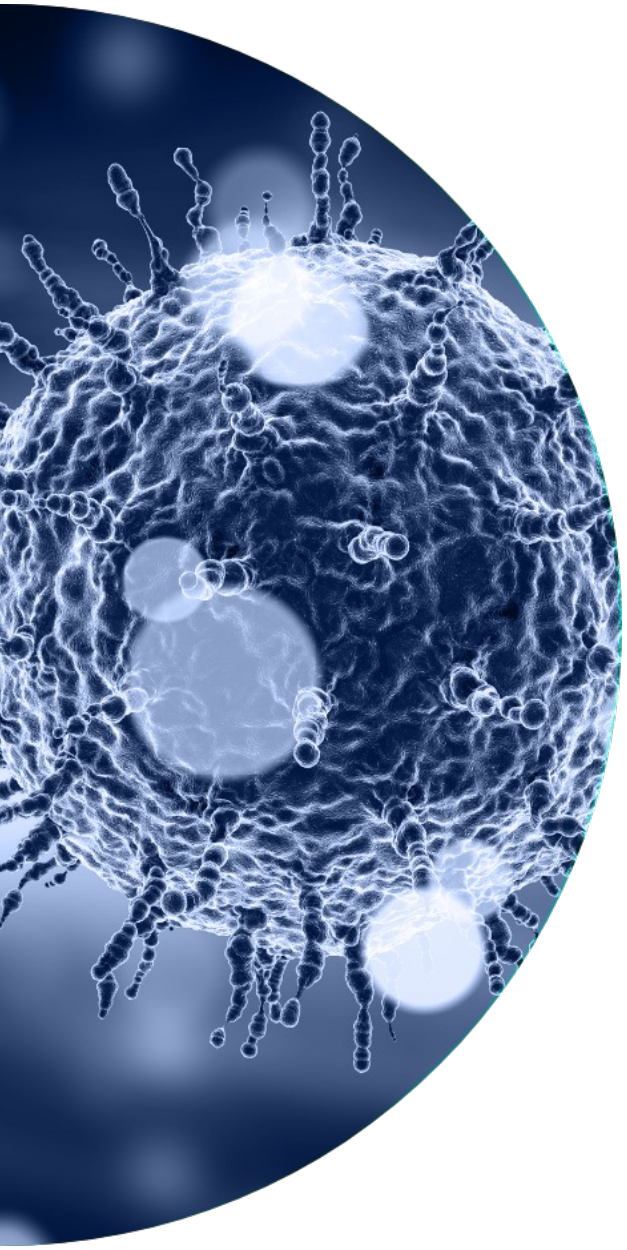


CANDEL THERAPEUTICS

Research & Development Day

Virtual | December 6, 2022

NASDAQ: CADL

Forward Looking Statements

This Presentation contains forward-looking statements and information. All statements other than statements of historical facts contained in this Presentation, including express or implied statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market size, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "target," "seek," "predict," "potential," "continue" or the negative of these terms or other comparable terminology. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market size, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this Presentation include, but are not limited to, statements about: the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs; our ability to efficiently discover and develop product candidates; our ability to initiate, recruit and enroll patients in and conduct our clinical trials at the pace that we project; our ability to obtain and maintain regulatory approval of our product candidates; our ability to compete with companies currently marketing or engaged in the development of treatments that our product candidates are designed to target; our reliance on third parties to conduct our clinical trials and to manufacture drug substance for use in our clinical trials; the size and growth potential of the markets for our product candidates and our ability to serve those markets; the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates; our ability to obtain and maintain adequate intellectual property rights; our estimates of our future expenses, revenue, capital requirements or our need for or ability to obtain additional financing; the potential benefits of strategic collaboration agreements, our ability to enter into additional strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise; our financial performance; developments and projections relating to our competitors or our industry; the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to, our preclinical studies or current and future clinical trials. We caution the recipient not to place considerable reliance on the forward-looking statements contained in this Presentation. The forward-looking statements in this Presentation speak only as of the date of this document, and we undertake no obligation to update or revise any of these statements. Our business is subject to substantial risks and uncertainties, including those referenced above.

Certain information contained in this Presentation relates to or is based on estimates, projections and other information concerning the Company's industry, its business and the markets for its programs and product candidates and studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this Presentation involves a number of assumptions; there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

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.

R&D Day 2022

December 6, 2022 (EST)

11:00 – 11:10 am	**Introduction to Candel Therapeutics**
11:10 – 11:20 am	**Intratumor viral immunotherapy: a new approach to induce systemic anti-tumor immunity**
11:20 – 11:30 am	**Clinical perspective on viral immunotherapy**
11:30 – 12:00 pm	**Phase 2 clinical trial of CAN-2409 in NSCLC**
12:00 – 12:10 pm	**Phase 1 clinical trial of CAN-2409 in combination with nivolumab and standard of care in newly diagnosed high-grade glioma**
12:10 – 12:25 pm	**Phase 1 clinical trial of CAN-3110 in recurrent high-grade glioma**
12:25 – 12:40 pm	**The enLIGHTEN™ Discovery Platform**
12:40 – 12:55 pm	**Penn – Candel discovery partnership: Combination therapy to overcome CAR-T resistance in solid tumors**
12:55 – 1:30 pm	**Closing and Q&A**

Speakers

Paul Peter Tak
MD, PhD, FMedSci
Candel Therapeutics

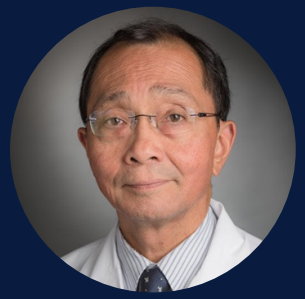
James P. Allison
PhD
MD Anderson Cancer Center & Parker Institute for Cancer Research

Padmanee Sharma
MD, PhD
MD Anderson Cancer Center

Charu Aggarwal
MD, MPH
Perelman School of Medicine at UPenn

Daniel H. Sterman
MD
NYU Langone Health

Roy Herbst
MD, PhD
Yale Cancer Center



Patrick Y. Wen
MD
Dana-Farber Cancer Institute & Harvard Medical School

E. Antonio Chiocca
MD, PhD
Brigham and Women's Hospital & Harvard Medical School

Francesca Barone
MD, PhD
Candel Therapeutics

Carl H. June
MD
Center for Cellular Immunotherapies at UPenn & Parker Institute for Cancer Research

Neil C. Sheppard
DPhil
Center for Cellular Immunotherapies at UPenn

CANDEL THERAPEUTICS

Candel Therapeutics

Paul Peter Tak, MD, PhD, FMedSci

CANDEL THERAPEUTICS

Paul Peter Tak, MD, PhD, FMedSci

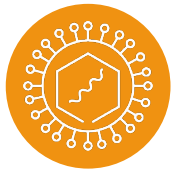
Candel Therapeutics

Dr. Paul Peter Tak is President, CEO, and Board Director of Candel Therapeutics. Dr. Tak received his medical degree from the Free University in Amsterdam and was trained as an internist and immunologist at Leiden University Medical Center, where he also received his PhD. He worked as a scientist at the University of California San Diego and next served as Professor of Medicine and Chair of the Department of Clinical Immunology and Rheumatology at Amsterdam University Medical Center. He has published extensively in peer-reviewed journals (> 590 publications, H-index 137, > 80,000 citations), received numerous awards, has been elected Fellow of the Academy of Medical Sciences, is an Honorary Senior Visiting Fellow at the University of Cambridge, and was recognized by PharmaVOICE100 in 2021. At GlaxoSmithKline, Dr. Tak served as Senior Vice President, Chief Immunology Officer, and Global Development Leader (2011-2018), and brought a large portfolio of investigational medicines to clinical development and approval.

Candel overview

- Two investigational medicines in the clinic and a discovery platform

- CAN-2409
  - Engineered, replication-defective adenoviral gene construct encoding herpes simplex virus (HSV)-thymidine kinase
  - Ongoing clinical trials in non-small cell lung cancer (NSCLC), pancreatic cancer, and prostate cancer
  - Pipeline in a product
  - **Phase 2 clinical trial data update in NSCLC**



- CAN-3110
  - Engineered, replication-competent HSV designed for tumor-specificity
  - Ongoing clinical trial in recurrent high-grade glioma (HGG)
  - Opportunity for creation of pipeline in a product by expansion of indications outside the brain
  - **Phase 1b clinical trial data update in recurrent HGG**

- enLIGHTEN™ Discovery Platform based on Advanced Analytics and HSV technology

- Company Update
  - Strong scientific support from high-profile Research Advisory Board
  - Significant unmet need and commercial opportunity for each selected indication
  - Cash and cash equivalents of $77.2M as of September 30, 2022; runway into Q1 2024

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

Paul-Peter Tak, M.D., Ph.D., FMedSci

President & Chief Executive Officer

gsk · sitryx · Flagship Pioneering · Amsterdam UMC University Medical Centers

Francesca Barone, M.D., Ph.D.

Chief Scientific Officer

Kintai Therapeutics · University of Birmingham

Christopher Matheny, Pharm.D., Ph.D.

Vice President, Development Leader

gsk

Seshu Tyagarajan, Ph.D., RAC

Chief Technical and Development Officer

Novartis · Merck · Roche · Biogen · Lilly

Jason Amello

Chief Financial Officer

genzyme · Akebia Therapeutics · saniona · Alaunos Therapeutics

Nathan Caffo

Chief Business Officer

ALX Oncology · presage · applied biosystems · Perlegen Sciences

Garrett Nichols, M.D., M.S.

Chief Medical Officer

gsk · ViiV Healthcare · Chimerix · istari Oncology

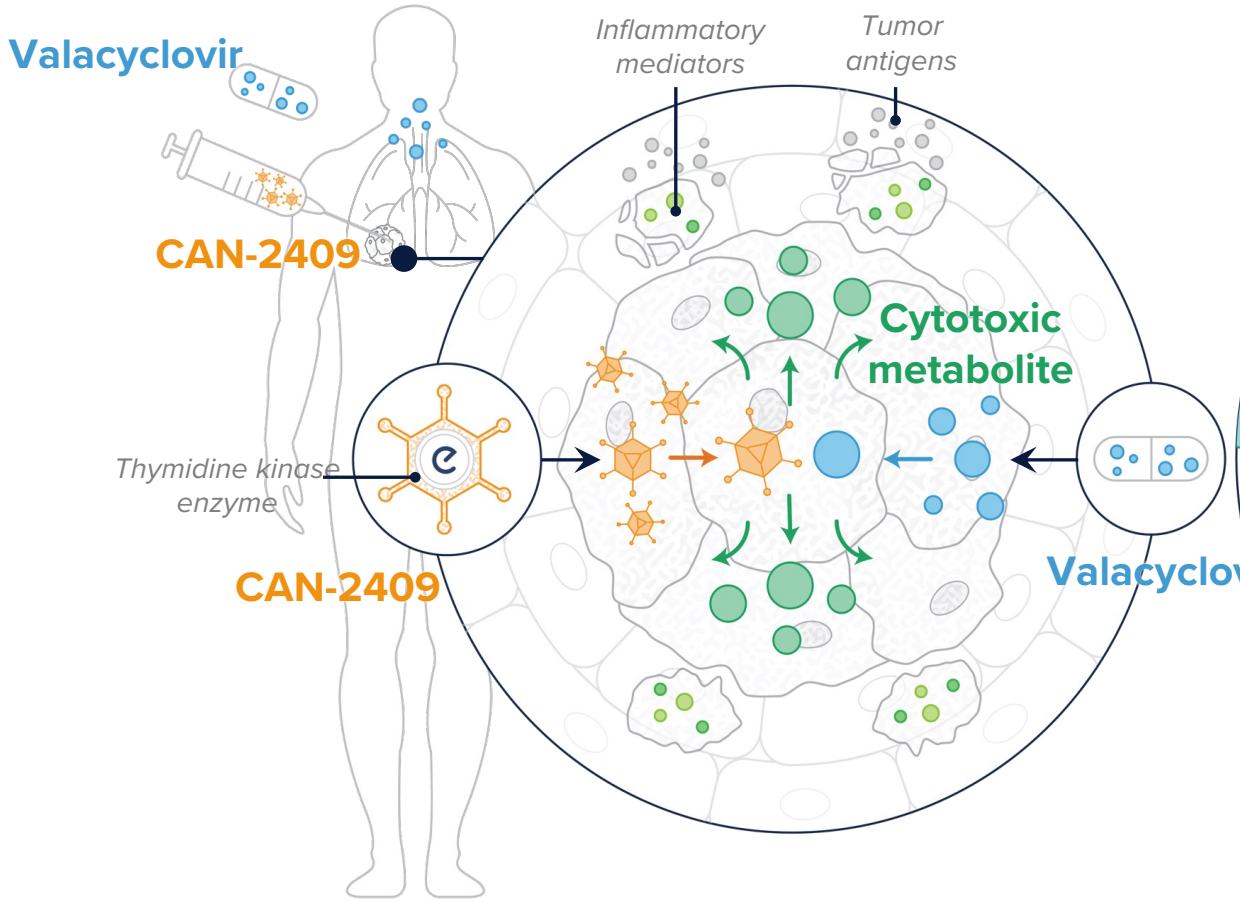
Susan Stewart, J.D.

Chief Regulatory Officer

Tokai Medical Products · genzyme · Abbott

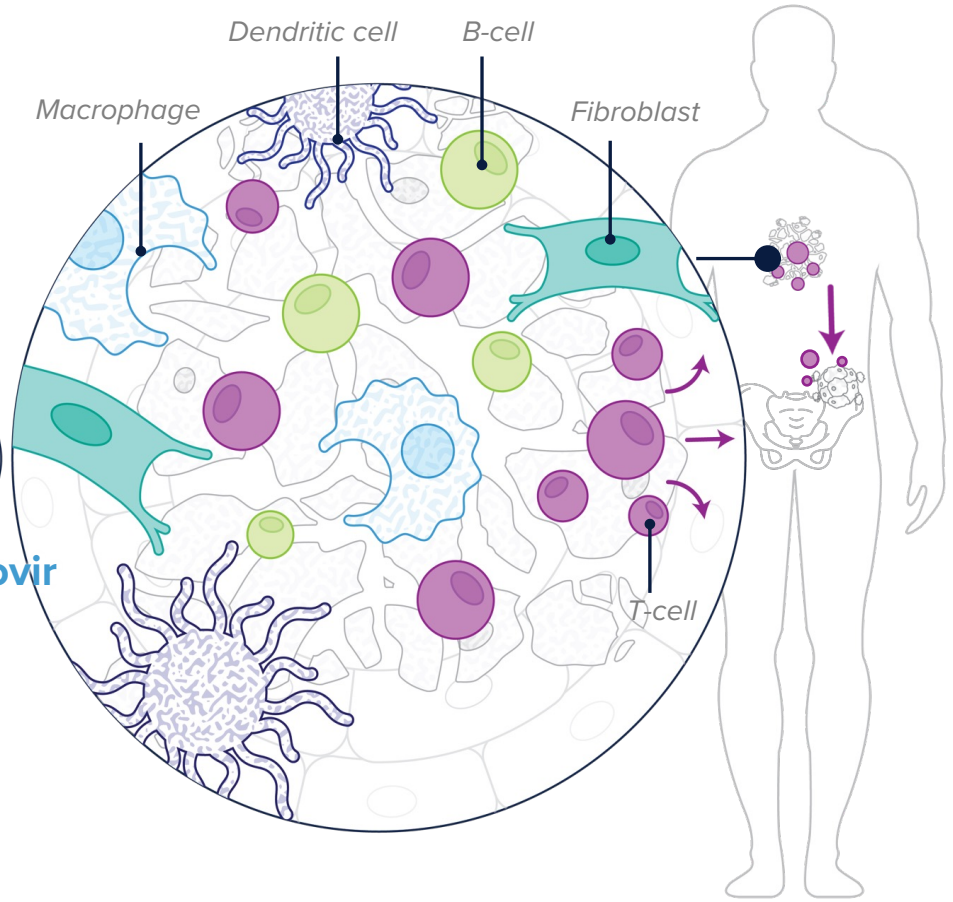
CAN-2409: Systemic immunotherapy delivered intratumorally

1. CAN-2409 locally administered combined with oral prodrug



2. Localized cytolytic mechanism combined with proinflammatory viral particles

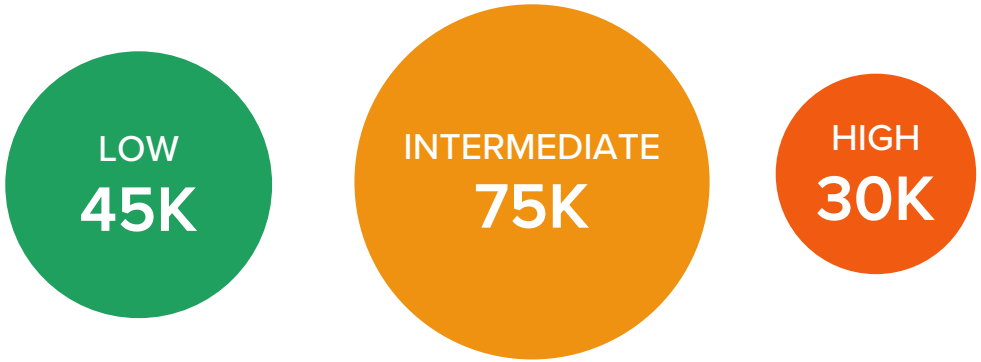
3. CAN-2409 induces CD8+ cytotoxic T cells



4. Local immunization yields systemic CD8+ T cell mediated against injected tumor and uninjected metastases

Prostate cancer: Significant unmet need

Incidence of localized prostate cancer in the US by risk level



- No new treatments approved for newly diagnosed, localized prostate cancer during the last 10+ years
- Currently available treatments are associated with significant side effects
- Significant opportunity for new treatment with favorable tolerability profile that will prevent disease progression

Target label for CAN-2409:
- Indicated in newly diagnosed localized prostate cancer in combination with radiotherapy +/- short-term ADT, in patients with intermediate- to high-risk disease
- Indicated in newly diagnosed localized prostate cancer in patients with NCCN-defined low-risk disease, or patients with intermediate-risk disease undergoing active surveillance[#]

[#] Market research combined with interviews with 22 KOLs (12 US; 10 EU) and 10 US payors. Dec 2020

Fully accrued phase 2 clinical trial of CAN-2409 in patients with prostate cancer (active surveillance)

PI: Dr. S. Eggener (U of Chicago)

N=187
Fully enrolled
Patients chose
active surveillance

2:1
Randomization

Active Surveillance + CAN-2409 + Valacyclovir
(2 injections)

Active Surveillance + Placebo + Valacyclovir
(2 injections)

Primary Endpoints

- Disease Free Survival

Secondary Endpoints

- Progression to radical treatment, pathological response/PSA kinetics
- Proactive Surveillance Score
- Quality of life
- Immunological biomarkers

NCT02768363

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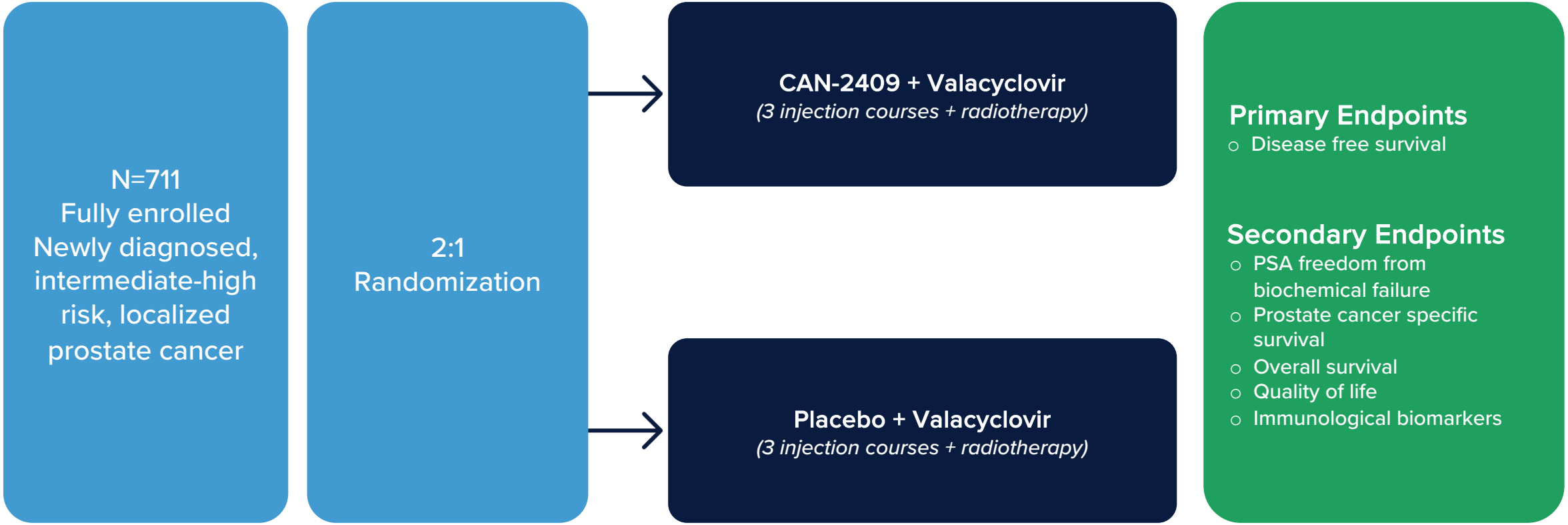
Fully accrued phase 3 clinical trial of CAN-2409 in patients with prostate cancer (newly diagnosed, intermediate/high risk)

PIs: Dr. T. DeWeese (JHU) and Dr. P. Scardino (MSKCC)



NCT01436968

Conducted under agreement with FDA under Special Protocol Assessment

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CAN-2409 is generally well tolerated in ongoing phase 2b clinical trial in patients with prostate cancer

(monotherapy; active surveillance population)

Study is still blinded
187 patients treated
362 injections performed

Most common PT (>=5%)	CTC grade				n=187
	1	2	3	4	Total (%)
Flu-like symptoms	40 (21)	20 (11)	1 (1)		61 (33)
Chills	39 (21)	13 (7)	1 (1)		53 (28)
Fever	39 (21)	9 (5)	1 (1)		49 (26)
Fatigue	27 (14)	10 (5)	1 (1)		38 (20)
Elevated AST/ALT	28 (15)	3 (2)	1 (1)		32 (17)
Elevated Creatinine	23 (12)	5 (3)	1 (1)	2 (1)	31 (17)
Headache	20 (11)	5 (3)			25 (13)
Urinary tract infection	1 (1)	15 (8)	2 (1)		18 (10)
Nausea	12 (6)	4 (2)			16 (9)
Low Hemoglobin	15 (8)				15 (8)
Diarrhea	10 (5)	3 (2)			13 (7)
Malaise	10 (5)	2 (1)			12 (6)
Hematuria	12 (6)				12 (6)
Urinary frequency	9 (5)	2 (1)			11 (6)
Urinary tract pain	6 (3)	3 (2)			9 (5)
Urinary urgency	7 (4)	2 (1)			9 (5)
Elevated Alkaline Phosphatase	8 (4)	1 (1)			9 (5)
Elevated Bilirubin	7 (4)	3 (2)			10 (5)

