2025 ASCO® ANNUAL MEETING

A Phase I/II study of the Safety and Efficacy of IP IMNN-001 in combination with N/ACT in patients newly-diagnosed with advanced EOC:

Updated Survival Analysis from OVATION-2 Trial

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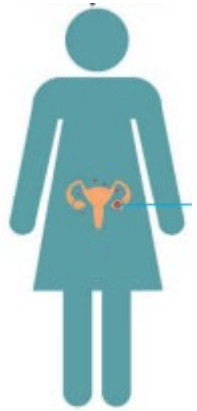
Key Takeaways

- OVATION-2 is a randomized, controlled study of IMNN-001, an IL-12 gene immunotherapy, intraperitoneally delivered in combination with neo/adjuvant chemotherapy (N/ACT) in newly diagnosed advanced epithelial ovarian cancer (EOC)
- The IMNN-001 nanoparticle-encased gene delivery system allows repeated safe and tolerable tumor-localized IL-12 delivery, avoiding immune-related adverse events associated with systemic IL-12 exposure
- After 31-month follow-up, the addition of IMNN-001 to SoC N/ACT provided a 13-month numerical survival advantage over N/ACT alone (46 vs 33 months) (data cutoff 12/2024)
- Increased activity was observed in HRD patients and those who received PARPi (median OS not yet reached in the IMNN-001 arm vs 37.1 months in the control arm)

Background

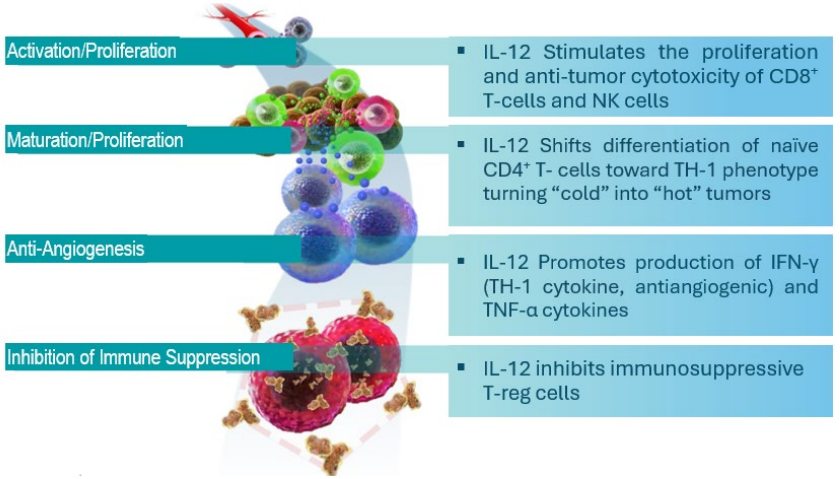
Immune approaches in EOC

- Immunotherapy is considered an attractive approach for the treatment of EOC due to a multifaceted, highly immunosuppressive (“cold”) tumor environment[1]
- The addition to ICIs in first or later lines EOC modestly improved ORR, but not OS (KEYNOTE, JAVELIN, KEYLYNK, DUO-O studies)[2-5]



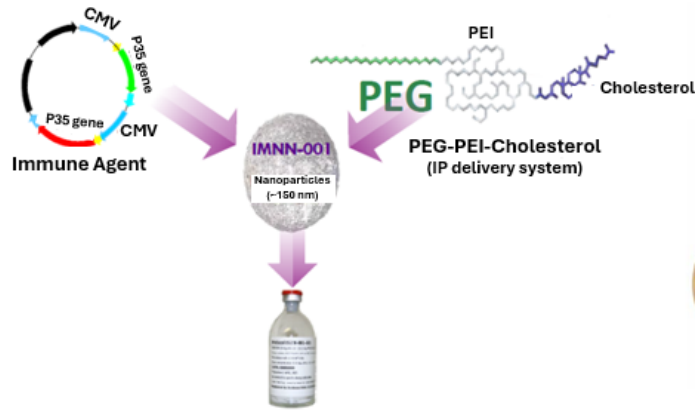
IMNN-001: MoA

- IMNN-001 is a novel IL-12 gene therapy investigational product
- IL-12 is a pleiotropic immuno-stimulatory cytokine with activity on both the innate and adaptive immune systems
- IL-12 converts the tumor microenvironment from ”cold” to ”hot”



