First in Human Data in Advanced Solid Tumors of NANT Cancer Vaccine: A Novel Temporospatial Orchestration of the Innate (NK) & Adaptive Immune System to Induce Antigen Cascade & Immunogenic Cell Death

Dr. Patrick Soon-Shiong

Society for Immunotherapy of Cancer (SITC)
November 7, 2018
Session Time: 2:00pm to 8:00pm
”Immune Escape: Current Understanding of Mechanisms and Advances in Therapeutics Approaches”

Disclosure & Forward Looking Statement

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DISCLOSURE:

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FORWARD-LOOKING STATEMENTS

These slides and the accompanying oral presentation contain forward-looking statements within the meaning of the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, that are based on management's beliefs and assumptions and on information currently available to our management. Forward-looking statements include, but are not limited to:

- our ability to pioneer immunotherapy, harness the power of the innate immune system, implement precision cancer medicine and change the current paradigm of cancer care;
- our expectations regarding the potential benefits of our strategy and technology;
- our ability to utilize multiple modes to induce cell death;
- our beliefs regarding the benefits and perceived limitations of competing approaches, and the future of competing technologies and our industry;
- our beliefs regarding the success, cost and timing of our product candidate development activities and clinical trials;
- the timing or likelihood of regulatory filings or other actions and related regulatory authority responses, including any planned investigational new drug (IND) filings or pursuit of accelerated regulatory approval pathways or orphan drug status and breakthrough therapy designations;
- our ability to implement an integrated discovery ecosystem and the operation of that planned ecosystem;
- our expectations regarding our ability to utilize the Phase I aNK clinical trial data to support the development our other product candidates;
- our ability to produce an "off-the-shelf" therapy;
- our beliefs regarding the potential manufacturing and distribution benefits associated with our product candidates, and our ability to scale up the production of our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidate and not infringe upon the intellectual property of others;
- the ability and willingness of strategic collaborators, including certain of our affiliates, to share our vision and effectively work with us to achieve our goals;
- the ability and willingness of various third parties to engage in research and development activities involving our product candidates, and our ability to leverage those activities; and
- regulatory developments in the United States and foreign countries.

Factors that could cause our results to differ materially from those expressed in forward-looking statements include, without limitation:

- the fact that our business is based upon the success of our aNK cells as a technology platform;
- our aNK platform and other product candidate families, including genetically modified taNK, haNK and t-haNK product candidates, will require significant additional clinical testing;
- even if we successfully develop and commercialize our aNK product candidate, we may not be successful in developing and commercializing our other product candidates either alone or in combination with other therapeutic agents;
- we may not be able to file INDs, to commence additional clinical trials on timelines we expect;
- we will need to obtain substantial additional financing to complete the development and any commercialization of our product candidates; and
- risks associated with our ability to enforce intellectual property rights.

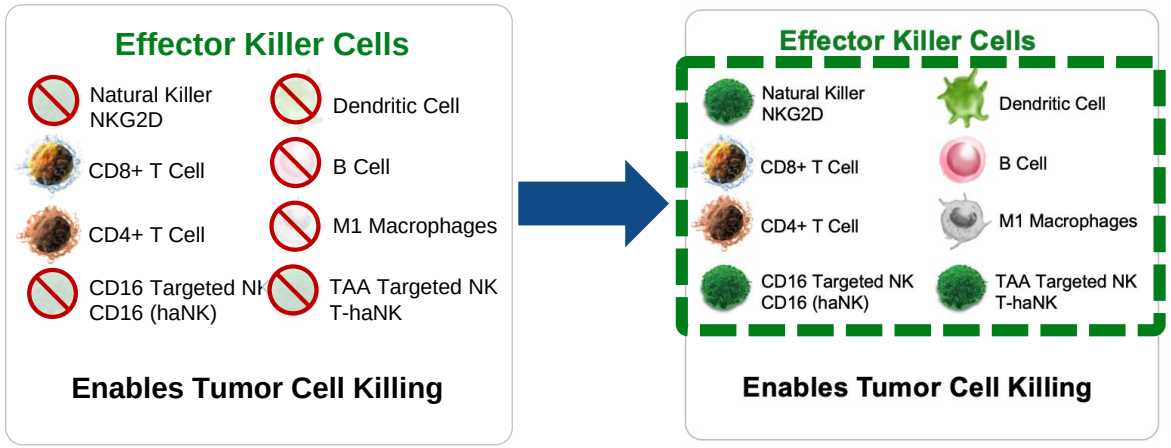
Forward-looking statements include statements that are not historical facts and can be identified by terms such as "anticipates," "believes," "could," "seeks," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should," "will," "would," or similar expressions and the negatives of those terms.

Forward-looking statements involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. We discuss these risks in certain filings we have made with the Securities and Exchange Commission for NantKwest, Inc. and NantHealth, Inc. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this presentation.

Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. No representation or warranty, express or implied, is given as to the completeness or accuracy of the information or opinions contained in this document and we do not accept any liability for any direct, indirect or consequential loss or damage arising from reliance on such information or opinions. Past performance should not be taken as an indication or guarantee of future performance. You should read this presentation completely and with the understanding that our actual future results may be materially different from what we expect.

Vision 2020+: Chemo Free Cancer Immunotherapy Beyond Checkpoint Inhibitors

- Pharma focus on Checkpoints and CAR T cells > 50 anti-PD-1/anti-PD-L1 agents are under development and another 80 are being developed in China. Only about 30% of patients treated with checkpoint blockers alone demonstrate objective responses.

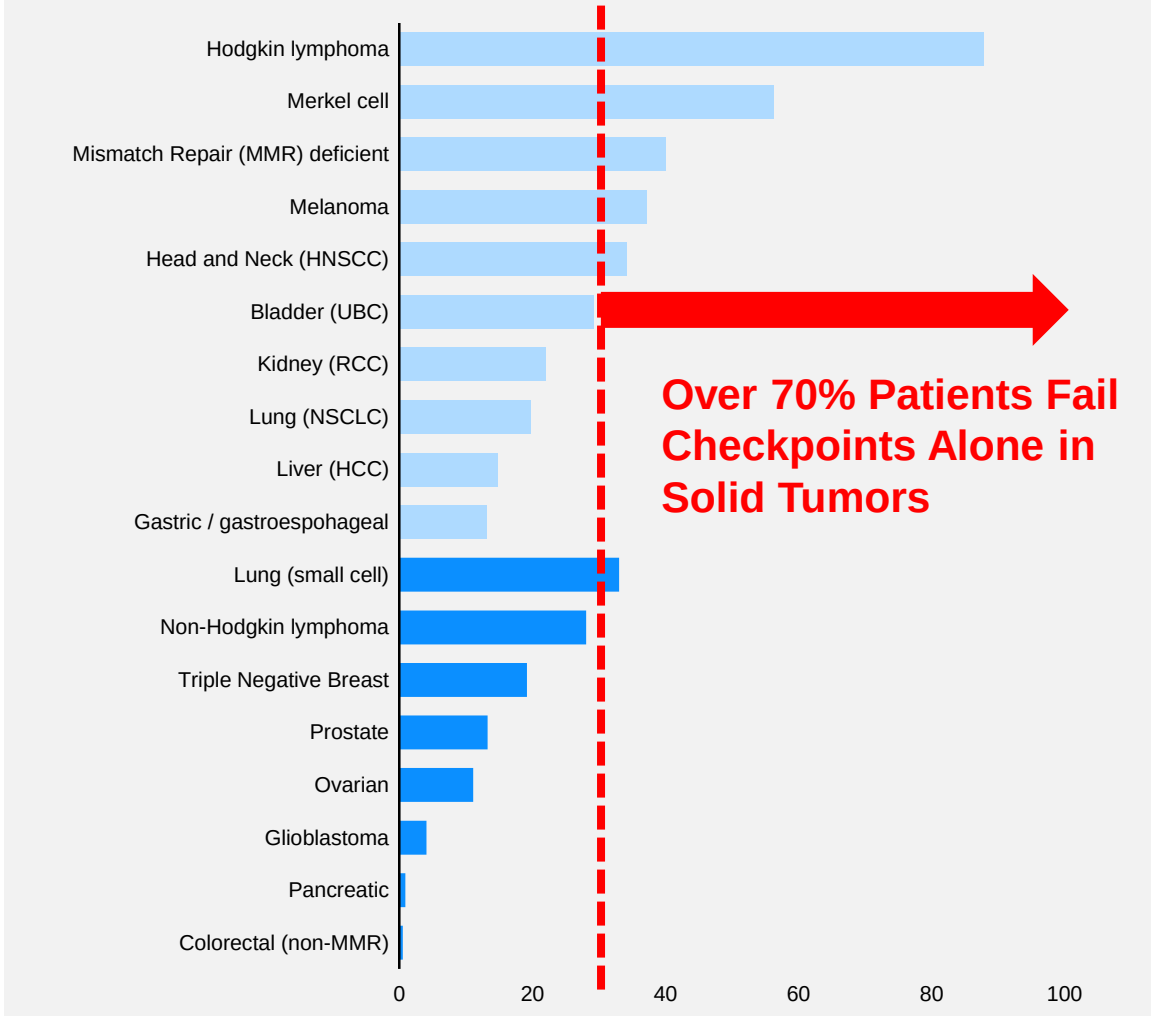


Current State with Checkpoints & CAR-T Therapies

Immunotherapy 2.0 Cancer Memory Vaccine

- **The Goal:** Orchestrate the entire immune system in a temporospatial protocol combining:
  - Metronomic low-dose nab-paclitaxel with low dose chemo-immunomodulators
  - Fusion proteins to induce endogenous stimulation of natural killer and T cells,
  - Supplemented with off-the-shelf targeted NK cell infusions and
  - Inducing T-cell memory via adenovirus and yeast vectors bearing tumor associated antigens and neoepitopes
  - Checkpoint Inhibitors - PD-1 or PD-L1
  - **The Cancer Memory Vaccine – CMV**
- **Vision 2020+:** Chemo-free biologically driven immunotherapy, inducing memory T-cells for the early treatment and prevention of cancer.

Anti-tumor efficacy of anti-PD-1 / PD-L1 inhibitors
Objective Response Rates (ORR)

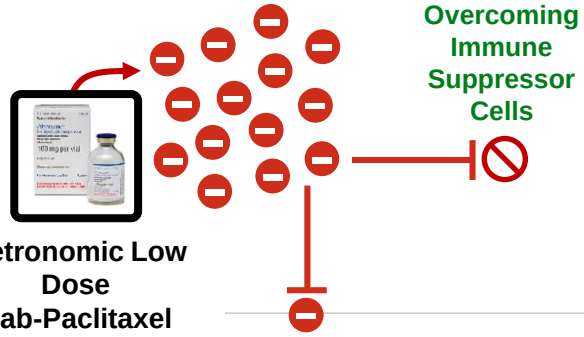


Source: Bloomberg.

Vision 2020+: Chemo Free Cancer Immunotherapy Beyond Checkpoint Inhibitors
Towards Immune Activated Cell Death & Immune Memory
Temporal Spatial Orchestration Towards Immunogenic Cell Death & Immune Memory

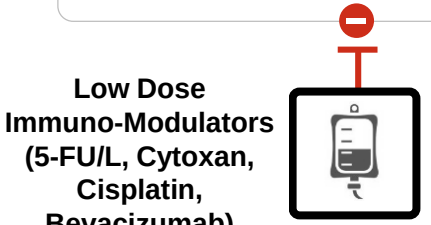
1 Hide Me Signals | **2 Find Me Signals** | **3 Kill Me Signals**

