ESMO Gastrointestinal Cancers Congress, July 2–5, 2025 Final Publication Number 134eP

Observed Survival Following Treatment With Leronlimab In Patients With Metastatic Colorectal Cancer

Benjamin A. Weinberg[1], Cyrus Arman[2], Joseph Meidling[2], Daniel L. Adams[3], Ari Baron[4], Melissa Palmer[5], Jacob P. Lalezari[2]

1. Lombardi Comprehensive Cancer Center, Washington, DC, USA; 2. CytoDyn Inc., Vancouver, WA, USA; 3. Creatv MicroTech, Monmouth Junction, NJ, USA; 4. Pacific Hematology-Oncology Associates, San Francisco, CA, USA; 5. Liver Consulting LLC, New York, NY, USA

BACKGROUND

- Higher CCR5/CCL5 expression is associated with: higher tumor mutational burden; higher dMMR; higher PD-L1 levels; and higher immune cell infiltration in the tumor microenvironment of pMMR tumors[1].
- Patients heterozygous for CCR5 (WT/Δ32-CCR5) tend to have a lower frequency of synchronous metastasis compared to patients wild-type for CCR5 (WT/WT)[2].
- In CRC it has been shown that CCL5/CCR5 signaling recruits T_{reg} to tumors and increases their ability to inhibit antitumor CD8+ cells[3].
- CCR5 inhibition delayed tumor growth in murine tumor models[4].
- In the PICCASSO phase 1 trial, in refractory pMMR MSS mCRC, treatment with pembrolizumab and maraviroc (small molecule CCR5 inhibitor) was associated with a higher-than-expected mOS (9.8 months [95%CI 5.59–20.02]) compared to <6 months based on historical data and was shown to have a beneficial safety profile[5].
- Leronlimab is a humanized monoclonal antibody that binds to and inhibits CCR5, blocking CCR5-mediated function.

MATERIALS & METHODS

- Study CD-09 (NCT04504942) was a phase 2, single arm, basket study of leronlimab in patients with CCR5+ locally advanced or metastatic solid tumors (Figure 1).
- Between Apr 2020 and Jan 2021, 81 patients were screened, and 16 patients enrolled, including 5 patients with CRC. Here we report retrospective follow up analysis on 5 patients with mCRC treated in study CD-09.

Figure 1. Study population in study CD-09

STUDY POPULATION

Patients with CCR5+ locally advanced or metastatic solid tumors: who have disease progression on standard therapy; who are receiving a standard anticancer treatment, but no subsequent approved treatment would be available upon progression; who are unable to receive standard therapy; or for whom standard therapy does not exist.

- Patients were to receive a target dose of 525 mg leronlimab once weekly by subcutaneous injection in combination with physician choice of standard-of-care chemotherapy and/or radiotherapy.
- Treatment could continue until progression of disease, unacceptable toxicity, or withdrawal of consent.
- Patients were followed up for survival status by clinic visits, or phone, or another method of contact every 3 months for 2 years after treatment discontinuation or until death.

RESULTS

- Patient median age was 51 years with a median of 1 prior lines of systemic therapy in the metastatic setting (Table 1).
- Patients received leronlimab: alone (N=1), with chemotherapy (N=2); with chemotherapy plus bevacizumab (N=1); and with chemotherapy plus bevacizumab plus pembrolizumab (N=1).
- Leronlimab was well tolerated with no dose limiting toxicities and no patients withdrew due to leronlimab treatment-related adverse events.

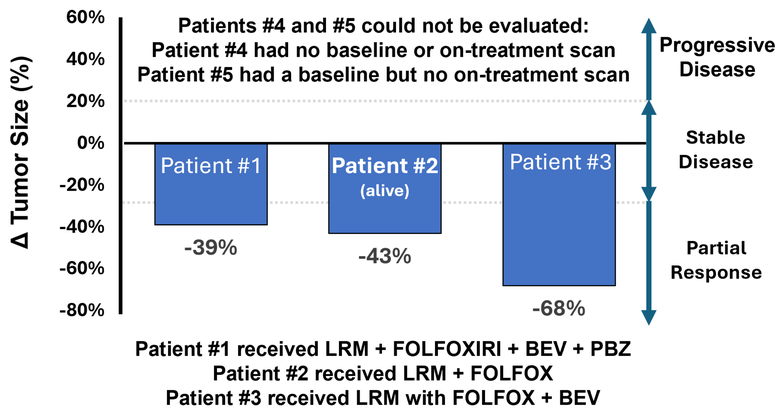
Table 1. Patient demographics and disease characteristics

Parameter	Value
Median age, years, (range)	51 (34–92)
Male Female	N=3 N=2
White Asian	N=4 N=1
Median prior lines systemic therapy, (range)	1 (1–3)
Median prior lines systemic therapy in metastatic, (range)	1 (1–2)
ECOG 0 ≥1	 N=3 N=2
CCR5+ TME Cellular Infiltrate Low/none (<1% positive leukocytes) Medium (1%–20% positive leukocytes) High (>20% positive leukocytes)	 N=1 N=1 N=3
Leronlimab starting dose 350 mg 525 mg	 N=2* N=3

* Subsequently increased to 525 mg in one patient

- mOS was 15.5 months with 3 patients having partial responses as measured by RECIST 1.1 (Figure 2).
- One patient, a White, 58-year-old female was diagnosed with stage II CRC in February 2018 and was subsequently diagnosed with liver metastasis in May 2020 initiating FOLFOX (May 2020) and leronlimab (350 mg increased to 525 mg) (July 2020). She underwent liver resection (margins clear) in September 2020. As of June 2025 she remains alive with no evidence of disease almost 5 years after initiating leronlimab.

