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Contact email: Richard.pestell@gmail.com

Long Term Survival with Leronlimab Treatment in Patients with Metastatic Triple-Negative Breast Cancer (mTNBC)

Richard G. Pestell[1,2], M. Cristofanilli[3], Milana Dolezal[4], Hallgeir Rui[5], Daniel L. Adams[6], A. Cyrus Arman[7], Joe Meidling[7], Bernie Cunningham[7], Jacob Lalezari[7], Hope S. Rugo[8]

Pennsylvania Cancer and Regenerative Medicine Research Center, Baruch S. Blumberg Institute, PA[1], The Wistar Cancer Center, PA[2]; Division of Hematology-Oncology, Weill Cornell Medicine, New York, NY, USA[3]; Stanford University School of Medicine, CA[4]; Department of Pharmacology, Physiology & Cancer Biology, Sidney Kimmel Cancer Center, Thomas Jefferson University, PA[5]; Creatv MicroTech, Inc., New Jersey[6]; CytoDyn, Vancouver, WA[7]; University of California San Francisco, San Francisco, USA[8]

ABSTRACT

CCR5 is a G protein coupled receptor that is overexpressed in ~95% of Metastatic Triple Negative Breast Cancer (mTNBC) and has been identified as a potential drug target blocking tumor motility and spread[1]. Leronlimab is a humanized monoclonal antibody that binds to and inhibits CCR5, blocking CCR5-mediated function, independently of hormone status

mTNBC is an aggressive subtype of breast cancer that has poor clinical outcomes[2]. In previously treated recurrent mTNBC, patient's median overall survival (mOS) have been found to be 6.6 months for 3rd line chemotherapy[2], ~11.8 months (4.3% complete response) for ≥2 line sacituzumab govitecan[3], and 9.9 months (3.5% complete response) for ≥1 line pembrolizumab+chemotherapy[4].

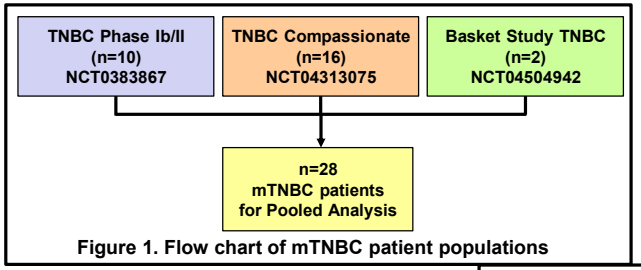


Figure 1. Flow chart of mTNBC patient populations

Table 1. Demographic Table (*=1 unknown)

Median Age (Range)	**48.5 (32-83)**
Median Prior metastatic therapies	**2 (0-5*)**
# Prior metastatic Therapies	
0	**2 (7%)**
1	**9 (32%)**
2	**9 (32%)**
≥3	**7 (25%)**
unknown	**1 (4%)**
ECOG	
0	**18 (64%)**
≥1	**10 (36%)**
Visceral	
None	**10 (36%)**
Positive	**18 (64%)**
Brain metastasis	**8 (29%)**
Prior Treatment with ICI	**9 (32%)**
ICI Treatment with or after	**7 (25%)**
PD-L1 (CPS)	
<1%	**8 (29%)**
≥1%	**18 (64%)**
≥10%	**5 (18%)**
unknown	**2 (7%)**
Leronlimab Dose	**16 (57%)**
350mg	**10 (36%)**
525mg (5 increased from 350mg)	**15 (53%)**
700mg	**3 (11%)**

MATERIALS & METHODS

Retrospective follow up analysis on 28 patients with mTNBC that were treated across three leronlimab clinical trials ((NCT03838367, N=10), (NCT04313075, N=16), (NCT04504942, N=2)). Treatment on NCT03838367 included leronlimab with carboplatin. NCT04313075 and NCT04504942 allowed physician's choice treatment. Leronlimab was administered weekly (350mg (n=10), 525mg (n=15) or 700mg (n=3)). 7 patients were treated with leronlimab in combination with atezolizumab (n=4), or subsequently with pembrolizumab (n=2) or nivolumab (n=1).