~ 33% patients experienced flu-like symptoms
< 1% infections requiring hospitalization

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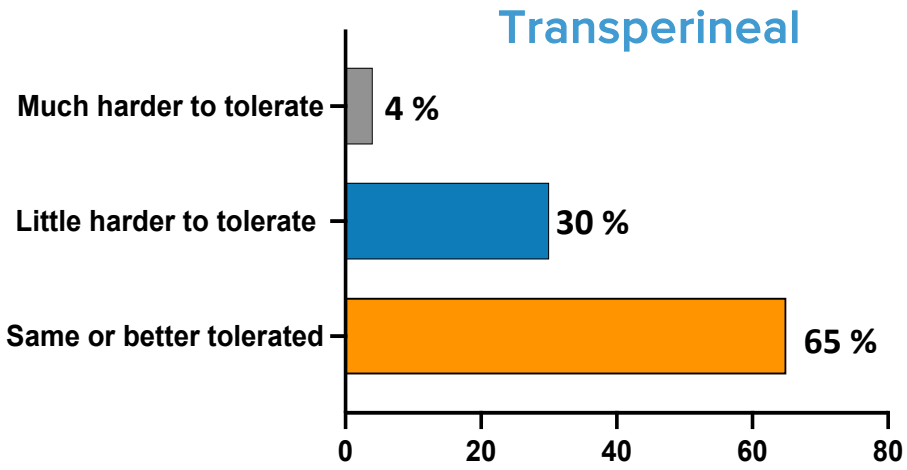
Most patients tolerate intra-prostate injection same or better than prostate biopsy

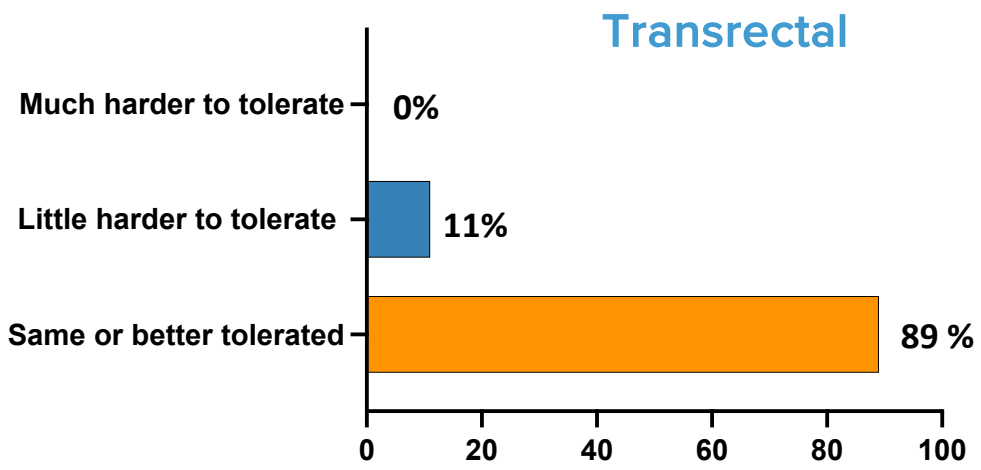
(ongoing phase 3 clinical trial; combined with radiotherapy +/- androgen deprivation therapy)

In total > 2,000 intra-prostate injections
(40% transperineal; 56% transrectal; 4% not reported)

"How did you tolerate the study procedure as compared to a prostate biopsy?"

Patient questionnaire substudy in 32 patients





Systemic immunotherapy delivered intratumorally

- Intra-tissue injection is a proven strategy for in situ vaccination
- Delivery designed to minimize systemic toxicity
- Systemic immune response: not all metastases need to be injected
- Durable responses after only 2-3 administrations
- Procedure is well tolerated by patients:
  - Administration to prostate takes 15-20 min in outpatient setting, often tolerated the same or better than prostate biopsy, which is a routine procedure in urology
  - Administration to lung tumor takes 15-20 min in outpatient setting via bronchoscopy, which is a routine procedure in pulmonary medicine
  - For future indications, any location can be reached using image-guided injection, robotic delivery, etc.
- Procedures with proven benefit/risk, patient tolerability, and cost-effectiveness will be implemented by clinicians
  - Stem cell transplantation, implant radiotherapy, interventional radiology, interventional cardiology

Candel overview

- Promising assets with near- and mid-term inflection points
  - CAN-2409: ***Systemic immunotherapy delivered intratumorally***
    - Phase 2 NSCLC; updated clinical data – to be presented today
      - Additional data expected in Q3 2023
    - Phase 3 HGG; ready to commence
    - Phase 2 pancreas preliminary data – expected Q4 2023
    - Phase 2 prostate cancer; localized, low- to intermediate-risk (active surveillance) – **readout expected Q4 2023**
    - Phase 3 prostate cancer; localized, intermediate- to high-risk – **readout expected Q4 2024**
  - CAN-3110: ***Replication-competent HSV with tumor-specificity***
    - Phase 1b recurrent HGG; updated clinical and biomarkers - presented at SITC and today
  - enLIGHTEN Discovery Platform based on use of Advanced Analytics and HSV technology
- Significant unmet need and commercial opportunity for each selected indication
- Management team with proven success in immunology, oncology, and development
- Cash and cash equivalents of $77.2M as of September 30, 2022
  - Funds currently planned operations into Q1 2024

Intratumor viral immunotherapy

James P. Allison, PhD

CANDEL THERAPEUTICS

James P. Allison, PhD

MD Anderson Cancer Center

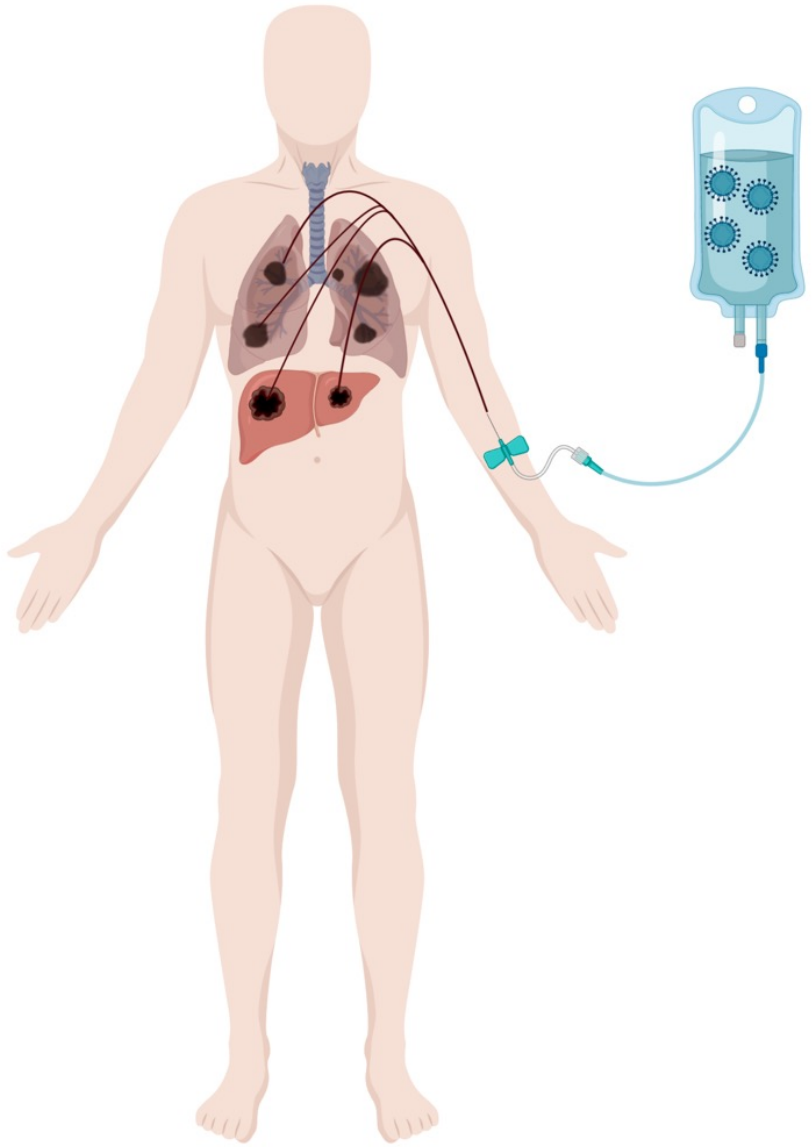
Dr. James Allison is the Regental Professor and Chair of the Department of Immunology, the Olga Keith Wiess Distinguished University Chair for Cancer Research, Director of the Parker Institute for Cancer Research, and the Executive Director of the Immunotherapy Platform at MD Anderson Cancer Center. His well-known research is focused on the mechanisms of T cell development and activation, development of novel strategies for tumor immunotherapy, and he is recognized as one of the first to isolate the T-cell antigen receptor complex protein. In 2018, Dr. Allison received the Nobel Prize in Physiology or Medicine for the discovery of cancer therapy by inhibition of negative immune regulation. Since April 2021, Dr. Allison has been on the Research Advisory Board for Candel.

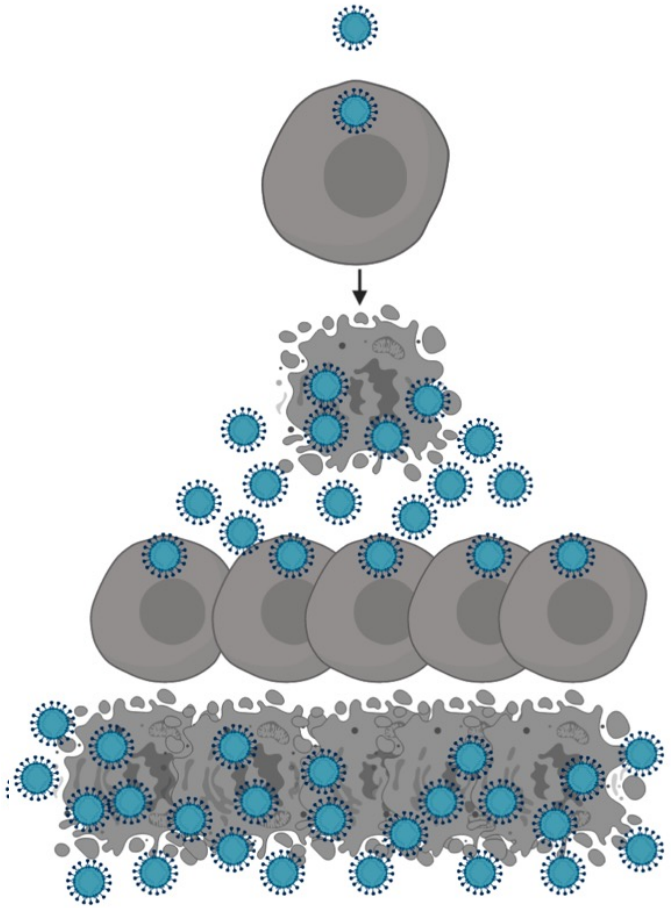
Intratumor viral immunotherapy:
A new approach to induce systemic anti-tumor immunity

Jim Allison, PhD
Regental Professor and Chair, Immunology
Vice-President, Immunobiology
Director, James Patrick Allison Institute
Executive Director, Immunotherapy Platform
Olga Keith Weiss Distinguished University Chair for Cancer Research
Distinguished Scholar, Cancer Prevention and Research Institute of Texas

Candel R&D Day 2022

How oncolytic viruses are thought to work





Primary infection

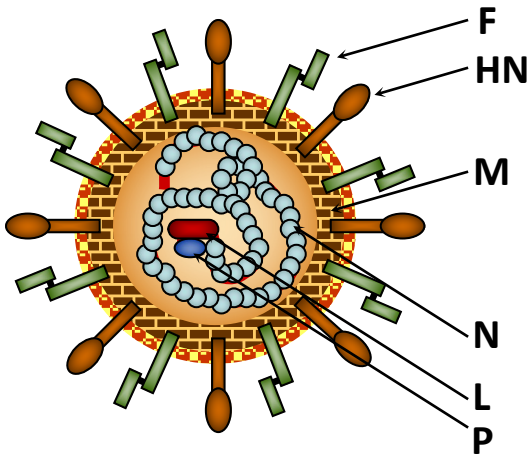
Virus amplification and tumor cell lysis

Secondary infection, Virus amplification, tumor cell lysis and virus spread

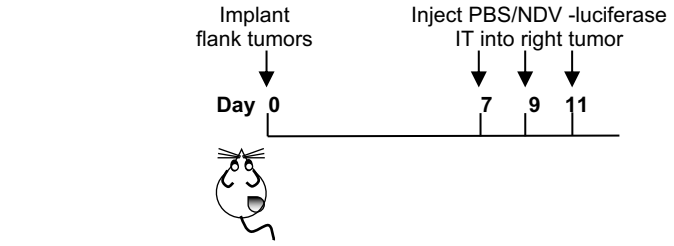
Inflammatory response

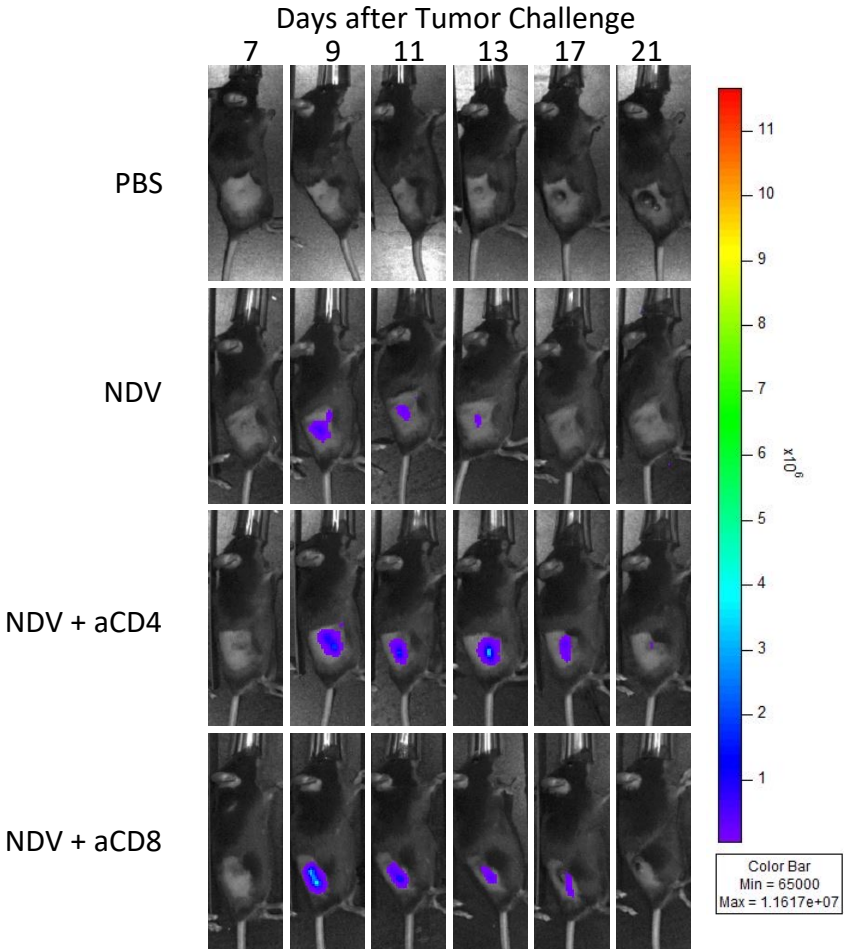
An example of viral immunotherapy: Newcastle Disease Virus (NDV)

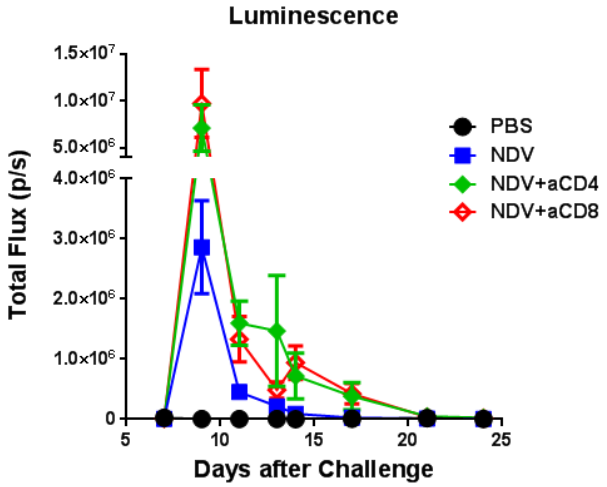
- **Family:** Paramyxoviridae: negative-strand RNA virus (same as mumps, HPIV, measles)
- **Natural host:** birds
- **Cell surface receptor:** sialic acid
- **Determinants of cancer cell-specificity:**
  - Deficiency in innate immune signaling
  - Resistance to apoptosis
- **Pathogenic types:** replication, pathogenicity (in birds) and oncolytic proficiency is determined by the viral fusion protein:
  - **Lentogenic** (nonpathogenic) strains: limited replication and lysis
  - **Mesogenic and velogenic** (pathogenic) strains: best replication and lysis

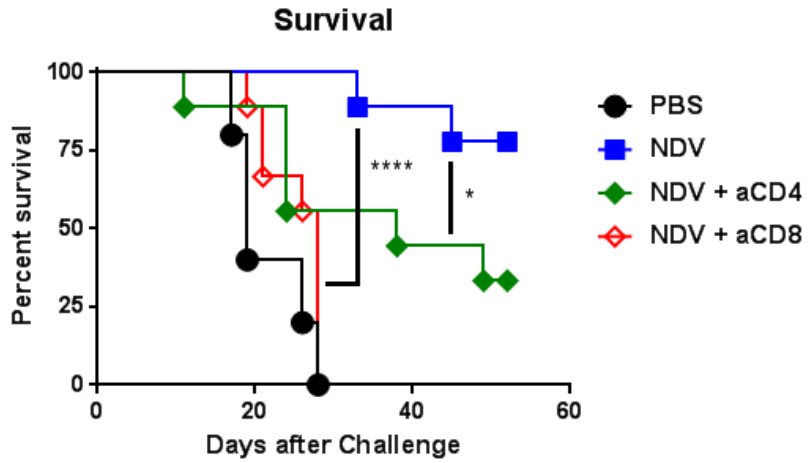


Therapeutic efficacy of oncolytic viruses is dependent on the adaptive immune response rather than virus replication

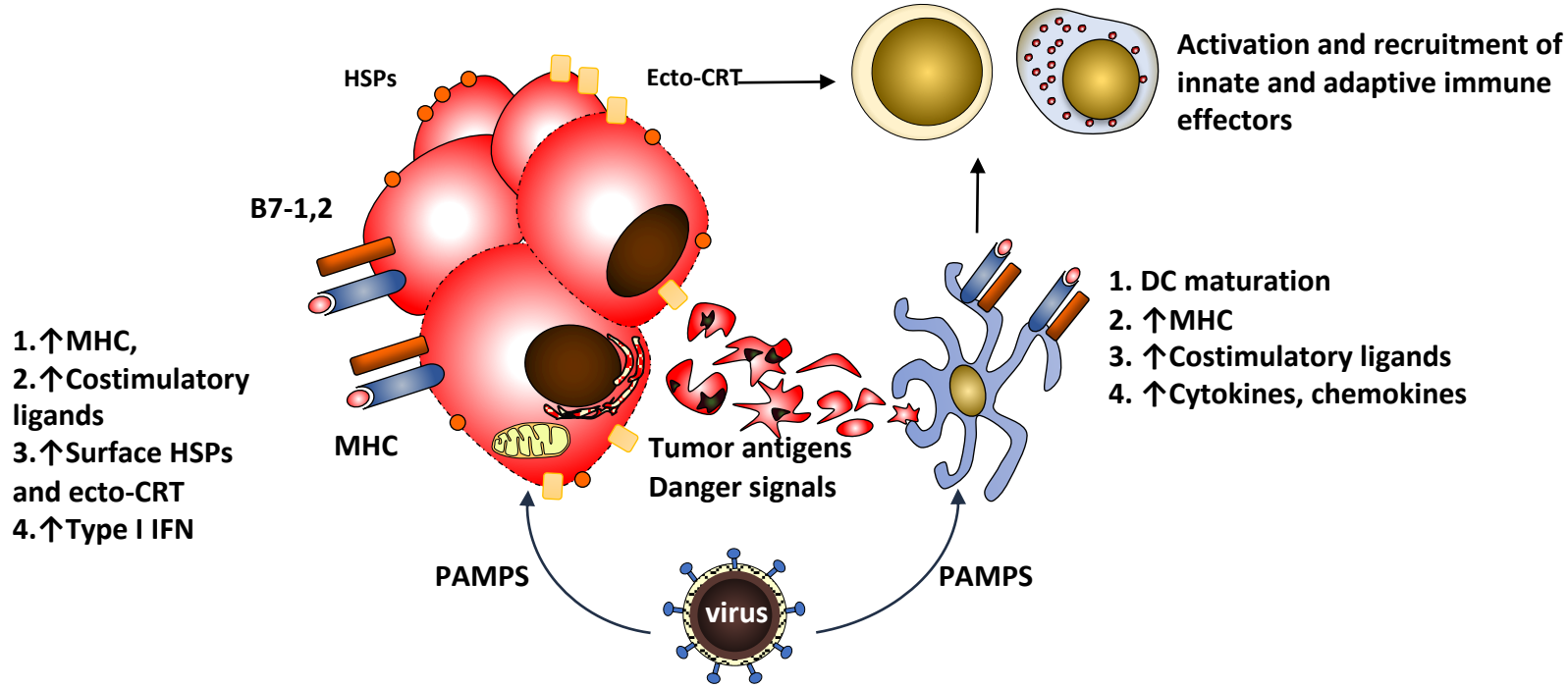






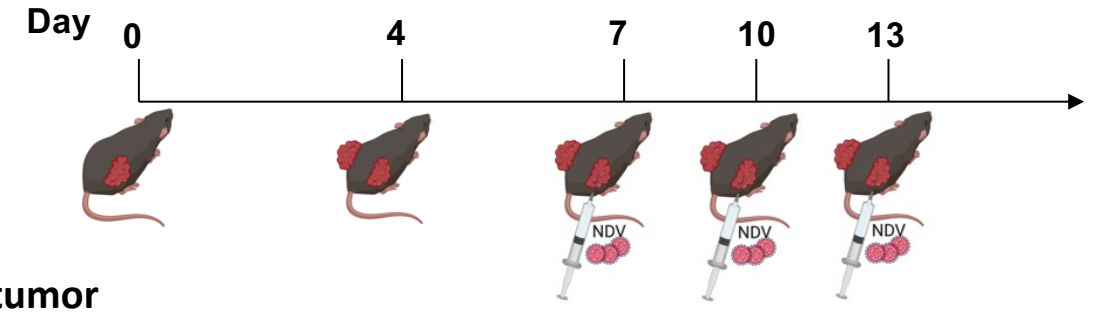


Oncolytic viruses don’t just lyse cancer cells, they make them more immunogenic

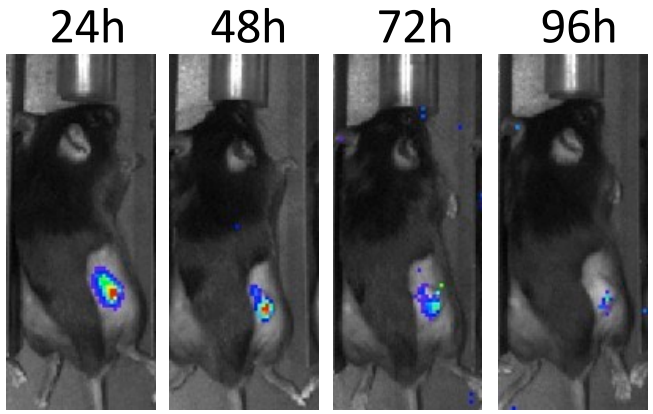


Zamarin D. and Wolchok J.D., *Molecular Therapy-Oncolytics* 1 (2014)