Step 1: Block Hide Me Signals

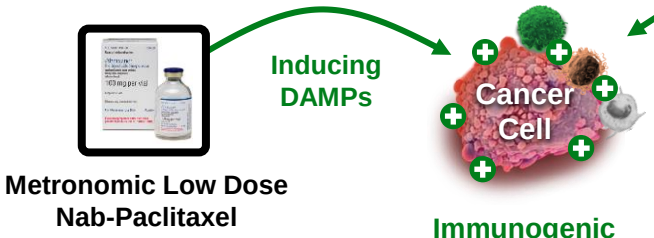


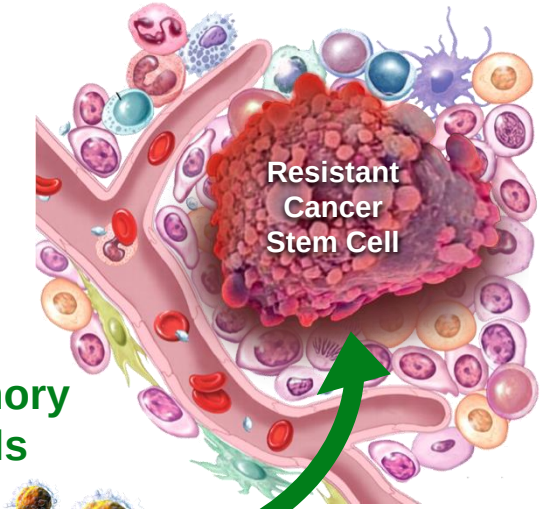
Immune Suppressor Cells

Enables Tumor Cell Growth



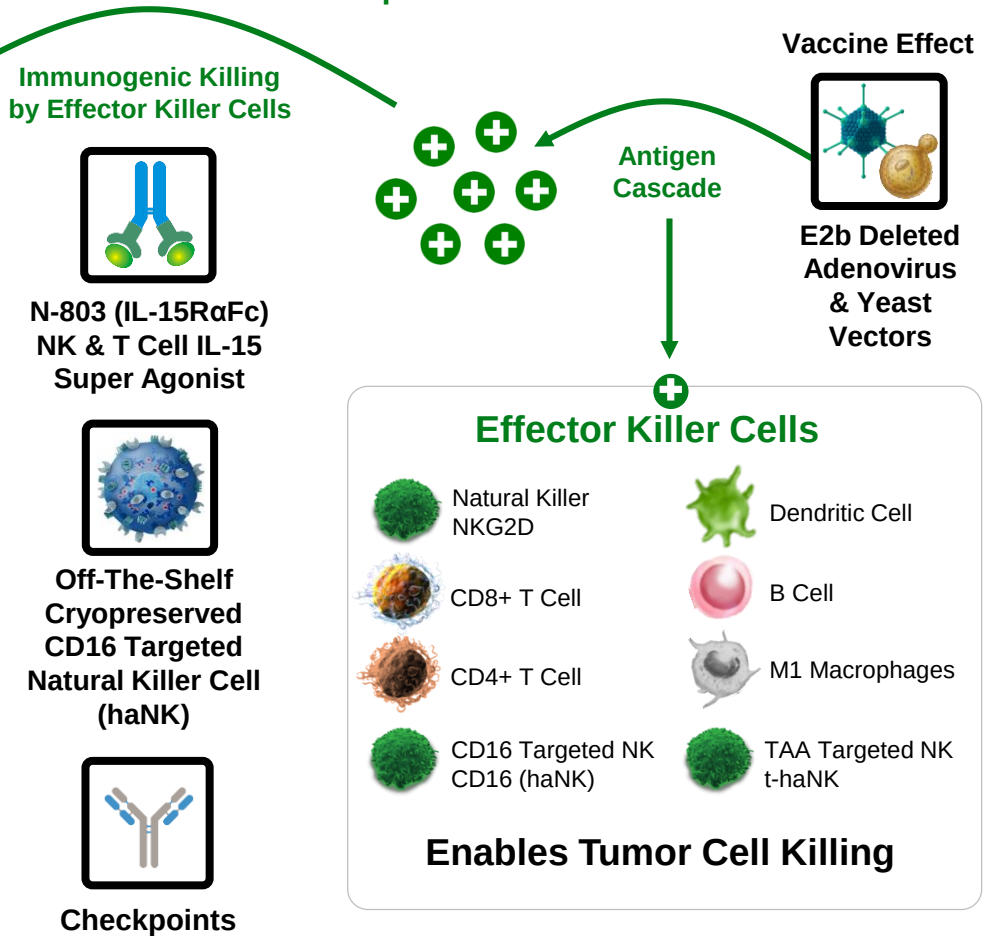
Step 2: Expose Find Me Signals





Immune Memory T & NK Cells

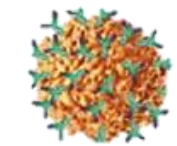
Step 3: Activate Effector Killer Cells



Cancer Memory Vaccine (CMV)

Orchestrated Over 21 Day Cycle

Day 1 – 4, 15

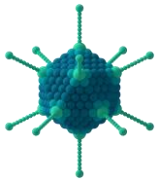


Nab Paclitaxel

Low Dose Metronomic
Nab Paclitaxel
+
Low Dose
Immuno-Modulators
(5-FU/L, Cystoxan,
Cisplatin, Bevacizumab)

+

Day 5



Adenovirus

Ad-CEA

Ad-MUC1

Ad-Brachyury

Ad-HER2

Day 5

Yeast

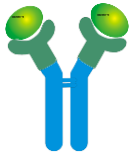
Ye-CEA

Ye-RAS

Ye-Brachyury

+

Day 9



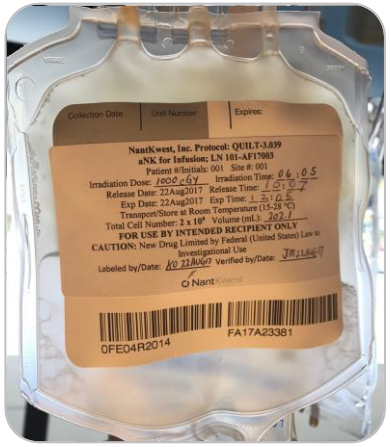
N-803

IL-15RαFc

Fusion Protein

+

Day 9, 11, 16



Natural Killer

NK CD16 Targeted haNK

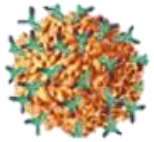
+

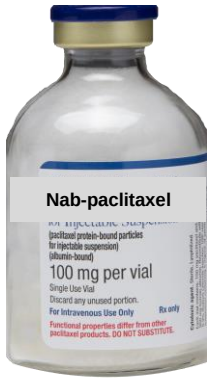
Day 9

Checkpoint

IgG1 PD-L1

History: Metronomic Nab-Paclitaxel (2005)





Nab Paclitaxel

Low Dose Metronomic
Nab Paclitaxel

(12) **United States Patent**
Desai et al.

(10) **Patent No.: US 8,735,394 B2**
(45) **Date of Patent: May 27, 2014**

(54) **COMBINATIONS AND MODES OF ADMINISTRATION OF THERAPEUTIC AGENTS AND COMBINATION THERAPY**

(75) Inventors: **Neil P. Desai**, Los Angeles, CA (US); **Patrick Soon-Shiong**, Los Angeles, CA (US)

(73) Assignee: **Abraxis BioScience, LLC**, Los Angeles, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 534 days.

(21) Appl. No.: **12/436,697**

(22) Filed: **May 6, 2009**

(65) **Prior Publication Data**

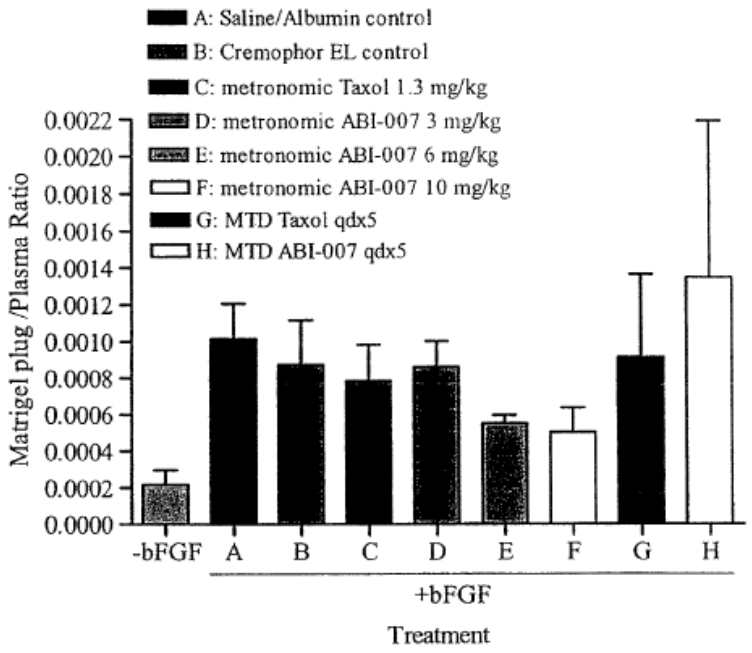
US 2009/0304805 A1 Dec. 10, 2009

Related U.S. Application Data

(63) Continuation of application No. PCT/US2007/023446, filed on Nov. 6, 2007, which is a continuation-in-part of application No. 11/594,417, filed on Nov. 6, 2006, now abandoned, which is a continuation-in-part of application No. 11/359,286, filed on Feb. 21, 2006, and a continuation-in-part of application No. 11/359,286, filed on Feb. 21, 2006.

(60) Provisional application No. 60/654,245, filed on Feb. 18, 2005.

FIG. 6



EP	0 577 215 A1	1/1994
EP	0 577 215 B1	1/1994

(Continued)

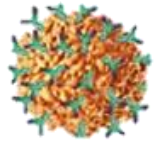
OTHER PUBLICATIONS

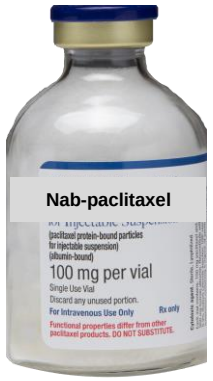
Adis Data Information BV. (Aug. 28, 2004). "Paclitaxel [Taxol] and Liposomal Doxorubicin [Caelyx] Cotherapy Appears to be an Effec-

2005

Metronomic

History: Metronomic Nab-Paclitaxel (2006)





Nab Paclitaxel

Low Dose Metronomic
Nab Paclitaxel

Influence of Formulation Vehicle on Metronomic Taxane Chemotherapy: Albumin-Bound versus Cremophor EL–Based Paclitaxel

Sylvia S.W. Ng,[1] Alex Sparreboom,[2] Yuval Shaked,[1] Christina Lee,[1] Shan Man,[1] Neil Desai,[3] Patrick Soon-Shiong,[3] William D. Figg,[2] and Robert S. Kerbel[1]

Abstract

Purpose: Low-dose metronomic chemotherapy treatments, especially when combined with 'dedicated' antiangiogenic agents, can induce significant antitumor activity without serious toxicity in various preclinical models. It remains unclear, however, whether some cytotoxic drugs are better suited for metronomic regimens than others. Paclitaxel appears to be a strong candidate for metronomic chemotherapy given its ability to inhibit endothelial cell functions relevant to angiogenesis in vitro at extraordinarily low concentrations and broad-spectrum antitumor activity. Clinically relevant concentrations of the formulation vehicle cremophor EL in Taxol, however, were previously reported to nullify the antiangiogenic effect of paclitaxel, the result of which would hamper its usefulness in metronomic regimens. We hypothesized that ABI-007, a cremophor EL–free, albumin-bound, 130-nm form of paclitaxel, could potentially alleviate this problem.

Experimental Design: The antiangiogenic activity of ABI-007 was assessed by multiple in vitro assays. The in vivo optimal dose of ABI-007 for metronomic chemotherapy was determined by measuring circulating endothelial progenitors in peripheral blood. The antitumor effects of metronomic and maximum tolerated dose ABI-007 and Taxol were then evaluated and compared in severe combined immunodeficient mice bearing human MDA-MD-231 breast cancer and PC3 prostate cancer xenografts.

Results: ABI-007 significantly inhibited rat aortic microvessel outgrowth, human endothelial cell proliferation, and tube formation. The optimal metronomic dose of ABI-007 was determined to be between 3 and 10 mg/kg. Metronomic ABI-007 but not Taxol, significantly suppressed tumor growth in both xenograft models. Furthermore, the antitumor effect of minimally toxic metronomic ABI-007 approximated that of the maximum tolerated dose of Taxol.

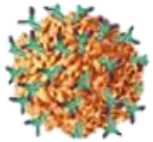
Conclusions: Our results underscore the influence of formulation vehicles on the selection of cytotoxic drugs for metronomic chemotherapy.

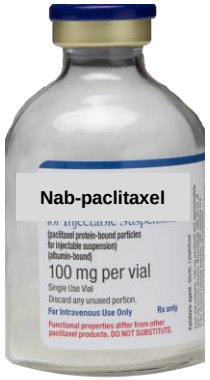
An alternative dosing regimen to pulsatile maximum tolerated dose (MTD) or "dose dense" and dose-intensive chemotherapy is "metronomic chemotherapy": the frequent administration of such drugs at close regular intervals with no prolonged breaks over long periods of time (1). The reduced toxicity and comparable or even increased efficacy of metronomic regimens compared with some MTD counterparts have been shown in a number of preclinical models (2, 3). In addition, metronomic chemotherapy regimens are particularly well suited for long-term combination with relatively non–toxic-targeted biological

2006

Metronomic

Current: Metronomic Low Dose Nab-Paclitaxel + Checkpoint (2018)





Nab Paclitaxel

Low Dose Metronomic
Nab Paclitaxel

Sept 2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer

L. Paz-Ares, A. Luft, D. Vicente, A. Tafreshi, M. Gümüş, J. Mazières, B. Hermes, F. Çay Şenler, T. Csőszi, A. Fülöp, J. Rodríguez-Cid, J. Wilson, S. Sugawara, T. Kato, K.H. Lee, Y. Cheng, S. Novello, B. Halmos, X. Li, G.M. Lubiniecki, B. Piperdi, and D.M. Kowalski, for the KEYNOTE-407 Investigators*

ABSTRACT

BACKGROUND

Standard first-line therapy for metastatic, squamous non–small-cell lung cancer (NSCLC) is platinum-based chemotherapy or pembrolizumab (for patients with programmed death ligand 1 [PD-L1] expression on ≥50% of tumor cells). More recently, pembrolizumab plus chemotherapy was shown to significantly prolong overall survival among patients with nonsquamous NSCLC.

METHODS

In this double-blind, phase 3 trial, we randomly assigned, in a 1:1 ratio, 559 patients with untreated metastatic, squamous NSCLC to receive 200 mg of pembrolizumab or saline placebo for up to 35 cycles; all the patients also received carboplatin and either paclitaxel or nanoparticle albumin-bound [nab]–paclitaxel for the first 4 cycles. Primary end points were overall survival and progression-free survival.

October 2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer

P. Schmid, S. Adams, H.S. Rugo, A. Schneeweiss, C.H. Barrios, H. Iwata, V. Diéras, R. Hegg, S.-A. Im, G. Shaw Wright, V. Henschel, L. Molinero, S.Y. Chui, R. Funke, A. Husain, E.P. Winer, S. Loi, and L.A. Emens, for the IMpassion130 Trial Investigators*

ABSTRACT

BACKGROUND

Unresectable locally advanced or metastatic triple-negative (hormone-receptor–negative and human epidermal growth factor receptor 2 [HER2]–negative) breast cancer is an aggressive disease with poor outcomes. Nanoparticle albumin-bound (nab)–paclitaxel may enhance the anticancer activity of atezolizumab.

METHODS

In this phase 3 trial, we randomly assigned (in a 1:1 ratio) patients with untreated metastatic triple-negative breast cancer to receive atezolizumab plus nab-paclitaxel or placebo plus nab-paclitaxel; patients continued the intervention until disease progression or an unacceptable level of toxic effects occurred. Stratification factors were the receipt or nonreceipt of neoadjuvant or adjuvant taxane therapy, the presence or absence of liver metastases at baseline, and programmed death ligand 1 (PD-L1) expression at baseline (positive vs. negative). The two primary end points were progression-free survival (in the intention-to-treat population and PD-L1–positive subgroup) and overall survival (tested in the intention-to-treat population; if the finding was significant, then it would be tested in the PD-L1–positive subgroup).