IMNN-001: Local IP delivery

- IMNN-001 is an IL-12 DNA-based plasmid encased in a lipopolymer nanoparticle delivery system enabling efficient cell transfection and durable, local secretion of the IL-12 protein at the tumor site[6].
- OVATION-1 Ph1 study demonstrated IP IMNN-001 delivery to be safe[7,8], avoiding the systemic toxicities from recombinant IL-12 when administered IV

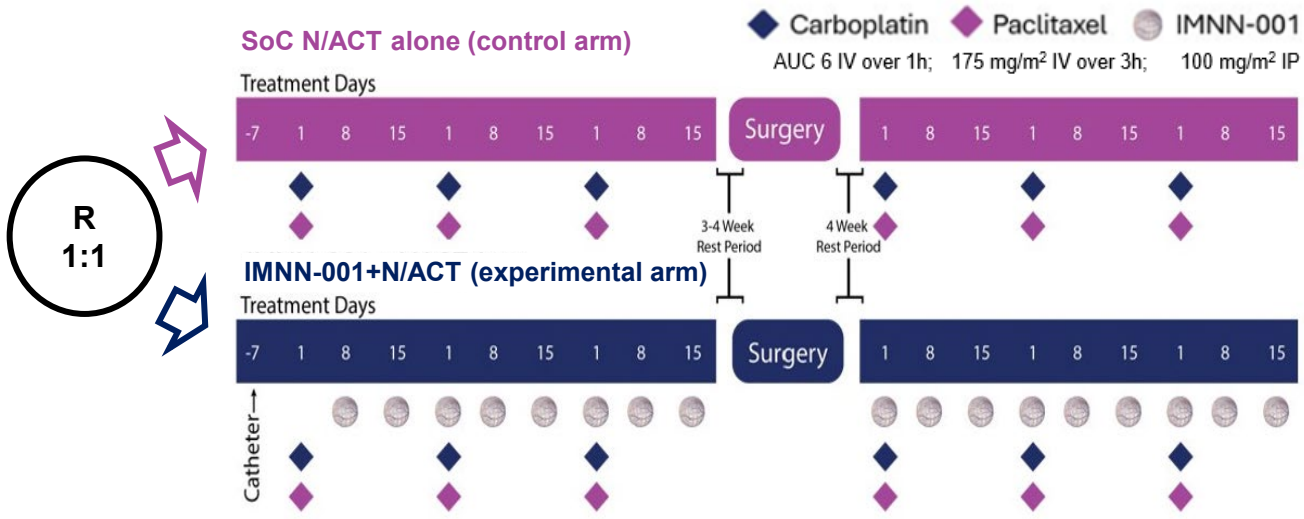


EOC: Epithelial ovarian cancer; ICIs: Immune checkpoint inhibitors; MoA: Mechanism of action; IL-12: Interleukine-12; IFN: Interferon; TNF: Tumor necrosis factor; T-reg: Regulatory T cells; CMV: Cytomegalovirus; PEG: Polyethyleneglycol; PEI: Polyethyleneimine; IP: Investigational product

