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Hyper-Engorged Cancer Associated Macrophage-Like Cells in Circulation Predict for Multi-Organ Metastatic Disease in Solid Tumors

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ABSTRACT

Patients with multiple organ metastases have poorer prognoses and higher tumor burden than those with single organ metastasis[1]. Cancer Associated Macrophage-Like Cells (CAMLs) are a circulating stromal cell subtype detected in the blood of patients with solid tumors[2]. While numerous studies have shown that ≥50um CAMLs predict poor clinical outcomes, meta-analysis of these studies have also suggested that Hyper-Engorged CAMLs ≥100um (heCAMLs) may be associated with multifocal metastatic disease and even worse outcomes[3]. In this prospective study, we evaluated the presence of heCAMLs in patients with metastatic disease, demonstrating a strong relationship with multi-organ spread and shorter Progression Free Survival (PFS) and Overall Survival (OS).

MATERIALS & METHODS

We prospectively recruited 151 patients with metastatic (m) mBreast (n = 58), mLung (n = 34), mProstate (n = 39), and mRenal (n = 20) cancers. Peripheral blood was collected prior to the induction of new treatment for metastatic cancer. CAMLs were isolated following standard CellSieve techniques, then imaged/measured using ZenBlue. Multi-organ metastasis was defined as spread to ≥2 distant organ sites, or any spread to the brain. Single factor analysis of variance (ANOVA) was used to compare heCAML presence in multi-organ metastases versus patients with single organ metastasis. Univariate and multivariate analysis was run to evaluate PFS and OS against heCAMLs, and all known clinical parameters.

Table 1. Patient Demographic Table (*Excludes 1 failed sample)

Demographic	Breast (n=58)	Lung (n=34)	Prostate (n=39)	Renal Cell (n=20)*
Age(Median):[Range]	57 [27-92]	62.5 [45-81]	73 [48-89]	61 [42-78]
Type of Metastasis				
Single Organ	18 (31%)	22 (65%)	20 (51%)	8 (40%)
Multi-Organ	40 (69%)	12 (35%)	19 (49%)	12 (60%)
Metastasis Location				
Bone	34 (59%)	10 (30%)	34 (87%)	6 (30%)
Brain	9 (16%)	9 (27%)	0 (0%)	4 (20%)
Liver	27 (47%)	5 (15%)	5 (13%)	5 (25%)
Local	5 (9%)	7 (21%)	1 (3%)	0 (0%)
Lung	15 (26%)	7 (21%)	6 (18%)	18 (90%)
Other	16 (28%)	4 (12%)	13 (33%)	6 (30%
heCAML Presence				
Absence	25 (43%)	27 (79%)	27 (69%)	11 (58%)
Presence	33 (57%)	7 (21%)	12 (31%)	8 (42%)
heCAML Presence Single Organ				
Absence	12 (67%)	20 (91%)	17 (85%)	7 (87%)
Presence	6 (33%)	2 (9%)	3 (15%)	1 (13%)
heCAML Presence Multi-Organ				
Absence	13 (32%)	7 (58%)	10 (53%)	4 (36%)
Presence	27 (68%)	5 (42%)	9 (47%)	7 (64%)

INTRODUCTION

Identifying predictive biomarkers that can differentiate between aggressive and non-aggressive metastases remain elusive in the field of precision oncology[4]. Due to significantly worsened survival associated with multi-organ metastases, there is a need for biomarkers that can predict for these patient subpopulations[1,4]. Prior prospective research on CAMLs suggest use as a universal, minimally invasive blood-based prognostic & predictive biomarker in multiple solid malignancies[2,3].