Figure 2. Patients with partial responses as measured by RECIST 1.1



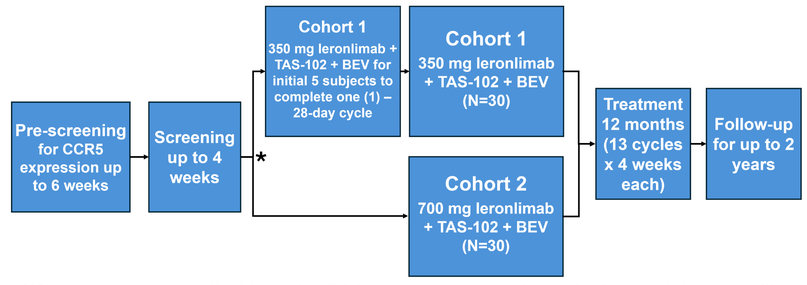
CONCLUSIONS

- Leronlimab was generally well tolerated with no leronlimab-related dose limiting toxicities observed.
- Leronlimab demonstrated potential clinical benefit in patients with mCRC.
- Though limited to 5 patients, these findings are encouraging and support further investigation of leronlimab in patients with MSS mCRC.

ONGOING STUDIES WITH LERONLIMAB IN CRC

- Figure 3 provides an overview of study CD-O-101 (NCT06699836) which is a phase 2 study currently recruiting patients in the USA to evaluate either weekly 350 mg or 700 mg leronlimab subcutaneously, with trifluridine + tipiracil (TAS-102) + bevacizumab in participants with CCR5+, MSS relapsed refractory mCRC.
- Tumor-infiltrating leukocytes will be scored based on the percentage of CCR5+ leukocytes with low <1%, medium 1%–20%, and high >20%.
- For further details regarding study CD-O-101 contact info@cytodyn.com.

Figure 3. Ongoing study (CD-O-101) of leronlimab in participants with CCR5+, MSS mCRC



*If patients are enrolled into the 700 mg arm, approximately 15 participants will be randomized 1:2 on 350 mg and 700 mg arms respectively in order achieve an overall 1:1 treatment assignment, thereafter randomization will proceed at 1:1

- Patients completing study CD-O-101 will be given the option to enter a roll-over study where they can continue to receive leronlimab. Patients who have progressed on the parent study will also be offered treatment with leronlimab in combination with an immune checkpoint inhibitor.

REFERENCES

1. Battaglin F, *et al*. J Immunother Cancer 2024;12:e007939
2. Suarez-Carmona M, *et al*. Oncoimmunology 2019;8(9):e1626193
3. Chang LY, *et al*. Cancer Res 2012;72(5):1092-102
4. Ward ST, *et al*. Br J Cancer 2015;112(2):319-28. (In eng). DOI: 10.1038/bjc.2014.572.
5. Haag GM, *et al*. Eur J Cancer 2022;167:112-122

ABBREVIATIONS

BEV = bevacizumab; CCL5 = C-C Chemokine Ligand 5; CCR5 = C-C Chemokine Receptor 5; CRC = colorectal cancer; dMMR = deficiency in mismatch repair; LRM = leronlimab; mCRC = metastatic colorectal cancer; mOS = median overall survival; MSS = microsatellite-stable; pMMR = mismatch repair proficient; PBZ = pembrolizumab; PD-L1 = programmed cell death ligand 1; TME = tumor microenvironment.

FUNDING SOURCES

This study was funded by CytoDyn Inc., Vancouver, WA, USA.

MEDICAL WRITING SUPPORT

Medical writing support was provided by Neil Buss, Nucleus Global, Switzerland, funded by CytoDyn Inc., Vancouver, WA, USA.

Disclosures for Benjamin A. Weinberg – Presenter

Honoraria: Primum, Caris Life Sciences; Consulting/Advisory: Merus, DoMore Diagnostics, Foundation Medicine, Agenus, Regeneron, CytoDyn; **Speakers' Bureau**: Sirtex, Seagen, Merus, Daiichi Sankyo/AstraZeneca, Natera, Jazz Pharmaceuticals, Pfizer; **Research Funding** (Institutional): Ipsen, Immune System Key, Merck, BioXcel Therapeutics. Email: benjamin.a.weinberg@gunet.georgetown.edu