

Breakfast Event during ASCO 2022 Annual Meeting



(NASDAQ: CADL)



Tipping the balance in favor of the immune system to fight cancer



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Forward Looking Statements

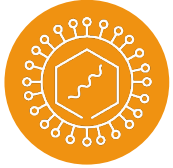
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These forward-looking statements are based on the beliefs of our management, as well as assumptions made by and information currently available to us. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. If such assumptions do not fully materialize or prove incorrect, the events or circumstances referred to in the forward-looking statements may not occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, except as required by law. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. Additional risks and uncertainties that could affect our business are included under the caption “Risk Factors” in our most recent report filed with the Securities and Exchange Commission.

Candel overview: Oncolytic viral immunotherapies

Two clinical stage investigational medicines and an innovative discovery platform



- **CAN-3110**

- Engineered, replication-competent herpes simplex virus with tumor-specificity
- Ongoing phase 1 clinical trial in recurrent HGG
- Potential for expansion of indications

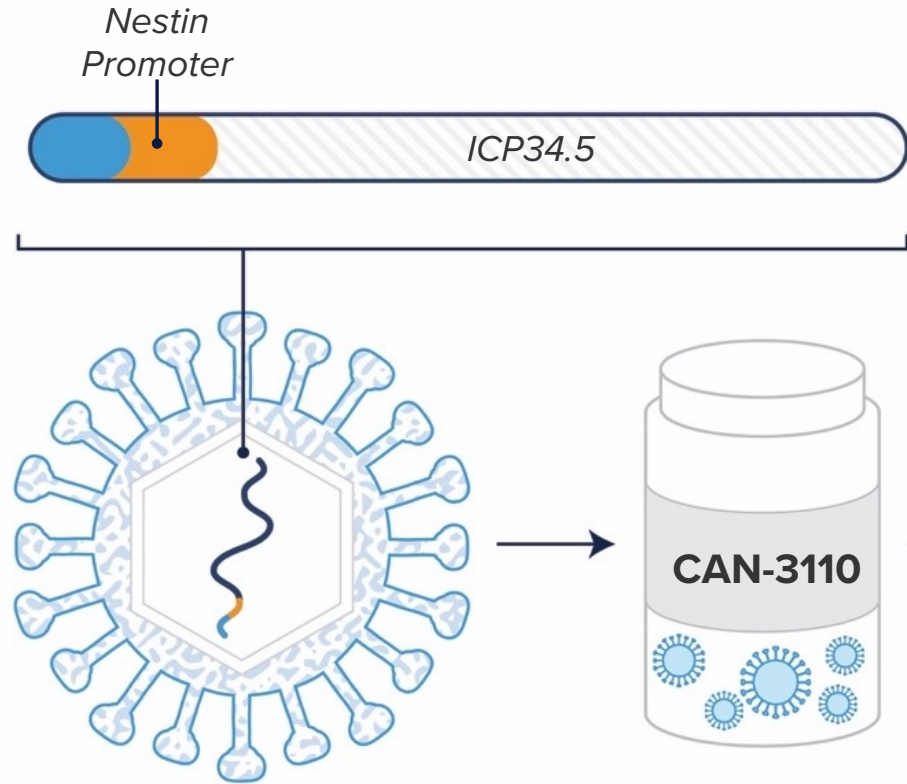


- **CAN-2409**

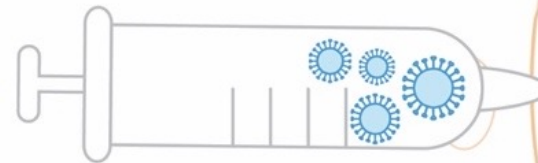
- Engineered, non-replicating adenoviral gene construct encoding HSV-thymidine kinase
- Ongoing clinical trials in NSCLC, high-grade glioma (HGG), pancreatic cancer, and prostate cancer
- Pipeline in a product

- **enLIGHTEN™** Discovery Platform based on HSV technology

CAN-3110: HSV “Nestin 34.5” construct

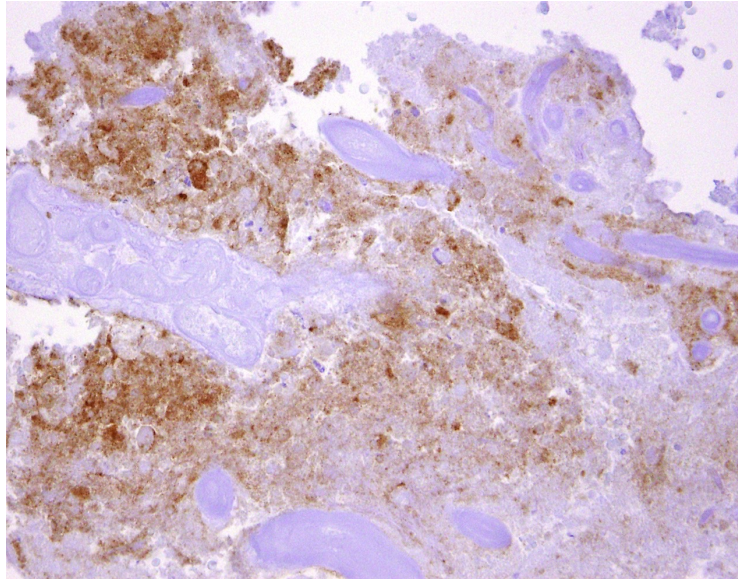


Nestin expression in tumor cells induces ICP34.5 expression, resulting in tumor-specific replication

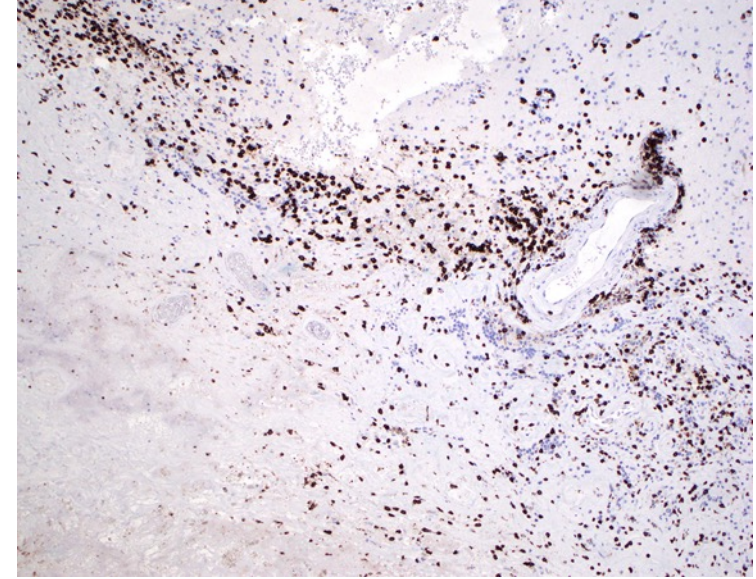


Virus expands in Nestin expressing tumor cells, causing oncolytic activity

Oncolytic HSV infection and CD8+ T cell infiltration after CAN-3110 treatment in patients with recurrent high-grade glioma



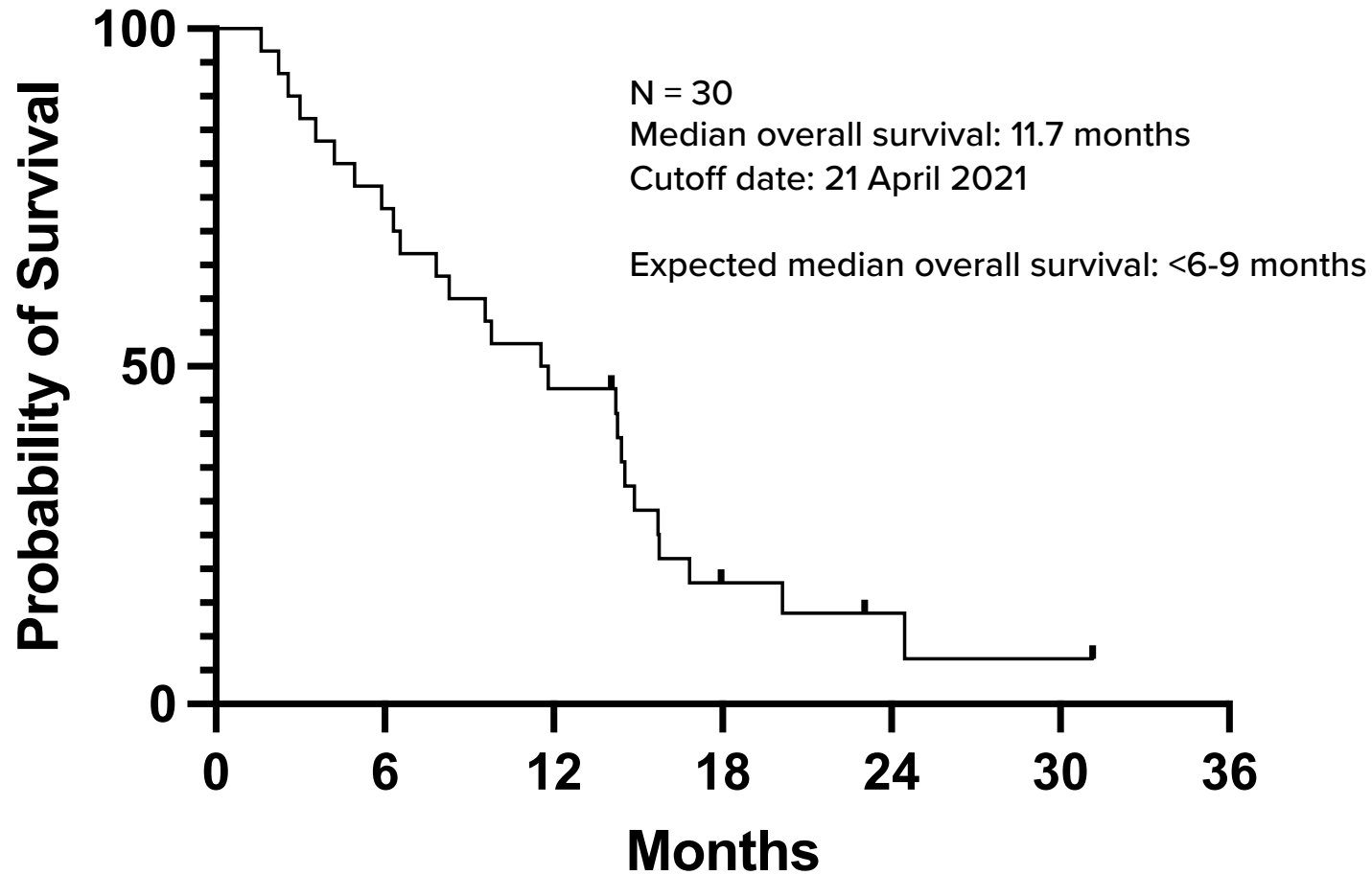
HSV1 antigen 6 weeks after injection of 1×10^6 pfu
 1.79×10^6 copies of viral DNA/mg
 2.97×10^5 copies of viral RNA transcript (ICP22)/mg



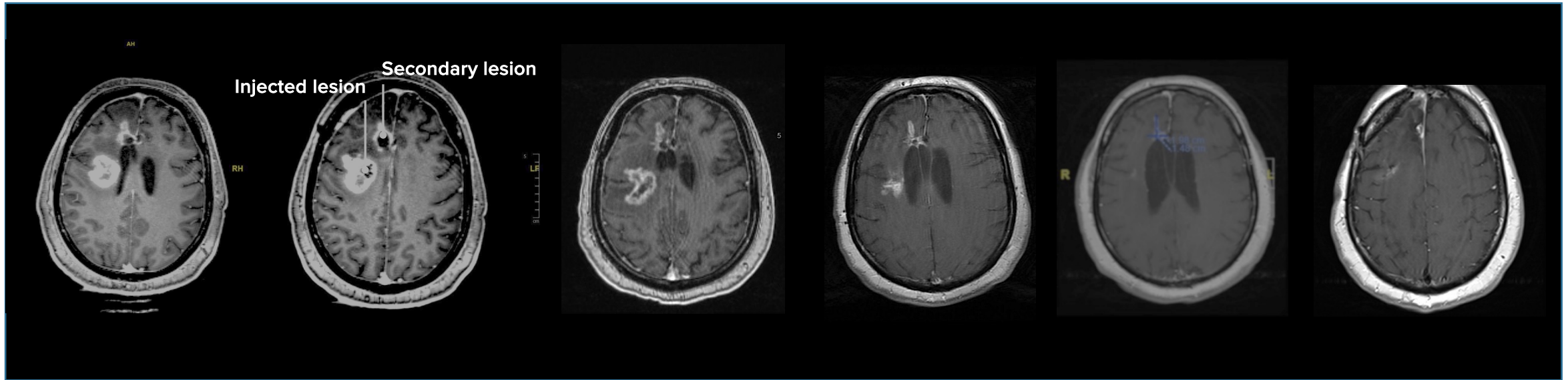
Infiltration by CD8+ cytotoxic T cells
(tumor infiltrating lymphocytes)

Post-treatment tissue (available in 18 patients) demonstrates persistence of HSV antigen and CD8+ T cell infiltrates
T cell receptor repertoire, transcriptomics, and single cell RNA sequencing analyses are ongoing

Survival in ongoing phase 1b clinical trial after single dose of CAN-3110 in recurrent high-grade glioma



Single agent activity of CAN-3110 in recurrent HGG patient with abscopal effect



Baseline

Day 0

Black hole within tumor
image is injection site
10⁶ PFU dose

Day 56

Reduction in contrast area
with no additional
treatment

Day 111

Patient back to work

Day 168

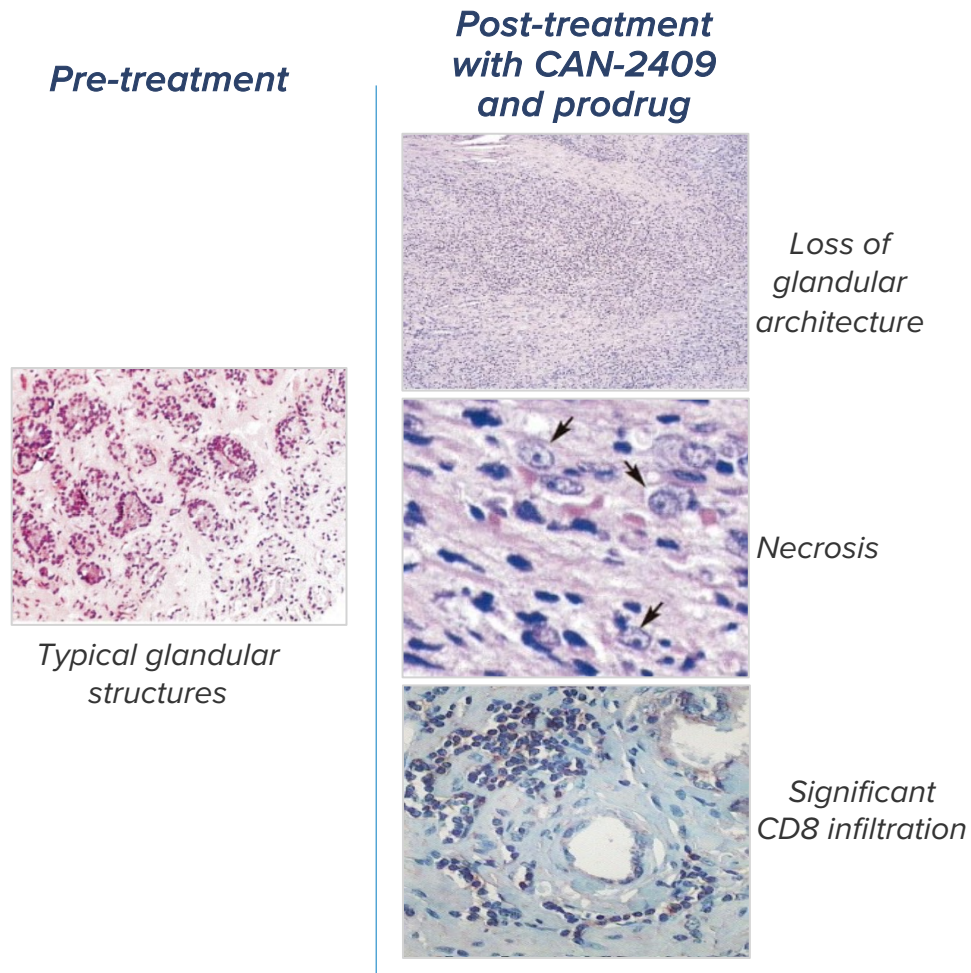
Day 280

56 YOM, IDH wild-type, MGMT partially methylated, right frontal mesial lesion initially treated with gross total resection, chemoradiation. Recurrences at two sites.