RESULTS

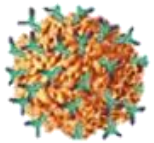
Checkpoint

PD-1 & PD-L1

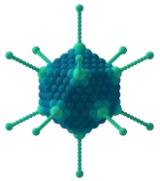
Cancer Memory Vaccine (CMV) - 2017

Orchestrated Over 21 Day Cycle

Day 1 – 4, 15

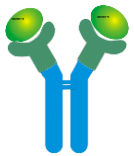


Day 5

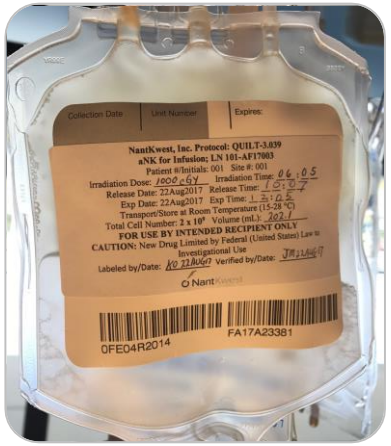


Day 5

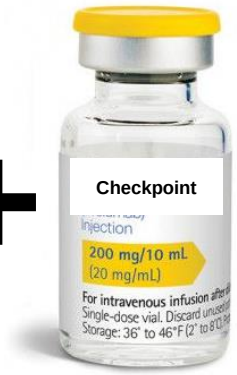
Day 9



Day 9, 11, 16



Day 9



Nab Paclitaxel

Low Dose Metronomic Nab Paclitaxel
+
Low Dose Immuno-Modulators (5-FU/L, Cytoxan, Cisplatin, Bevacizumab)

Adenovirus

Ad-CEA

Ad-MUC1

Ad-Brachyury

Ad-HER2

Yeast

Ye-CEA

Ye-RAS

Ye-Brachyury

N-803

IL-15RαFc

Fusion Protein

Natural Killer

NK CD16 Targeted haNK

Checkpoint

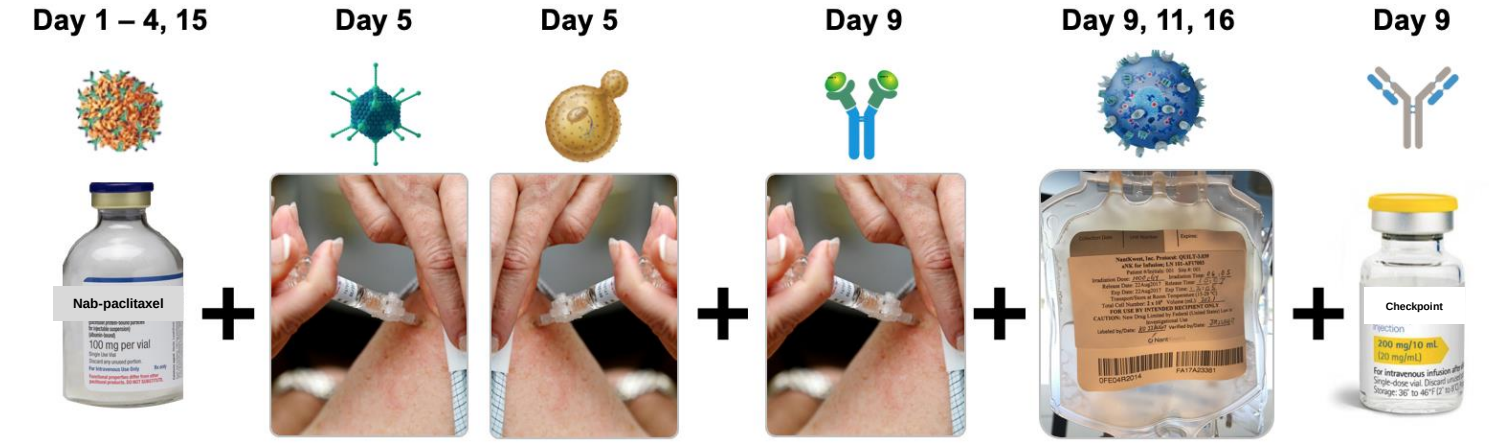
IgG1 PD-L1

Cancer Memory Vaccine (CMV)

Orchestrated Over 21 Day Cycle

August 2017 – October 2018

First in Human Clinical Results of 300 Doses of CD16 Targeted, Off-the-shelf Cryopreserved Natural Killer Cells (haNK) in a Novel Cancer Memory Vaccine Immunotherapy Combination In 30 Patients with Advanced Metastatic Cancer Refractory To Multiple Previous Therapies



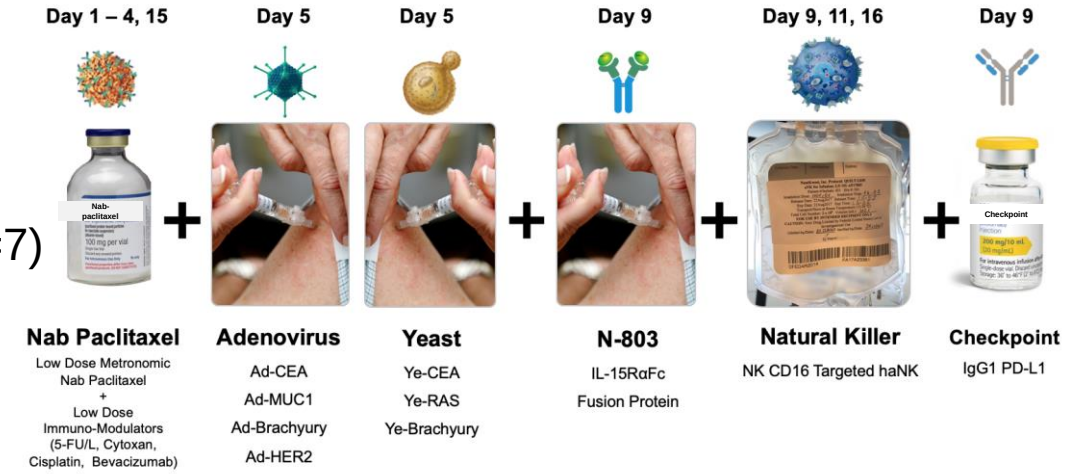
Clinical Results of Patients Receiving haNK, Fusion Proteins, and/or Cancer Memory Vaccine (N=30)

Advanced Highly Refractory Metastatic Patient Population Receiving haNK Alone (N=6)

- 3rd Line or Greater – Advanced Solid Tumors in haNK (N=6)

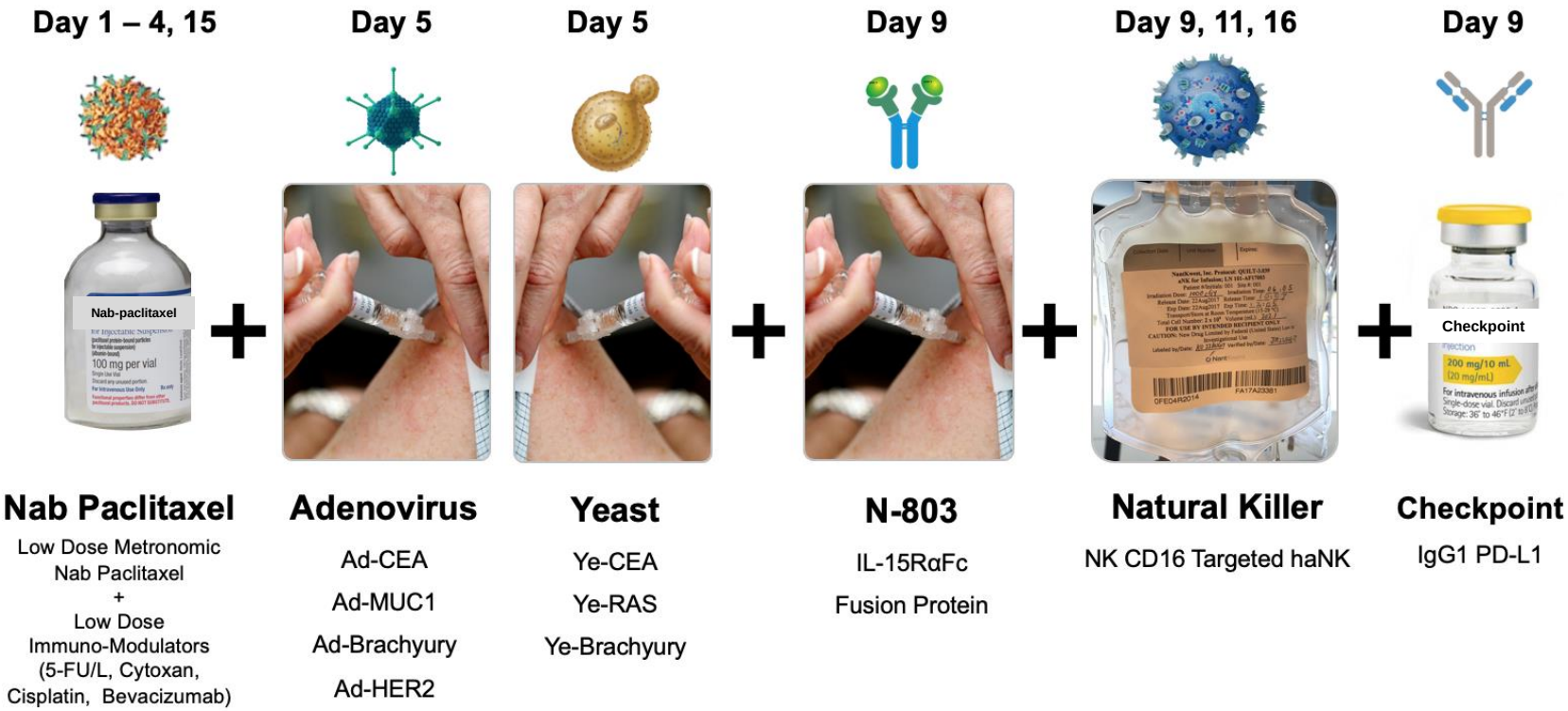
Advanced Highly Refractory Metastatic Patient Population Receiving Cancer Memory Vaccine Combination (N=24)

- 3rd Line or Greater – Metastatic Pancreatic Cancer (N=12)
- 4th Line or Greater – Metastatic Triple Negative Breast Cancer (N=7)
- 4th Line or Greater – Metastatic Head & Neck (N=4)
- 3rd Line or Greater – Metastatic Colon Cancer (N=1)



Safety Data of 300 Doses of haNK
Including 276 Doses of haNK in Cancer Memory Vaccine Combination

August 2017 – October 31, 2018



- Zero incidence of cytokine release syndrome
- No immune related adverse events

- 24 doses of haNK administered as a single agent
- 276 doses of haNK administered in combination with Cancer Memory Vaccine
- 300 doses of haNK administered in an outpatient setting in highly refractory advanced cancer patients

Safety Data of Cancer Memory Vaccine (CMV) Combination In Highly Refractory Metastatic Pancreatic Cancer

- Patients received 15.2 ± 7.0 (mean ± SD) doses of haNK per patient, with a total of 152 doses administered with no evidence of cytokine release syndrome (CRS).

- In the CMV treatment regimen, haNK cell therapy was administered concurrently with the PD-L1 IgG1 antibody avelumab. No immune-related treatment-emergent or haNK-related immune related AEs occurred.

- The most common treatment-emergent, treatment-related grade ≥ 3 AEs were neutropenia (8 of 10 patients) and anemia (6 of 10 patients), consistent with AEs associated with chemotherapy.

Safety Data of Cancer Memory Vaccine (CMV) Combination In Highly Refractory Metastatic Triple Negative Breast Cancer and Head & Neck Cancer

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

Efficacy Data of 300 Doses of haNK

Including 276 Doses of haNK in Cancer Memory Vaccine Combination

August 2017 – October 31, 2018

Day 1 – 4, 15

Nab Paclitaxel

Low Dose Metronomic
Nab Paclitaxel
+
Low Dose
Immuno-Modulators
(5-FU/L, Cytoxan,
Cisplatin, Bevacizumab)

+

Day 5

Adenovirus

Ad-CEA

Ad-MUC1

Ad-Brachyury

Ad-HER2

Day 5

Yeast

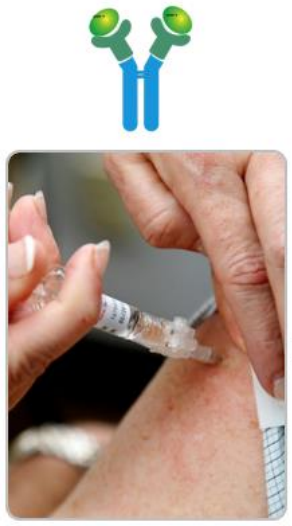
Ye-CEA

Ye-RAS

Ye-Brachyury

+

Day 9



N-803

IL-15RαFc

Fusion Protein

+

Day 9, 11, 16

Natural Killer

NK CD16 Targeted haNK

+

Day 9

Checkpoint

IgG1 PD-L1

Advanced Refractory Metastatic Pancreatic Cancer

Gemcitabine Package Insert 1st Line Pancreatic Cancer

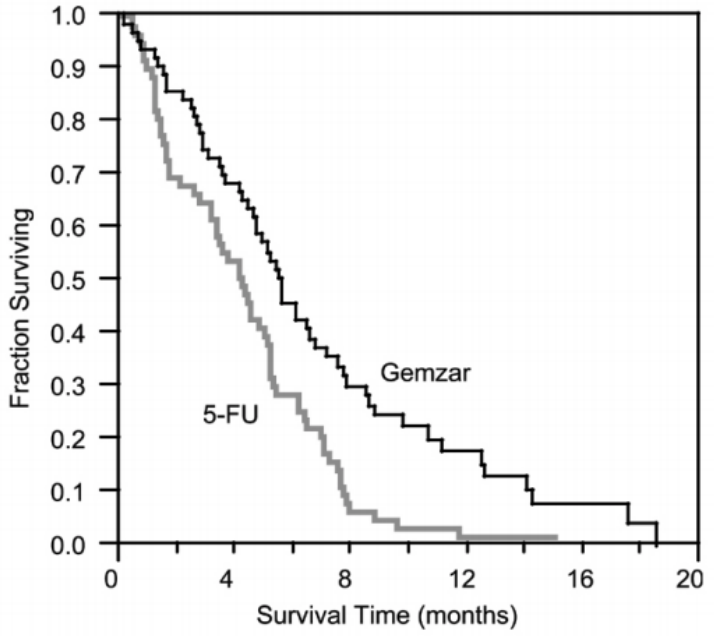
Section 14.4 Pancreatic Cancer The safety and efficacy of Gemzar was evaluated in two trials, a randomized, single-blind, two-arm, active-controlled trial conducted in patients with locally advanced or metastatic pancreatic cancer who had received no prior chemotherapy and in a single arm, open-label, multicenter trial conducted in patients with locally advanced or metastatic pancreatic cancer previously treated with 5-FU or a 5-FU-containing regimen.