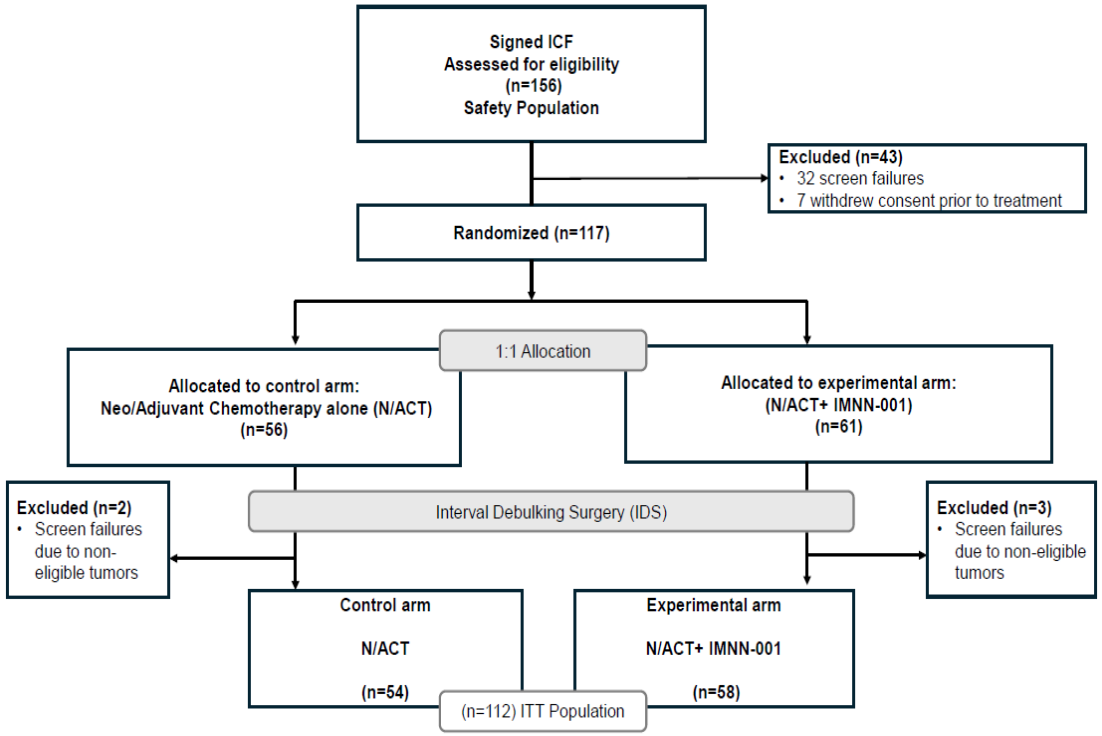
(1) Blanc-Durand, Front Immunol, 2023 (2) Matulonis et al., Ann Oncol, 2019 (3) Pujade-Lorraine et al., Lancet Oncol, 2021 (3) Powell et al., Gynecol Oncol, 2025 (4) GSK Press Release, 2024 (5) Harter et al., Gynecol Oncol, 2025 V190 Supp1 (6) Answer et.al, Gene Ther, 2020 (7) Alvarez et al., Gynecol Oncol 2014 (8) Thaker et al., Clin Cancer Res, 2021

OVATION-2 Phase I/II Study in EOC N/ACT +/- IMNN-001

Study Schema (NCT03393884)



Consort Diagram



- A 15-patient **safety lead-in phase 1** monitored a 100 mg/m^2 dose of IMNN-001 given IP in combination with N/ACT SoC before opening the phase 2 recruitment
- **Ph2 Endpoints**: Primary: Safety and PFS
  Secondary: OS, ORR, Surgical response, Chemotherapy Response Score, Serologic response rates
- **No** endpoints were **powered for statistical significance**

Demographics and Exposure

Demographics

- Overall well-balanced [only somewhat higher risk group in the IMNN-001 arm (ECOG and stage)]

Exposure

- Median number of CT cycles was 6 in both arms
- Median number of IMNN-001 doses was 6 (0-17)
- Dose intensity of IMNN-001 in the overall period was 35.3% (62.5% in the NACT period and 11.1% in the ACT period)

Demographics (ITT Population)

Characteristics		Control arm N/ACT (N=54)	Experimental arm IMNN-001 + N/ACT (N=58)
Age (years)	Mean (SD)	64.4 (8.3)	64.2 (10.6)
Weight (kg)	Mean (SD)	76.8 (18.2)	74.8 (20.3)
BSA (m^2)	Mean (SD)	1.84 (0.23)	1.81 (0.27)
ECOG 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 n (%)	Yes	9 (16.7)	10 (17.2)
	No	41 (75.9)	41 (70.7)
	Unknown	4 (7.4)	7 (12.1)
HRD Mutation n (%) (excluding BRCA mutations)	Yes	10 (18.5)	12 (20.7)
	No	38 (70.4)	40 (69.0)
	Unknown	6 (11.1)	6 (10.3)

BSA: Body Surface Area; ECOG: Eastern Cooperative Group; HRD: Homologous Recombination Deficient; N/ACT: neo/adjuvant chemotherapy; SD: Standard Deviation.