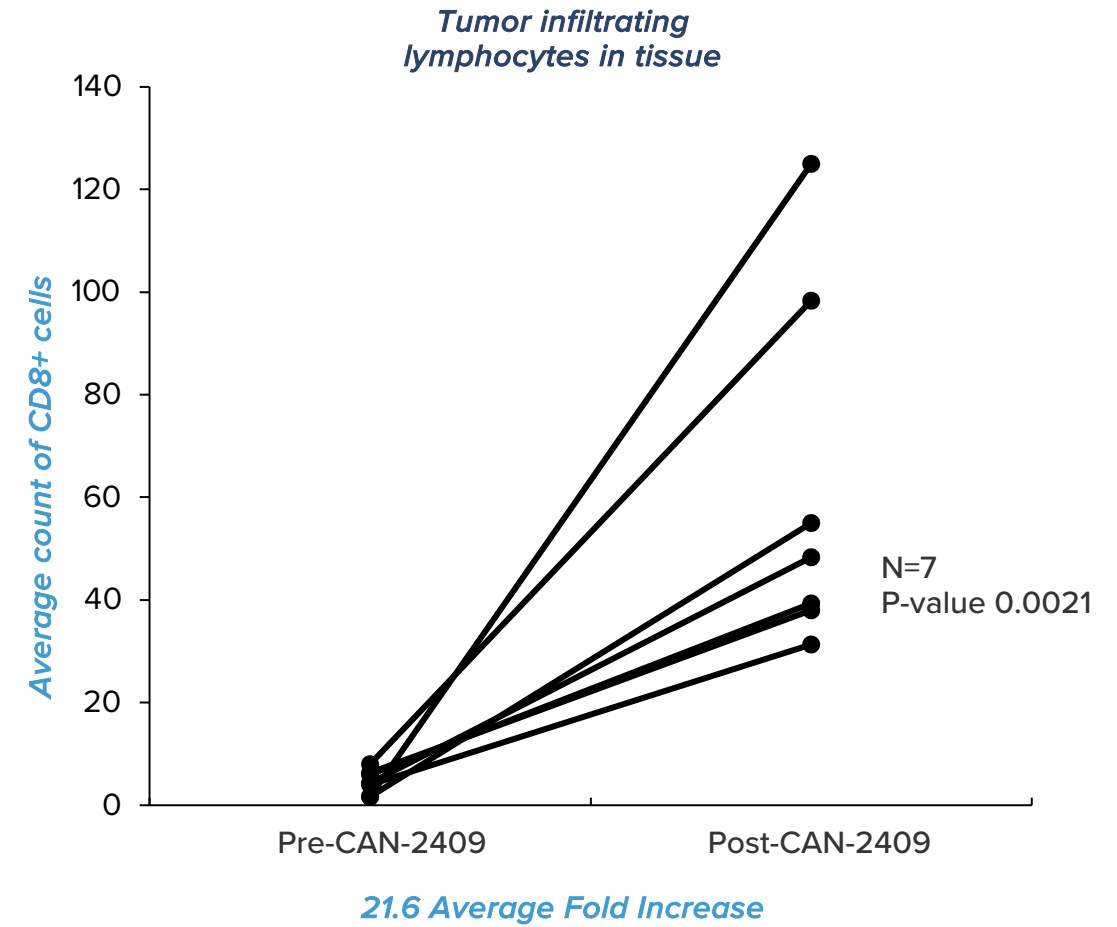
**Clinical effect on injected tumor
and uninjected tumor**

CAN-2409 treatment: Induction of CD8+ tumor-infiltrating lymphocytes in prostate cancer and pancreatic cancer

PROSTATE CANCER PH 1/2 STUDY

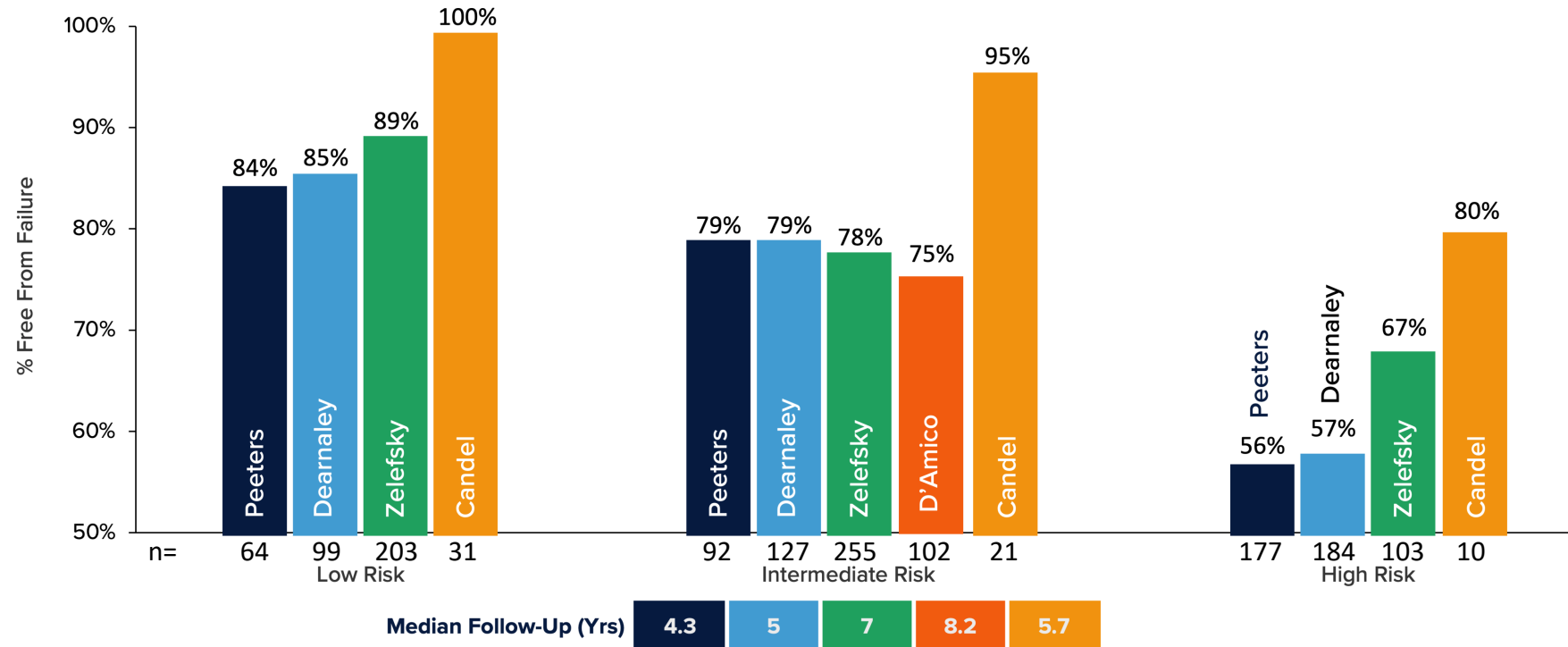


PANCREATIC CANCER PH 1/2 STUDY



Clinical evidence supports ongoing clinical trials of CAN-2409 in prostate cancer and pancreatic cancer

Completed phase 2 trial of CAN-2409 shows consistently improved freedom from failure rates in newly diagnosed, localized prostate cancer



- Pathological complete response (pCR) observed in 93% of the biopsies available at 2yrs (37%-73% in control populations)
- Low risk patients achieved PSA < 2ng/ml in 77% of CAN-2409 treated patients versus 58% in control populations
- Significant increase in activated CD8+ T cells compared to baseline (p=0.0003)

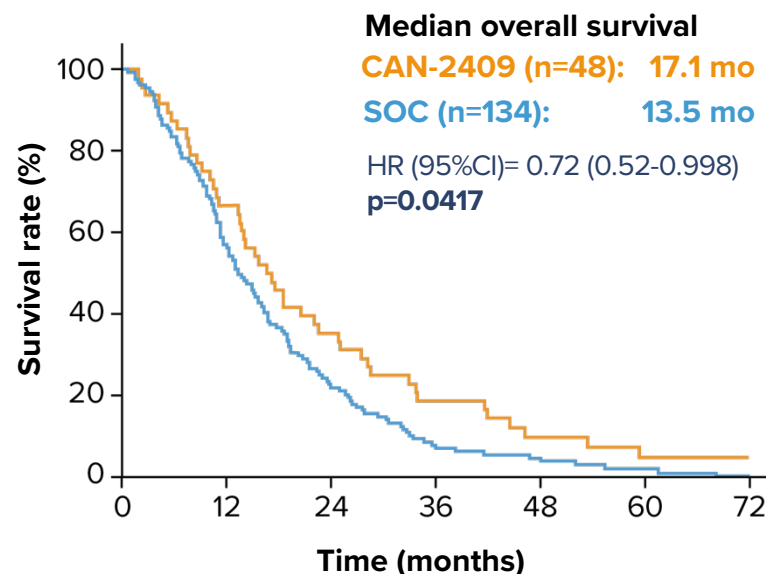
Clinical evidence supports ongoing phase 3 clinical trial of CAN-2409 in combination with SoC as first line treatment

Failure was measured from the start date of treatment until the date of treatment failure defined as clinical failure or biochemical failure, whichever first, according to the Phoenix ASTRO consensus (Nadir +2)

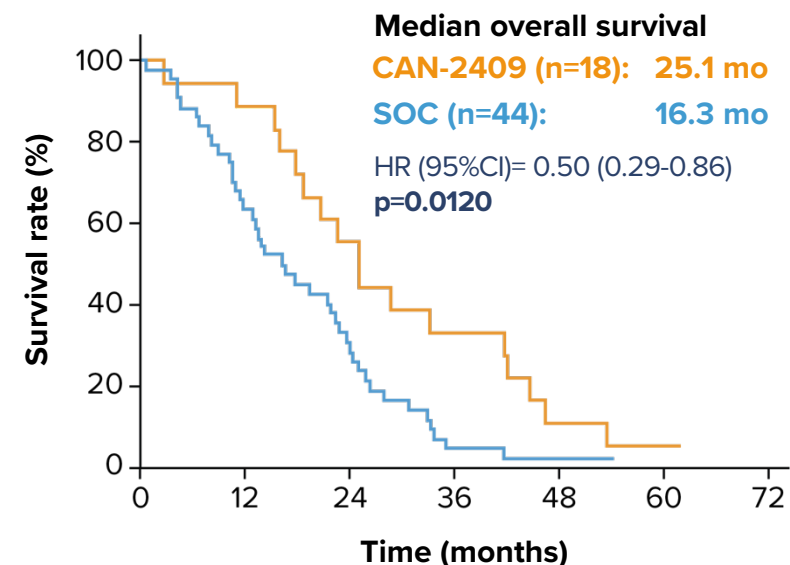
Significant survival benefit after CAN-2409 treatment in HGG

Compared to contemporary controls fulfilling the same inclusion and exclusion criteria

All patients:
All high-grade glioma,
All resection extent



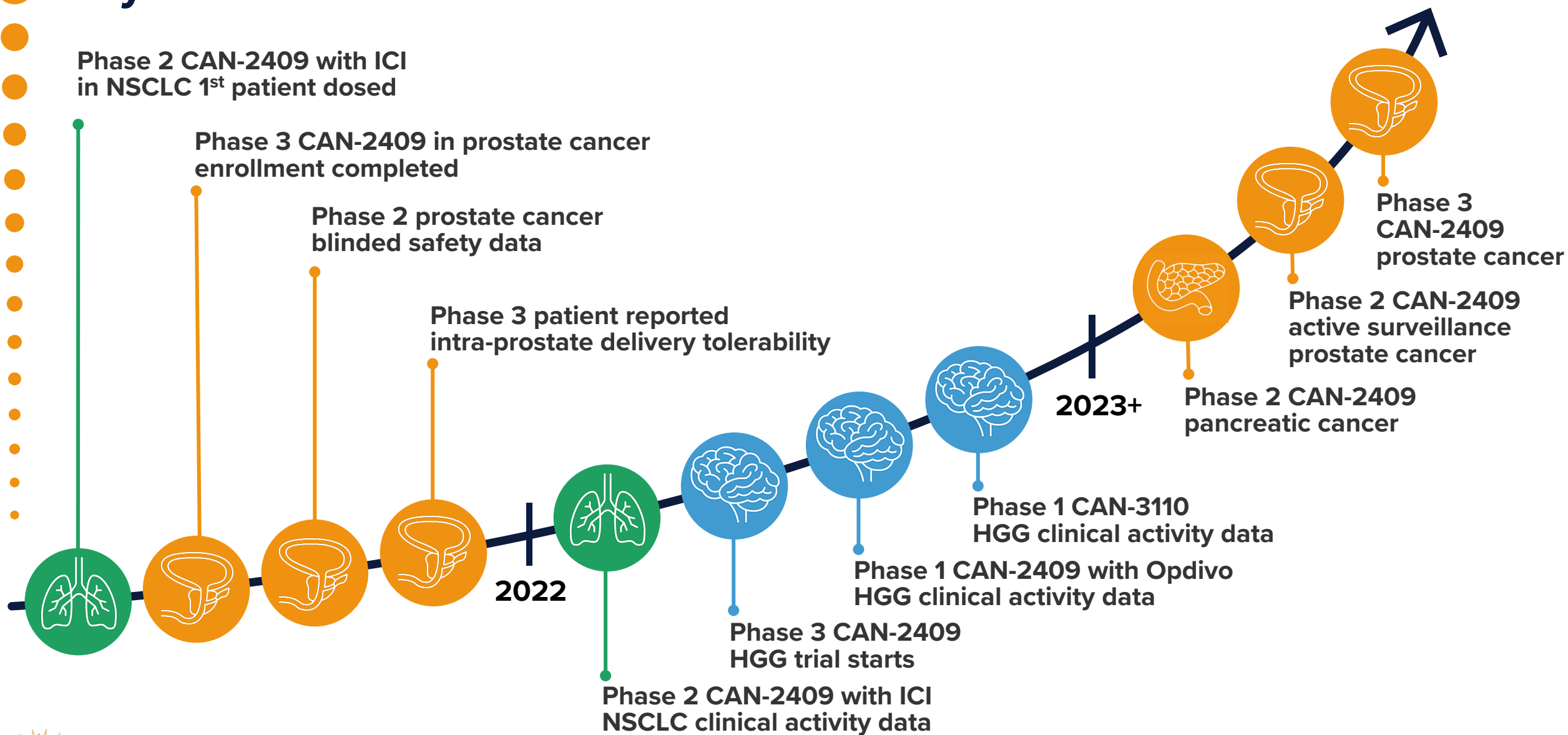
Prespecified subgroup:
glioblastoma with gross total resection



54% Relative improvement
(8.8 mo median survival benefit)

Clinical evidence supports adaptive phase 3 clinical trial of CAN-2409 in high-grade glioma patients undergoing Gross Total Resection and standard of care chemoradiation (reviewed with FDA)

Key achievements and future milestones



Leadership team with decades of experience in oncology, immunology, and drug development



Paul-Peter Tak, M.D., Ph.D., FMedSci
President & Chief Executive Officer



Nathan Caffo
Chief Business Officer



Christopher Matheny, Pharm.D., Ph.D.
Vice President, Development Leader



Seshu Tyagarajan, Ph.D., RAC
Chief Technical and Development Officer



Francesca Barone, M.D., Ph.D.
Chief Scientific Officer



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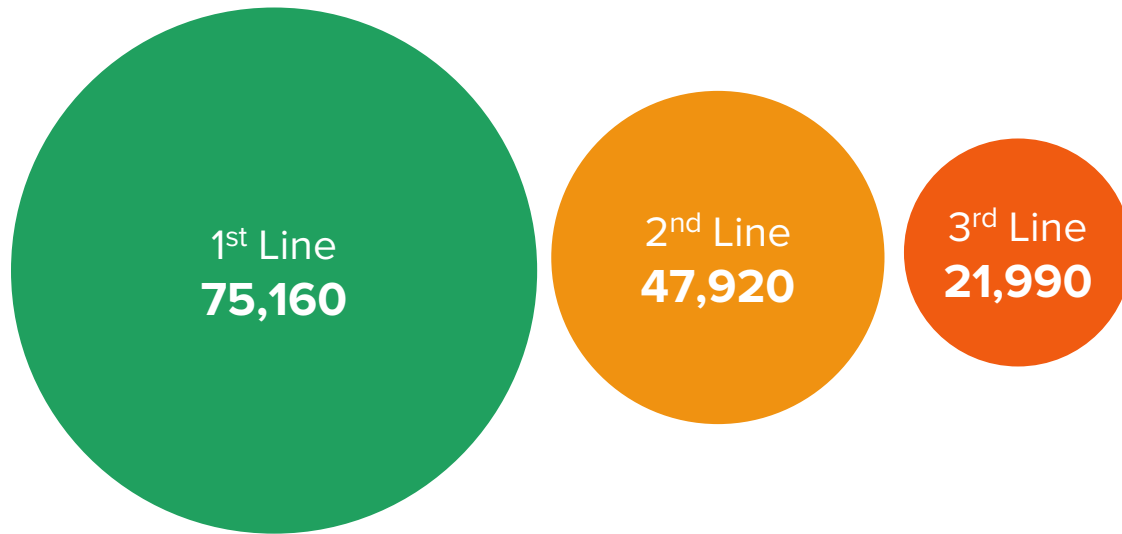


Padmanee Sharma, M.D., Ph.D.

