CAMLs are a circulating stromal cell subpopulation that accurately predicts resistance and progression in treatment naïve lung cancer patients receiving definitive radiotherapy

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ABSTRACT
Cancer Associated Macrophage-Like cells (CAMLs) are a recently described circulating stromal cell common to the peripheral blood of cancer patients hypothesized to be a mechanism in cancer pathogenesis. We have previously described that treatment naïve patients with circulating CAMLs ≥50µm is a significant independent prognostic indicator of progression free survival (PFS) in a variety of cancers. However, the clinical value of CAMLs in specific diseased cohorts as it relates to predicting response to treatment has not been evaluated. We present the results of a prospective study on treatment naïve lung cancer patients before induction, and if possible directly after completion, of definitive radiotherapy to determine if CAMLs are predictive of cancer progression within 2 years.

RESULTS
- CAMLs were found in 93% of BL samples averaging 3.2 CAMLs/7.5mL.
- At BL, patients with CAMLs of ≥50 µm had reduced PFS (HR=2.9) (Figure 2)
- At T1 patients with CAMLs of ≥50 µm had further reduced PFS (HR=7.7) (Figure 2)
- At BL, 90% of patients with a ≥50 µm CAML progressed in 2 years vs 46% of patients with <50 µm CAML (Figure 2)
- At T1, enlarged CAMLs were more accurate at predicting progression, with 92% of ≥50 µm CAML patients progressing vs 21% of patients with <50 µm CAMLs. (Figure 3)
- 100% of patients that had ≥50 µm CAMLs at both BL and T1 progressed. (Figure 3)

CONCLUSIONS
CAML sizes were prognostic both at pretreatment baseline as well as any change in size that occurred during and/or after therapy. Giant CAMLs could represent a population of tumor stroma cells that may promote tumor progression Monitoring the presence of giant CAMLs and their sizes through the course of radiation therapy may predict cancer progression or death Prospective validation of giant CAMLs as a blood-based biomarker for risk stratification is ongoing through a R43/SBIR grant, results pending.

MATERIALS & METHODS
A 2 year single blind prospective study was undertaken, testing the relationship of enlarged CAMLs (≥50µm) to PFS of lung cancer patients before & after induction of definitive radiation therapy. To achieve a 2-tailed 95% power (n=0.05) we recruited a training set of 55 patients, all with pathologically confirmed lung cancer. Stage I (n=13), Stage II (n=7), Stage IIIA (n=10), Stage IIIB (n=18) & Stage IV (n=7). Baseline (BL) blood samples were taken prior to start of therapy. If possible, a 2nd blood samples (T1) was taken after completion of radiotherapy (~60 days), n=46 patients. Blood was filtered by CellSieve™ filtration and CAMLs quantified. Analysis by CAML size of <50 µm or ≥50 µm was used to evaluate PFS hazard ratios (HRs) by censored univariate & multivariate analysis.

REFERENCES
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