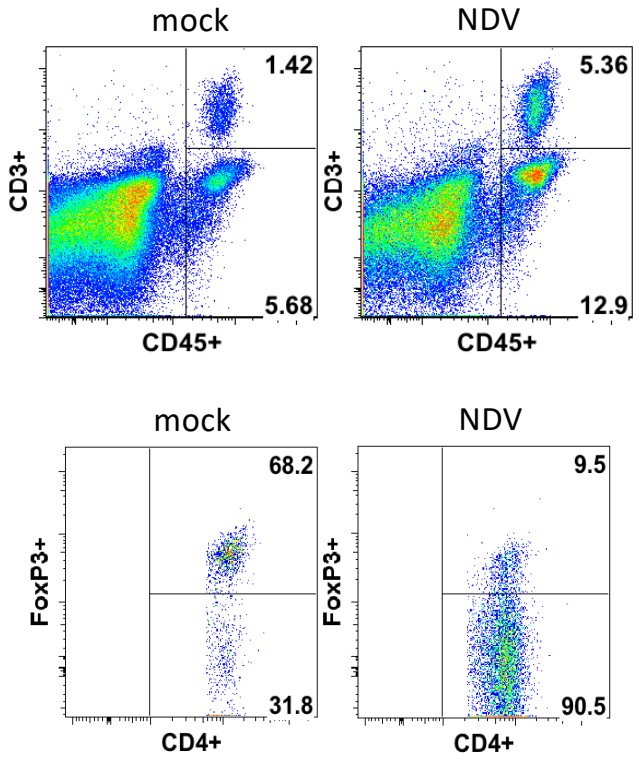
Systemic immune effects of intratumoral NDV treatment

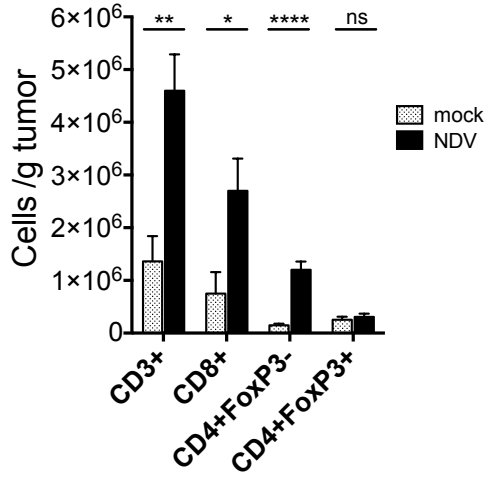


Virus-treated tumor



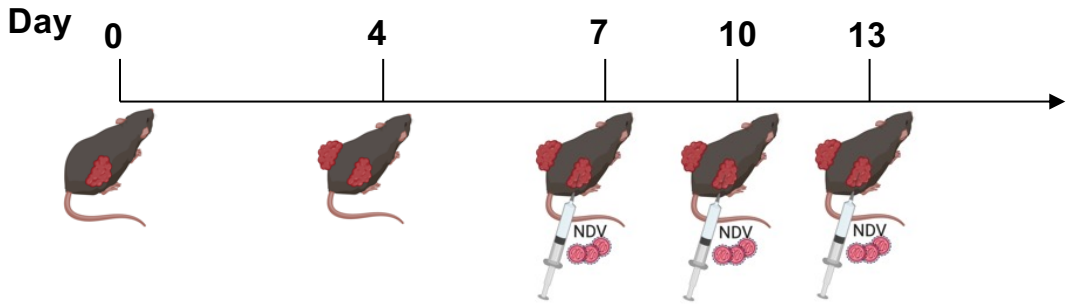
Distant tumor

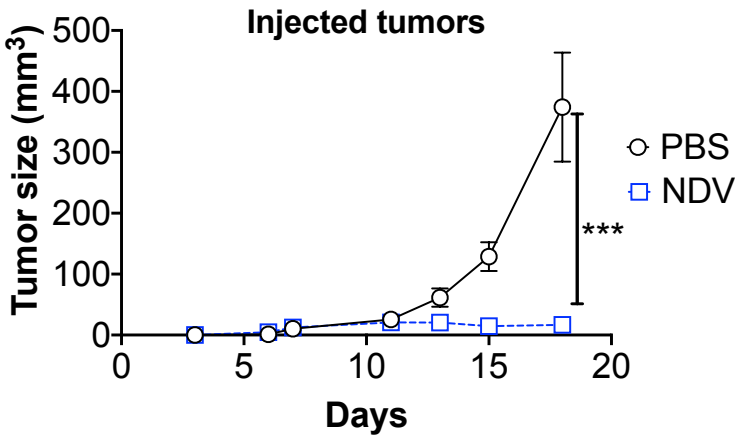


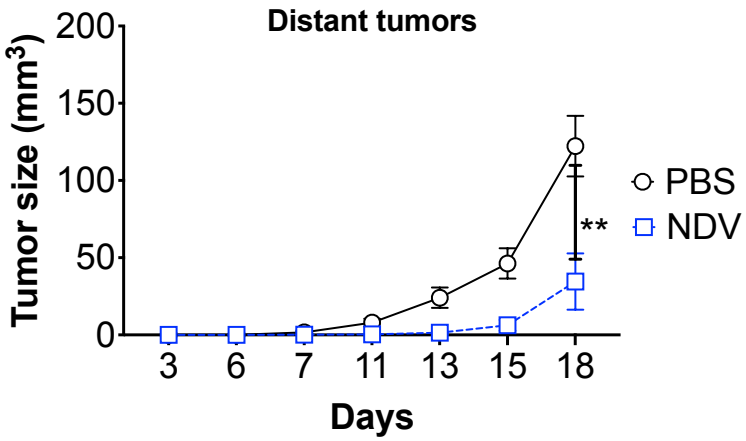


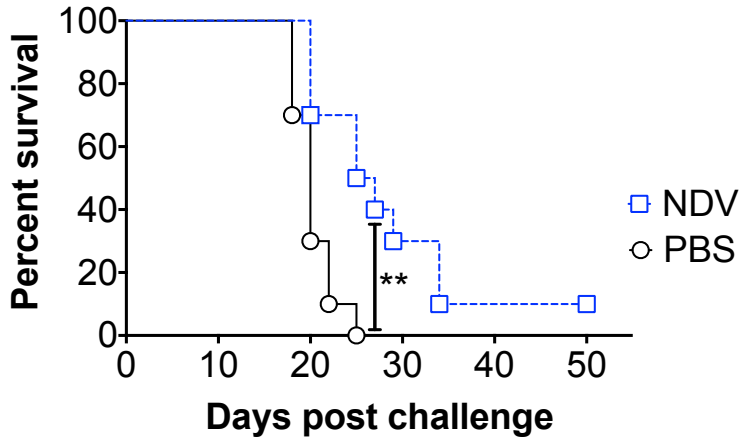
Zamarin D, Wolchok JD, Allison JP. *Sci. Transl. Med.* 2014 5:226ra

Intratumoral NDV controls virus-injected and distant tumors



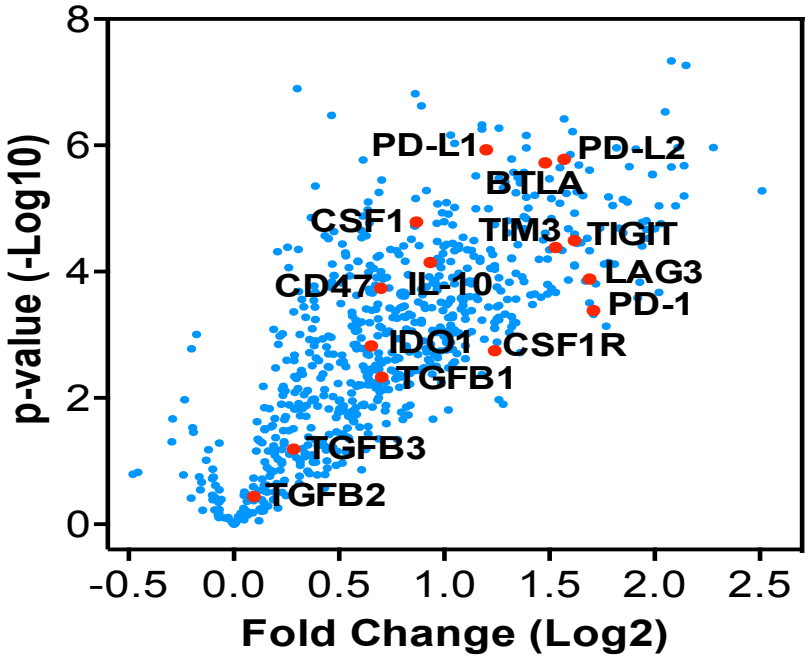


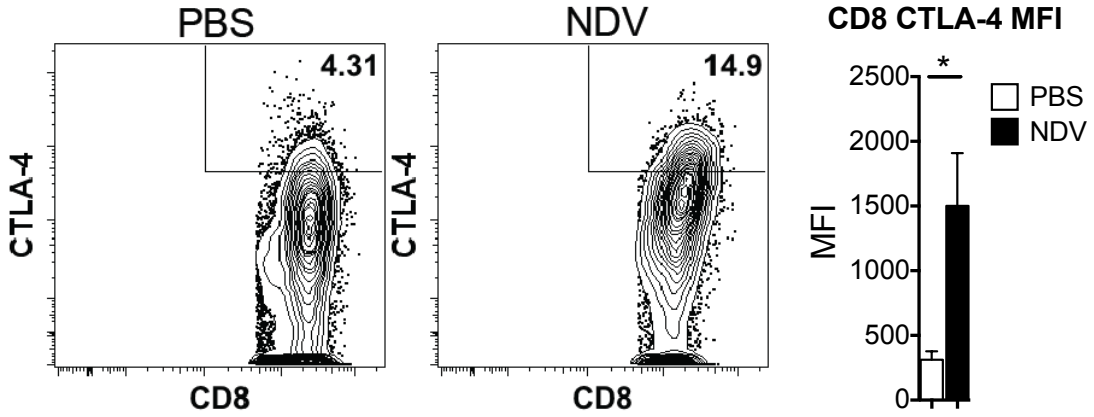


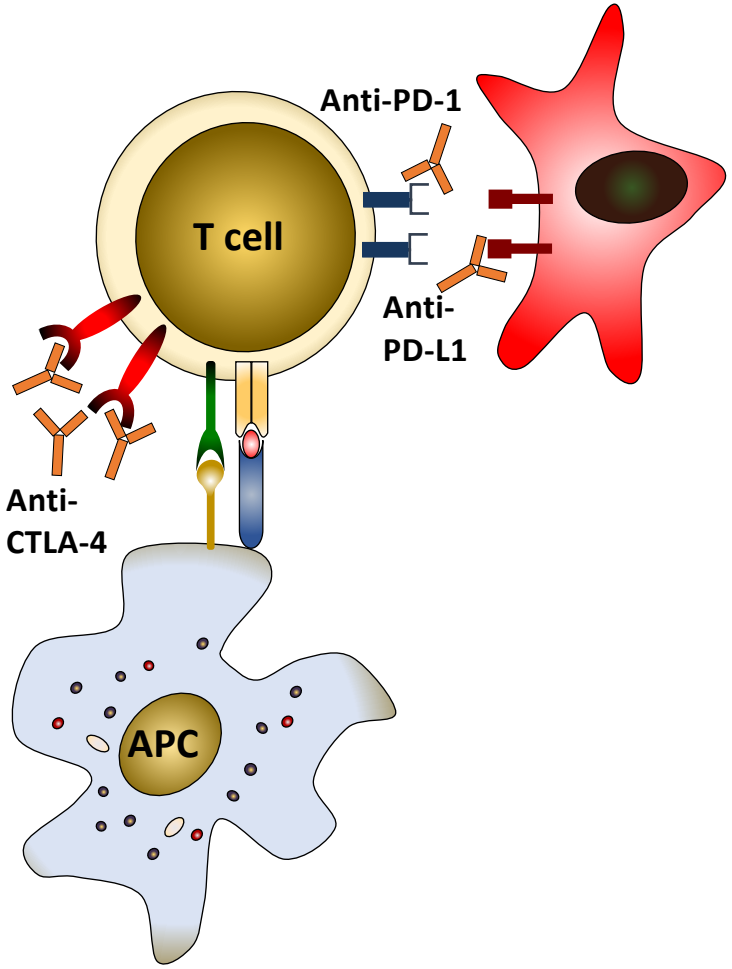


Zamarin D, Wolchok JD, Allison JP. *Sci. Transl. Med.* 2014 5:226ra

NDV upregulates a range of immune negative feedback pathways in tumors

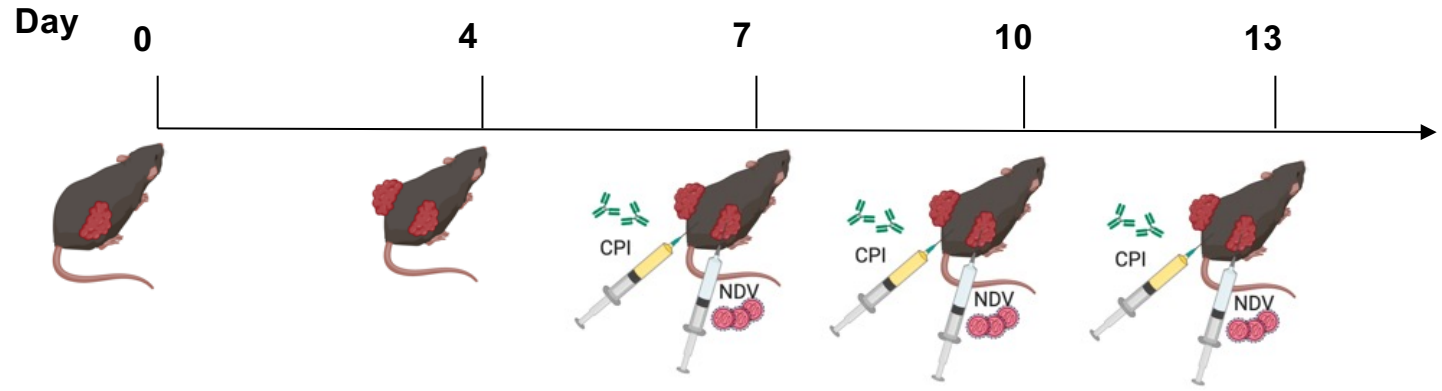


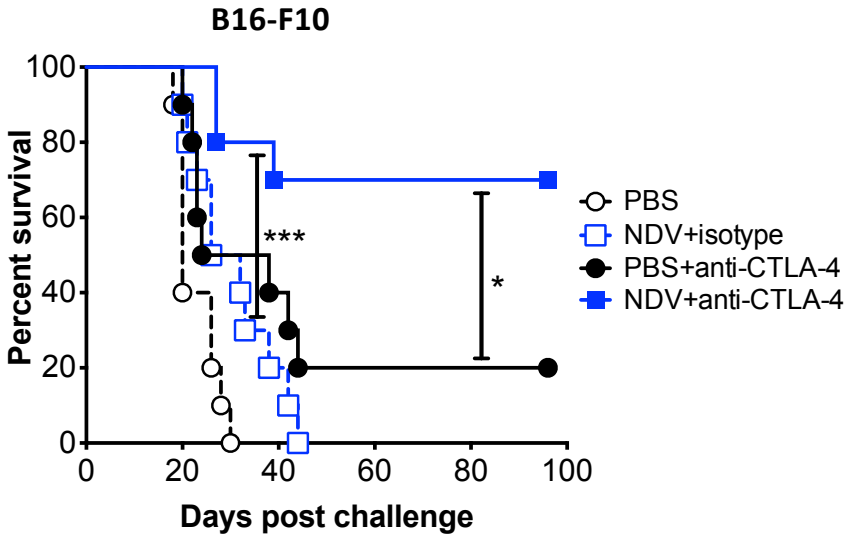


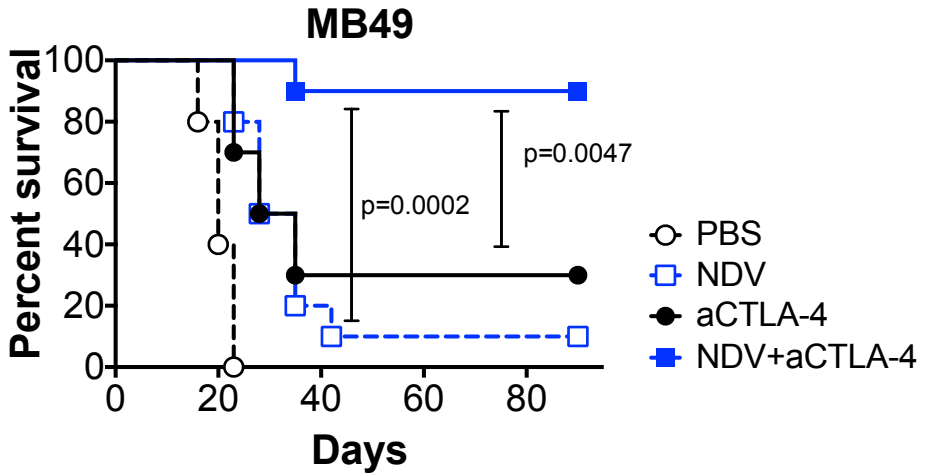


Immune checkpoint blockade

Intratumoral NDV with systemic immune checkpoint blockade leads to rejection of the treated and distant tumors

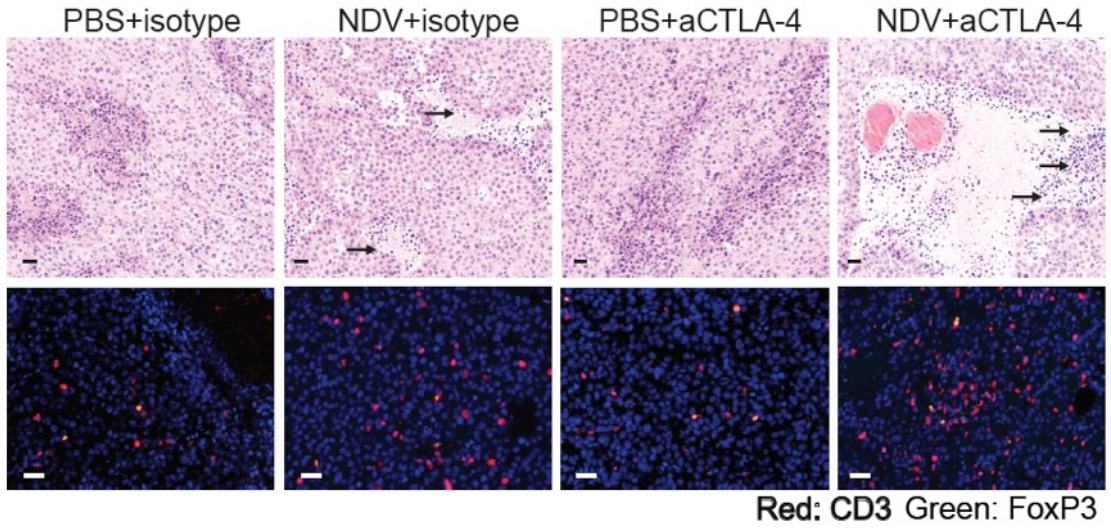


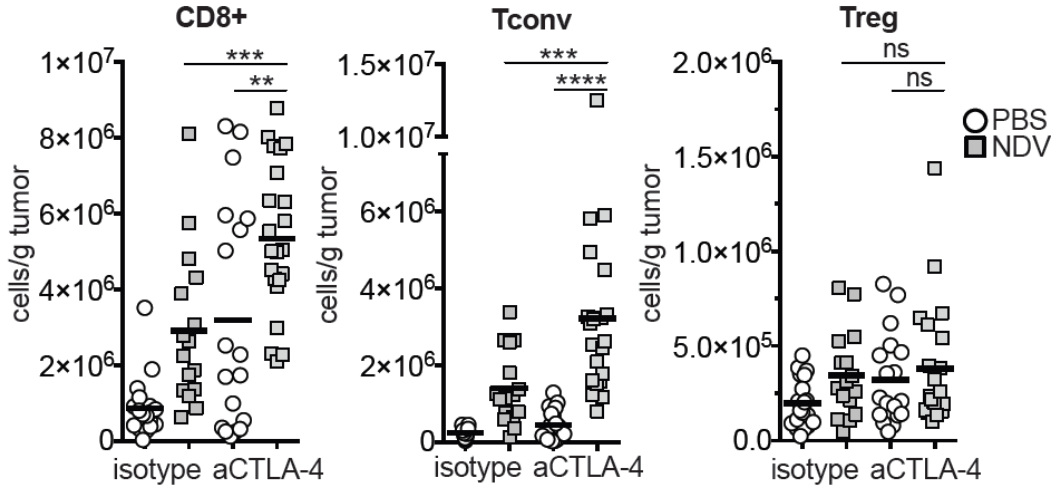




Zamarin D, Wolchok JD, Allison JP. *Sci. Transl. Med.* 2014 5:226ra

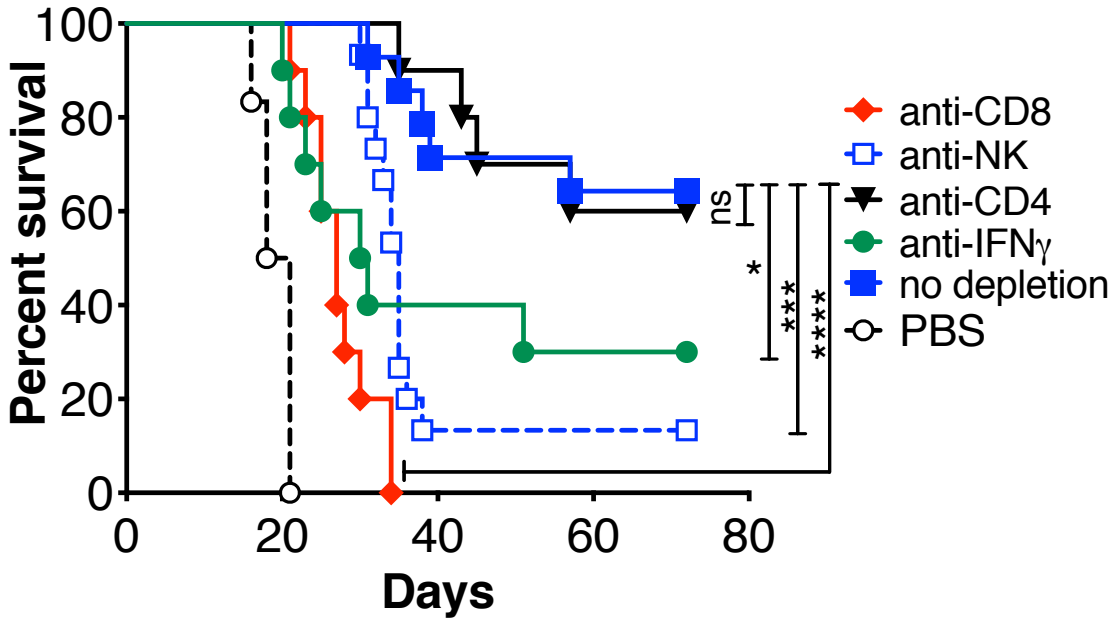
Combination therapy with NDV and CTLA-4 blockade induces inflammatory changes in distant tumors