17

Survival Median (95% CI) p-value[b]	5.7 months (4.7, 6.9)	p=0.0009	4.2 months (3.1, 5.1)
Time to Disease Progression Median (95% CI) p-value[b]	2.1 months (1.9, 3.4)	p=0.0013	0.9 months (0.9, 1.1)

[a] Karnofsky Performance Status.

[b] p-value for clinical benefit response calculated using the two-sided test for difference in binomial proportions. All other p-values are calculated using log rank test.



Median Survival of 5.7 Months With Gemcitabine

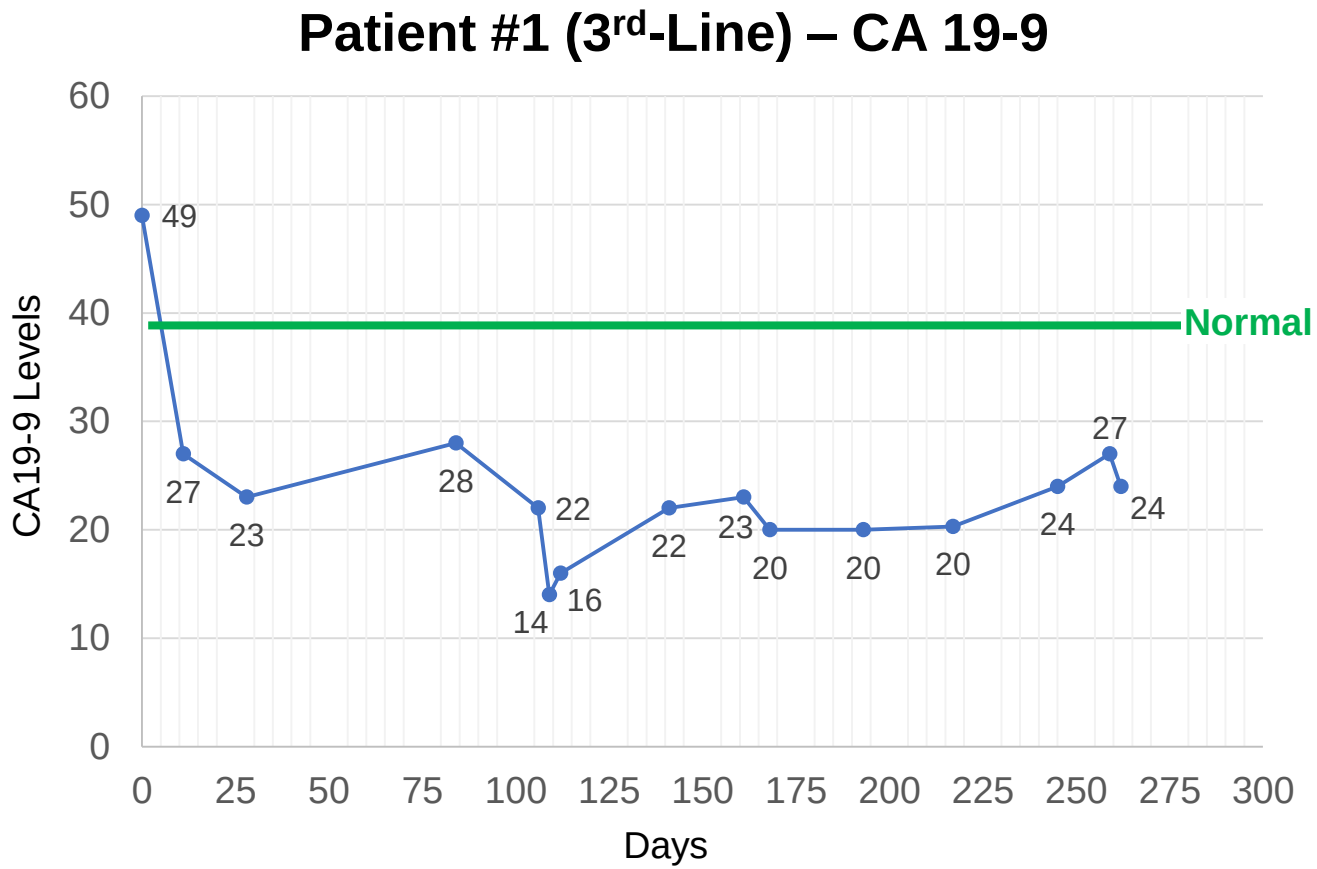
Confirmed Response Rate 0%

Case Study Patient #1: Cancer Memory Vaccine

3rd Line Cancer Patient - Failed Standard Chemo

35 year old male with metastasis to liver and lung failed first line (nab-paclitaxel, 5-FU/LV, Oxaliplatin, Gemcitabine) and second line (5-FU/LV, bevacizumab, nab-paclitaxel, Vitamin D/C, Oxaliplatin) chemotherapy

- First dosing of Cancer Memory Vaccine on August 14, 2017
- Received **13 cycles** to date
- CA 19-9 Normalized from a high of 49 to 20
- Patient pain free to date (Oct 2018)
- Weight gain of 10 lbs
- 20% reduction by RECIST of tumor mass
- **Progression Free Survival 8.6 months with Survival of 14 months to date (October 2018)**

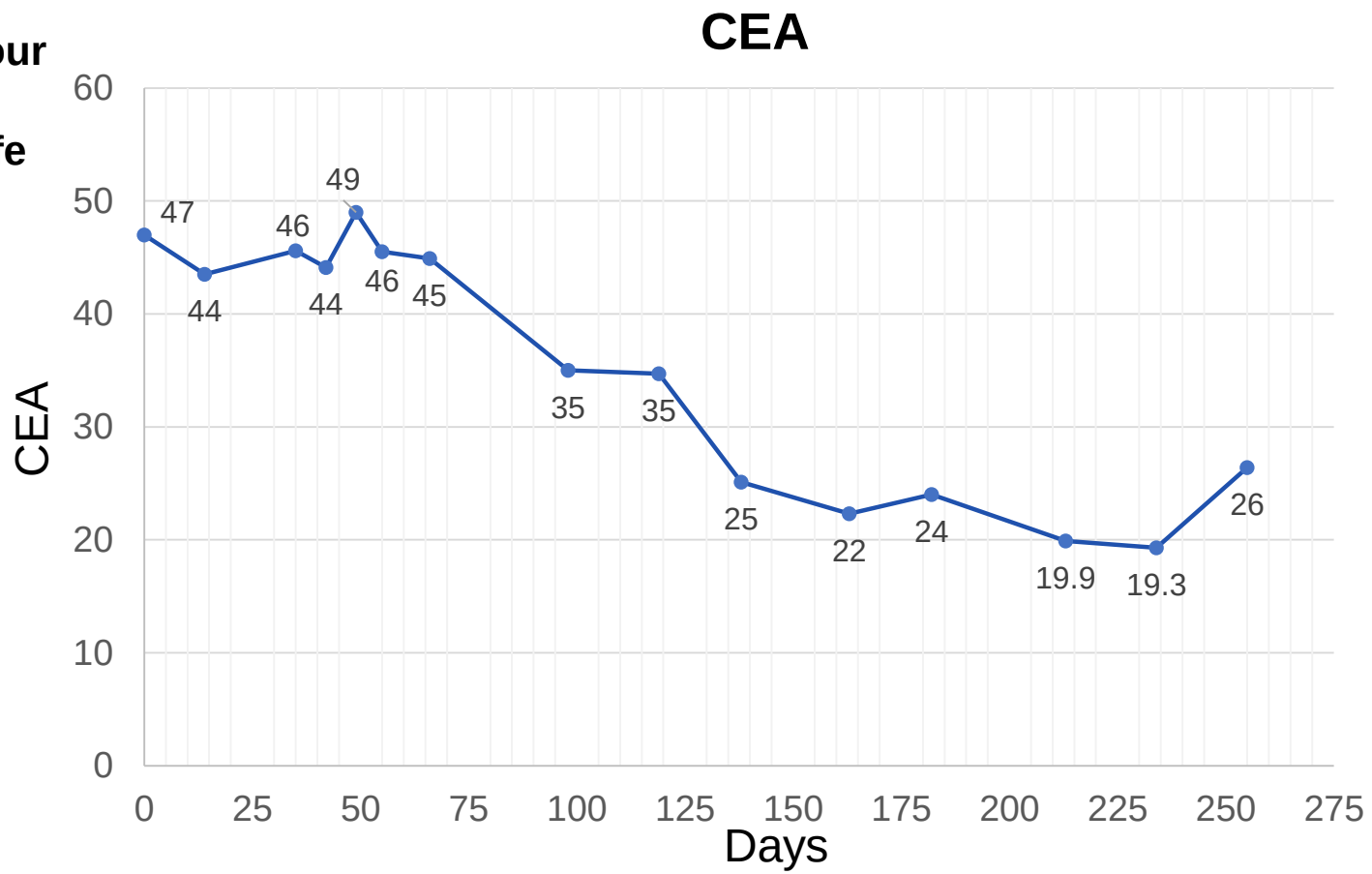


Case Study Patient #2: Cancer Memory Vaccine

4th Line Cancer Patient - Failed Standard Chemo

63 year old male with metastasis to liver failed four prior lines of therapy including: FOLFIRINOX, Gemcitabine, Nab-Paclitaxel, Erlotinib, Cyberknife

- First dosing of CMV on October 2, 2017
- Received **14 cycles**
- CEA dropped >50% from a high of 45 to 20
- No DLTs over **14 cycles** to date
- **Stable disease for 8 months with reduction of CEA**
- **PFS: 9.1 months**
- **Underwent Whipple surgical resection**
- **Survival 13 months to date (Nov 2018)**
- **3 Months post Whipple to date (Nov 2018)**

