(NASDAQ:DRTS)

Investor Presentation

Mar 11, 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

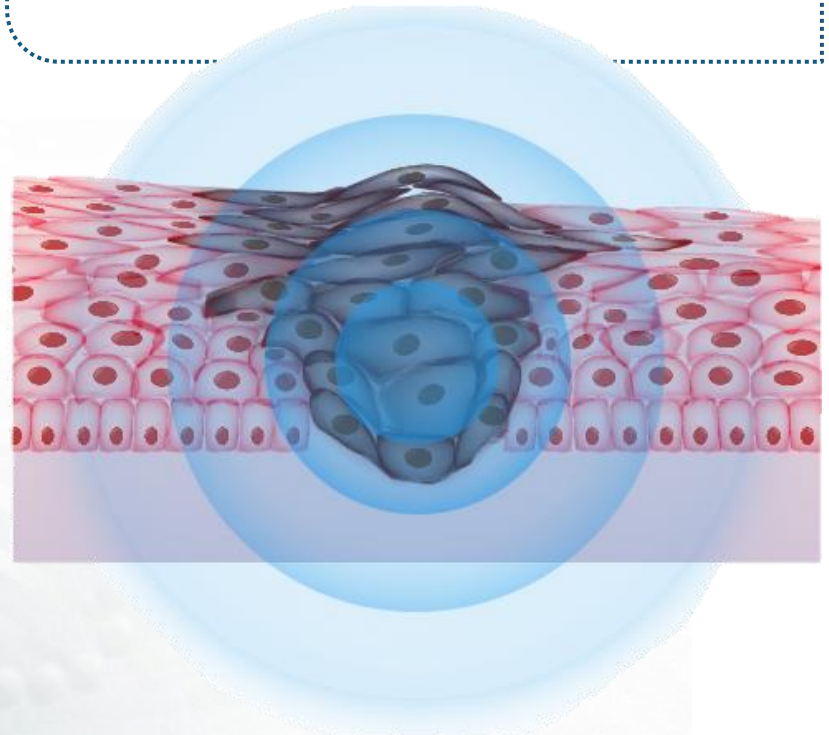
- Broad potential applicability for local tumor control, together with signs of compelling immuno-stimulatory activity
- Platform technology has the potential to be utilized alone or synergistically with other cancer treatment modalities
- Milestones and data from multiple clinical trials in various 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

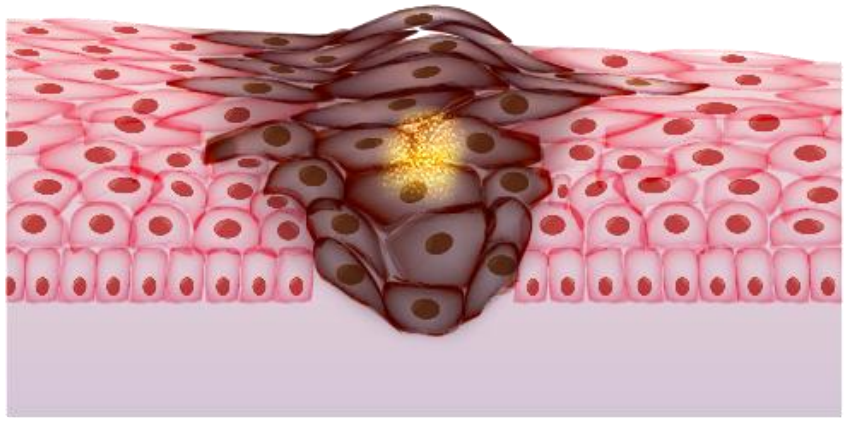
Beta/Gamma Radiation

Long therapeutic range with risk to surrounding organs



Alpha Radiation

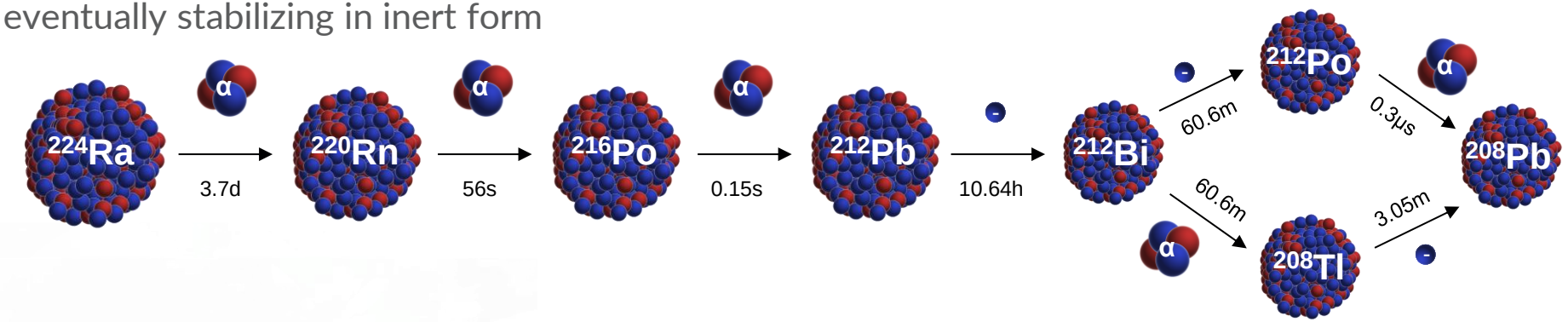
Short range in tissue limits damage to surrounding organs but also limits coverage



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

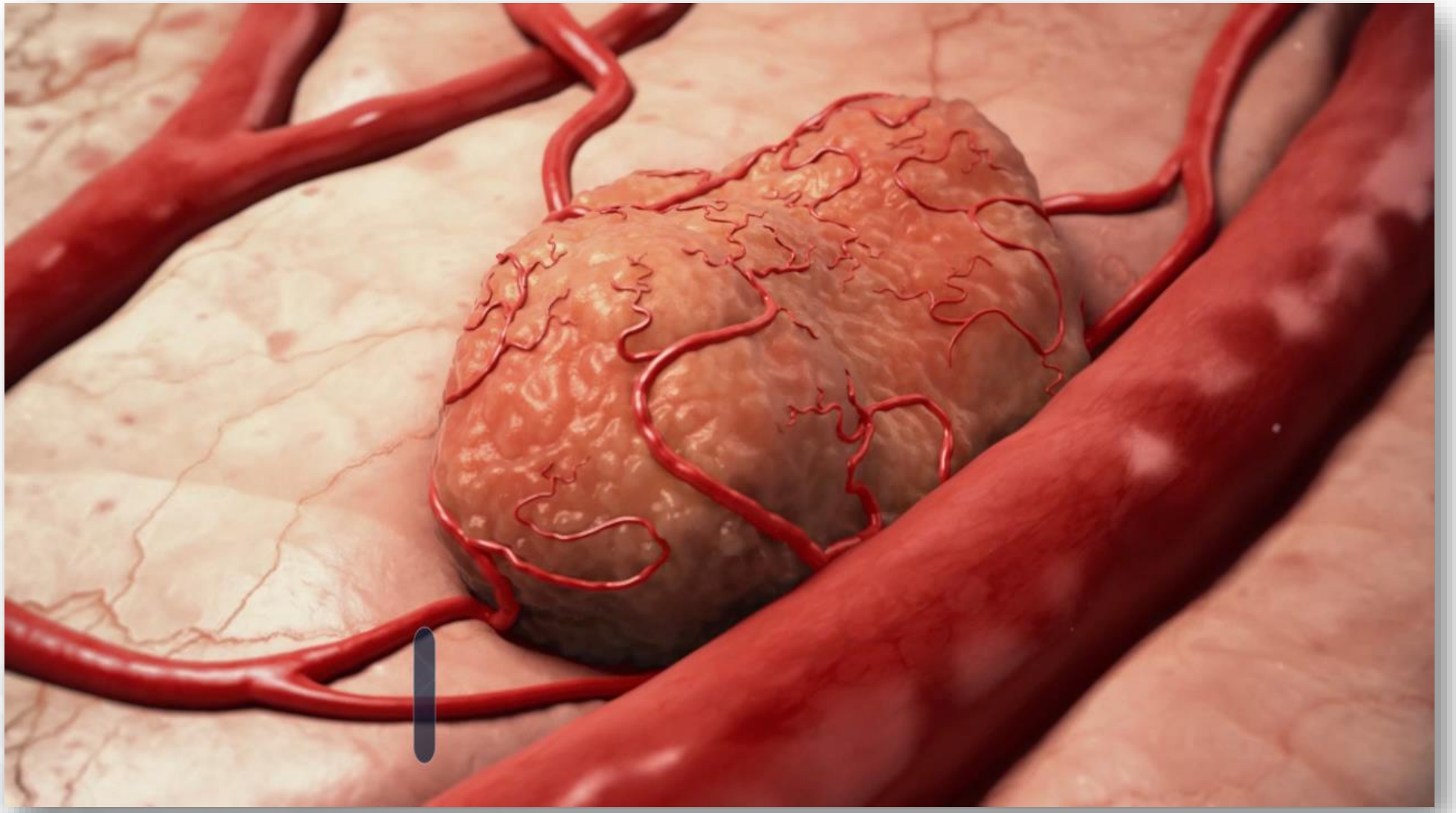


Alpha DaRT

- 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



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)

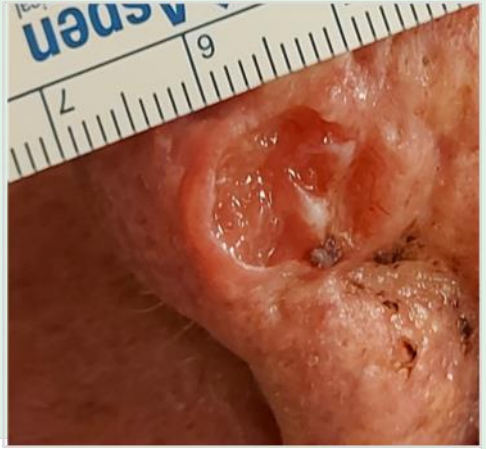
Treatment of hundreds of tumors to date:

- 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

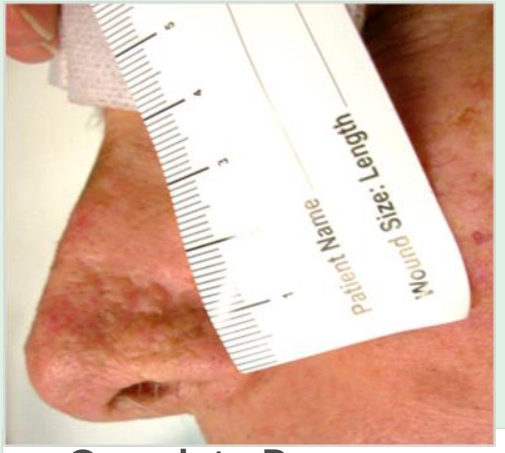
Pivotal trial ("ReSTART") underway in the U.S. for recurrent cutaneous SCC

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** **No treatment-related serious AEs**
Response Rate	**100% Complete Response Rate**



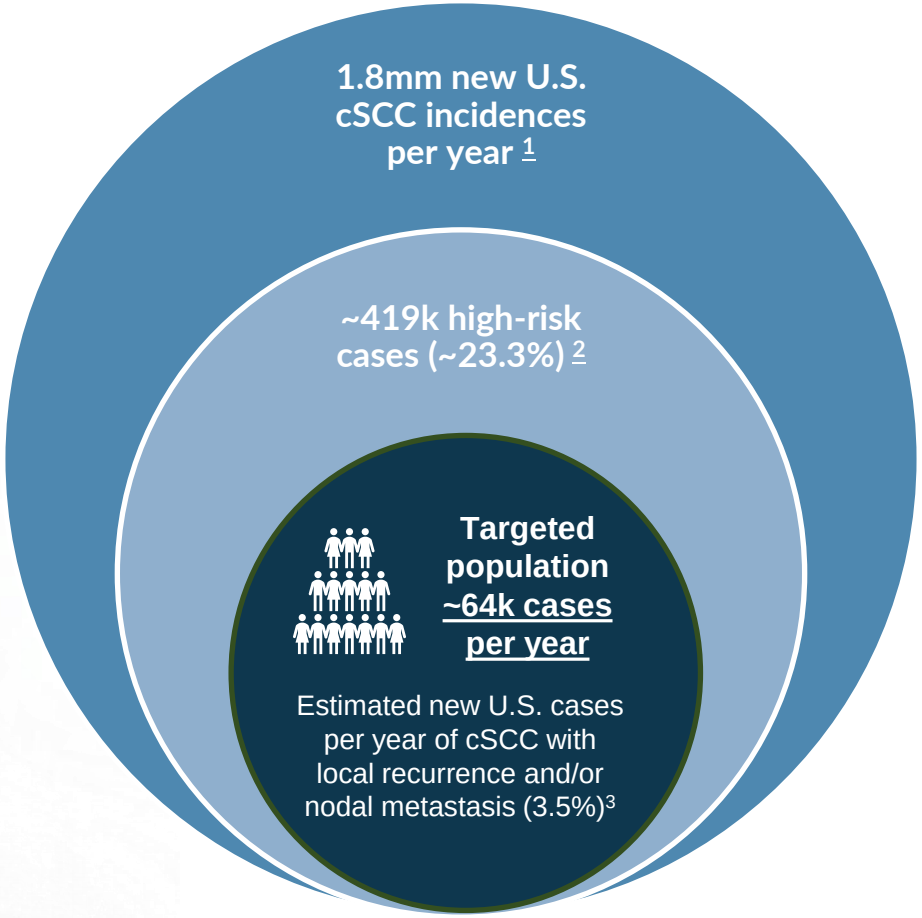
Simulation Day



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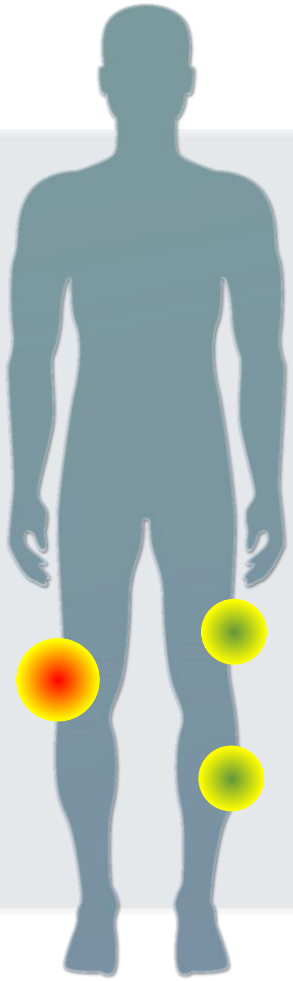
Case Study: Potential Systemic Immune Effect Observed in One cSCC Patient Where a Second, Untreated Lesion Manifested CR

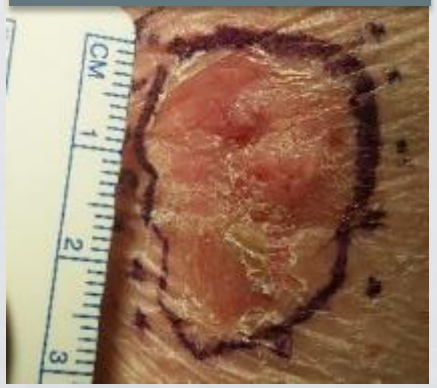
Complete Response + Potential Systemic Immune Effect



Treated Tumor

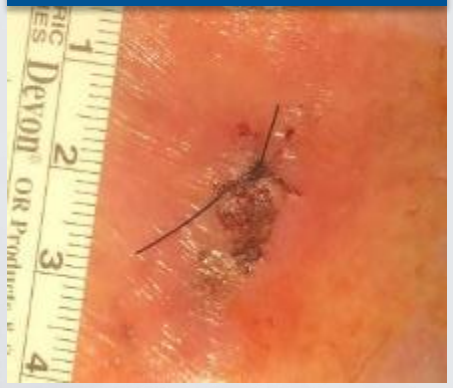
Before

30-Nov-17



After

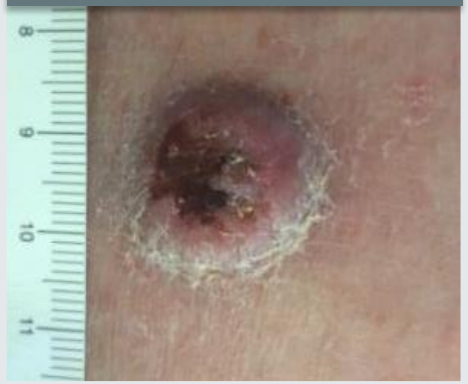
29-Dec-17



Untreated Tumors

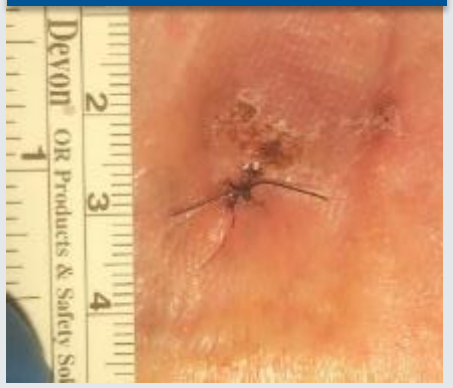
Before

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)

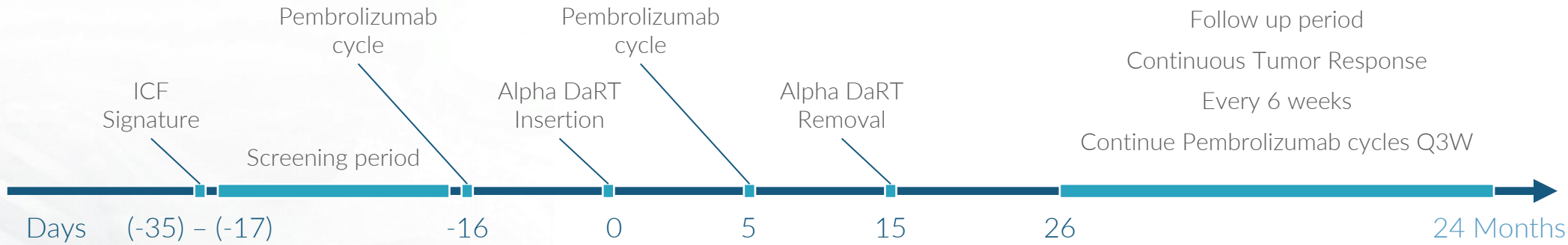
No **previous treatment for metastatic disease**

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 laHNSCC
- 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)