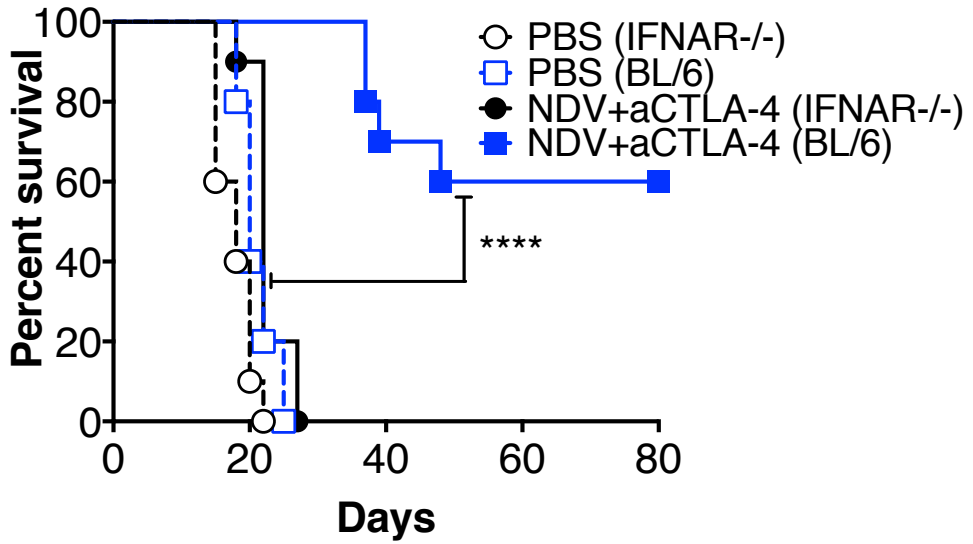




Anti-tumor activity of NDV combination therapy is dependent on CD8 cells, NK cells, IFNγ, and type I IFN

Depletion of specific immune cell subtypes

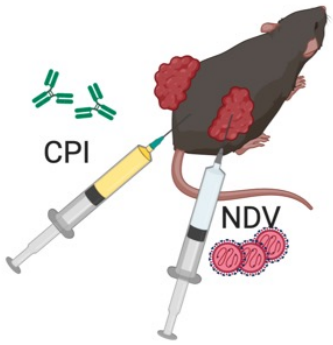




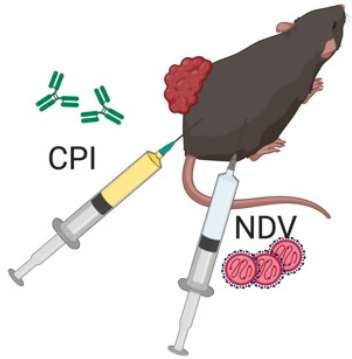
Zamarin D, Wolchok JD, Allison JP. *Sci. Transl. Med.* 2014 5:226ra

Virus delivery to the tumor is essential for the abscopal response

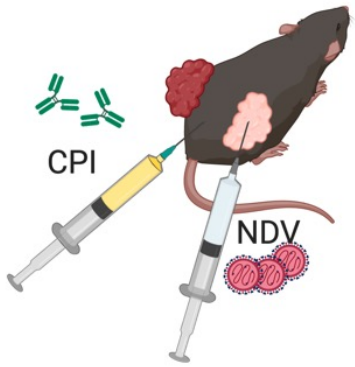
B16-B16



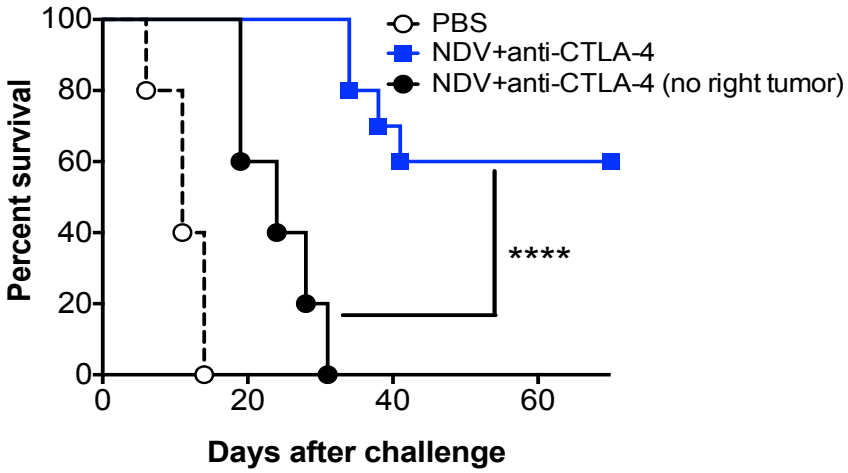
B16-no right tumor



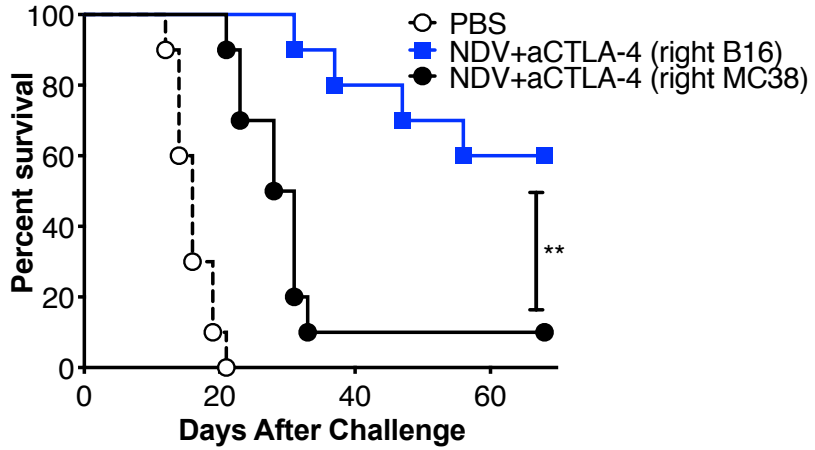
B16-MC38



No right tumor

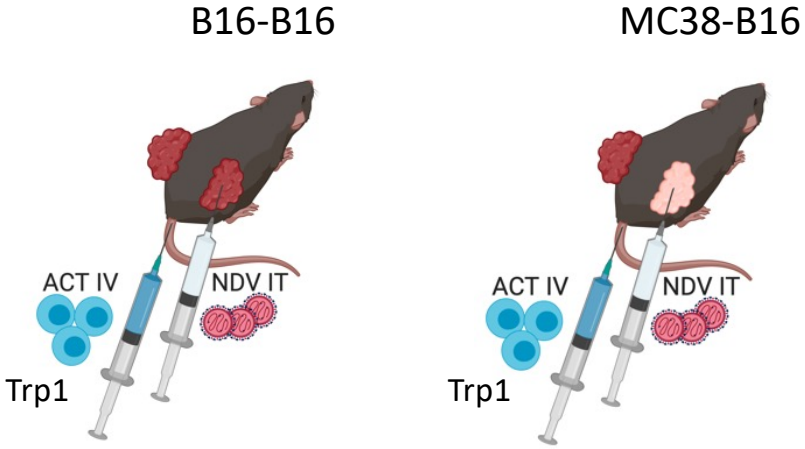


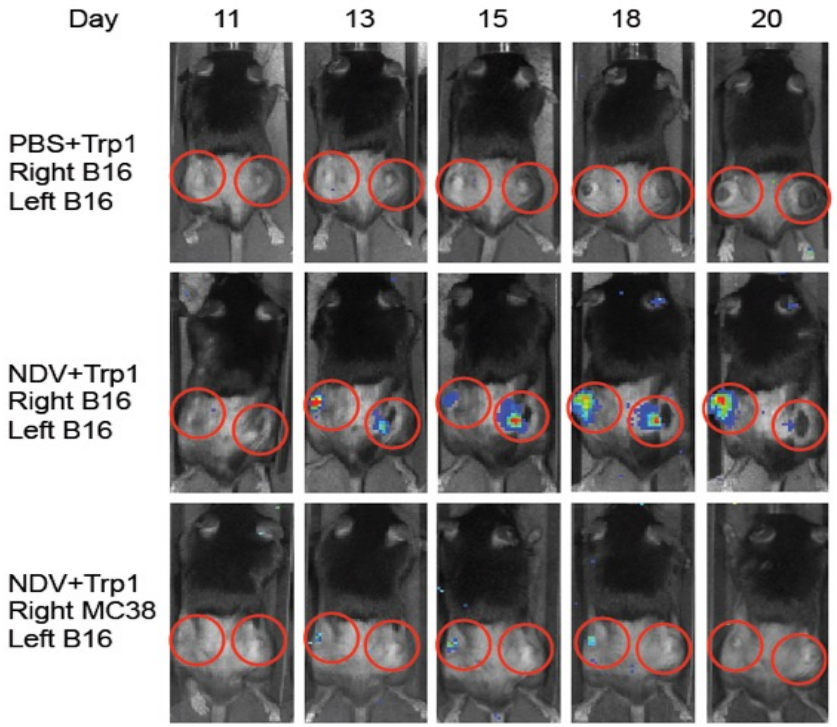
Right MC38 tumor



Zamarin D, Wolchok JD, Allison JP. *Sci. Transl. Med.* 2014 5:226ra

Infection of a tumor sharing antigens with distant tumors is required for priming of T cells specific for distant tumors





Clinical perspectives on viral immunotherapy

Padmanee Sharma, MD, PhD

Padmanee Sharma, MD, PhD

MD Anderson Cancer Center

Dr. Padmanee Sharma is an immunologist and oncologist whose research work is focused on investigating mechanisms and pathways within the immune system that facilitate tumor rejection or elicit resistance to immune checkpoint therapy. She is a Professor in the departments of Genitourinary Medical Oncology and Immunology, Associate VP of Immunobiology and the T.C. and Jeanette D. Hsu Endowed Chair in Cell Biology at MD Anderson Cancer Center. She is also the inaugural Scientific Director for the Immunotherapy Platform and the Director of Scientific Programs for the James P. Allison Institute at MD Anderson Cancer Center. She's written and conducted multiple innovative immunotherapy clinical trials, with emphasis on obtaining patients' tumor samples for in-depth laboratory studies, including the first neoadjuvant trial with immune checkpoint therapy and first clinical trial with immune checkpoint therapy for patients with bladder cancer. Her studies have identified novel resistance mechanisms to immune checkpoint therapy, including loss of interferon (IFN) signaling, $VISTA^{+}$ immunosuppressive cells, increased EZH2 expression in T cells, TGF-β signaling in bone metastases, and $CD73^{+}$ myeloid cells in GBM. These data have led to initiation of new research studies focused on developing rational combination immunotherapy strategies for the treatment of cancer patients. As a result of her outstanding contributions to the field of cancer immunotherapy, Dr. Sharma was selected as a member of the American Society for Clinical Investigation (ASCI) as well as awarded the Emil Frei III Award for Excellence in Translational Research in 2016, the Coley Award for Distinguished Research for Tumor Immunology in 2018, the Women in Science with Excellence (WISE) award in 2020, the Heath Memorial Award in 2021 and the Randall Prize for Excellence in Cancer Research in 2021.

Clinical perspectives on viral immunotherapy

Padmanee Sharma, MD, PhD

CAN-2409 in non-small cell lung cancer

Charu Aggarwal, MD, MPH

Daniel H. Sterman, MD

Roy Herbst, MD, PhD

CANDEL THERAPEUTICS

Charu Aggarwal, MD, MPH
Perelman School of Medicine at UPenn

Dr. Charu Aggarwal is the Leslye Heisler Associate Professor of Medicine in the Hematology-Oncology Division at the University of Pennsylvania's Perelman School of Medicine. She is also an active member of the Abramson Cancer Center where she serves as Physician Leader for the clinical research program for Airways Malignancies. Dr. Aggarwal specializes in the management of patients with lung and head and neck cancer, with a specific and clinical research focus on the development of novel immunotherapeutic approaches, and the discovery and application of biomarkers to guide therapy and monitor treatment. She is a co-principal investigator for Candel's phase 2 clinical trial of CAN-2409 followed by valacyclovir in combination with standard of care immune checkpoint inhibitors in patients living with late-stage NSCLC.

Daniel H. Sterman, MD
NYU Langone Health

Dr. Daniel Sterman is the Thomas and Suzanne Murphy Professor of Pulmonary and Critical Care Medicine in the Departments of Medicine and Cardiothoracic Surgery at the New York University Grossman School of Medicine, Director of the Division of Pulmonary, Critical Care, and Sleep Medicine, and Director of the Multidisciplinary Pulmonary Oncology Program at NYU Langone Health in New York City. For more than two decades, Dr. Sterman has focused on the translation of laboratory discoveries from the bench to the bedside: conducting multiple human clinical trials of gene therapy and vaccine therapy for lung cancer, mesothelioma, and other pleural malignancies. Dr. Sterman obtained his MD from Weill Cornell Medical College of Cornell University. He is a co-principal investigator for Candel's phase 2 clinical trial of CAN-2409 followed by valacyclovir in combination with standard of care immune checkpoint inhibitors in patients living with late-stage NSCLC.

Roy Herbst, MD, PhD
Yale Cancer Center

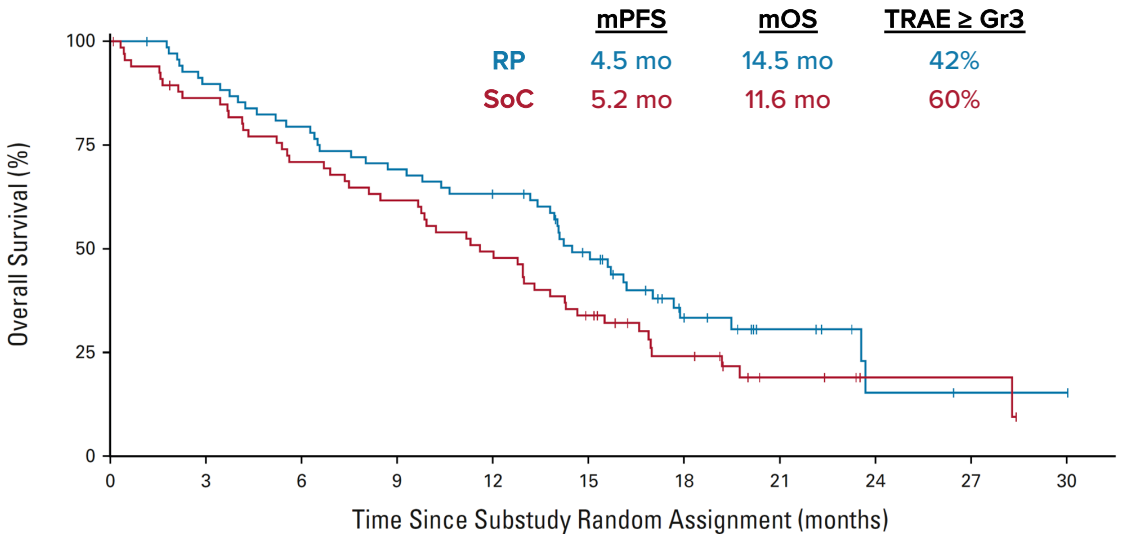
Dr. Roy Herbst is the Ensign Professor of Medicine (Medical Oncology) and Professor of Pharmacology; Director, Center for Thoracic Cancers; Deputy Director, Clinical Affairs; Assistant Dean for Translational Research, Office of the Dean, School of Medicine; Chief of Medical Oncology, Yale Cancer Center and Smilow Cancer Hospital; and Associate Cancer Center Director, Translational Science. Dr. Herbst is best known for his work in developmental therapeutics and the personalized therapy of non-small cell lung cancer, in particular the process of linking genetic abnormalities of cancer cells to novel therapies. His work has led to the approval of several therapies such as gefitinib, cetuximab, bevacizumab, and axitinib. Dr. Herbst authored a high-profile review of the 20-year progress in lung cancer as well as authored or co-authored more than 350 publications including peer-reviewed journal articles, abstract, and book chapters. Since April 2021, he has been on Candel's Research Advisory Board.

ICIs have transformed treatment of advanced NSCLC, but most patients still progress and long-term survival is low

- After progression, 2L SoC is chemotherapy, associated with poor prognosis and significant toxicity
- Recent Ph2 and Ph3 trials have explored alternative approaches post ICI progression

Ph2 ramucirumab + pembrolizumab (RP) vs chemotherapy (SoC)

Lung-MAP substudy



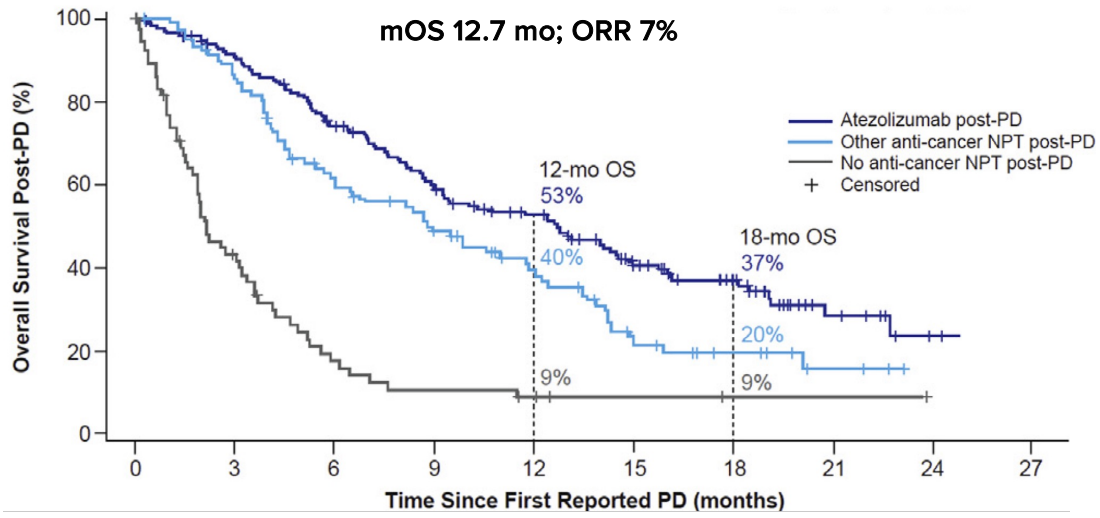
Reckamp K. et al. J Clin Onc 2022;40:2295-2306

Ph3 evaluating treatment beyond progression with atezolizumab

OAK study

168 (of 332) patients treated with atezolizumab were treated beyond progression (TBP)

mOS 12.7 mo; ORR 7%



Gandara D. et al. J Thorac Onc 2018;13:1906-1918

ICI: immune checkpoint inhibitor, mPFS: median PFS, mOS: median overall survival; ORR: overall response rate, TRAE: treatment-related adverse event, SoC: standard of care

Phase 2 clinical trial of CAN-2409 in advanced NSCLC (LuTK02)

Enrolls spectrum of disease to support signal generation and refinement of the patient population

Stage III/IV non-resectable NSCLC with suboptimal response to first-line ICI

CAN-2409 and valacyclovir (2 courses)

with standard of care anti-PD-1/PD-L1 +/- chemotherapy

→ **Cohort 1** Stable Disease (>18 wks ICI)

→ **Cohort 2** Progressive Disease (>18 wks ICI)

→ **Cohort 3*** Refractory Disease (>9 wks ICI)

**Cohort 3 closed as of Jun 2022*

Primary Endpoints
- Response by RECIST criteria
- Safety

Secondary Endpoints
- Overall survival
- Progression free survival
- Quality of life
- Immunological biomarkers
- Response by iRECIST and itRECIST (Exploratory)