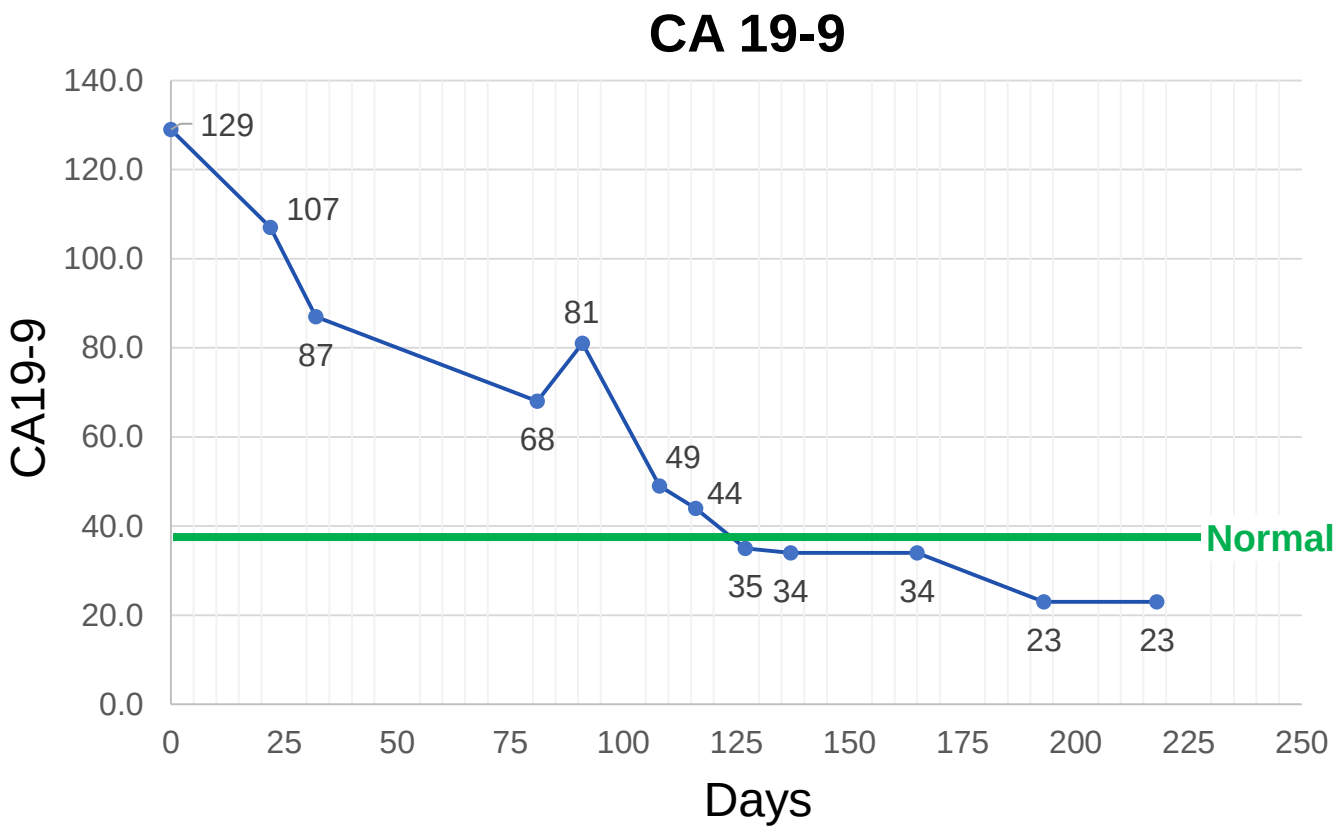


Case Study Patient #3: Cancer Memory Vaccine

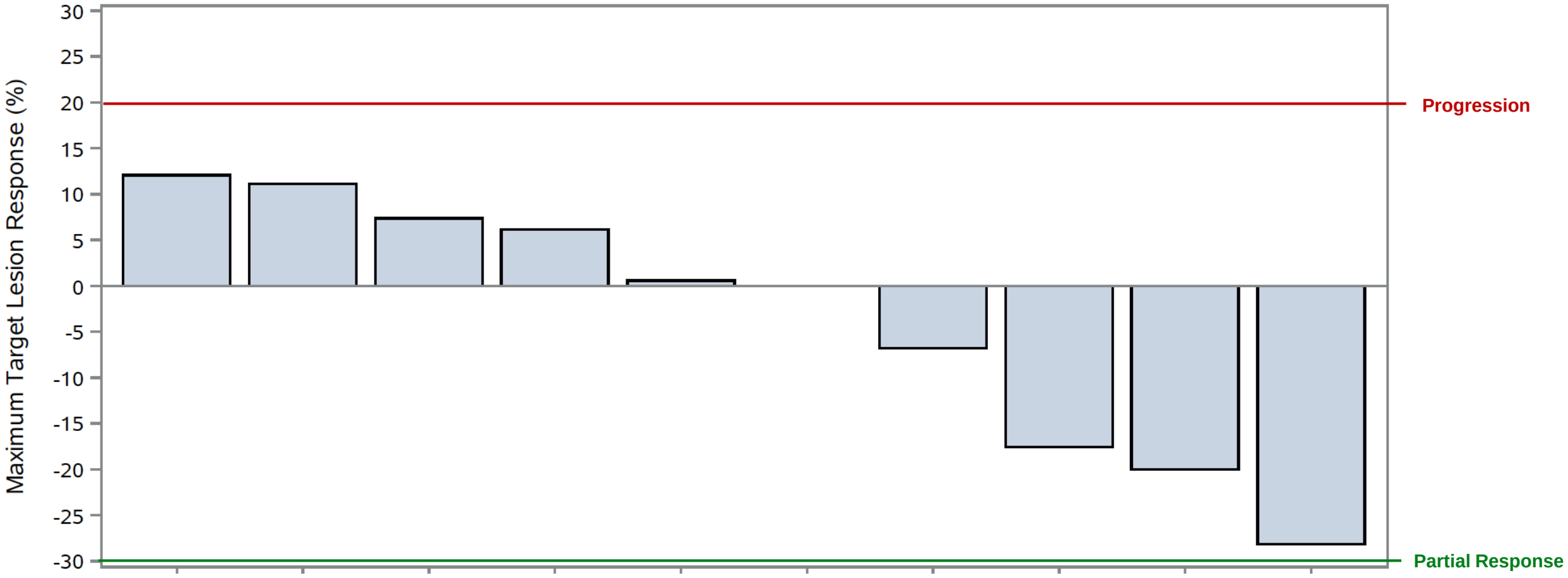
3rd Line Metastatic Pancreatic Cancer Patient

50 year old female failed 2 prior lines of therapy (FOLFIRINOX, SBRT)

- Cachetic with active weight loss at time of initiation of trial and on high dose methadone pain medications BID
- First dosing of CMV on Sept 4, 2017
- Received **14 cycles** to date
- CA 19-9 Dropped >50% from a high of 129 to 23 (normal)
- Pain completely resolved and patient methadone free from cycle 2
- Weight gain, 12 lbs.
- **Stable disease for 4.4 months with reduction of CA-19-9, weight gain and pain-free 7 months.**
- **Normalized CA19-9**
- **Progressed with survival of 9.6 months**



Best Response of Target Lesions in First 10 Patients with 3rd Line or Greater Metastatic Pancreatic Cancer



100% Stable disease in target lesions at 8 weeks in first 10 patients receiving CMV

Summary of CMV in 3rd Line or Greater Metastatic Pancreatic Cancer

- **Disease Control Rate (DCR): 90%**
  9 of 10 patients maintained stable disease (SD) for ≥ 8 weeks.

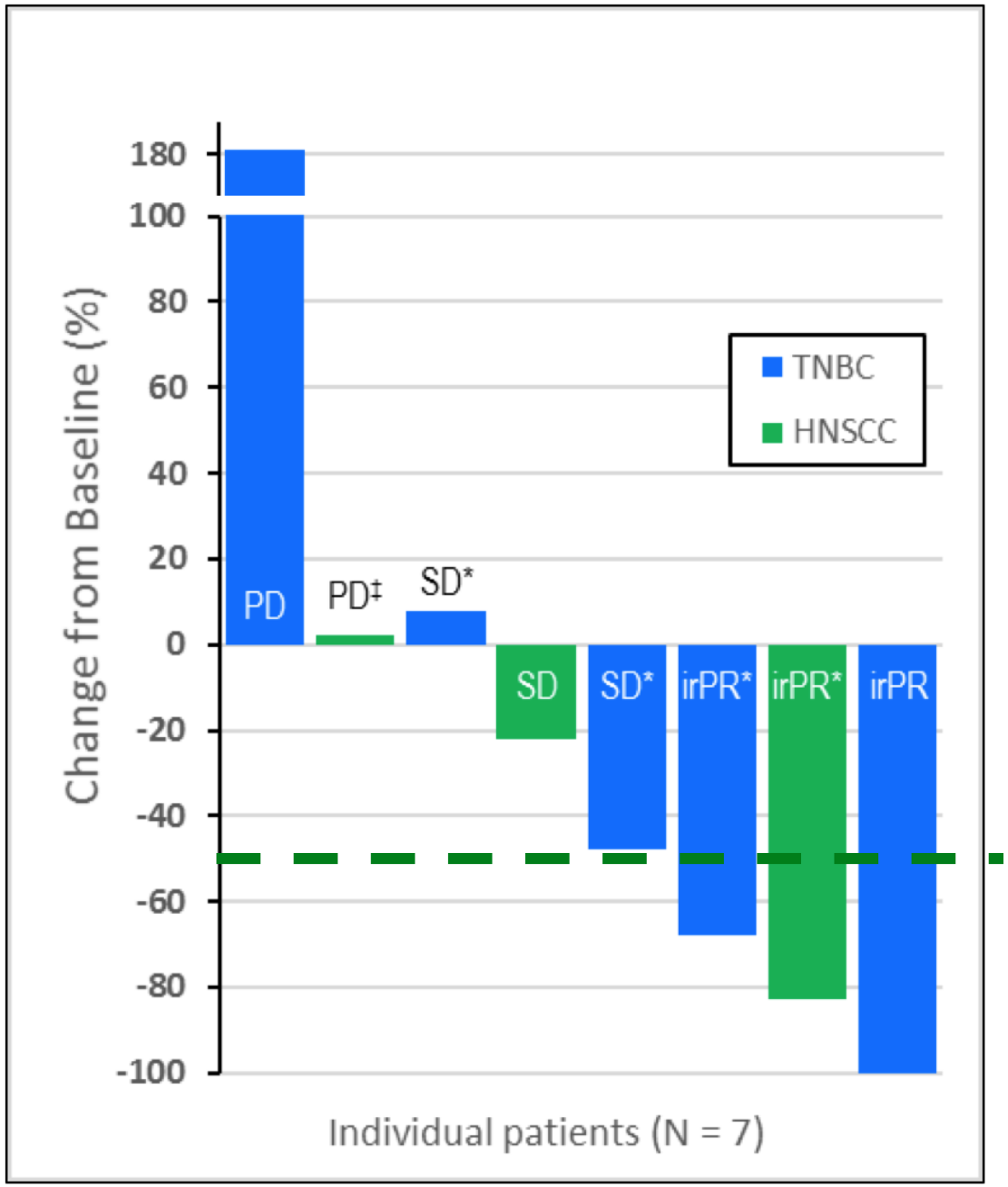
- **Median PFS: 5.8 months**
  (95% confidence interval [CI]: 3.3 months - 8.8 months)

- **Median OS: 9.5 months**
  (95% CI: 5.0 months - upper limit not yet reached)

Median overall survival of 9.5 months in these patients who had greater than **3rd line** disease compares favorably with historical median overall survival in **1st line** pancreatic cancer patients receiving gemcitabine alone of 5.7 months or gemcitabine + Abraxane of 8.7 months

Advanced Refractory Metastatic TNBC & HNSCC

Best Target Lesion Response in Greater than 3rd Line TNBC and HNSCC



- 80% disease control in patients with TNBC with advanced disease ranging from 4th to 6th line therapy.
- 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.
- 3 of 8 Evaluable Patients Experienced irPRs

- *Continue to Receive CMV Therapy on Study

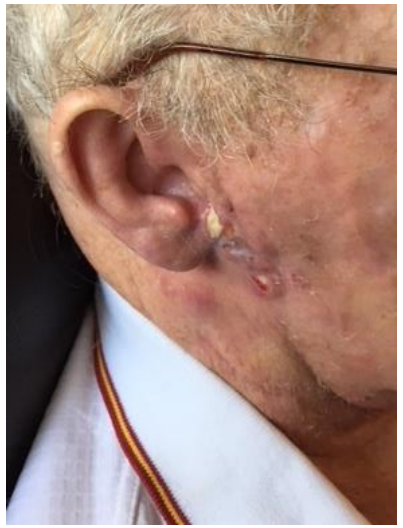
Efficacy of CMV in 4th Line Metastatic Head & Neck

- Disease control rate (DCR) is 67% for 2 of 3 evaluable patients who experienced stable disease (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% reduction in tumor size from baseline).

Patient 002 History: 76 Year Old Male with 5th Line Metastatic Head & Neck Cancer

Patient 3090-001-002

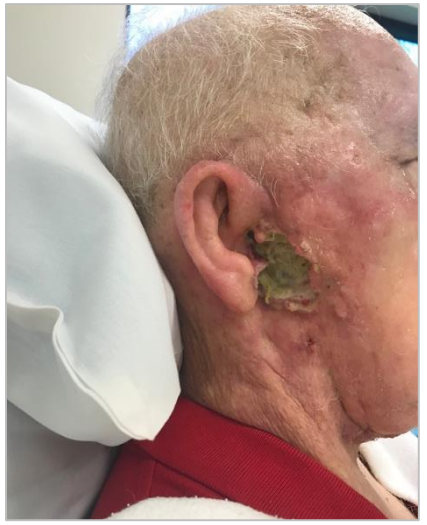


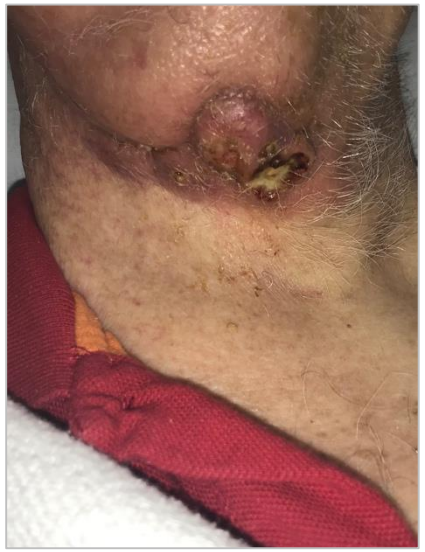
Recurrence After Surgery & Radiation
1st Line & 2nd Line

Progressed On Chemotherapy:
Docetaxel
Carboplatin
5-FU
3rd Line

Progressed On Checkpoint:
Pembrolizumab
4th Line

Presented with 5th Line Metastatic Disease for NANT Cancer Vaccine
Day 1
May 14, 2018

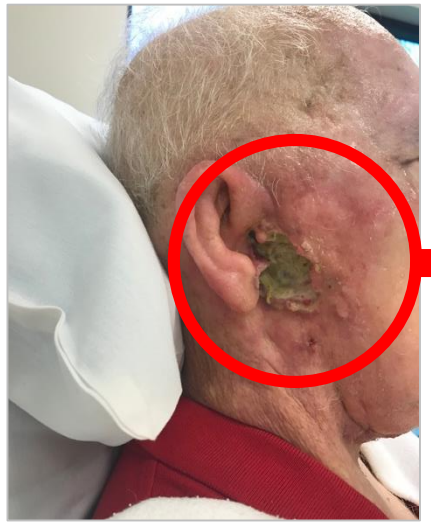




Complete Response with NANT Head & Neck Cancer Vaccine

Patient 3090-001-002

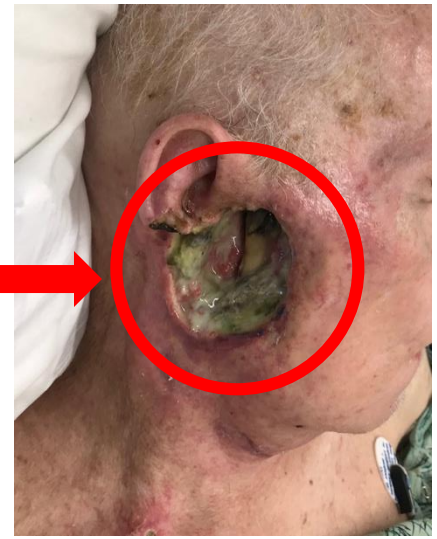
Day 1
May 14, 2018
5th Line Metastatic
Head & Neck Cancer
Large Tumor Mass
Penetrating to
Temporomandibular Joint



