NANT Cancer Vaccine (NCV): An Orchestration of Immunogenic Cell Death by Overcoming Immune Suppression and Activating Natural Killer (NK) and T Cell Therapy in Patients with Greater Than 3rd-Line Triple-Negative Breast Cancer (TNBC) or Head and Neck Squamous Cell Carcinoma (HNSCC)

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Background

TNBC and HNSCC
- Advanced TNBC and HNSCC are aggressive cancers with limited treatment options.¹ ² ³
- TNBC and HNSCC share cytological and molecular features, including originating in epithelial or epithelial-like cells, resistance to treatment with nab-paclitaxel, and VEGF expression as a poor prognostic factor.⁴ ⁵ ⁶

NANT Cancer Vaccine (NCV)
- The NCV includes metronomic low-dose nab-paclitaxel (Abraxane) and low dose radiation therapy with cryopreserved off-the-shelf CD16 targeted natural killer cells (haNK) and cytokine NK & T cell superagonist IL-15RaoSu/Fc (N-803) combined with E2b-deleted adenovirus (Ad) & yeast (Ye) tumor associated antigen vaccines, and checkpoint inhibitors.
- All treatment was administered in the outpatient setting without G-CSF support.
- The NCV is anticipated to reduce immunosuppression in the tumor microenvironment, while increasing immune-mediated cell death, cytotoxic dendritic and T cell activity, and innate immune responses.⁷ ⁸ ⁹
- Ongoing phase 1b/2 studies for TNBC (QUILT-3.067; NCT03387085) and HNSCC (QUILT-3.090; NCT03387111) seek to evaluate the safety of the NCV and establish preliminary estimates of efficacy.
- As of October 2018, 98 doses of haNK and NCV Vaccine has been administered in 11 patients (7 TNBC, 4 HNSCC, See Table 1)

Methods

Study Design
- Non-randomized, open-label, Phase 1b/2 trials.
- Combination low dose metronomic chemotherapy, immunotherapy and CD16 haNK administered over a 3-week induction cycle for up to 1 year.

Enrollment Criteria
- Histologically confirmed or unresectable TNBC that has progressed on or after anthracycline-based chemotherapy; or HNSCC with progression on or after platinum-based chemotherapy and anti-PD-1/PD-L1 therapy.
- ≥ 18 years old with ECOG performance status of 0–2.

Endpoints
- Primary endpoints: Incidence of treatment-emergent adverse events (AEs) and serious AEs (SAEs).
- Secondary endpoints: overall response rate (ORR), progression-free survival (PFS), overall survival (OS), duration of response (DOR), disease control rate (DCR), and quality of life by patient-reported outcomes (PROs).

Results

Safety
- Four patients with HNSCC received 44 doses of CD16 haNK with NCV.
- Seven patients with TNBC received 54 doses of CD16 haNK with NCV.
- No patient experienced cytokine release syndrome or immune related adverse events from CD16 haNKS or the immune components of NCV.
- Three HNSCC patients experienced chemotherapy related DLTs.
- No TNBC patients experienced chemotherapy related DLTs.

Table 2: Chemotherapy Related AE Incidence by Patient

<table>
<thead>
<tr>
<th>Nebu</th>
<th>HNCCC</th>
<th>Nebu</th>
<th>HNCCC</th>
<th>Nebu</th>
<th>HNCCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>Grade ≥ 3</td>
<td>SAEs</td>
<td>Any AE</td>
<td>Grade ≥ 3</td>
<td>SAEs</td>
</tr>
<tr>
<td>6 (100%)</td>
<td>5 (83%)</td>
<td>2 (33%)</td>
<td>4 (100%)</td>
<td>4 (100%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Grade ≥ 3</td>
<td>SAEs</td>
<td>Neutropenia</td>
<td>Grade ≥ 3</td>
<td>SAEs</td>
</tr>
<tr>
<td>1 (17%)</td>
<td>1 (17%)</td>
<td>0</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>Grade ≥ 3</td>
<td>SAEs</td>
<td>Pyrexia</td>
<td>Grade ≥ 3</td>
<td>SAEs</td>
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<tr>
<td>4 (67%)</td>
<td>2 (33%)</td>
<td>0</td>
<td>4 (100%)</td>
<td>1 (25%)</td>
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Efficacy
- **Head & Neck**: DCR is 67% for 2 of 3 evaluable patients who experienced SD for ≥ 8 weeks. 1 patient with 5th line HNSCC experienced a pathologically confirmed complete response. This patient showed resolution of an ulcerated right parotid mass (~100% change in tumor size from baseline; Figure 1).
- Progression was recorded on a subsequent assessment, resulting in a confirmed iPR.
- **TNBC**: DCR is 80% in 4 of 5 patients with SD in 2 patients and iPR in 2 patients, with treatment still ongoing.
- For all patients, Figure 2 shows the timeline of NCV treatment for all enrolled patients (11 total). Figure 3 shows the best target lesion response for patients with ≥ 1 evaluable imaging assessment (8 patients).

Figure 1: Resolution of an HNSCC Parotid Tumor

Figure 2: Timeline of Treatment with NCV Therapy

Figure 3: Best Target Lesion Response

As of October 2018, 7 of 11 enrolled patients continue to be treated with NCV therapy. ³Magnitude of PD unavailable. ⁴Continue to receive NCV therapy on study.

Conclusions
- The Nant Cancer Vaccine (NCV) treatment regimen was tolerated in all patients who received haNK without evidence of cytokine release syndrome or immune related adverse events after a total 98 infusions.
- These findings suggest that haNK cell therapy given in combination with low-dose chemotherapy, localized radiation, and immune modulators may be safely used in treatment of patients with advanced TNBC and HNSCC.
- In heavily pretreated patients with advanced cancer, the NCV treatment regimen has yielded preliminary positive clinical results with 80% disease control in patients with TNBC with advanced disease ranging from 4th to 6th line therapy.
- Furthermore, in patients with advanced Head & Neck cancer ranging from 4th to 6th line therapy demonstrated 67% disease control, with a pathologically confirmed complete response in one patient.

References and Acknowledgements

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