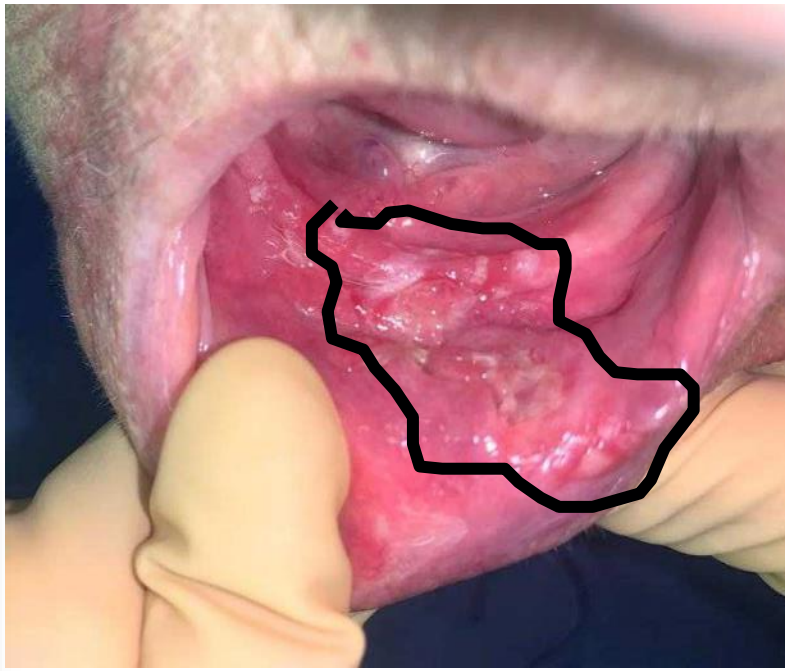
No Related SAEs

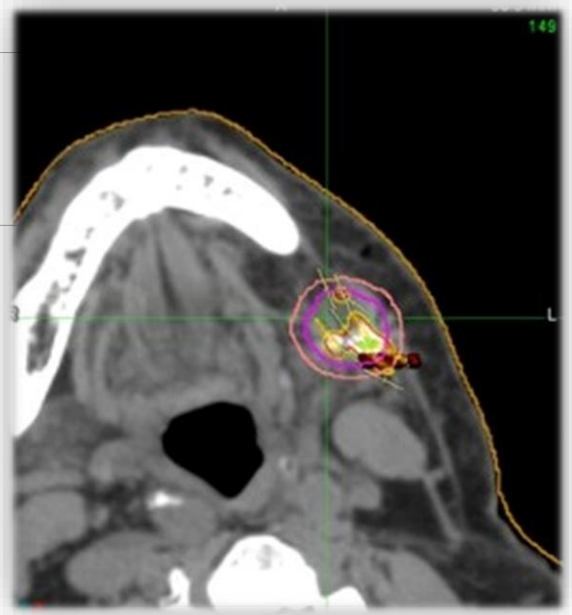
HNCPI-00-01-003

Pembrolizumab Combination Case Study

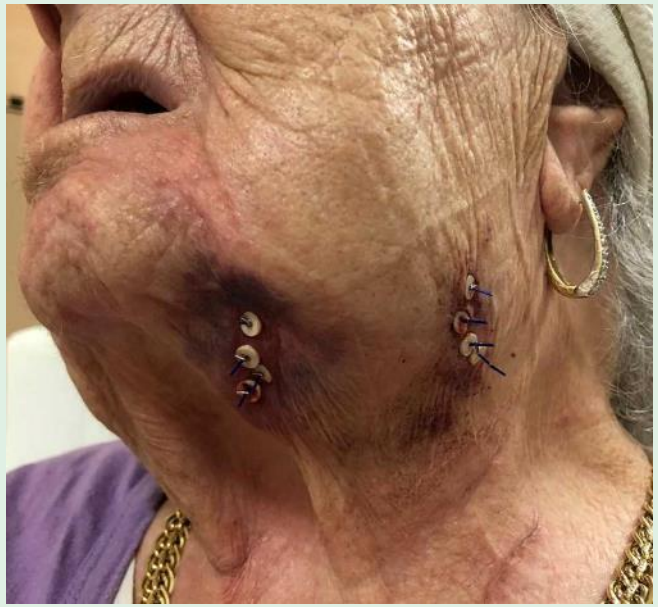
Case Background – HNCPI-00-01-003

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 • Dementia • ECOG3
Cancer Stage	• Stage IV • T2N1M1

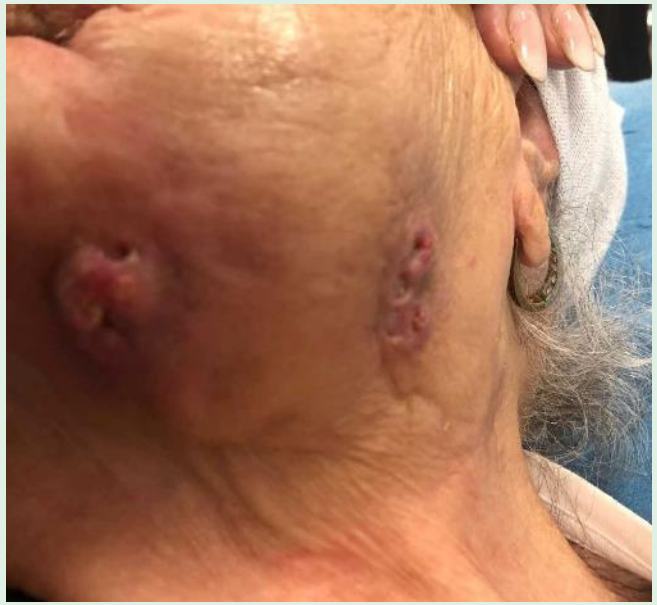




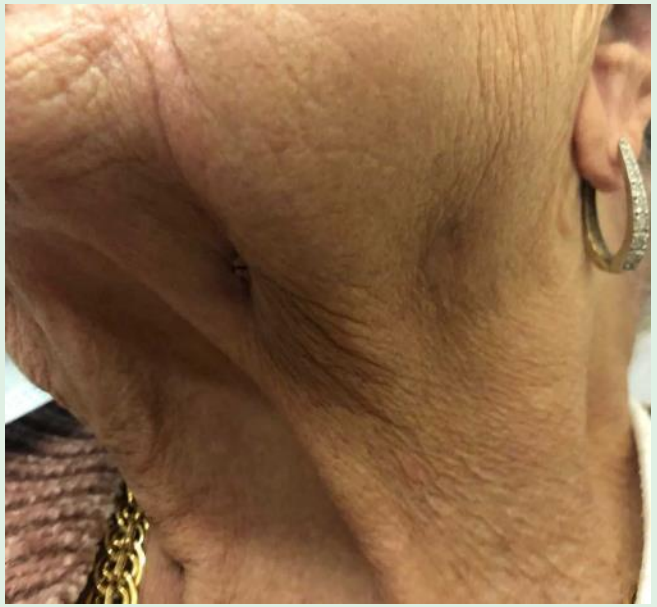
Alpha DaRT Treatment



Alpha DaRT Insertion
Sept-2022



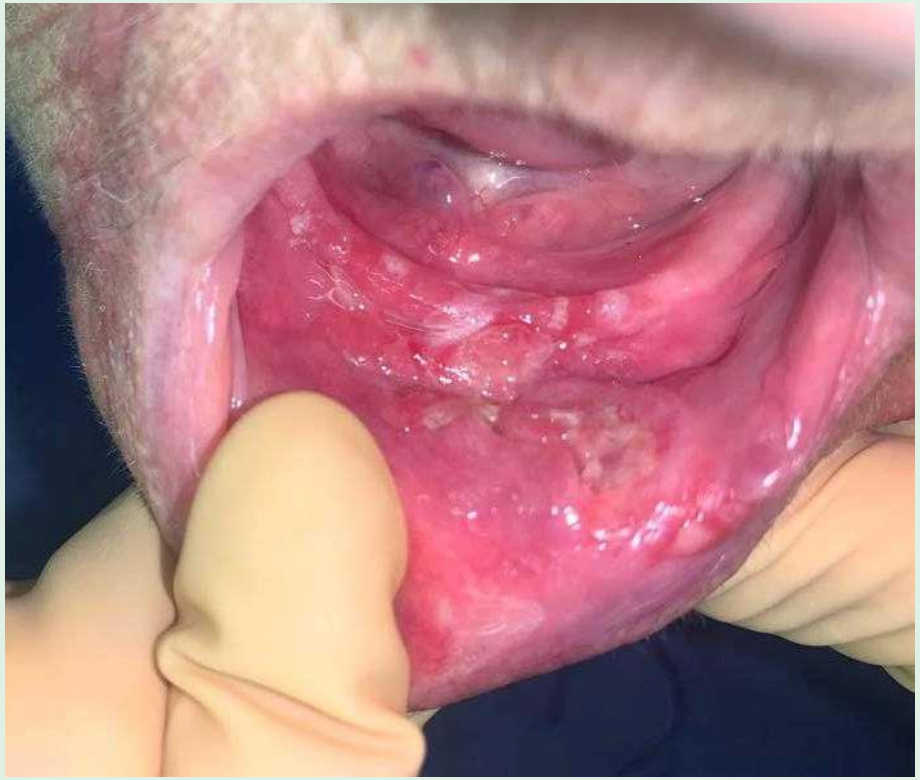
After Alpha DaRT Removal
Oct-2022



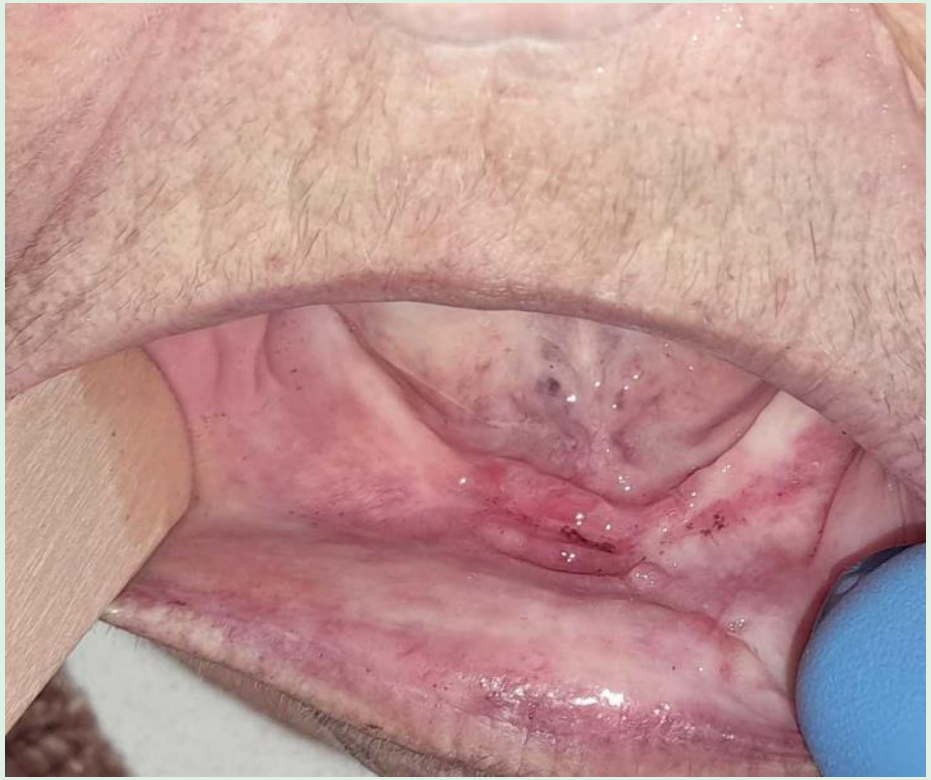
Follow-Up

Jan-2023

Clinical Follow-Up

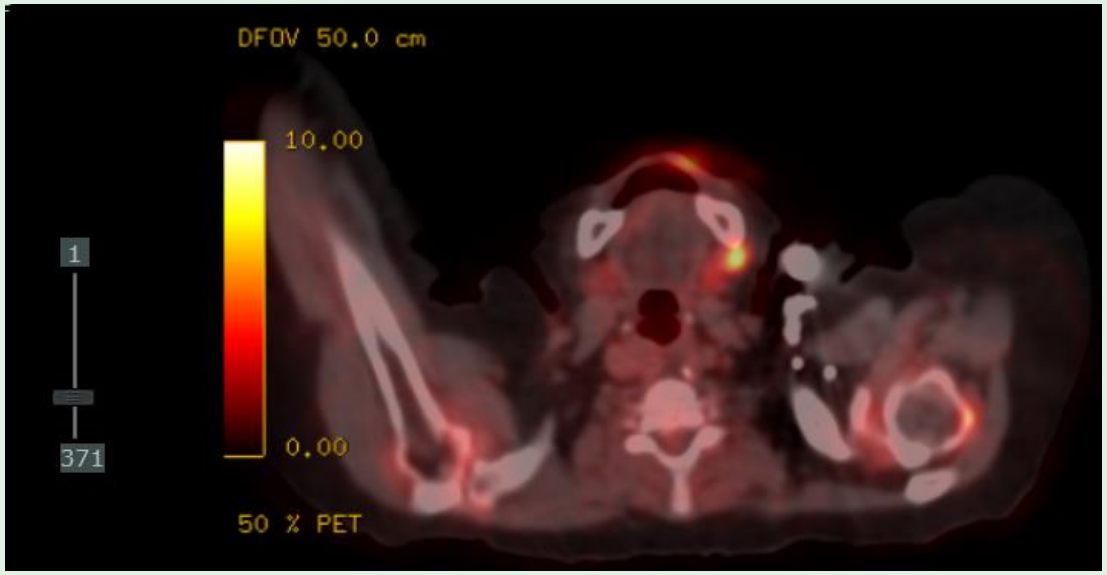


Pre-Treatment

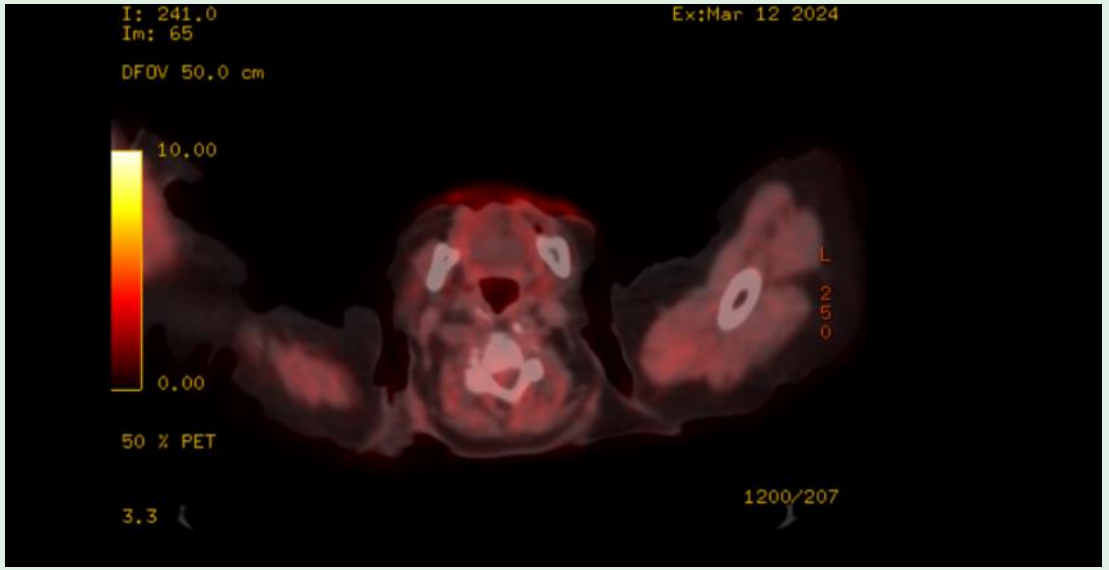


Nine Weeks Post Treatment

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

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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

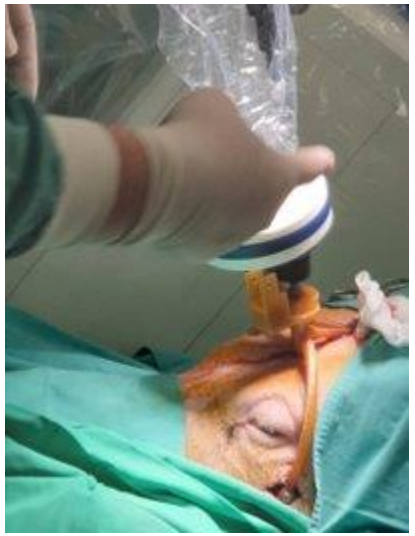
- Pancreas – clinical trial underway
- Liver – clinical trial underway
- Lung – clinical trial underway
- Prostate – clinical trial underway
- Brain – GBM + Brain Mets
- Breast
- Rectum

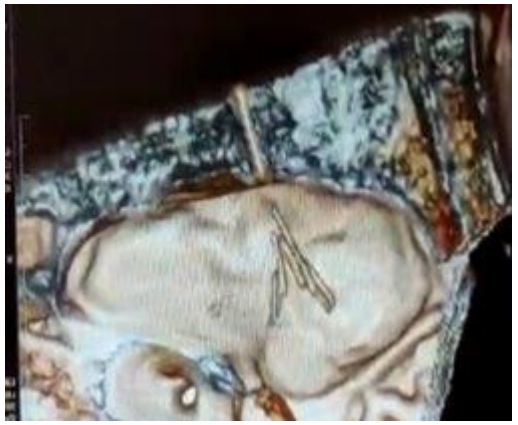
CHUM
Centre hospitalier de l'Université de Montréal

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

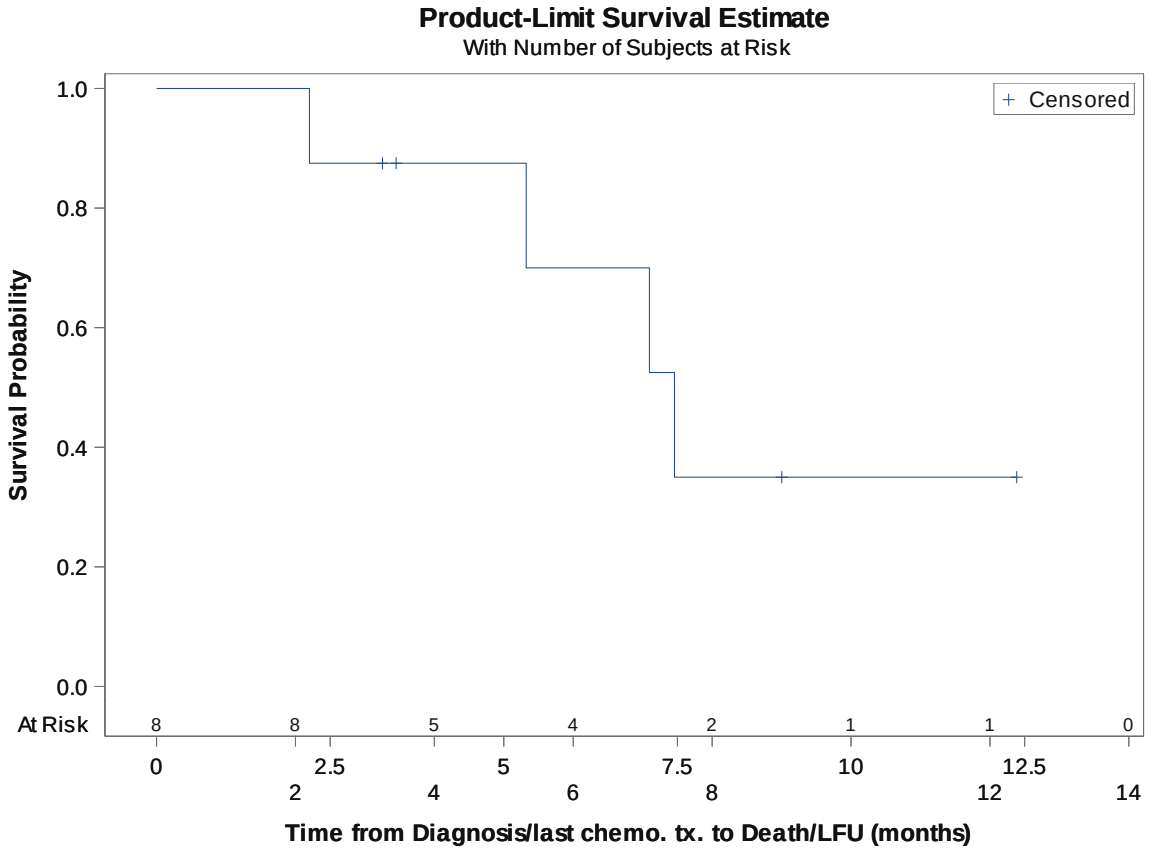
Of n=33 patients analyzed, 13 have died
The remaining 20 (and the five newer patients) remain alive

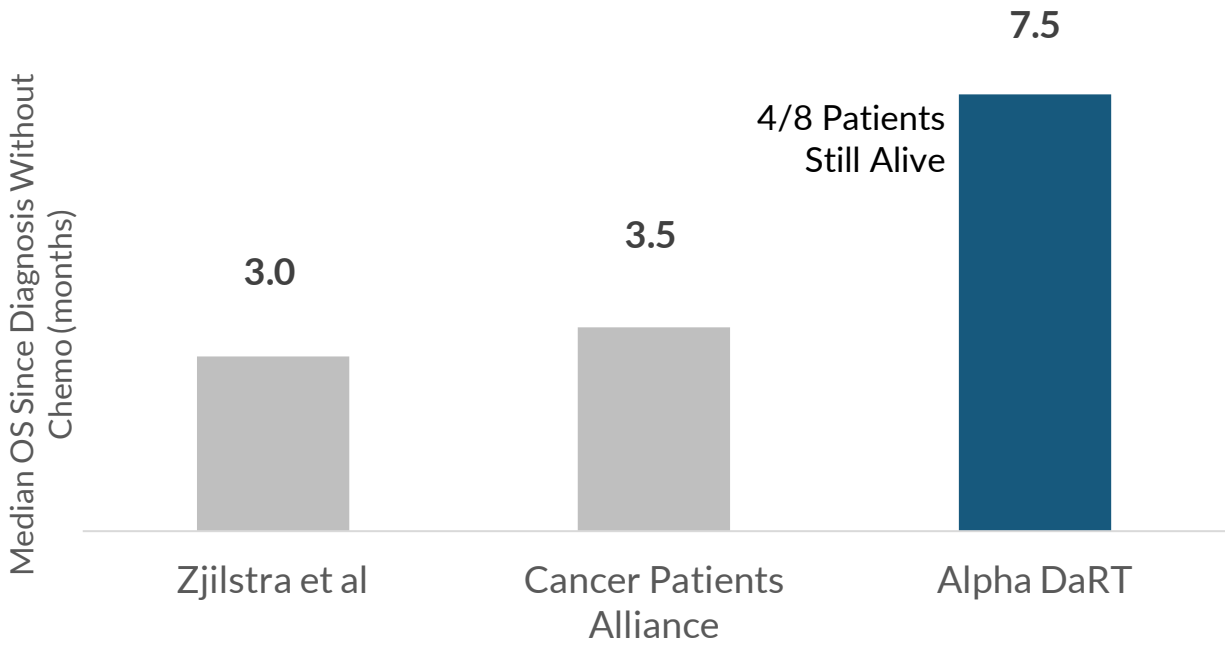
In light of the **heterogeneity of the population**, we conducted ad-hoc analyses **of key sub-groups** to offer context vs. expected OS for each group