NCT04495153

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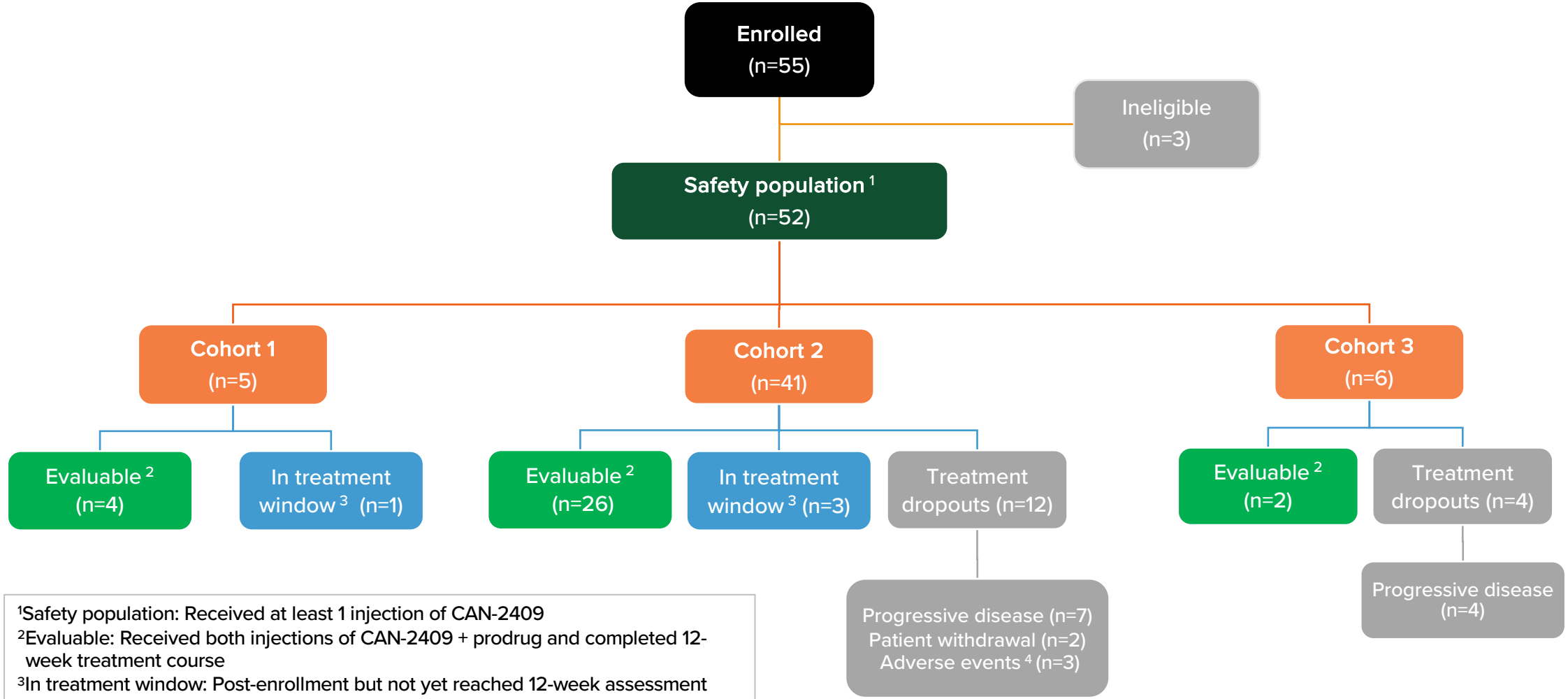
LuTK02 Consort diagram



[1]Safety population: Received at least 1 injection of CAN-2409
[2]Evaluable: Received both injections of CAN-2409 + prodrug and completed 12-week treatment course
[3]In treatment window: Post-enrollment but not yet reached 12-week assessment
[4]Adverse events: Empyema grade 3 possibly related to study drug, pneumonia grade 3 and bullous dermatitis grade 3 unrelated to study drug

Cohort 3 closed as of Jun 2022

As of cutoff date
21 Oct 2022

Patient demographics and characteristics

52 patients who received at least 1 dose of CAN-2409 comprise the safety population

Age	Years
Median (Range)	68.5 (43-88)
Sex	**n (%)**
Female	21 (40)
Male	31 (60)
Race	**n (%)**
Black/African American	7 (13)
Asian	1 (2)
White	41 (79)
Unknown	3 (6)
Ethnicity	**n (%)**
Not Hispanic or Latino	48 (92)
Not Reported	4 (8)
PD-L1 Expression	**n (%)**
<1%	22 (42)
1-49%	15 (29)
≥50%	10 (19)
Unknown	5 (10)

Baseline ECOG	n (%)
0 or 1	21 (40); 31 (60)
Smoking History	**n (%)**
Former or current	41 (79); 7 (13)
Tumor Stage	**n (%)**
Stage III	8 (15)
Stage IV	44 (85)
Histology	**n (%)**
Non-Squamous	37 (71)
Squamous	15 (29)
ICI at study entry	**n (%)**
Durvalumab	2 (4)
Nivolumab	5 (10)
Nivolumab/Ipilimumab	1 (2)
Pembrolizumab	44 (85)
Chemotherapy at study entry	**n (%)**
Pemetrexed	17 (33)
None	35 (67)

CANDEL THERAPEUTICS

As of cutoff date
21 Oct 2022

CAN-2409 treatment is generally well tolerated

Treatment-related adverse events reported in ≥5% of recipients

SOC/Adverse Event (≥5%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total (n=52)
Gastrointestinal disorders					
Constipation	2 (4)	1 (2)			3 (6)
Nausea	7 (13)				7 (13)
Vomiting	3 (6)				3 (6)
General disorders and administration site conditions					
Chills	3 (6)				3 (6)
Fatigue	11 (21)	3 (6)			14 (27)
Pyrexia	7 (13)		1 (2)		8 (15)
Investigations					
Alanine aminotransferase increased	3 (6)				3 (6)
Aspartate aminotransferase increased	3 (6)				3 (6)
Blood creatinine increased	5 (12)	1 (2)			6 (12)
Musculoskeletal and connective tissue disorders					
Muscular weakness	2 (4)	1 (2)			3 (6)
Respiratory, thoracic and mediastinal disorders					
Cough	2 (4)	1 (2)			3 (6)
Dyspnea	2 (4)	3 (6)			5 (10)

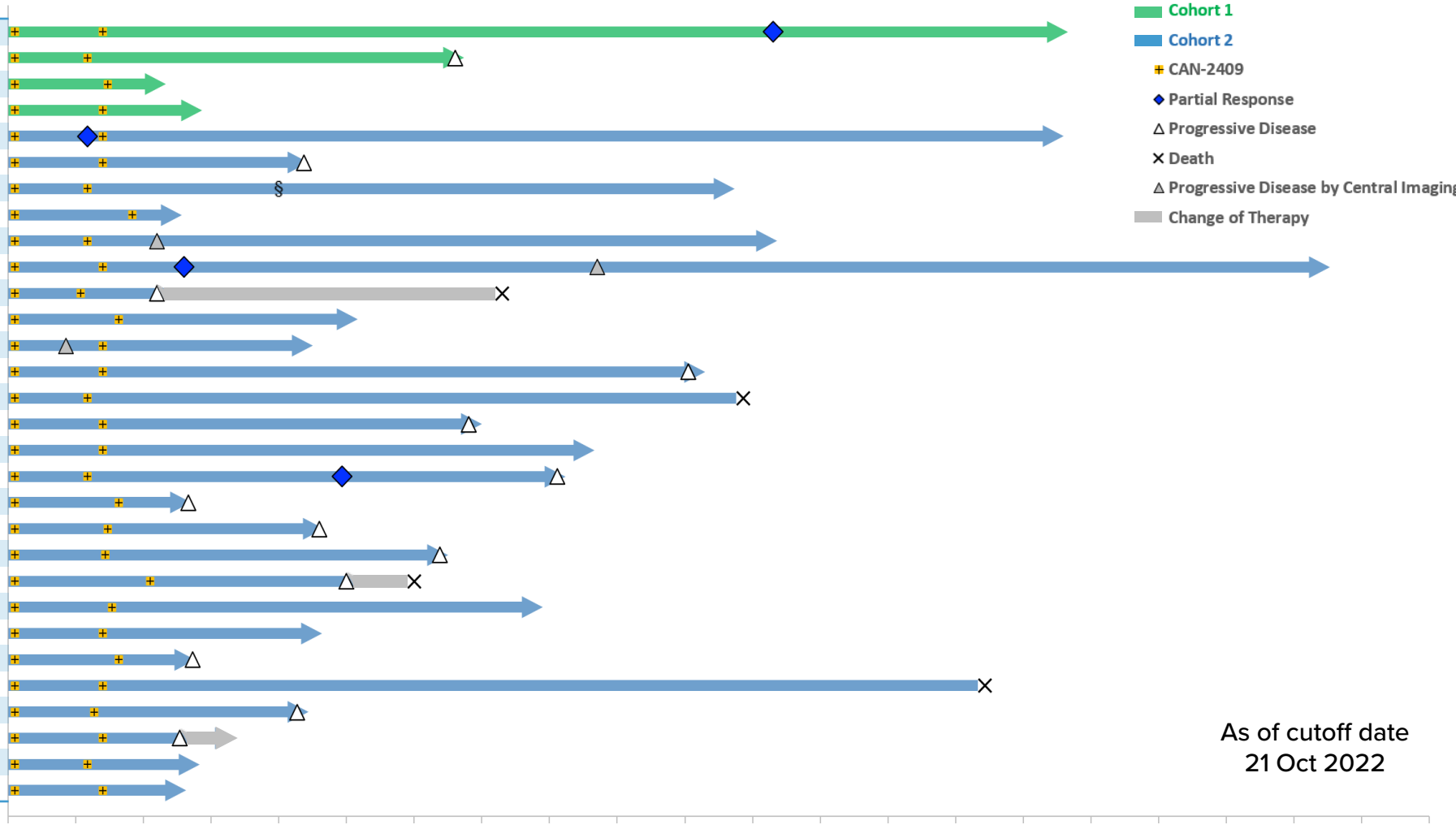
- Majority of treatment-related AEs (TRAEs) were mild
- No DLTs or treatment-related AEs ≥Gr4 reported
- Only five Gr3 TRAEs were reported: single occurrences of pyrexia, empyema, lymphocyte count decreased, platelet count decreased, and pneumonitis
- No serious injection-related complications

As of cutoff date
21 Oct 2022

CAN-2409 is associated with durable disease stabilization

Swimmer plot of evaluable patients in Cohorts 1 and 2 (n=30)

Subject ID	PD-L1	ICI Regimen*	Time on ICI (mo)**
PA-003	< 1%	Pembro/pemetrex	15.5
PA-007	< 1%	Pembro/pemetrex	5.0
UH-001	< 1%	Pembro	6.7
VB-007	< 1%	Pembro	7.8
MU-002	N/A	Pembro	16.6
MU-004	< 1%	Pembro	5.2
NY-001	1-49%	Pembro	7.0
NY-003	1-49%	Nivo	12.1
NY-004	≥ 50%	Pembro	11.7
NY-007	< 1%	Nivo	16.2
NY-008	1-49%	Pembro	10.3
NY-013	1-49%	Durva	13.3
NY-015	≥ 50%	Pembro	6.3
PA-005	< 1%	Pembro/pemetrex	19.1
PA-006	< 1%	Pembro/pemetrex	8.2
PA-008	< 1%	Pembro	11.1
PA-010	< 1%	Pembro/pemetrex	11.8
PA-011	≥50%	Pembro	13.2
PA-013	1-49%	Pembro/pemetrex	45.2
RV-001	1-49%	Nivo	38.4
UC-001	1-49%	Pembro	13.0
UC-002	1-49%	Pembro	16.6
VB-003	1-49%	Pembro	10.8
VB-005	1-49%	Pembro/pemetrex	12.1
VB-009	< 1%	Durva	12.1
VC-001	< 1%	Pembro/pemetrex	5.4
VC-004	1-49%	Pembro/pemetrex	5.4
VC-006	≥50%	Pembro	15.1
VC-007	1-49%	Pembro/pemetrex	5.7
VC-008	<1%	Pembro/pemetrex	6.4

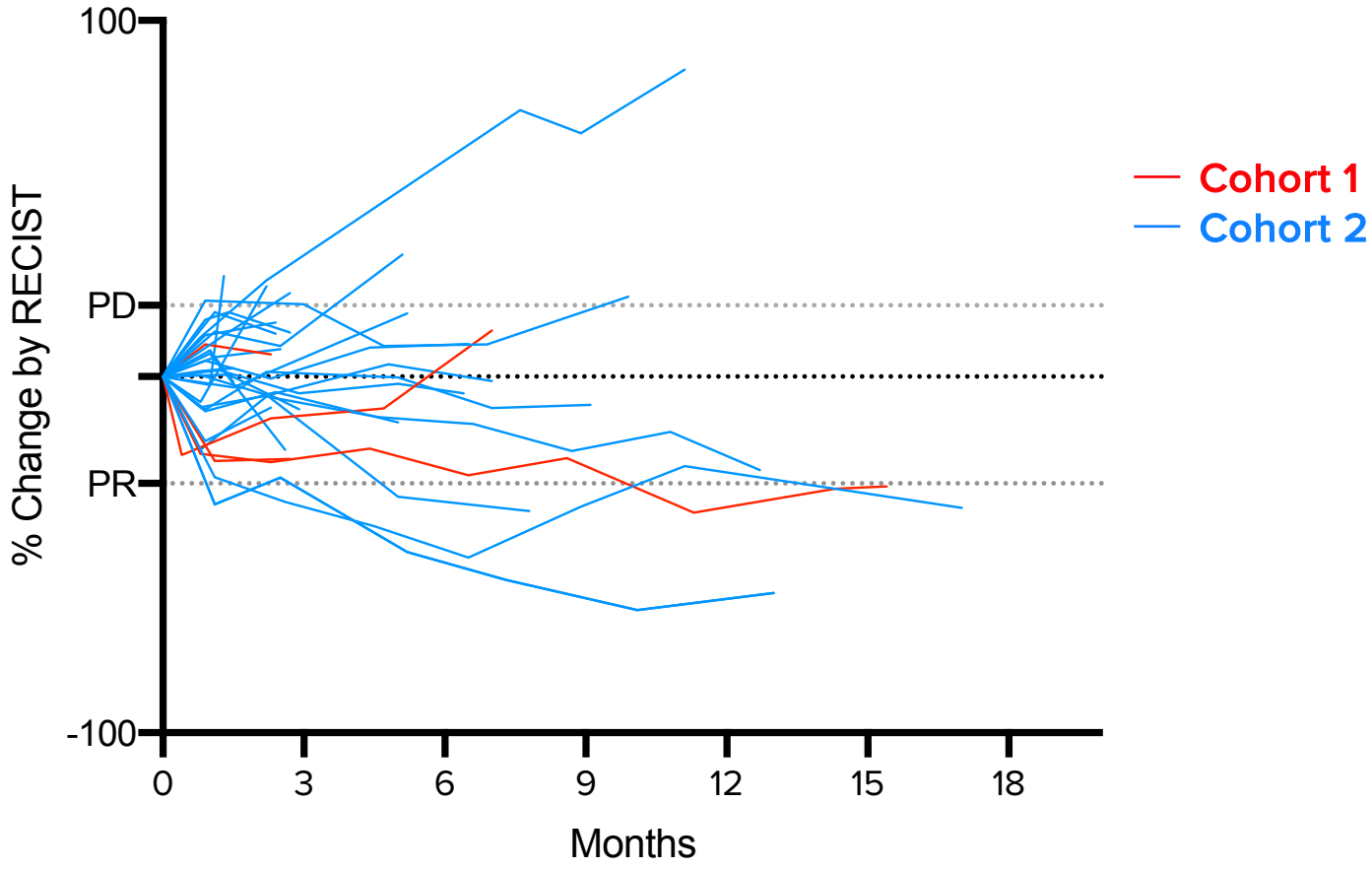


As of cutoff date
21 Oct 2022

* ICI Regimen: At enrollment to study
** Time on ICI: Initiation of ICI before enrollment to first CAN-2409 injection
§ Irradiation included target lesion, no longer RECIST evaluable

CAN-2409 is associated with durable disease stabilization

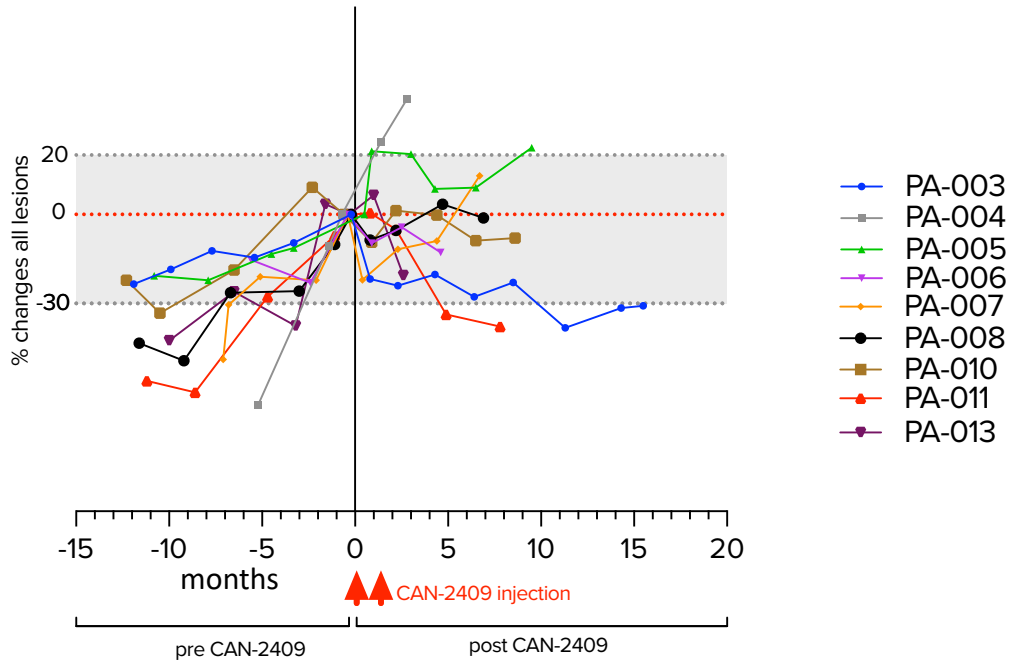
Spider plot of evaluable patients in Cohorts 1 and 2 (n=30)



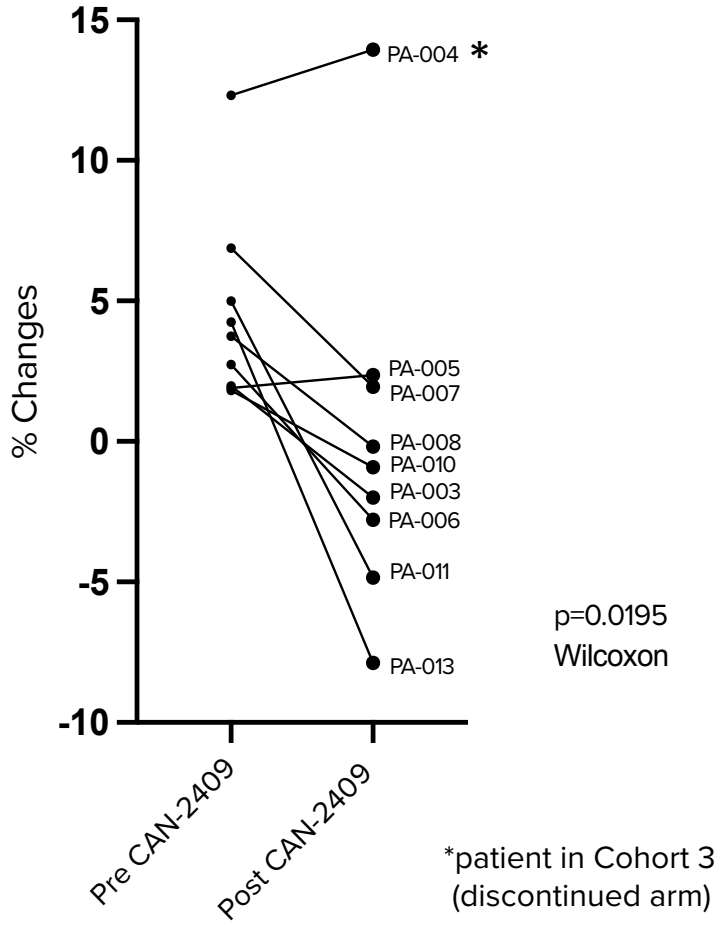
As of cutoff date
21 Oct 2022

CAN-2409 favorably changes the trajectory of tumor growth

Tumor trajectories pre-study and following CAN-2409 administration



Monthly tumor growth rate



*patient in Cohort 3 (discontinued arm)

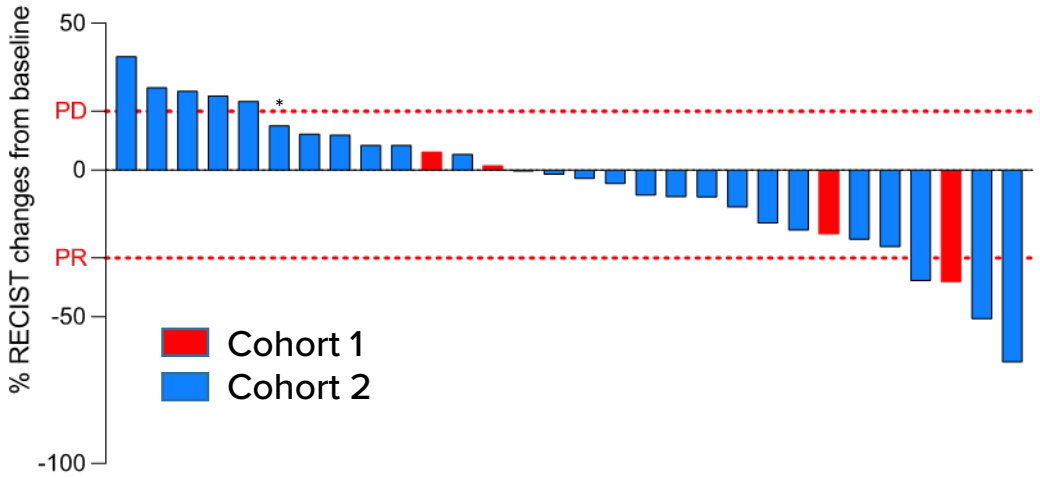
- Serial scans available for up to one year prior to treatment with CAN-2409 in 9 patients
- Monthly tumor growth rate calculated pre-study (during prior therapy of ICI +/- chemo) and on-study, based on total sum of diameters assuming linear growth rate