*Professor of Genitourinary Medical Oncology and
Immunology
MD Anderson Cancer Center*

Non-small cell lung cancer opportunity for CAN-2409

Prevalence of NSCLC in the US*



- Patients treated with immune checkpoint inhibitors often combined with chemotherapy as 1st line treatment
- Median overall survival 22 months
- < 40% of patients survive > 30 months
- Opportunity to improve response by teaching the immune system how to recognize the cancer cells

Target label for CAN-2409: Indicated as adjunct to standard-of-care immune checkpoint inhibitor treatment (+/- chemotherapy) in stage III / IV NSCLC patients not responding to first-line or later ICI treatment[#]



First report from a phase 2 clinical trial of CAN-2409 in inadequate responders to immune checkpoint inhibitors for stage III/IV NSCLC

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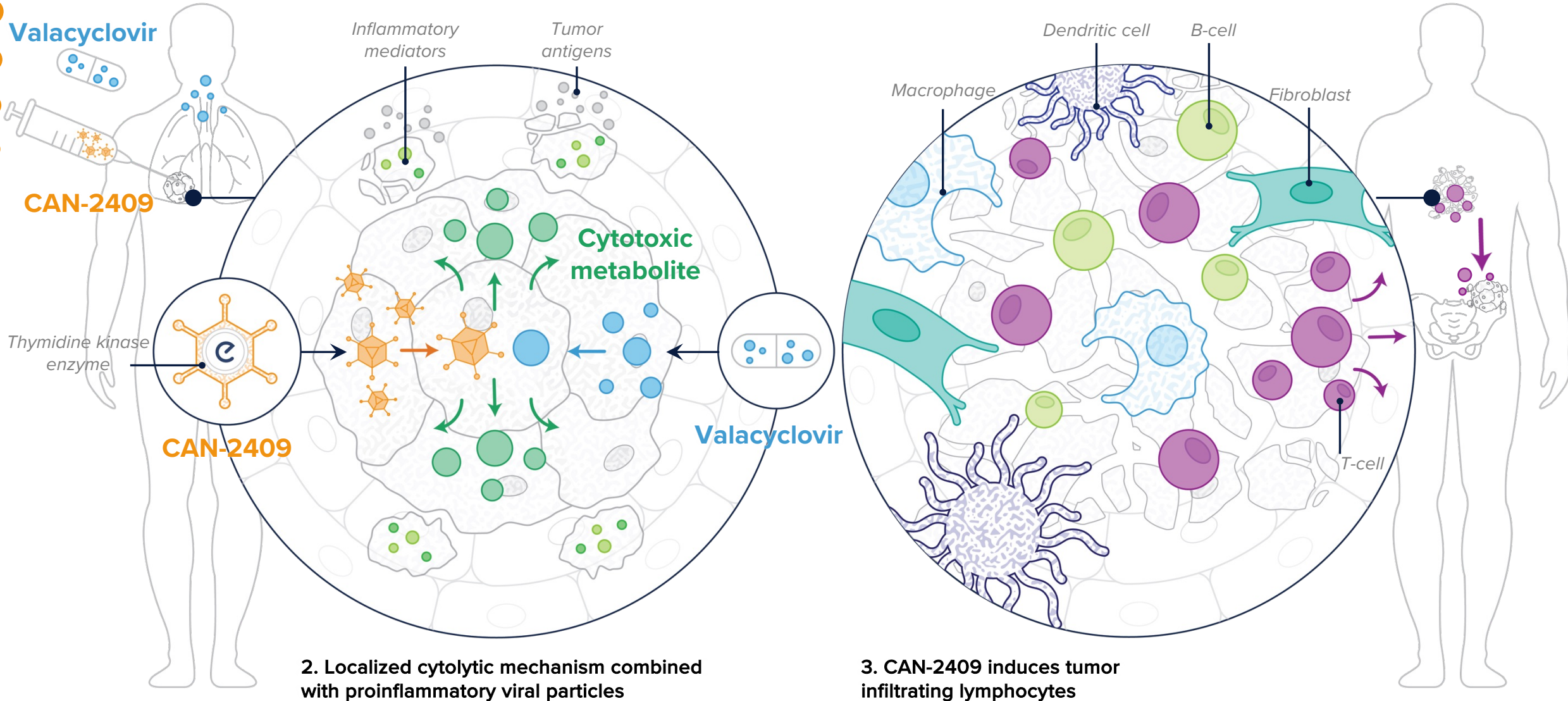
Daniel Sterman, MD

Thomas and Suzanne Murphy Professor of Pulmonary and Critical Care Medicine, at the New York University Grossman School of Medicine, and Director of the Division of Pulmonary, Critical Care, and Sleep Medicine, and Director of the Multidisciplinary Pulmonary Oncology Program at NYU Langone Health

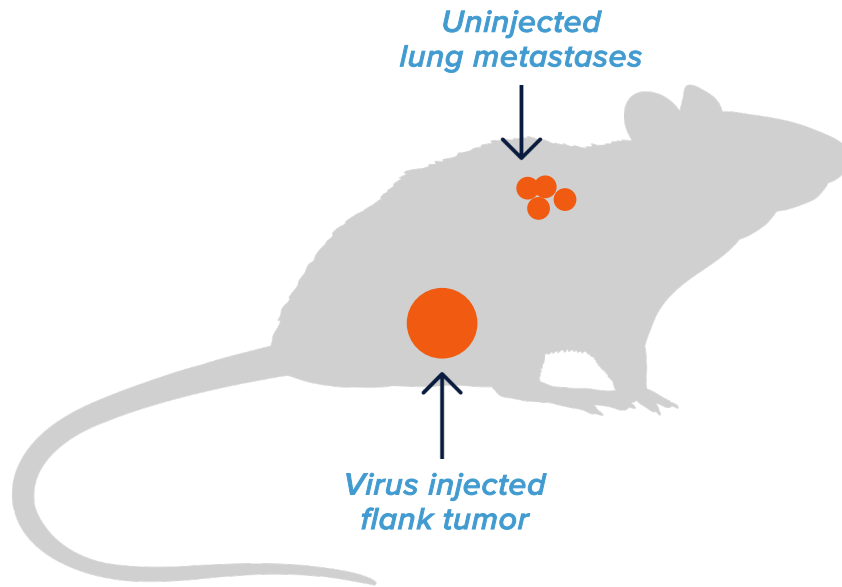
Conflict of interest disclosure: Nothing to disclose

CAN-2409: Mechanism of action

1. CAN-2409 locally administered and oral prodrug



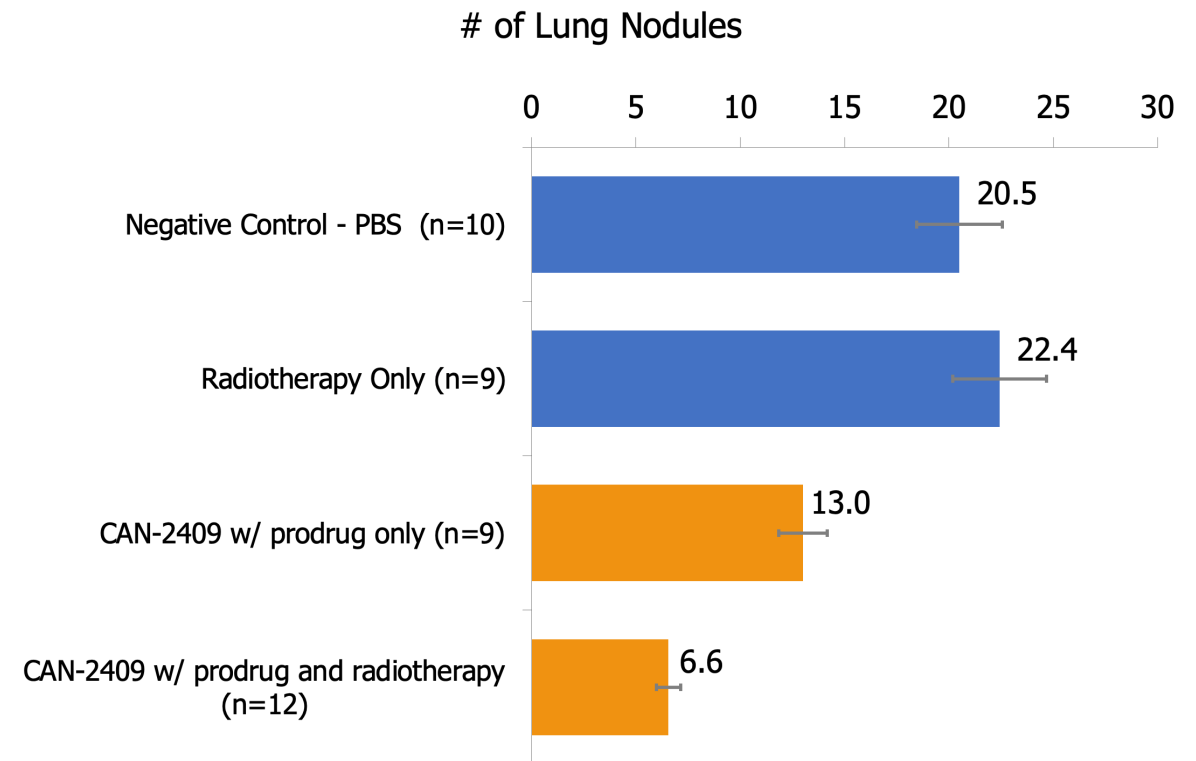
CAN-2409 teaches the immune system how to fight cancer in injected tumor and uninjected metastases



Mice receive one of four treatment regimens

1. PBS
2. Radiotherapy
3. CAN-2409 with prodrug
4. CAN-2409 with prodrug plus radiotherapy

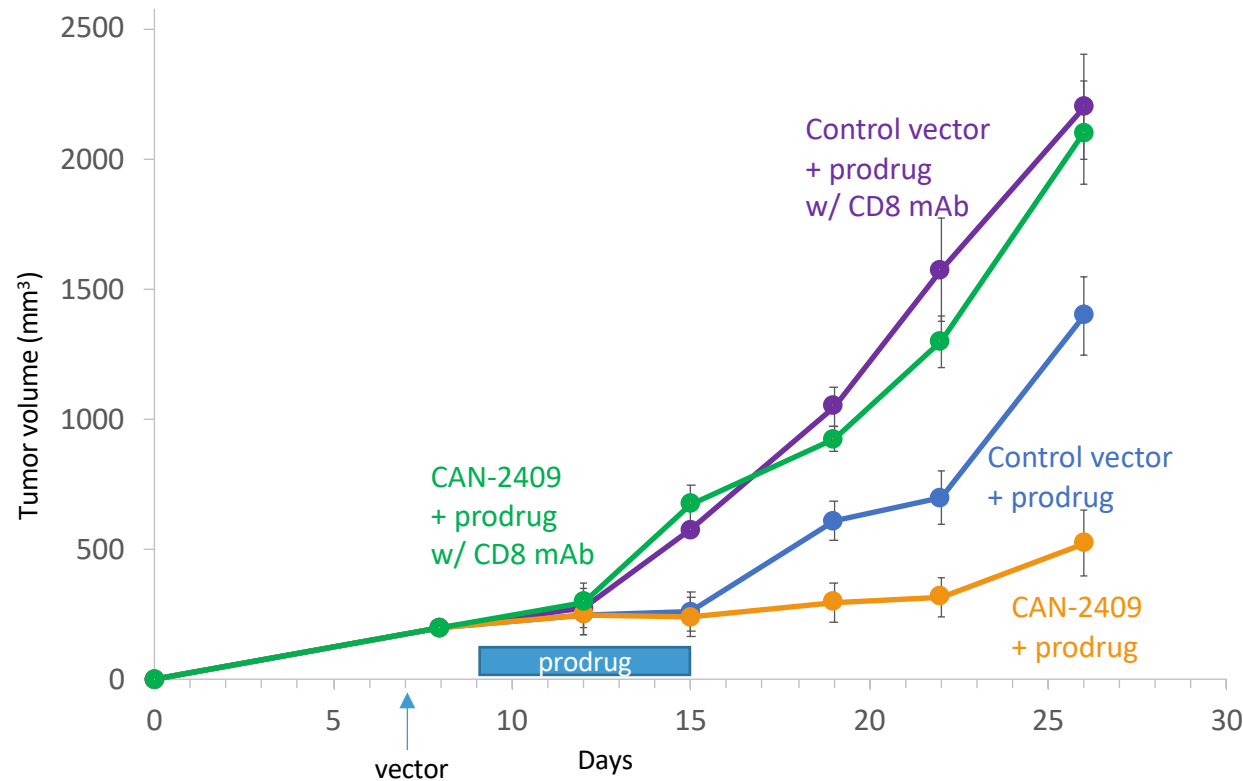
Decrease in uninjected lung metastases



Model of prostate cancer: RM-1 cells in C57BL/6 mice

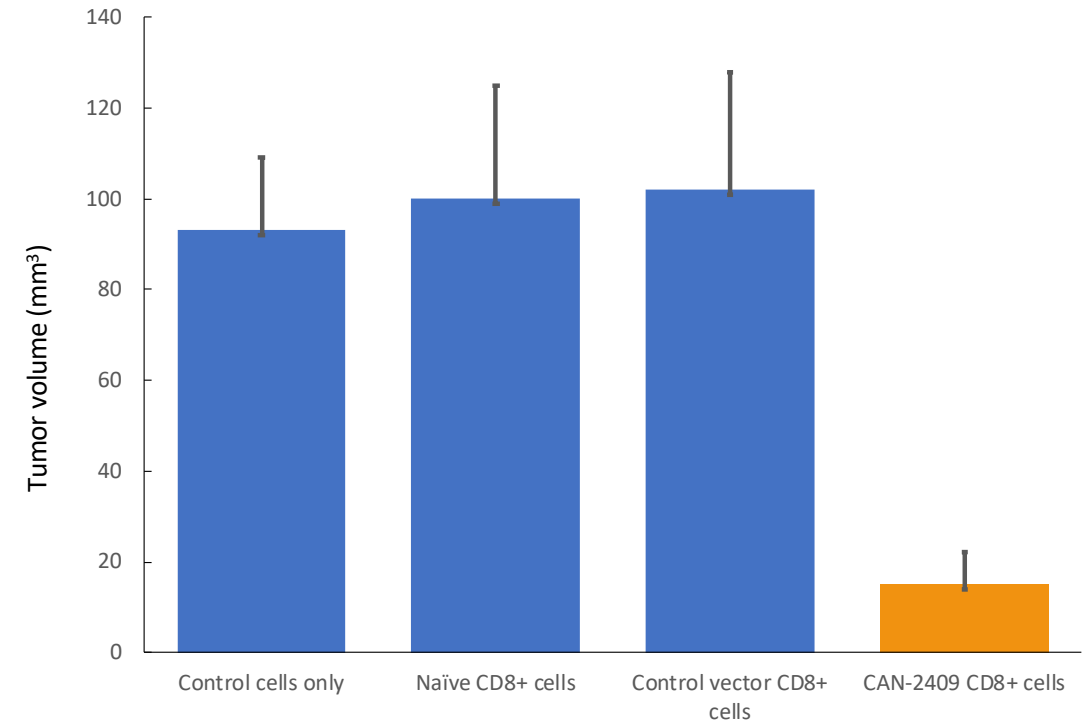
Chhikara M et al. Mol Ther 2001; 3:536-42