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)

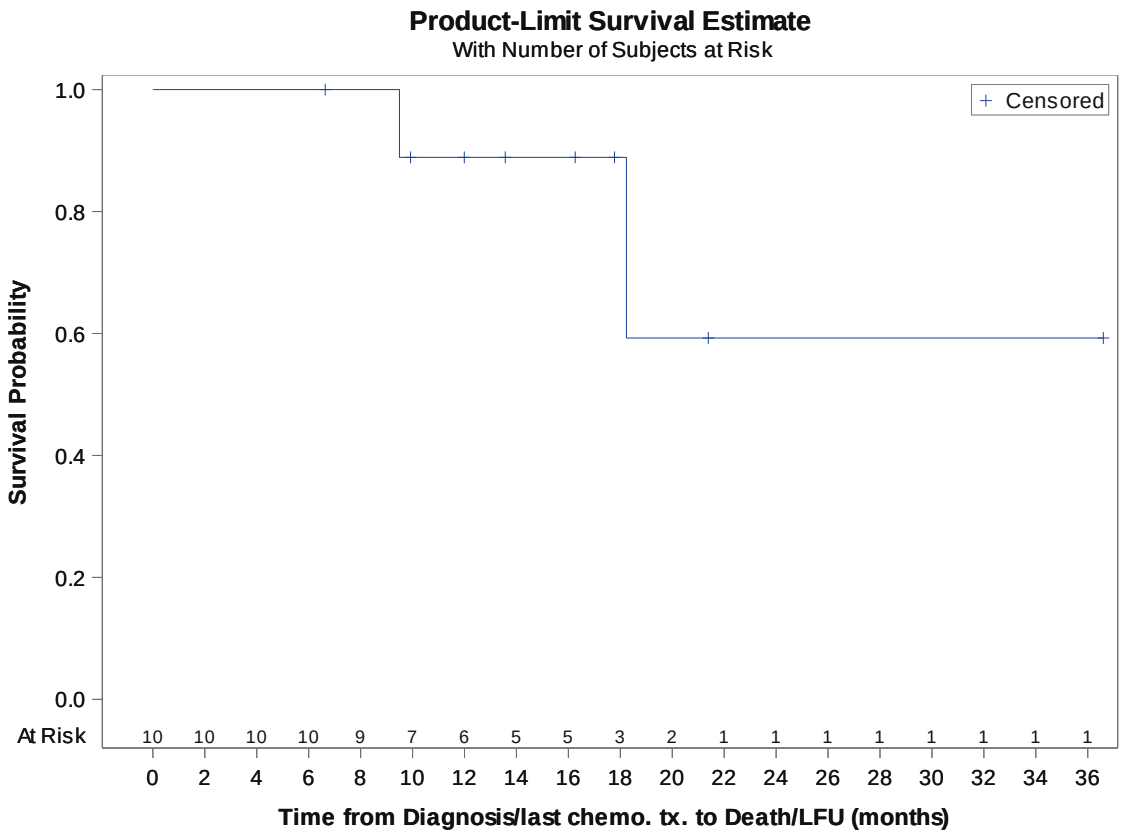


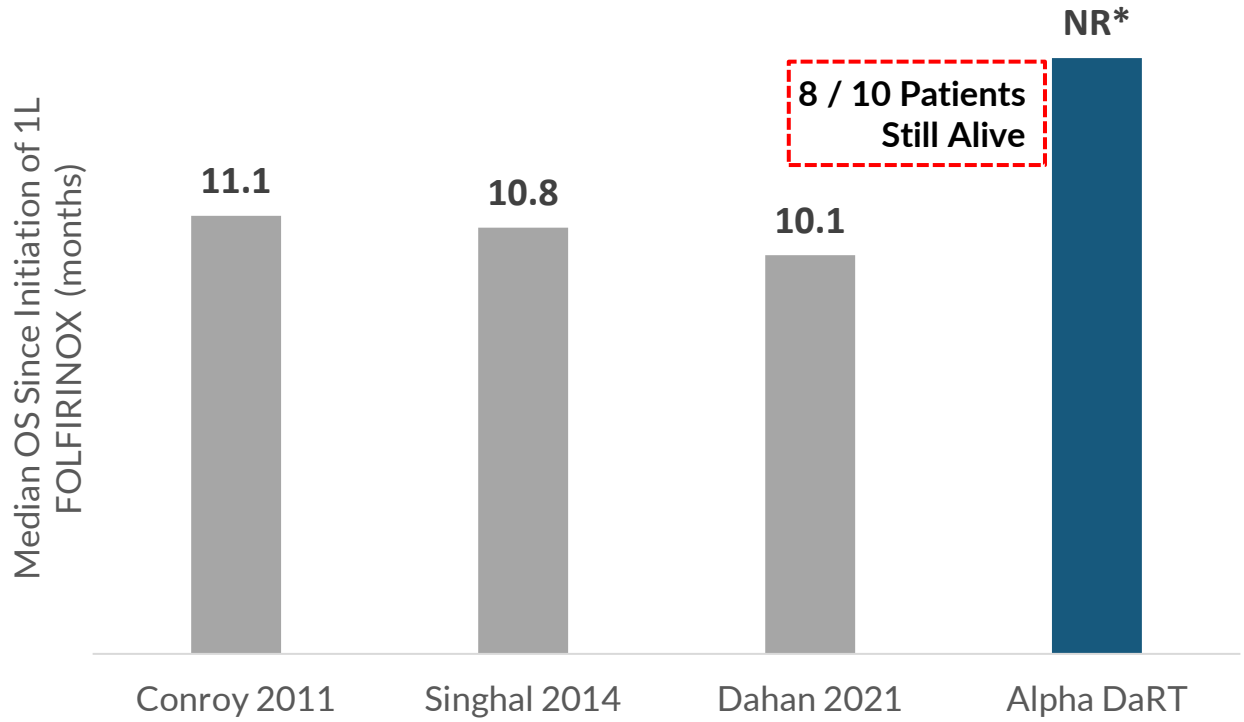


Note: Median follow-up in Alpha DaRT group of 6.3 months
Results as of January 8, 2025
For Illustrative Purposes Only - no head-to-head clinical study has been conducted comparing Alpha DaRT to other products or candidates. Differences exist between trial designs, subject characteristics and other factors, 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:

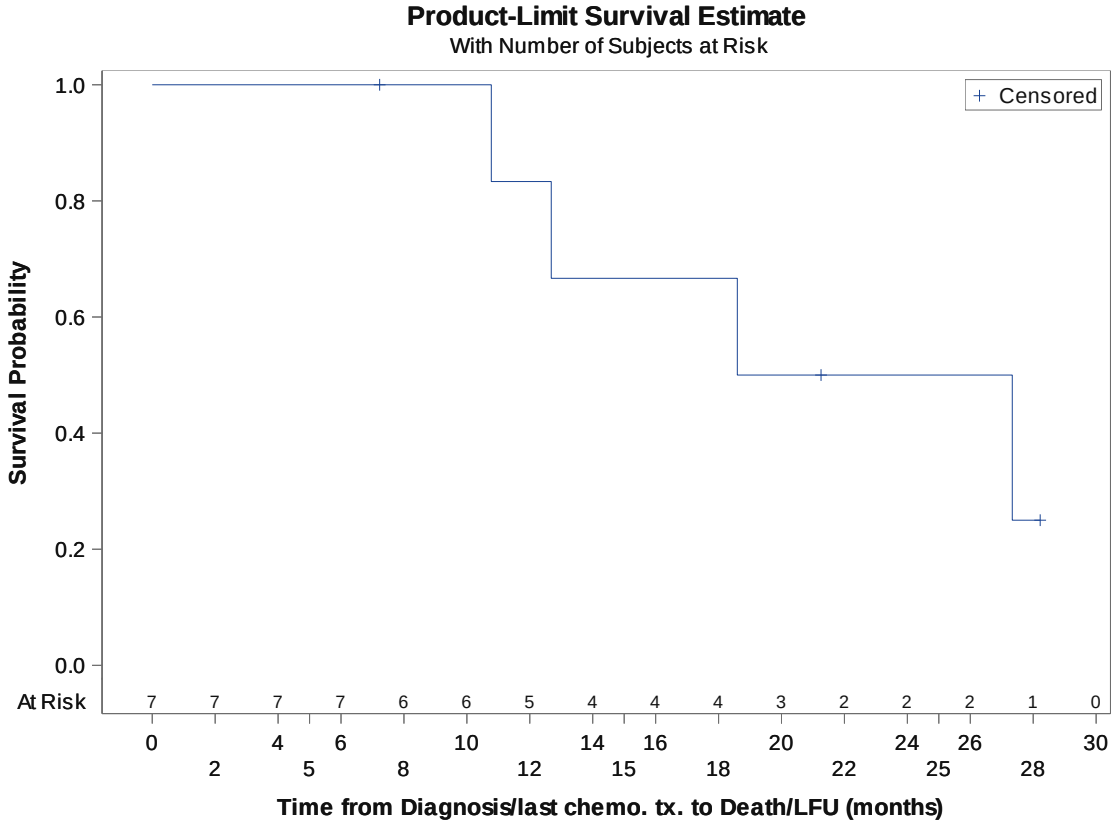
Thierry Conroy et al., FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer. New England Journal of Medicine (2011). DOI: 10.1056/NEJMoa1011923

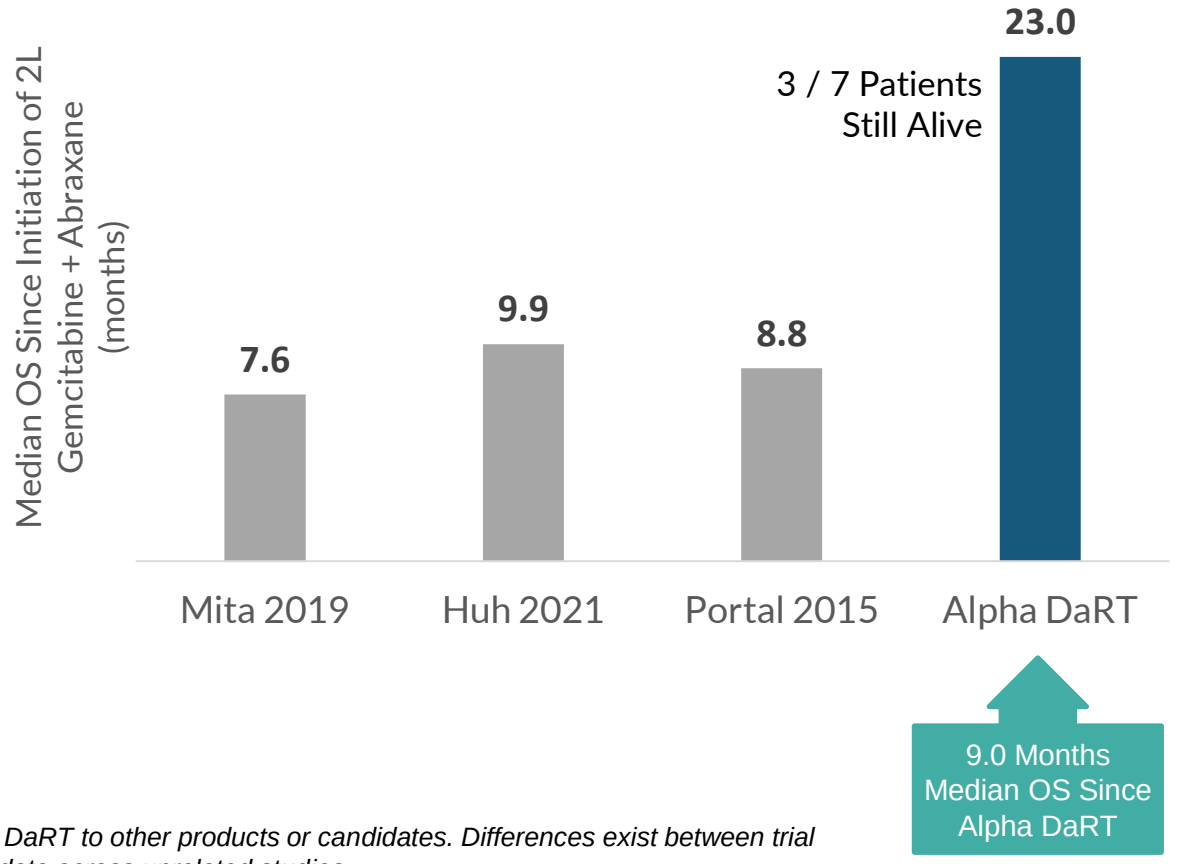
Singhal MK, et al. A phase III trial comparing FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. Ann Oncol. 2014;25(suppl 4):iv210–53.

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)

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

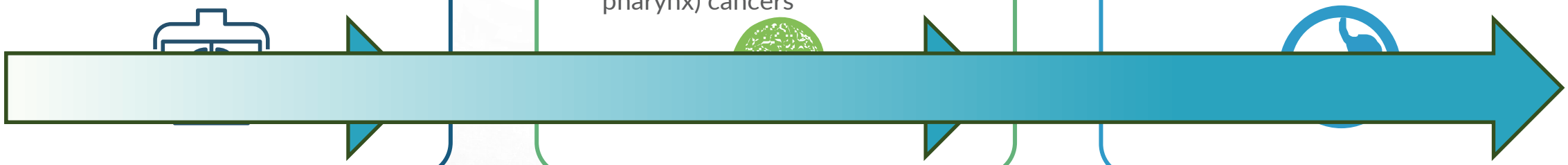
- Localized tumors that are not surgical candidates and tumors that recur after surgery and are **resistant to other** therapies, specifically radiotherapy
- Alpha DaRT to be evaluated as **a later line therapy**
- Tumor types we are targeting include **SCC, H&N SCC and prostate**

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**



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

Financial Position

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

AlphaTAU

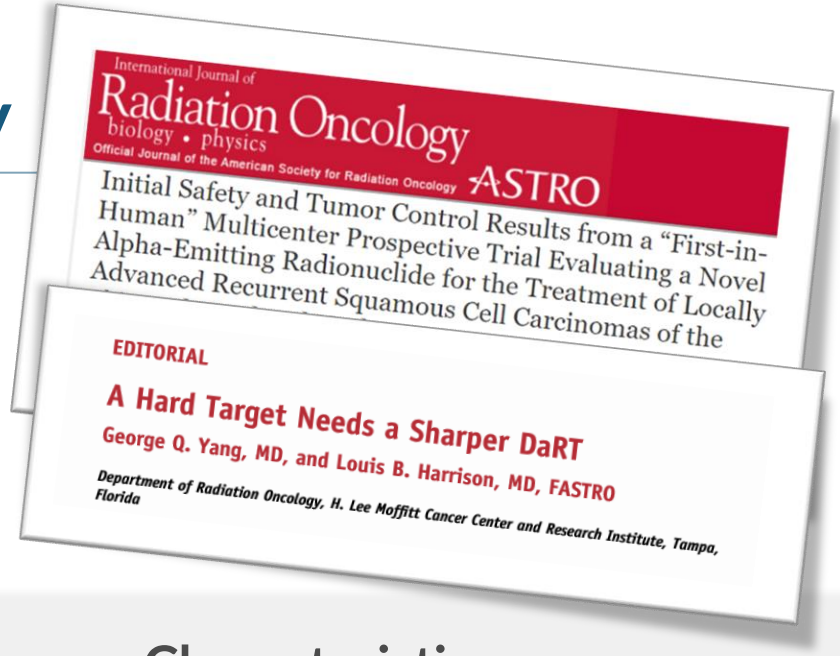
Saving Lives Globally

Appendix

Backup Slides

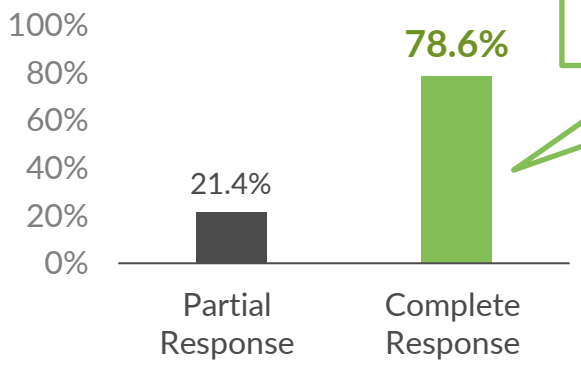
First in Human Skin / Head & Neck SCC Study

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

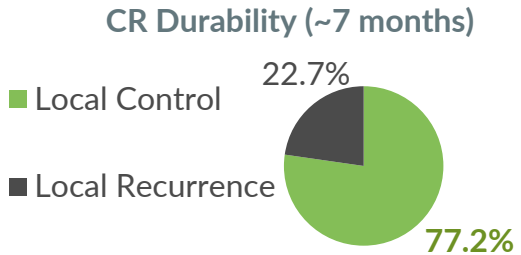


Efficacy Results

Overall Response (n=28)



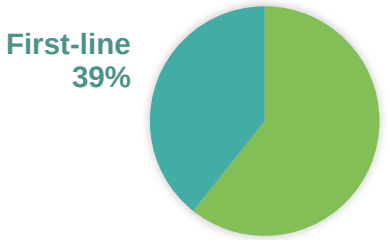
CR Durability (~7 months)



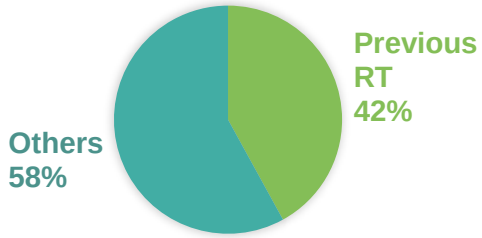
Baseline Disease Characteristics

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

Previous Treatment[1]



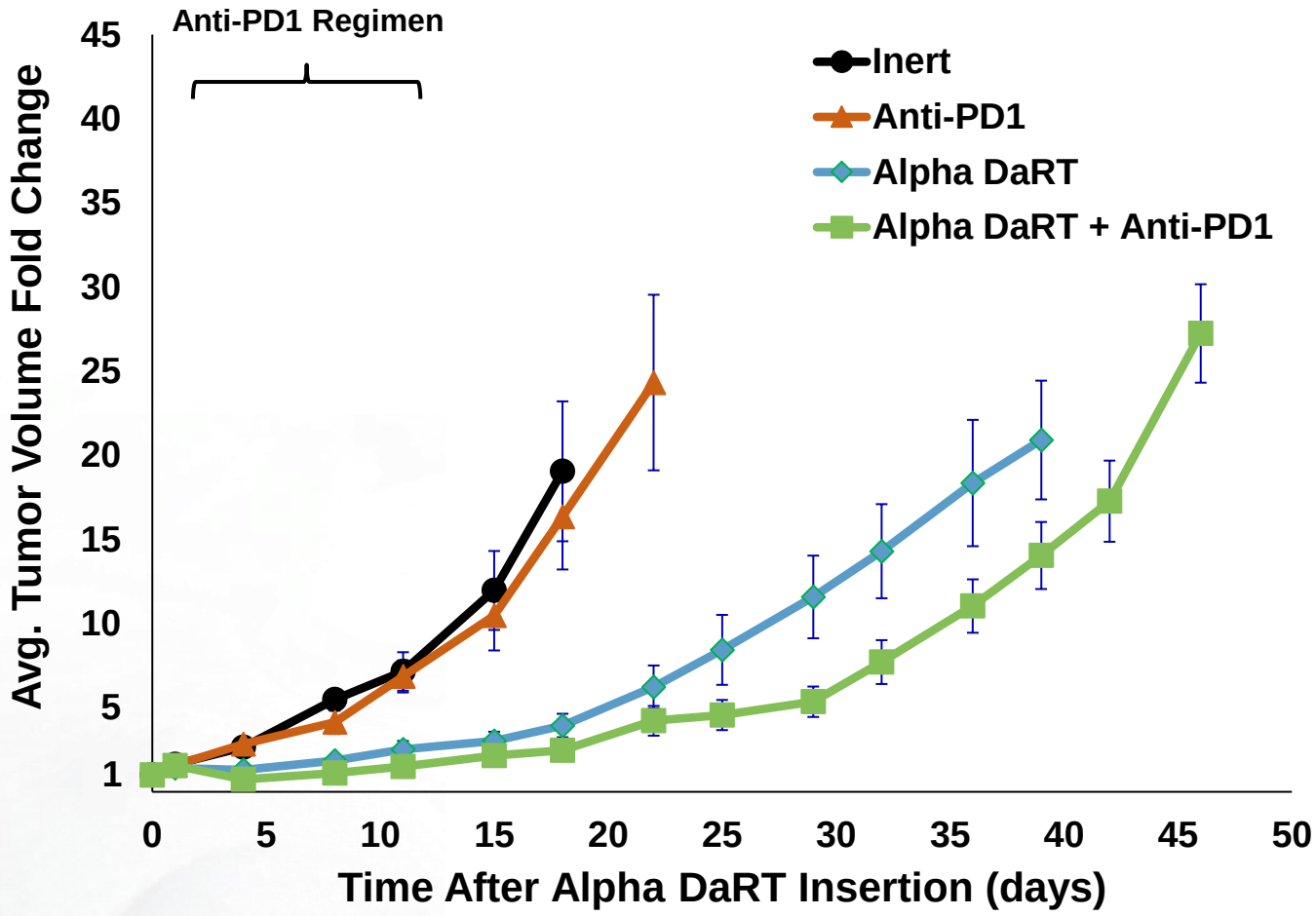
Previous Radiotherapy (RT)



[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.

