Clinical utility of circulating tumor cell (CTC) analysis in patients with metastatic NSCLC receiving first-line chemotherapy

Lara Kujtan[1], Cecile Rose T. Vibat[2], Veena M. Singh[2], Kevin F. Kennedy[3], Anuj Shrestha[1], Sheshadri Madhusudhana[1], Jacob Smeltzer[4], Ashiq Masood3,[1,4], Janakiraman Subramanian[1,4]

[1]University of Missouri at Kansas City, Kansas City, USA, [2]Biocept, Inc., San Diego, USA, [3]St. Luke's Hospital, Kansas City, USA
[4]Saint Luke's Cancer Institute, Kansas City, USA

BACKGROUND

-Liquid biopsy is a minimally invasive and cost-effective means of cancer biomarker evaluation to select appropriate treatment and monitor disease burden.

-CTC enumeration may have prognostic and predictive potential for patients receiving chemotherapy. [1-3]

-We performed a prospective study to enumerate and characterize CTCs in the peripheral blood of patients with advanced non-small cell lung cancer (NSCLC).

OBJECTIVE

-To determine the proportion of patients with metastatic non-small cell lung cancer with detectable CTCs.

METHODS

-Single arm prospective study conducted at two institutions.

-Patients had histologically proven NSCLC and were eligible for systemic cytotoxic chemotherapy.

-Venous blood samples were obtained for CTC analysis before administration of chemotherapy on treatment days (D) 1, 8, 22 and 43, and at disease progression.

-CTC enumeration was performed using a 10 antibody capture cocktail targeting a wide spectrum of CTC phenotypes. CTC capture and identification of both cytokeratin (CK) positive (epithelial) and cytokeratin negative (mesenchymal, stem cell) CTCs were undertaken in a patented microchannel. CTC capture and biomarker analysis were conducted at a CLIA-certified, CAP accredited laboratory.

-Continuous variables were compared using one-way analysis of variance. Categorical variables were compared using chi-square or Fisher's exact test. The Kaplan-Meier method was used for survival estimates.

RESULTS

-Twenty-eight patients have been enrolled to date in this ongoing study: 19 (67.9%) adenocarcinoma, 9 (32.1%) squamous cell carcinoma.

RESULTS

-Of 27 patients with blood collections at D1 (treatment start), 16 (59.2%; 11 adenocarcinoma, 5 squamous) had detectable CTCs. For patients with detectable D1 CTCs, CTC count at D8 decreased in 14/15 (93.3%; 11 adenocarcinoma, 4 squamous) subjects, and was unchanged in 1 individual (6.7%; adenocarcinoma).

-Among patients with undetectable CTCs at D1, CTCs remained undetectable in 6/11 (54.5%; 4 adenocarcinoma and 2 squamous) and increased in 2/11 (18.1%; one each of adenocarcinoma and squamous) of subjects. Three subjects did not have D8 results available.

-Patients with 1-5 CTCs at D1 had a mean progression free survival (PFS) 188.9 days; patients with > 5 CTCs at D1 had a mean PFS of 109 days; patients with 0 CTCs at D1 had a mean PFS of 129.7 days (p=0.25).

-Patients in the 1-5 CTC group had a mean survival of 269.6 days, while patients in the >5 CTC group had a mean survival of 182.5 days; patients with 0 CTCs at D1 had a mean survival of 152.9 days (p=0.16; Figure 2).

Figure 1: Progression free survival based on Day 1 CTC enumeration

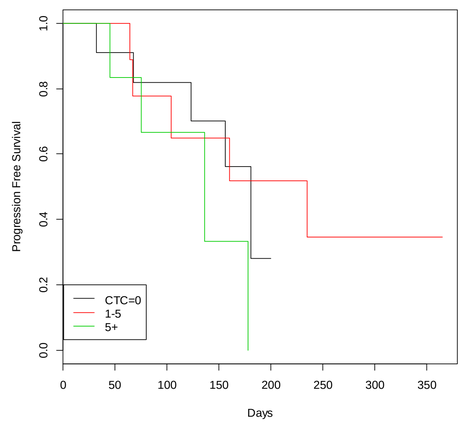
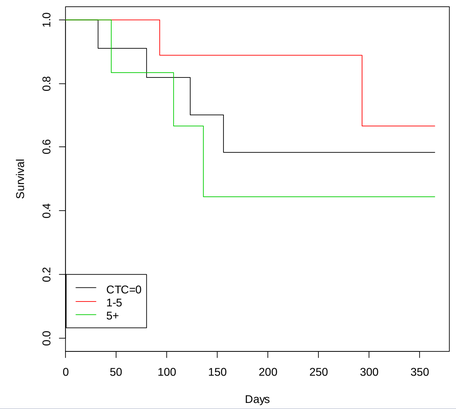


Figure 2: Overall survival based on Day 1 CTC enumeration



CONCLUSIONS

-CTCs were detected in ~60% of patients with advanced NSCLC.

-In subjects with detectable CTCs prior to chemotherapy, CTC count declines within a week after starting chemotherapy in >90% patients.

-In patients with detectable CTCs, >5 CTCs prior to starting treatment is associated with worse survival compared to 1-5 CTCs.

-The CTC methodology employed enables analysis of a spectrum of CTC phenotypes and their potential biological implications.

-Further data from this ongoing study may provide additional insight into the role of CTC analysis applied to clinical practice.

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Corresponding author: J. Subramanian – jsubramanian@saint-lukes.org