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Phase I/II study of Safety and Efficacy of Intraperitoneal IMNN-001 with Neoadjuvant Chemotherapy of Paclitaxel and Carboplatin in Patients Newly Diagnosed with Advanced Epithelial Ovarian Cancer

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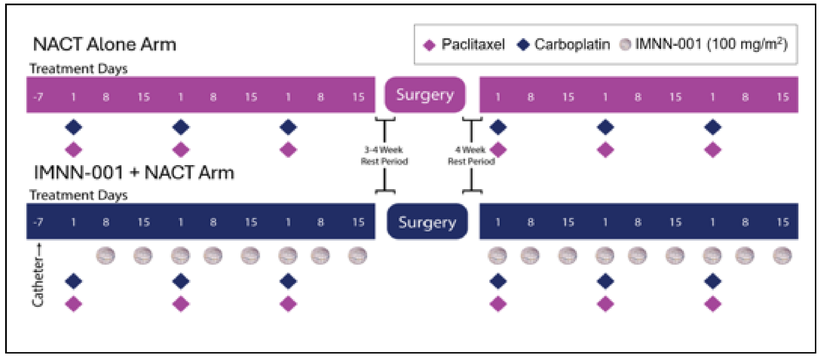
BACKGROUND

- Ovarian cancer remains the leading cause of death among gynecologic cancers. With approximately 20,000 cases diagnosed each year in the US, 80% of which are diagnosed in late stage (III/IV), it is estimated that >60% will die within 5 years of diagnosis[1,2]
- Patients with bulky stage III-IV disease who are not surgical candidates typically undergo three cycles of platinum-based neoadjuvant chemotherapy (NACT) 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]
- IMNN-001 is an IL-12 DNA 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 (IP) delivery also avoids the toxicities associated with systemic recombinant IL-12.[8]
- OVATION-2 (NCT03393884) is a randomized, controlled study assessing IMNN-001 in addition to neoadjuvant and adjuvant chemotherapy for the treatment of newly diagnosed epithelial ovarian cancer (EOC). The trial was open label due to intraperitoneal delivery of IMNN-001.
- We are reporting the findings from the recent primary database lock of the Phase I/II study evaluating the use of weekly IP IMNN-001 in combination with neoadjuvant and adjuvant chemotherapy in newly diagnosed EOC cancer patients eligible for NACT.

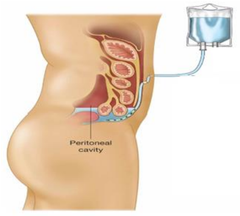
STUDY DESIGN AND METHODS



Primary Endpoint = Progression Free Survival (PFS)
Secondary Endpoints = OS, Chemotherapy-Response-Score (CRS), Surgical-Response-Score (SRS), and Objective-Response-Rate (ORR)
Participants could also receive PARP inhibitor maintenance which occurred more frequently in the control vs. experimental arm (44% vs. 32.8%).
OVATION-2 was not powered for hypothesis testing; however, PFS and OS are summarized using the estimate of the hazard ratio (HR) and corresponding confidence interval (CI). Percent response is reported for other endpoints.

ADMINISTRATION – IP CATHETER

- Subcutaneously implantable intraperitoneal silicone catheters are used to deliver IMNN-001 to the peritoneal cavity.



CONTACT INFORMATION

- NCT03393884 on https://clinicaltrials.gov
- For questions, please contact Imunon at clinical@imunon.com

PATIENT POPULATION

- Patients newly diagnosed with EOC were eligible.
- Participant characteristics were balanced except for an increased proportion of stage IV disease, and lesser proportion of ECOG PS=0 in the experimental arm.
- Participants with a pathogenic BRCA mutation and/or HRD status were balanced across the control & experimental arms.