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

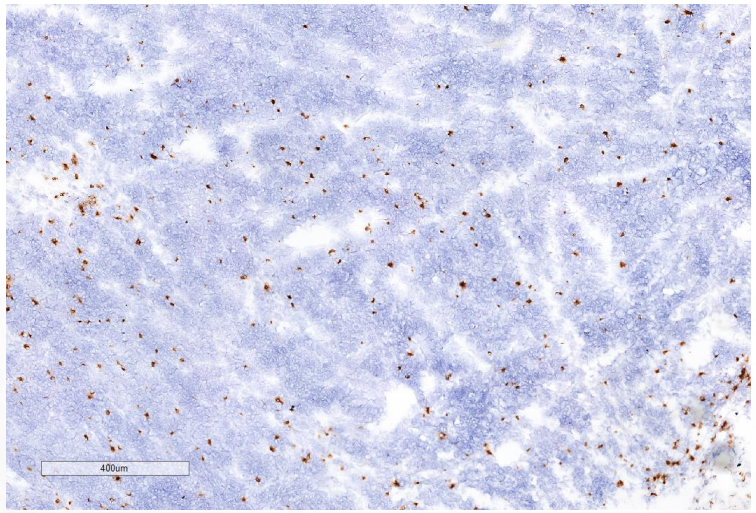
While mice with the SQ2 squamous cell carcinoma model showed little to no effect when treated with a murine anti-PD1 agent, the observed effect was larger for the combination with Alpha DaRT than for Alpha DaRT on its own



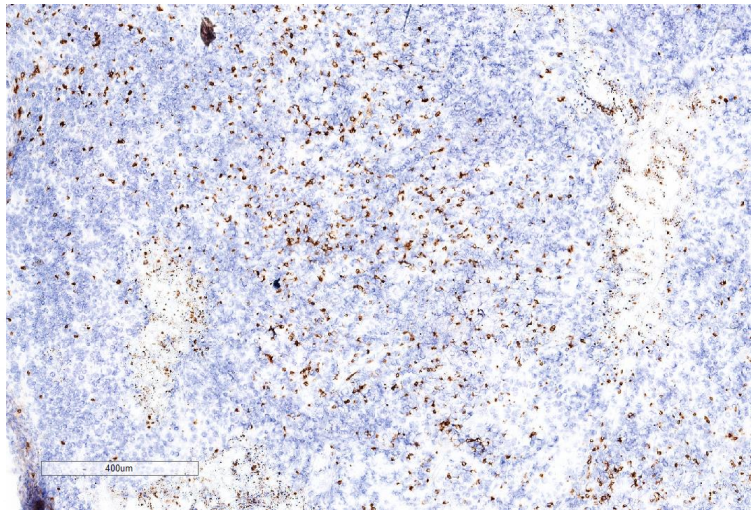
Alpha DaRT Increased Infiltration of CD3+ T-cells Into the Tumor

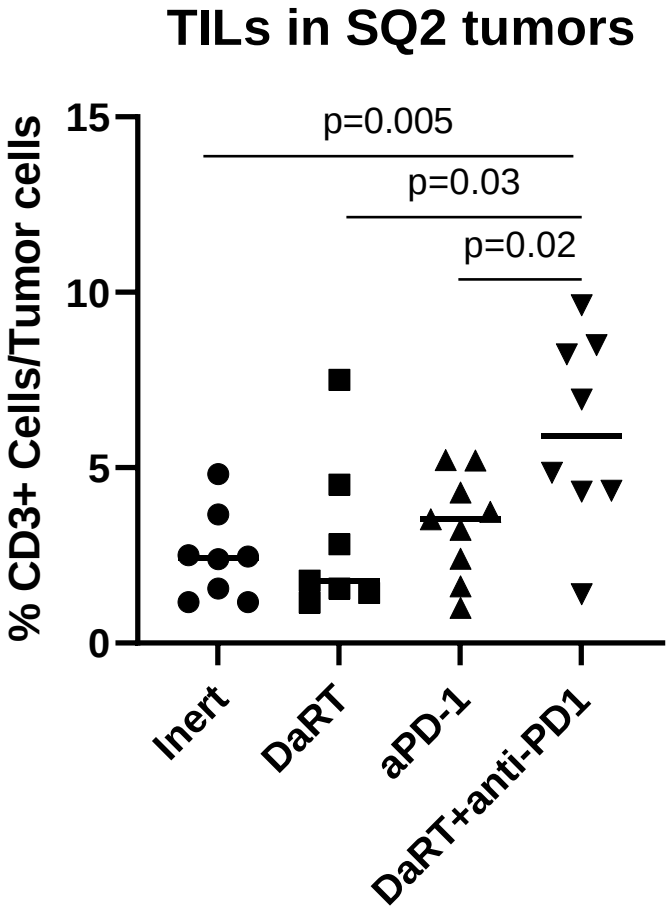
The combination of Alpha DaRT with anti-PD1 demonstrated the highest level of TILs in mice with SQ2 SCC tumors, suggesting potential to potentiate the checkpoint blockade

anti PD-1



Alpha DaRT + anti PD-1

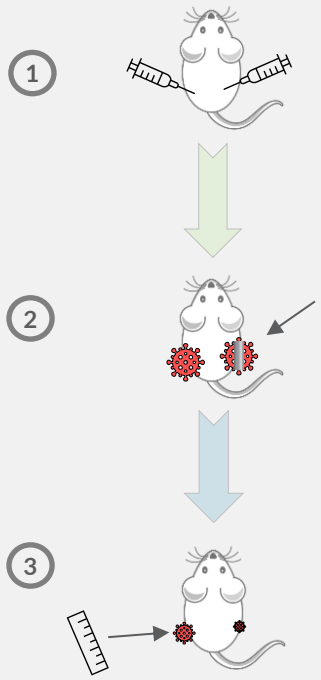




Immune Response Observed Even in “Cold” Pancreatic Tumor Model

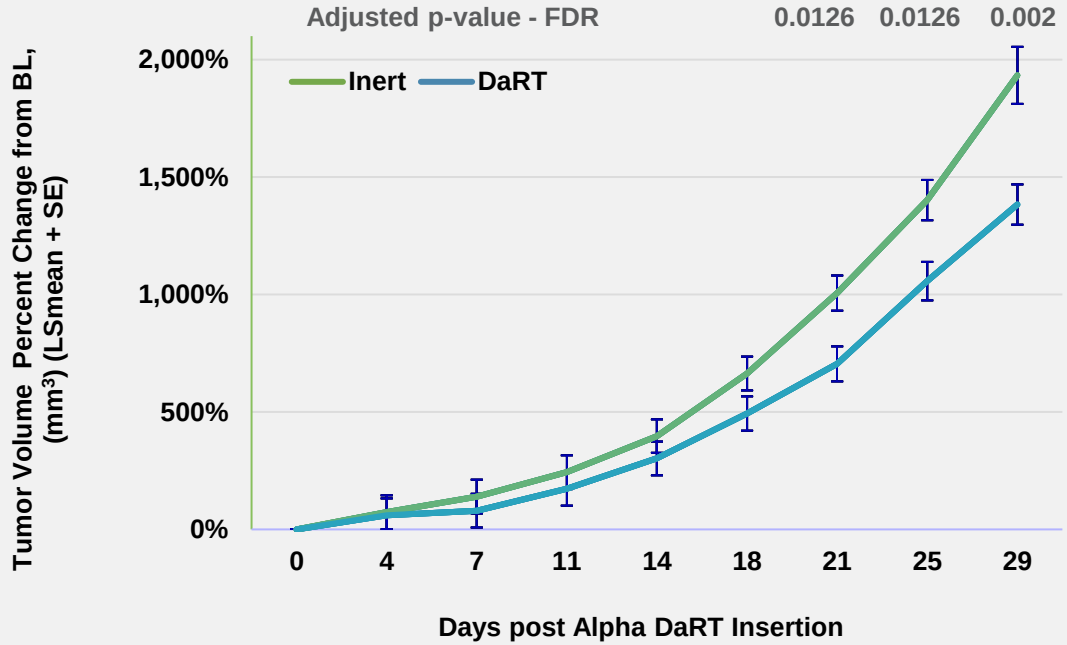
When treating one pancreatic cancer tumor with Alpha DaRT sources instead of inert sources, a statistically significant decline in secondary tumor growth rate was seen

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.

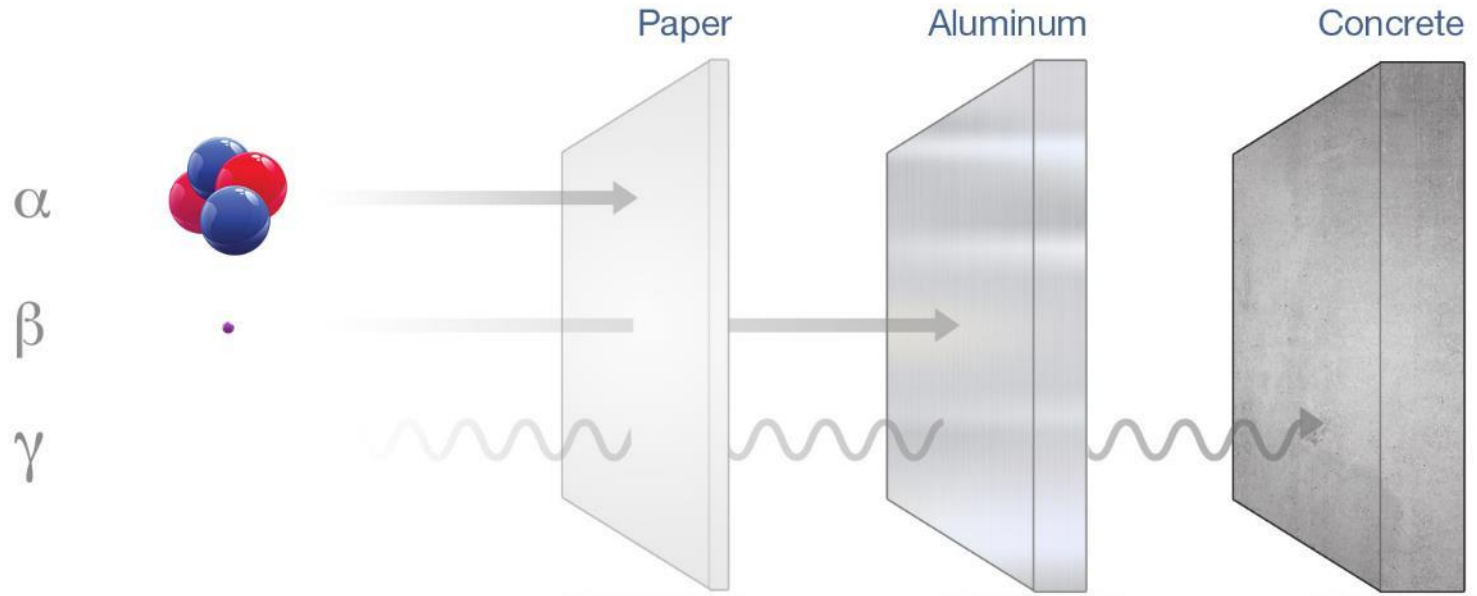
Development Pipeline

- **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

Types of Radioactive Decay

Due to the mass of the alpha particle, in comparison to beta particle, alpha has a low penetration power. This means that the outside layer of the human skin, for example, can block these particles.

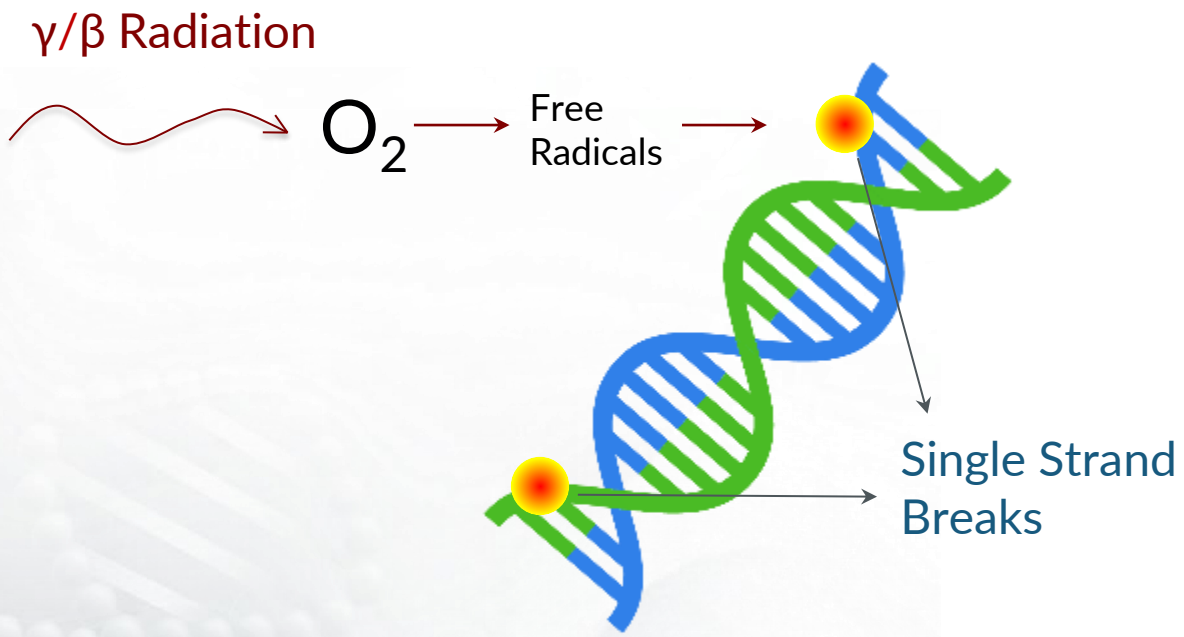


Potent Alpha Radiation: Extensively Damages the DNA

Local radiation therapy with gamma or beta radiation is a mainstay of cancer treatment, but requires high local dose to be effective, as it primarily relies on single-strand breaks in a process relying on oxygen. Alpha radiation can be significantly more efficient given its ability to destroy both strands of the DNA directly, requiring lower levels of radiation

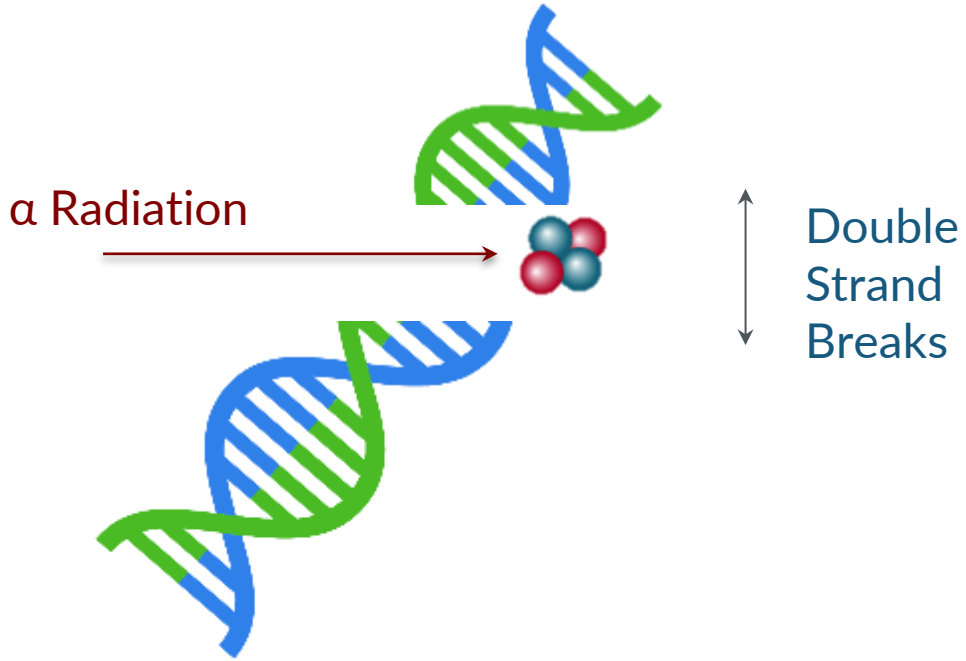
Conventional Gamma/Beta Radiation

- Indirectly damaging the DNA
- Dependent on oxygen presence
- **Repairable single strand breaks**



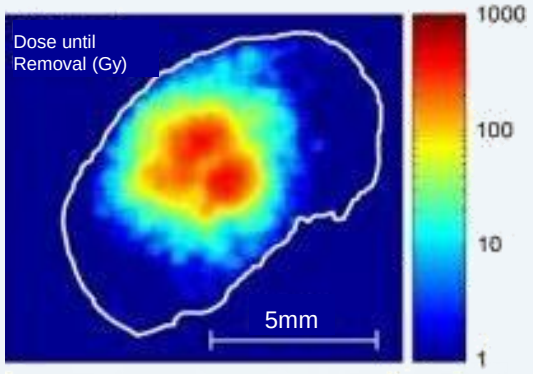
Alpha Radiation

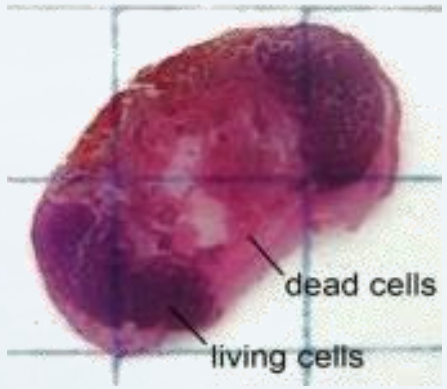
- Directly damaging the DNA
- Independent of oxygen presence
- **Irreparable double strand breaks**



Alpha DaRT Has a Unique Potential to Preserve Healthy Tissues

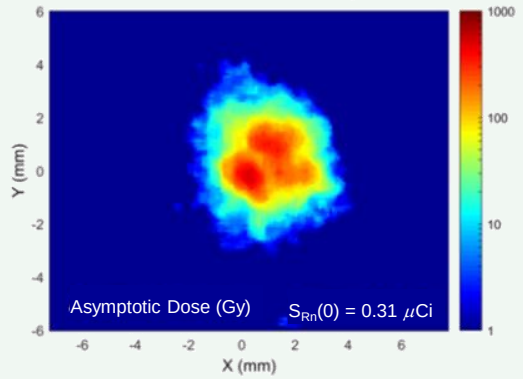
Alpha DaRT is unique in its potential to deliver a high dose of radiation in a very conformal form, with sharp dose drop-off outside of a 5mm range



