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Changes in Circulating Tumor Associated Cells Predicts Progression Free and Overall Survival in Metastatic TNBC Patients after Induction with the Anti-CCR5 Drug Leronlimab

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ABSTRACT

Metastatic triple negative breast cancer (mTNBC) is a highly invasive breast cancer subtype that has limited treatment options and poor clinical outcomes. Recently, the C-C chemokine receptor 5 (CCR5) was identified in preclinical models as a potential drug target that inhibits pro-migratory tumor progression in breast cancer. Leronlimab (PRO 140), a humanized IgG4κ monoclonal antibody, is a competitive inhibitor of CCR5 with 3 active clinical trials ongoing in patients with TNBC (**Figure 1**). Here we report on a preliminary pooled analysis of n=28 mTNBC patients to evaluate effects of Leronlimab on two subtypes of circulating tumor-associated cells (TACs) as an early predictor of drug response with end point outcomes of progression free survival (PFS) and Overall Survival (OS).

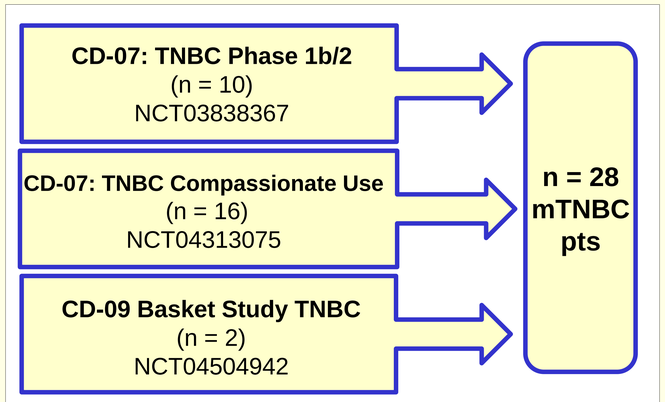

Figure 1. Flow chart of mTNBC patient populations

INTRODUCTION

mTNBC is an aggressive subtype of BC that lacks estrogen, progesterone, or HER2 receptors, which has limited targeted therapeutic agents and high recurrence rates[1]. CCR5 is a motility marker that was identified as a potential drug target that inhibits tumor progression in BC by blocking tumor motility and tumor spread[2]. Leronlimab (PRO 140) is an anti-CCR5 inhibitor that blocks CCR5-mediated motility, independent of hormone status. However, CCR5 is largely expressed in motile cells, so primary and metastatic biopsies often lack CCR5 expression. Recently we have shown that CCR5 is found on two types of circulating TACs, Circulating Tumor Cells (CTCs) and pro-tumorigenic Cancer Associated Macrophage-Like cells (CAMLs) (**Figure 2**) which predicts tumor motility and increased progression[3,4].

MATERIALS & METHODS

Blood samples were drawn from mTNBC patients from 3 blinded prospective clinical drug studies (**Figure 1**) to evaluate TACs. All subjects received ≥1 dose of Leronlimab (range 1-33 doses), ranging from 350mg – 700mg, with 4 subjects having dose escalation. Anonymized peripheral blood samples were available from (n=28) patients, prior to drug induction (BL) and after one treatment dose (T1), ~26 days. TACs were isolated using the CellSieve Microfiltration system and changes in TACs were quantified by the LifeTracDx™ assay. An univariate analysis was used to analyze changes in TACs to predict for PFS and OS over 12 months.

RESULTS

- CTCs were found in 29% (n = 8/28) of BL samples.
- CAMLs were found in 96% (n = 27/28) of BL samples.
- The absence/drop of CTCs at T1 was significant for improved PFS and OS (**Figure 3A and 3B**)
- CAMLs or CTCs were evaluable in 100% of patients
- 75% of patients had a decrease in CTCs or CAMLs after 1 dose of Leronlimab
- Increases of TACs (CTCs or CAMLs) at T1 were highly significant in predicting for worse PFS and worse OS (**Figure 3C and 3D**)

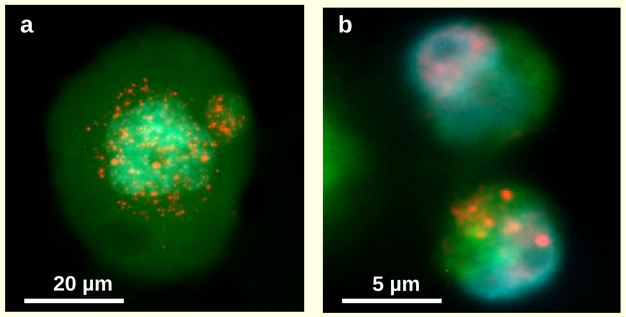

Figure 2. CCR5 expression in a CAML (a) and CTC (b) from mTNBC disease (Red = CCR5, Blue = nucleus, Green = Cytoplasm).

