San Antonio Breast Cancer Symposium, December 9–12, 2025 Poster presentation number PS5-02-30

Contact email: milanad@stanford.edu

Prolonged survival following PD-L1/PD-1 immune checkpoint inhibitor therapy after leronlimab induced PD-L1 upregulation on cancer-associated macrophage-like cells and circulating tumor cells in patients with metastatic or locally advanced triple-negative breast cancer

Milana V. Dolezal[1], Vandana G. Abramson[2], Namita Chittoria[3], Sima Ehsani[4], Richard G. Pestell[5,6], Hope S. Rugo[7], Hallgeir Rui[8], Daniel L. Adams[9], Joseph Meidling[10], Max Lataillade[10], Jacob P. Lalezari[10]

[1]Stanford University School of Medicine, Stanford, CA, [2]Vanderbilt-Ingram Cancer Center, Nashville, TN, [3]University of Utah Huntsman Cancer Institute, Salt Lake City, UT, [4]University of Arizona Cancer Center, Tucson, AZ, [5]Pennsylvania Cancer and Regenerative Medicine Research Center, Wynnewood, PA, [6]The Wistar Cancer Center, Philadelphia, PA, [7]City of Hope Comprehensive Cancer Center, Duarte, CA, [8]Thomas Jefferson University, Philadelphia, PA, [9]Creatv MicroTech, Inc., Monmouth Junction, NJ, [10]CytoDyn, Inc., Vancouver, WA.

INTRODUCTION

- Metastatic triple-negative breast cancer (mTNBC) is a particularly difficult-to-treat breast cancer subtype with pretreated mTNBC having a very poor prognosis.[1-3]
- In a US real-world study in patients with mTNBC who started first-line treatment, 51% of patients were subsequently treated with a second-line and 26% with a third-line treatment, while approximately 34% did not survive to receive next-line treatment after first- or second-line treatment.[4]
- Among patients with locally recurrent, inoperable, or mTNBC treated with the immune checkpoint inhibitor (ICI) pembrolizumab plus chemotherapy, median overall survival (mOS) is greater for patients with a PD-L1 combined positive score (CPS) of ≥10, (23.0 months), compared to patients with a CPS score of <10, (14.7 months).[5]
- In an analysis of 2,250 breast cancer patients, more than 95% of TNBC tumors were positive for C-C chemokine receptor 5 (CCR5).[6]
- Leronlimab is a humanized monoclonal antibody that blocks CCR5 and reduces TNBC metastases by >98% in preclinical models.[7]

MATERIALS & METHODS

- This is a retrospective follow-up analysis of 28 women with mTNBC, treated across three leronlimab clinical trials: NCT03838367 (N=10); NCT04313075 (N=16); and NCT04504942 (N=2).
- Treatment on NCT03838367 specified treatment with leronlimab plus carboplatin. NCT04313075 and NCT04504942 allowed physician's choice treatment in combination with leronlimab.
- Allocation to leronlimab dose (350 mg QW SC, 525 mg QW SC, or 700 mg QW SC) and criteria for dose modifications of leronlimab were pre-specified in the respective protocols.
- Overall, 7 patients were treated with leronlimab in combination with, or followed by, atezolizumab (n=4), pembrolizumab (n=2) or nivolumab (n=1).
- PD-L1 immunohistochemistry (IHC): PD-L1 membrane staining was assessed with 22C3 pharmDx IHC (Agilent/Dako) and reviewed by a board-certified pathologist using combined positive score (CPS; PD-L1$^+$ tumor + immune cells) × 100 / tumor cells).
- Blood samples were collected before leronlimab treatment (BL) to measure cancer-associated macrophase-like cells (CAMLs) and circulating tumor cells (CTCs), and their aggregate average PD-L1 expressions by immunofluorescence. Follow-up samples (T1) were taken ~48 days later to evaluate changes in CAMLs/CTCs, and their aggregate average PD-L1 expressions. A numerical increase, or decrease, in CTC/CAML numbers between BL and T1 was defined as a negative prediction, or positive prediction, respectively (Fig. 3).