Response to CAN-2409 is dependent on CD8+ T cells and transferable in mouse models of cancer



Depletion of CD8+ cells eliminated effect

Esophageal cancer model (AKR) flank tumors in C57Bl/6 mice (n = 8 per group)



CD8+ cells from 'cured' mice administered CAN-2409 protected naïve mice from tumor challenge

Winn Assay: Lung cancer model (TC-1) flank tumors in C57Bl/6 mice (n = 5 per group)

Phase 1 mechanistic trial in resectable NSCLC: Safety and feasibility of intratumoral administration of CAN-2409

Evidence of monotherapy activity both via biomarkers and clinical response

Newly diagnosed
stage I-III
suspected
operable
NSCLC

N=12 completing
treatment and
surgical resection

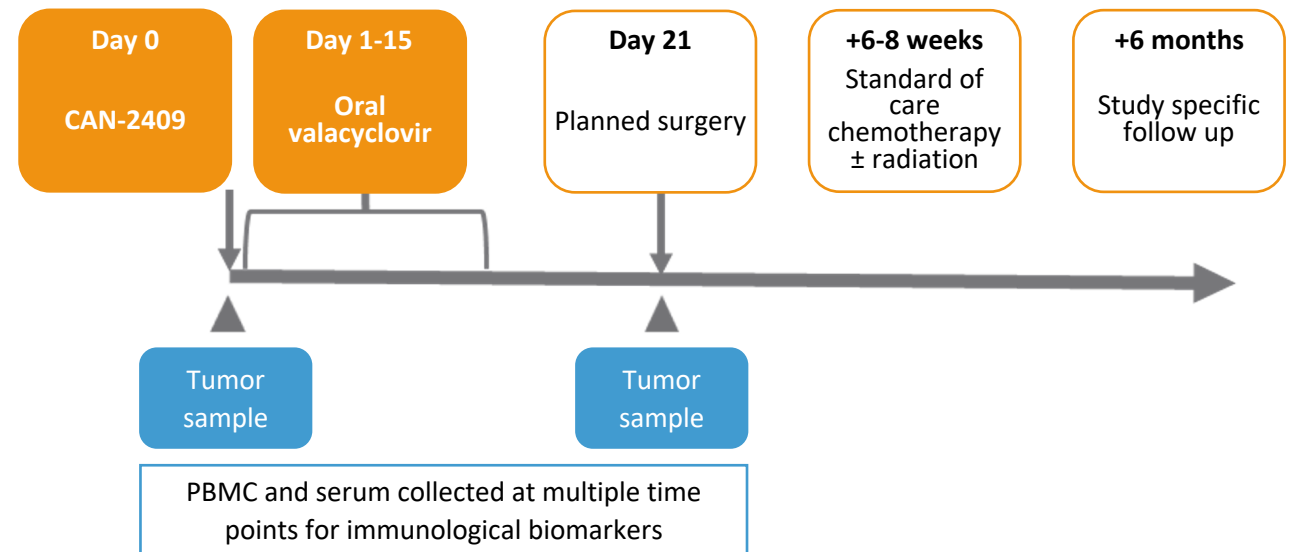
CAN-2409 and
valacyclovir
(one course)

3+3 dose
escalation

Injected into tumor
during SoC staging
procedure
(endobronchial or
direct injection)

No other therapy

CAN-2409 dose levels:
 2.5×10^{11} , 5×10^{11} , 1×10^{12} VP

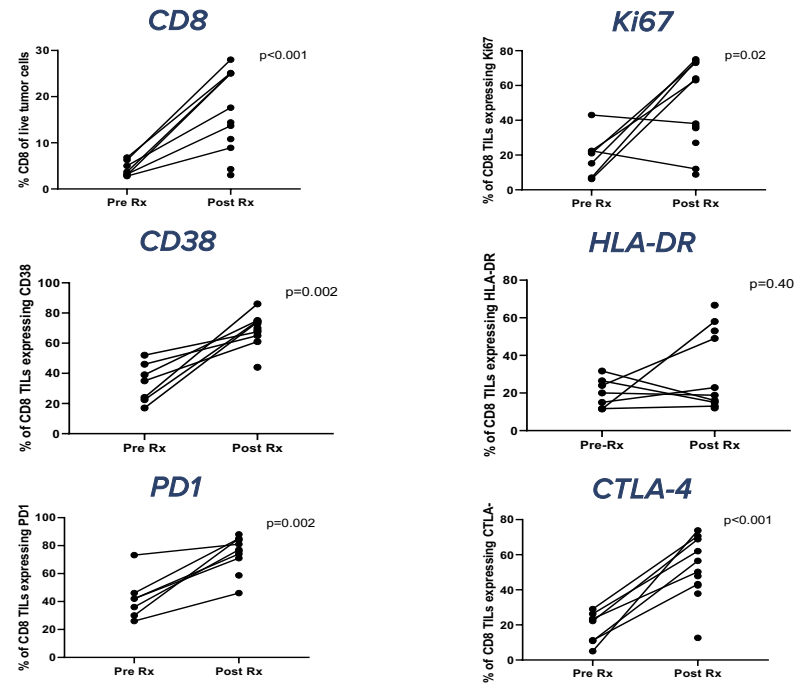


Principal investigators:
Dr S Singhal (UPenn) and Dr S Albelda (UPenn)

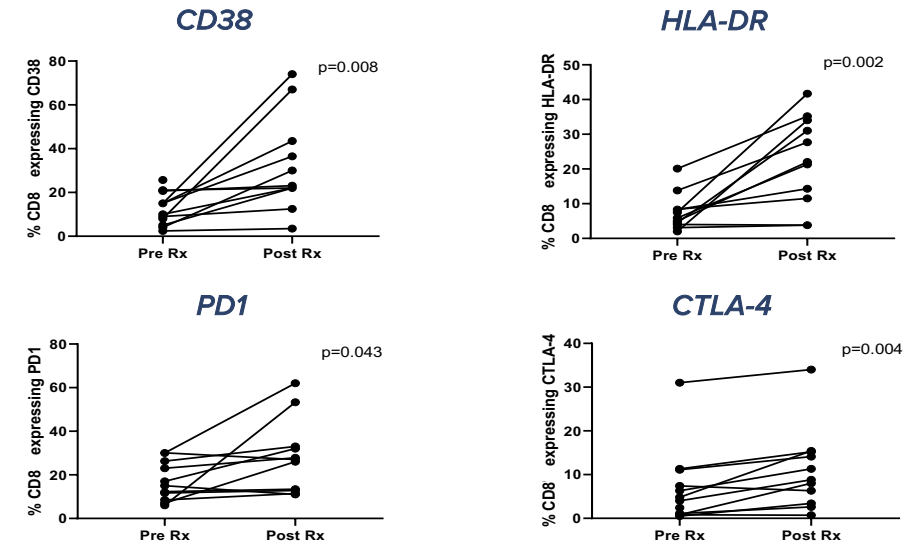
CAN-2409 stimulates local and systemic CD8+ T-cell response in patients with NSCLC

Non-small cell lung cancer Ph 1 study (n=12)

TISSUE

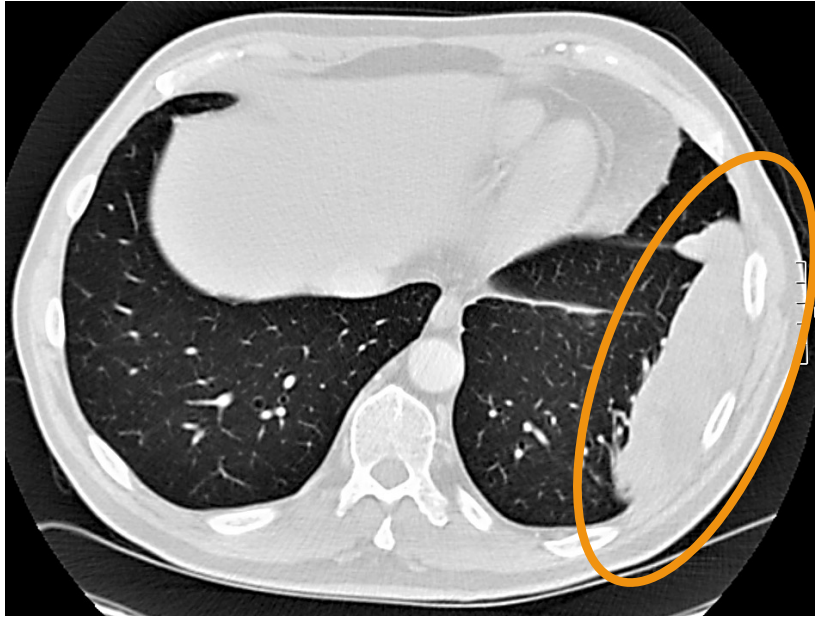


PERIPHERAL BLOOD



Monotherapy activity of CAN-2409 in NSCLC

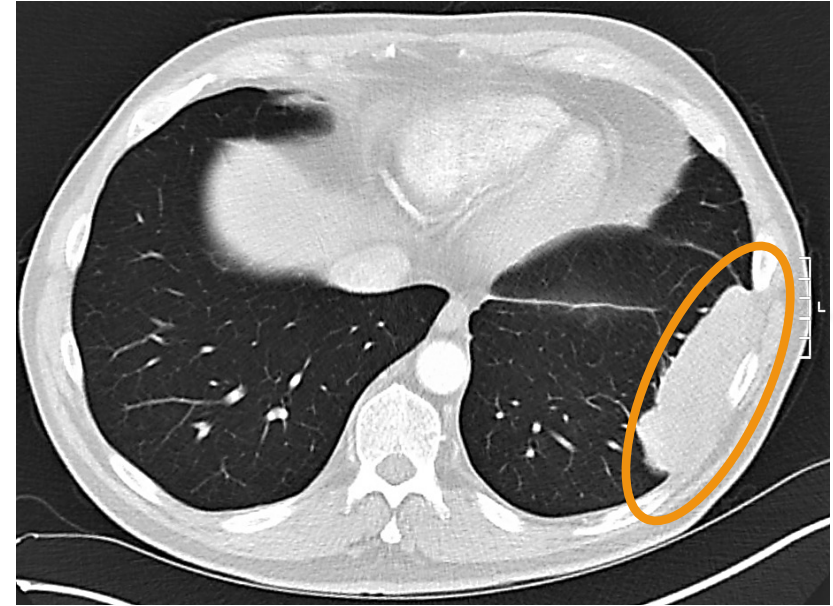
70 yr old male with a 14.8 cm stage IIIA sarcomatoid carcinoma



Day 0

Tumor Dimensions: 148 x 40 x 82 mm

10^{12} vp dose



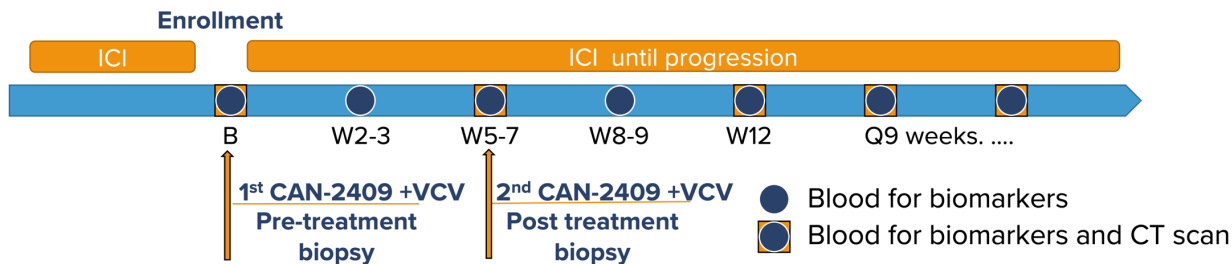
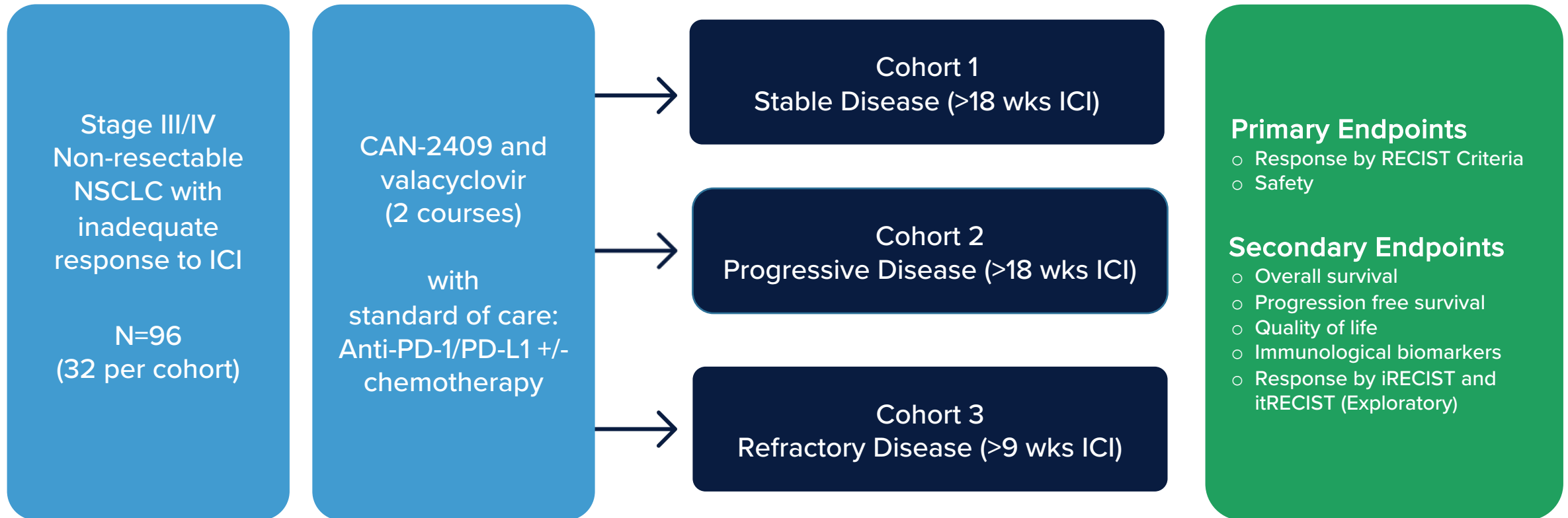
Day 22

Tumor Dimensions: 100 x 34 x 75 mm

Nearly 50% decrease in tumor volume* at 3 weeks after CAN-2409 monotherapy

Predina JD et al. Mol Ther 2020; 29:1-13

Current, ongoing phase 2 clinical trial of CAN-2409 in combination with ICI in stage III/IV NSCLC



ASCO 2022 Annual Meeting
Abstract # 9037
Poster session June 6, 2022 8:00-11:00 CDT

Demographics

35 patients enrolled between October 2020 and April 2022

Age	Years
Median (range)	69 (43-88)
Sex	n (%)
Male	20 (57)
Female	15 (43)
Race	n (%)
White/Caucasian	30 (86)
Black/African American	3 (9)
Smoking History	n (%)
Never	4 (11)
Former or current	28 (80); 3 (9)
ECOG Status at Enrollment	n (%)
0 or 1	14 (40); 21 (60)