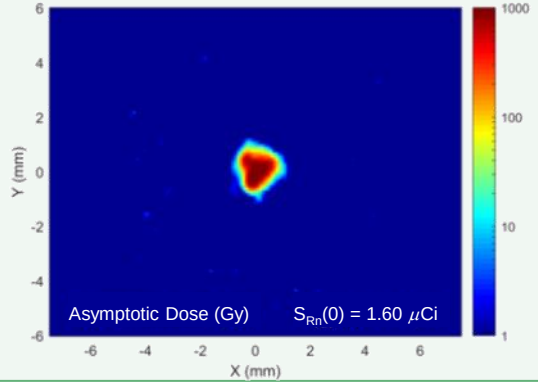


The range of the Alpha DaRT was observed to be meaningfully more extensive in tumor tissue than in healthy tissue in animal studies

Diffusion in SCC



Diffusion in healthy tissue



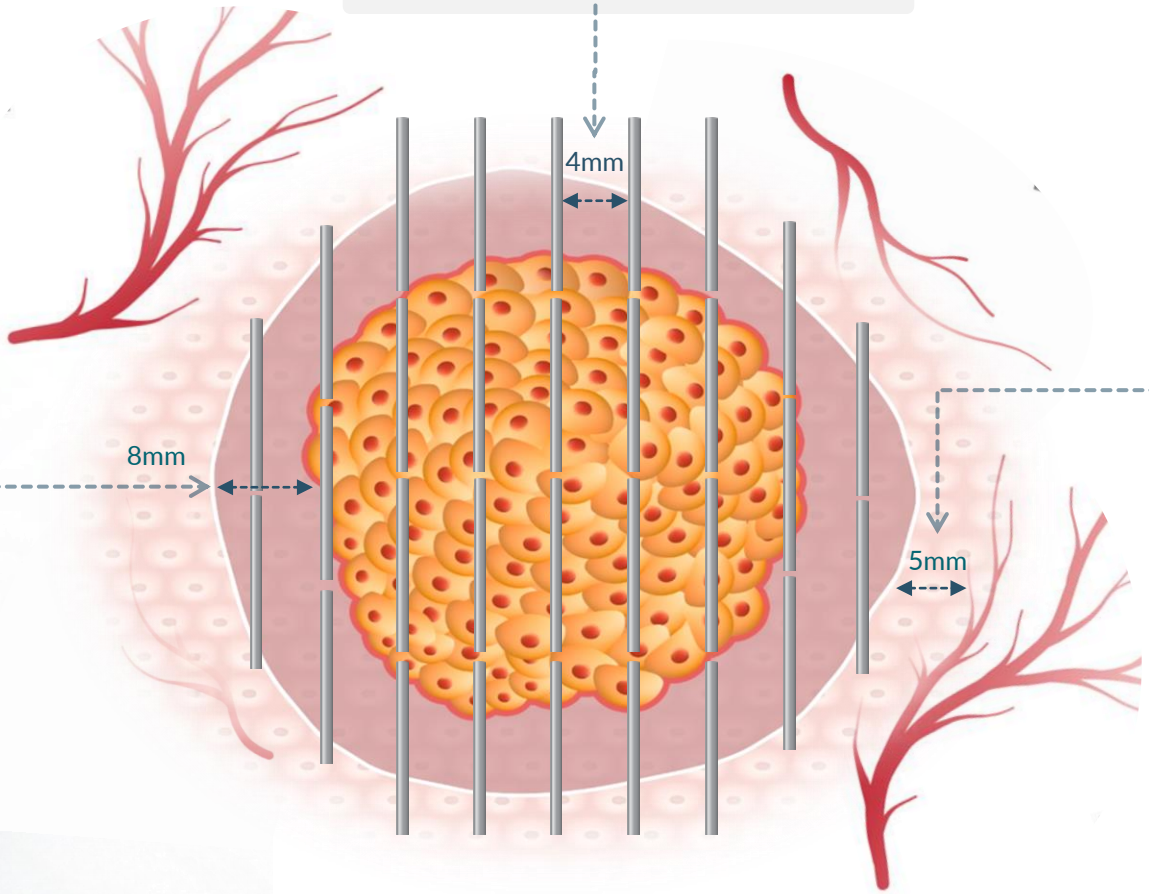
Alpha DaRT Source Placement

Through a series of Alpha DaRT injections to the tumor, spread a few millimeters apart, a clinician can potentially deliver alpha radiation to the full geometry of the tumor while taking care to avoid sensitive healthy tissue around the tumor

< **5 mm** between sources

Coverage of margins of **8 mm** (last source to be placed **5 mm** outside of the tumor)

5 mm safety distance from critical organs



Our Applicators Allow Delivery Into Both Superficial & Internal Tumors

We Have a Total of Seven Applicators Which Have Been Developed for a Range of Potential Uses to Accommodate for:

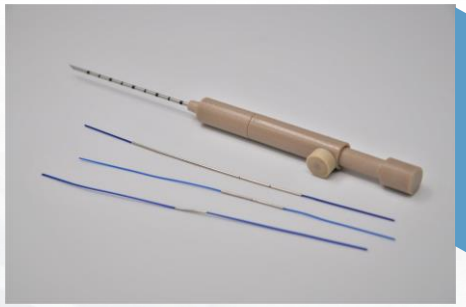
Treatment delivery method | **Duration of implantation** | **Tumor Location**

Temporary Implants (Superficial Tumors)

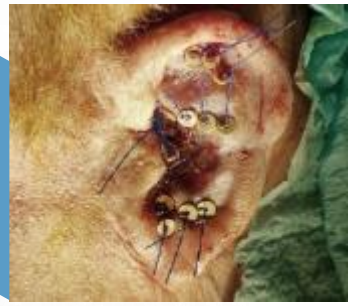
Applicators are supplied preloaded, sealed and designed for immediate use

Sources are hollow and strung onto a surgical suture, allowing the clinician to insert the sources into the tumor and leave the suture in place

Alpha DaRT Needle Applicator



Needle Applicator in Action

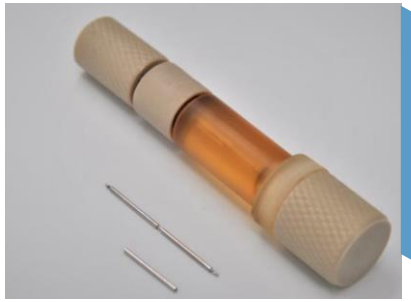


Example Indication: Superficial Tumors.
sources are affixed to a biocompatible suture and loaded inside the needle

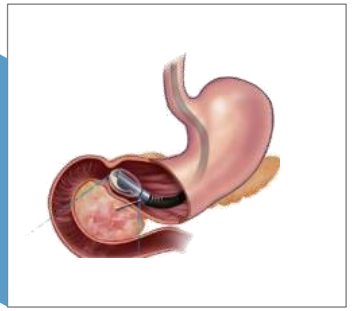
Permanent Implants (Internal Tumors)

Applicators are designed to allow clinicians flexibility to receive the sources preloaded, or load the sources in the course of treatment, and to select how many sources to deliver

Loading Device



Procedure: FNA in Conjunction with Endoscopic Ultrasound

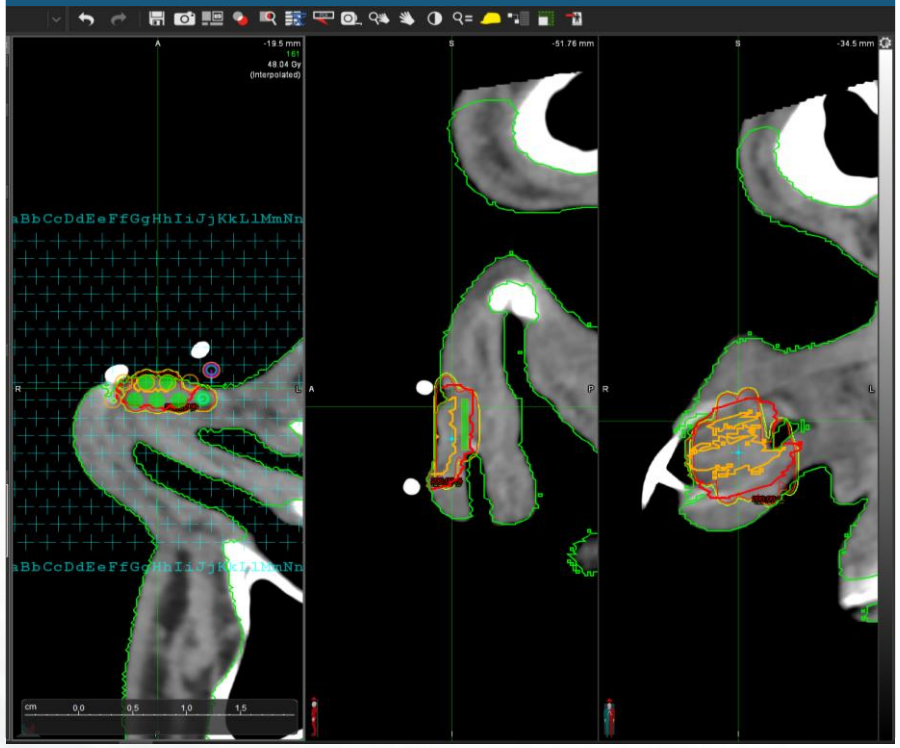


Example Indication: Pancreatic Tumors.
Device is designed to be fitted to existing needles such as standard Fine Needle Aspirator (FNA) to ultimately deliver sources into the tumor

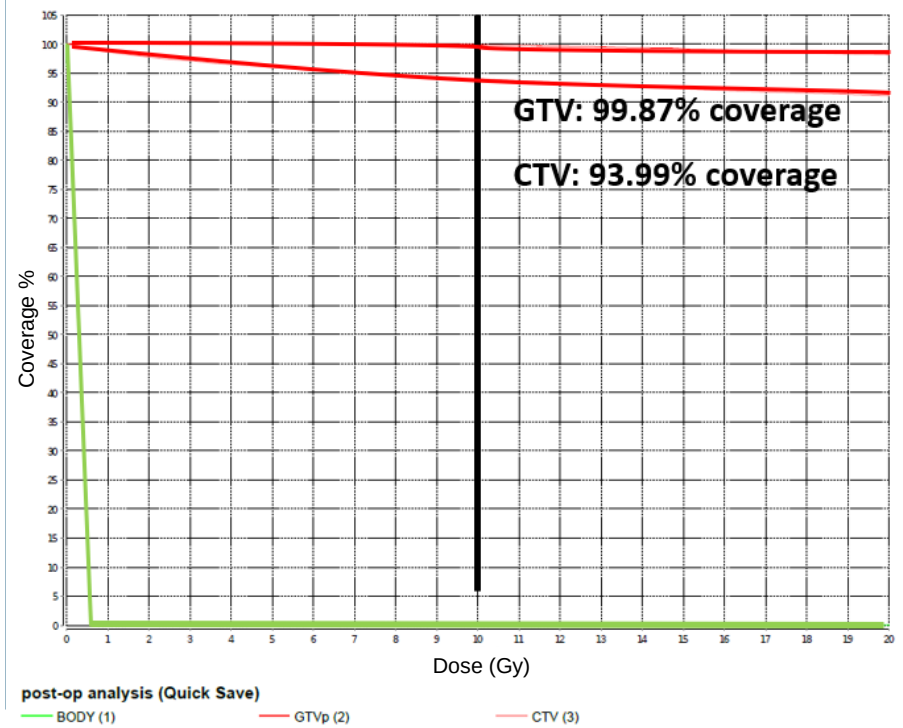
Treatment Planning in Partnership with MIM Software

Treatment planning software may serve to increase the precision and robustness of Alpha DaRT use, by allowing the clinician to calculate the alpha-specific dosimetry for the desired plan before treatment, and then check the tumor coverage post treatment

Pre-Treatment Planning



Post-Treatment Dosimetry Confirmation

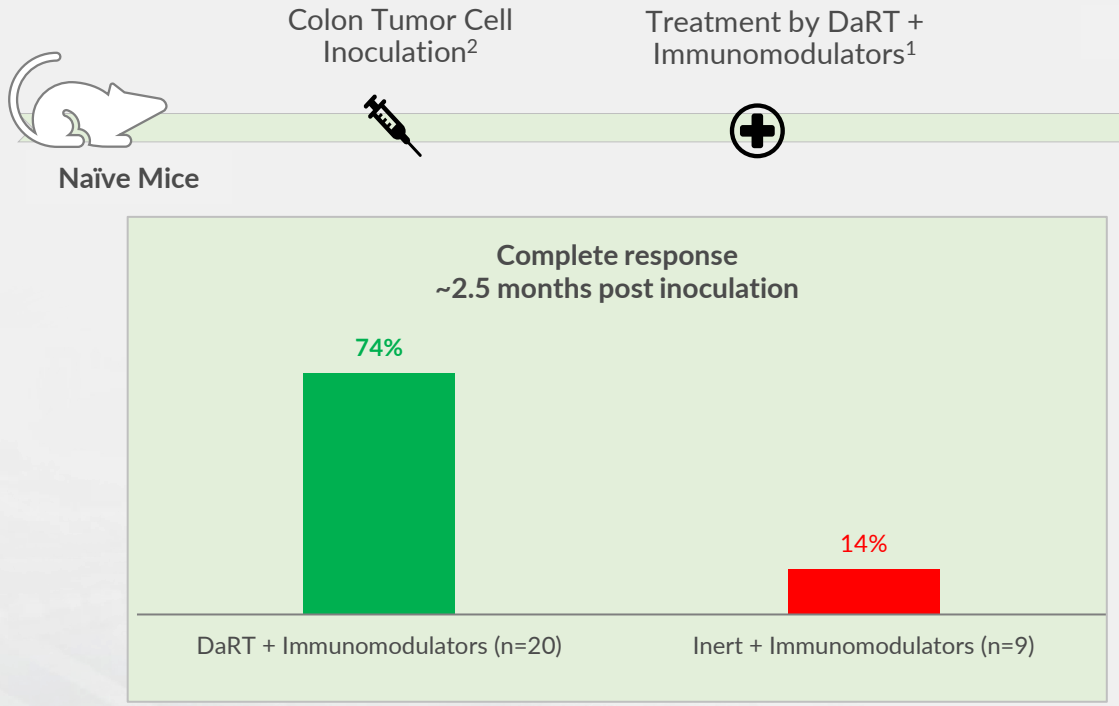


Alpha Tau has announced an agreement with MIM Software for continued collaboration on Alpha DaRT treatment planning, including development of new features and support for the Alpha DaRT across multiple potential indications, integration into all clinical trials involving the Alpha DaRT, and bundling the MIM software with the Alpha DaRT for future commercial sales.

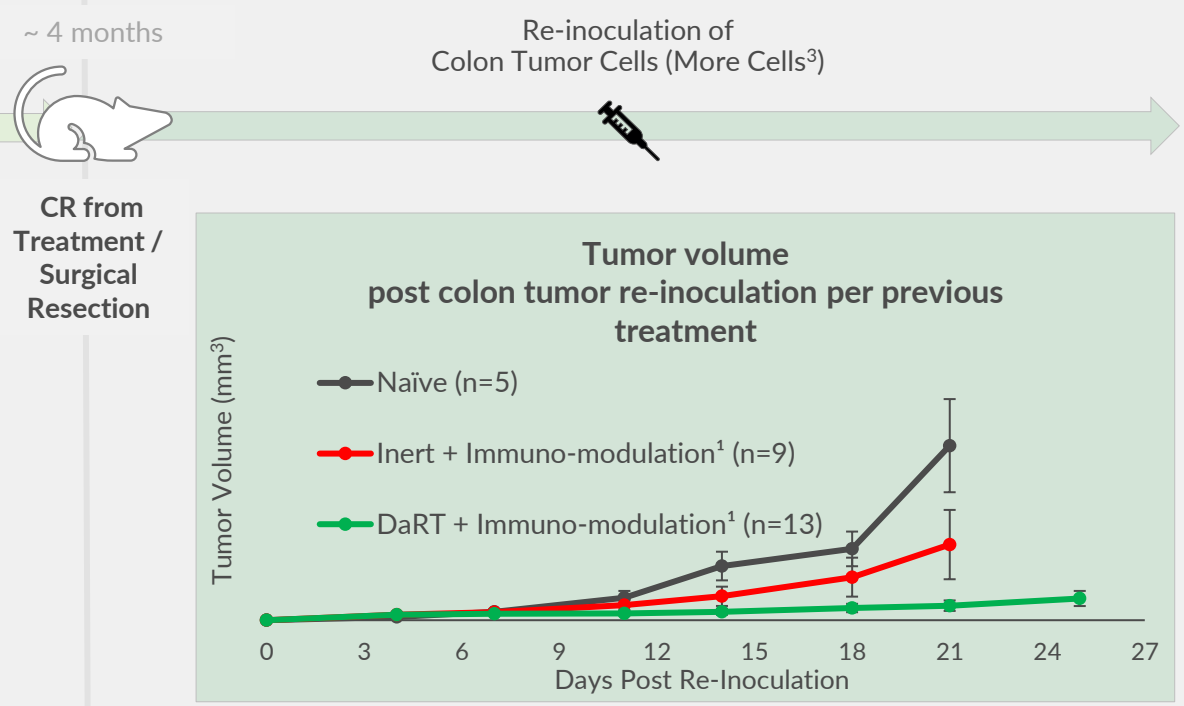
Observed Cancer-Specific Immune Protection (1/2)

In challenging mice 4 months after treatment, those previously treated by the Alpha DaRT displayed a meaningful retained protection against regrowth of the same tumor type, as compared to the two control groups

Tumor Treatment by DaRT + Immunomodulators[1]

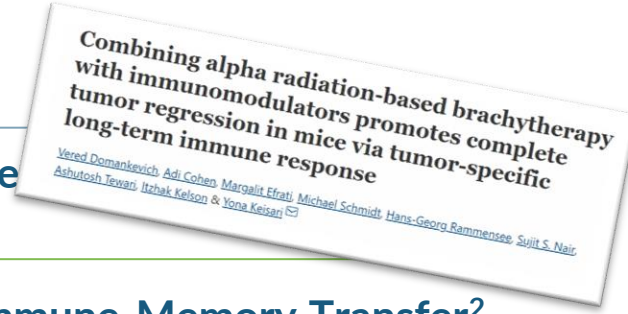


Tumor Re-Inoculation after Treatment by DaRT + Immunomodulators vs. Inert[1]



(1) Three groups of mice were inoculated with 5 x 10^5 CT26 tumor cells and then treated with (1) DaRT + CP, Sildenafil and 2xCpG, N=10 (2) DaRT + CP, Sildenafil and CpG, N=10 or (3) inert + CP, Sildenafil and 2xCpG, N=9. Complete responders or tumor-resected mice were re-challenged ~4 months after DaRT with 5 x 10^6 CT26 tumor cells.
(2) CT26 5 x 10^5.
(3) CT26 5 x 10^6.