RESULTS

- Patients, median age was 48.5 years (range 32–83), patients received a median of 2 prior lines of metastatic therapy (range 0–5) (**Table 1**).
- Leronlimab was well tolerated with five grade 1 and two grade 2 treatment-related adverse events (TRAEs), plus expected chemo-related adverse events (AEs).
- No patients withdrew due to leronlimab TRAEs. No dose-limiting toxicities (DLTs) were observed up to the 700 mg QW SC dose.
- For all 28 patients, mOS after starting leronlimab treatment was 7.1 months (95% CI: 4.8–17.7 months) with survival at years 1, 2, 3, and 4 of 35.7%, 21.4%, 17.9% and 17.9%, respectively (**Fig. 1**).

Fig 1. OS among the overall population

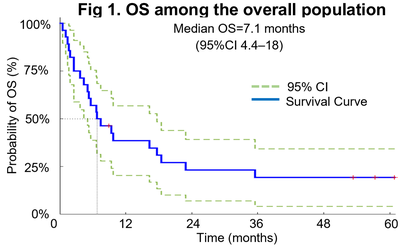
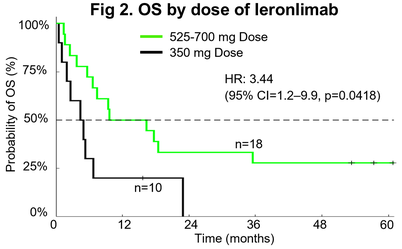


Fig 2. OS by dose of leronlimab



- OS in subgroups of interest were assessed using univariable analyses without adjusting for differences in baseline characteristics. It is therefore possible that there were differences between subgroups.
- Compared to patients treated with the 350 mg QW SC dose of leronlimab, patients treated with either the 525 or 700 mg QW SC dose of leronlimab demonstrated significantly longer survival (HR 3.44, 95% CI: 1.2–9.9; P=0.0418) (**Fig. 2**).
- Compared to patients with an increase in CTCs/CAMLs after starting leronlimab, patients with a reduction in CTCs/CAMLs demonstrated longer survival (HR 7.11, 95% CI: 2.5–20.2; P=0.0007) (**Fig. 3**).
- Patients treated with leronlimab in combination with, or followed by, an ICI (N=7) demonstrated significantly longer survival compared to patients (N=21) who were not treated with leronlimab in combination with, or followed by an ICI (HR 4.14, 95% CI: 1.7–10.2; P=0.0041) (**Fig. 4**).
  - As of 22 September 2025, all 5 patients treated with leronlimab in combination with, or followed by an ICI, and who significantly induced PD-L1 in their CTCs/CAMLs, were alive after a median of 60.9 months since initiating treatment with leronlimab.
  - Two patients treated with leronlimab in combination with, or followed by an ICI, but who failed to significantly induced PD-L1 in their CTCs/CAMLs died (one at 5.0 months, and one at 5.6 months after starting leronlimab).
- Treatment with leronlimab (any dose) was associated with a significant upregulation of PD-L1 in circulating cells (i.e. CTCs and/or CAMLs) in 76% (n=16/21) of patients with post-baseline data (**Fig. 5**)
  - Among the subset of patients who received leronlimab at a dose of 525 mg or 700 mg QW SC 88% (n=15/17) significantly upregulated PD-L1 in circulating cells.

Table 1. Baseline and study treatment characteristics (N=28)		Value
Median age, years (range)		48.5 (32–83)
Median number prior metastatic therapies†		2 (0–5)
Number of prior metastatic therapies†	0 1 2 ≥3	2 (7%) 9 (32%) 9 (32%) 7 (25%)
ECOG	0 ≥1	18 (64%) 10 (36%)
Metastasis	None Positive Brain	10 (36%) 18 (64%) 8 (29%)
Prior treatment with ICI		9 (29%)
PD-L1 (CPS scores)‡	<1% ≥1% (includes ≥10%) ≥10%	8 (29%) 18 (64%) 5 (18%)
ICI treatment with or after leronlimab		7 (25%)
Leronlimab dose	350 mg QW SC 525 mg QW SC (5 increased from 350 mg QW) 700 mg QW SC	10 (36% 15 (53%) 3 (11%)

†Unknown for 1 patient; ‡Unknown for 2 patients; ICI = immune checkpoint inhibitor; QW = once weekly; SC = subcutaneously.