Safety

- Most TEAEs and Serious TEAS related to treatment were gastrointestinal and cytopenias
- TEAEs of special interest were abdominal pain (66% in experimental vs 28% in control), and cytokine release syndrome with no reported events
- Abdominal pain was the most common cause of IMNN-001 dose reduction (12% of patients but only 3% discontinued treatment)
- No serious systemic toxicity or immune-related events reported
- 1 pt died in each arm, unrelated to IMNN-001

TEAE: Treatment Emergent Adverse Event; STEAE: Serious TEAE. (*) Dose reduction for IMNN-001 was 80 mg/m2 from the intended 100 mg/m2 (#) 2 additional patients had dose reductions due to port issues.(&) Occurring in the same patient.

Safety (Safety Population)

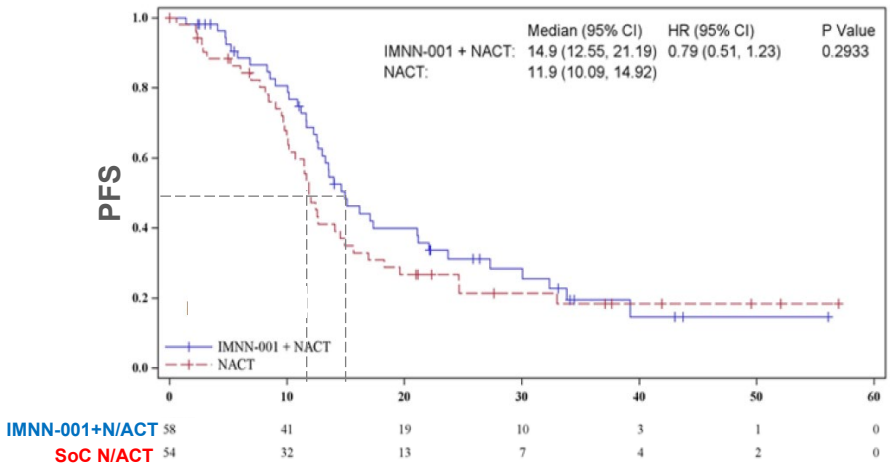
Subjects with at Least One, n (%)	Control arm (N/ACT) n=58	Experimental arm (IMNN-001 + N/ACT) N=59
TEAEs	56 (96.6)	59 (100)
STEAEs	21 (36.2)	43 (72.9)
TEAEs of special interest	16 (27.6)	39 (66.1)
Abdominal Pain	16 (27.6)	39 (66.1)
Cytokine Release Syndrome	.	.
TEAEs leading to IMNN-001 dose reduction*#	NA	9 (15.2)
Abdominal Pain	NA	7 (11.9)
Others (deconditioning)	NA	1 (1.7) each
TEAE Leading to Study Drug D/C	.	14 (23.7)
Abdominal pain	.	2 (3.4)
Respiratory failure		2 (3.4)
Others (n=8)	.	1 (1.7) each
TEAE Leading to death	1 (1.7)	1 (1.7)
Pancytopenia	.	1[&] (1.7)
Upper GI hemorrhage	1 (1.7)	.
Respiratory failure	.	1[&] (1.7)

Serious TEAEs (IMNN-001 or N/ACT related) with incidence >10% in the experimental arm				
	Total	**Grades1&2**	**Grade 3**	**Grade 4**
Thrombocytopenia	9 (15.3)	1 (1.7)	4 (6.8)	4 (6.8)
Nausea	7 (11.9)	3 (5.1)	5 (8.5)	.
Abdominal pain	8 (13.6)	.	8 (13.6)	.
Febrile neutropenia	7 (11.9)	.	7 (11.9)	.
Anemia	7 (11.9)	.	7 (11.9)	.
Vomiting	6 (10.2)	1 (1.7)	5 (8.5)	.
Pyrexia	6 (10.2)	5 (8.5)	1 (1.7)	.