Observed Cancer-Specific Immune Protection (2/2)



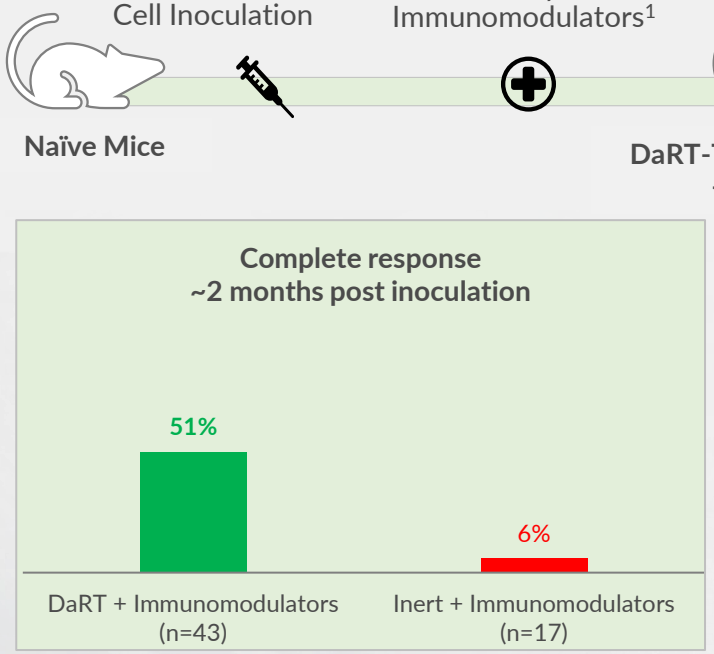
This activity was then shown to be tumor-specific – the challenge only resisted regrowth of the same tumor line. It was also shown to be transferrable via the transfer of splenocytes

Tumor Treatment by DaRT + Immunomodulators

Colon[3] Tumor Cell Inoculation

Treatment by DaRT + Immunomodulators[1]

Naïve Mice

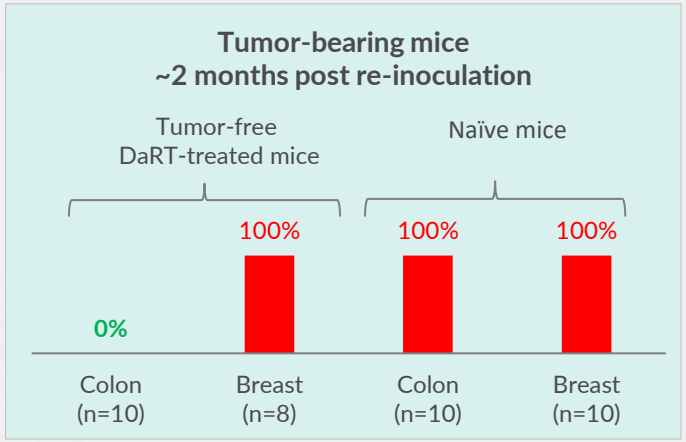


Tumor Re-Inoculation[2] (Challenge Assay)

DaRT-Treated Tumor-free + Naïve Mice

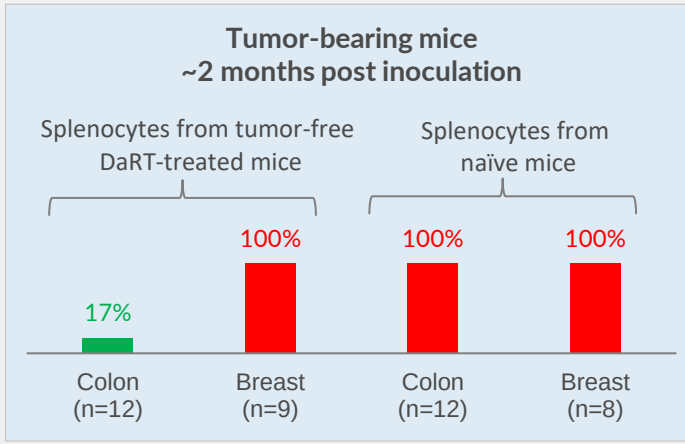
Colon[3] / Breast[4] Tumor Cell Re-inoculation

Naïve Mice



Immune-Memory Transfer[2] (Winn Assay)

Inoculation of Colon[3] / Breast[4] Tumor Cells + **Splenocytes** from Tumor-free Pretreated Mice



(1) Immuno-modulation refers to a combination of low dose CP, Sildenafil and CpG.
(2) Mice with CR from DaRT + immuno-modulators (n = 18) and naïve mice (n = 20) were inoculated with 5 x 10^5 CT26 or DA3 cells 52 days post inoculation (Challenge Assay). Naïve mice were injected intradermally with splenocytes from either naïve or CT26-bearing mice treated by DaRT and immunomodulators, coupled with CT26 or DA3 tumor cells (Winn assay). The presented results are based on cumulative data from two different experiments.
(3) CT26 5 x 10^5.
(4) DA3 5 x 10^5.

Impressive Efficacy & Safety Data Collected in Long-Term Follow-Up


cancers

Article

Extended Follow-Up Outcomes from Pooled Prospective Studies Evaluating Efficacy of Interstitial Alpha Radionuclide Treatment for Skin and Head and Neck Cancers

MDPI

Aron Popovtzer [1,*], Aviram Mizrachi [2], Mark A. D'Andrea [3], Noam A. VanderWalde [4], Noga Kurman [2], Eli Rosenfeld [2], Ran Ben-Hur [2], Salvatore Roberto Bellia [5], Giacomo Feliciani [5], David Silvern [2], Anna Sarnelli [5], Matthew T. Ballo [4], Pradeep Patra [4], Gil'ad N. Cohen [6], Antonio L. Damato [6], Yotam Shkedy [7], Robert B. Den [8,9], Christopher A. Barker [6], Tomer Charas [7] and Nir Hirshoren [1]

Data Set Description

Data collected from four feasibility trials in unresectable, recurrent, or locally advanced head and neck or skin cancers

81 treated lesions in 71 patients

Median follow-up of 14 months (range: 2-51 months)

Efficacy Results

- ✓ 89% of treated lesions achieved complete response (CR)
- ✓ 77% two-year local recurrence-free survival (LRFS)

Safety Results

- ✓ ~20% of patients had acute grade 2 toxicities and no patients had acute grade 3 or higher toxicities
- ✓ No grade 2 or higher late toxicities observed 6 months post-treatment

Short-term local responses led to durable long-term control in difficult-to-treat tumors

Canada Pancreas Trial Baseline Characteristics

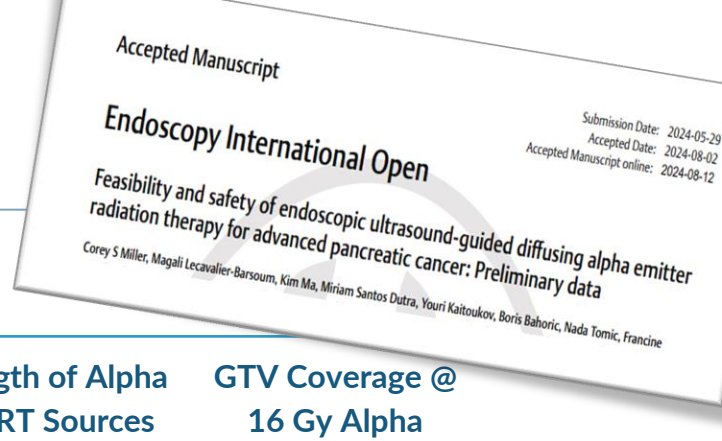
Subject ID	Age (years)	Sex	ECOG Score	Tumor Stage	Tumor Location	Pancreatic Cancer Inoperability	Prior Treatments	Length of Alpha DaRT Sources (cm)	GTV Coverage @ 16 Gy Alpha Radiation Dose
PANC-101-02-001	78	M	1	Stage IV	Pancreatic head/ uncinate	Metastatic disease	Chemotherapy: Gemcitabine and Paclitaxel; Gemcitabine	3	8%
PANC-101-02-002	68	F	2	Stage III	Pancreatic head	Unresectability	Chemotherapy: FOLFIRINOX (fluorouracil+leucovorin +oxaliplatin+irinotecan); Gemcitabine and Paclitaxel	11	13%
PANC-101-02-003	69	F	0	Stage II	Pancreatic head/neck	Unresectability	Chemotherapy: FOLFIRINOX; Abraxane and Gemcitabine	21	44%
PANC-101-02-004	84	F	1	Stage IV	Pancreatic head	Metastatic disease	Chemotherapy: Capecitabine	22	12.5%
PANC-101-02-005	71	F	0	Stage IV	Pancreatic neck	Metastatic disease	None	24	29.5%

Safety and Feasibility Outcomes

- **Successful delivery** to all 5 patients
- All patients were **discharged** from the hospital **on the same day** as the procedure
- All device- or procedure-associated adverse events (2) were **mild** (Grade 1)
- **No Grade 3** or higher associated events
- All SAEs were **not associated with** the Alpha DaRT or the procedure

Note: Results as of November 28, 2023

Early Response Data


Accepted Manuscript

Endoscopy International Open

Submission Date: 2024-05-29
Accepted Date: 2024-08-02
Accepted Manuscript online: 2024-08-12

Feasibility and safety of endoscopic ultrasound-guided diffusing alpha emitter radiation therapy for advanced pancreatic cancer: Preliminary data

Corey S Miller, Magali Lecavalier-Barsoum, Kim Ma, Miriam Santos Dutra, Youri Kaitoukov, Boris Bahoric, Nada Tomic, Francine

Subject ID	Age (years)	Sex	ECOG Score	Tumor Stage	Tumor Location	Pancreatic Cancer Inoperability	Prior Treatments	Length of Alpha DaRT Sources (cm)	GTV Coverage @ 16 Gy Alpha Radiation Dose
Progressive Disease; Death ~3 months after treatment								3	8%
Progressive Disease; Death ~3 months after treatment								11	13%
Stable Disease at 28 days; Partial Response at 69 days								21	44%
Stable Disease at 28 and 98 days								22	12.5%
Stable Disease at 28 days								24	29.5%

Note: Results as of November 28, 2023

Patient Characteristics

Including the first five patients from the interim data released in late 2023, a total of **n = 41 patients have been treated** thus far with pancreatic cancer across the three trials

	Canada (n=24)	**Israel (n=17)**		
Characteristic (n)	PANC-101	PANC-02	ALL-00	Total
Gender				
Male	10	7	6	23
Female	14	2	2	18
Median Age	70	75	72	71
Cancer Stage				
2	4	1	0	5
3	4	3	2	9
4	16	5	6	27
Previous/concurrent lines of chemotherapy				
0	7	1	1	9
1	9	3	3	15
2	8	5	4	17

Highlights of Interim Feasibility and Safety Results

100% success in delivering Alpha DaRT sources (feasibility)

Strong safety results

- Total of 151 adverse events (AEs) reported
- 38 were associated with Alpha DaRT (possibly, probably or definitely related), of which 29 were mild (Grade 1), five were moderate (Grade 2) and four were severe (Grade 3), of which three were SAEs
- Three related SAEs included:
  - Two cases of elevated liver functions:
    - One patient hospitalized and discharge
    - One patient declined to hospitalize and recovered at home
  - One case of sepsis – stabilized, hospitalized and discharge

Note: Results as of January 8, 2025

Possibly-, Probably- or Definitely-Related Adverse Events (by CTCAE)

CTCAE Coded Term	1 – Mild	2 – Moderate	3 – Severe	4 – Life-Threatening	5 – Death	Total
Abdominal pain	6		1			7
Fatigue	5	2				7
Anorexia	3	1				4
Not yet coded	2	1	1			4
Nausea	3					3
Blood bilirubin increased	1		1			2
Gallbladder obstruction	1	1				2
Alkaline phosphatase increased	1					1
Back pain	1					1
Bloating	1					1
Chills	1					1
Gastroesophageal reflux disease	1					1
Sepsis			1			1
Stomach pain	1					1
Vomiting	1					1
Weight loss	1					1
Total	29	5	4	0	0	38

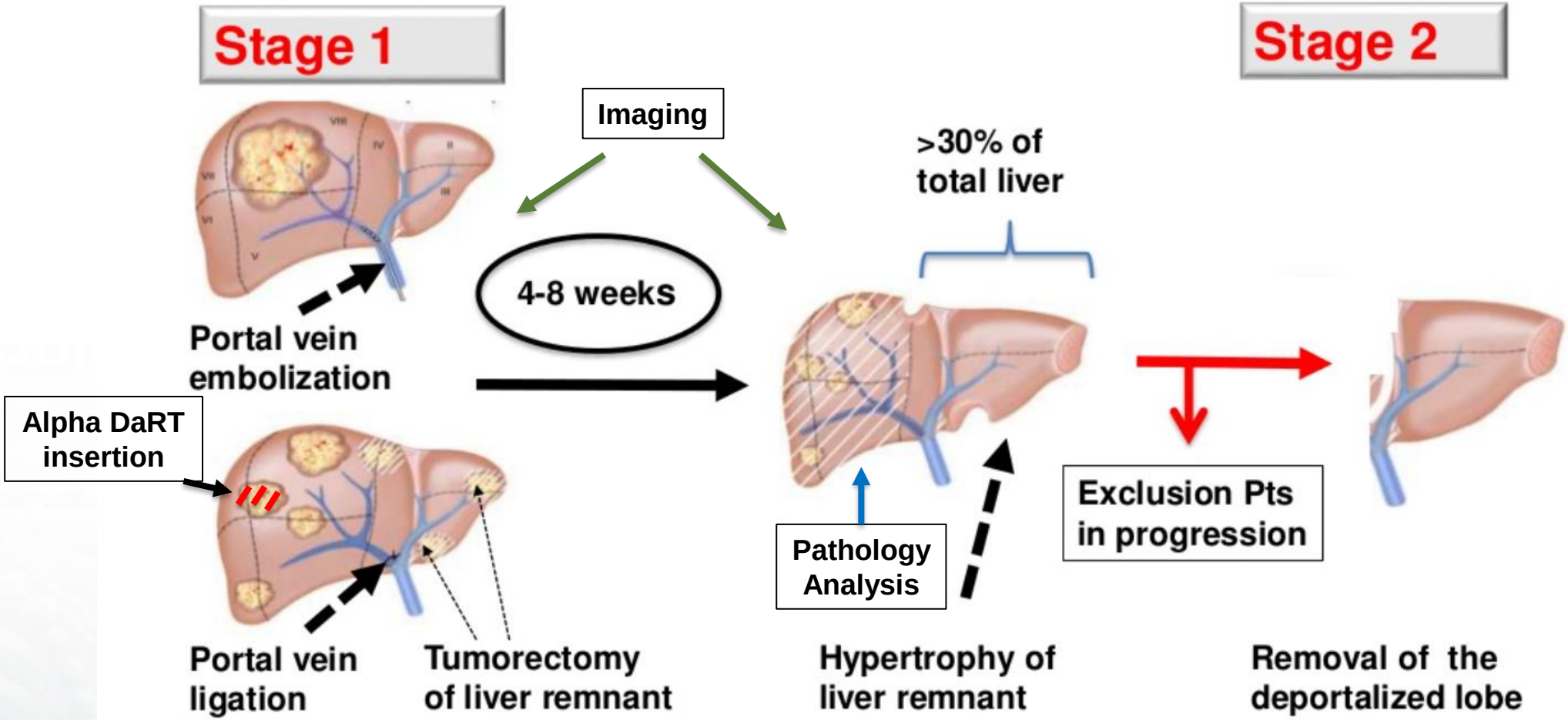
Internal Organs

A Feasibility and Safety Study of Intratumoral Diffusing Alpha Radiation Emitters for the Treatment of Liver Metastases

CTP-LIV-00

Study Schema

Liver study



Clavien et al. Strategies for safer liver surgery. NEJM, 2017

Outline of Liver Metastases Study - CTP-LIV-00

Primary objectives: Evaluate feasibility & safety of Alpha DaRT implanted in liver metastases

Secondary / exploratory objectives: Evaluate pathological and radiological response, determine immunological impact, stratify differences in response by histopath. growth patterns (vascular / immuno.)

Key Eligibility Criteria

Referred for a **two-staged hepatectomy** to resect liver metastases of colorectal cancer

No prior use of **systemic investigational agents** for primary cancer

Sample size N = 10 patients

Treatment and Procedure

Treatment plan based on CT scan or MRI

Sources 0.7 mm in diameter and 1 cm in length

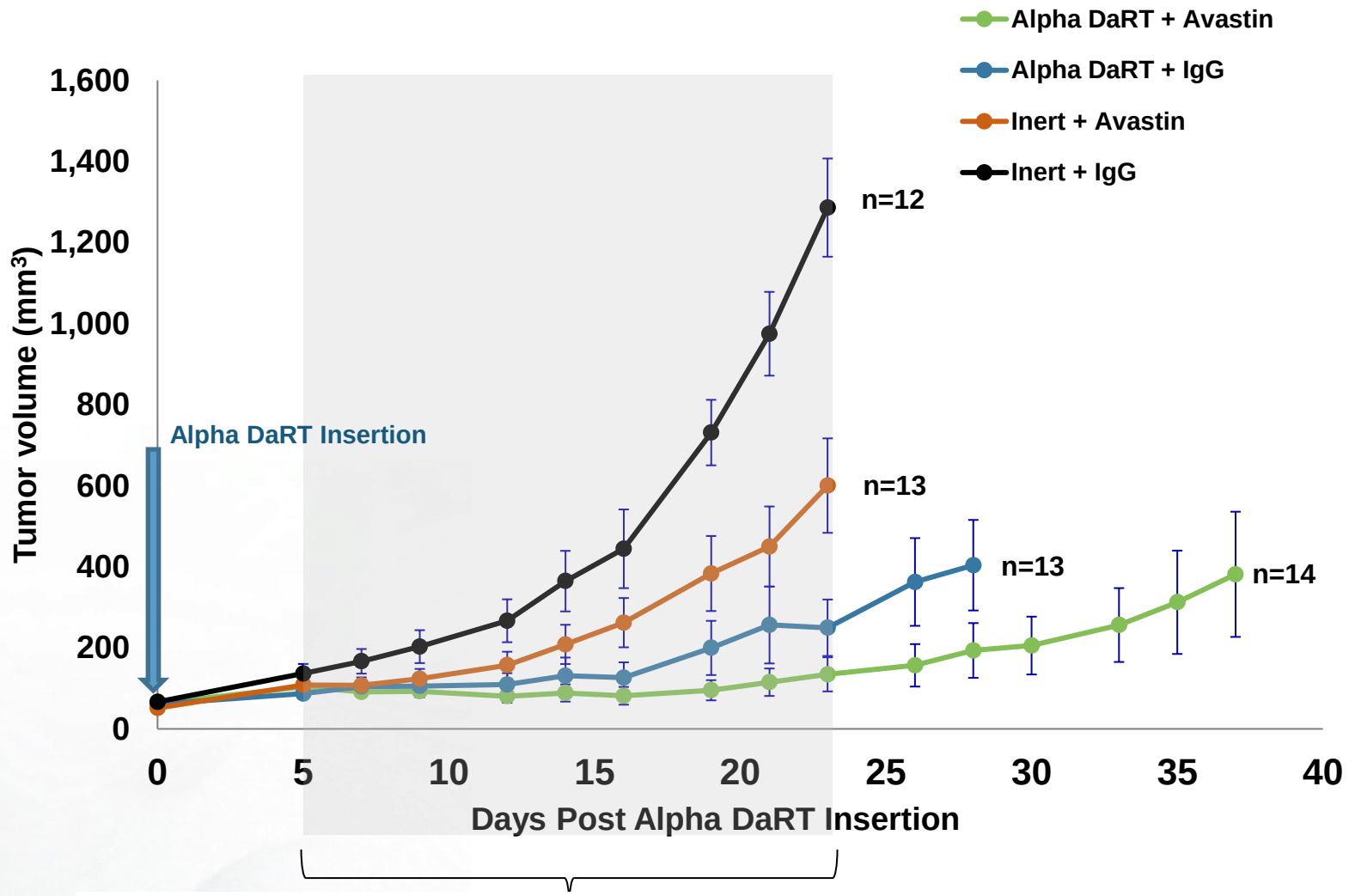
Activity per source 3 µCi

General anesthesia

Timeline

- **1st operation:** one side of the liver is cleared from its metastases & Alpha DaRT sources are implanted in the other side of the liver
- 3 - 4 cycles of **chemotherapy** (6 - 8 weeks)
- **2nd operation:** The liver lobe containing the metastasis with the sources is resected, to leave the patient with a disease-free liver

Alpha DaRT + Avastin Combo Showed Attenuated Growth of GBM Xenografts



Simple Radioactive Supply Chain

Delivery does not require any special handling and simple planning ensures on-time arrival

Alpha DaRT is shipped in Excepted Packages (low levels of radioactivity) or Type A packages, and may therefore be dispatched in suitable applicators by standard courier, requiring no special handling or protective gear in transit

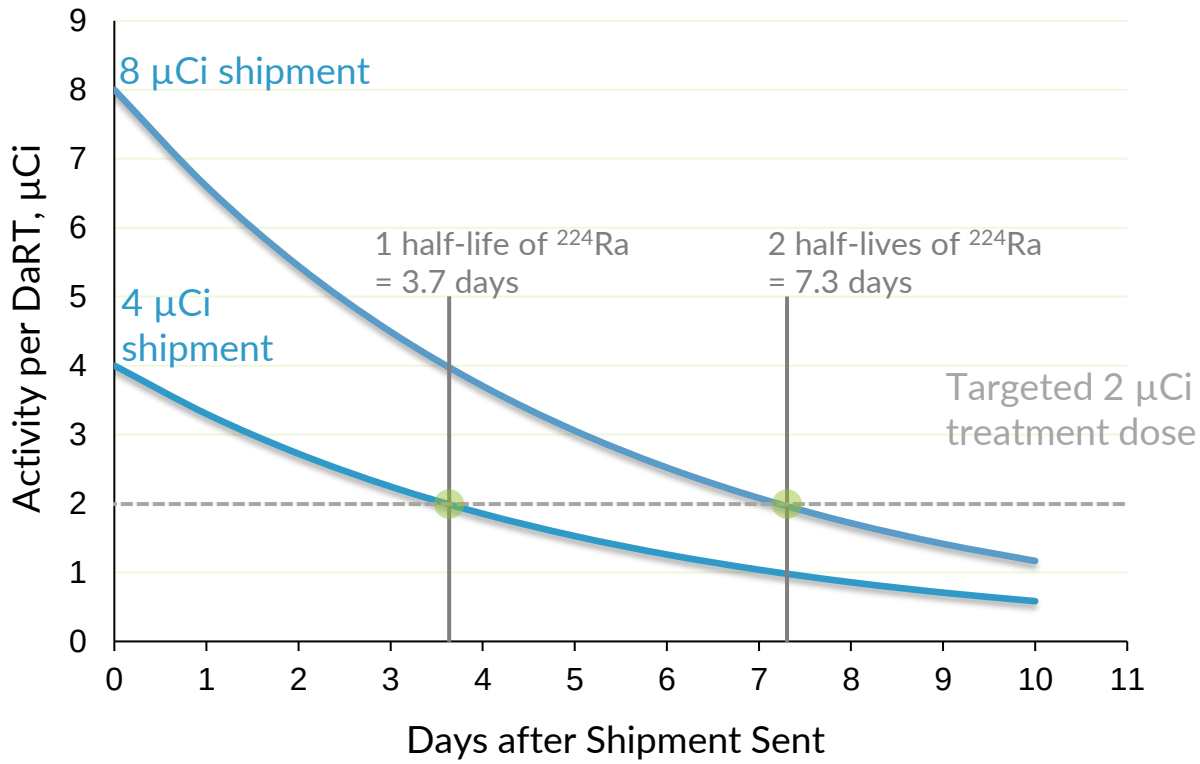
Radioactive Material Excepted Package

This package contains radioactive material, excepted package and is in all respects in compliance with the applicable international and national governmental regulations.

