
(NASDAQ:DRTS)

# Investor Presentation

February 2025

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# The Alpha Tau Mission

## Alpha DaRT

A novel approach using localized alpha particle radiotherapy designed to precisely destroy solid tumors while sparing surrounding healthy tissue

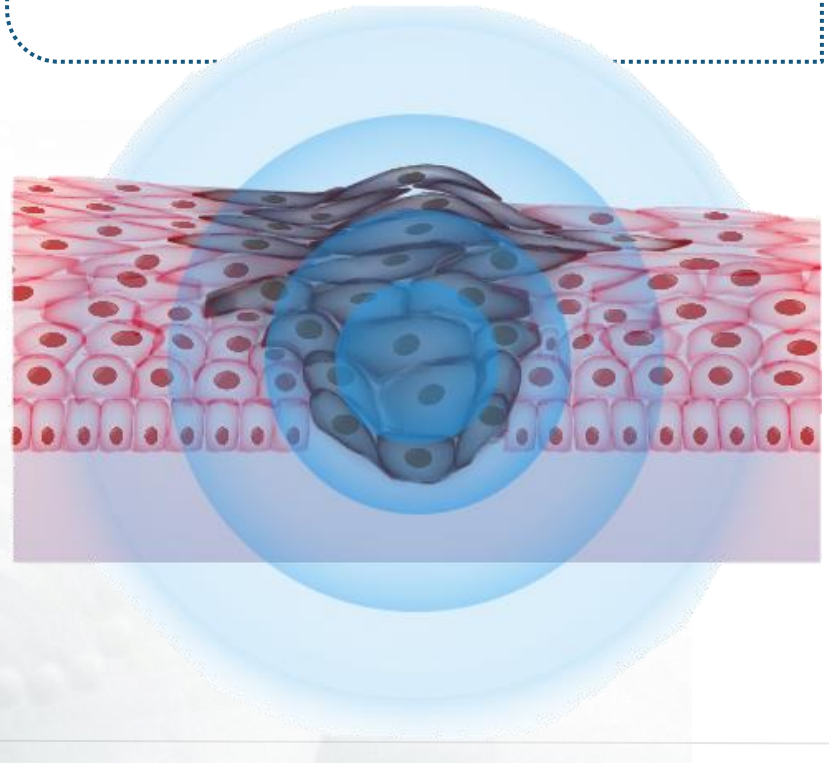
- Broad potential applicability for local tumor control, together with signs of compelling immuno-stimulatory activity
- Platform technology has the potential to be utilized alone or synergistically with other cancer treatment modalities
- Milestones and data from multiple clinical trials in various phases in different indications expected in 2025 and 2026
- 1st potential U.S. marketing authorization in 2026, with significant market opportunity across multiple tumor types

# Alpha Radiation is Focal - Short Range Limits Clinical Use

**Whereas beta and gamma radiation can penetrate tissue with sufficient range to facilitate tumor coverage (while risking damage to healthy tissue), alpha radiation has short range in tissue (<100 µm), which limits its clinical usefulness in local delivery**

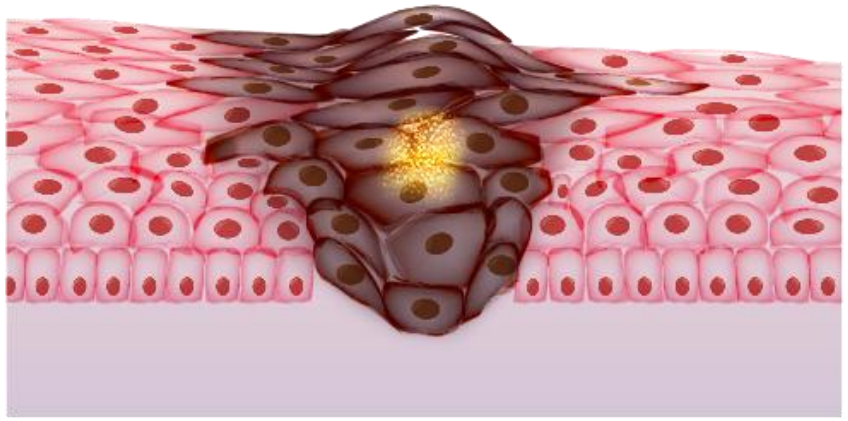
## Beta/Gamma Radiation

Long therapeutic range with risk to surrounding organs



## Alpha Radiation

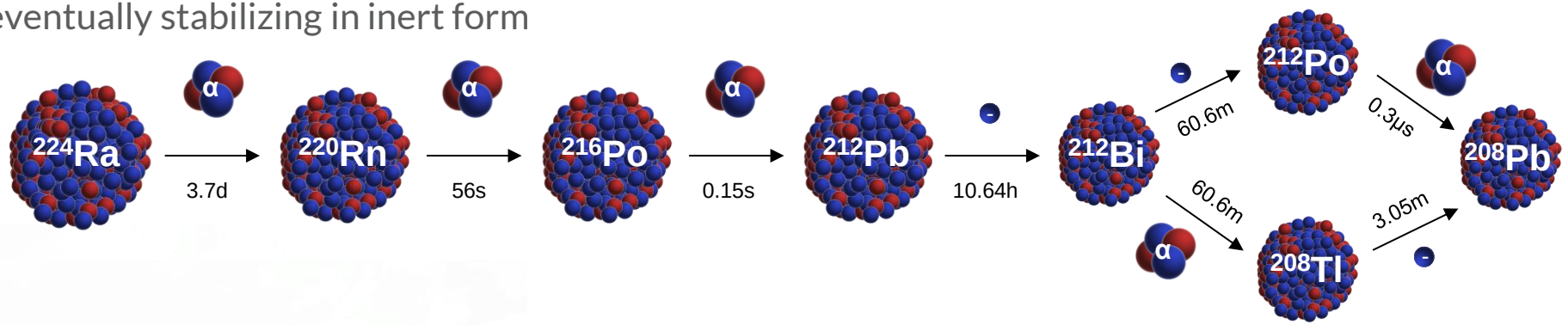
Short range in tissue limits damage to surrounding organs but also limits coverage



# Alpha DaRT Technology is Designed to Overcome These Limitations

## $^{224}$Ra Decay Chain

- Alpha DaRT leverages the innate decay chain of Radium-224
- The decay chain of Radium-224 includes four alpha particles
- Radium-224 has a half-life of ~3.7 days, while the remaining decay chain has a total half-life of approximately 12 hours, before eventually stabilizing in inert form




## Alpha DaRT

- The Alpha DaRT utilizes stainless steel or titanium sources that are impregnated with Radium-224
- When the Alpha DaRT source is injected into the tumor, the radium remains attached to the source while its daughter atoms detach, emitting cytotoxic alpha particle payloads as they move deeper into the tumor until eventually stabilizing

**Alpha DaRT is designed to overcome the range limitations of alpha particles through precise release of alpha emitters into the tumor, generating a potent and tight distribution of alpha radiation**

# Alpha DaRT - Diffusing Alpha-emitters Radiation Therapy

https://www.youtube.com/watch?v=nwfzJHm0fTQ

# Therapeutic Focus

**We are focused on delivering solutions to three markets that we believe would be best served by the unique characteristics of the Alpha DaRT**

## Localized & Unresectable

- Localized tumors that are not surgical candidates and tumors that recur after surgery and are **resistant to other** therapies, specifically radiotherapy
- Alpha DaRT to be evaluated as **a later line therapy**
- Tumor types we are targeting include **SCC, H&N SCC and prostate**

## Metastatic

- Alpha DaRT being evaluated for its potential to induce an **immune response** in **metastatic** tumors
- Alpha DaRT being evaluated **in combination with checkpoint inhibitors** as an adjuvant therapy
- Tumor types we are targeting include **liver, breast and H&N** (which includes lip, oral cavity, salivary glands, oropharynx & pharynx) cancers

## High Unmet Need

- Solid tumors that have **limited treatment options** with limited standard of care offering
- Alpha DaRT could potentially target **broad patient populations**
- Tumor types we are targeting include **GBM and pancreatic cancer**

# Initial Foray into Superficial Tumors

Alpha DaRT first tested in superficial tumors – tumors of the skin or head & neck, due to:

- Ease of access
- Straightforward control
- Ongoing monitoring
- Strong initial preclinical data in Squamous Cell Carcinoma (SCC)

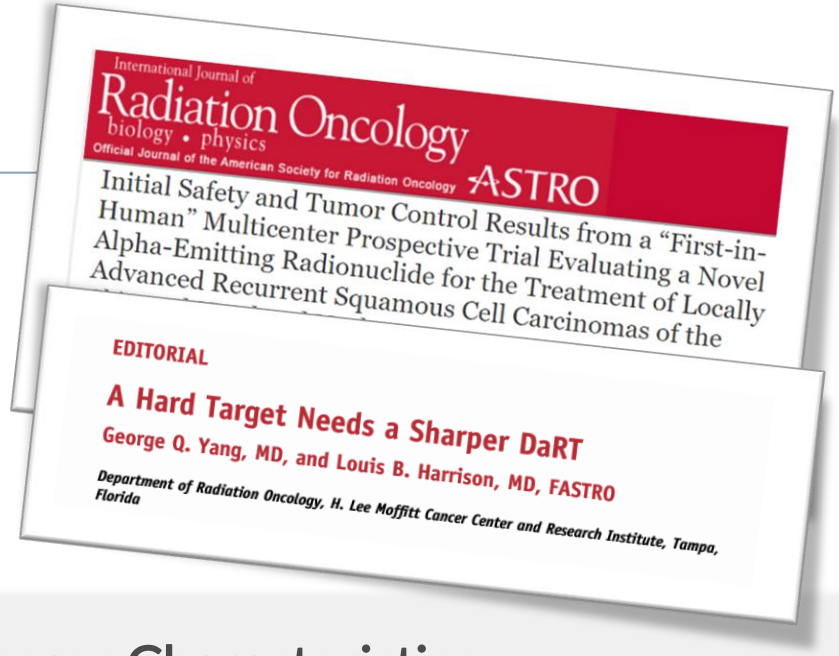
Treatment of hundreds of tumors to date:

- Indicated a mild safety profile
- Generated marketing authorization in Israel to treat SCC of the skin or oral cavity
- Allowed us to submit to PMDA in Japan for marketing authorization to treat recurrent head & neck cancer

Pivotal trial ("ReSTART") underway in the U.S. for recurrent cutaneous SCC

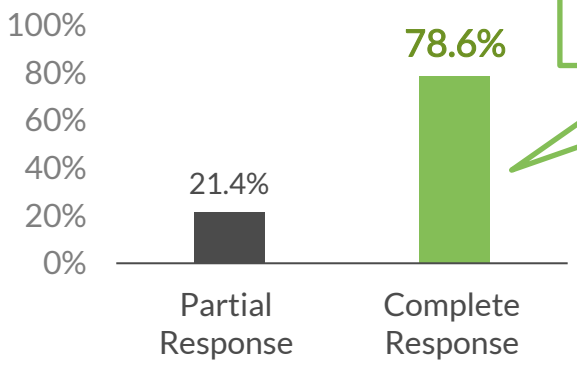
# First in Human Skin / Head & Neck SCC Study