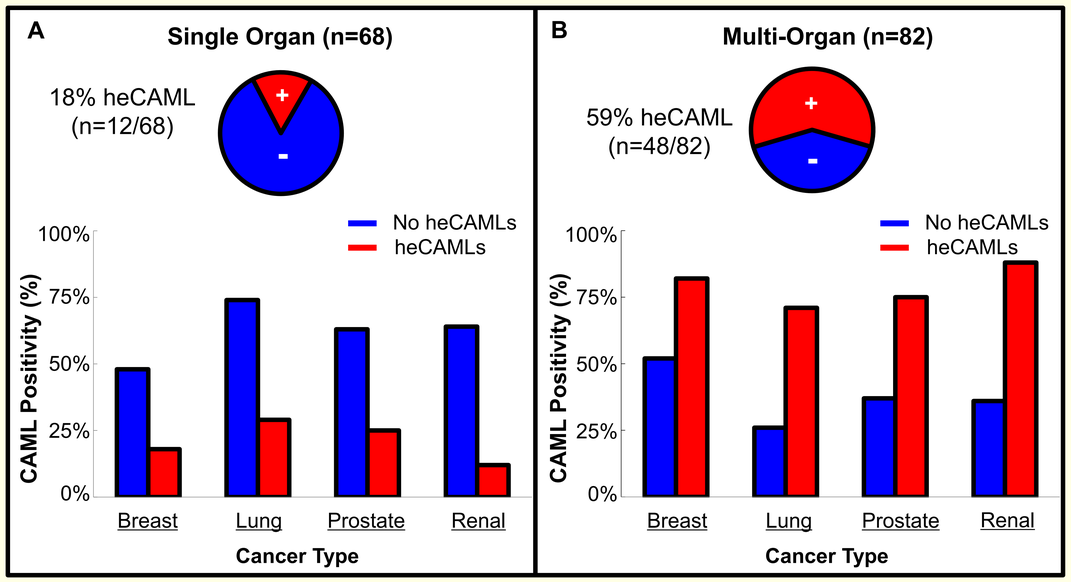

Figure 1. Distribution of heCAML presence in (A) single organ and (B) multi-organ metastatic patients by cancer type.

RESULTS

- Multi-organ metastases were present in 55% (n=83/150) of the patients **(Table 1)**
- heCAMLs were found in 59% (n=49/83) of patients with multi-organ metastases **(Fig. 1)**
- heCAMLs were found in 16% (n=11/67) of patients with single organ metastasis
- heCAML presence appeared to indicate multi-organ metastasis in mbreast (82% vs. 52%, **p=0.006**), mlung (71% vs. 26%, **p=0.025**), mprostate (75% vs. 37%, **p=0.029**), and mrenal (88% vs. 36%, **p=0.025**) (**Fig. 1B**)
- In all n=150 patients, patients with heCAMLs had significantly shorter PFS (HR = 1.67, 95%CI = 1.13-2.45, **p = 0.013**) & OS (HR = 2.05, 95%CI = 1.24-3.39**, p = 0.008**) (**Fig. 2**)

CONCLUSIONS

- From a single blood draw, we identified that patients with heCAMLs are more likely to have multi-organ metastases
- heCAML presence predicted for significantly shorter PFS (HR=1.67) and OS (HR=2.05)
- heCAML presence prior to initiation of new treatment may predict for multi-organ metastases, thus requiring more aggressive treatment regimes
- Larger prospective validation cohorts on local and non-local disease are needed to validate these preliminary findings

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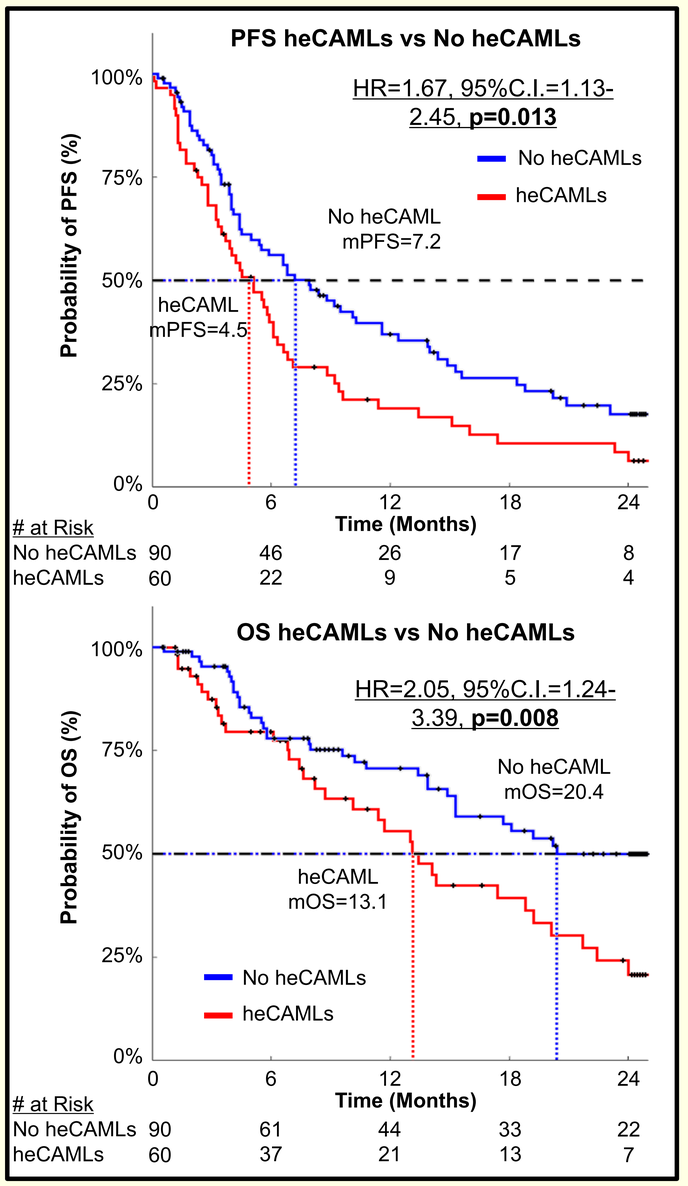
Figure 2. Kaplan Meiers comparing heCAML presence in patients with metastatic disease



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