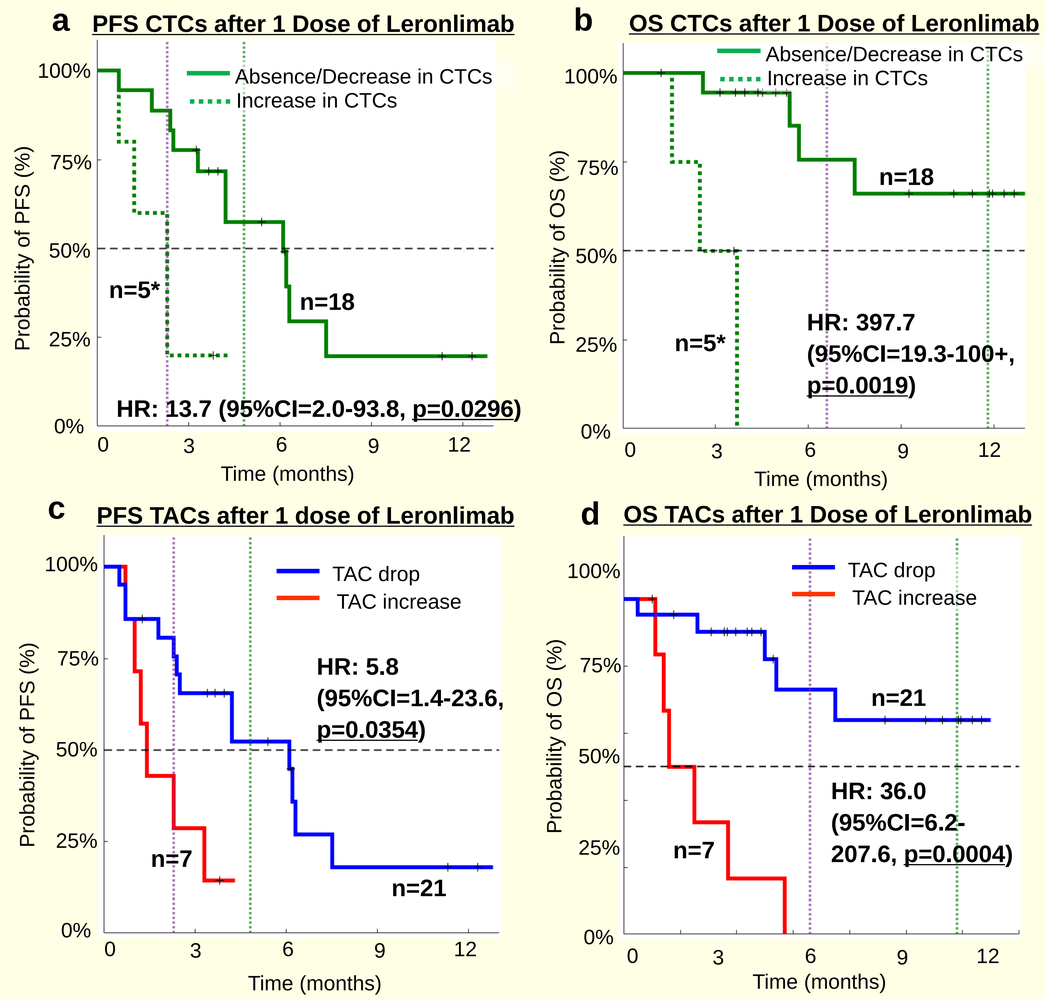

Figure 3. PFS and OS of n=28 treated with Leronlimab. Vertical Purple Dashed Reference Line = median of the standard of care chemotherapy. Vertical Green Dashed Reference Line = median of Trodelvy®.

CONCLUSIONS

- Measuring CAMLs or CTCs is possible in 100% of the patient population.
- The absence or drop in CTCs at T1 predicts improved survival.
- Increases in TACs at T1 significantly predicts for patients with worse survival.
- Treatment with Leronlimab resulted in rapid decreases in TACs in 75% of patients which correlated with improved survival.
- Drug toxicity and further patient clinical outcomes are ongoing

FUNDING SOURCES

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