- 100% overall response rate
- Durable responses observed
- Responses observed within days
- Well tolerated; no systemic toxicity observed

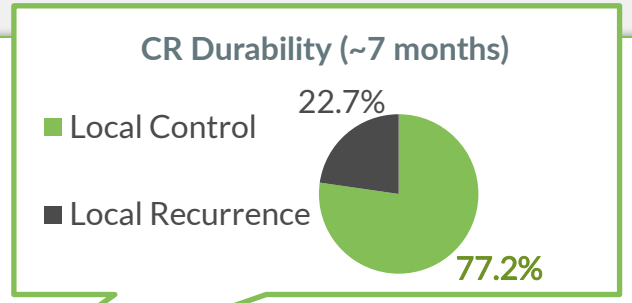



## Efficacy Results

### Overall Response (n=28)



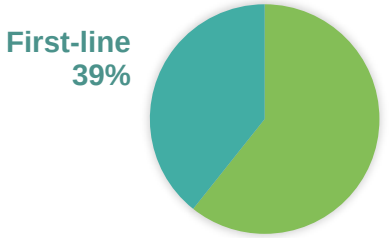

### CR Durability (~7 months)



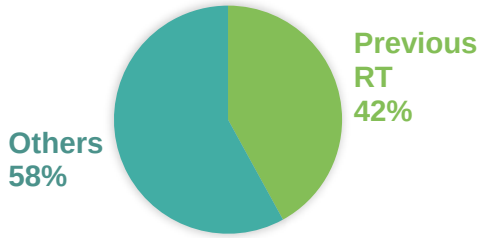

## Baseline Disease Characteristics

### Activity observed against radioresistant tumors (Patient median age = 80.5 years)

Previous Treatment[1]



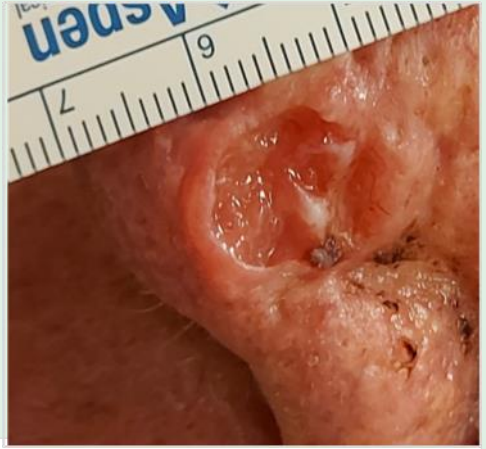

Previous Radiotherapy (RT)



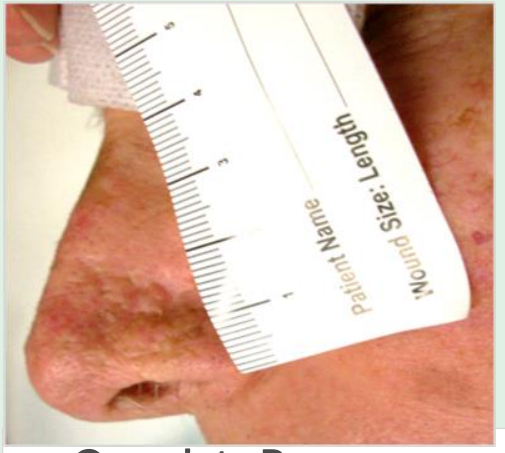

[1] Most patients (60.7%) had recurrent and previously treated disease by either surgery, prior external beam radiotherapy or both; 13 of 31 (42%) had received prior RT.

# U.S. Skin Cancer Pilot Study Leading to Pivotal Study


| U.S. Pilot Feasibility Study | |
|---|---|
| Locations | 5 centers – led by Memorial Sloan Kettering Cancer Center |
| # of Patients Treated | 10 |
| **Adverse Events** | **22 reported AE's, most were mild or moderate**<br>**No treatment-related serious AEs** |
| **Response Rate** | **100% Complete Response Rate** |



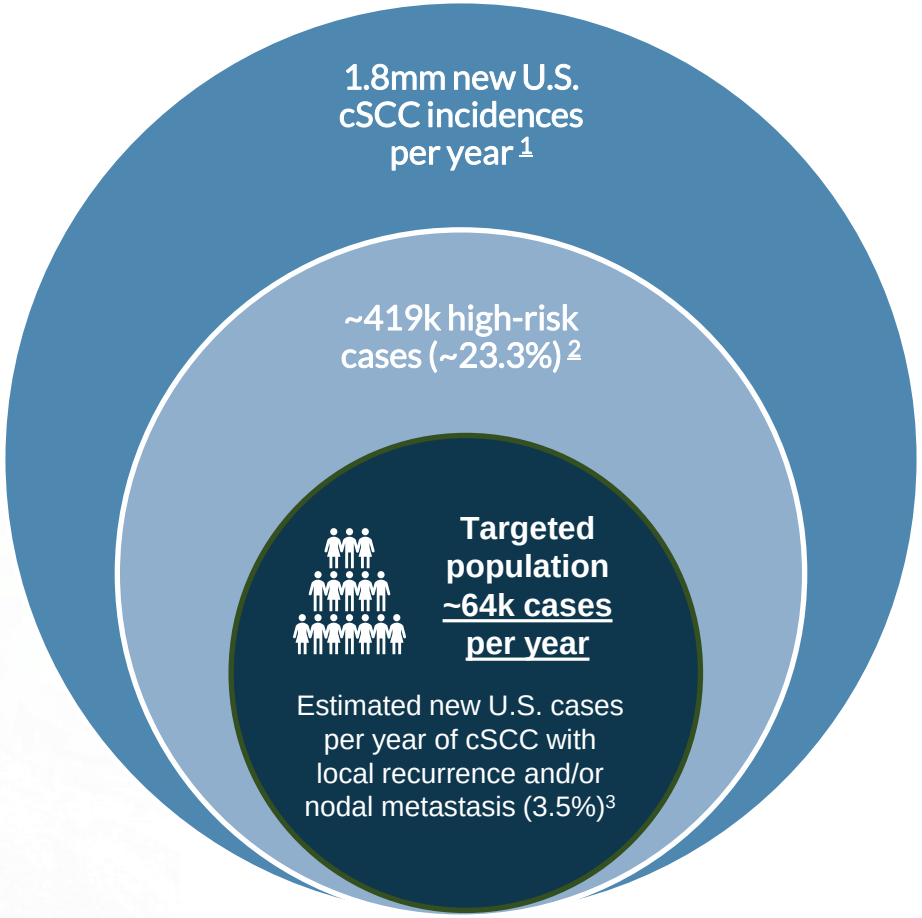
Simulation Day




Complete Response
12 weeks

| Multicenter Pivotal Recurrent SCC Study | |
|---|---|
| Locations | Multiple centers, including UCLA, Emory University, Mayo Clinic, etc. |
| # of Patients | 86 |
| Primary Objectives | Overall Response Rate, Durability of Response @ 6 months, adverse events assessment |
| Targeted Completion of Recruitment | Q3 2025 |

# Potential cSCC Patient Breakdown - Estimated U.S. Incidence




[1] https://www.skincancer.org/blog/our-new-approach-to-a-challenging-skin-cancer-statistic/

[2] Evaluation of American Joint Committee on Cancer, International Union Against Cancer, and Brigham and Women's Hospital Tumor Staging for Cutaneous Squamous Cell Carcinoma
*Pritesh S. Karia, Anokhi Jambusaria-Pahlajani, David P. Harrington, George F. Murphy, Abrar A. Qureshi, and Chrysalyne D. Schmults. Journal of Clinical Oncology 2014 32:4, 327-334*

[3] Factors Predictive of Recurrence and Death From Cutaneous Squamous Cell Carcinoma: A 10-Year, Single-Institution Cohort Study
*Schmults CD, Karia PS, Carter JB, Han J, Qureshi AA. JAMA Dermatol. 2013;149(5):541–547. doi:10.1001/jamadermatol.2013.2139*

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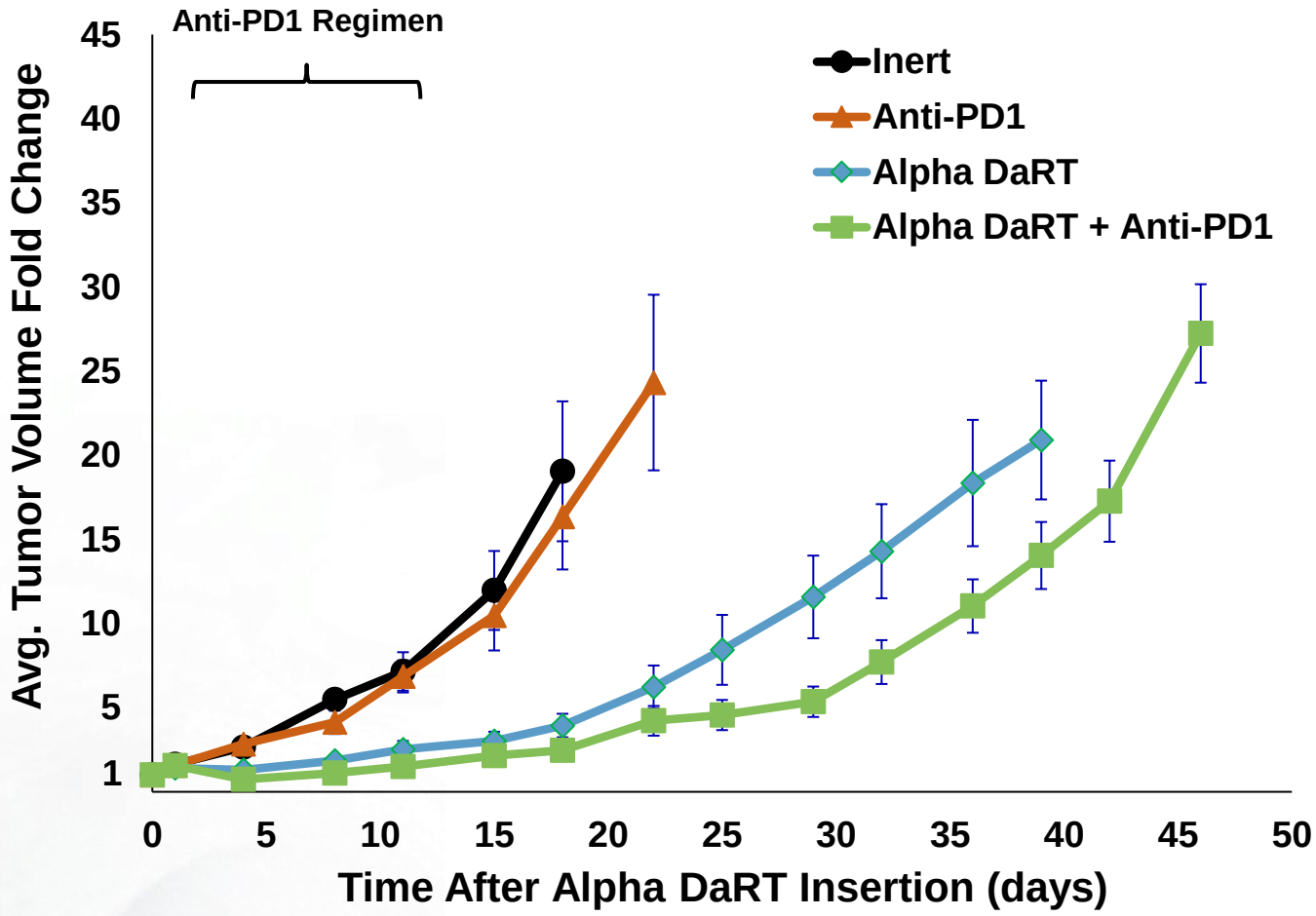
# Alpha DaRT Elicits Effect from anti-PD1 in SCC Mouse Model (SQ2)