Results Efficacy: PFS (Primary endpoint) and Response

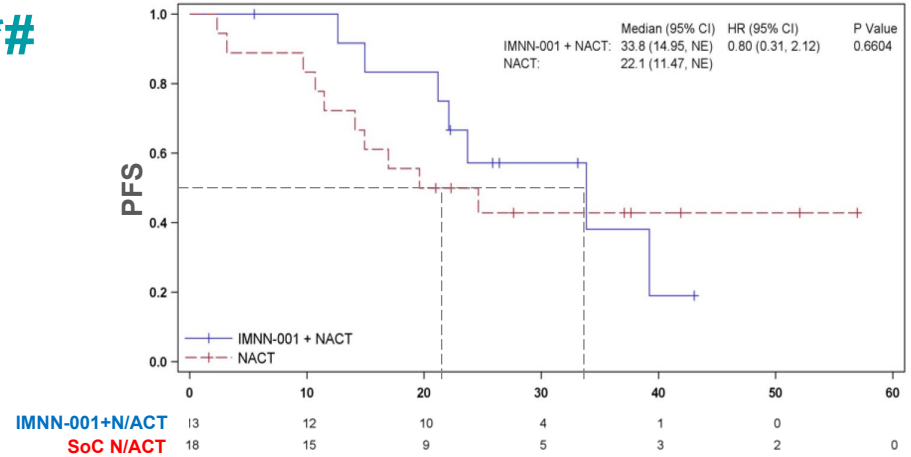
ITT

- **IMNN-001 Δ3 mo** to **SoC** PFS (**14.9** vs **11.9**) HR: 0.79



PARPi Treated*#

- **IMNN-001 Δ3 11.7mo** to **SoC** PFS (**33.8** vs **22.1**) HR:0.8



Response, ITT

- **IMNN-001** increased **R0** and **CRS 3**

Endpoint	N/ACT n=54	IMNN-001 + N/ACT N=59
Objective Response Rate n (%) (ORR=CR+PR) prior surgery	31 (57.4)	31 (53.4)
Best Overall Response n (%)		
CR	1 (1.9)	1 (1.7)
PR	30 (55.6)	30 (51.7)
SD	12 (22.2)	12 (20.7)
PD	4 (7.4)	0
NE	1 (1.9)	2 (3.4)
Serologic response n (%)		
Yes	43 (79.6)	44 (75.9)
No	6 (11.1)	10 (17.2)
NA	5 (9.3)	4 (6.9)
Surgical response* n (%)		
R0	25 (52.1)	31 (64.6)
R1	14 (29.2)	5 (10.4)
R2	9 (18.8)	12 (25.0)
CT Response score* n (%)		
CRS3	6 (13.0)	12 (26.1)
CRS2	24(52.2)	18 (39.1)
CRS1	16 (34.8)	16 (34.8)

(*) PARPi treated in first line maintenance before first PD
(#) in Non-PARPi treated subgroup (n=81): PFS was 13.3 vs 10.2 mo HR 0.63 no statistically significant (ss)

