NANT Triple Negative Breast Cancer (TNBC) Vaccine: Molecularly-Infomed Integrated Immunotherapy
Combining Innate High-Affinity Natural Killer (haNK) Cell Therapy with Adenoviral & Yeast-based Vaccines and Immune Checkpoint Inhibitor to Induce T-Cell Responses in Patients with TNBC Who Have Progressed on or after Standard-of-Care Therapy

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BACKGROUND
TNBC is an aggressive subtype of breast cancer with limited treatment options for which immunotherapy has demonstrated clinical benefit in selected patients [1]. We hypothesized rationally-based, thoughtfully-sequenced orchestration of both innate and adaptive immune system responses would elicit anti-tumor efficacy. We further hypothesize that by activating the entire immune system, the immunogenic cell death in this disease will be durable and associated with a low risk of adverse events. Here we describe a first-in-human novel combination immunotherapy protocol of chemoradiation, checkpoint inhibition, cytokine-induced NK & T cell activation [2], & off-the-shelf high-affinity NK (haNK) cell infusion.

RESULTS

Figure 2: Demographics, Adverse events (AEs) & toxicity. Nine TNBC pts have been treated to date in an outpatient setting. Eight of these had previously chemotherapy-related neutropenia and/or anemia. Grade ≥3 haNK-related AEs (fever and fatigue) were observed in 3 pts. No patient withdrew due to SAEs. No pts experienced cytokine release syndrome.

Figure 3: Response to treatment & progression-free survival (PFS). (A) The maximum target lesion response percent based on RECIST1.1 criteria is shown for each patient. To date, the (early) disease control rate (DCR) combining Complete Response, Partial Response, and Stable Disease (CR+PR+SD) is 78% (7/9 pts) and the Overall Response Rate (ORR = PR+CR) is 67% (6/9 pts) using irC. Two pts (22%, 3/9) achieved a CR. (B) Median PFS is 13.7 months; seven (7) pts are alive, and the duration of responses ranges from 2 to 12 months over 4 patients. Each patient was studied on study date.

Figure 4: PBMC T cell receptor (TCR) diversity in response to treatment. Patients with significant tumor regressions showed >30 fold change in the Shannon Wiener Diversity Index (SWDI) in comparison to the baseline. Patients 001, 008 and 009 were ‘super-responders’ with the lowest SWDI at baseline and dramatic surges in SWDI post induction suggesting activation and/or expansion of anti-tumor T cell clones.

KEY FINDINGS
- The Overall Response Rate (ORR) to orchestrated treatment in QUILT 3.067 is 67%
- Disease Control Rate (DCR) of 78%
- Complete Response (CR) rate of 22%
- No cytokine release syndrome
- No patients withdrew due to SAEs
- Protocol was successfully administered exclusively in an outpatient setting
- T cell receptor diversity shows potential as a predictive biomarker for response to the therapeutic approach used here.

CONCLUSIONS
The early efficacy of the novel, combinatorial, sequenced & orchestrated treatment approach presented here warrants further study in expanded clinical trials. In addition, the utility of TCR profile as a biomarker for response should be further explored & validated.

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REFERENCES

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