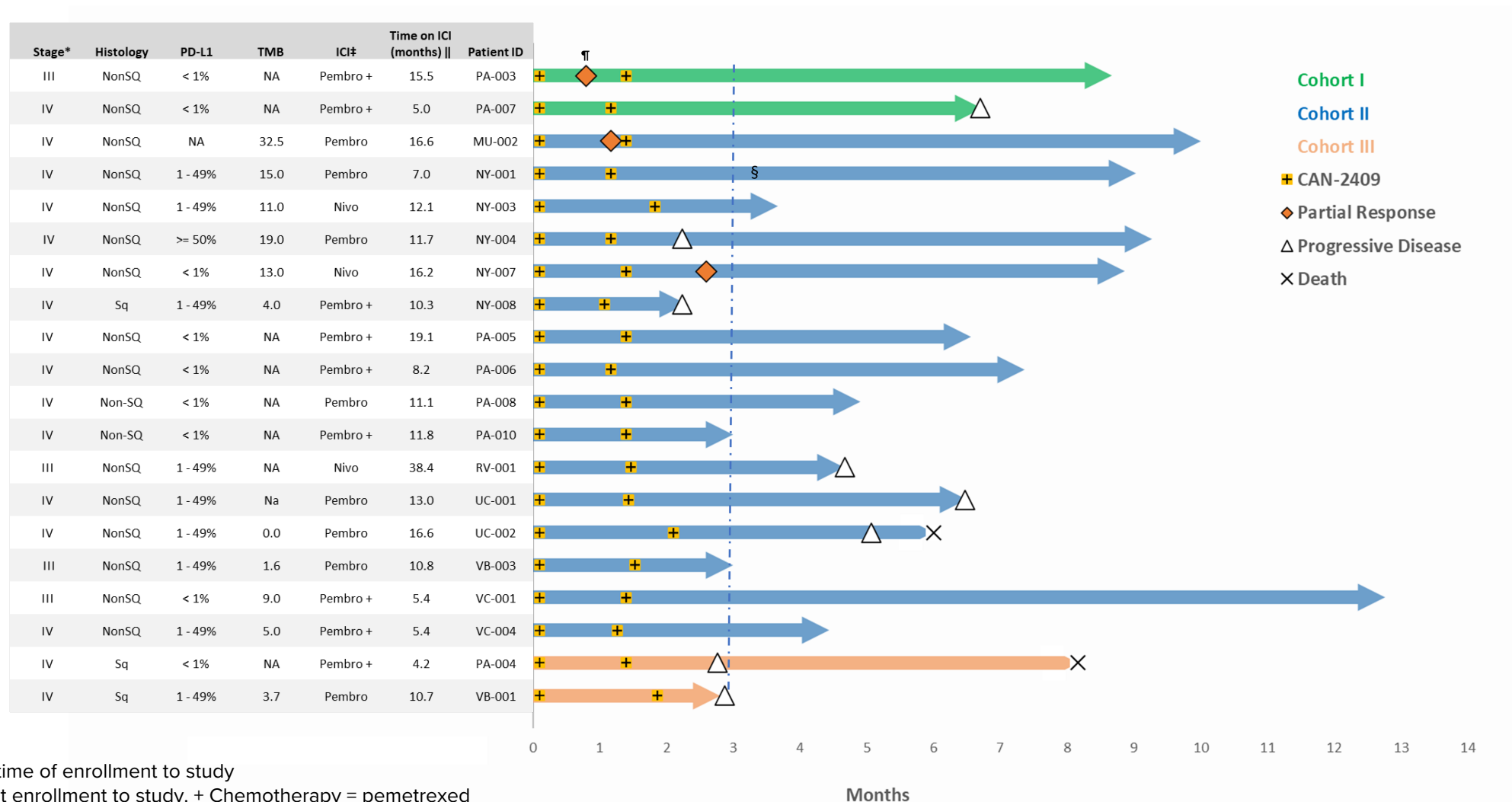
Most frequent treatment-related adverse events

Generally, CAN-2409 was shown to be well tolerated with no Grade 4 and few Grade 3 events

SOC/Adverse Event (>10%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Total patients (n=35)
General disorders and administration site conditions				
Chills	4 (11)			4 (11)
Fatigue	8 (22)	4 (11)		12 (33)
Injection site reaction	4 (11)			4 (11)
Pyrexia	6 (17)		2 (6)	7 (20)
Investigations				
Blood creatinine increased	4 (11)	1 (3)		4 (11)

Swimmer plot for all evaluable patients

20 patients received 2 courses of CAN-2409 with valacyclovir and were evaluable at 12 weeks



* Stage: at time of enrollment to study

‡ SOC ICI: at enrollment to study. + Chemotherapy = pemetrexed

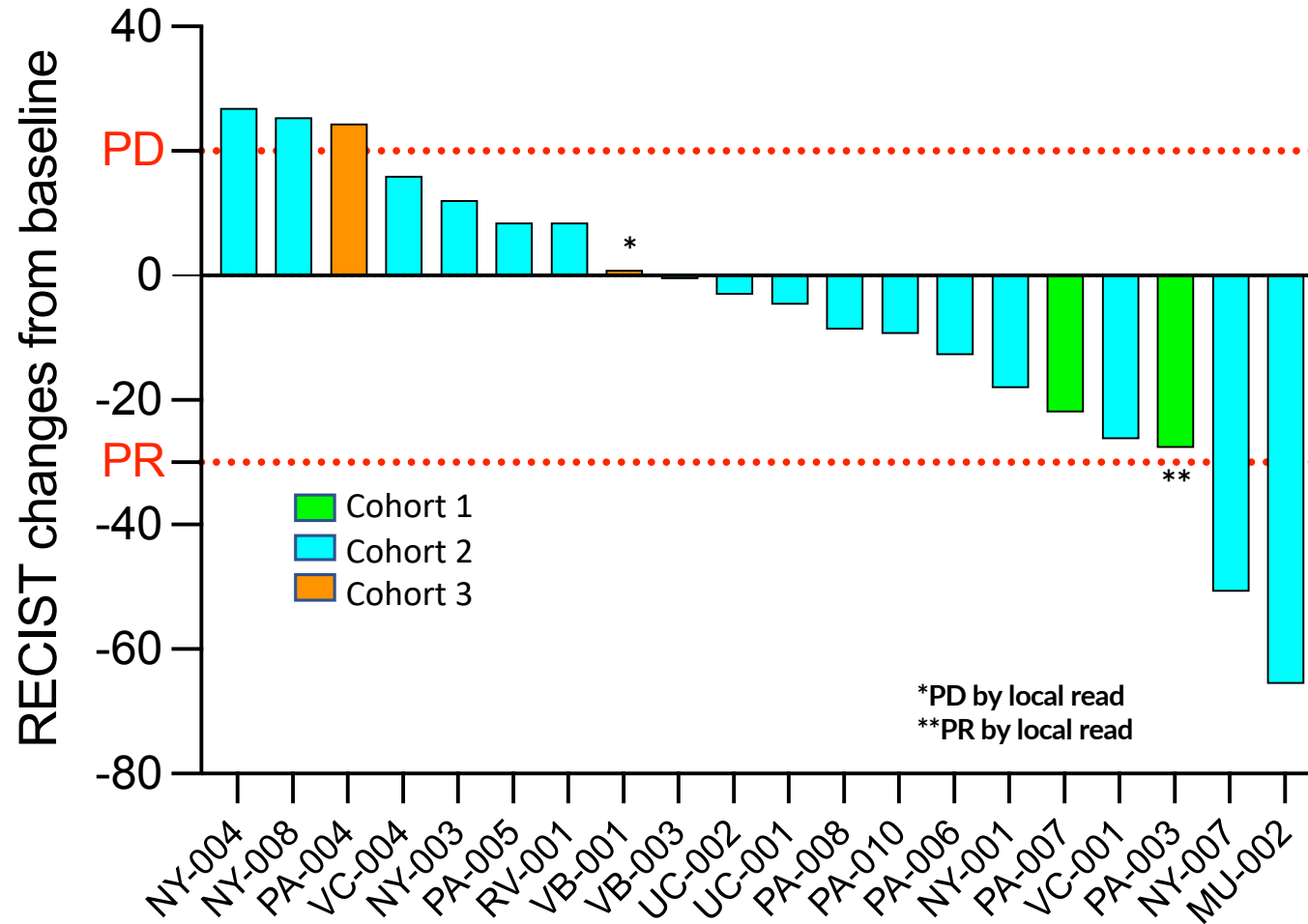
|| Time on SOC ICI prior to Study Enrollment: Initiation of ICI to first CAN-2409 injection

¶ PR by local read

§ Irradiation included target lesion, no longer RECIST evaluable

Radiographic best responses for all evaluable patients

Majority of patients experienced reduction in tumor burden



Encouraging clinical responses

Disease control rate in cohort 2 of 87.5% in patients who were progressing at trial entry

Cohort	Completed 12-week treatment	PR	SD	PD	DCR	DoR for PR (w)	DoR for SD (w)
1	2	1**	1	0	50%	24.1+	26.9
2	16	2	12	2	87.5%	26.7-37.9+	5.4+ - 50.4+
3	2	0	0	2*	0%	n/a	n/a

PR= partial response; SD= stable disease; PD= progressive disease;

DCR = disease control rate

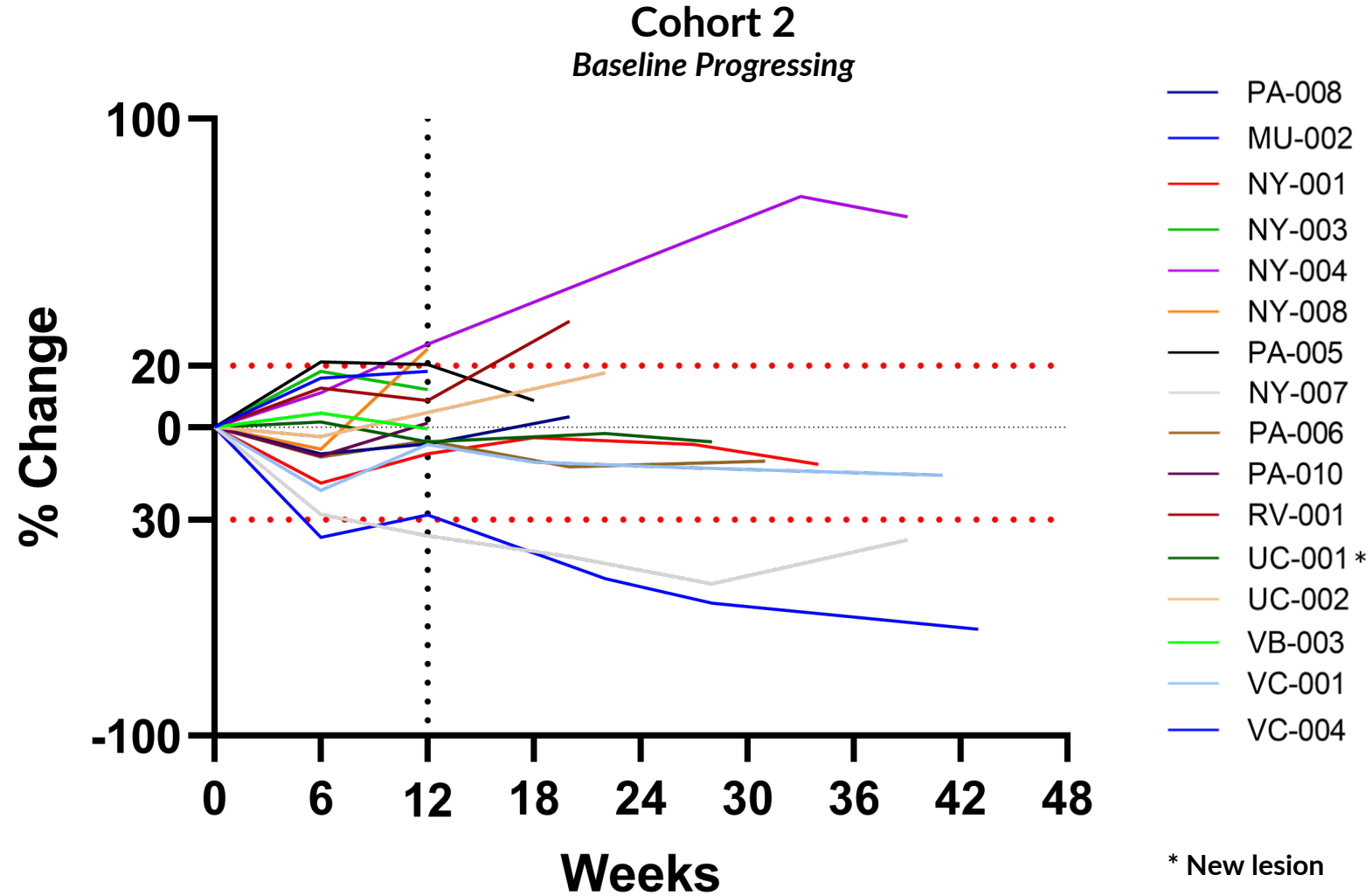
DoR PR= weeks from PR to progression; DoR SD=weeks from SD to progression

+ongoing response

*PD by local read; **PR by local read

Spider plot of cohort 2 suggests durable and stable response

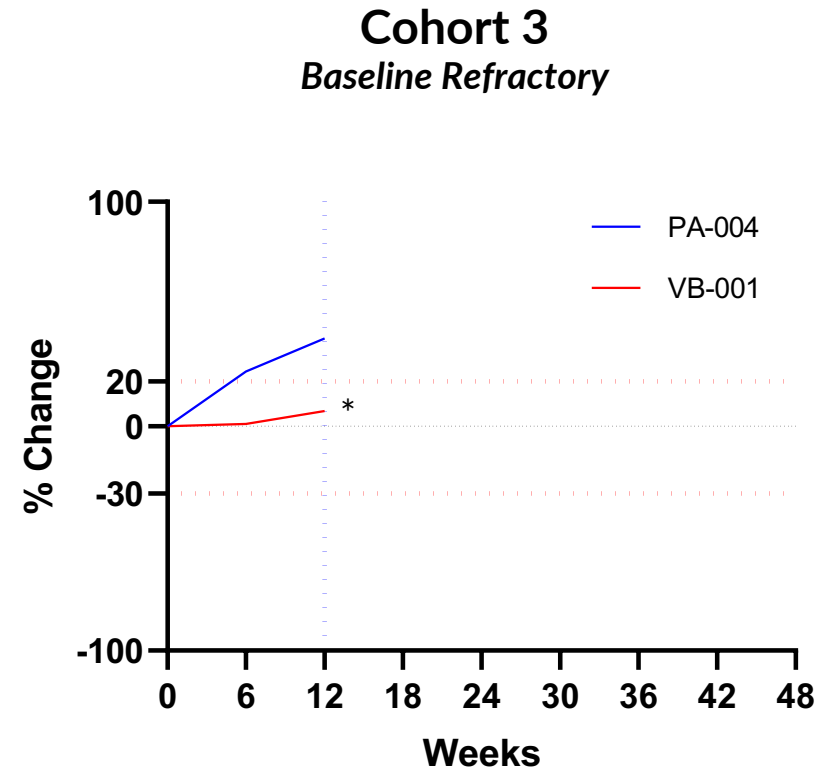
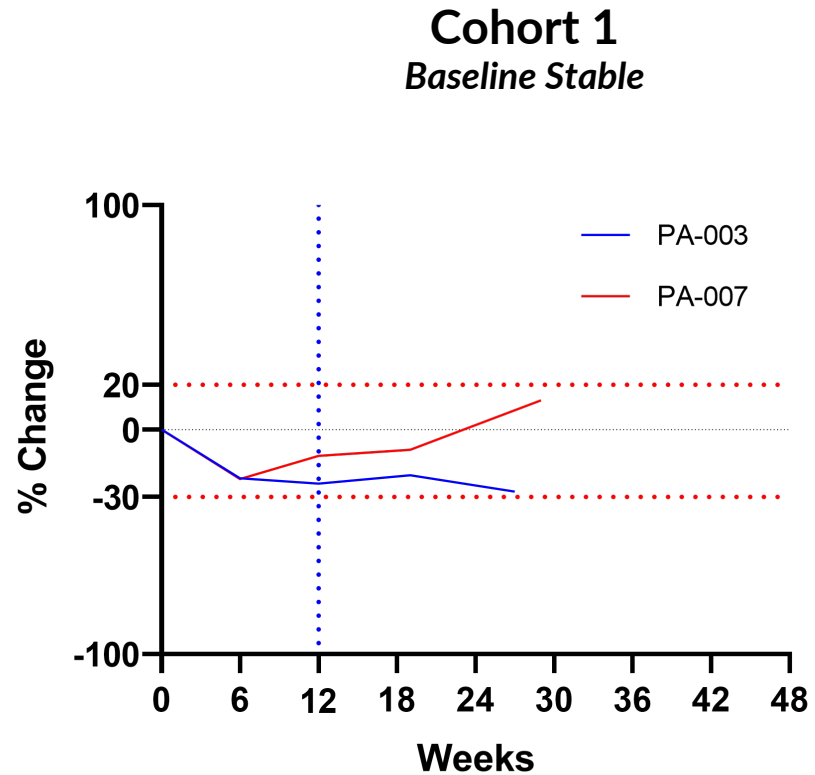
CAN-2409 led to disease stabilization in most patients who were progressing at entry