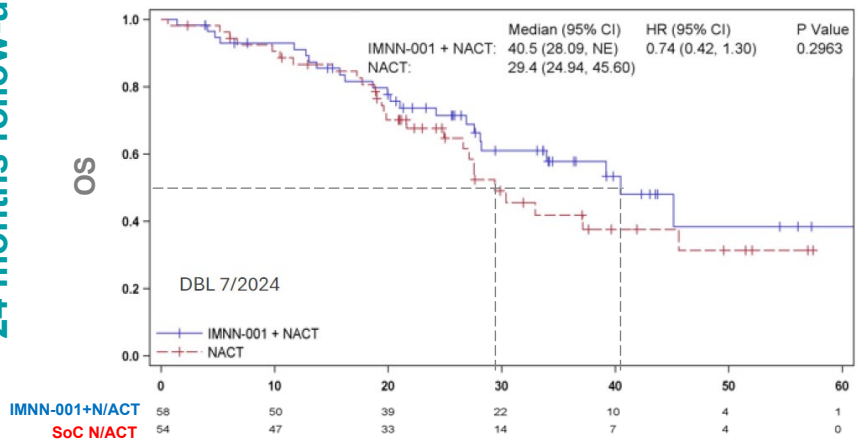
Results Efficacy: OS (13 mo benefit at 31 mo FU)

ITT

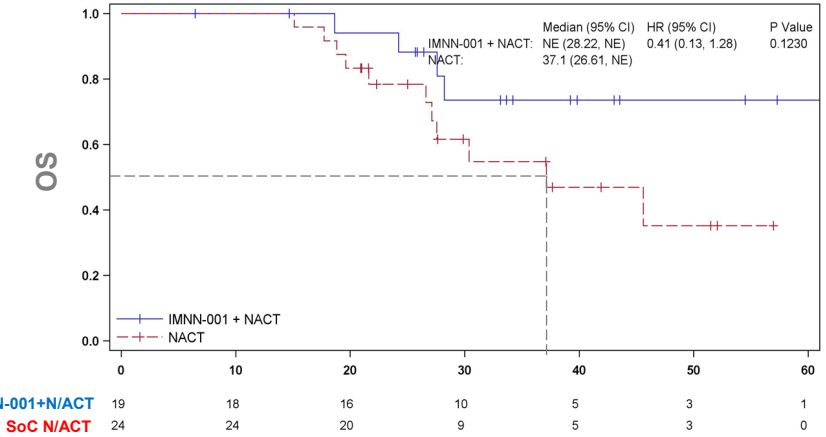
PARPi treated[#$]