Fig 3. OS by change in CTCs/CAMLs

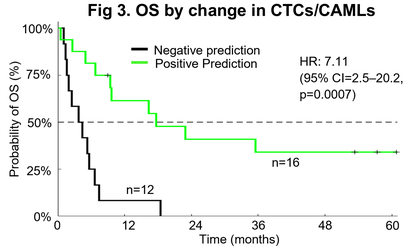


Fig 4. OS by treatment with ICIs

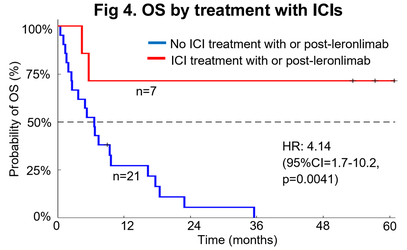
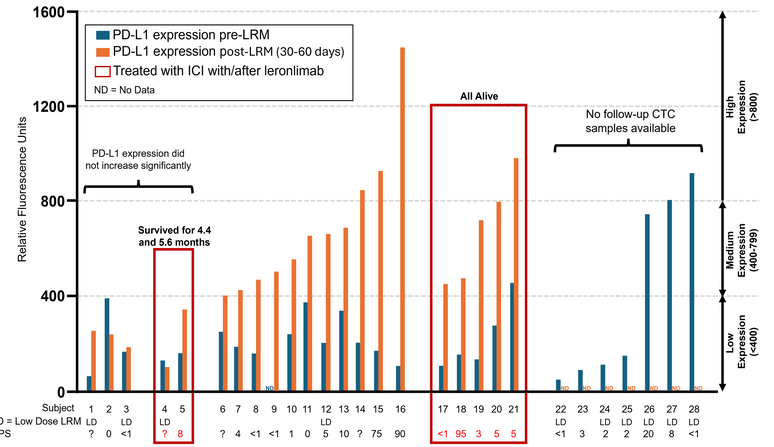


Fig 5. PD-L1 expression in CTCs/CAMLs before/after leronlimab Induction



CONCLUSIONS

- Leronlimab was well-tolerated with few TRAEs and no DLTs.
- Among all 28 patients, mOS was 7.1 months, with 5 patients (17.9%) still alive after a median of 60.9 months since starting treatment with leronlimab.
- Patients treated with either the 525 or 700 mg dose of leronlimab demonstrated significantly longer survival compared with patients treated with the 350 mg dose of leronlimab.
- Patients with a reduction in CTCs/CAMLs after starting leronlimab demonstrated significantly longer survival compared with patients with an increase in CTCs/CAMLs.
- Patients who were treated with leronlimab in combination with, or followed by, an ICI demonstrated prolonged survival. As of 22 September 2025, all 5 of the patients treated with leronlimab, in combination with, or followed by, an ICI, and who significantly induced PD-L1 in their CTCs/CAMLs were alive after a median of 60.9 months.
- Treatment with leronlimab was associated with a significant upregulation of PD-L1 in circulating cells (i.e. CTCs or CAMLs).
- Upregulation of PD-L1 with leronlimab treatment may "prime" the PD-L1 positivity in the tumor and its microenvironment. Thus, it may increase the proportion of patients eligible for treatment with an ICI and synergize with ICI efficacy. Further studies are warranted to confirm these findings.

FUNDING SOURCES / MEDICAL WRITING SUPPORT / DISCLOSURES

Funded by CytoDyn Inc. The presenting author, Dr. Dolezal is an advisor to CytoDyn Inc. Medical writing support was provided by Neil Buss, Nucleus Global, Switzerland, funded by CytoDyn Inc., Vancouver, WA, USA.

REFERENCES

1. Bardia A, et al. J Clin Oncol 2024;42(15):1738-1744.
2. Cabel L, et al. Breast 2021;56:18-25.
3. Winer EP, et al. Lancet Oncol 2021;22(4):499-511.
4. Punie K, et al. Oncologist 2025;30(3).
5. Cortes J, et al. N Engl J Med 2022;387(3):217-226.
6. Velasco-Velázquez M, et al. Cancer Res 2012;72(15):3839-50.
7. Jiao X, et al. Breast Cancer Res 2021;23(1):11.