Characteristics		NACT Alone (Control Arm) (N=54) n (%)	IMNN-001 + NACT (Experimental Arm) (N=58) n (%)
Age (years)	Mean (SD)	64.4 (8.34)	64.2 (10.56)
	Median	64.5	66.0
	Min, Max	45, 82	39, 82
Weight (kg) at Baseline	Mean (SD)	76.75 (18.247)	74.77 (20.349)
	Median	75.50	74.90
	Min, Max	43.2, 129.0	42.6, 128.4
BSA (m2) at Baseline	Mean (SD)	1.842 (0.2302)	1.811 (0.2667)
	Median	1.840	1.805
	Min, Max	1.33, 2.49	1.33, 2.49
ECOG Score at Baseline, n (%)	0	35 (64.8)	30 (51.7)
	1	17 (31.5)	25 (43.1)
	2	2 (3.7)	3 (5.2)
Cancer Stage, n (%)	IIIB	5 (9.3)	3 (5.2)
	IIIC	30 (55.6)	33 (56.9)
	IV	12 (22.2)	18 (31.0)
	Missing	7 (13.0)	4 (6.9)
BRCA Mutation Status, n (%)	Yes	9 (16.7)	10 (17.2)
	No	41 (75.9)	41 (70.7)
	Unknown	4 (7.4)	7 (12.1)
HRD Mutation Status, n (%)	Yes	10 (18.5)	12 (20.7)
	No	38 (70.4)	40 (69.0)
	Unknown	6 (11.1)	6 (10.3)
BRCA Mutation and/or HRD Mutation Status, n (%)	Yes	16 (29.6)	18 (31.0)
	No or Unknown	38 (70.4)	40 (68.9)

SAFETY

- The Safety Population (N = 117) is used for all safety analyses and is defined as all participants who received at least 1 cycle of chemotherapy.
- Weekly IP delivered IMNN-001 at a dose of 100 mg/m^2 was safe and well-tolerated. The most common AEs attributed at least possibly related to IMNN-001 were (listed by descending order): nausea, abdominal pain, fatigue, diarrhea, vomiting, and fever. Pain management protocols were found to be effective.
- There were no reports of cytokine release syndrome, an AE of special interest, or any other serious immune related adverse events (see table below, left side).
- An increased frequency of gastrointestinal events (e.g., abdominal pain, nausea, vomiting) as well as anemia, neutropenia and thrombocytopenia were observed in the experimental arm.
- This increased frequency of hematologic AEs may be attributed to the protocol design, in that participants on the experimental arm were sampled/evaluated for safety weekly compared to every 3 weeks in the control arm. The sampling in the experimental arm includes the time when participants are anticipated to nadir from their chemotherapy. For a proper comparison, we have analyzed the data to evaluate the effects of increased sampling and to apply corrections (see table below, right side). Given the known hematologic effect associated with chemotherapy, the DSMB found the toxicity reported in the experimental arm to be uncompelling clinically.

Immune Related Adverse Events in Safety Population

Immune Related Adverse Event	Chemotherapy Alone (Control Arm) (N=58) n (%)	Chemotherapy + IMNN-001 (Experimental Arm) (N=59) n %
Cytokine release syndrome	0	0
Allergic reactions[1]	7 (12.1)	5 (8.5)
Rashes	4 (6.9)	6 (10.2)
Thyroid disorders	1 (1.7)	0
Pneumonitis	0	0
Hepatitis	0	0

[1] Attributable to chemotherapy and not to IMNN-001

Grade 3 and Greater Hematologic Treatment Emergent Adverse Events at Matching Timepoints in Safety Population

Grade	NACT Alone (Control Arm) (N=58) n (%)	IMNN-001 + NACT (Experimental Arm) (N=59) n (%)
Grade 4 frequency corresponding to Day 1 lav draws	5 (8.6)	11 (18.6)
Grade 3 frequency corresponding to Day 1 lav draws	14 (24.1)	14 (23.7)
Total grade 3 or grade 4 frequency corresponding to Day 1 lav draws	16 (27.6)	22 (37.3)

EFFICACY

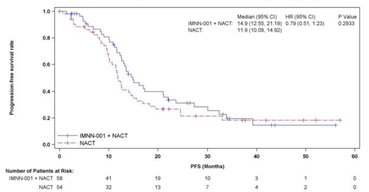
- 112 participants (ITT population) were enrolled with a median follow-up of 24 months at data cutoff (21Jun2024).
  - Median PFS was 14.9 months for experimental arm vs. 11.9 months for the control with HR:0.79 (0.51, 1.23)
  - Median OS was 40.5 months for experimental arm vs. 29.4 months for the control with HR:0.74 (0.42, 1.30)
- A subgroup analysis of participants having received PARP inhibitor regardless of exposure to IMNN-001 during the treatment included an n=31 of PARPi first line and an n=43 PARPi any line:
  - Median PFS for experimental arm was 33.8 months vs. 22.1 months for control with HR:0.80 (0.31, 2.12)
  - Median OS was not reached for experimental arm vs. 37.1 months for control with HR:0.41 (0.13, 1.28)

