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OVATION Study

Phase I study of the safety and activity of formulated IL-12 plasmid administered intraperitoneally in combination with standard neoadjuvant chemotherapy in patients with newly diagnosed advanced stage ovarian cancer

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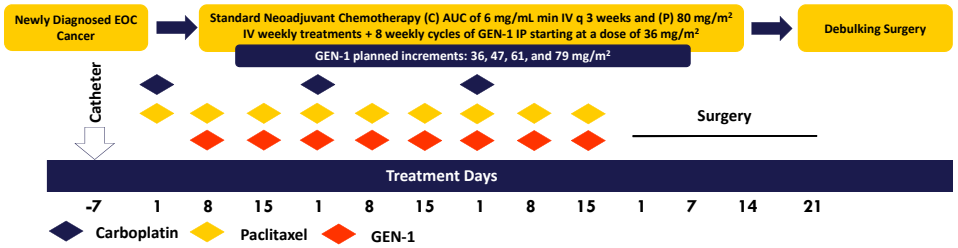
BACKGROUND

- Ovarian cancer is the fifth most lethal type of cancer among women in the United States, causing an estimated 14,000 deaths annually.[1-2]
- Patients with bulky stage III-IV disease who are not surgical candidates typically undergo three cycles of platinum-based neoadjuvant chemotherapy (NAC) followed by interval debulking surgery (IDS).[3]
- The goal of IDS is a complete cytoreduction of all macroscopic visible disease. Data shows that complete cytoreductions are associated with a significant increase in overall survival (OS).[4,5,6,7]
- GEN-1 is an IL-12 plasma vector encased in a nanoparticle delivery system. The encasement enables cell transfection followed by persistent, local secretion of the IL-12 protein at therapeutic levels, providing efficacy by recruiting an anti-cancer immune response. The localized intraperitoneal delivery also avoids the toxicities associated with systemic recombinant IL-12.
- Previous Phase I study in platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal (EOC) patients (n = 13) with escalating GEN-1 dosed to 24 mg/m^2 in combination taxane and carboplatinum (T/C) had an anti-tumor response of 17% complete response, 33% partial response and 42% stable disease.[8]
- We are reporting the interim findings of the ongoing Phase I study evaluating the use of weekly intraperitoneal (IP) GEN-1 in combination with dose-dense weekly T/C every three weeks in newly diagnosed EOC cancer patients undergoing NAC.

STUDY DESIGN AND METHODS

- Standard 3+3 design with approximate 30% dose increments between successive cohorts of patients. Dose levels of GEN-1 in conjunction with carboplatin (C) and paclitaxel
- Tolerated dose is confirmed when 6 patients are treated at a dose level and <2 patients experience a dose-limiting toxicities (DLTs)



CONCLUSIONS

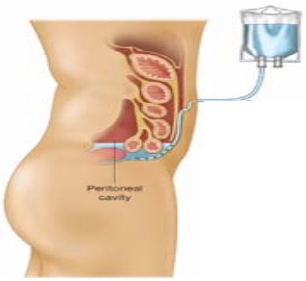
- Adding weekly IP GEN-1 to neoadjuvant T/C is safe and appears to be active in newly diagnosed EOC patients.
- Within this regimen, GEN-1 appears to be tolerable up to 79 mg/m^2 with further dose escalation possible. Additionally, other combination treatments at these higher doses of GEN-1 are being evaluated.
- Confirmatory cohort enrollment is still ongoing and final results will be provided in the second half of 2017. These patients continue to be followed for progression (up to two years following IDS).
- The translational data from this study is being reported separately.

CONTACT INFORMATION

- NCT02480374 on https://clinicaltrials.gov
- For questions, please contact Lauren Musso at lmusso@celsion.com

ADMINISTRATION – INTRAPERITONEAL CATHETER

- Subcutaneously implantable intraperitoneal silicone catheters are used to deliver GEN-1 to the peritoneal cavity.



PATIENT POPULATION

- Patients newly diagnosed with EOC were eligible; patients who received prior radiotherapy or chemotherapy to any portion of the abdominal cavity and/or pelvis were excluded.

Characteristic	Cohort 1 (n=3)	Cohort 2 (n=3)	Cohort 3 (n=3)	Cohort 4 (n=3)	Total (n=12)
Stage					
IIIB	1	0	0	0	1
IIIC	1	3	1	2	7
IV	1	0	2	1	4
Histology					
Serous	3	3	3	3	12
CA-125					
Minimum	246	372	907	273	246
Median	362	934	1145	458	683
Maximum	423	957	1313	2006	2006

SAFETY

- The safety evaluation period is based on the first 4 doses of GEN-1 administered to each patient.
- The DSMB has reviewed data from the first 4 cohorts of patients. To date, 12 patients have been reviewed and no DLTs have been declared.
- Most common adverse events reported, regardless of causality, have been nausea, anemia, neutropenia, abdominal cramping, fatigue, and anorexia.
- Most common toxicities reported, which can be attributed to GEN-1, have been neutropenia, nausea, abdominal cramping, fatigue, anorexia, vomiting, anemia, and chills.
- The most severe AEs included > Grade 3 neutropenia, anemia, vomiting, and abdominal pain. No Grade 5 events have been recorded.
- One patient experienced Grade 2 fevers associated with GEN-1 but responded to acetaminophen and fluids.
- One patient did not undergo IDB while on-study due to pulmonary embolism and severe deconditioning due to underlying cancer. This patient has since improved and will have IDB.

EFFICACY

- In total, 12 patients were assessed for RECIST and 11 patients were assessed for Debulking Status and Pathologic Response.
- Control rate is 100% and response rate is 75%.
- All efficacy assessments are investigator reported.

RECIST Response	Cohort 1 (n=3)	Cohort 2 (n=3)	Cohort 3 (n=3)	Cohort 4 (n=3)	Total (n=12)
Complete Response	1	0	0	0	1
Partial Response	0	2	3	3	8
Stable Disease	2	1	0	0	3
Interval Debulking Status	**Cohort 1 (n=3)**	**Cohort 2 (n=2)**	**Cohort 3 (n=3)**	**Cohort 4 (n=3)**	**Total (n=11)**
R0	2	0	2	2	6
R1	1	2	0	1	4
R2	0	0	1	0	1
Pathological Response	**Cohort 1 (n=3)**	**Cohort 2 (n=2)**	**Cohort 3 (n=3)**	**Cohort 4 (n=3)**	**Total (n=11)**
cPR	1	0	0	0	1
micoPR	1	1	1	2	5
macroPR	1	1	2	1	5

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