

SAFETY AND CLINICAL ACTIVITIES OF THE ACID PH-SENSITIVE ANTI-CTLA-4 MAB ONC-392 IN OVARIAN CANCER PATIENTS

¹John Hays*, ²Tianhong Li, ²Hui Chen, ³George Zahrah, ³Richard Frank, ⁴John Hamm, ⁵Merry-Jennifer Markham, ⁵Thomas George, ⁶Eric Whitman, ⁷Mark Goldstein, ¹Kai He, ⁸Rohit Joshi, ⁹Dan Chen, ⁹Yang Liu, ⁹Pan Zheng, ¹David O'Malley. ¹The Ohio State University James Cancer Center, Columbus, OH, United States; ²UC Davis Cancer Center, Sacramento, CA, United States; ³Norwalk Health, Norwalk, CT, United States; ⁴Norton Healthcare, Louisville, KY, United States; ⁵University of Florida Cancer Center, Gainesville, FL, United States; ⁶Atlantic Health, Morristown, NJ, United States; ⁷Center for Cancer and Blood Disorders, Frederick, MD, United States; ⁸Cancer Research SA, Adelaide, Australia; ⁹OncoC4, Inc., Rockville, MD, United States

Background Despite extensive effort, no immunotherapy has been approved for ovarian cancer patients. Ovarian cancer patients who fail more than two lines of systemic therapies have very poor prognosis. ONC-392 is an acid pH-sensitive anti-CTLA-4 antibody that preserves CTLA-4 recycling and avoids lysosomal degradation. ONC-392 is more effective for immunotherapy but largely devoid of immunotherapy-related adverse events (irAE) in preclinical studies. Our previous dose escalation study has established an RP2D for monotherapy at 10.0 mg/kg.¹ Here we report safety and clinical response of ovarian cancer patients to monotherapy of ONC-392 at 10.0 mg/kg in dose finding and dose expansion studies (NCT04140526, Part A and Part C Arm L).

Methods Thirty four patients with advanced/metastatic ovarian cancer, including primary peritoneal cancer and fallopian tube cancer, who have progressive disease after prior systemic treatments, including chemotherapy, targeted therapy or checkpoint inhibitors have been enrolled. Four patients were enrolled in Part A monotherapy dose finding with defined doses. Thirty patients in expansion cohort had ONC-392 administered via IV infusion with starting two doses of 10.0 mg/kg, Q3W, followed by 6.0 mg/kg Q3W. The primary endpoints are safety and objective response rate (ORR) using RECIST 1.1 criteria.

Results Thirty-four patients have received 1-11 cycles of ONC-392 treatment. The safety data set consists of 32 patients. The median age is 67.5 (range 40-82), White/Asian/Black: 27/3/2, and 5 Hispanic. The median follow up is 17 weeks. Treatment related AEs (TRAEs) were observed in 26 (81%) patients. Grade 3 TRAEs were observed in 10 pts (31%): myocarditis (1), diarrhea (2), immune-mediated colitis or colitis (4), immune hepatitis (1). Grade 4 TRAE in 1 patient with hypotensive shock (3%). No grade 5 AE was observed. Among 26 evaluable patients, the CR/PR/SD/PD numbers are 1/3/15/7 (ORR=15%, DCR=73%) (figure 1).

Conclusions The safety profile of 10.0 mg/kg x 2, followed by 6.0 mg/kg Q3W is comparable to patients who received substantially lower doses other CTLA-4-targeting drug in the ovarian cancer patients. While the number of evaluable patients is small, the preliminary assessment suggests ONC-392 monotherapy has clinical activity among patients who has failed multiple lines of systemic therapy. The available data support continuous clinical testing of ONC-392 in ovarian cancer. A new Phase 2 study with combination of ONC-392 and pembrolizumab will initiated in Q32022 (ONC-392-004, MK3475-E24, GOG-3081).

Acknowledgements The study is sponsored by OncoC4, Inc.

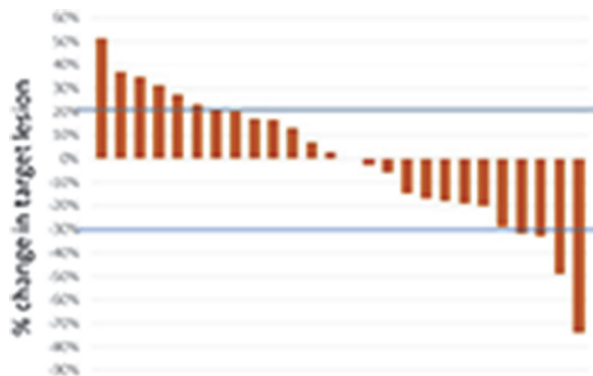
Trial Registration NCT04140526.

REFERENCE

1. Li T, Tang M, Kelly K, et al. First-in-human study of the first acid pH-sensitive and recycling CTLA-4 antibody that preserves the immune tolerance checkpoint to

avoid immunotherapy-related adverse events in cancer patients. *J Immunother Cancer*. 2021; 9(5 Suppl 2): A998.

Ethics Approval This study obtained ethic approval from WCG IRB with study #20193108 or the local institutional IRBs. All participants gave informed consent before taking part of the study.



Abstract 564 Figure 1 Best response with ONC-392 in ovarian cancer. Best response with ONC-392 monotherapy in ovarian cancer patients

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.0564>