Summary of Surgical, Chemotherapy, and Objective Response Rate in ITT Population prior to Interval Debulking Surgery[1]

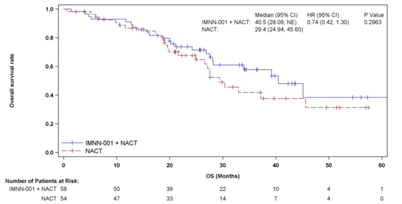
Category	NACT Alone (Control Arm) (N=54)	NACT + IMNN-001 (Experimental Arm) (N=58)
Surgical Response[2]		
R0	25 (52.1)	31 (64.6)
R1	14 (29.2)	5 (10.4)
R2	9 (18.8)	12 (25.0)
Chemotherapy Response Score[2]		
1	16 (34.8)	16 (34.8)
2	24 (52.2)	18 (39.1)
3	6 (13.0)	12 (26.1)
Best Overall Response, n (%)		
Complete Response (CR)	1 (1.9)	1 (1.7)
Partial Response (PR)	30 (55.6)	30 (51.7)
Objective Response Rate (ORR), n (%)[3]	31 (57.4)	31 (53.4)
Serologic Response[4]		
Yes	43 (79.6)	44 (75.9)
No	6 (11.1)	10 (17.2)
Not Applicable	5 (9.3)	4 (6.9)

[1] The trial was not powered for statistical significance on any trial endpoint, and the p-values from all secondary endpoints were not statistically significant.
[2] Percentages are based on number of patients in each treatment group, excluding those with missing or not applicable assessments.
[3] ORR is defined as the proportion of participants with objective evidence of CR or PR prior to debulking surgery.
[4] Serologic response evaluates proportion of participants with at least 50% reduction in CA-125 from baseline, among participants that the baseline value is at least twice the upper limit of the reference range and within 2 weeks prior to treatment initiation (≤ 14 days).

Kaplan-Meier Plot of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 in the ITT Population



Kaplan-Meier Plot of Overall Survival in the ITT Population



CONCLUSIONS

- IMNN-001 (dose 100 mg/m^2) shows a promising effect on survival and an acceptable safety profile in patients with newly diagnosed advanced epithelial ovarian cancer.
- Results across endpoints show a consistent treatment effect.
- A Phase III study is being designed to confirm these preliminary findings. FPI is anticipated for Q1 2025.

REFERENCES

1. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2023;74:12-49.
2. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024; 74:229-263.
3. NCCN Guidelines Version3.2024
4. du Bois A, Reuss A, Pujade-Lauraine E et al. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d' Investigateurs Nationaux Pour les Etudes des Cancers de l' Ovaire (GINECO). Cancer 2009; 115: 1234–1244.
5. van der Burg ME, van Lent M, Buyse M et al. The effect of debulking surgery after induction chemotherapy on the prognosis in advanced epithelial ovarian cancer. Gynecological Cancer Cooperative Group of the European Organization for Research and Treatment of Cancer. N Engl J Med 1995; 332: 629–634.
6. Vergote I, Tropé CG, Amant F et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med 2010; 363: 943–953.
7. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. J Clin Oncol. 2002; 20(5):1248–59.
8. P.H. Thaker, W.H. Bradley, C.A. Leath III, C. Gunderson Jackson, N. Borys, K. Anwer, L. Musso, J. Matsuzaki, W. Bshara, K. Odunsi, R.D. Alvarez. GEN-1 in Combination with Neoadjuvant Chemotherapy for Patients with Advanced Epithelial Ovarian Cancer: A Phase I Dose-Escalation Study. Clinical Cancer Research; 2021 Oct 15; 27(20):5536-5545.