24 months follow-up

- **IMNN-001 Δ 11.1 mo** to **SoC** OS (**40.5** vs **29.4**) HR:0.74

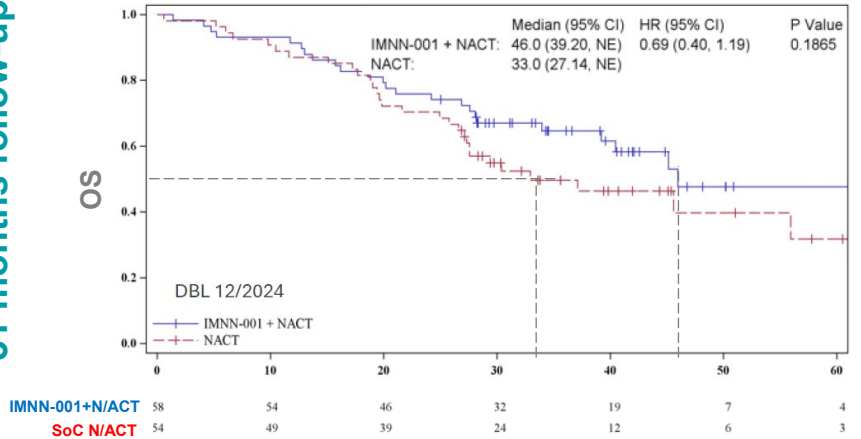


- **IMNN-001 vs SoC** (**NE** vs **37.1**) HR:0.41

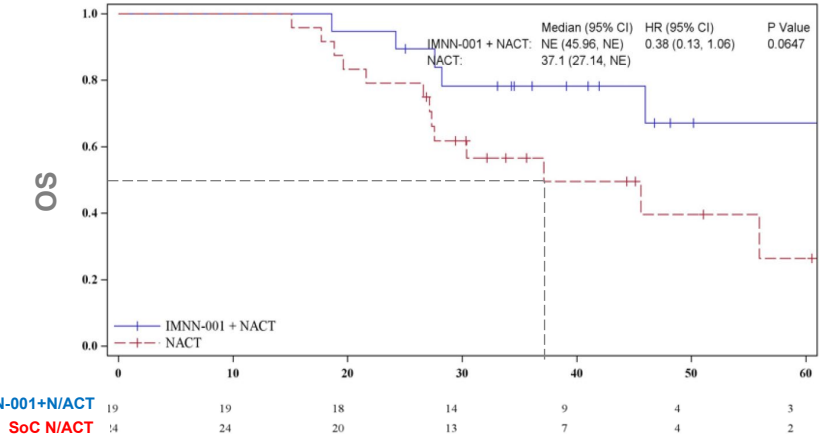


31 months follow-up

- **IMNN-001 Δ 13 mo** to **SoC** OS (**46.0** vs **33.0**) HR:0.69



- **IMNN-001 vs SoC** (**NE** vs **37.1**) HR:0.38



(#) 31 mo Follow-up for Non-PARPi treated subgroup (n=69): OS was 40.5 vs 29.4 mo HR 0.83 no statistically significant (ss)
($) 31 mo Follow-up for BRCAm/HRD subgroup (n=34): OS was NE vs NE mo HR 0.49 no ss

Limitations and supportive data

- A remarkable 13-month numerical benefit in OS is detected in this study with the addition of IMNN-001 to SoC 1L treatment in EOC; however, this study was not powered for statistical significance. A confirmatory Phase 3 study powered for OS is underway (NCT06915025)

- IMNN-001's benefit signal is further supported by:

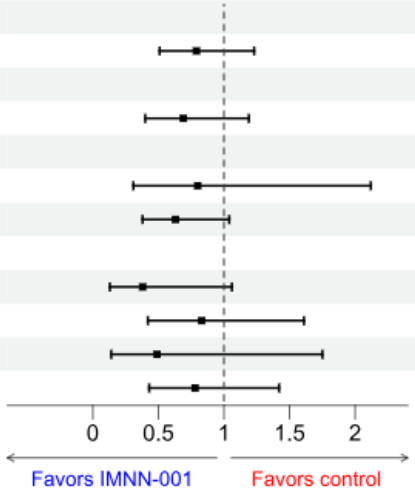
1) Benefit observed in all subgroups analyzed

2) A 6.5-month reduction of negative treatment effects in a post-hoc analysis using a statistical method to assess the totality of treatment effect, an endpoint composed of PFS+ OS

IMNN-001's Benefit in PFS and OS is observed in all subgroups analyzed

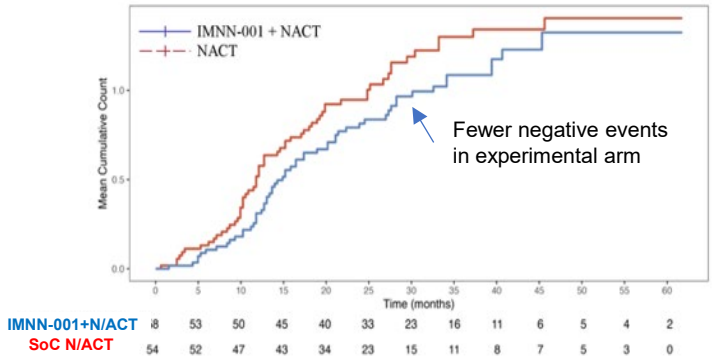
Endpoint	n	HR (95% CI)
Primary		
Progression Free Survival (PFS)	112	0.79 (0.51 to 1.23)
Secondary		
Overall Survival (OS)	112	0.69 (0.40 to 1.19)
PFS Subgroup		
PARP treated patients*	31	0.80 (0.31 to 2.12)
Non-PARP treated patients*	81	0.63 (0.38 to 1.04)
OS Subgroups		
PARPi treated patients	43	0.38 (0.13 to 1.06)
Non-PARPi treated patients	69	0.83 (0.42 to 1.61)
HRDpos [BRCAm and/or HRD]	34	0.49 (0.14 to 1.75)
HRP	78	0.78 (0.43 to 1.42)