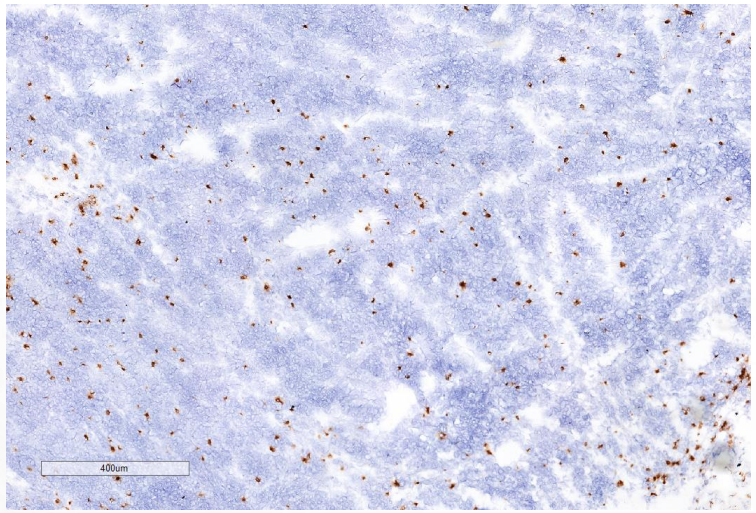
While mice with the SQ2 squamous cell carcinoma model showed little to no effect when treated with a murine anti-PD1 agent, the observed effect was larger for the combination with Alpha DaRT than for Alpha DaRT on its own



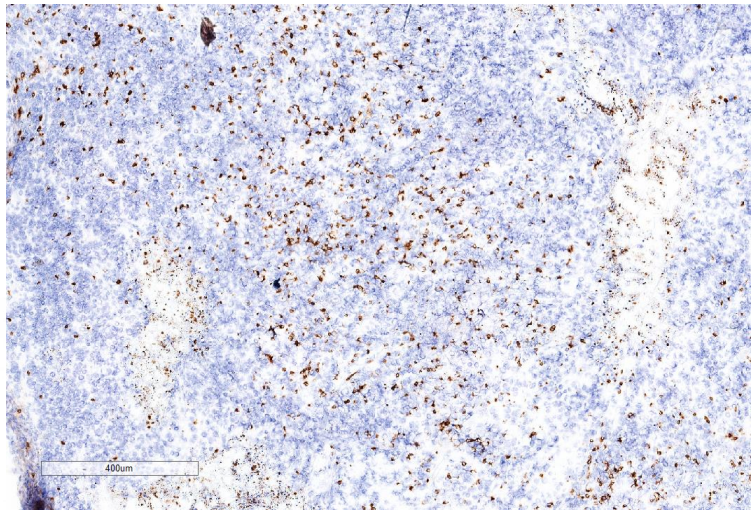
# Alpha DaRT Increased Infiltration of CD3+ T-cells Into the Tumor

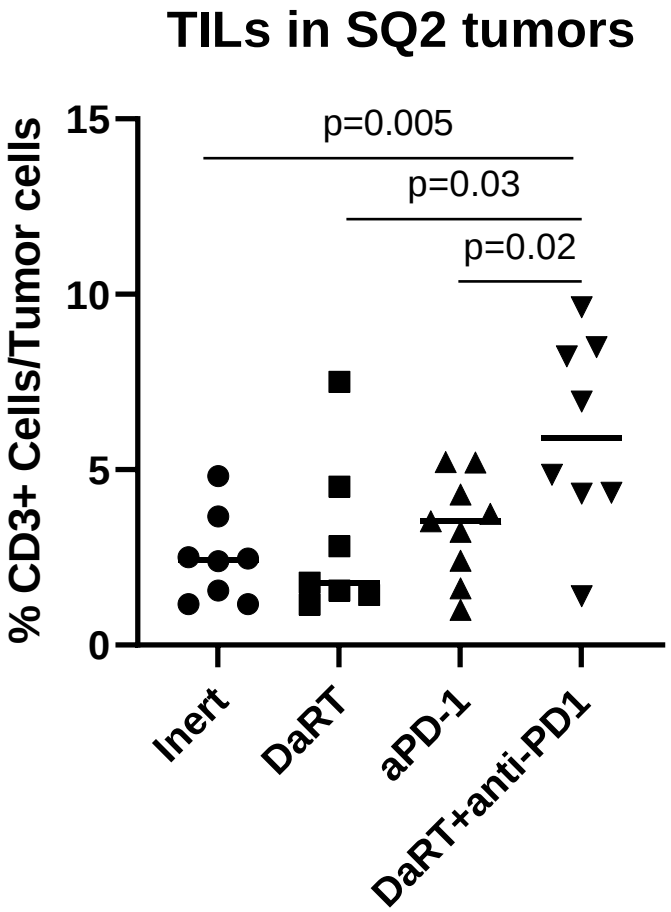
The combination of Alpha DaRT with anti-PD1 demonstrated the highest level of TILs in mice with SQ2 SCC tumors, suggesting potential to potentiate the checkpoint blockade

anti PD-1



Alpha DaRT + anti PD-1

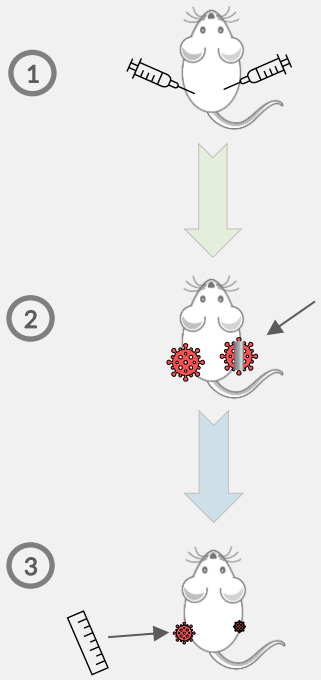




# Immune Response Observed Even in "Cold" Pancreatic Tumor Model

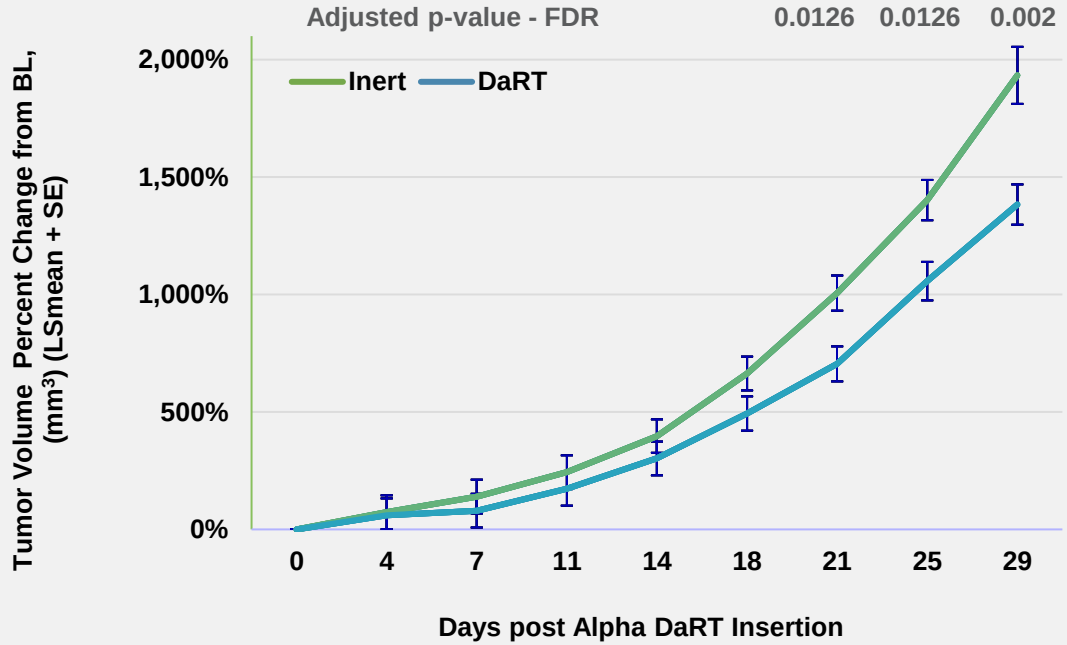
## When treating one pancreatic cancer tumor with Alpha DaRT sources instead of inert sources, a statistically significant decline in secondary tumor growth rate was seen

### Experiment Design



1. Intracutaneous inoculation of two Panc02 or KPC tumors
2. Insertion of Alpha DaRT sources into primary tumor after 9-10 days
3. Measurement of the secondary tumor volume over time

### Secondary Tumor Growth (Untreated)




**Similar results also observed when examining the Panc02 and KPC tumor models individually rather than grouped into a larger analysis.**

The percent change in tumor volume over time was assessed and compared between the groups with Repeated Measures ANOVA models, applying a False Detection Rate (FDR) correction for multiple comparisons.

