Phase 2 QUILT 88 trial of DAMP inducers combined with IL15 superagonist, N-803 and anti PDL1-t-haNK cell therapy more than doubles historical overall survival with 3rd to 6th line advanced Pancreatic Cancer

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BACKGROUND

Pancreatic cancer will claim an estimated 47,050 lives in the USA in 2020. In patients with advanced disease (>3rd line) the median overall survival is 3 months. We hypothesize that effective response against pancreatic cancer requires a coordinated approach that orchestrates both the innate and adaptive immune system. We further hypothesize that by orchestrating the activation of the entire immune system, we could accomplish immunogenic cell death with durable responses in this previously immunotherapy unresponsive disease. We describe a novel combination immunotherapy protocol of low-dose chemo-radiation to enhance antigen cascade and reduce MDSC's, cytokine-induced NK and T cell activation and proliferation via N-803 (Anktiva, IL-15 cytokine fusion protein), and off-the-shelf PDL1-targeted high-affinity NK cell (PD-L1 t-haNK) infusion.

STUDY EXPERIMENTAL TREATMENT

Days 1 and 15, every 4 weeks:
- Nab-paclitaxel
- Gemcitabine

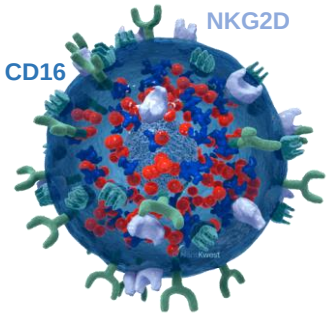
Days 1–5 and 15–19, every 4 weeks:
- Cyclophosphamide

Days 1, 8, 15, and 22; for first cycle only:
- SBRT (not to exceed 8 Gy, exact dose to be determined by the radiation oncologist)

Day 8, every 4 weeks:
- Aldoxorubicin HCl
- N-803 (15 µg/kg SC)

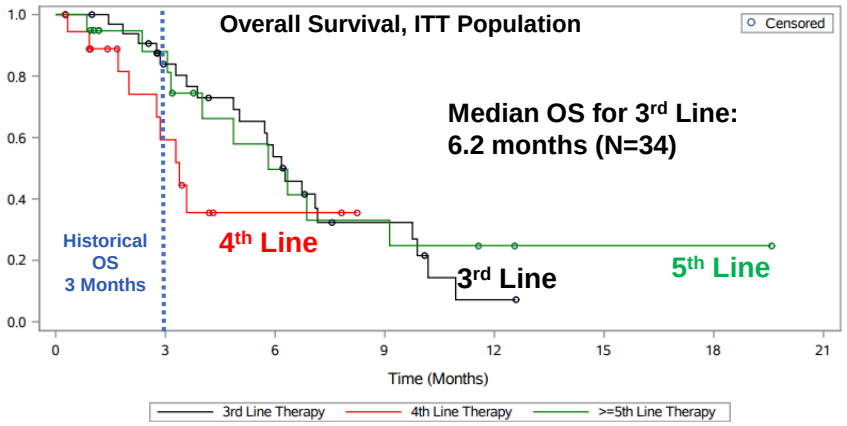
Days 1, 8, and 15; every 4 weeks:
- PD-L1 t-haNK (~2 × 109 cells/dose IV)

PD-L1 t-haNK



PD-L1 t-haNK
NKG2D
PD-L1/CD16/erIL2

RESULTS



Median OS for ITT (≥ 3rd, 4th and 5th line): 5.8 months (N=78)

TABLE 1

Demographics	N / (%)
Age	62 (24, 78)
Age≥65	42%
M:F	58/42
ECOG 0-1	96%
Metastasis	93%

TABLE 2

Any grade TR-AE >10%	%
Chills	47
Pyrexia	46
injection site rxn	40
fatigue	36
anemia	50
neutropenia	19
thrombocytopenia	13
vomiting	28
nausea	26
stomatitis	13
decreased appetite	14
infusion rxn	13

TABLES 1,2,3: **Demographics, Treatment related Adverse Events (AEs), TR G3+AEs:** Median 3 cycles (1,18),

TABLE 3

Grade ≥3 TR AE ≥5%	%
anemia	41
neutropenia	29
thrombocytopenia	17
fatigue	5

KEY FINDINGS

- Nant Cancer Vaccine (NCV) **more than doubled median OS** versus historical OS (Manax ASCO GI 2019) of 3 months after >2L
- In QUILT 88 median OS in **3rd line** subjects (n=34) was **6.2 months** (95% CI: 4.9, 9.8)
- Overall survival for ITT population (N=78) of **3rd, 4th and 5th line is 5.8 months** (95% CI: 4.0, 6.9)
- Treatment related (TR) SAE's were uncommon (6%), no TR deaths were reported
- All treatments were performed as outpatient
- Treatment ongoing for 25 patients

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REFERENCES

1. Fabian KP, Padget MR, Donahue RN, Solocinski K, Robbins Y, Allen CT, Lee JH, Rabizadeh S, Soon-Shiong P, Schlom J, Hodge JW. PD-L1 targeting high-affinity NK (t-haNK) cells induce direct antitumor effects and target suppressive MDSC populations. J Immunother Cancer. 2020 May;8(1):e000450. doi: 10.1136/jitc-2019-000450. PMID: 32439799; PMCID: PMC7247398.
2. Lee MY, Robbins Y, Sievers C, *et al.* Chimeric antigen receptor engineered NK cellular immunotherapy overcomes the selection of T-cell escape variant cancer cells. *Journal for ImmunoTherapy of Cancer* 2021;**9**:e002128. doi: 10.1136/jitc-2020-002128
3. Wolfson B, Franks SE, Hodge JW. Stay on Target: Reengaging Cancer Vaccines in Combination Immunotherapy. Vaccines (Basel). 2021 May 15;9(5):509. doi: 10.3390/vaccines9050509. PMID: 34063388; PMCID: PMC8156017.
4. Chu Y, Nayyar G, Jiang S, Rosenblum JM, Soon-Shiong P, Safrit JT, Lee DA, Cairo MS. Combinatorial immunotherapy of N-803 (IL-15 superagonist) and dinutuximab with ex vivo expanded natural killer cells significantly enhances in vitro cytotoxicity against GD2+ pediatric solid tumors and in vivo survival of xenografted immunodeficient NSG mice. J Immunother Cancer. 2021 Jul;9(7):e002267. doi: 10.1136/jitc-2020-002267. PMID: 34244307; PMCID: PMC8268924.

SCAN ME

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