As of cutoff date 21 Oct 2022

Evidence that CAN-2409 improves disease control

Most patients entering trial with progressive disease achieved disease control

Waterfall plot



Summary of efficacy

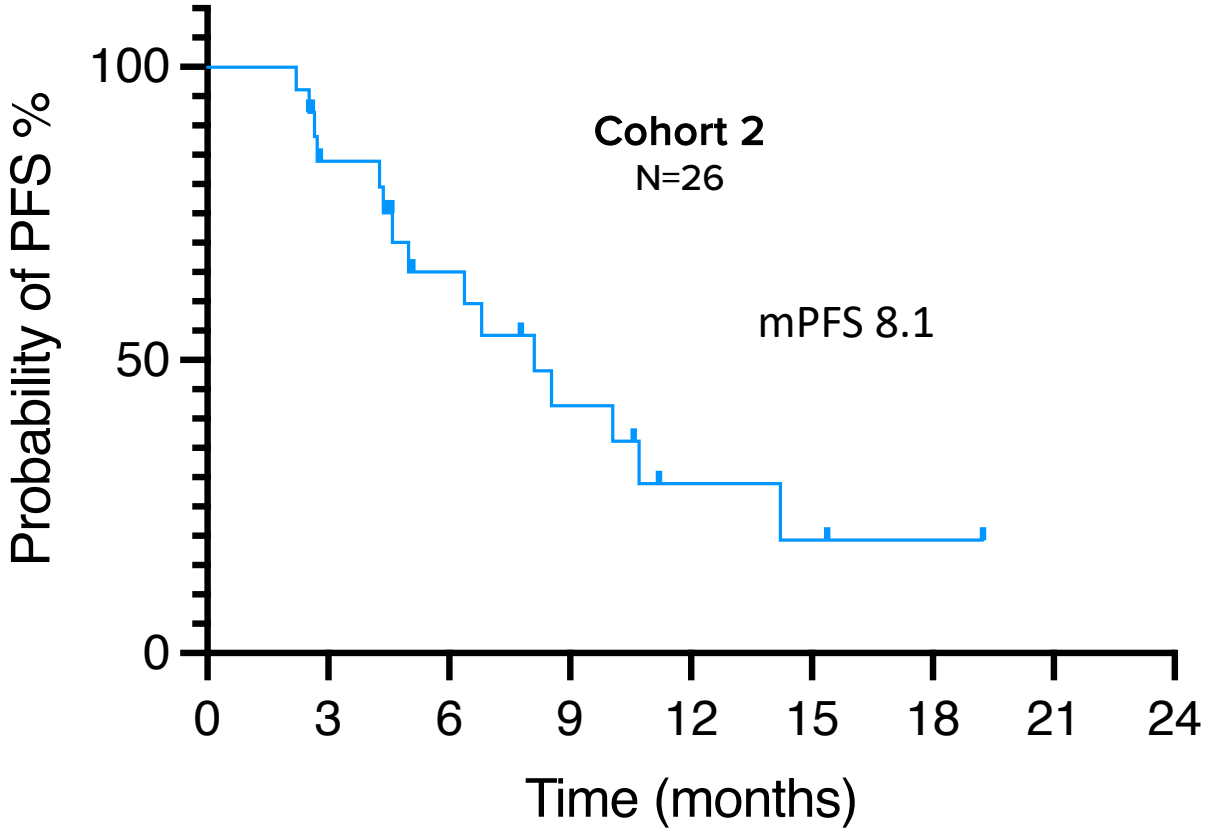
Cohort/ Pre-trial status	N	PR	SD	PD	ORR or DCR	DoR for PR (mo)	SD duration (mo)
1 SD at study entry	4	1	3	0	ORR 25% DCR N/A	4.1+	1.4+ to 6.2
2 PD at study entry	26	3	17	6	ORR 12% DCR 77%	2.8 to 14.2+	1.4+ to 11.6

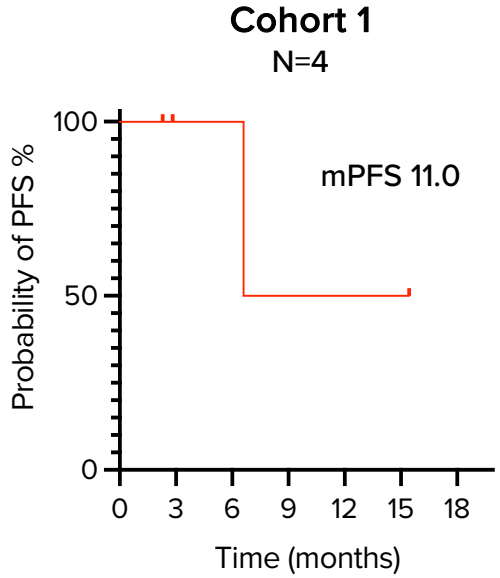
Data shown based on blinded independent central review (BICR) of radiographic data per RECIST 1.1 in evaluable patients
Evaluable patients are those receiving 2 courses of CAN-2409 + prodrug and completed 12-wk treatment window
*new lesion
+ indicates response is ongoing
ORR: overall response rate, DCR: disease control rate, DoR: duration of response, PR: partial response, SD: stable disease, PD: progressive disease

CANDEL THERAPEUTICS

As of cutoff date
21 Oct 2022

Slowing tumor growth may translate into PFS benefit



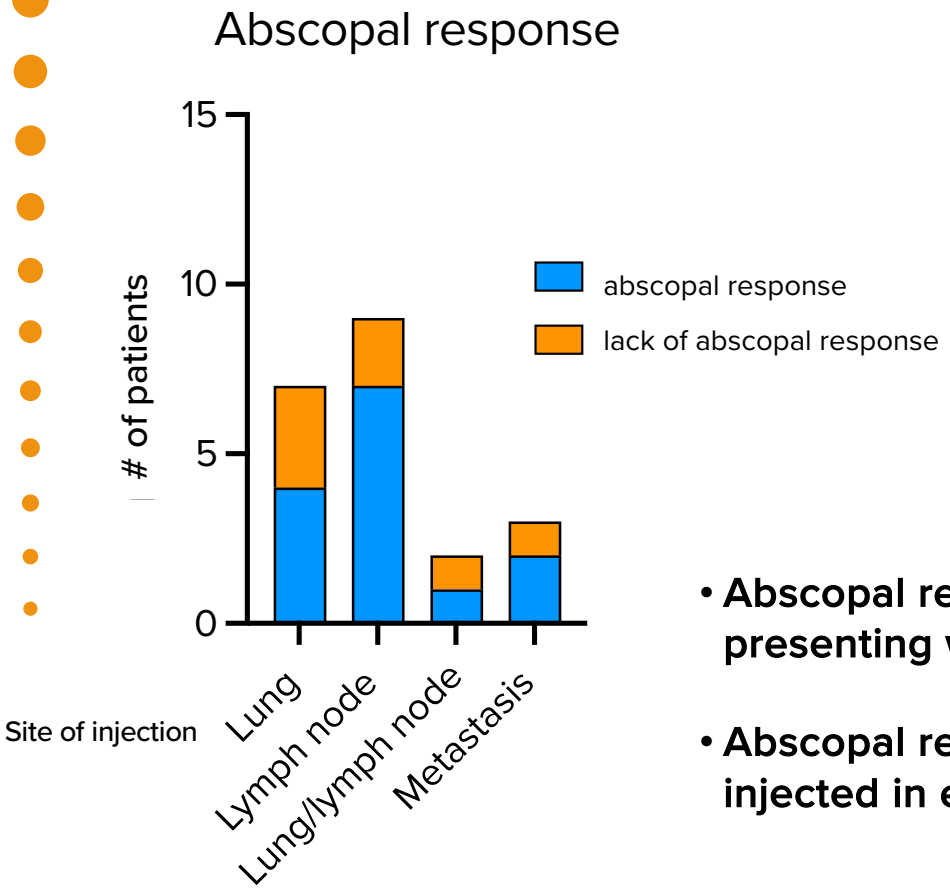


- Progression free survival (PFS) in evaluable patients receiving both courses of CAN-2409 + prodrug and completed 12-wk treatment window based on progression per Investigator assessment
- Median follow up 11.2 mo for Cohort 2
- 47% (14/30) patients censored (ongoing SD, PR)

As of cutoff date
21 Oct 2022

Local injection induces systemic anti-tumor activity

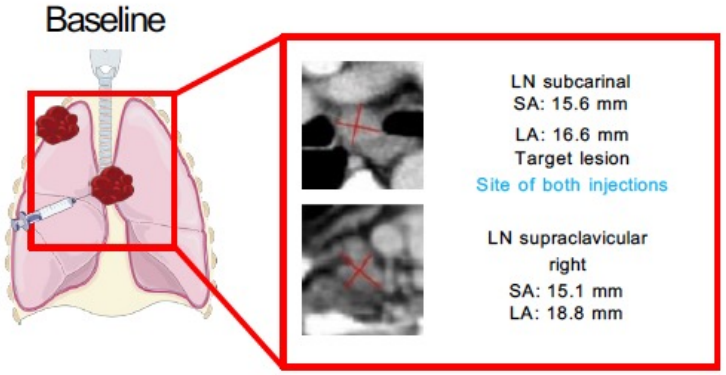
Regression of uninjected lesions

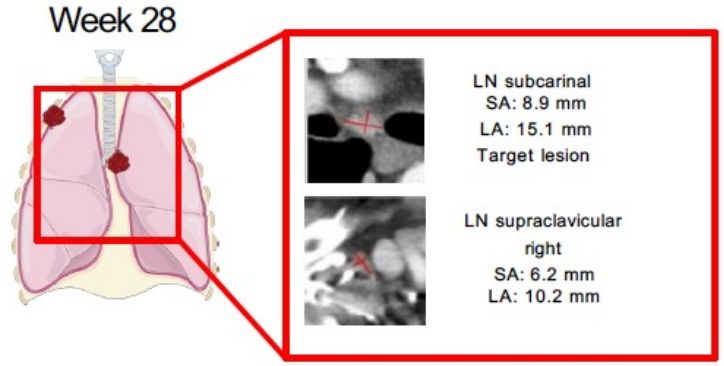


NY-007: Patient with partial response and evidence of abscopal effect

NY-007 (Cohort 2)
- 74M, Stage IV Nonsq
- PD-L1 <1%
- Diagnosed Feb'19
- Platinum-based chemo Feb–Jul'19
- Nivolumab monotherapy Sep'19 through trial
- PR by local and central read

1st injection (baseline) and 2nd injection (week 6)





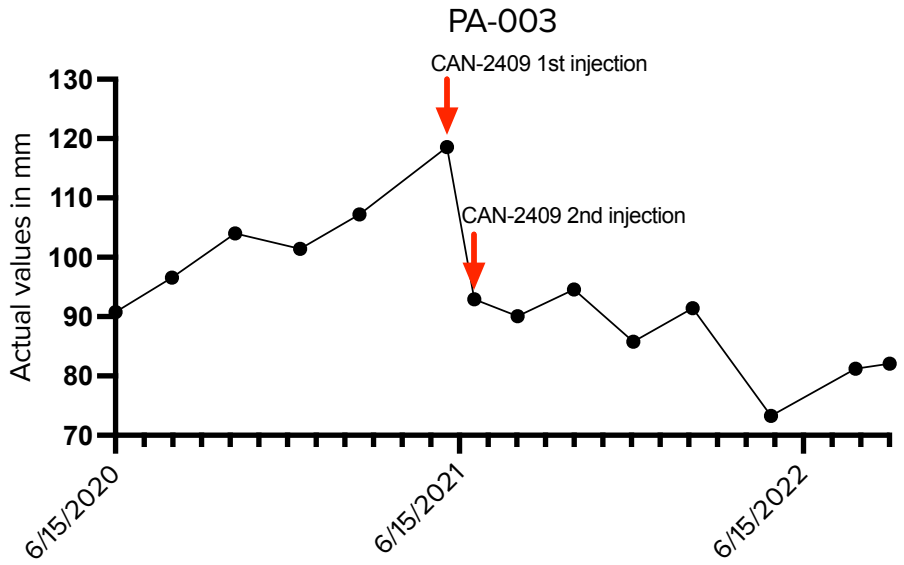
- **Abscopal response in 14/21 patients (67%) presenting with multiple lesions***
- **Abscopal response was observed in patients injected in either lymph nodes and/or lung lesions**

* Decrease of at least 5% observed in at least one noninjected lesion

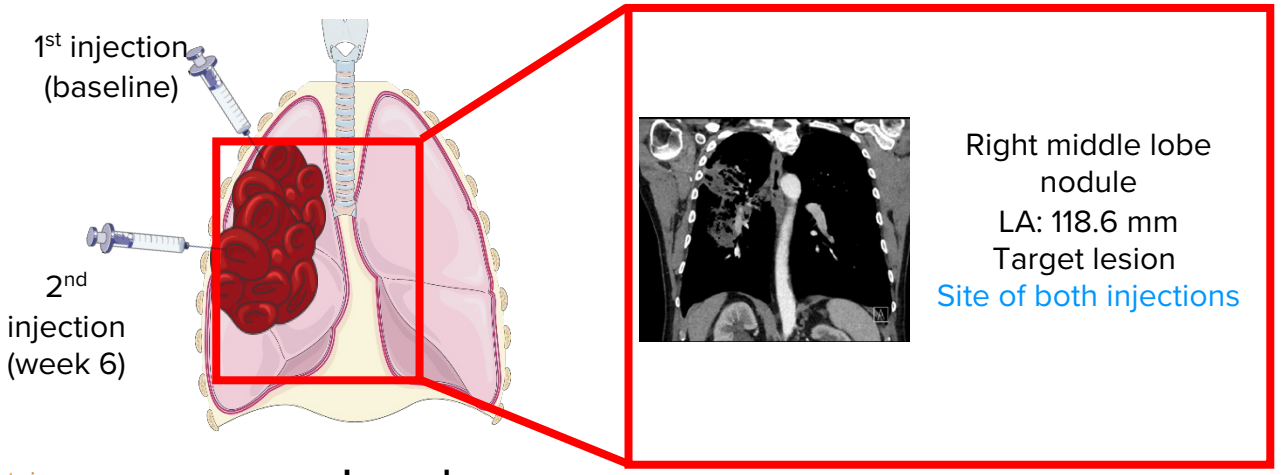
Partial response in extended lung mass with durable post-treatment tumor regression (> 1 yr)

PA-003 (Cohort 1)

- 73 yo M, Stage III Nonsq
- PD-L1<1%
- Diagnosed Jan'20
- Started pembro + carbo + pemetrexed Feb'20
- Pembro + pemetrexed Jun'20 through trial

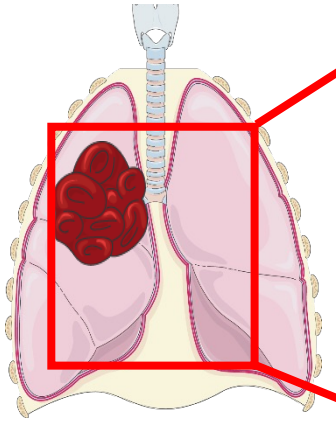


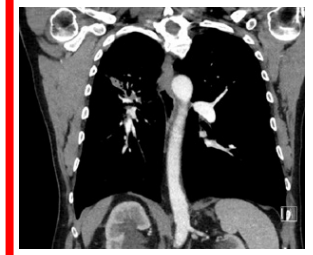
Baseline



Right middle lobe nodule
LA: 118.6 mm
Target lesion
Site of both injections

Week 28





Right middle lobe nodule
LA: 85.8 mm
Target lesion

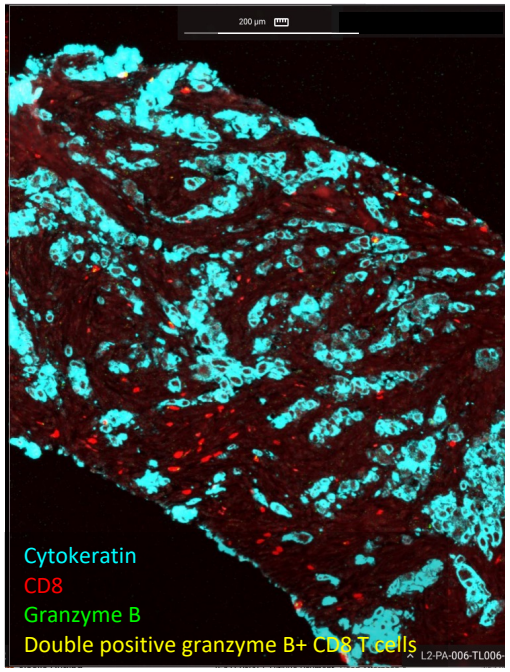
Legend
RECIST target lesions (red)

LN: lymph node, LA: long axis, SA: short axis

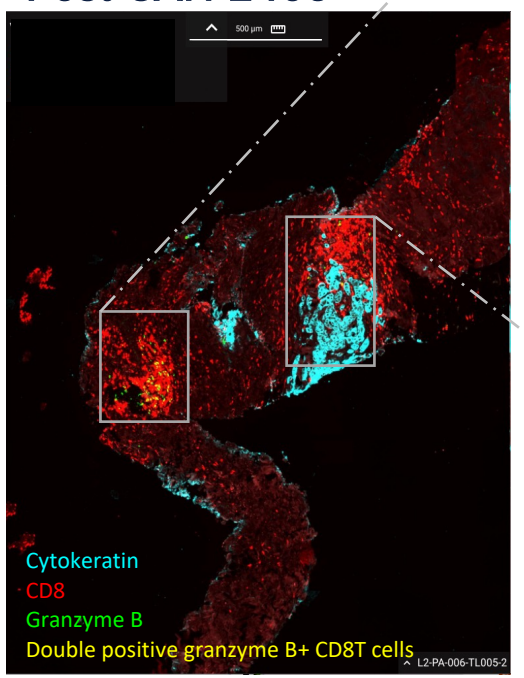
CAN-2409 induces expansion of CD8+ granzyme B+ T cells in the tumor microenvironment

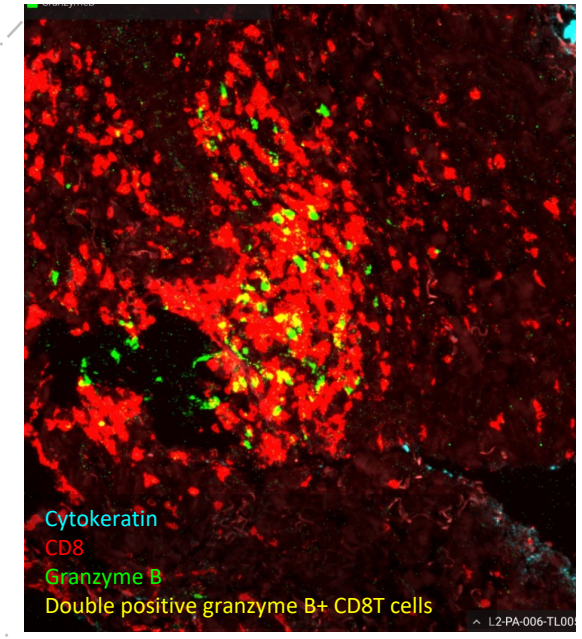
PA006

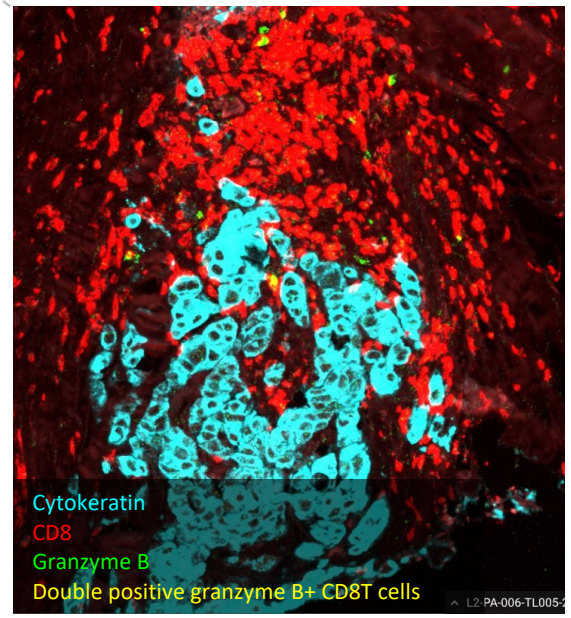
Pre CAN-2409



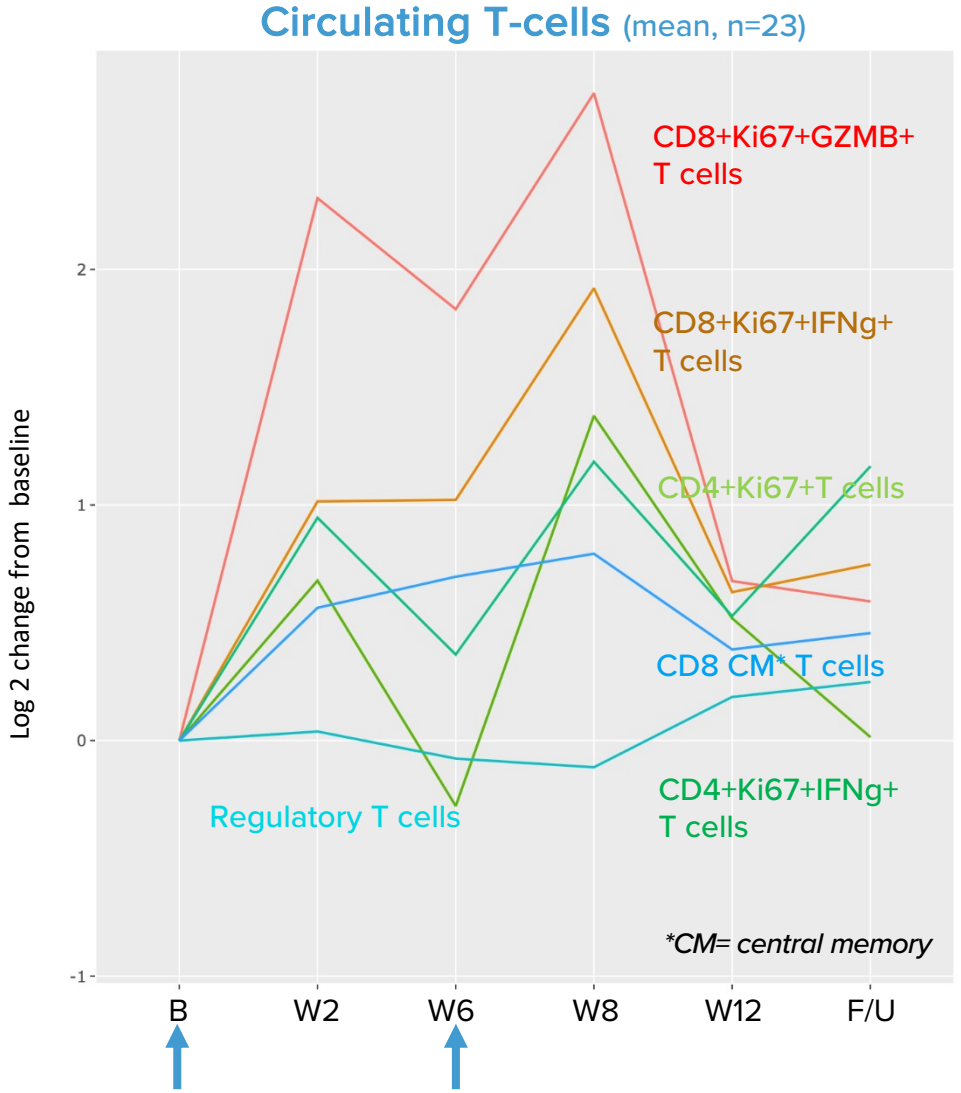
Post CAN-2409

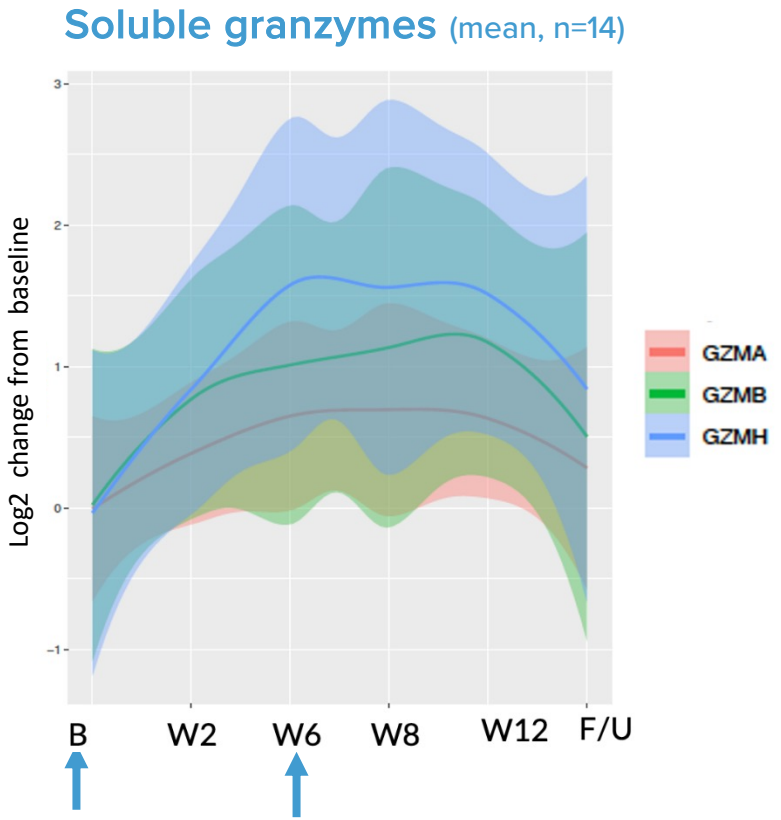






CAN-2409 significantly increases frequency of circulating cytotoxic T cells and levels of soluble granzymes