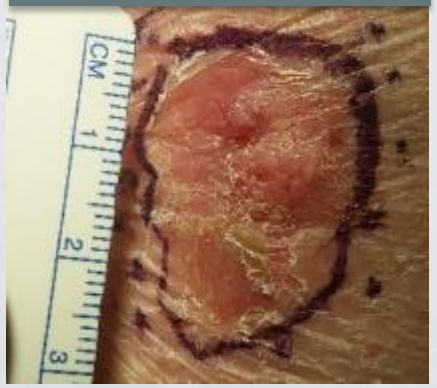
# Case Study: Potential Systemic Immune Effect Observed in One cSCC Patient Where a Second, Untreated Lesion Manifested CR


Complete Response + Potential Systemic Immune Effect

## Treated Tumor

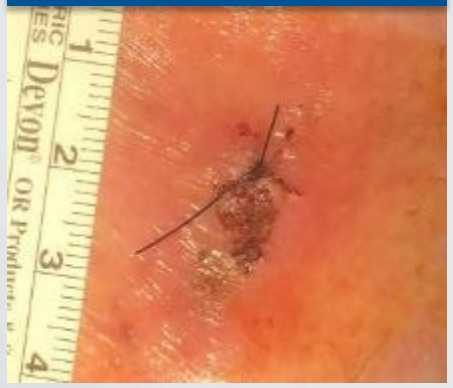
Before

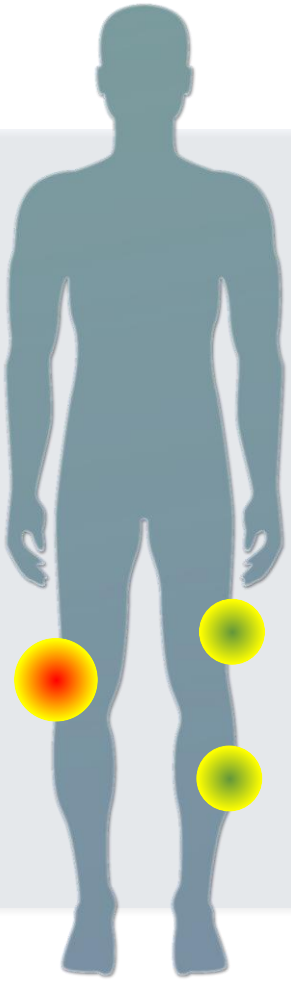
30-Nov-17



After

29-Dec-17

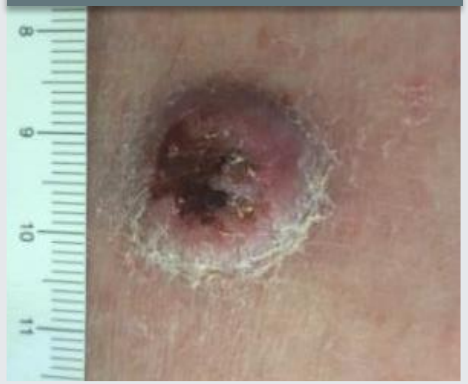




## Untreated Tumors

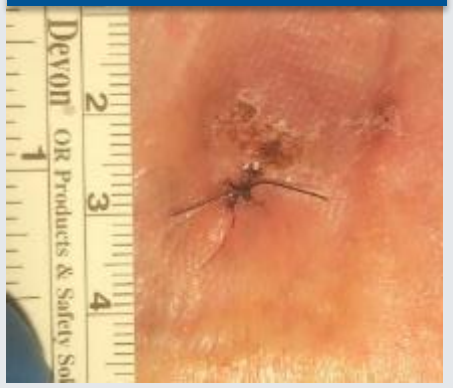
Before

30-Nov-17



After

29-Dec-17



# Outline of Checkpoint Inhibitor Combination Trial – CTP-HNCPI-00

## Key Eligibility Criteria

Recurrent unresectable or metastatic head and neck squamous cell carcinoma (like KEYNOTE-048)

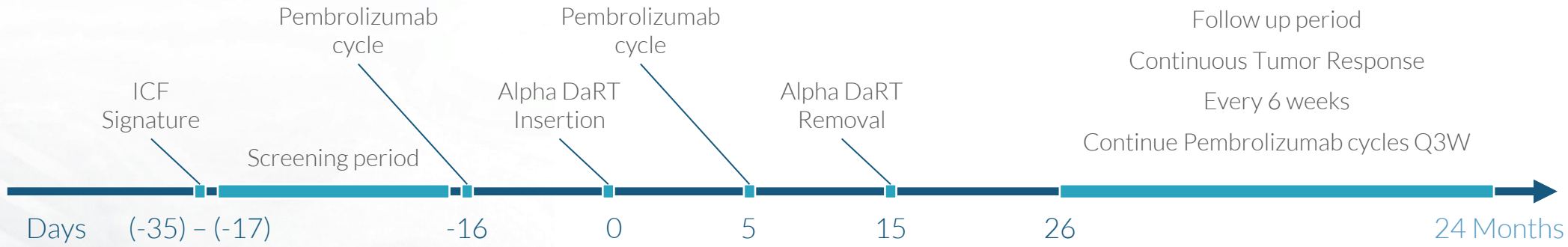
No previous treatment for metastatic disease

## Benchmark Comparator

KEYNOTE-048: Benchmark comparator data for 1L Pembrolizumab in patients with recurrent or metastatic HNSCC[1]

| Population | Benchmark Regimen | Systemic ORR | Systemic CR % |
|---|---|---|---|
| PD-L1 CPS ≥ 20 | Pembrolizumab Alone | 23% | 8% |
| PD-L1 CPS ≥ 1 | Pembrolizumab Alone | 19% | 5% |
| Total population | Pembrolizumab Alone | 17% | 5% |

## Treatment Regimen




[1]*Benchmark data provided for illustrative purposes only. Not a head-to-head trial*

*Source: Burtness, B. et al (2019). Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. The Lancet. doi:10.1016/s0140-6736(19)32591-7*

# Early Interim Data Show Strong Systemic Responses

- As of January 9, 2025, eight patients were treated with Alpha DaRT and pembrolizumab in the study
- Baseline characteristics:
  - 3 female / 5 male
  - Mean age of 73 years (range 61-96)
  - 6 mHNSCC / 2 IaHNSCC
- Patients received an average of 4 cycles of pembrolizumab (range 2-9)
- Systemic responses observed:
  - Three complete responses
  - Three partial responses
  - Two patients died prior to evaluation
- Only two Alpha DaRT-related adverse events, both were Grade 1 (mild)

**37.5%**
**Systemic Complete Responses**

**75%**
**Systemic Objective Response Rate (CR + PR)**

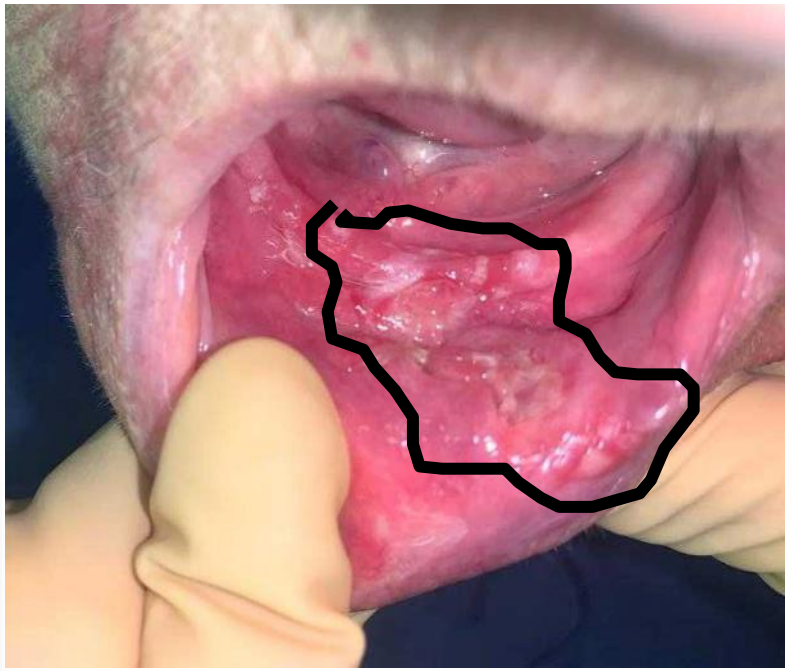
**No Related SAEs**

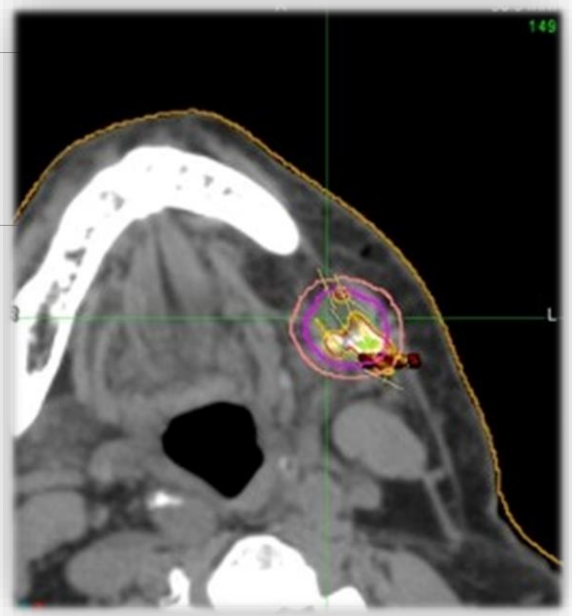
HNCPI-00-01-003

# Pembrolizumab Combination Case Study

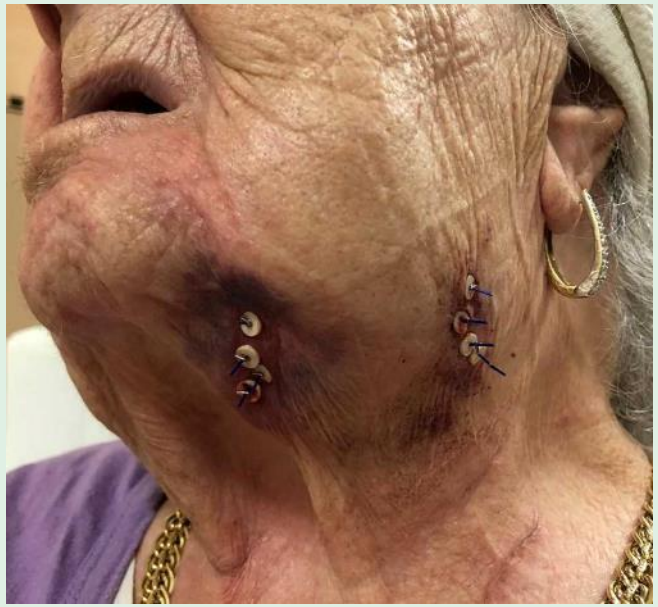
# Case Background – HNCPI-00-01-003

| | |
|---|---|
| Age | 96 |
| Sex | Female |
| Tumor Type | SCC |
| Date of First Diagnosis | Jul-2022 |
| Location | Alveolar ridge & lip plus dermal involvement |
| Prior Treatments | None |
| Medical Background | • Cardio<br>• Dementia<br>• ECOG3 |
| Cancer Stage | • Stage IV<br>• T2N1M1 |

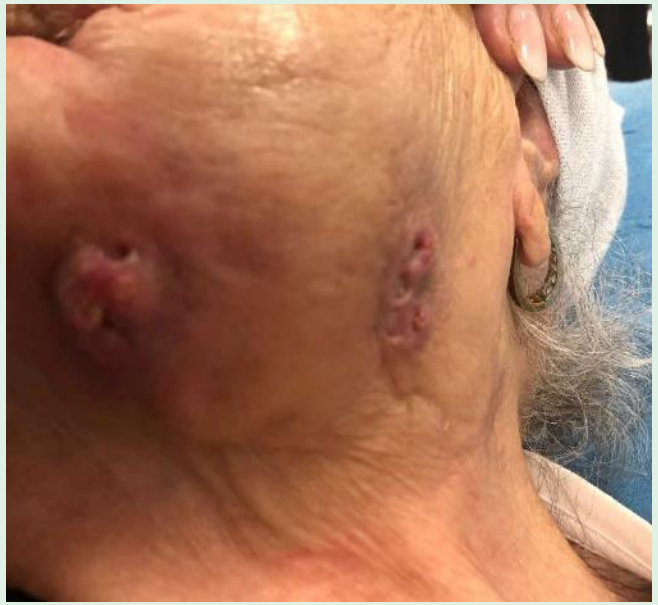




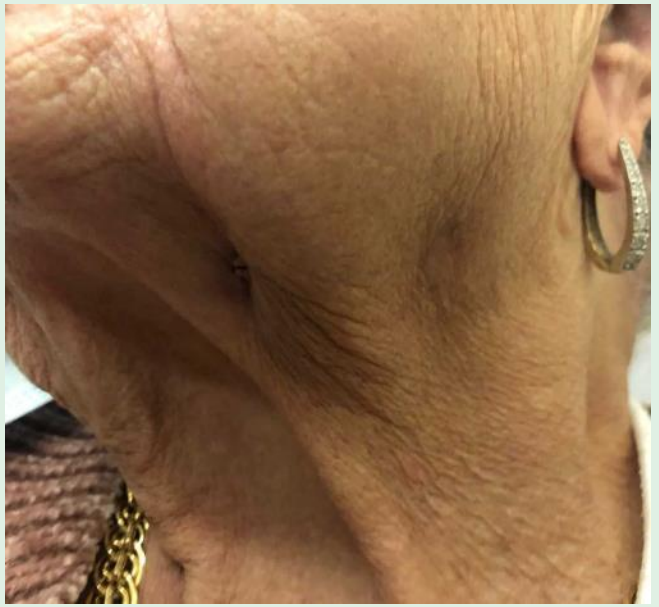
# Alpha DaRT Treatment



**Alpha DaRT Insertion**
Sept-2022



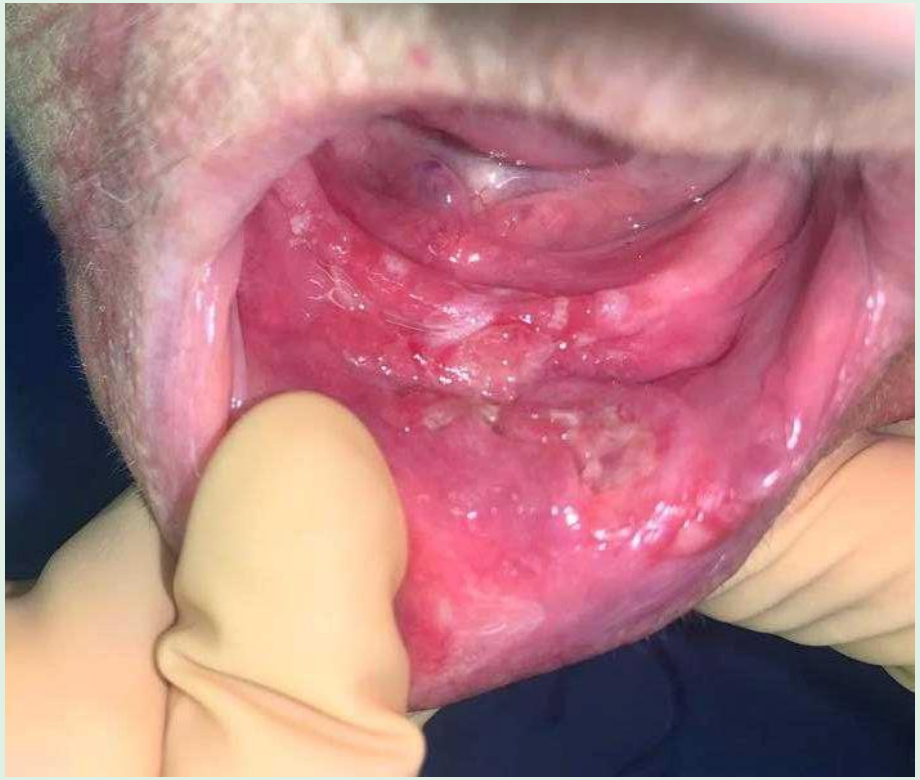
**After Alpha DaRT Removal**
Oct-2022



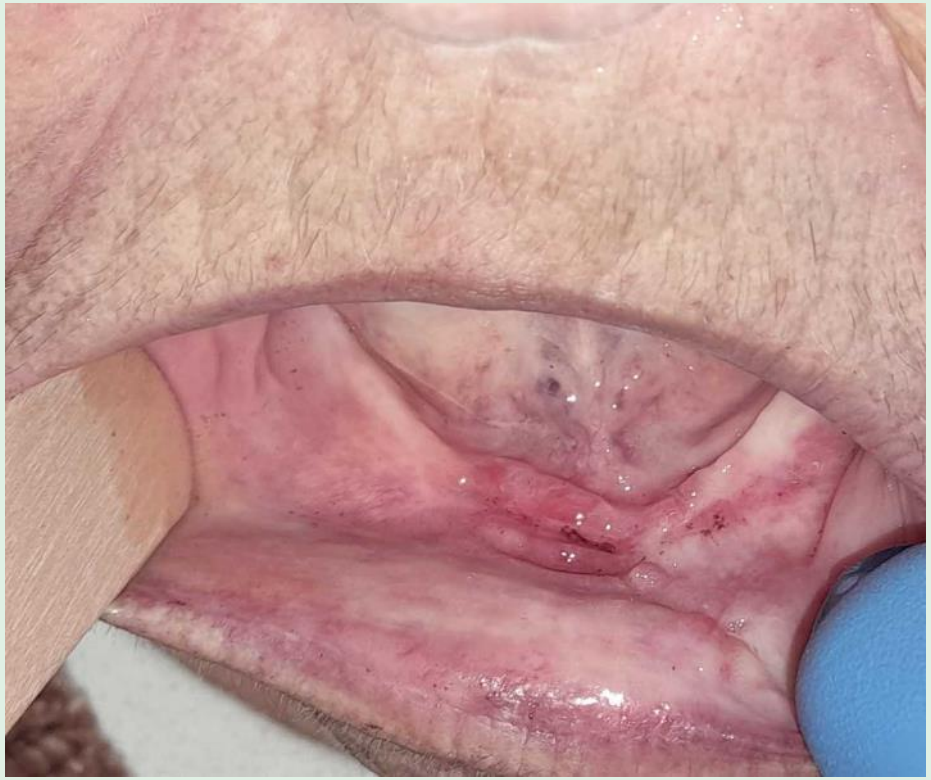
**Follow-Up**

Jan-2023

# Clinical Follow-Up

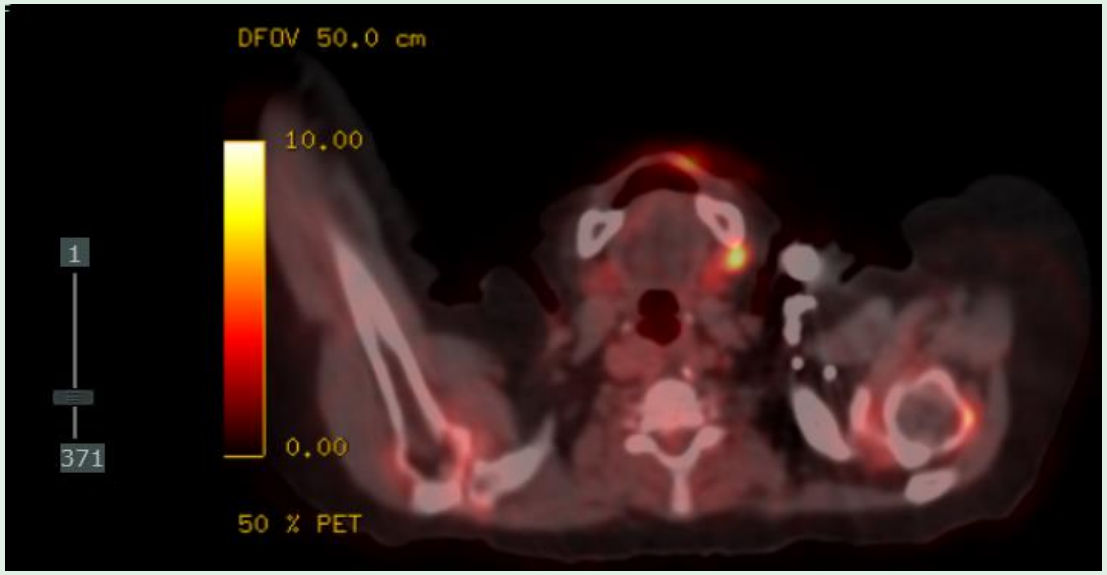


Pre-Treatment

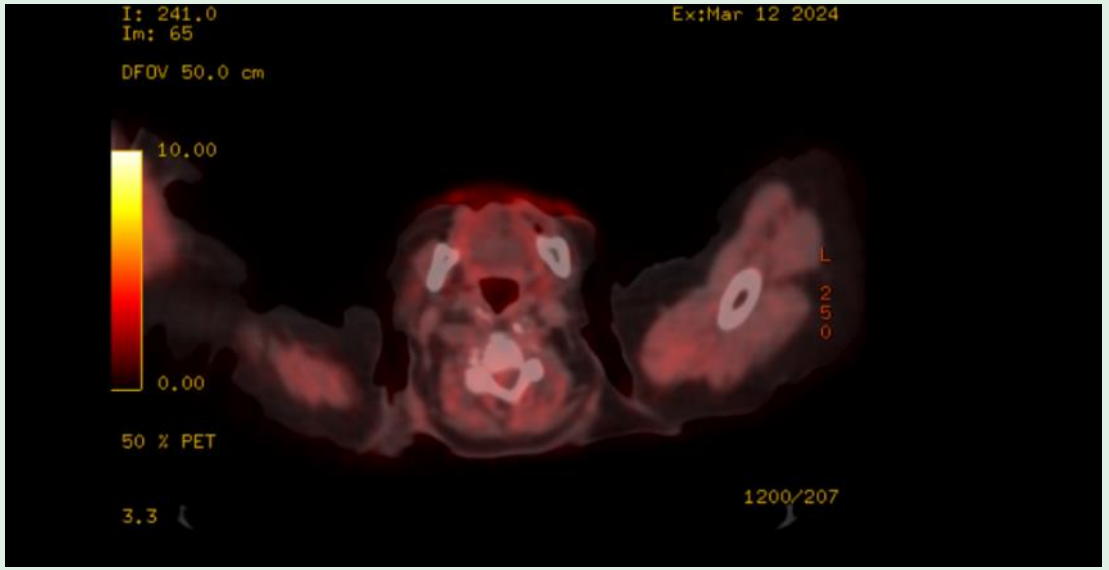


Nine Weeks Post Treatment

# PET Follow-Up




Pre-Treatment
Aug-2022




Post-Treatment
Mar-2024

# Patient Status

- Patient stopped Pembrolizumab after 12 months
- Patient still alive with no evidence of disease at October 2024 followup