Limited patient numbers in cohorts 1 and 3

Cohort 1: challenging recruitment because stable disease in NSCLC was considered acceptable by treating physician

Cohort 3: patients were often too ill to get to the 2nd CAN-2409 administration



* New lesion

Patient with partial response defined by local read in extended lung lesion and consolidation

PA-003 (Cohort 1)

73M, Stage III Non-SQ

PD-L1<1%

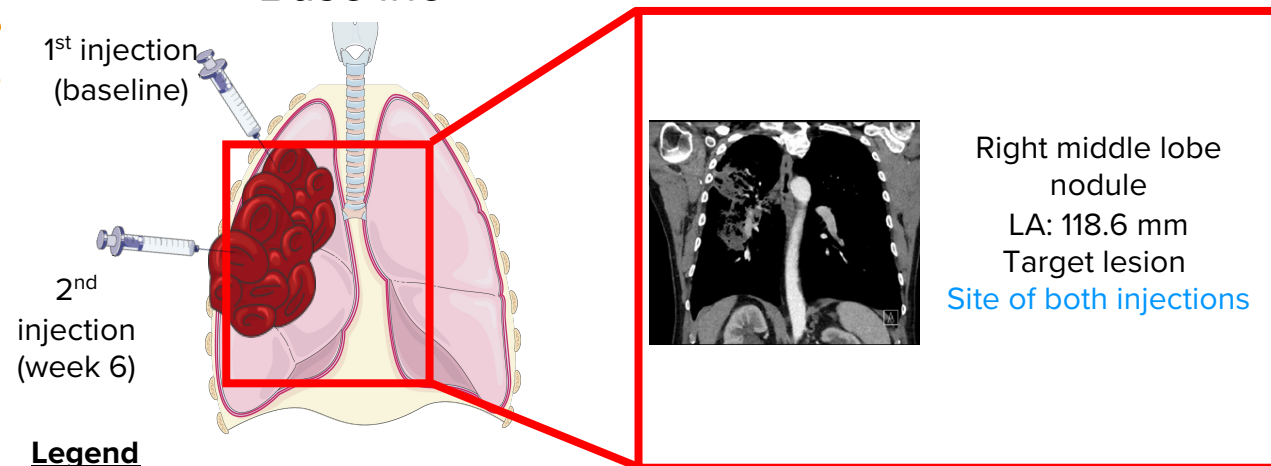
Diagnosed Jan'20

Started pembro + carbo + pemetrexed
Feb'20, pembro + pemetrexed cont.
from Jun'20 through trial

PR by local read

Schematics to show general lesion injection orientation; not to scale
LN = lymph node; LA = long axis; SA = short axis

Baseline

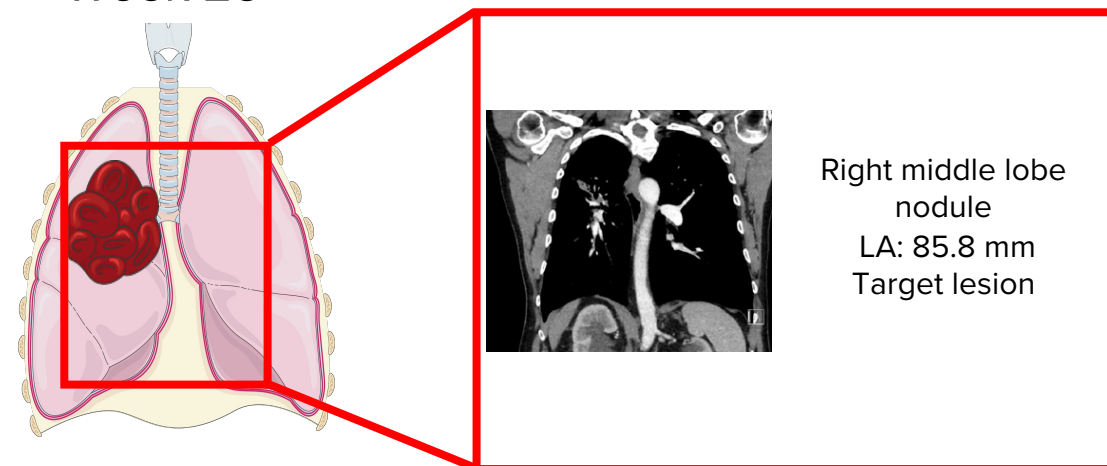


Legend

RECIST target lesions (red)

Non-target lesions (green)

Week 28



Patient with partial response and evidence of abscopal effect

NY-007 (Cohort 2)

74M, Stage IV Non-SQ

PD-L1 <1%

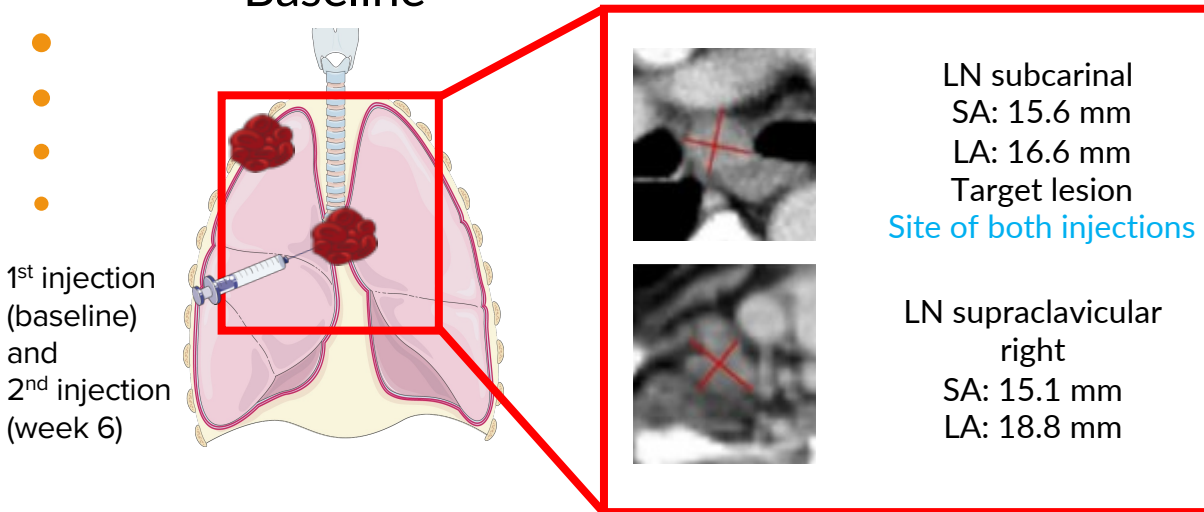
Diagnosed Feb'19

cisplatin/etoposide Feb'19 to Jul'19,
nivolumab monotherapy from Sep'19
thru trial

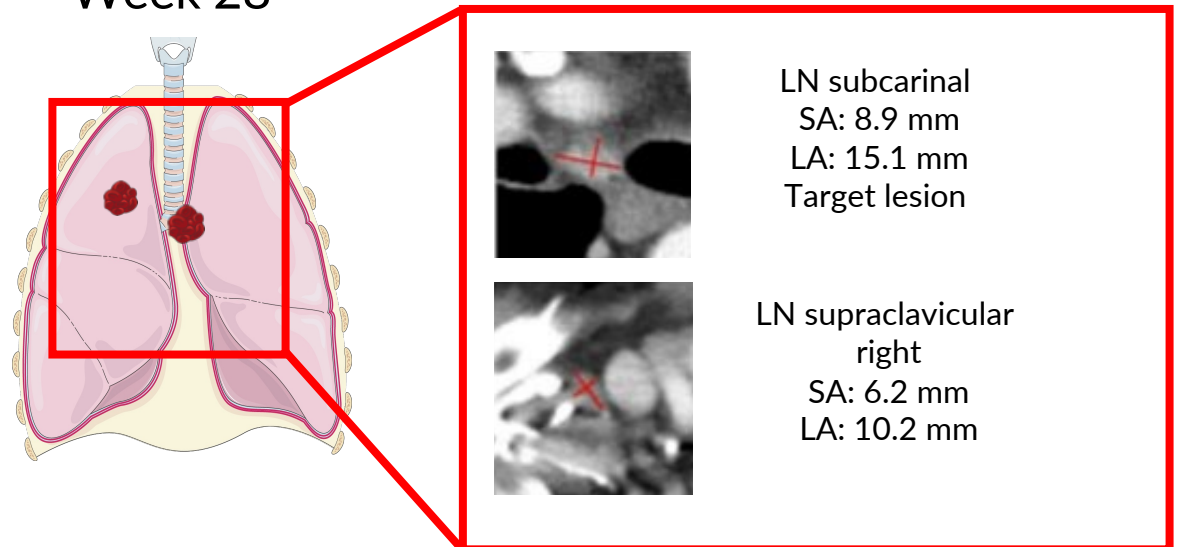
PR by local and central read

*Schematics to show general lesion injection orientation; not to scale
LN = lymph node; LA = long axis; SA = short axis*

Baseline



Week 28



Legend

RECIST target lesions (red)

Non-target lesions (green)

Patient with partial response and evidence of abscopal effect

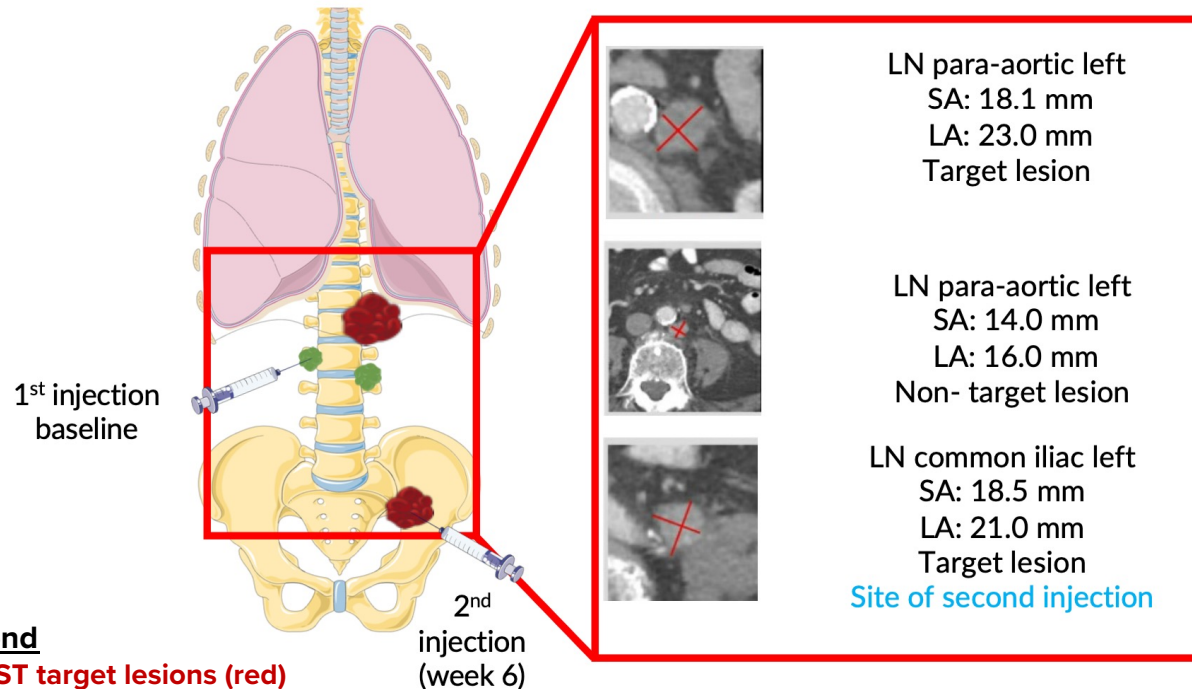
MU-002 (Cohort 2)

69F, Stage III 2013, Stage IV 2019; Non-SQ; PD-L1 unknown; Started pembro monotherapy Jan'20 through trial

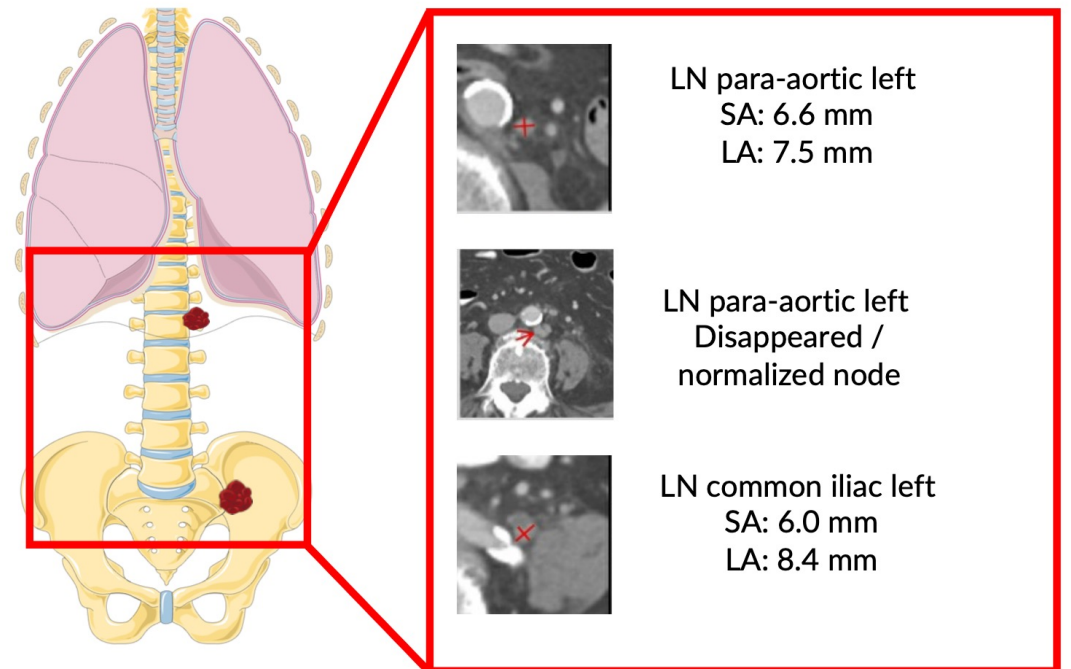
PR by local and central read

*Schematics to show general lesion injection orientation; not to scale
LN = lymph node; LA = long axis; SA = short axis*