UN 2910

The information for this package need not appear on the Notification to Captain (NOTOC)

Alpha DaRT Radioactive Decay



Personalized treatment, shipped out on a per-patient basis

Simple planning ensures that an Alpha DaRT arrives with the required amount of ^{224}Ra available, even when allowing for radioactive decay, based on the known half-life of the ^{224}Ra

Global Manufacturing Facilities

For efficient commercial operations, we look to establish manufacturing operations in multiple regions of the world, to enable relatively short shipping times to our core markets

Hudson, New Hampshire
(Under Construction)

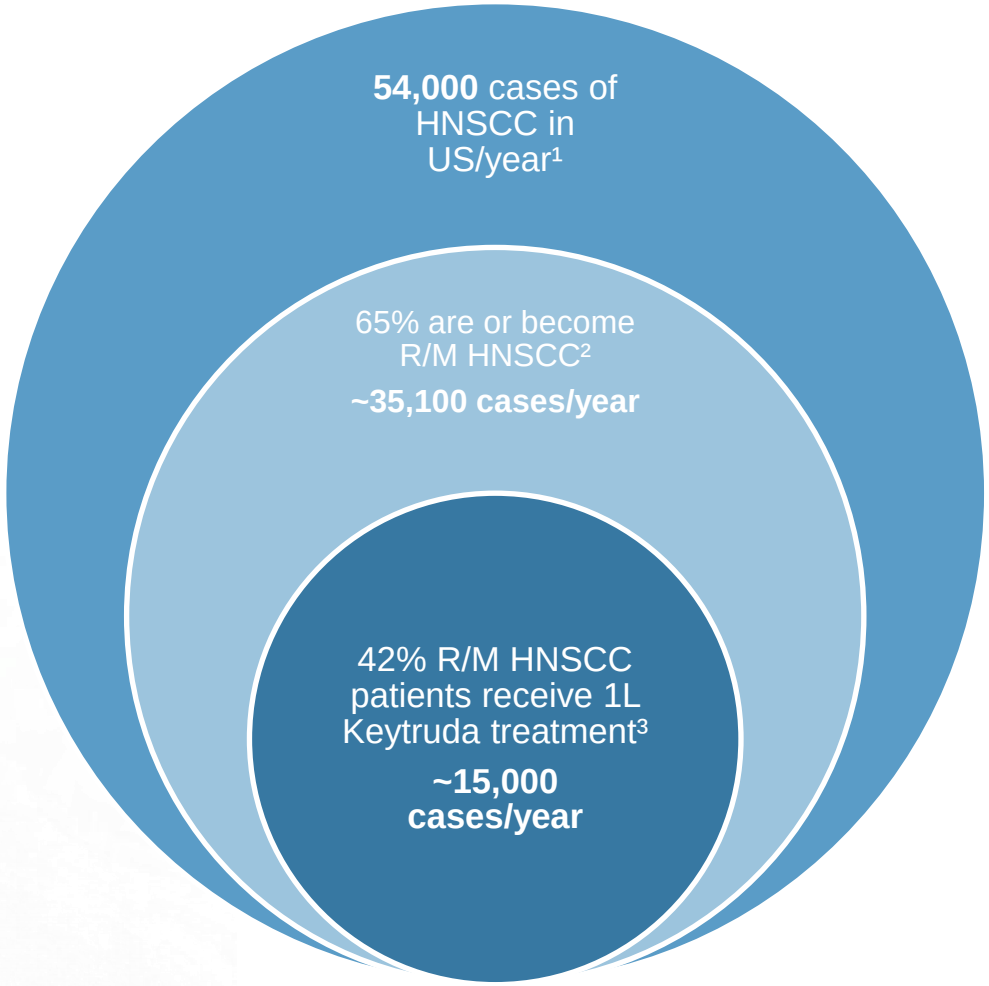
Jerusalem
(~400,000 sources per year – Ramping Up)

Lawrence, Massachusetts
(Ramping Up)

Jerusalem
(Land Granted – Facility in Planning)

Togane, Japan
(In Design)

HNSCC Patient Breakdown



[1]*Epidemiology, Risk Factors, and Prevention of Head and Neck Squamous Cell Carcinoma* Adam Barsouk, John Sukumar Aluru, Prashanth Rawla, Kalyan Saginala, Alexander Barsouk. *Med. Sci.* 2023, *11*(2), 42; https://doi.org/10.3390/medsci11020042

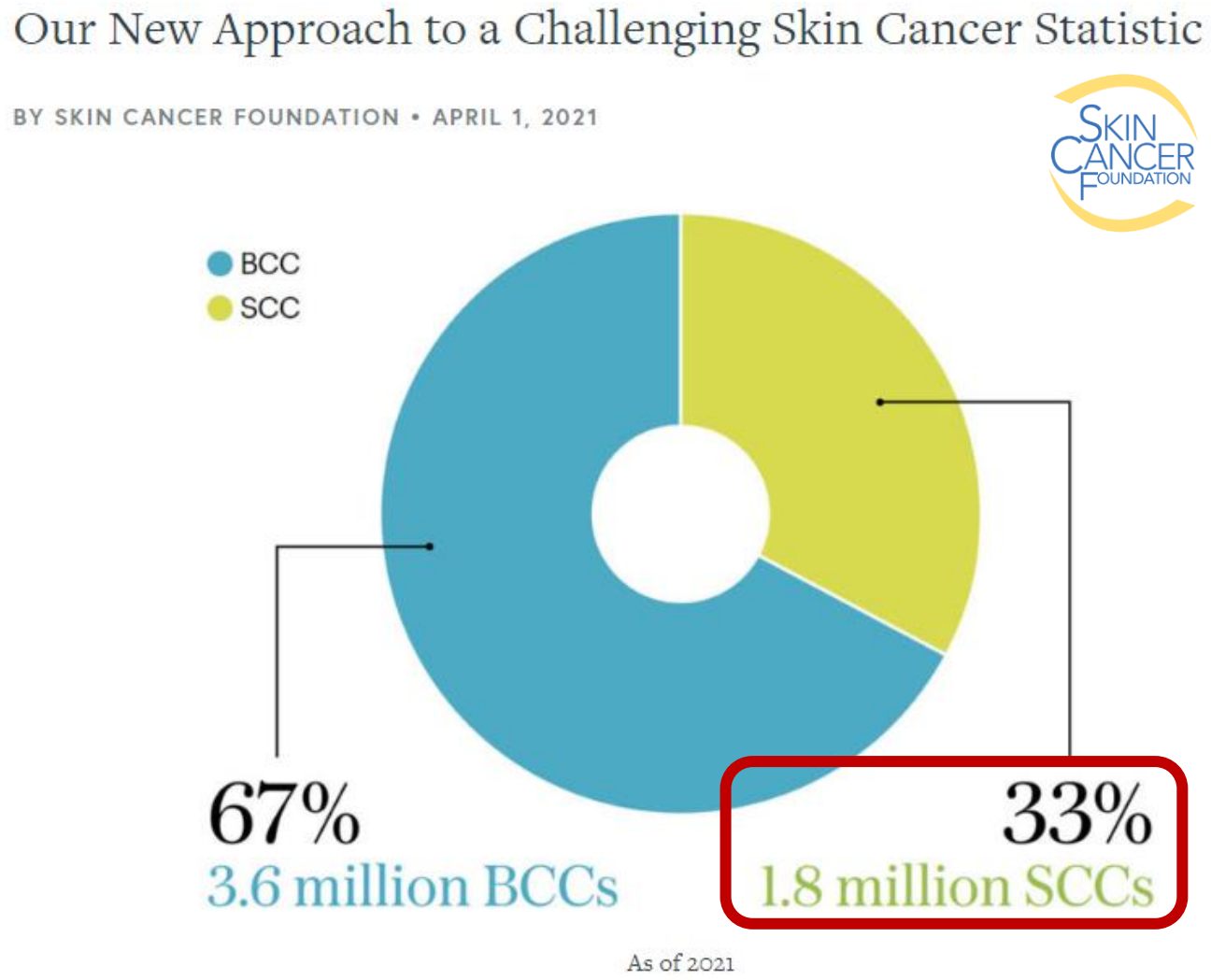
[2]*Recent Advances and Future Directions in Clinical Management of Head and Neck Squamous Cell Carcinoma* Jameel Muzaffar, Shahla Bari, Kedar Kirtane, Christine H. Chung *Cancers* 2021, *13*(2), 338; https://doi.org/10.3390/cancers13020338

[3]*Real-world treatment patterns and outcomes among individuals receiving first-line pembrolizumab therapy for recurrent/metastatic head and neck squamous cell carcinoma* Christopher M Black, Glenn J Hanna, Liya Wang, Karthik Ramakrishnan, Daisuke Goto, Vladimir Turzhitsky, Gleicy M Hair Front Oncol. 2023 May 22;13:1160144. https://doi.org/10.3389/fonc.2023.1160144

Appendix

Analysis of U.S. Market Opportunity in Cutaneous Squamous Cell Carcinoma

U.S. Annual Cutaneous Squamous Cell Carcinoma Incidence



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

Risk Stratification Per NCCN Guidelines

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Squamous Cell Skin Cancer

NCCN Guidelines Index
Table of Contents
Discussion

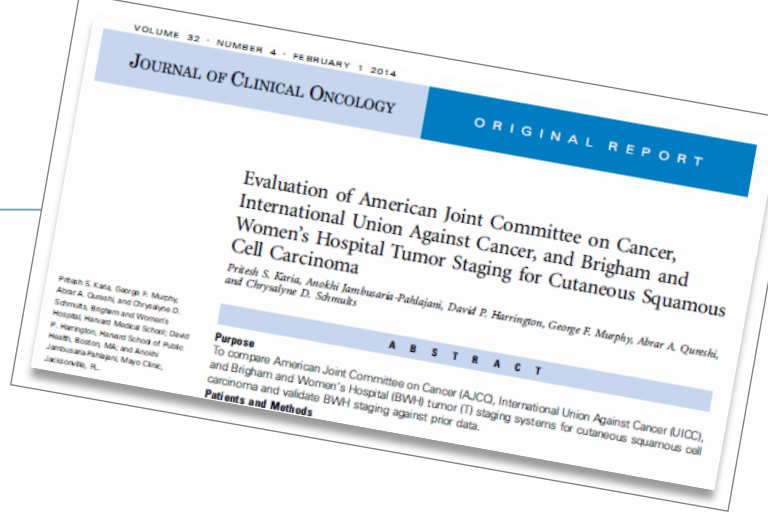
STRATIFICATION TO DETERMINE TREATMENT OPTIONS AND FOLLOW-UP FOR LOCAL CSCC BASED ON RISK FACTORS FOR LOCAL RECURRENCE, METASTASES, OR DEATH FROM DISEASE

Risk Group[a]	Low Risk	High Risk	Very High Risk
Treatment options	SCC-2	SCC-3	SCC-3
H&P			
Location/size[b]	Trunk, extremities ≤2 cm	Trunk, extremities >2 cm – ≤4 cm	>4 cm (any location)
		Head, neck, hands, feet, pretibia, and anogenital (any size)[e]	
Clinical extent	Well-defined	Poorly defined	
Primary vs. recurrent	Primary	Recurrent	
Immunosuppression	(-)	(+)	
Site of prior RT or chronic inflammatory process	(-)	(+)	
Rapidly growing tumor	(-)	(+)	
Neurologic symptoms	(-)	(+)	
Pathology (SCC-A)			
Degree of differentiation	Well or moderately differentiated		Poor differentiation
Histologic features: Acantholytic (adenoid), adenosquamous (showing mucin production), or metaplastic (carcinosarcomatous) subtypes	(-)	(+)	Desmoplastic SCC
Depth[c,d]: Thickness or level of invasion	<2 mm thick and no invasion beyond subcutaneous fat	2–6 mm depth	>6 mm or invasion beyond subcutaneous fat
Perineural involvement	(-)	(+)	Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring ≥0.1 mm
Lymphatic or vascular involvement	(-)	(-)	(+)

Focus Patients

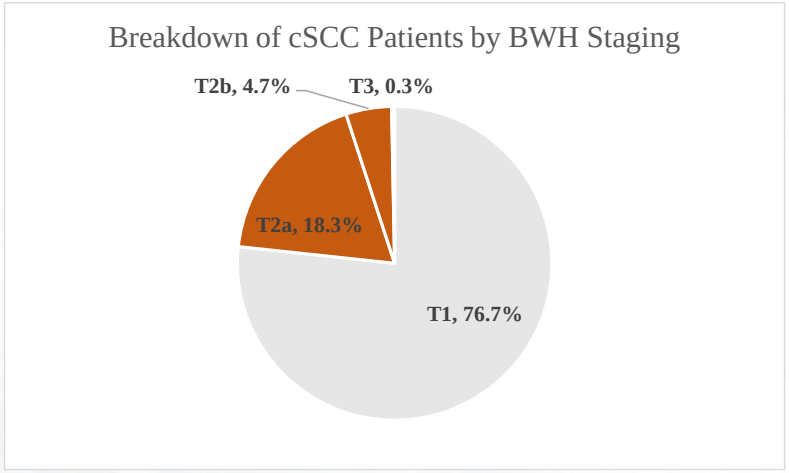
Source: NCCN Guidelines for Cutaneous SCC: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf

How Many Are “High/Very-High Risk”?
Staging from Brigham & Women’s Hospital (BWH) Researchers



BWH Tumor Stage	Description
T1	0 high-risk factors*
T2a	1 high-risk factor
T2b	2-3 high-risk factors
T3	≥ 4 high-risk factors

*Note: High-risk factors include tumor diameter ≥ 2 cm, poorly differentiated histology, perineural invasion ≥ 0.1 mm, or tumor invasion beyond fat (excluding bone invasion which automatically upgrades tumor to BWH stage T3).
Compare to high-risk factors from NCCN Guidelines on previous page!



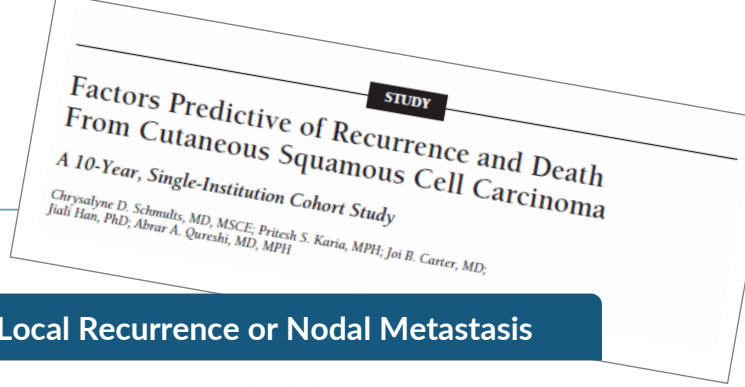
23.3% of cSCC are stages T2a – T3 (high-risk, i.e., at least 1 risk factor)

At 1.8 million cSCC incidences per year, that translates into **~419k high-risk cases per year**!

Source: 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

What Are cSCC Outcomes Like?

Data from Brigham & Women's Hospital (BWH) Researchers


STUDY

Factors Predictive of Recurrence and Death From Cutaneous Squamous Cell Carcinoma

A 10-Year, Single-Institution Cohort Study

Chrysalyne D. Schmults, MD, MSCE; Pritesh S. Karia, MPH; Joi B. Carter, MD; Jiali Han, PhD; Abrar A. Qureshi, MD, MPH

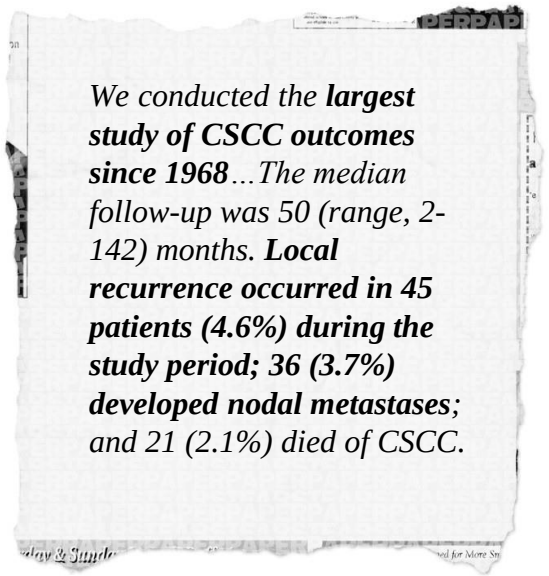
NCCN Risk Factors Correspond to Recurrence and Metastatic Outcomes

Table 3. Results of Univariate Analysis for Outcomes of Interest

	LR		NM		DSD		ACD	
	SHR (95% CI)	*P* Value	SHR (95% CI)	*P* Value	SHR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age, y								
<70	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
70-80	2.1 (1.1-3.9)	.02	1.2 (0.6-2.5)	.66	1.1 (0.4-2.7)	.89	1.7 (1.4-2.0)	<.001
>80	1.7 (0.8-3.8)	.17	1.0 (0.4-2.8)	.99	0.9 (0.2-3.3)	.88	2.5 (2.0-3.1)	<.001
Sex								
Female	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Male	1.6 (0.9-3.0)	.11	2.4 (1.0-5.5)	.04	2.8 (1.9-8.3)	.06	1.9 (1.6-2.3)	<.001
Tumor diameter, cm								
<2	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
≥2	8.9 (5.1-15.7)	<.001	15.2 (6.6-35.2)	<.001	28.5 (9.4-86.3)	<.001	1.0 (0.8-1.3)	.75
Tumor differentiation								
Well	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Moderate	2.7 (1.3-5.9)	.01	5.6 (1.6-19.1)	.006	2.5 (0.6-11.2)	.23	1.3 (1.1-1.6)	.02
Poor	10.4 (5.4-19.0)	<.001	29.8 (10.2-87.0)	<.001	19.4 (6.4-58.5)	<.001	1.7 (1.3-2.1)	<.001
Tumor depth								
Dermis	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Subcutaneous fat	5.9 (3.0-11.7)	<.001	7.2 (2.8-18.1)	<.001	8.8 (2.8-27.8)	<.001	1.5 (1.1-2.0)	.006
Beyond fat	24.4 (12.9-46.1)	<.001	43.0 (19.6-93.2)	<.001	51.4 (19.1-137.8)	<.001	1.7 (1.2-2.6)	.008
Perineural invasion								
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	8.8 (4.8-16.4)	<.001	14.5 (7.1-29.8)	<.001	11.3 (4.5-28.1)	<.001	1.7 (1.2-2.3)	.003
Lymphovascular invasion								
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	5.7 (2.4-13.4)	<.001	2.7 (0.6-11.3)	.17	2.1 (0.3-15.3)	.47	1.3 (0.8-2.1)	.33
Tumor location								
Other	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Head or neck (excluding ear and temple)	2.5 (1.5-4.4)	.001	2.4 (1.3-5.0)	.009	1.8 (0.8-4.3)	.18	1.1 (0.9-1.3)	.34
Ear	3.8 (1.4-10.4)	.01	3.1 (0.9-11.0)	.03	2.6 (0.8-9.0)	.12	1.4 (1.0-1.9)	.03
Temple	3.2 (1.1-9.0)	.03	3.8 (1.2-12.5)	.03	1.8 (0.2-13.5)	.56	1.5 (1.0-2.3)	.07
Perianal	17.4 (4.1-72.4)	<.001	64.3 (12.4-321.1)	<.001	39.0 (10.7-142.4)	<.001	1.0 (0.3-4.0)	.79
Genitalia	15.0 (2.6-88.2)	.003	69.4 (14.6-329.8)	<.001	47.6 (8.0-282.4)	<.001	0.9 (0.2-5.4)	.78

Abbreviations: ACD, all-cause death; DSD, disease-specific death; HR, hazard ratio; LR, local recurrence; NM, nodal metastasis; SHR, subhazard ratio.