As of cutoff date 21 Oct 2022

p-values range from 25×10^{-3} to 626×10^{-6}

B baseline
F/U follow-up

Bronchoscopic delivery of CAN-2409 is a simple extension of existing care for NSCLC patients and is well tolerated

Therapeutic delivery tool based on extensive experience with bronchoscopic biopsy, a routine outpatient procedure (15 min, outpatient setting)

Transbronchial needle injection (TBNI) presents similar complication rate as biopsy (extremely rare)

Latest generation of TBNI includes ultrasound-guided transbronchial injection of lymph nodes and robotic bronchoscopy (already in use in LuTK02)

Majority of lung and thoracic lymph node lesions are accessible for outpatient bronchoscopic injection

DeMaio A, Sterman D. Eur Respir Rev 2020; 29: 200028

Promising picture of safety, clinical activity and immune changes

Favorable safety/tolerability profile in comparison to SoC 2L options

- Only two administrations with relatively simple procedure; most TRAEs were Gr1/2

Consistent induction of local and systemic cytotoxic T cell response

- Increased infiltration of CD8+ T cells in the tumor microenvironment, systemic expansion of effector T cells and increase in soluble granzyme B in peripheral blood

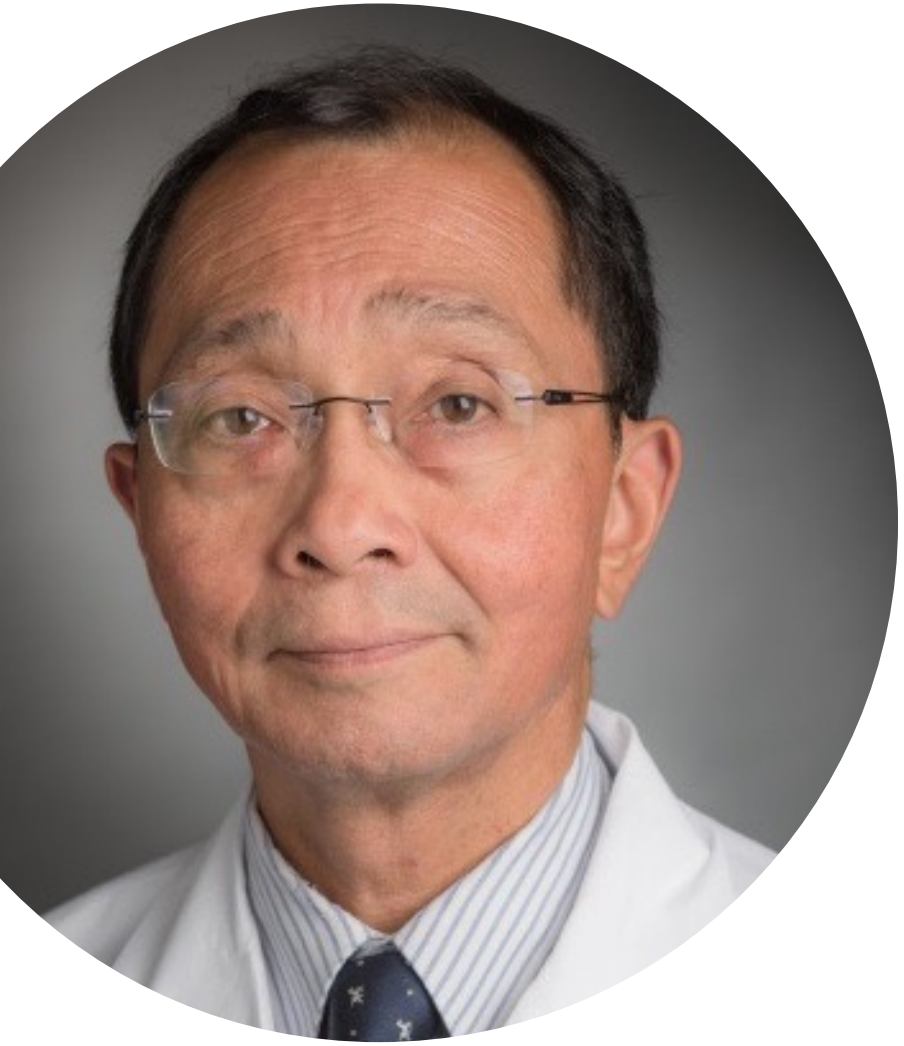
Robust evidence of local and systemic anti-tumor activity

- CAN-2409 favorably changed the trajectory of tumor progression
- Decrease in tumor size of RECIST target lesions in most patients
- Reduction in uninjected tumor lesions: 14/21 patients (67%)
- ORR of 13% (4/30) across cohorts 1 and 2
- DCR of 77% (20/26) in patients entering trial with progressing disease (cohort 2)
- Sustained and ongoing clinical responses of longer than 1 year
- Durable disease stabilization translating into promising preliminary PFS

CAN-2409 + nivolumab in high-grade glioma

Patrick Y. Wen, MD

CANDEL THERAPEUTICS



Patrick Y. Wen, MD

Dana-Farber Cancer Institute & Harvard Medical School

Dr. Patrick Y. Wen is a Professor of Neurology at Harvard Medical School, and Director of the Center for Neuro-Oncology at Dana-Farber Cancer Institute in Boston, MA. Dr. Wen's research focuses on development of new novel therapies for brain tumors, especially targeted molecular agents. His other clinical interests include neurologic complications of cancer. Dr. Wen graduated from the Medical College of St. Bartholomew's Hospital, University of London, completed his internal medicine training at the University of London postgraduate hospitals and his neurology residency in the Harvard-Longwood Neurology Training Program. Dr. Wen is a principal investigator on Candel's open label phase 1 clinical trial of CAN-2409 plus valacyclovir in combination with nivolumab and standard of care in newly diagnosed high-grade glioma.

Phase 1 clinical trial of CAN-2409 in combination with nivolumab and standard of care in newly diagnosed high-grade glioma

R&D Day
December 6, 2022

Data cutoff as of September 30, 2022

Immunosuppressive tumor microenvironment and negative prognostic factors determine poor prognosis in high-grade glioma patients

High-grade glioma tumor microenvironment is characterized by poor T cell infiltrate, enrichment in M2 suppressive macrophages and suppressive microglia

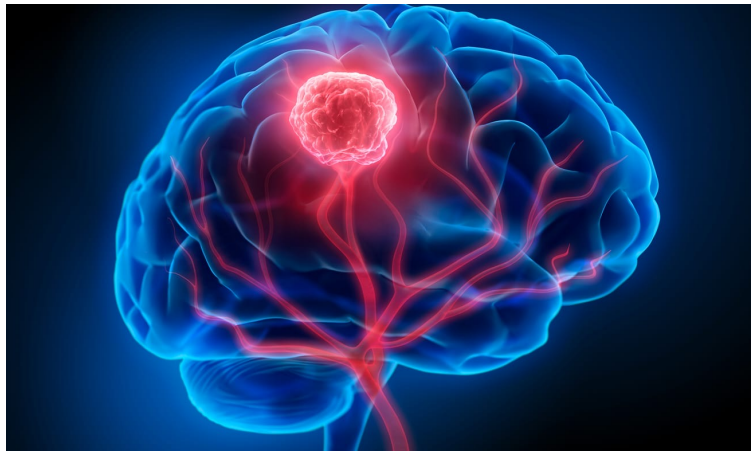
Median overall survival < 15 months

Radiation and temozolomide induce lymphopenia

Corticosteroids may impact immune response

Negative prognostic factors influencing survival:

Age, sex, MGMT* methylation status, IDH**, extent of tumor resection



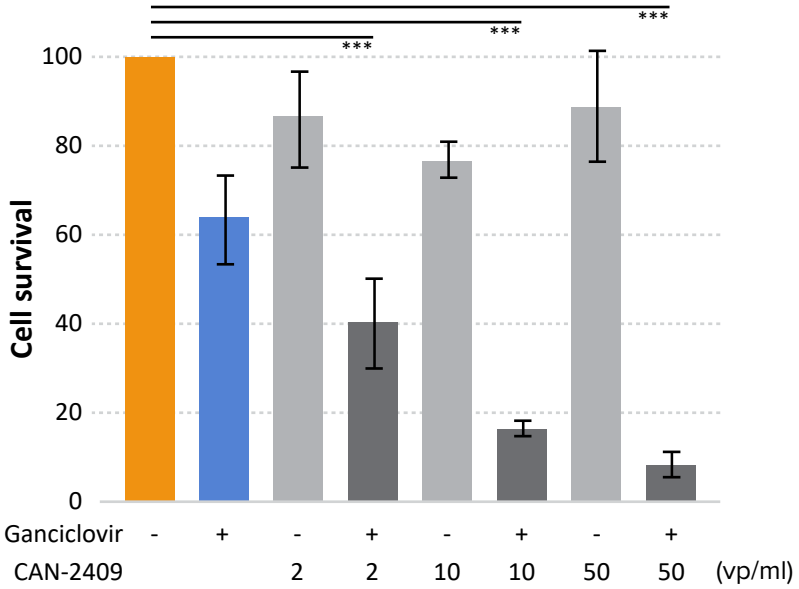
High grade glioma

**O6-methylguanine-DNA methyl-transferase (MGMT) gene promoter*
***Isocitrate dehydrogenase*

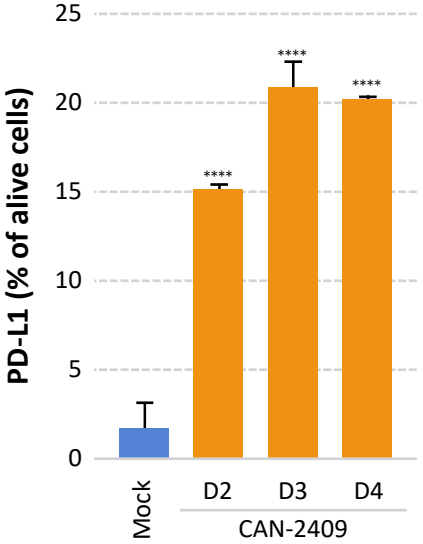
Weller M et al. Nat Rev Neurol 2017; 13:363-374
Grossman SA et al. Clin CA Res 2011; 17:5473-5480
Chongsathidkiet P et al Nat Med 2018; 24:1459-1468

Potential opportunity for combination therapy with immune checkpoint inhibitor: improved effect in mouse model of high-grade glioma

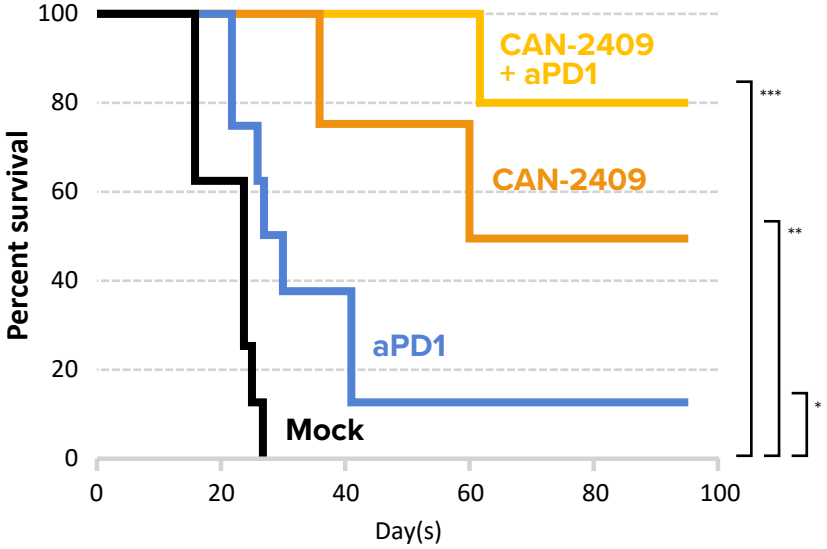
Induction of cell death



Induction of PD-L1 expression



Improved survival



Model: In vitro experiments with murine CT-2A-Luc HGG cells

***p ≤ 0.001, ****p ≤ 0.0001

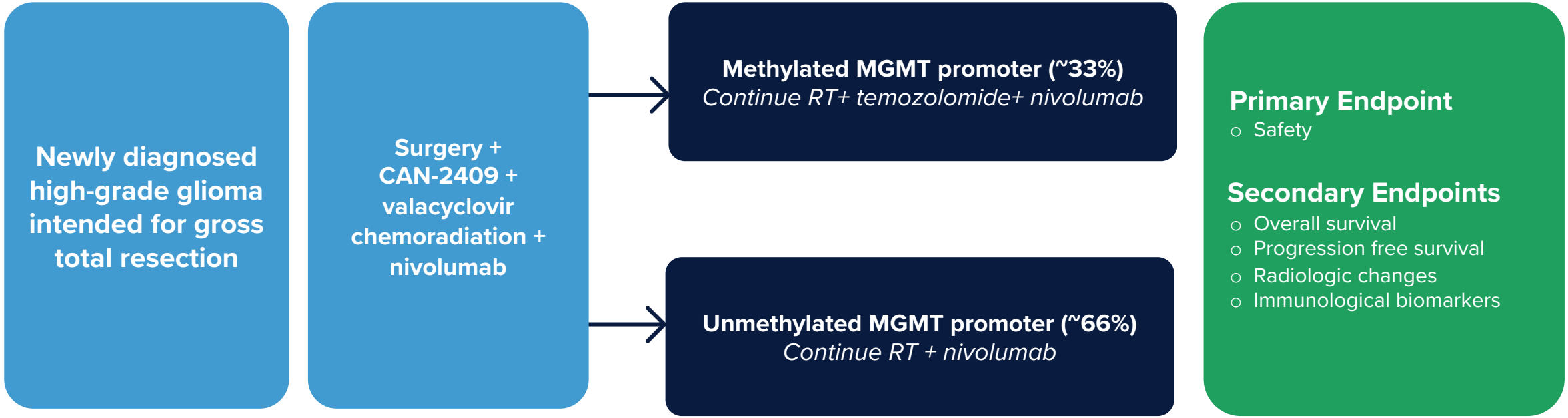
Model: Intracranial injection of murine CT-2A-Luc HGG cells in mice

N=26; ***p≤ 0.001, **p ≤ 0.01, *p≤ 0.05

Speranza MC et al. Neuro Oncol 2018; 20:225-235

Phase 1 clinical trial of CAN-2409 plus valacyclovir combined with nivolumab in high-grade glioma

A protocol of the Adult Brain Tumor Consortium (ABTC) in collaboration with Bristol-Myers Squibb (BMS) and Candel Therapeutics, Inc.



NCT03576612

Methodology for primary endpoint:
Evaluate safety of the combination of CAN-2409 +VCV + nivolumab +/- temozolomide (TMZ)
Enrolment in sets of 9 patients (~3 methylated and 6 unmethylated)
If DLT rate ≤33%, proceed with next set of 9 patients
Target ~12 methylated and ~24 unmethylated evaluable patients

Patient demographics safety population (41 patients)

Characteristic	N (%)
Age	
Median age (years)	62
Range	28-81
Sex	
Female	14(34)
Male	27(66)
Race	
White/Caucasian	34(83)
Black/African American	3(7)
American Indian or Alaska Native	1(2)
Asian	1(2)
Not reported	2(5)
Ethnicity	
Not Hispanic or Latino	38(93)
Hispanic or Latino	1(2)
Unknown	1(2)
Not reported	1(2)

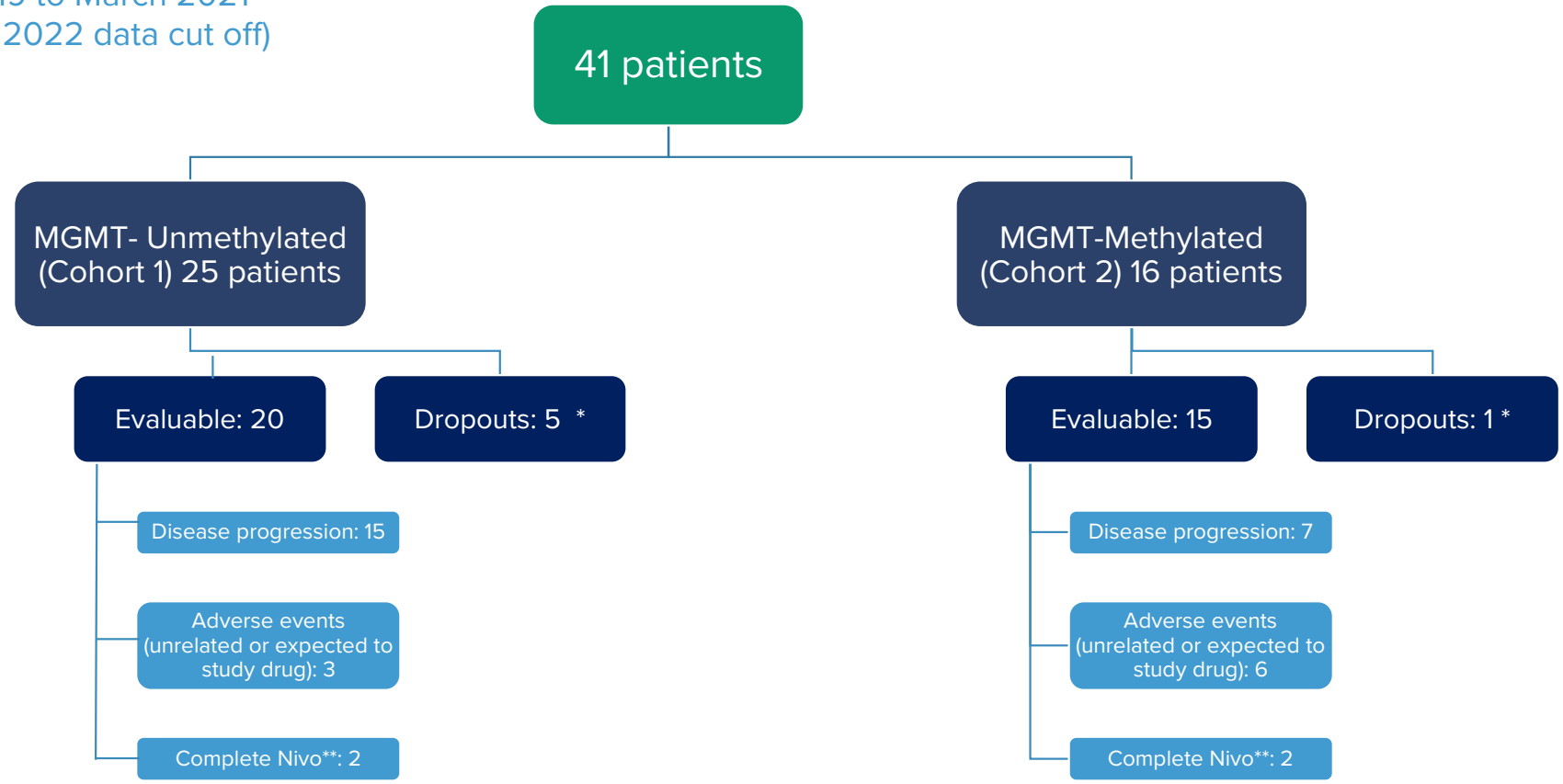
Characteristic	N (%)
KPS* (Baseline)	
Median KPS	90
Range	80-100
KPS (Day 15)	
Median KPS	80
Range	20-100
MGMT	
Methylated	16(39)
Unmethylated	25(61)
IDH**	
Wild type	39(95)
Mutant	2(5)
Histopathologic diagnosis	
Glioblastoma	40(98)
Diffuse astrocytoma	1(2)
Type of resection	
Gross total resection	30(73)
Subtotal resection	11(27)

*Karnofsky Performance Scale
**IDH Isocitrate dehydrogenase

As of cutoff date
30 Sep 2022

CONSORT diagram

Enrollment February 2019 to March 2021
9 patients alive (30 Sep 2022 data cut off)

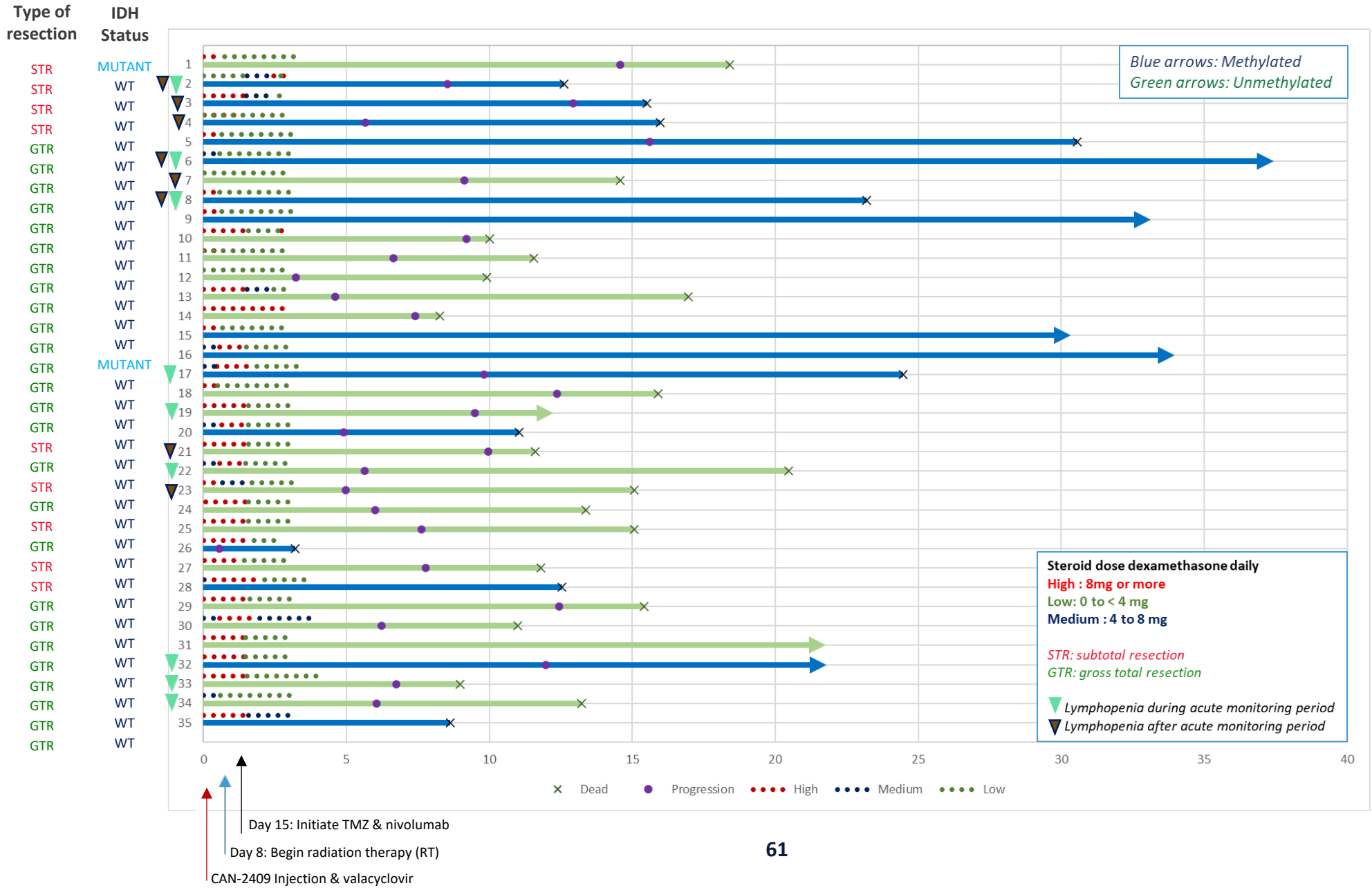


***Received 26 nivolumab infusions*

**Received less than 80% of any planned dose of treatment regimen for reasons unrelated to study treatment*

Evaluable : Patients who completed >80% of treatment during the acute monitoring period (2 weeks after the 4th dose of nivolumab).
Safety population: Any patient who received investigational agent.