Baseline



Week 42

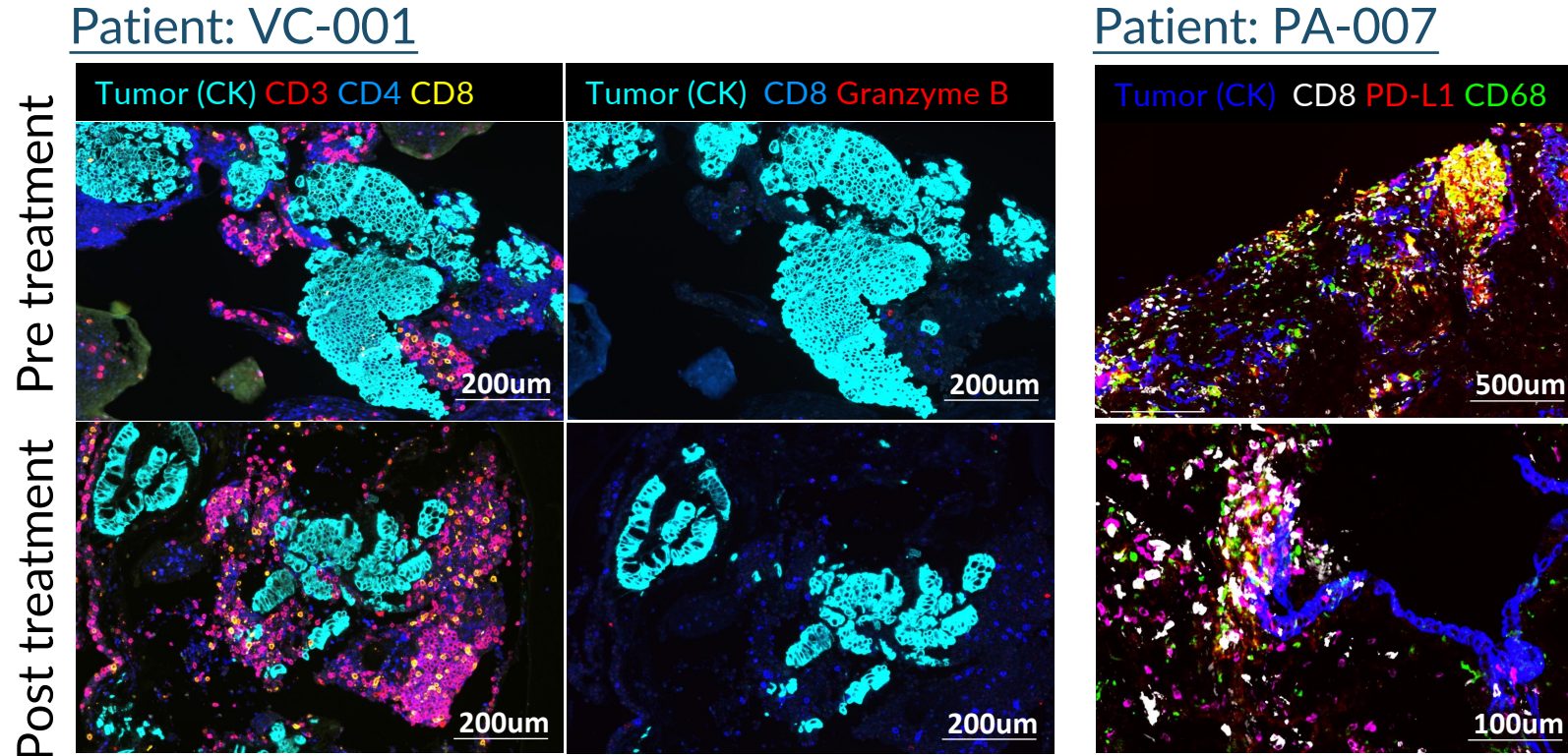


Legend

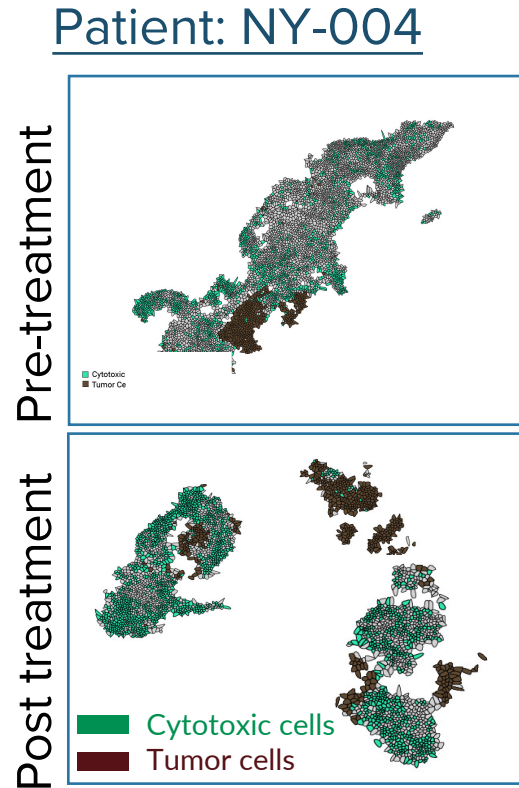
RECIST target lesions (red)

Non-target lesions (green)

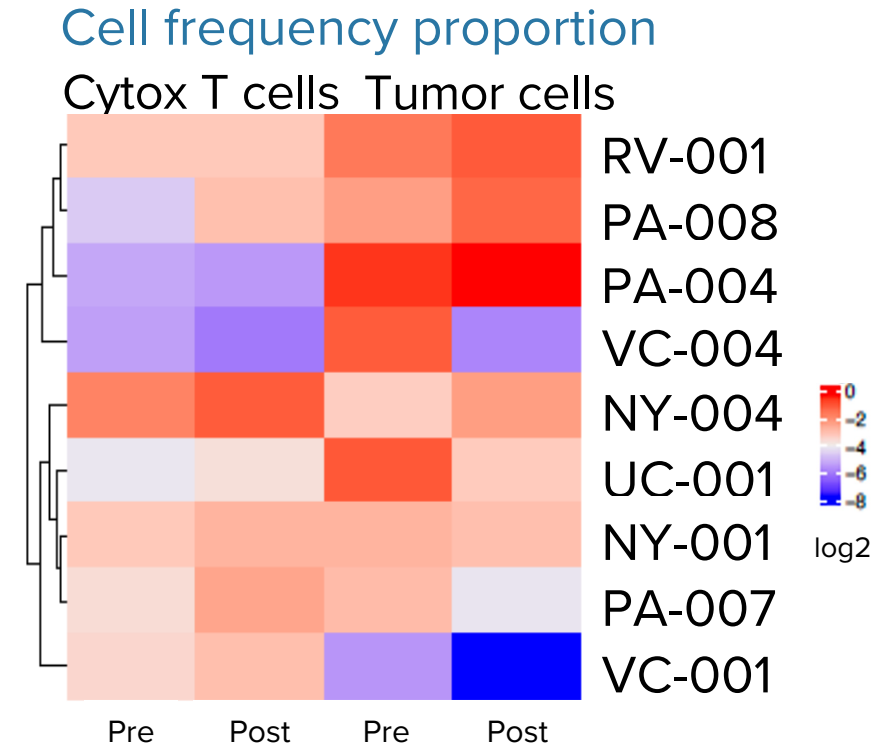
CAN-2409 increases immune cell infiltration in post-treatment tumor biopsies



Frequency analysis demonstrates enrichment in cytotoxic T cells

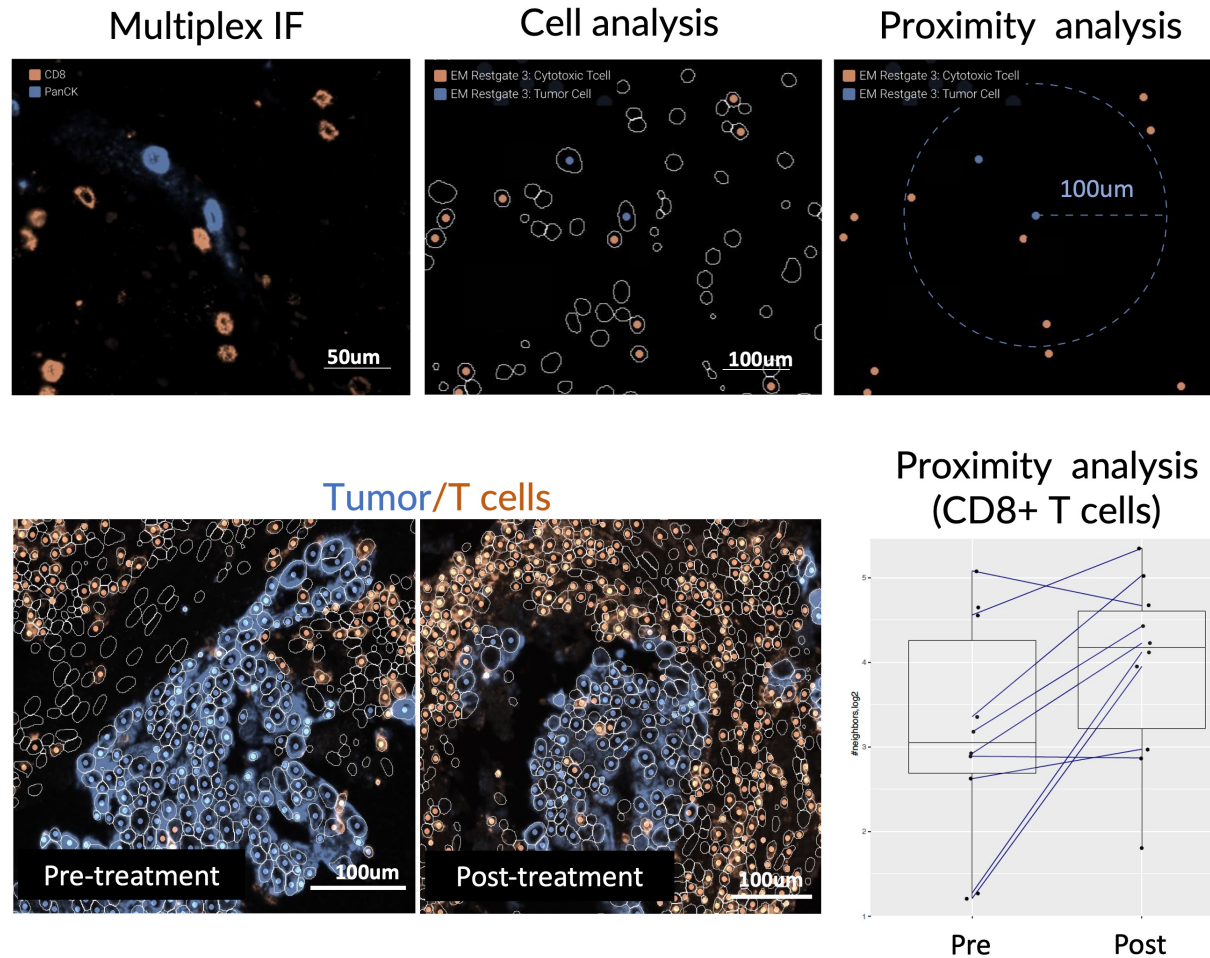


Vorenoi diagram illustrating frequency analysis methodology for patient NY-004 in pre- and post-treatment samples



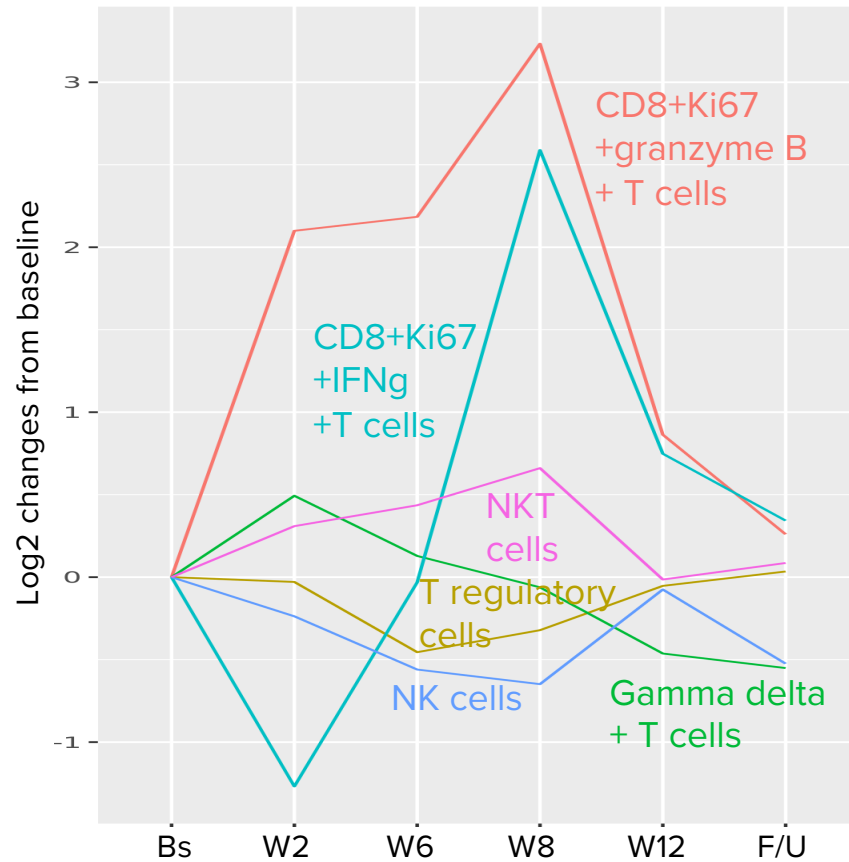
Heat map summarizing frequency data for paired biopsy samples for 9 eligible patients

Increased aggregation of cytotoxic T cells in post treatment biopsies



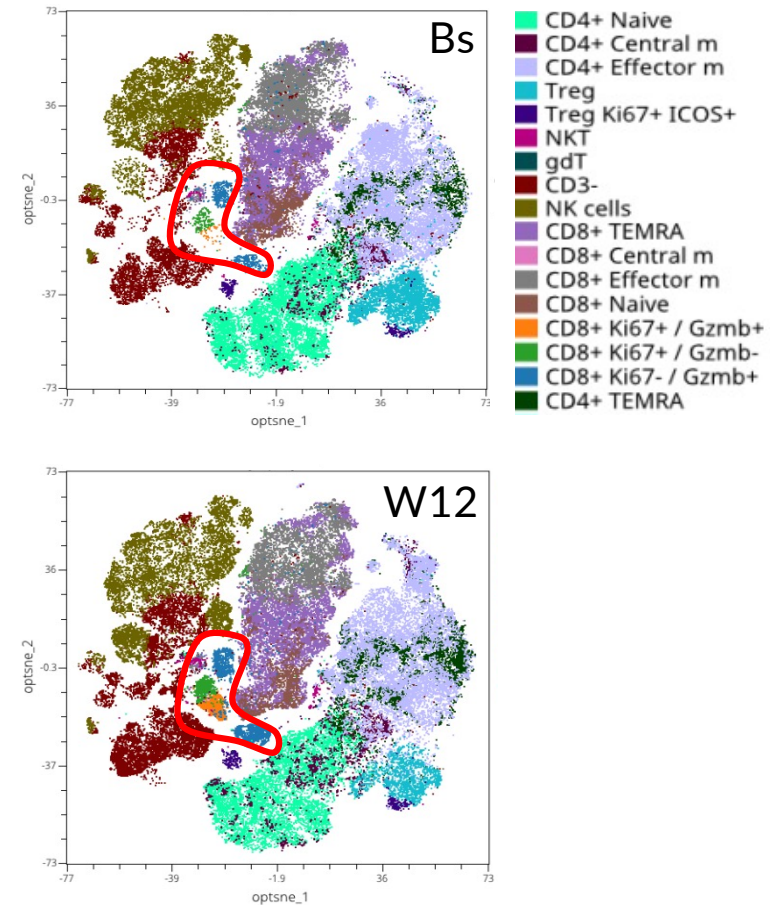
Proximity analysis was applied to immunofluorescence (IF) stained samples to evaluate number of CD8+ cytotoxic cells within a distance of 100um radius from tumor cells. Significant difference was observed in post treatment samples (paired patient data represented $p=0.0149$ t-test).