Estimate of Patient Pool with Local Recurrence or Nodal Metastasis



*We conducted the **largest study of CSCC outcomes since 1968**…The median follow-up was 50 (range, 2-142) months. **Local recurrence occurred in 45 patients (4.6%) during the study period; 36 (3.7%) developed nodal metastases**; and 21 (2.1%) died of CSCC.*

1.8 million incidences per year, with 4.6% local recurrence and another 3.7% nodal metastasis, translates into **~148 thousand recurrent / metastatic cases per year**

Source: 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

Alpha DaRT – Analyst Views on Potential Treatment Selling Price

Wall street analysts' views – not company view

>$20K

H.C. WAINWRIGHT & CO.

"We estimate that Alpha DaRT may be priced at over $20,000 per treatment course per patient"

April 2023

$60K

PIPER | SANDLER

"We've conservatively assumed an ASP per procedure of $60K, although payment rates for therapies such as NVCR's Optune ($100K+) represents upside opportunity to our estimates if DRTS could secure a commensurate therapy payment rate."

April 2022

$65K

CANTOR Fitzgerald

Alpha DaRT Gross Price	$65,000
% Price Growth	2%

Source: Cantor Fitzgerald Estimates

April 2022

$125K

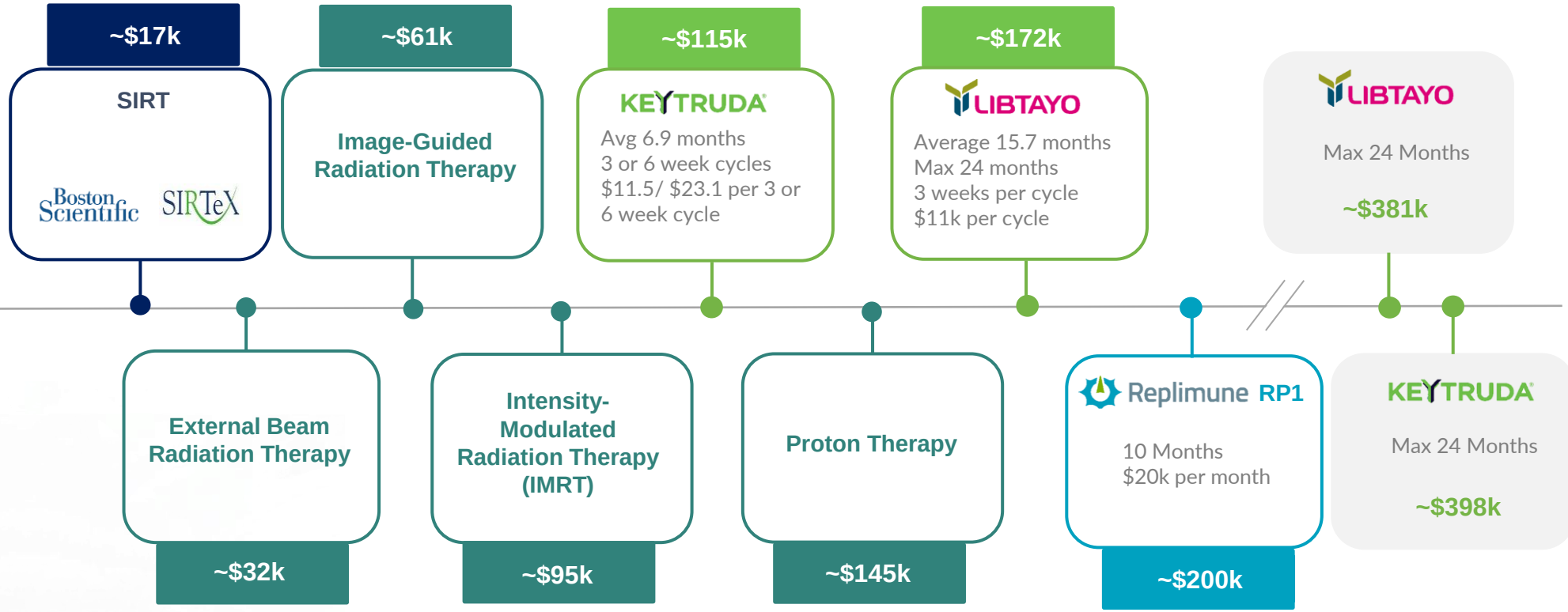
citi

"We model per-patient pricing at $125,000 at launch, consistent with the annualized cost of cancer immunotherapies (i.e., cemiplimab)."

December 2023

Benchmarking of U.S. Treatment Prices

- **Local radiotherapy medical device (competing liver radioembolization products)**
- **Local radiation therapy for adjuvant cSCC**
- **Locally injected drug product candidate for cSCC**
- **FDA comparator systemic therapies for pivotal trial statistics**



Note: ReSTART trial inclusion criteria envisions usage when standard radiation therapy is not indicated, and uses systemic therapies as historical control arms

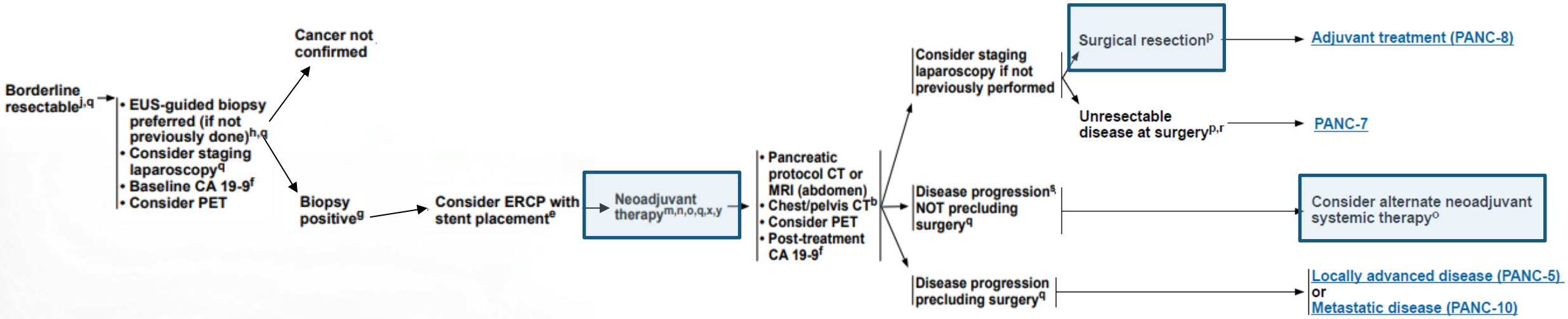
Source for SIRT pricing: https://www.sirtex.com/Media/womp5u2s/Sirtex%20Coding%20Guide_Hosp%20%28HEPRA-US-001-02-24%293.pdf
Source for cSCC radiation therapy pricing: https://ncbi.nlm.nih.gov/pmc/articles/PMC10826833/#:~:text=Based%20on%20four%20radiation%20treatment,patient%2C%20detailed%20in%20Table%201B-
Source for Libtayo price:https://www.ncbi.nlm.nih.gov/books/NBK596646/
Source for Libtayo average treatment length: https://www.libtayohcp.com/cscc/efficacy/response-duration
Source for Libtayo max treatment length: https://www.medicalnewstoday.com/articles/drugs-libtayo-dosage#dosage
Source for Keytruda avg treatment length: https://www.merck.com/news/fda-approves-expanded-indication-for-mercks-keytruda-pembrolizumab-in-locally-advanced-cutaneous-squamous-cell-carcinoma-cscc/
Source for Keytruda price: https://www.keytruda.com/financial-support/
Source for Keytruda treatment cycle: https://www.keytrudahcp.com/dosing/options/
Source for Keytruda max price: https://www.keytrudahcp.com/dosing/options/
Source for RP1 Replimune: Barclays research model as of 24-Feb-2024 for Replimune Group Inc

Appendix

The Role of Local Therapies in Treating Pancreatic Cancer

II Pancreatic Adenocarcinoma Stage II: Borderline Resectable
NCCN Guidelines

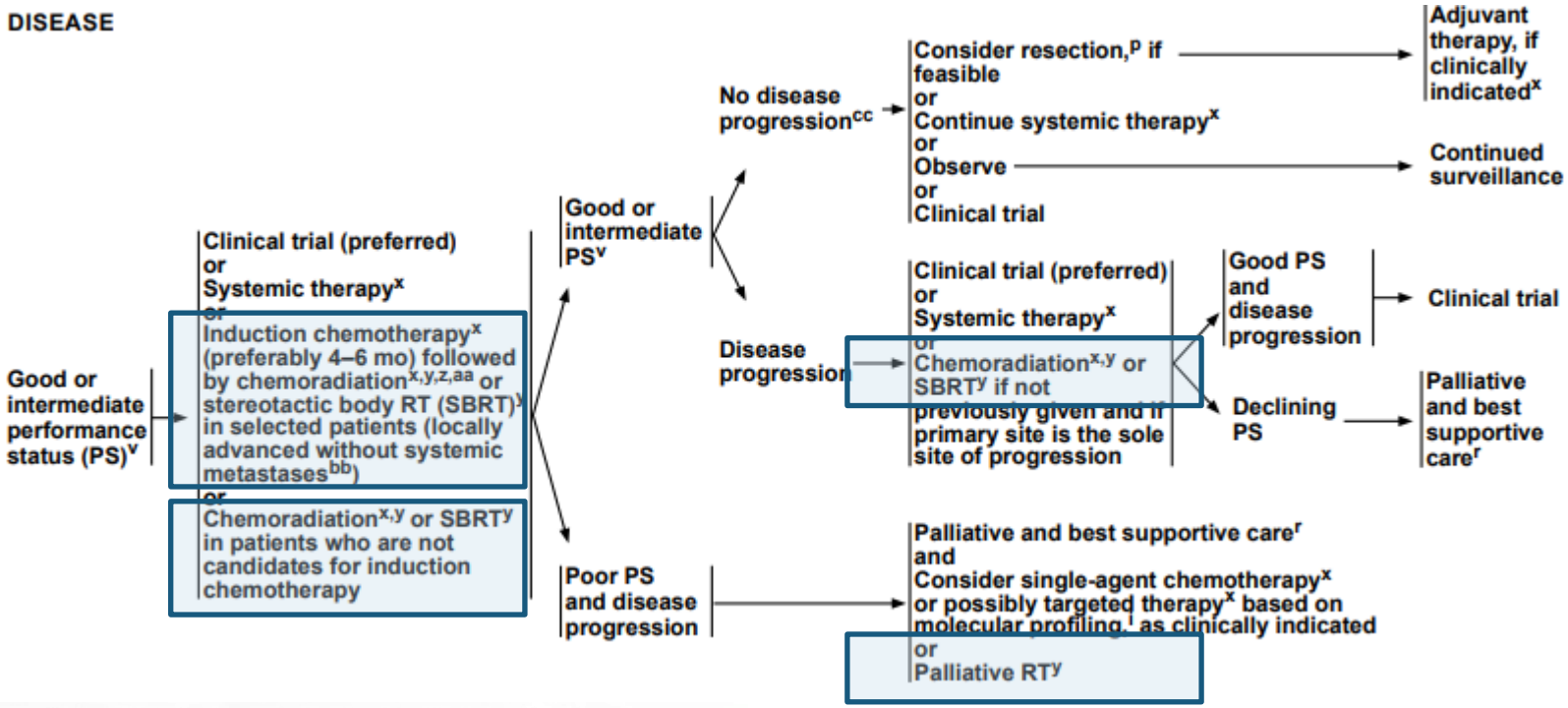
"RT (Radiation Therapy) in the neoadjuvant setting may lead to an increased likelihood of a margin negative resection and local control"
- NCCN Guidelines



With borderline resectable patients, the goal of therapy is to downstage the patient with neoadjuvant therapy where possible, in an attempt to enable definitive local therapy, i.e., surgery. Radiation therapy is also used as one of these potential neoadjuvant therapies

Source: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf

III Pancreatic Adenocarcinoma Stage III: Locally Advanced
NCCN Guidelines



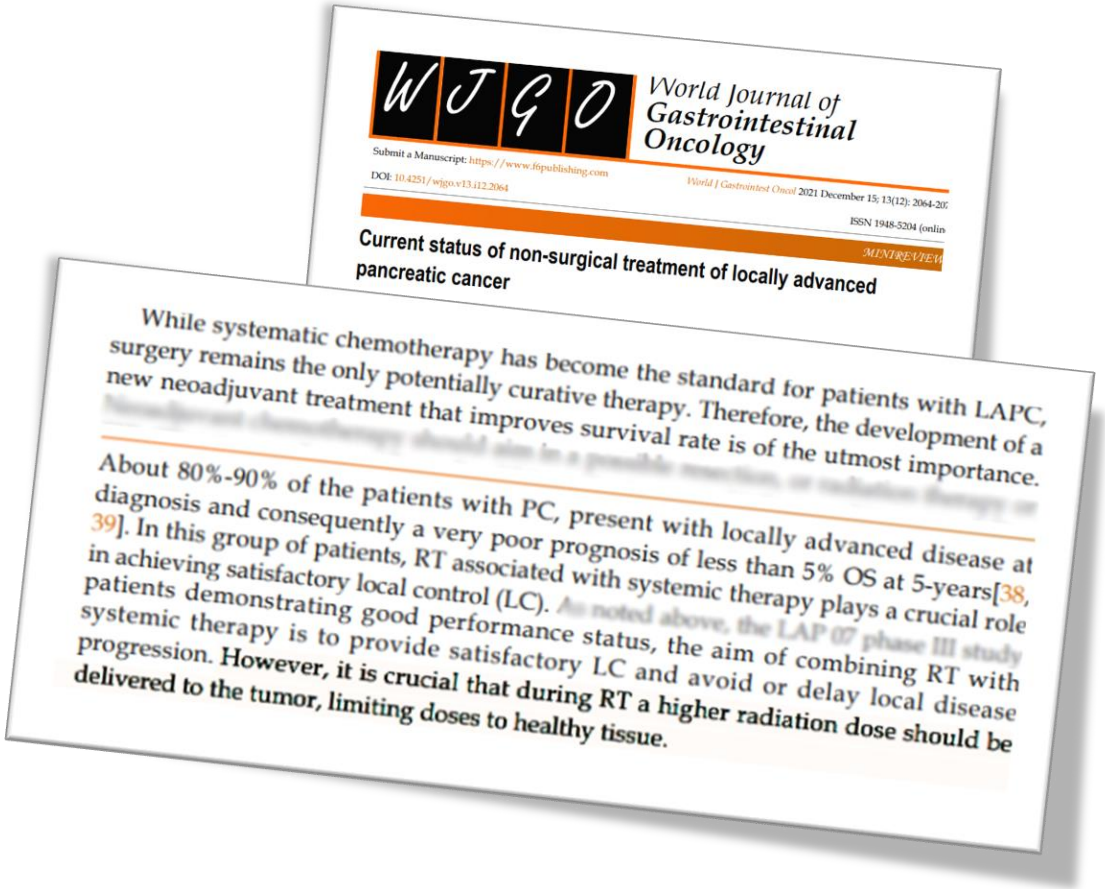
For locally advanced patients, whose tumor has not yet reached distant metastases, radiation therapy plays an important role in therapy, whether in the form of radiation alone (such as SBRT) or in combination with chemotherapy as a radiosensitizer (i.e., chemoradiation), and at later stages, for palliative purposes.

Source: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf

Perspectives on Treating Non-Metastatic Pancreatic Cancer

Retrospective Study of 13 Years of PDAC Patients at Single Oncology Center in Australia, Focus on Non-Metastatic Patients

Therapy Received	n=134	%	Median OS (months)
Chemotherapy only	18	13.5%	23
Chemotherapy + radiation	43	32%	34
Chemotherapy + surgery	34	25%	45
Cyberknife	2	1.5%	17
Trimodality	37	28%	47

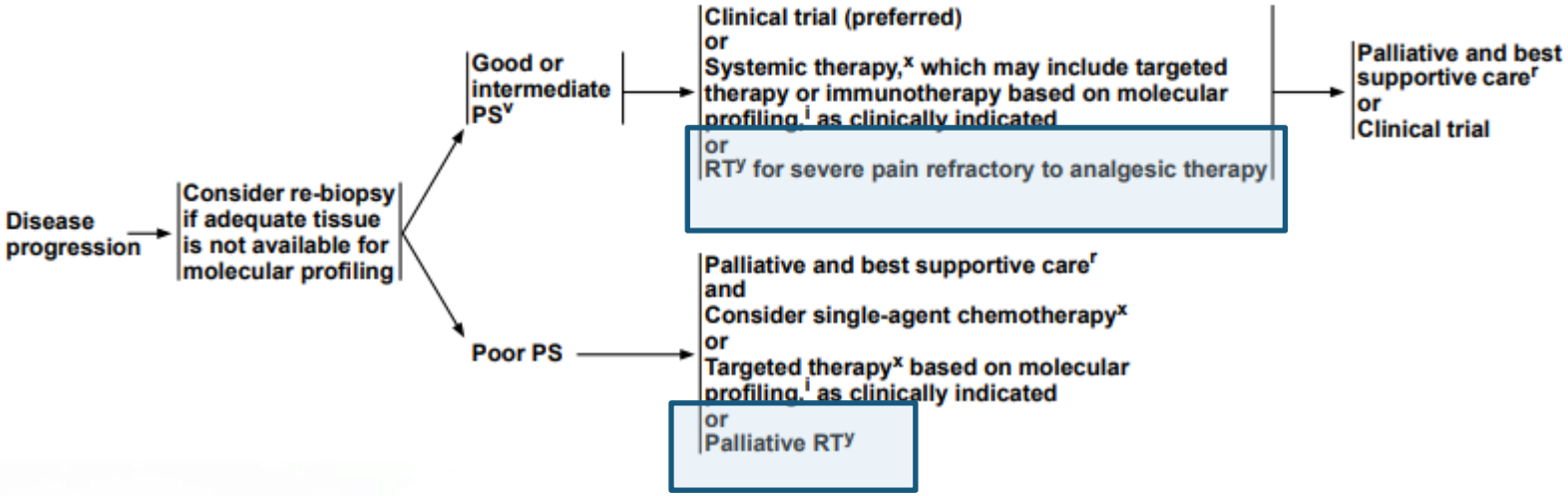


When examining a sample of treatment paradigms for non-metastatic patients, over 85% received one or more local therapies as part of their care.
These patients also had better OS outcomes

For LAPC, there is a dire need to find better forms of neoadjuvant treatment toward curative outcomes, as well as better forms of local control and delay of disease progression, especially radiation therapy with more potent doses that spare surrounding healthy tissue

Sources:
https://jgo.amegroups.org/article/view/79949/html
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8713317/

IV Pancreatic Adenocarcinoma Stage IV : Metastatic
NCCN Guidelines



- Even in the metastatic setting / for progressive disease, where a systemic therapy will be dominant, radiation therapy already plays an important role in palliative care.
- Of course, should a radiation therapy demonstrate a reproducible systemic anti-tumor immunity effect in a metastatic PC setting, then the potential for shifting the paradigm for treatment of late-stage PC is tremendous.

Source: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf