

1234eTiP - OVATION-3: A randomized phase III trial evaluating the safety and efficacy of intraperitoneal IL-12 gene therapy administered in combination with standard neoadjuvant and adjuvant chemotherapy (N/ACT) in newly-diagnosed patients with advanced epithelial ovarian cancer (EOC)



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BACKGROUND

- IMNN-001, an **IL-12 DNA-gene therapy nanoparticle** that showed a favorable benefit/risk ratio when administered intraperitoneally (IP) in combination with Neo and Adjuvant IV Chemotherapy (N/ACT) in women with advanced Epithelial Ovarian Cancer (EOC).¹⁻²
- In the **OVATION-2 randomized phase 2 study (NCT03393884)**, **IMNN-001+SoC N/ACT demonstrated a clinically meaningful numerical OS benefit of 13 months (mo) vs N/ACT alone (40.5 vs 27.6 mo; HR 0.70)**. In the PARPi-treated subgroup of patients, OS HR was 0.42 (NE vs 37.1mo). Local delivery of IL-12 with IMNN-001 was safe, with no serious immune-related adverse events. Most common IMNN-001 adverse reactions were abdominal pain and pyrexia.³
- OVATION-3 Phase 3 trial is designed to confirm the OS benefit and safety of IMNN-001+SoC N/ACT for advanced EOC patients.**

IMNN-001 DELIVERY AND MECHANISM OF ACTION

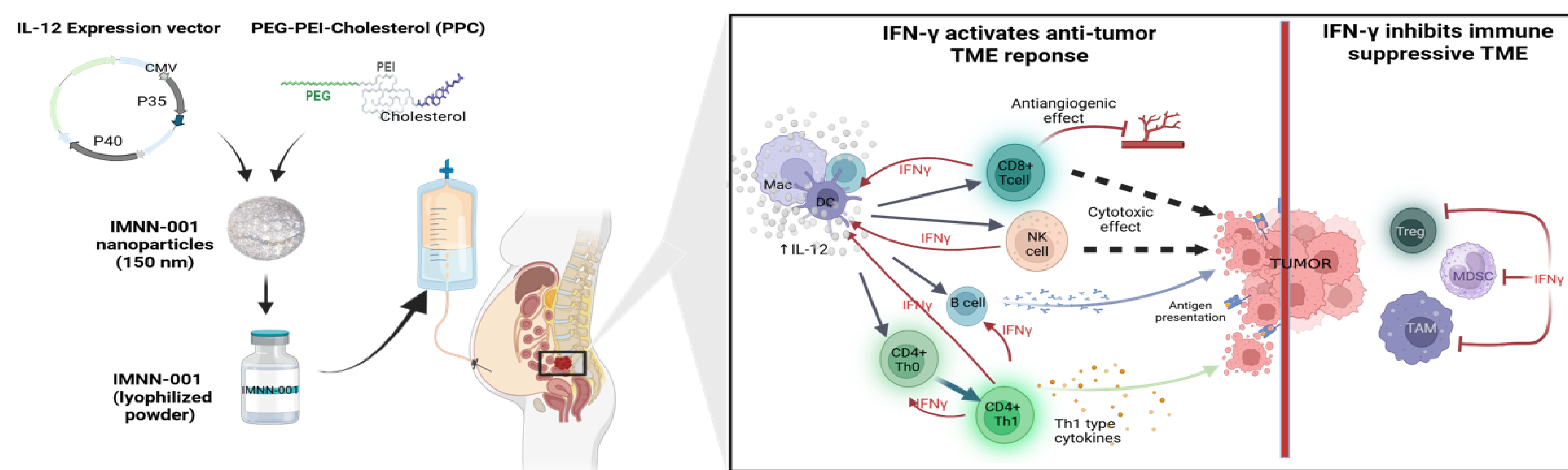


Figure 1: Left: IMNN-001, comprised of a plasmid expressing the p35 and p45 subunits of hIL-12 encased in a synthetic lipopolymer delivery system composed of a polyethylenimine (PE) backbone covalently linked to polyethylene glycol (PEG) and cholesterol, is delivered intraperitoneally in the clinic.⁴ Right: The expression of hIL-12 by cells in the tumor microenvironment (TME) through its downstream mediators (IFN- γ and other cytokines) activates the innate and adaptive immune systems and inhibits immune suppressive cells, turning the TME from cold to hot and providing anti-tumor activity.^{2,5,6}