# Therapeutic Focus

**We are focused on delivering solutions to three markets that we believe would be best served by the unique characteristics of the Alpha DaRT**

## Localized & Unresectable

- Localized tumors that are not surgical candidates and tumors that recur after surgery and are resistant to other therapies, specifically radiotherapy
- Alpha DaRT to be evaluated as a later line therapy
- Tumor types we are targeting include SCC, H&N SCC and prostate

## Metastatic

- Alpha DaRT being evaluated for its potential to induce an immune response in metastatic tumors
- Alpha DaRT being evaluated in combination with checkpoint inhibitors as an adjuvant therapy
- Tumor types we are targeting include liver, breast and H&N (which includes lip, oral cavity, salivary glands, oropharynx & pharynx) cancers

## High Unmet Need

- Solid tumors that have limited treatment options with limited standard of care offering
- Alpha DaRT could potentially target broad patient populations
- Tumor types we are targeting include GBM and pancreatic cancer

# Focus on Internal Organ Treatments

We continue to make progress across internal organ programs, with trials underway in multiple targeted indications and others in various stages of planning and start-up

## Internal Organs in Focus

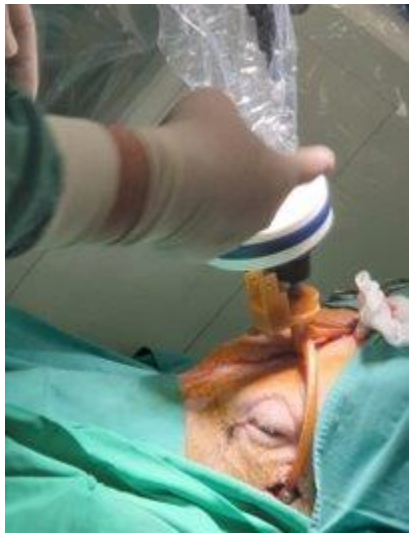
- Pancreas – clinical trial underway
- Liver – clinical trial underway
- Lung – clinical trial underway
- Prostate – clinical trial underway
- Brain – GBM + Brain Mets
- Breast
- Rectum

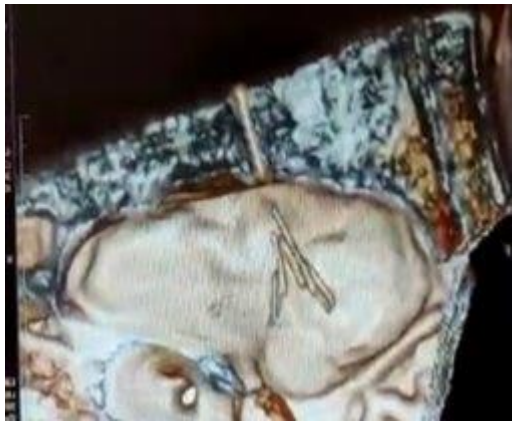
CHUM
Centre hospitalier de l'Université de Montréal

HADASSAH UNIVERSITY MEDICAL CENTER
Founded by Hadassah, the Women's Zionist Organization of America

HGJ | JGH

RAMBAM Health Care Campus





# Interim Pancreatic Cancer Results - Overview of Trial Design

Three trials treating pancreatic cancer patients in parallel:

- CTP-PANC-101 monotherapy treatment at 2 sites in Montreal, Canada – up to 37 patients total
- CTP-PANC-02 monotherapy treatment at 1 site in Jerusalem, Israel – up to 15 patients total
- CTP-ALL-00 flexible basket trial at 1 site in Jerusalem, Israel – no specified limit on number of patients

Following initial results, there are some situations where chemotherapy has been used in the first two trials

- CTP-PANC-101 allows chemotherapy 30 days after Alpha DaRT treatment
- CTP-PANC-02 was modified to allow concomitant chemotherapy

Therefore, after initially embarking on monotherapy exploration, **a small number of patients from all three trials have received chemotherapy treatment alongside or following Alpha DaRT treatment**

Due to the exploratory nature of the trials, they do not focus on a specific patient sub-population but rather a broad mix of patients with non-resectable pancreatic cancer

# High Disease Control Rate Observed

Among the 41 patients treated, 33 had a measured objective response, with 5 patients awaiting response evaluation and 3 who discontinued prior to evaluation. Results are presented below using Best Overall Response (BOR) for those with a measured response.

| | | |
|---|---|---|
| **Including first two patients (heavily underdosed / feasibility only)** | **18%** Objective Response Rate (CR + PR) | **91%** Disease Control Rate (CR + PR + SD) |
| **Excluding first two patients (heavily underdosed / feasibility only)** | **19%** Objective Response Rate (CR + PR) | **97%** Disease Control Rate (CR + PR + SD) |

*Note: Results as of January 8, 2025*

# Highlights of Overall Survival (OS) Data

## Key Caveats:

- The data are still **relatively immature, but ongoing**
- Trial designs were **focused on feasibility and safety**, without the frequent monitoring visits common in studies focused on precise measurement of survival
- Five patients treated since Nov 25, 2024, and three patients who exited the study very shortly after treatment, in all cases with insufficient time to reach objective response measurement, were excluded from OS analysis for lack of data maturity
  - Therefore, a total of n = 33 patients are evaluated for OS using Kaplan-Meier analysis

| Population | OS Since Diagnosis / Initiation of Last Chemotherapy (mo) | OS Since Alpha DaRT Treatment (mo) |
|---|---|---|
| Overall Population (n=33) | 18.6 | 10.9 |

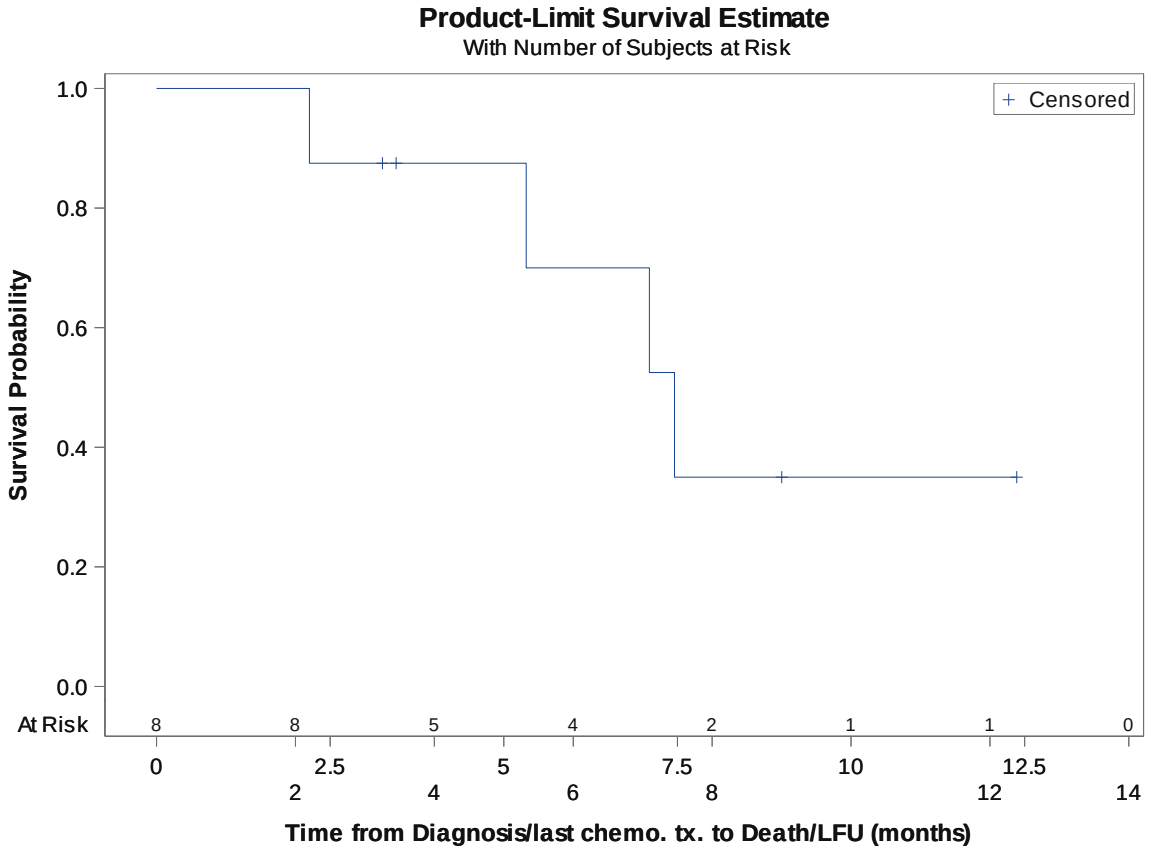
**Of n=33 patients analyzed, 13 have died**
**The remaining 20 (and the five newer patients) remain alive**