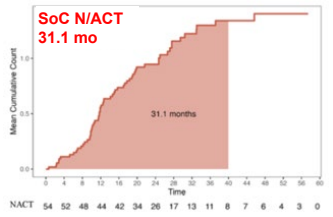
* In 1st line maintenance—before first PD

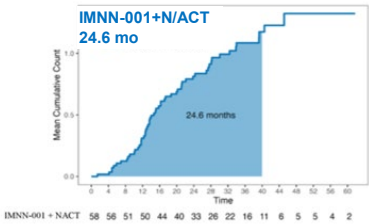


IMNN-001's Totality of Treatment effect* (PFS+OS)

IMNN-001 shows **6.5 mo reduction of negative treatment effects vs SoC** (p=0.0375)







Top mean cumulative count curves demonstrate fewer negative events over time with IMNN-001+N/ACT treatment than with the control N/ACT alone treatment. Areas under the curve (AUC) below represent average time lost due to undesirable outcomes for the experimental (24.6 mo) and control arm (31.1 mo) (p=0.0375)

(*) Wang, X., et al., JAMA Netw Open, 2023. **6**(6): p. e2319055.

Conclusions

- OVATION-2, a randomized controlled Phase I/II study of IMNN-001, an IL-12 gene immunotherapy, delivered intraperitoneally in combination with neo/adjuvant chemotherapy in newly-diagnosed advanced epithelial ovarian cancer (EOC), was safe and yielded clinically meaningful benefits to patients over the SoC in terms of PFS, OS, Surgical Response and Chemotherapy Response score

- The IMNN-001 nanoparticle-encased gene delivery system allows safe and tolerable repeated delivery of tumor-localized IL-12, avoiding immune-related adverse events associated with systemic IL-12 exposure

- After 31-month follow-up, the addition of IMNN-001 to SoC neo/adjuvant chemotherapy (N/ACT) provided a 3-month numerical PFS and a 13-month OS advantage over N/ACT alone (46 vs 33 months)

- Increased activity is observed in HRD patients and for those who received maintenance PARPi (the median OS not yet reached in the IMNN-001 arm vs 37.1 months in the control arm)

- A confirmatory randomized phase 3 study (NCT06915025) is underway to evaluate the safety and efficacy of IMNN-001 plus N/ACT compared to N/ACT alone and will further explore the contribution of BRCA/HRD status to IMNN-001 efficacy

Acknowledgements

- To the patients and their families who made this trial possible
- To the clinical study teams for their excellent work
- The study is supported by IMUNON Inc.

Lay Summary Slide

- **What did this research tell us?**

This OVATION-2 study is a clinical trial exploring the effects of adding an immunotherapy (IMNN-001, a delivery interleukin-12 system) to standard of care chemotherapy (CT) for women with newly-diagnosed advanced stage ovarian cancer. IL-12 is a molecule that stimulates the body immune defenses to attack tumor cells. One hundred twelve women were randomized to either standard of care CT or to CT + IMNN-001 and treated for approximately 24 weeks. This Phase 2 trial established that the IMNN-001 formulation of IL-12 could be safely administered. Results from this study suggest that IMNN-001 treatment may increase life-expectancy and may provide other benefits when combined with CT.

- **Who does this research impact?**

Ovarian cancer is frequently diagnosed at an advanced stage, after it has spread. Controlling advanced-stage ovarian cancer with currently available first-line treatments is frequently difficult, and new, safe and better treatments are needed.

- **What does this mean for patients right now?**

While the results of the OVATION-2 trial are promising, the activity and safety of IMNN-001 must be repeated and proven in a larger trial. A phase 3 trial of IMNN-001 in combination with CT is underway in the US and Canada (OVATION-3, NCT06915025). The investigators in OVATION-2 and OVATION-3 hope that these studies will provide a new therapeutic modality to benefit women with ovarian cancer.