CAN-2409 increases circulating cytotoxic T cells and decreases circulating T regulatory cells



Flow cytometry quantitation of cytotoxic cells and T regulatory cells; average values for subpopulations at specific time points from 14 patients' PBMCs

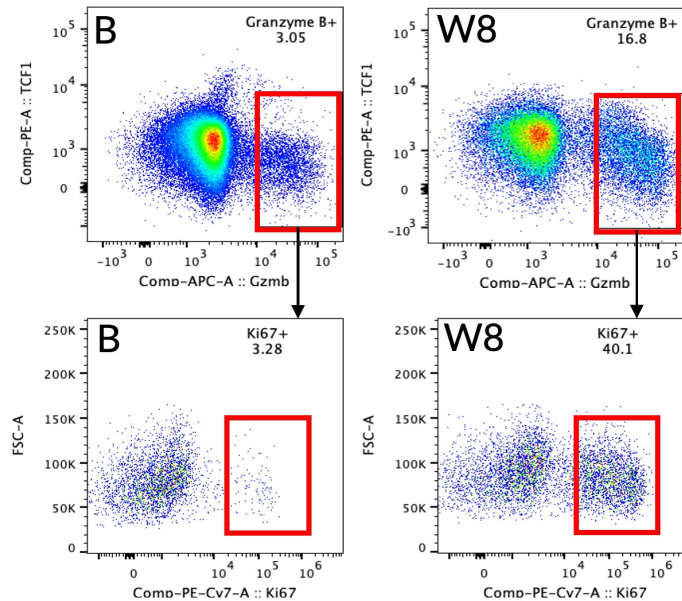
Patient: NY-007



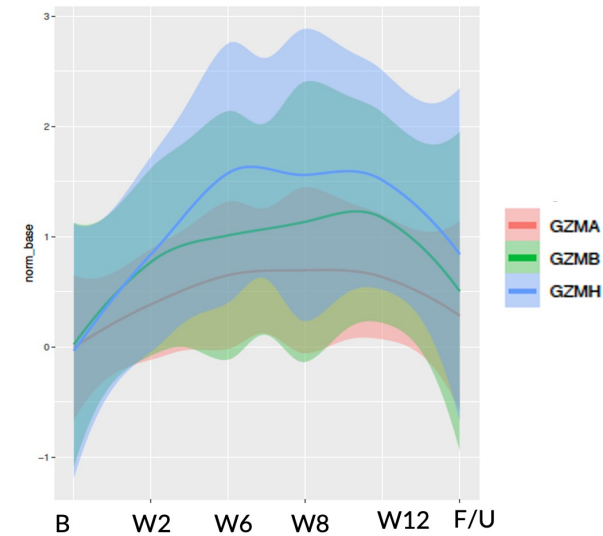
t-SNE plot representing patient MU-002 at baseline and 12 w demonstrating changes in the T cells and NK subpopulations (red outline)

CAN-2409 induces an increase in circulating CD8+Ki67+granzyme B+ T cells associated with elevated soluble granzyme A, B, and H levels

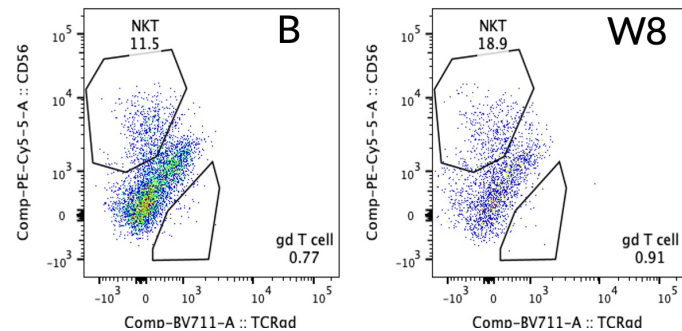
Increase in granzyme B+Ki67+CD8 T cells



Soluble granzyme A, B and H increase over time

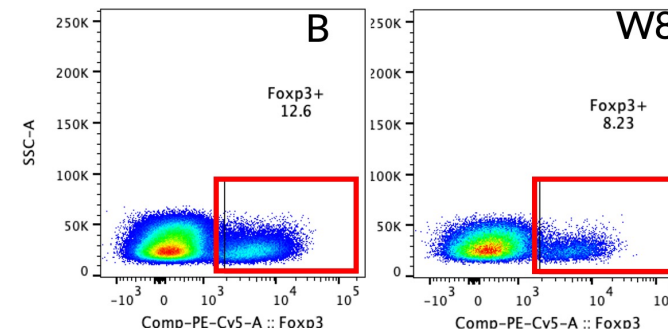


Post treatment increase in NK- T cells



Post treatment reduction in T-reg

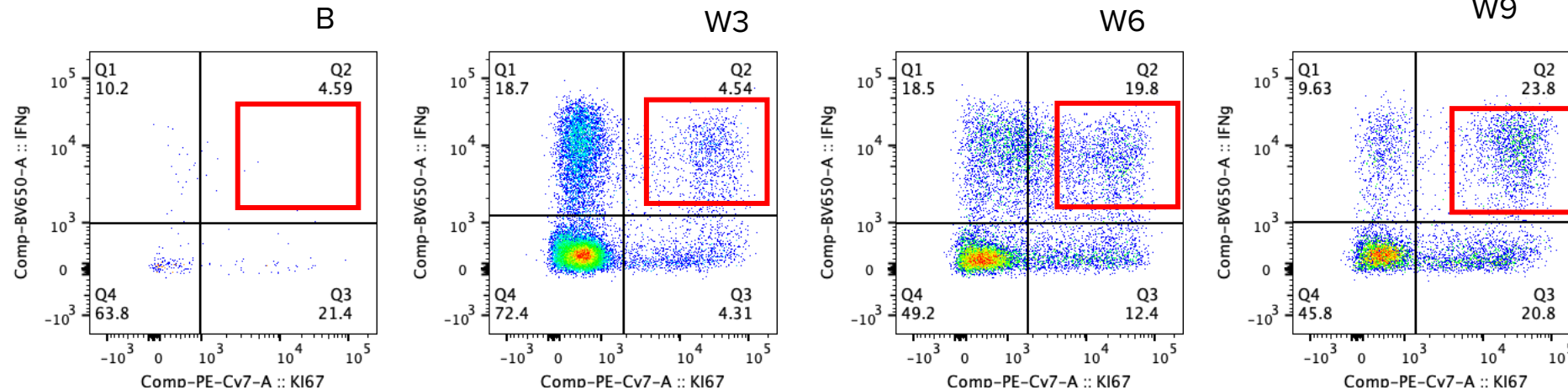
Gated on CD4



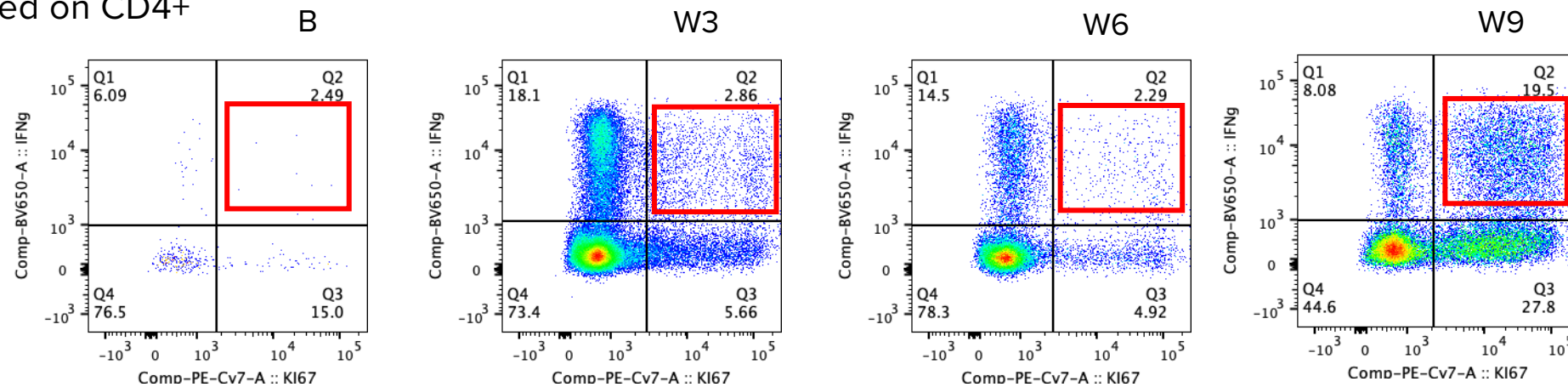
CAN-2409 induces a systemic increase in proliferating CD8+ and CD4+ IFN γ producing effector cells

Patient: PA-003

Gated on CD8+



Gated on CD4+



Biomarker analysis summary

Biomarker data consistent with hypothesized mechanism of action

- Post treatment tumor biopsies:
 - Increased infiltration of cytotoxic T cells
 - Increased T cell aggregation in proximity to tumor cells
- Post treatment peripheral blood samples:
 - Increased actively proliferating, granzyme B positive T cells
 - Increased actively proliferating, CD4+ and CD8+ IFN γ + T cells
 - Increased levels of soluble granzymes A, B, and H

Summary of data from ongoing phase 2 clinical trial:

- Experimental treatment with CAN-2409 plus valacyclovir in patients with advanced NSCLC and an inadequate response to first-line ICI (\pm chemo) who continued ICI treatment appears to be generally well tolerated
- Encouraging preliminary activity in the first 20 evaluable patients at 12 weeks post-treatment:
 - Evidence for disease regression in both injected and uninjected lesions
 - In Cohort 2 (patients who entered the study with progressive disease), a DCR of 87.5% with durable disease stabilization ongoing in 10 out of 16 patients
 - Partial Response in 3 patients
 - Increased infiltration by cytotoxic T cells in the tumor microenvironment associated with increased levels of soluble granzymes A, B, and H as well as granzyme B positive T cells in the peripheral blood
- These data are consistent with the hypothesis that CAN-2409 induces immunization against tumor antigens in the injected tumor and uninjected metastases



Perspective on clinical trial of CAN-2409 and anti-PD-1 in patients with NSCLC and inadequate response to anti-PD-1 agents

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Chief of Medical Oncology at the Yale Cancer Center and Smilow Cancer Hospital

Conflict of interest disclosure: Member of Candell's Research Advisory Board

Key Findings

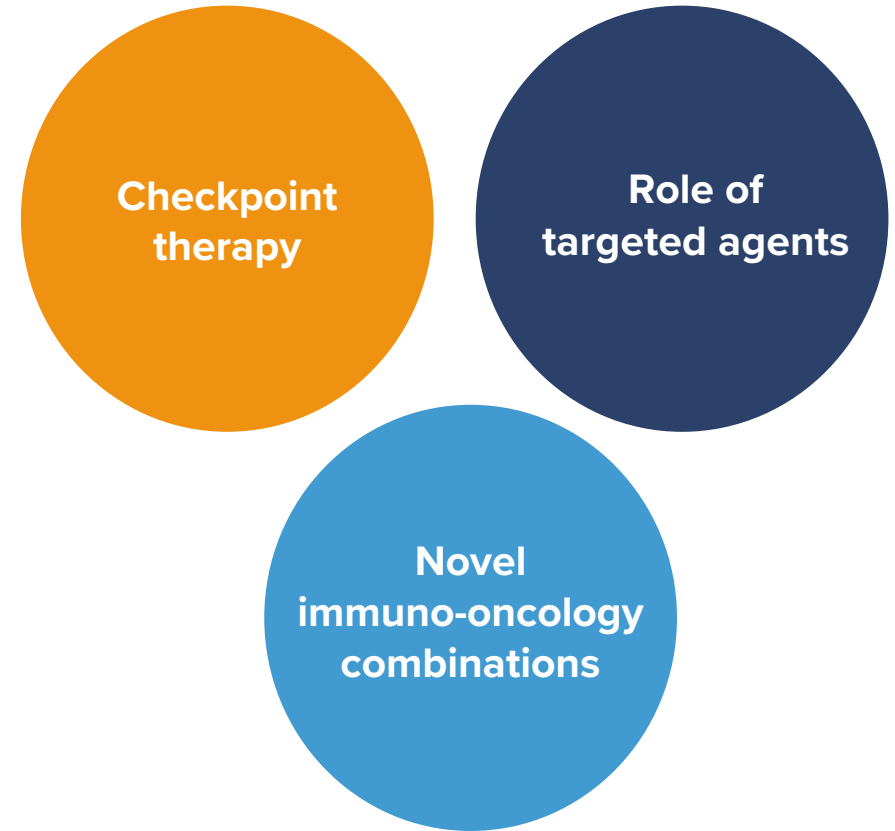
- Experimental treatment with CAN-2409 plus valacyclovir in patients with advanced NSCLC and an inadequate response to first-line ICI (\pm chemo) who continued ICI treatment appears to be well tolerated
- Encouraging preliminary activity in the first 20 evaluable patients at 12 weeks post-treatment:
 - Evidence for disease regression in both injected and uninjected lesions
 - In Cohort 2 (patients who entered the study with progressive disease), a DCR of 87.5% with durable disease stabilization ongoing in 10 out of 16 patients
 - PR in 3 patients
 - Increased infiltration by cytotoxic T cells in the tumor microenvironment associated with increased levels of soluble granzymes A, B, and H as well as granzyme B positive T cells in the peripheral blood
- These data are consistent with the hypothesis that CAN-2409 induces immunization against tumor antigens in the injected tumor and uninjected metastases

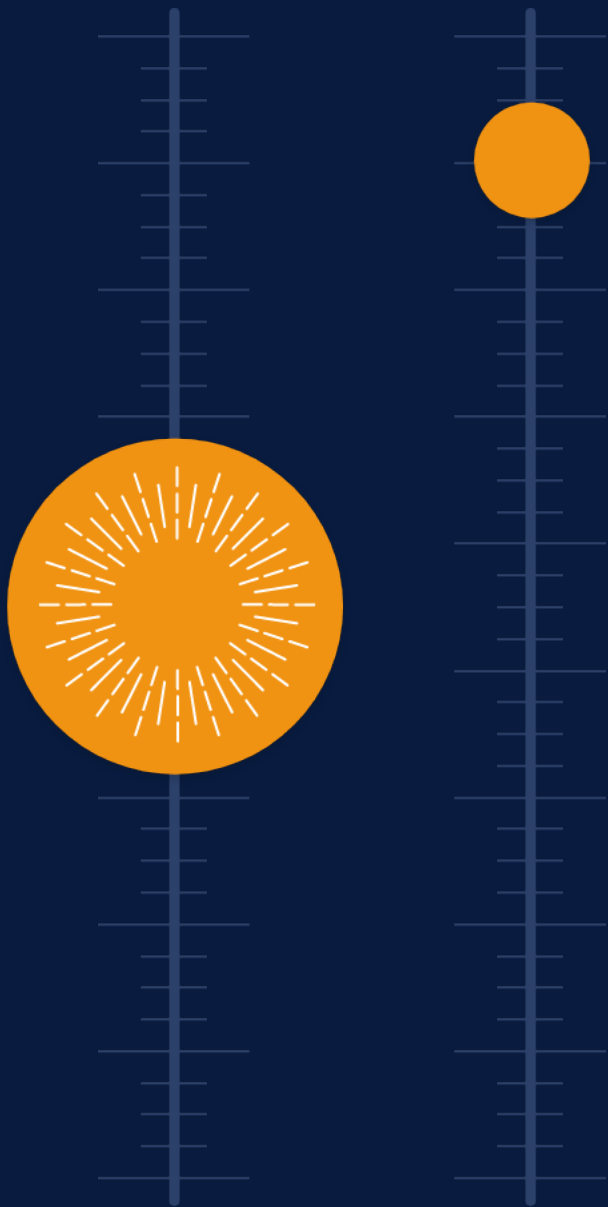
NSCLC landscape

Experience in treating NSCLC



Current treatment paradigm





Q&A





Q&A

- How important is achieving stable disease in NSCLC patients?
- What has been the response rate in PD-1 progressing patients treated beyond progression with anti-PD-1 or other agents?
- What is your view of the monotherapy data for CAN-2409?
- How quickly did patients experience tumor shrinkage? PRs?
- Do you think you might get better response rates by retreatment patients with CAN-2409?
- Do you think CAN-2409 has a unique opportunity in low PD-L1 tumors?