recombinant human STING (CTD) was evaluated using isothermal titration calorimetry (ITC) compared to the endogenous ligand 2',3'-cGAMP. Antitumor efficacy was evaluated in multiple syngeneic tumor models, including the TC-1 model which overexpresses HPV16 E6 and E7 with the ONM-500 vaccine in combination with anti-PD-1 checkpoint inhibitor. Long-term anti-tumor memory was evaluated in a follow-up rechallenge study after 60 days in tumor-free animals.

**Results** Characterization of ONM-500 nanovaccine shows reproducible particle chemi-physical properties and antigen loading. The nanoparticle size substantiates the effective lymph node accumulation for antigen cross-presentation in dendritic cells following subcutaneous administration. ITC studies with human STING demonstrated effective binding by ONM-500 adjuvant. The nanovaccine anti-tumor efficacy was previously demonstrated in melanoma, colorectal, and HPV-associated syngeneic tumor models. In TC-1 tumors, ONM-500 nanovaccine containing full-length E6/E7 protein showed 100% overall survival at 55 days (figure 1). Tumor growth inhibition was also improved over E7 antigen peptide formulated nanovaccine. A rechallenge study demonstrated long-term antigen-specific anti-tumor memory response.

**Conclusions** ONM-500 STING-activating nanovaccines effectively deliver antigens in vivo to lymph nodes to elicit antigen-specific CTL response. The anti-tumor efficacy in multiple tumor models demonstrates the potential of ONM-500 as a general STING agonist cancer vaccine platform, and full-length E6/E7 incorporated ONM-500 is being developed for HPV-associated cancers.

**Ethics Approval** All animal procedures were performed with ethical compliance and approval by the Institutional Animal Care and Use Committee of the University of Texas Southwestern Medical Center (Protocol No. 2017-101954) and Pennsylvania State College of Medicine (Protocol No. 47682).

### REFERENCES


1. Luo M, Wang H, Wang Z, Cai H, Lu Z, Li Y, Du M, Huang G, Wang C, Chen X, Porembka MR, Lea J, Frankel AE, Fu YX, Chen ZJ, Gao J. A STING-activating nanovaccine for cancer immunotherapy. *Nat Nanotechnol* 2017; **12**:648–654.
2. Luo M, Liu Z, Zhang X, Han C, Samandi LZ, Dong C, Sumer BD, Lea J, Fu YX, Gao J. Synergistic STING activation by PC7A nanovaccine and ionizing radiation improves cancer immunotherapy. *J Control Release* 2019; **28**:154–160.


## In-Progress clinical trials

### P858 AN OPEN-LABEL, MULTI-CENTER TRIAL OF INO-5401 AND INO-9012 DELIVERED BY ELECTROPORATION (EP) IN COMBINATION WITH CEMIPLIMAB IN SUBJECTS WITH NEWLY-DIAGNOSED GLIOBLASTOMA (GBM)


[1]Jeffrey Skolnik*, [2]David Reardon, [3]Steven Brem, [3]Arati Desai, [3]Stephen Bagley, [4]Sylvia Kurz, [5]Macarena de la Fuente, [6]Seema Nagpal, [7]Mary Welch, [1]Brian Sacchetta, [1]Sarah Bartra, [8]Amy-Lee Bredlau, [8]Israel Lowy, [1]Kimberly Kraynyak, [1]Matthew Morrow, [1]Trevor McMullan, [1]Jean Boyer. *[1]Inovio, Plymouth Meeting, PA, USA; [2]Dana Farber Cancer Institute, Boston, MA, USA; [3]University of Pennsylvania, Philadelphia, PA, USA; [4]New York University, New York, USA; [5]University of Miami, Miami, USA; [6]Stanford University, Stanford, USA; [7]Columbia University, New York, USA; [8]Regeneron, Tarrytown, NY, USA*


10.1136/LBA2019.12

**Background** GBM is one of the most deadly cancers and treatment is surgery, followed by radiation (RT) and temozolomide (TMZ) daily during RT followed by cycles of TMZ for select patients.[1] New immunotherapies, such as checkpoint inhibition, may benefit patients with GBM. T cell-enabling therapies, in combination with checkpoint inhibition, may improve overall survival (OS). In this study, a novel antigen-specific T cell-generating therapy, INO-5401 (synthetic DNA plasmids encoding for human telomerase [hTERT], Wilms Tumor-1 [WT-1] and prostate specific membrane antigen [PSMA]), plus INO-9012 (synthetic DNA plasmid encoding for IL-12), with the PD-1 checkpoint inhibitor, cemiplimab, was given to patients with newly-diagnosed GBM to evaluate tolerability, immunogenicity and clinical efficacy of the combination.

**Methods** Phase I/II, single arm, two cohort study (A: MGMT Promoter Unmethylated, B: MGMT Promoter Methylated). The primary objective is to evaluate the safety of INO-5401 and INO-9012 followed by EP with CELLECTRA® 2000 in combination with cemiplimab. Secondary objectives include the evaluation of preliminary clinical efficacy and immunogenicity. Treatment is with 9 mg INO-5401 with 1 mg INO-9012 every three weeks (Q3W) for four doses, then Q9W; and cemiplimab (350 mg IV Q3W). RT is given as 40 Gy over three weeks; TMZ is given concurrent with radiation (Cohorts A and B), followed by maintenance TMZ (Cohort B).

**Results** 52 patients were enrolled onto this study; 32 in Cohort A and 20 in Cohort B. 18 were women (35%) and 47 were white (90%). The median age was 60 years (range 19-78 years). The most common Grade $\geq$3 adverse events were elevations in alanine or aspartate aminotransferase (ALT/AST; 5 patients), and tumor inflammation/edema (5 patients); there was one Grade 5 unrelated event of urosepsis. The only related SAE reported in more than one patient was pyrexia. 22 patients (42%) reported immune-related AEs, with the most common being elevations in ALT or AST (8 patients), and were reported most commonly within the first nine weeks of treatment. The safety profile was consistent with that of patients with GBM and of checkpoint inhibitors. ELISpot assessments performed to date demonstrated the majority of patients have T cell responses to INO-5401. PFS6 was 75% (95% CI 56.6, 88.5) in Cohort A (preliminary; Cohort B pending).

**Conclusions** INO-5401 + INO-9012 with cemiplimab has an acceptable safety profile, is immunogenic and is potentially efficacious in patients with newly-diagnosed GBM. This combination is promising; survival results will be updated next year.

**Trial Registration** NCT03491683.

**Ethics Approval** This study was approved by New York University institution's Ethics Board; approval number i17-00764.

### REFERENCES


1. Stupp R, *et al*. (2009). Lancet Oncology, **10**(5):459–466.


### P859 ASSOCIATION OF IMMUNOPHARMACODYNAMIC RESPONSES OF IMPRIME PGG PLUS PEMBROLIZUMAB WITH CLINICAL BENEFIT IN METASTATIC TRIPLE NEGATIVE BREAST CANCER (TNBC) SUBJECTS FAILING FRONT-LINE CHEMOTHERAPY


[1]Nadine Ottoson, [1]Nandita Bose*, [1]Anissa Chan, [1]Xiaohong Qiu, [1]Ben Harrison, [1]Richard Walsh, [1]Paulette Mattson, [1]Michele Gargano, [1]Joanna Cox, [2]Michael Chisamore, [1]Mark Uhlik, [1]Jeremy Graff. *[1]Biothera Pharmaceuticals, Eagan, MN, USA; [2]Merck and Co., Inc., Rahway, NJ, USA*


10.1136/LBA2019.13