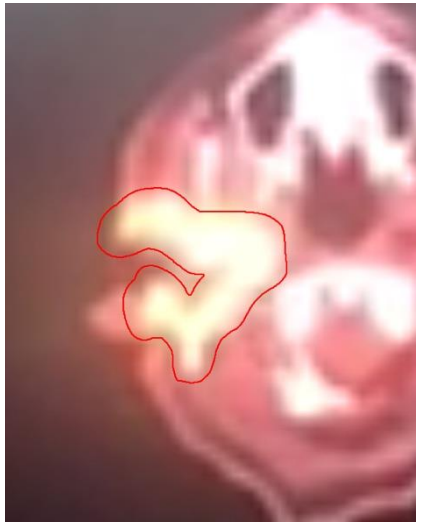
Day 1 - Pre Treatment
May 14, 2018

NK Cell & T-Cell Eradication of Tumor

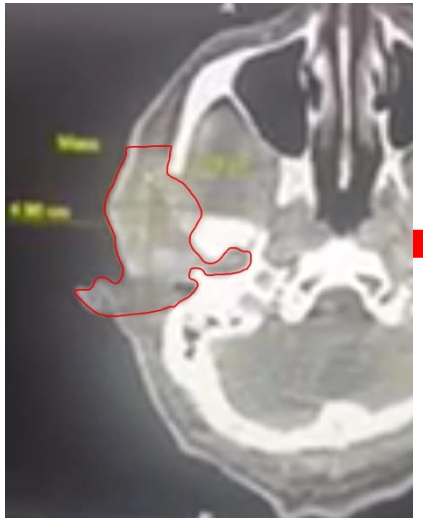
Complete Response After 2 Cycles of NANT Cancer Vaccine



Cycle 3 **- Day 62**
July 15, 2018



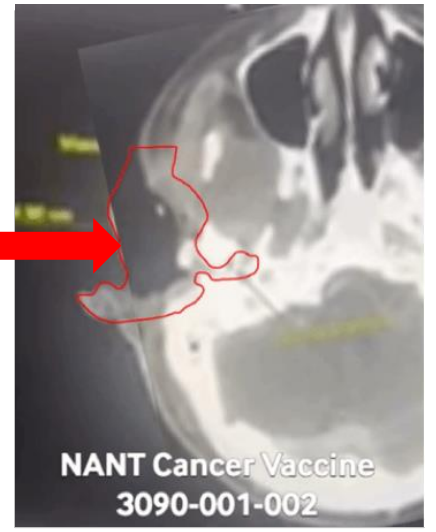
PET Scan Day 1



Pre-Treatment
Day 1

NK Cell & T-Cell Eradication of Tumor

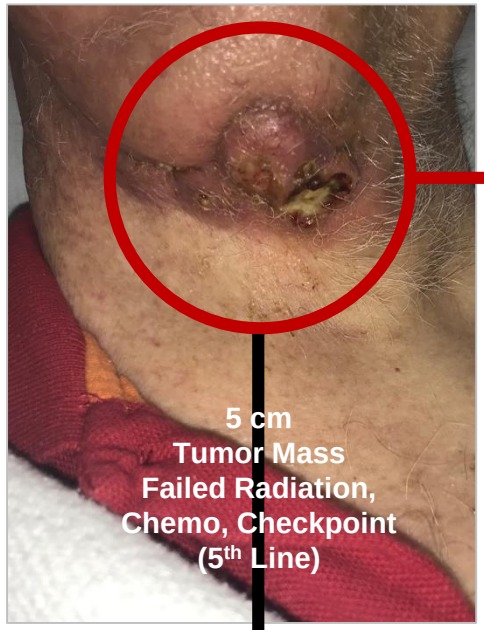
Complete Response After 2 Cycles of NANT Cancer Vaccine

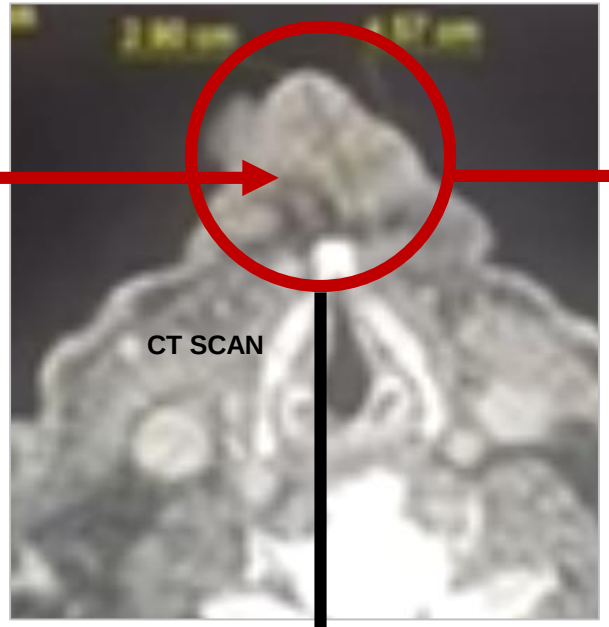


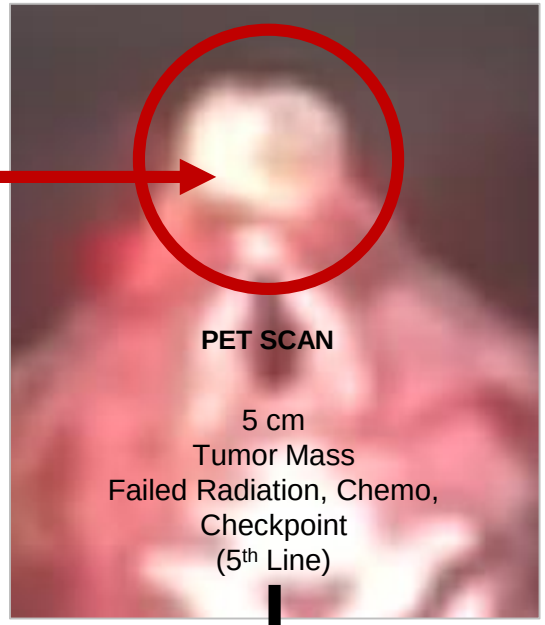
CT Scan **Day 1**

Complete Response in 5th Line Metastatic Head & Neck Cancer After 2 Cycles of NANT Cancer Vaccine

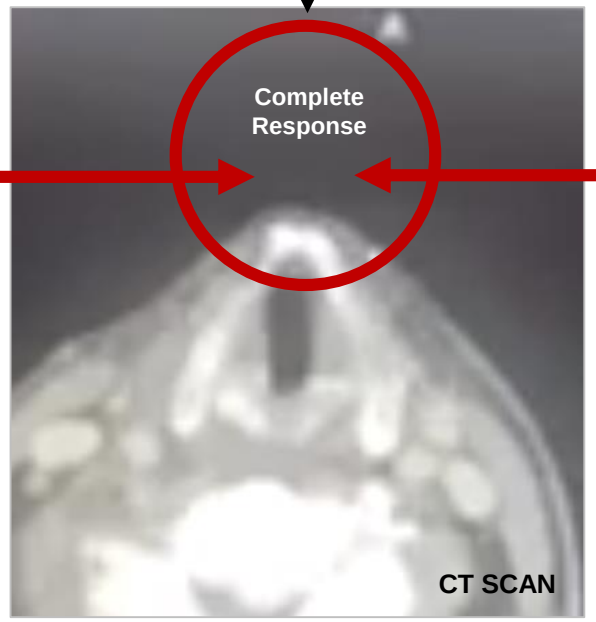
Patient: 3090–001-002
Pre-Treatment
5th Line







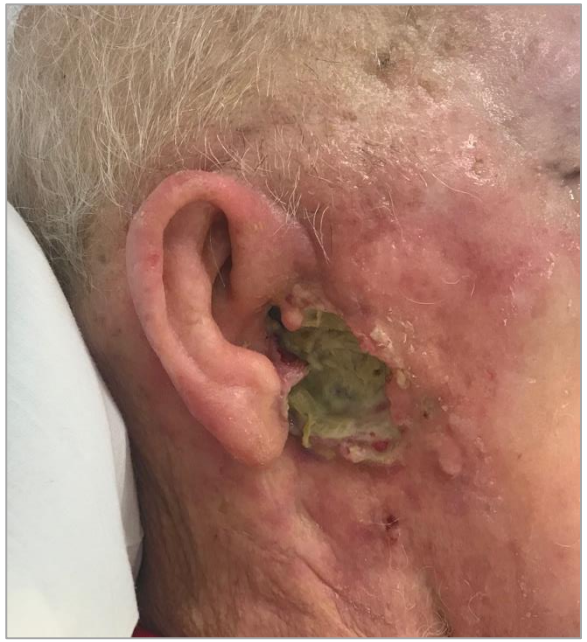
Complete Remission Post NANT Cancer Vaccine Treatment
After 2-Cycles

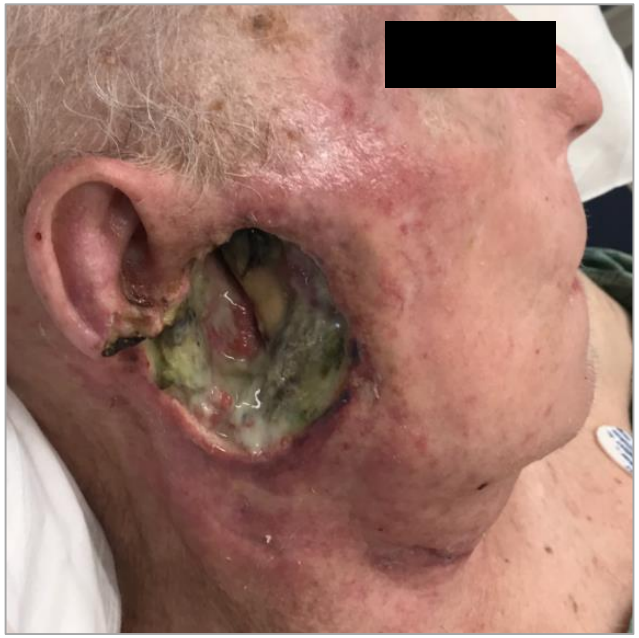


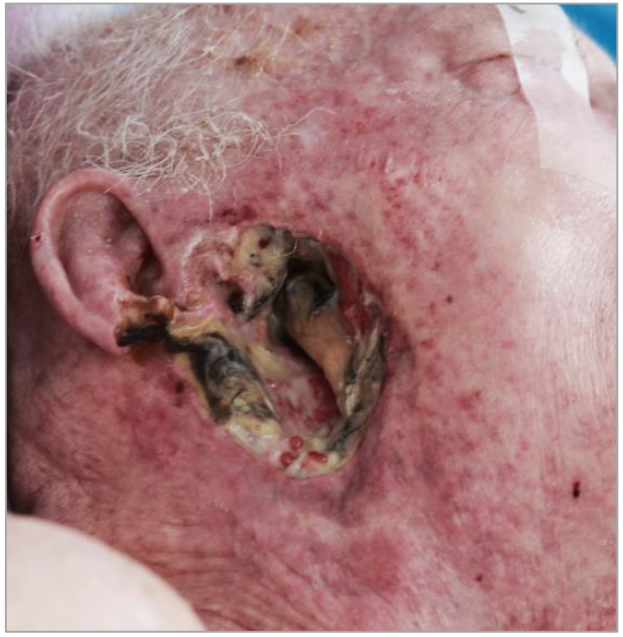
Tumor Mass Completely Resolved After 60 Days (2 Cycles, July 15, 2018)

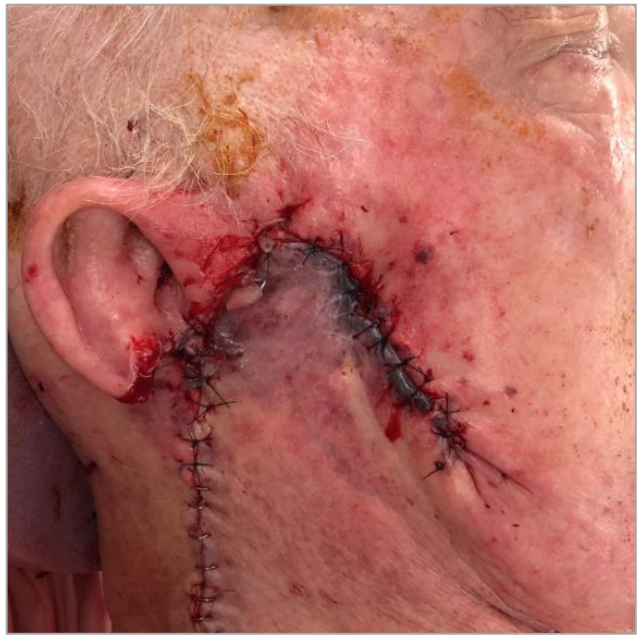
Phase I Result: Complete Response (5th Line Metastatic Head & Neck)

Patient 3090-001-002









Day 1
May 14, 2018
76yr old Male with
5th Line Metastatic
Head & Neck Cancer
Large Tumor Mass Penetrating
to Temporomandibular Joint