RESULTS

- Patient median age=48.5 years & median=2 prior lines in the metastatic setting (**Table 1**)
- Leronlimab was well tolerated with 5 grade 1 & 2 grade 2 treatment related adverse events (TRAEs), plus chemo related AEs.
- No patients withdrew due to leronlimab TRAEs. No Dose Limiting Toxicities (DLTs) were observed after dose escalation to 700 mg (n=10).
- Pooled analysis showed mPFS=3.8, mOS 6.8 months, and both 3 & 4-year survival of 17.9% from induction of leronlimab (**Fig 2**)
- In a post hoc analysis, the number of CTCs/CAMLs dropped in 43% (n=12/28) of patients after leronlimab induction, and upregulation of PD-L1 was seen in 81% (n=17/21) of patient's CTCs/CAMLs (**Figs 3 & 4**)
- 5 patients treated with leronlimab are currently alive and were treated in combination, or subsequently, with immunotherapy PD-L1 checkpoint inhibitors (ICI) (**Figs 4 & 5**)

Figure 2. Overall Survival in leronlimab Treated Population

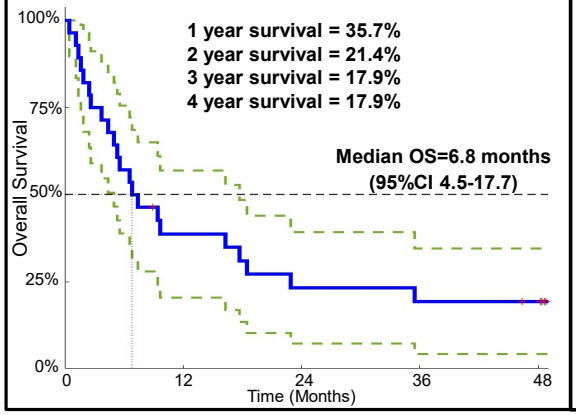
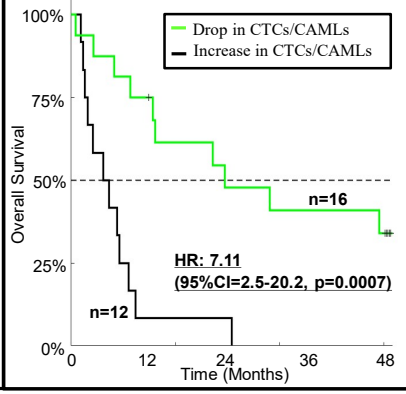


Figure 3. Drop in CTC/CAML Number after leronlimab Prognosticates Survival



CONCLUSIONS

- Leronlimab was well-tolerated with few TRAEs
- Significant upregulation of PD-L1 in circulating cells (i.e. CTCs or CAMLs) was identified in 76% (n=16/21) of patients after leronlimab, and in 88% (n=15/17) of patients who received a 525mg or 700mg dose (**Fig 4**)
- Patients treated with leronlimab in combination with PD-L1 ICIs had prolonged survival (**Figs 4 & 5**)
- N=5/5 patients who induced PD-L1 in their CTCs/CAMLs and treated with ICI concurrently or subsequently with leronlimab were alive after 48 months, with n=4/5 currently NED (these n=5 patients had 4 median lines of any prior therapy)
- Upregulation of PD-L1 after leronlimab along with the increased overall survival observed with the combination of leronlimab & PD-L1 ICIs warrants prospective evaluation in future mTNBC studies

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Figure 4. Leronlimab Induction of PD-L1 Expression in CTC/CAMLs

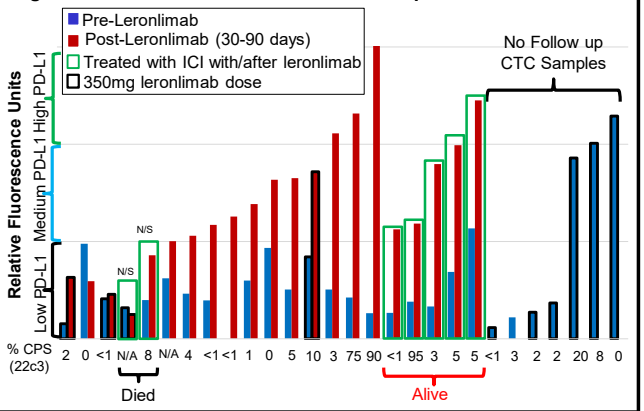

Figure 5. Overall Survival by leronlimab Treatment ± ICI therapy