TRIAL DESIGN: OVATION-3 Phase III study (NCT06915025)

Screening

Suspected Stage III_{bc}/IV EOC patients recommended to received NACT

Homologous recombinant repair test & staging¹

1. Homologous recombinant repair status and tumor stage required prior to randomization

Diagnostic Laparoscopy

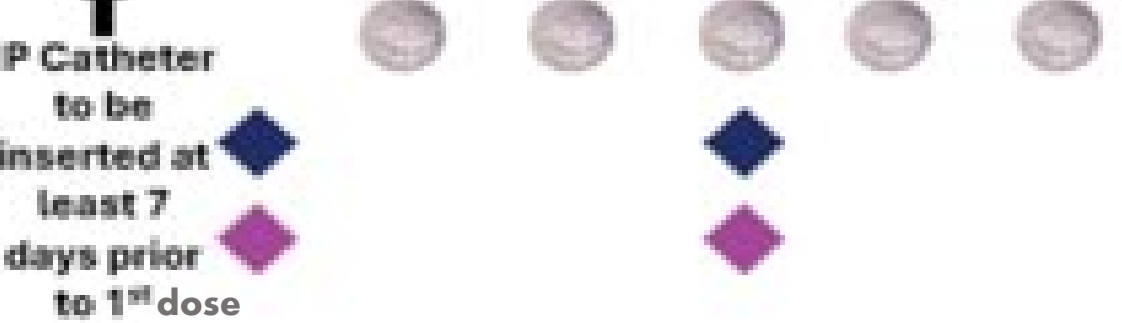
R¹ (1:1)

Frontline Therapy

Chemotherapy Alone (Control Arm)



IMNN-001 + Chemotherapy (Experimental Arm)



Dosage

- Paclitaxel: 175 mg/m² over 3 hours
- Carboplatin: AUC 6 IV over 1 hour
- IMNN-001: 100 mg/m² (experimental arm only)

Maintenance Therapy

PARPi treatment: HRD⁺ participants only

PARPi treatment: HRD⁻ participants only

EOT visit

- N=500 to enroll in US and EU
- PRIMARY ENDPOINT:** OS (>95% statistical power)
- SECONDARY ENDPOINTS** include Chemotherapy Response Score, Surgical Response Score and ORR
- EXPLORATORY ENDPOINTS** include IMNN-001's local and systemic immune effects, QoL and ctDNA analysis

MAIN ELIGIBILITY CRITERIA

- Female, ≥ 18 years old, ECOG 0-2.
- Histologically confirmed diagnosis of high-grade non-mucinous epithelial ovarian (serous, endometrioid, carcinosarcoma, mixed epithelial pathologies), fallopian tube, or peritoneal cancer Stage III_{b/c} or IV (FIGO) with no prior treatment for this disease.
- Eligible to receive neoadjuvant chemotherapy but no intent to receive bevacizumab.
- Confirmed biomarker tumor status (HRD vs. HRP).
- WCHBP must have a negative serum pregnancy test before initiation of therapy and practice an effective form of contraception. No breastfeeding allowed.
- Adequate bone marrow, renal, hepatic function, and neuropathy grade ≤ 1 .
- No active infection, uncontrolled illness or active hepatitis or HIV (undetectable viral load).
- No prior treatment with IMNN-001 or requiring systemic immunosuppressive therapy (i.e., steroid use not related to chemotherapy administration).
- No bowel obstruction, sub-occlusive mesenteric disease, abdominal or gastrointestinal fistula, gastrointestinal perforation, or intra-abdominal abscess.
- No uncontrolled hypersensitivity to treatment drugs or their excipients.
- No in treatment for active autoimmune disease.
- No prior radiotherapy to any portion of the abdominal cavity or pelvis. Or any prior chemotherapy for any abdominal or pelvic tumor.
- No history of CNS disease.
- No interference with the placement of the IP catheter for study drug administration.

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P.H.T receives consulting fees and owns stock from Imunon.

REFERENCES

(1) Thaker et al., *Future Oncol*, 2019; (2) Thaker et al., *Clin Cancer Res*, 2021; (3) Thaker et al., *Gynecol Oncol*, 2025; (4) Anwer et al., *Gene Ther*, 2009; (5) Geils et al., *J. Gene Med*, 2024; (6) Thaker et al., Poster: AACR Advances in OC Research meeting 2025