NANT Cancer Vaccine

Day 62
July 15, 2018
Complete Response
No Evidence of Tumor
After 2 Cycles

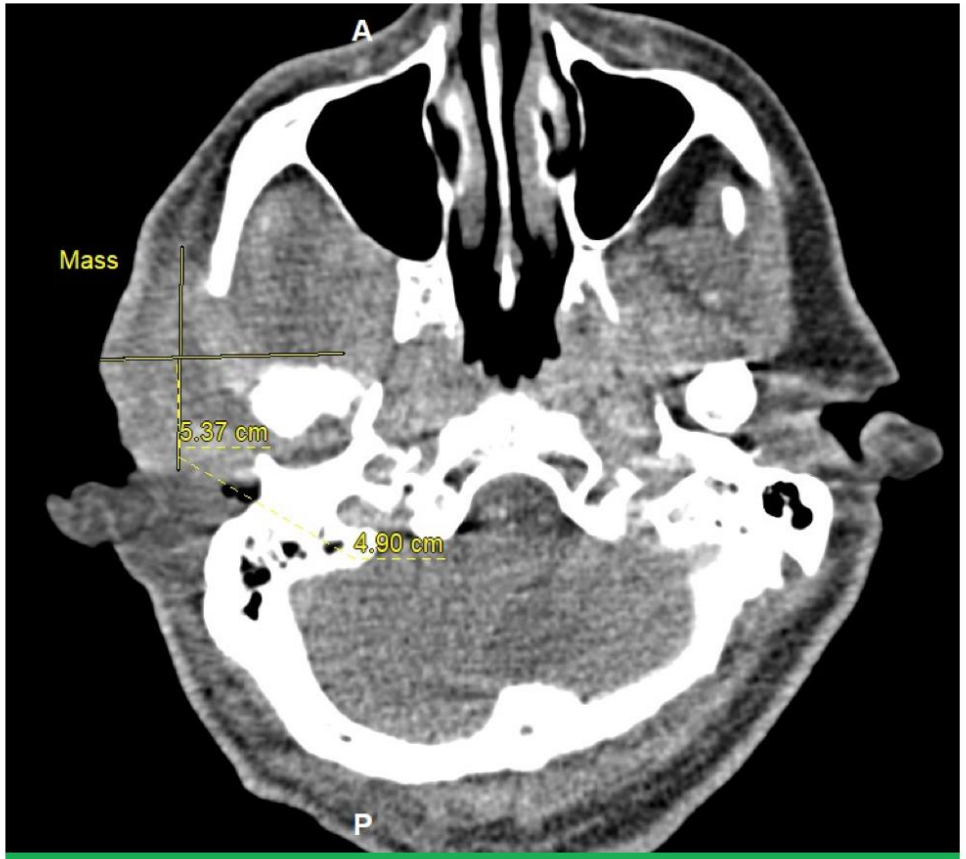
Surgical Debridement

Day 65
July 18, 2018
Complete Response
No Evidence of Tumor
Wound Debridement

Surgical Flap Repair

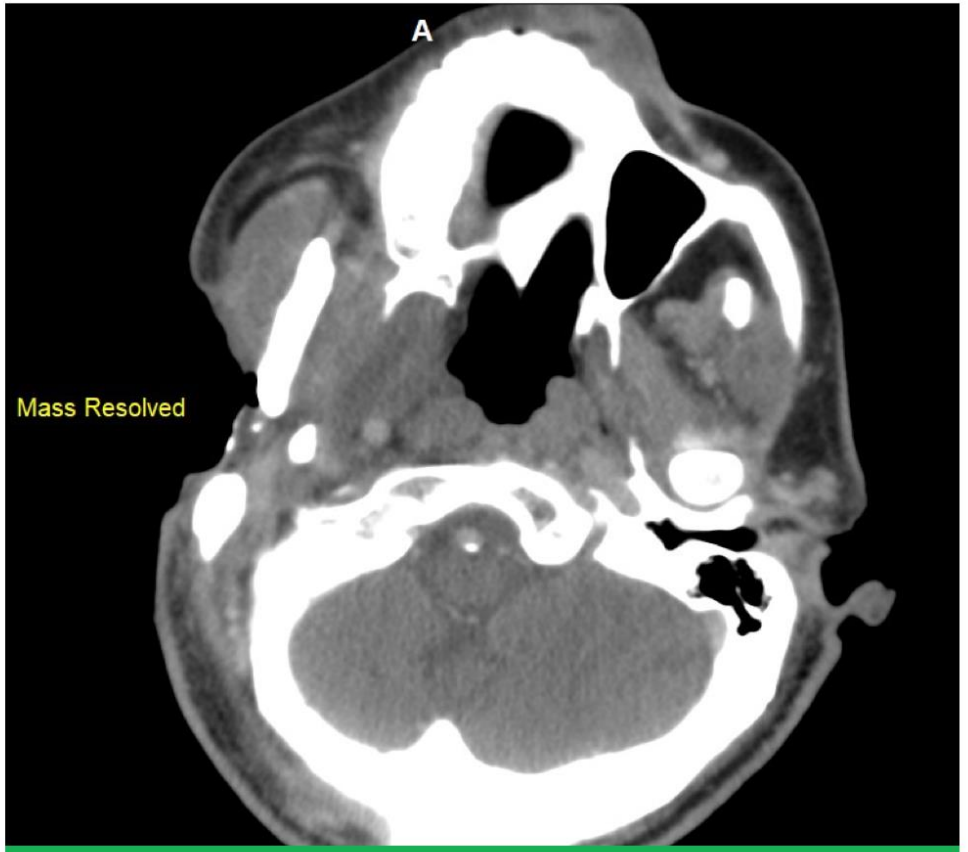
Day 65
July 18, 2018
Surgical Flap Repair

Figure 1: Resolution of an HNSCC Parotid Tumor



May 4, 2018: Baseline imaging assessment. Ulcerated right parotid mass.

NCV treatment initiated May 2018



June 22, 2018: Complete resolution of parotid tumor, with no evidence of disease.

Efficacy of CMV in 4th Line Metastatic TNBC

- Disease control rate (DCR) is 80% in 4 of 5 patients with stable disease (SD) in 2 patients and partial response (irPR) in 2 patients

- To date, 6 out of 7 (86%) patients are ongoing treatment

Patient #01 (4th Line): 57 Year-Old Female with Metastatic TNBC

Patient 3067-001-001

1st-Line
Doxorubicin
Cytoxan

→

2nd-Line
XRT
Letrozole

→

Progressed
3rd-Line
Capecitabine
Nab-paclitaxel

→

Presented
4th-Line
NANT Cancer
Vaccine Trial

March 27, 2018
Day 1

→

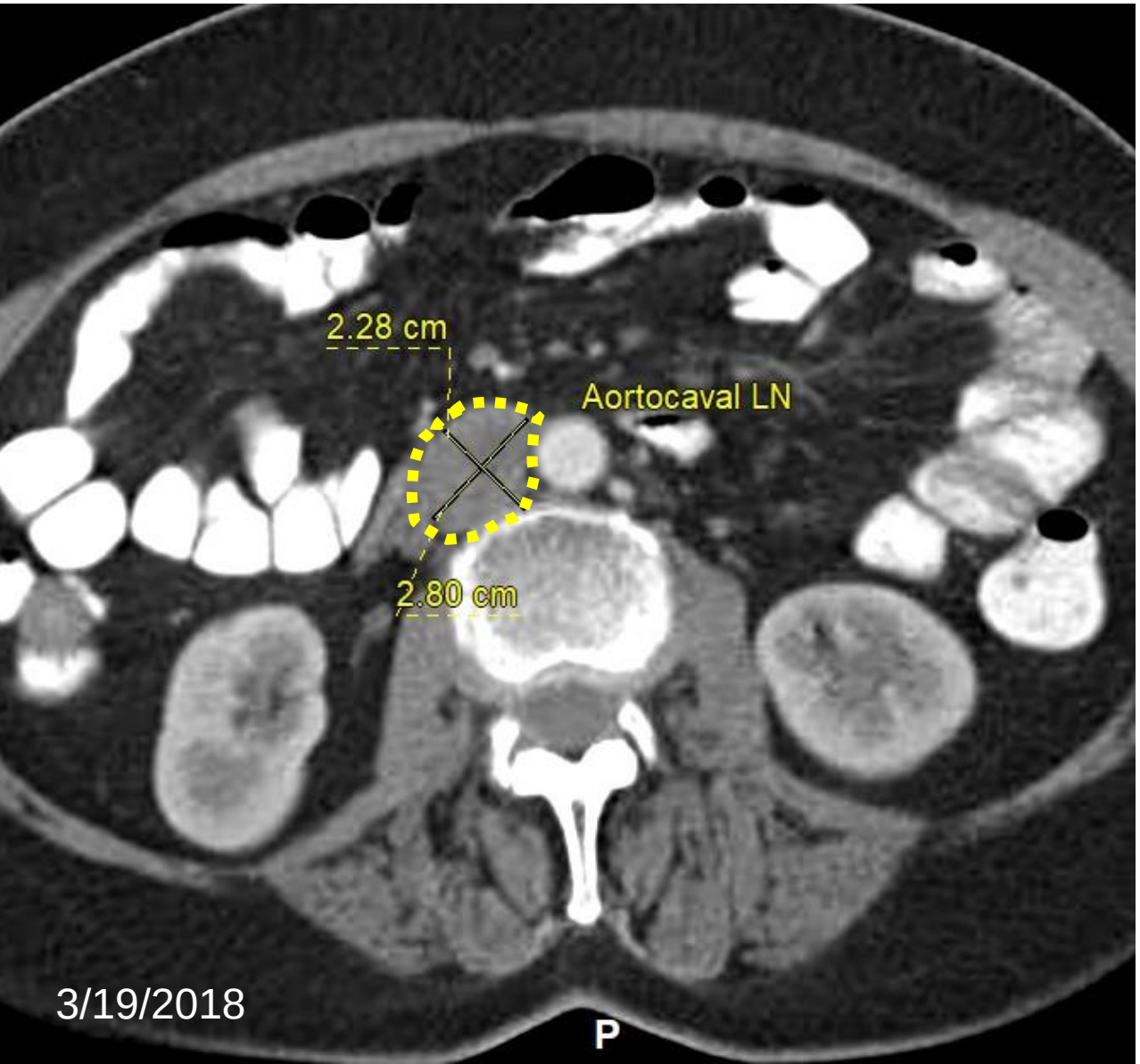
First Observation of Partial Response
July 10, 2018
Day 105

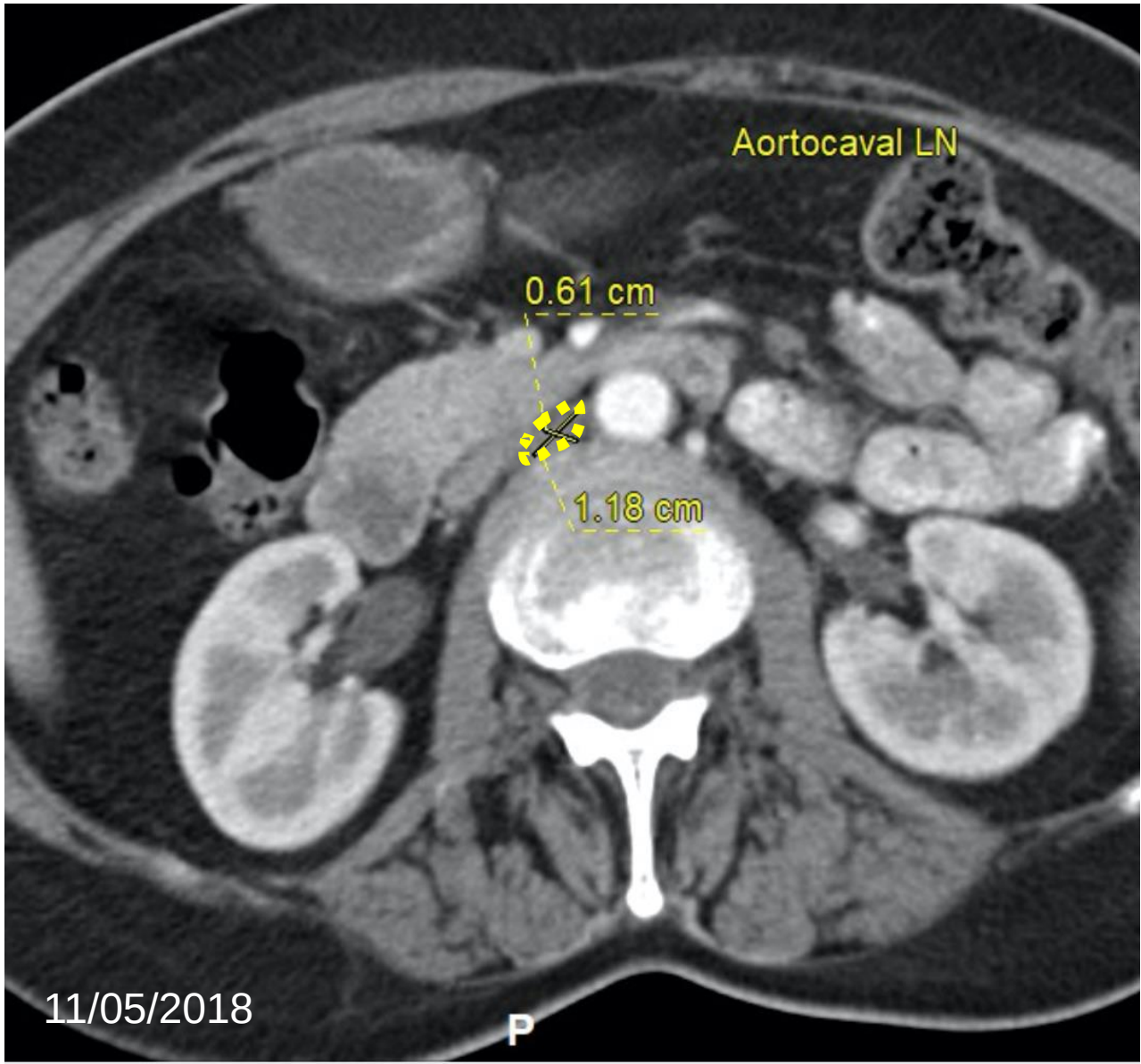
- Received **4 cycles** to date
- Patient pain-free
- 1 DLT managed with dose reduction of cisplatin
- No immune-related AEs