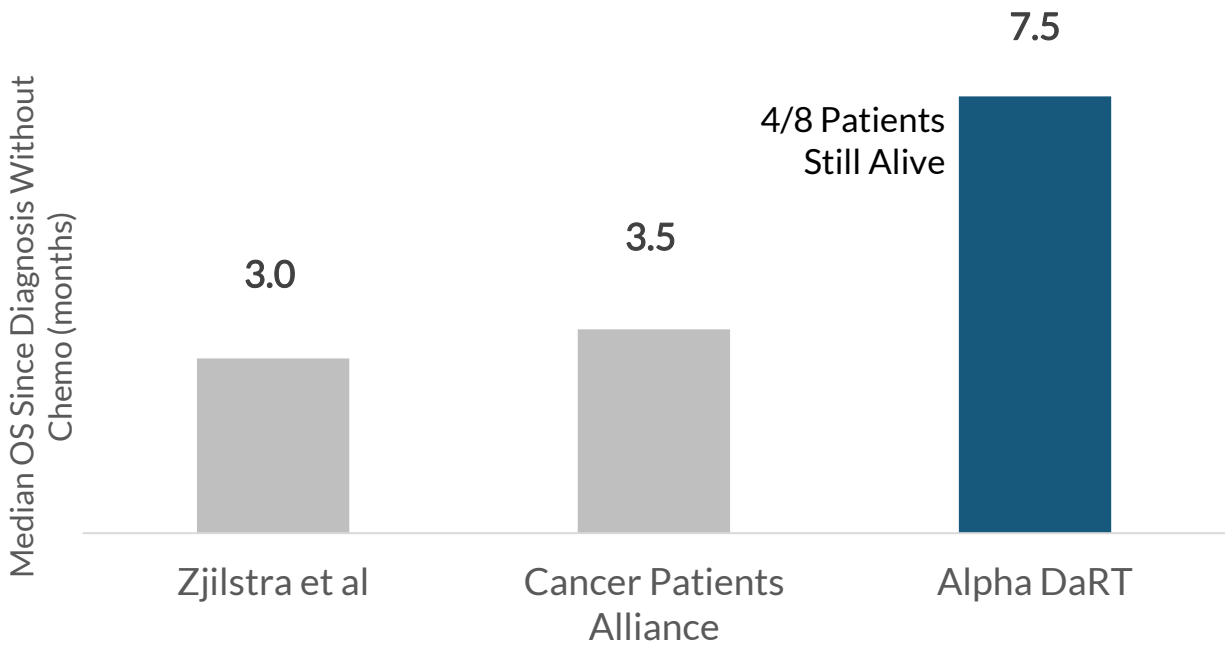
In light of the **heterogeneity of the population**, we conducted ad-hoc analyses **of key sub-groups** to offer context vs. expected OS for each group

*Note: Results as of January 8, 2025*

# Analysis of Overall Survival in Key Sub-Populations (1/3)

## Newly Diagnosed / Not Eligible for Chemotherapy (n=8)

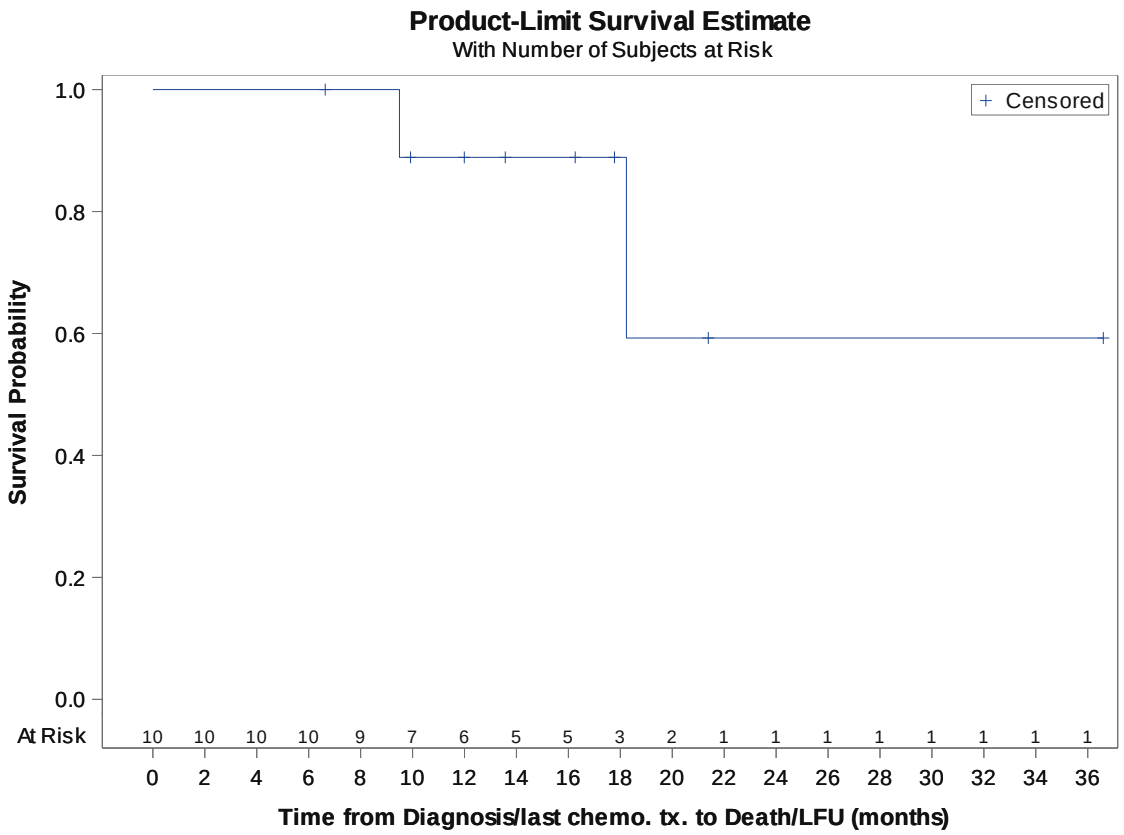


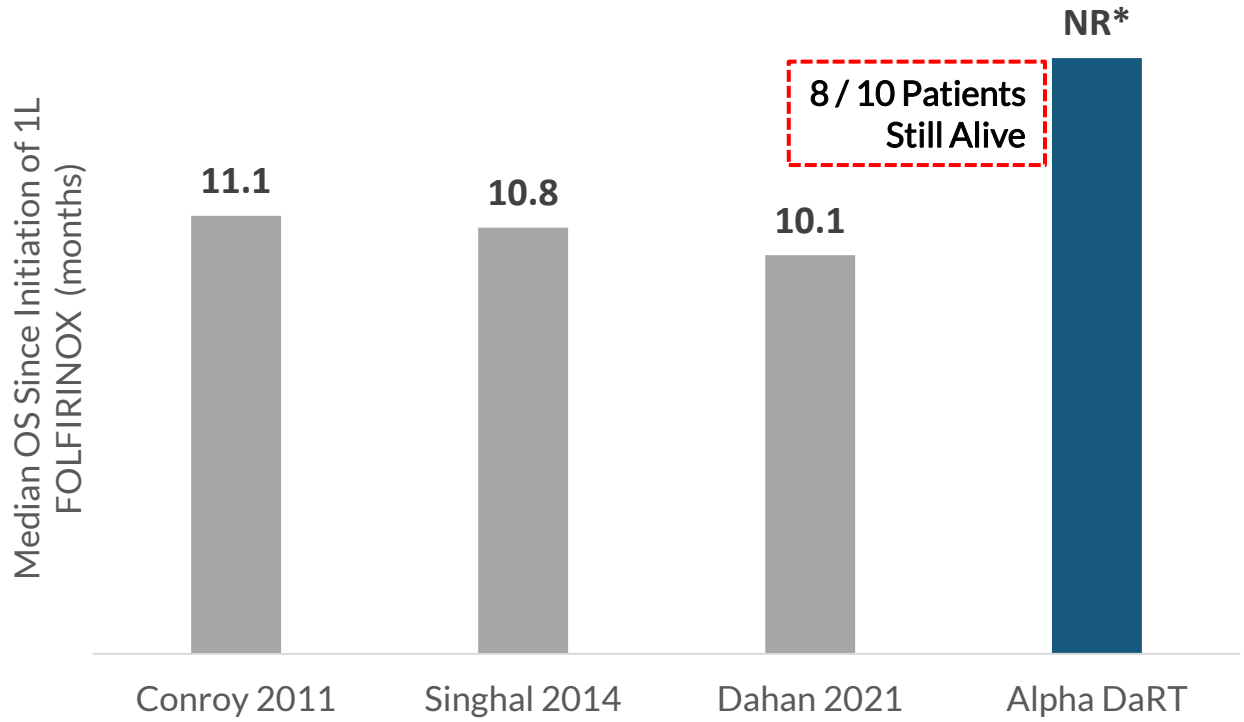




*Note: Median follow-up in Alpha DaRT group of 6.3 months*
*Results as of January 8, 2025*
*For Illustrative Purposes Only - no head-to-head clinical study has been conducted comparing Alpha DaRT to other products or candidates. Differences exist between trial designs, subject characteristics and other factors, and caution should be exercised when comparing data across unrelated studies*
*Sources:*
*Zijlstra, M. et al (2018). Patient characteristics and treatment considerations in pancreatic cancer: a population based study in the Netherlands. https://doi.org/10.1080/0284186X.2018.1470330*
*https://pancreatica.org/pancreatic-cancer/pancreatic-cancer-prognosis/*

# Analysis of Overall Survival in Key Sub-Populations (2/3)

## Metastatic (Stage IV) Patients After 1L FOLFIRINOX (n=10)




** Median Kaplan-Meier estimate was not reached (NR); median follow-up time was 15.1 months*

*For Illustrative Purposes Only - no head-to-head clinical study has been conducted comparing Alpha DaRT to other products or candidates. Differences exist between trial designs, subject characteristics and other factors, and caution should be exercised when comparing data across unrelated studies*

*Note: Results as of January 8, 2025*

*Sources:*

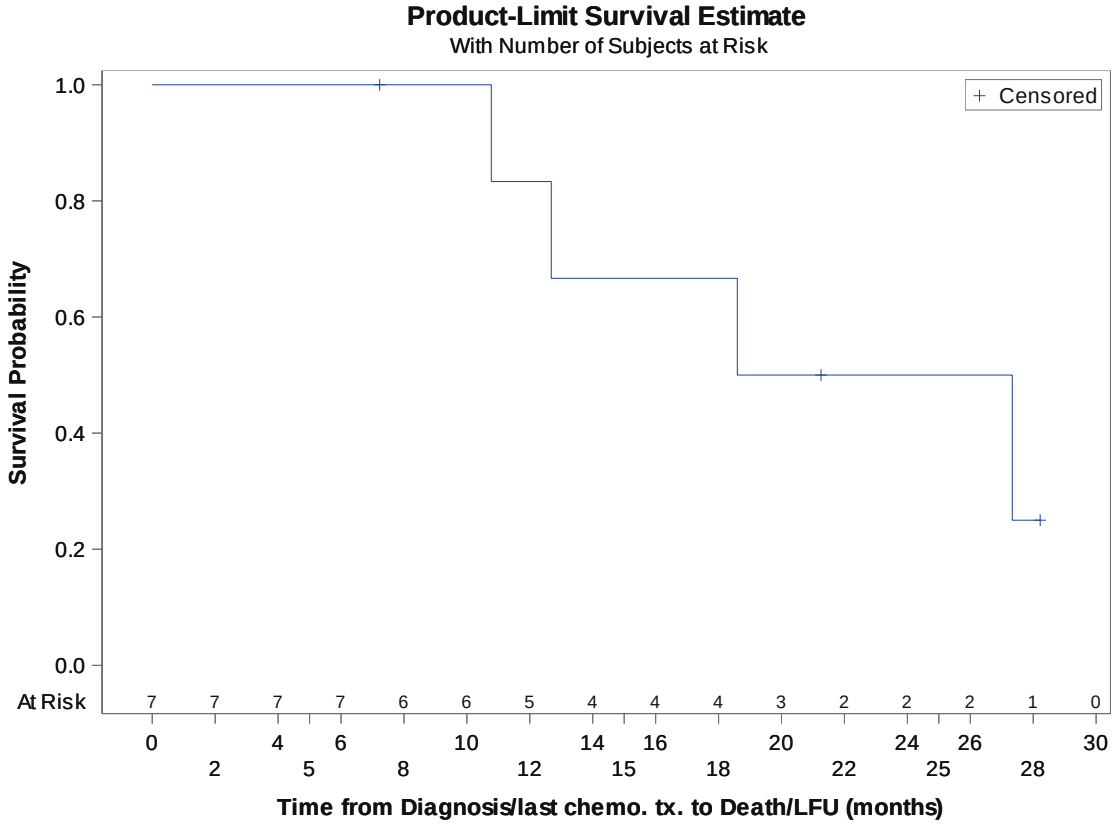
*Thierry Conroy et al., FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer. New England Journal of Medicine (2011). DOI: 10.1056/NEJMoa1011923*

