7 & mOS=21.7 (**Fig. 3**).

CONCLUSIONS

- These initial models confirm that both CTCs and enlarged CAMLs are prognostic indicators of worse PFS and OS.
- The simultaneous quantification both CTCs and CAMLs allows for more accurate pan-cancer risk stratification in an array of cancer pt populations.
- Additional clinical variables incorporated into the models may allow better risk subtyping and possibly forecast optimal treatment regimens.

REFERENCES

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