- **Current Radiographic Response:**
  - RECIST 1.1: **71% decrease**
  - irRC: **90% decrease**

Patient #01 (4th Line): 57 Year-Old Female with Metastatic TNBC

90% Tumor Reduction Immune Related Response Criteria (irRC)





BCG Unresponsive
Non-Muscle Invasive Bladder Cancer

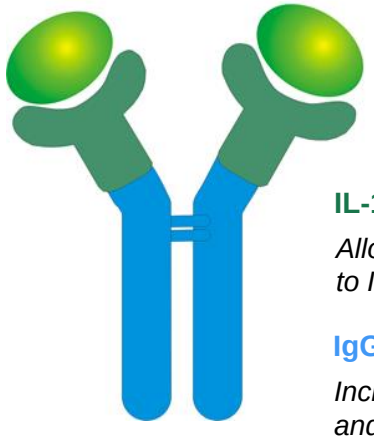
Early Phase 2 Clinical Results of IL-15RαFc Superagonist N-803 With BCG in BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer (NMIBC) Patients Demonstrating 86% CR of Carcinoma In Situ (CIS)

Augmenting Immunity with an IL-15 Superagonist: N-803

- N-803 (also known as ALT-803) is a novel IL-15 receptor superagonist engineered to have a longer serum half-life and 30-fold greater activity vs. IL-15
- N-803 promotes natural killer (NK) and $CD8^+$ T-cell expansion and activation in vivo without expanding immunosuppressive regulatory T cells

N-803

IL-15 Superagonist



IL-15N72D

IL-15 alteration N72D enhances binding 10-fold to βγ complex

IL-15Rα

Allows transpresentation selectively to IL-2R βγ chain

IgG1 Fc

Increases serum half-life and lymphoid distribution

N-803 promotes natural killer (NK) and $CD8^+$ T-cell expansion and activation in vivo without expanding immunosuppressive regulatory T cells

N-803 + BCG in High-Risk NMIBC – Phase I Results

Durable Complete Responses in 9 out of 9 Patients

Dose (intravesicular instillation)	Patient	Stage	Response Assessments							
			W12	6M	9M	12M	15M	18M	21M	24M
100 µg	1	T1	CR	CR	CR	CR	CR	CR	CR	CR
	2	Ta	CR	CR	CR	CR	CR	CR	CR	CR
	3	T1	CR	CR	CR	CR	CR	CR	CR	CR
200 µg	4	T1	CR	CR	CR	CR	CR	CR	CR	CR
	5	Tis (CIS)	CR	CR	CR	CR	CR	CR	CR	CR
	6	T1	CR	CR	CR	CR	CR	CR	CR	CR
400 µg	7	T1	CR	CR	CR	CR	CR	CR	CR	CR
	8	Tis (CIS)	CR	CR	CR	CR	CR	CR	CR	CR
	9	Ta	CR	CR	CR	CR	CR	CR	CR	CR

9 of 9 (100%) patients disease-free at 24 months

N-803 has earned ***Fast Track*** **designation** from the FDA based on the strength of these results.

Ongoing Phase II Results: Combination of IL-15 Superagonist N-803 plus BCG in BCG-Unresponsive NMIBC

Cohort	Sex / Age	Stage	Response Assessments*			
			3 Months	6 Months	9 Months	12 Months
Cohort 1 Unresponsive Carcinoma In-Situ (CIS) [with or without Ta/T1 papillary disease]	M / 72	CIS	CR	CR	CR	CR →
	M / 73	CIS	PR	PD ✖		
	M / 55	CIS + T1	PR	CR →		
	M / 68	CIS + T1	CR →			
	M / 63	CIS + T1	CR →			
	M / 80	CIS + Ta	CR →			
	M / 66	CIS + Ta	CR →			
Cohort 2 Unresponsive high-grade Ta/T1 papillary disease	M / 64	T1	DF	DF	DF	DF →
	F / 66	T1	DF	DF	DF	**
	M / 89	Ta	DF	DF	DF →	
	F / 63	Ta	DF	DF →		
	M / 90	T1	DF	DF →		
	M / 74	T1	DF →			
	M / 63	T1	DF →			
	M / 88	T1	DF →			

→ Subject ongoing in study ✖ Progressive disease

CR, complete response; DF, disease free; PD, progressive disease. * For the CIS with or without Ta/T1 papillary disease cohort, CR is defined as negative cystoscopy and negative (including atypical) urine cytology; or positive cystoscopy with biopsy-proven benign or low-grade Ta NMIBC and negative cytology; or negative cystoscopy with malignant urine cytology if cancer is found in the upper tract or prostatic urethra and random bladder biopsies are negative. For the high-grade Ta/T1 papillary disease cohort, disease-free is defined as absence of high-grade Ta (excluding low-grade Ta), any grade T1, persistent or new CIS, disease progression, cystectomy, change in therapy, and death (any cause). ** Patient had treatment delays due to AEs of dysuria and urgency and then decided to discontinue treatment after 4 doses; patient was alive at 6-month and 9-month follow up and survival status will continue to be collected per protocol.

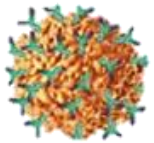
Conclusions

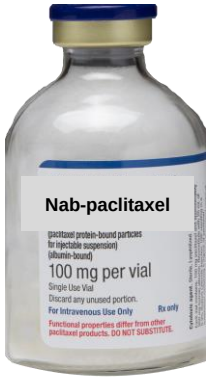
- **CIS Cohort: 6 out of 7 (86%) complete response (CR)** in subjects in the CIS [with or without Ta/T1 papillary disease] cohort
- **Papillary Cohort: 8 out of 8 (100%) remain disease free (DF)** with no evidence of disease recurrence in any of the patients in the high-grade Ta/T1 papillary disease cohort to date, ranging from 3 to 12 months in duration
- Treatment is well tolerated with no immune related AEs
- AE profile was generally consistent with what would be expected in subjects receiving BCG alone[11]
- Enrollment is actively proceeding
- N-803 + BCG demonstrated promising evidence of clinical activity in patients who failed BCG therapy, in both the CIS and papillary disease cohorts

Cancer Memory Vaccine (CMV)

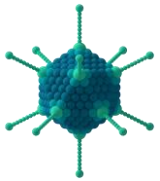
Orchestrated Over 21 Day Cycle

Day 1 – 4, 15



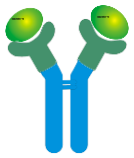


Day 5

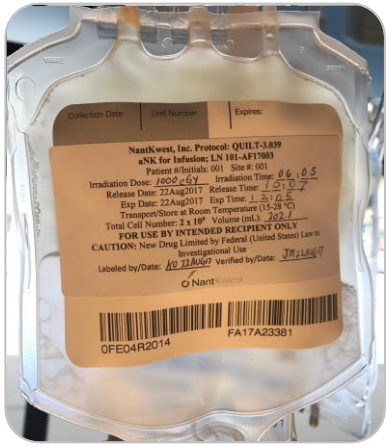


Day 5

Day 9



Day 9, 11, 16



Day 9

Nab Paclitaxel

Low Dose Metronomic Nab Paclitaxel
+
Low Dose Immuno-Modulators (5-FU/L, Cytoxan, Cisplatin, Bevacizumab)

Adenovirus

Ad-CEA

Ad-MUC1

Ad-Brachyury

Ad-HER2

Yeast

Ye-CEA

Ye-RAS

Ye-Brachyury

N-803

IL-15RαFc

Fusion Protein

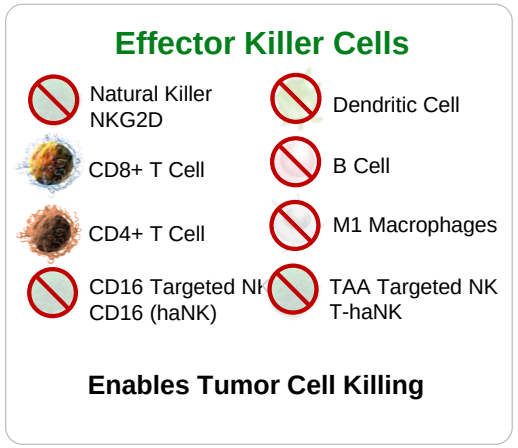
Natural Killer

NK CD16 Targeted haNK

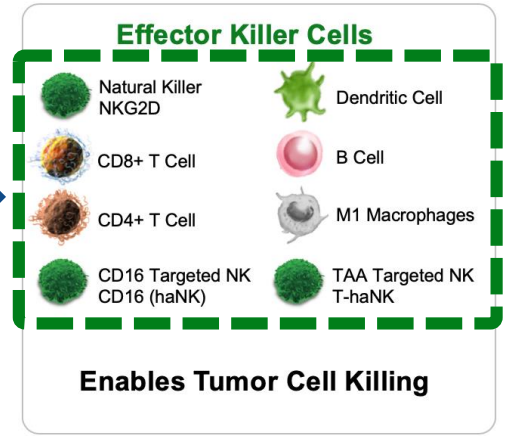
Checkpoint

IgG1 PD-L1

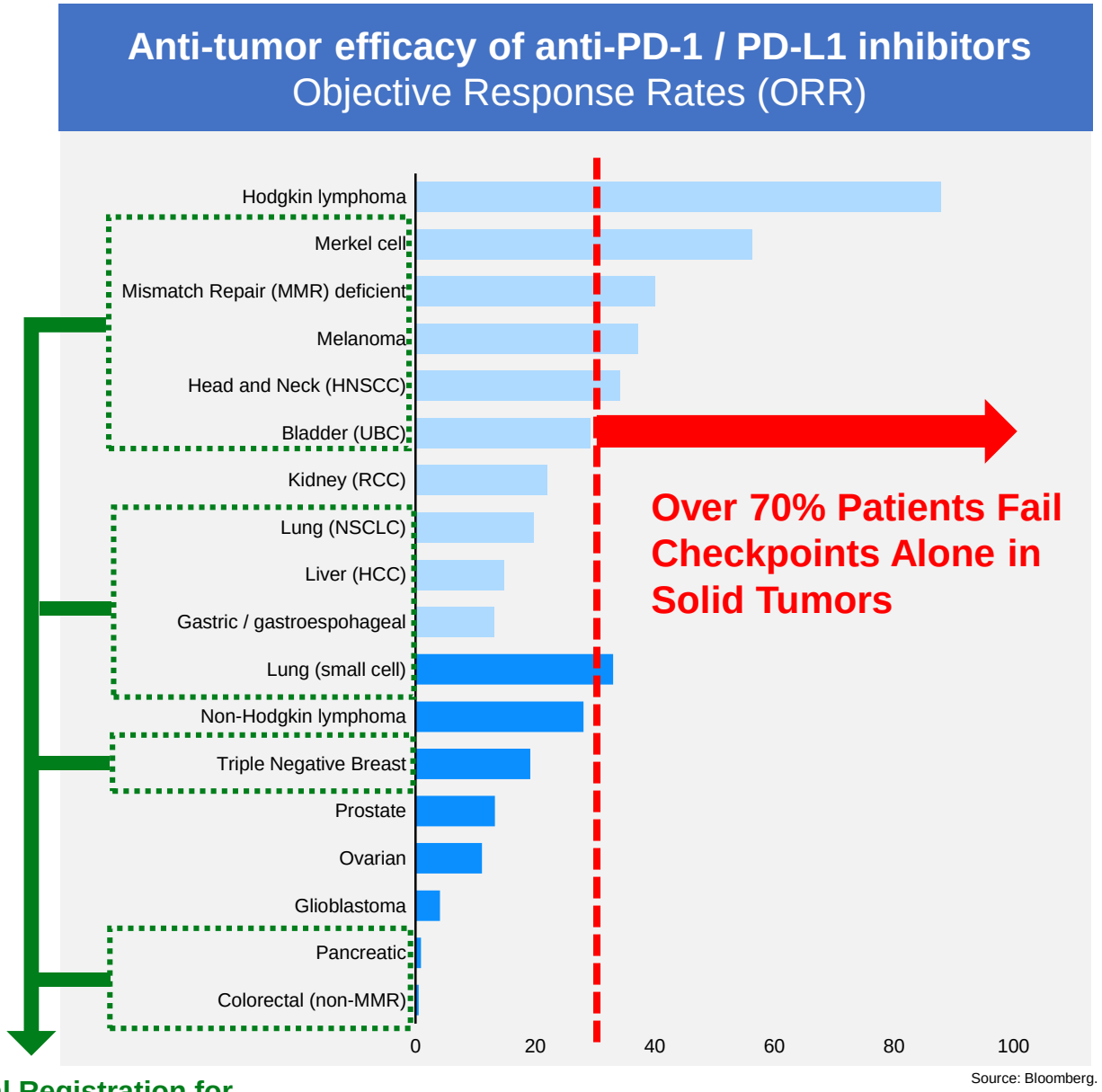
Vision 2020+: Chemo Free Cancer Immunotherapy Beyond Checkpoint Inhibitors



Current State with Checkpoints & CAR-T Therapies



Immunotherapy 2.0 Cancer Memory Vaccine



Source: Bloomberg.

- **The Goal:** Orchestrate the entire immune system in a temporal spatial protocol combining:
  - Metronomic low-dose nab-paclitaxel with
  - Fusion proteins to induce endogenous stimulation of natural killer and T-cells,
  - Supplemented with off-the-shelf targeted NK cell infusions and
  - Inducing T-cell memory via adenovirus and yeast vectors bearing tumor associated antigens and neoepitopes
  - Checkpoints - PD-1 and PD-L1
  - **(Cancer Memory Vaccine)**

- **Vision 2020+:** Chemo-free biologically driven immunotherapy, inducing memory T-cells for the early treatment and prevention of cancer.

Clinical Trial Registration for Cancer Memory Vaccine