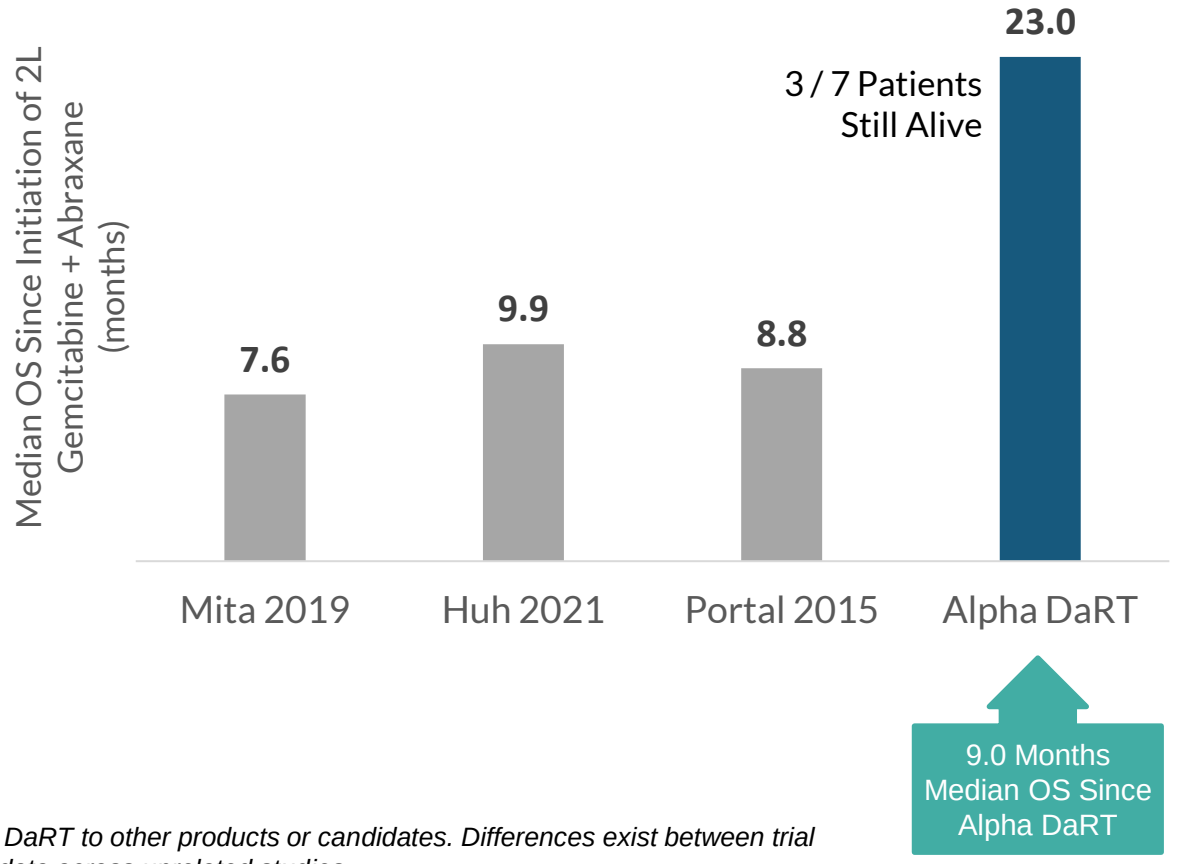
*Singhal MK, et al. A phase III trial comparing FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. Ann Oncol. 2014;25(suppl 4):iv210–53.*

*Laetitia Dahan et al., Randomized Phase II Trial Evaluating Two Sequential Treatments in First Line of Metastatic Pancreatic Cancer: Results of the PANOPTIMOX-PRODIGE 35 Trial. JCO 39, 3242-3250(2021). DOI:10.1200/JCO.20.03329*

# Analysis of Overall Survival in Key Sub-Populations (3/3)

## Progressed After 2L Gemcitabine-Abraxane (n=7)




*Note: Median follow-up in Alpha DaRT group of 18.9 months*

*For Illustrative Purposes Only - no head-to-head clinical study has been conducted comparing Alpha DaRT to other products or candidates. Differences exist between trial designs, subject characteristics and other factors, and caution should be exercised when comparing data across unrelated studies*

*Note: Results as of January 8, 2025*

*Source:*

*Mita N, Iwashita T, Uemura S, Yoshida K, Iwasa Y, Ando N, Iwata K, Okuno M, Mukai T, Shimizu M. Second-Line Gemcitabine Plus Nab-Paclitaxel for Patients with Unresectable Advanced Pancreatic Cancer after First-Line FOLFIRINOX Failure. J Clin Med. 2019 May 29;8(6):761. doi: 10.3390/jcm8060761. PMID: 31146420; PMCID: PMC6616879*

*Huh G, Lee HS, Choi JH, Lee SH, Paik WH, Ryu JK, Kim YT, Bang S, Lee ES. Gemcitabine plus Nab-paclitaxel as a second-line treatment following FOLFIRINOX failure in advanced pancreatic cancer: a multicenter, single-arm, open-label, phase 2 trial. Ther Adv Med Oncol. 2021 Nov 10;13:17588359211056179. doi: 10.1177/17588359211056179. PMID: 34790261; PMCID: PMC8591648.*

*Portal A et al. Nab-paclitaxel plus gemcitabine for metastatic pancreatic adenocarcinoma after Folfirinox failure: an AGEO prospective multicentre cohort. Br J Cancer. 2015 Sep 29;113(7):989-95. doi: 10.1038/bjc.2015.328. Epub 2015 Sep 15. PMID: 26372701; PMCID: PMC4651133.*

# Breakdown of Pancreatic Cancer Incidence by Stage

## FACS National Cancer Database - 2008-2017 All Types Hospitals in All States

There are over half a million new cases of pancreatic cancer per year. Approx. 67k of them are in the U.S.

Focus Area: 87%

| Stage | I | II | III | IV |
|---|---|---|---|---|
| | Resectable | Borderline Resectable | Locally Advanced | Metastasized |
| Percent of Total | 13% | 29% | 10% | 48% |

87% of pancreatic cancer cases (approx. 59k in the US) are not eligible for surgical resection

*Note: Excludes cancers of stage "unknown" or "N/A" - data from 1400 Hospitals*
*Source:* https://www.facs.org/media/ztllhkfu/cancer-cases-reported-to-the-ncdb-by-tumor-type-and-ajcc-stage.pdf
https://gco.iarc.who.int/media/globocan/factsheets/cancers/13-pancreas-fact-sheet.pdf
https://www.cancer.org/cancer/types/pancreatic-cancer/about/key-statistics.html

# Pancreatic Cancer Clinical Trial: USA Pilot

N=15

Newly Diagnosed
**Locally Advanced Pancreatic Cancer**

N=15

Newly Diagnosed
**Metastatic Pancreatic Cancer**

**AlphaDaRT**
**Insertion**
(During Cycles 1-4)

8-12 cycles of **mFOLFIRINOX**

**1**

**Primary Endpoint:**

Incidence of Treatment-Emergent Adverse Events

**2**

**Secondary Endpoints:**

Overall Survival
Progression-Free Survival
Pain Improvement
Surgical Resectability (LA cohort only)

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## High Unmet Need

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- Alpha DaRT could potentially target broad patient populations
- Tumor types we are targeting include GBM and pancreatic cancer

# Anticipated Milestones

| Geography | Target Indication | H1 2025 | H2 2025 | H1 2026 |
|---|---|---|---|---|
| United States | Recurrent Cutaneous SCC | | Completion of multi-center pivotal trial recruitment | Data Readout + Potential FDA submission |
| | Pancreatic Cancer | First Patient in Pilot Study | Complete Recruitment in Pilot Study | Readout from Pilot Study |
| | Recurrent GBM | Early Feasibility Study IDE | | Readout from Early Feasibility Study |
| Israel | Brain Cancer (GBM or Metastases) | Targeted first patient treated | | |
| Europe | Pancreatic Cancer (French Multicenter) | | Targeted first patient treated | |
| Japan | Head & Neck Cancer | PMDA Response | | |

Clinical | Regulatory

# Development Pipeline

- FDA Breakthrough Device Designation received for certain uses in skin cancer and GBM

| Geography | Target Indication | Pre-Clinical Research | Feasibility Trial | Pivotal Trial | Marketing Authorization | Anticipated Milestones |
|---|---|---|---|---|---|---|
| North America | Rec. Cutaneous SCC | | U.S. | | | • Complete patient recruitment in Q3 2025 |
| | Pancreatic Cancer | | U.S. | | | • IDE received, targeting first patient Q2 2025 |
| | Recurrent GBM | | U.S. | | | • Targeting IDE for early feasibility study in Q2 2025 |
| | Pancreatic Cancer | | Canada | | | |
| | Liver Metastases | | Canada | | | |
| Israel | Skin & Oral SCC | | | | | |
| | All Skin & Oral Cancers | | | | | |
| | Ia/mHNSCC (combo with pembrolizumab) | | | | | • Exploring U.S. IDE submission for similar study |
| | Pancreatic Cancer | | | | | |
| | Lung Cancer | | | | | |
| | Brain (GBM + mets) | | | | | • Targeting first patient in H1 2025 |
| | Prostate Cancer | | | | | |
| Europe | Skin Cancers | | | | | |
| | Vulvar SCC | | | | | |
| | Pancreatic Cancer | | | | | • Targeting first patient in H2 2025 in French trial |
| Japan | Head & Neck Cancer | | | | | • Targeting PMDA response in Q2 2025 |

# Financial Position

- Public Since Mar-2022 (NASDAQ:DRTS)
- $68.4mm in Cash & Deposits at Q3 2024
- 2+ Years of Cash Runway

# AlphaTAU

## Saving Lives Globally