Evaluable subject progress (35 patients)



As of cutoff date
30 Sep 2022

Safety profile of the combination of CAN-2409 plus valacyclovir and nivolumab in patients receiving surgery, radiation and TMZ

- No unexpected serious adverse events were observed
- Adverse events considered at least possibly related to CAN-2409, valacyclovir or nivolumab during acute monitoring period (0-71 days) are shown below

Most common adverse events occurring in >10% of patients

Adverse Event	CTC grade				Total=41
	1	2	3	4	N (%)
Fatigue	11 (27)	4 (10)	1 (2)	0	16 (39)
Nausea	9 (22)	1 (2)	2 (5)	0	12 (29)
ALT increased	9 (22)	0	1 (2)	0	10 (24)
Headache	6 (15)	0	2 (5)	0	8 (20)
Anemia	3 (7)	3 (7)	1 (2)	0	7 (17)
Fever	5 (12)	2 (5)	0	0	7 (17)
AST increased	7 (17)	0	0	0	7 (17)
Hyponatremia	4 (10)	2 (5)	1 (2)	0	7 (17)
Vomiting	4 (10)	1 (2)	1 (2)	0	7 (17)
Platelet count decreased	4 (10)	0	0	2 (5)	6 (15)
Blood bilirubin increased	4 (10)	1 (2)	0	0	5 (12)

Additional grade 3-4 adverse events occurring in >1 patient

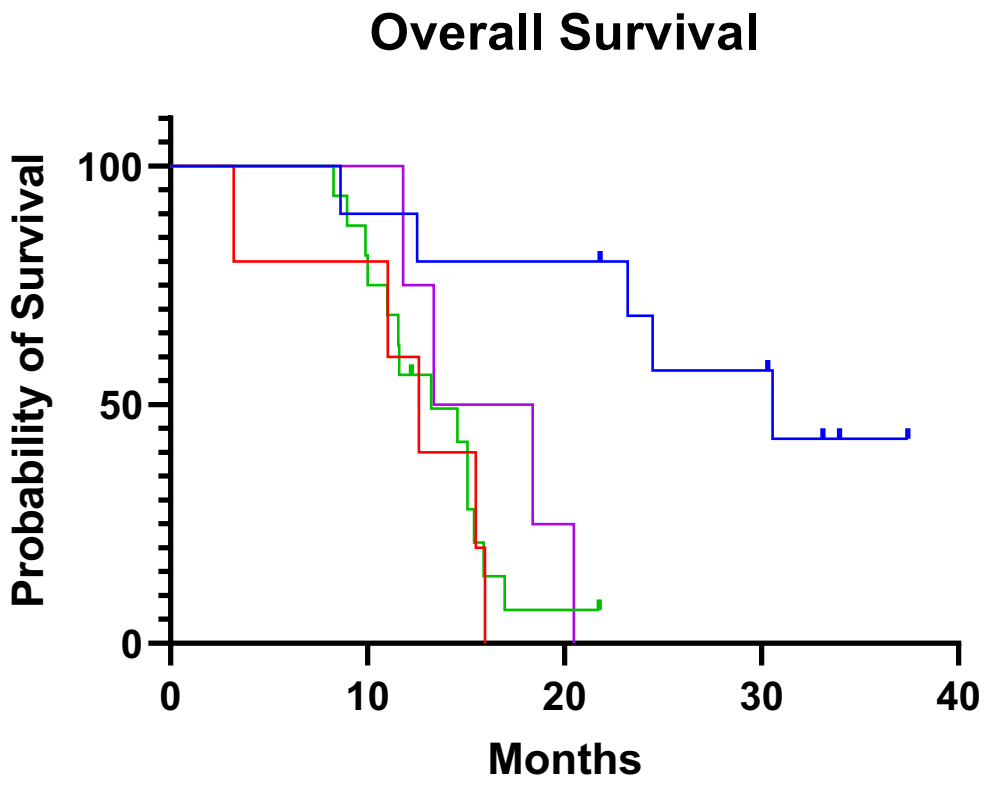
Event	CTC grade		Total=41
	3	4	N (%)
Neutrophil count decreased	1 (2)	1 (2)	2 (5)
Acute kidney injury	2 (5)	0	2 (5)
Hypertension	2 (5)	0	2 (5)

9 discontinuations due to adverse events:

- 3 expected temozolomide toxicity (myelosuppression)
- 3 expected nivolumab toxicity (1 aseptic meningitis, 2 AST/ALT increase)
- 2 due to underlying disease symptoms
- 1 unrelated medical event (prostate cancer)

As of cutoff date
30 Sep 2022

Evaluable population survival curves: MGMT methylation status and extent of resection



Methylated GTR Median OS: 30.6 m (n=10)
Methylated STR Median OS: 12.6 m (n=5)
Unmethylated GTR Median OS: 13.2 m (n=16)
Unmethylated STR Median OS: 15.9 m (n=4)

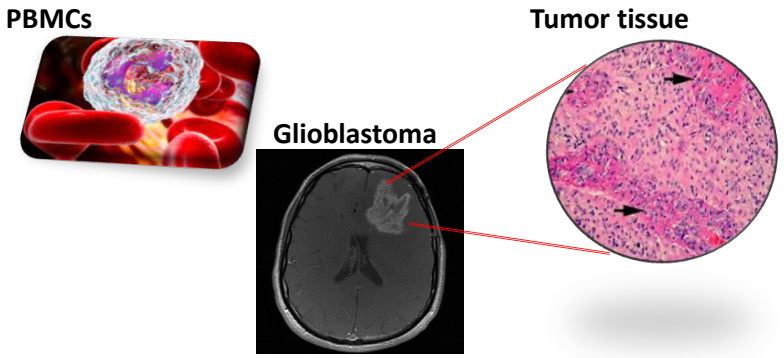
Median OS for all: 15.1 m (n=35)

As of cutoff date
30 Sep 2022

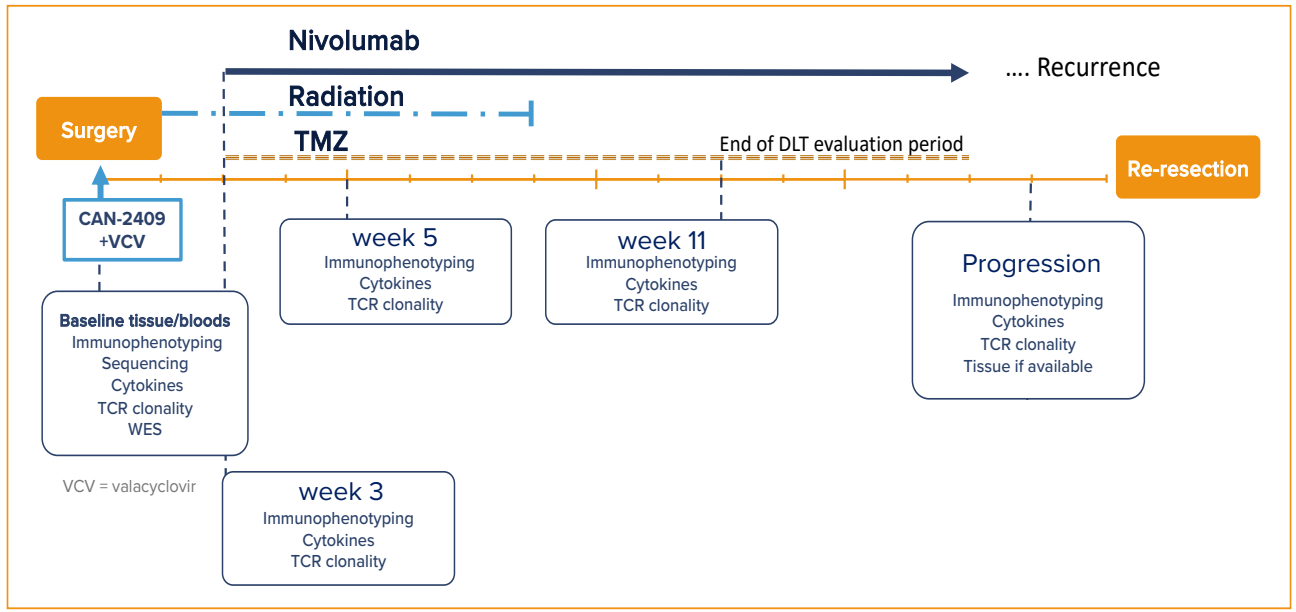
GTR – gross total resection
STR – subtotal resection
OS – overall survival

Immune profiling in collaboration with CIMAC-CIDC

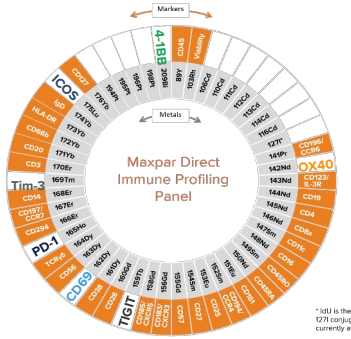
Longitudinal analysis in both tumor and peripheral blood:

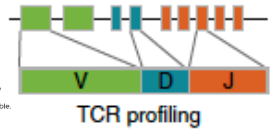


CYTOF
WES
RNAseq
TCR sequencing
mRNA Seq
OLINK proteomics
MIBI on brain samples

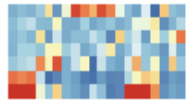


CIMAC-CIDC
Immuno-Oncology
Biomarkers Network

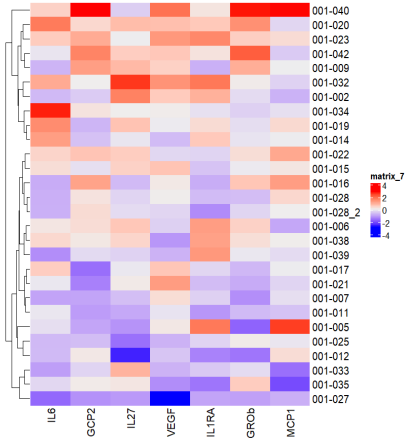


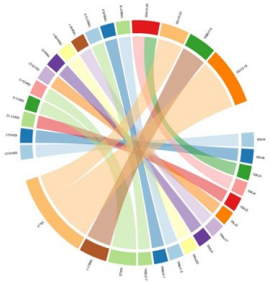


TCR profiling



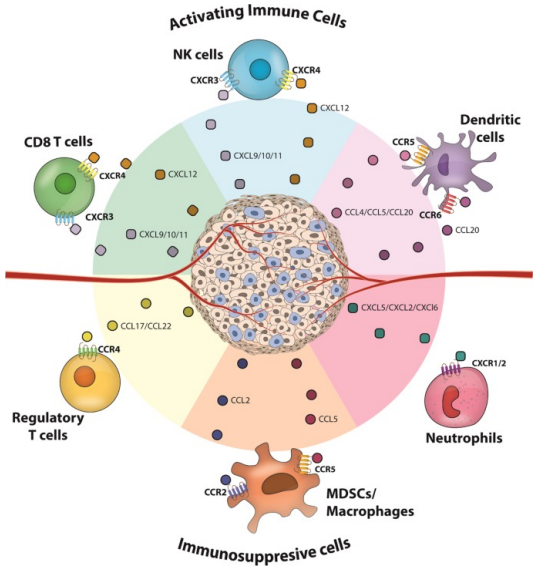
Expression analyses





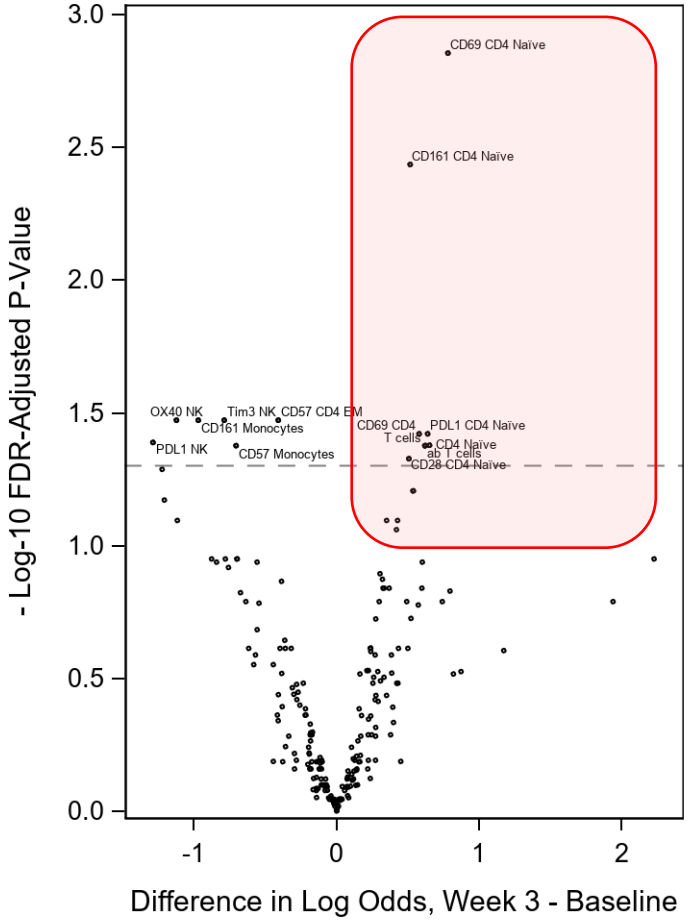
Single administration of CAN-2409 to the resection bed after removal of the tumor elicits strong systemic immune response

Key effector cells in antitumoral response

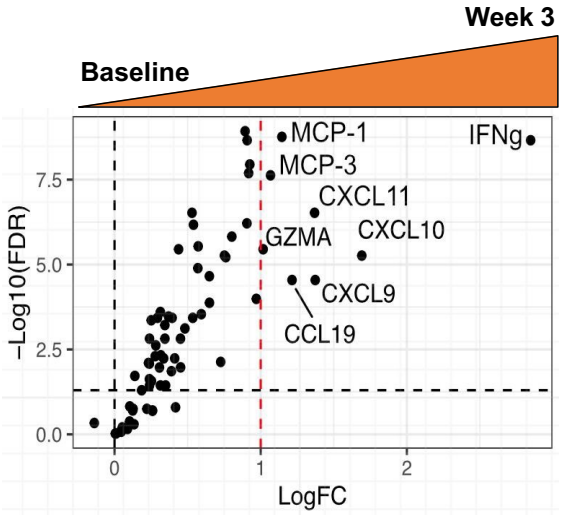


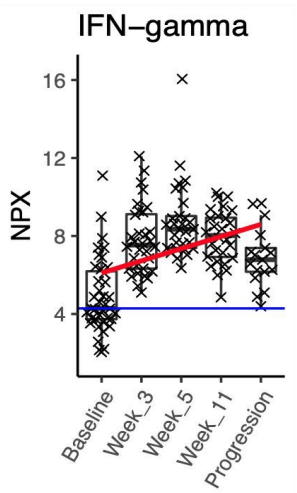
Kohli K et al. Cancer Gene Ther 2020; 29: 10–21

CyTOF data on longitudinal samples



OLINK data on longitudinal samples

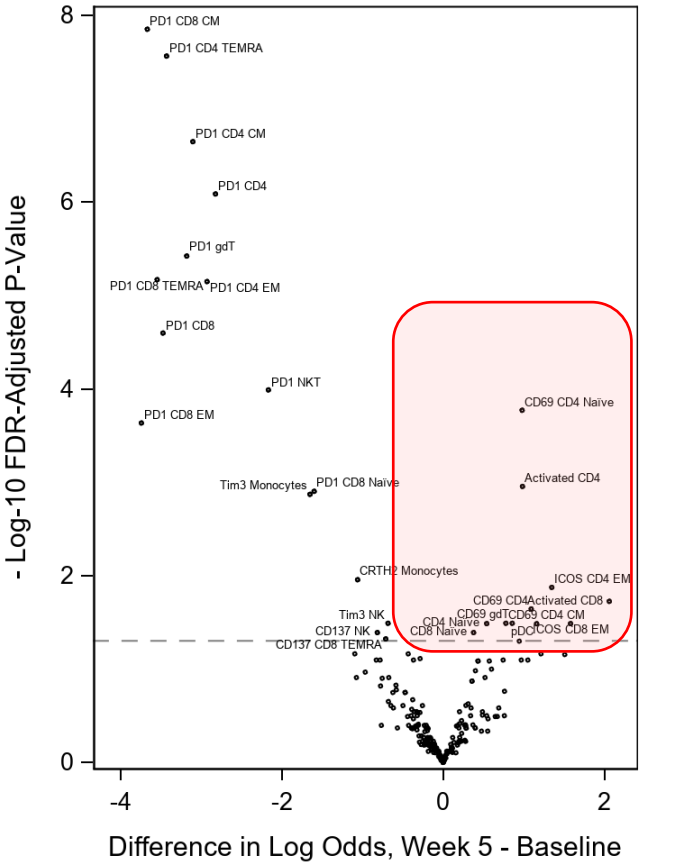




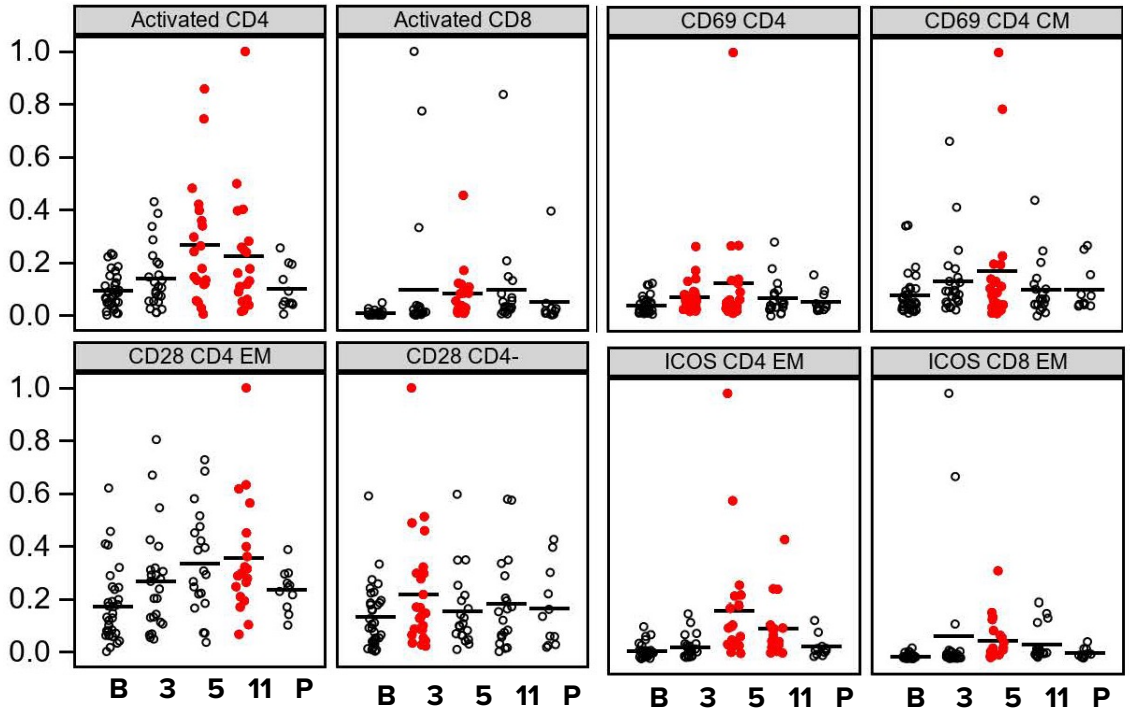
LogFC>1, FDR<0.05

Combination of CAN-2409 and nivolumab shows expansion of activated CD4 and CD8 T cells and decreased exhaustion

CyTOF data on longitudinal samples

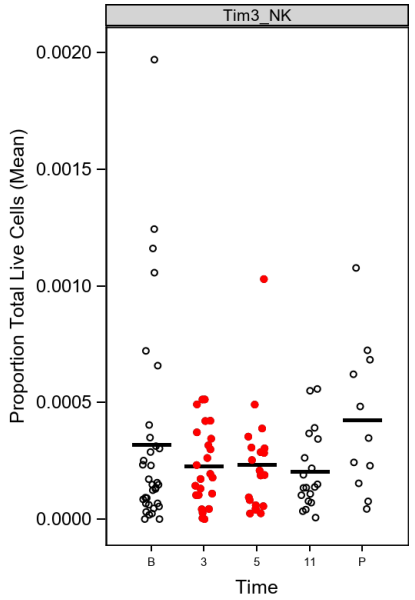


Increased T cell activation



Time post treatment (weeks)

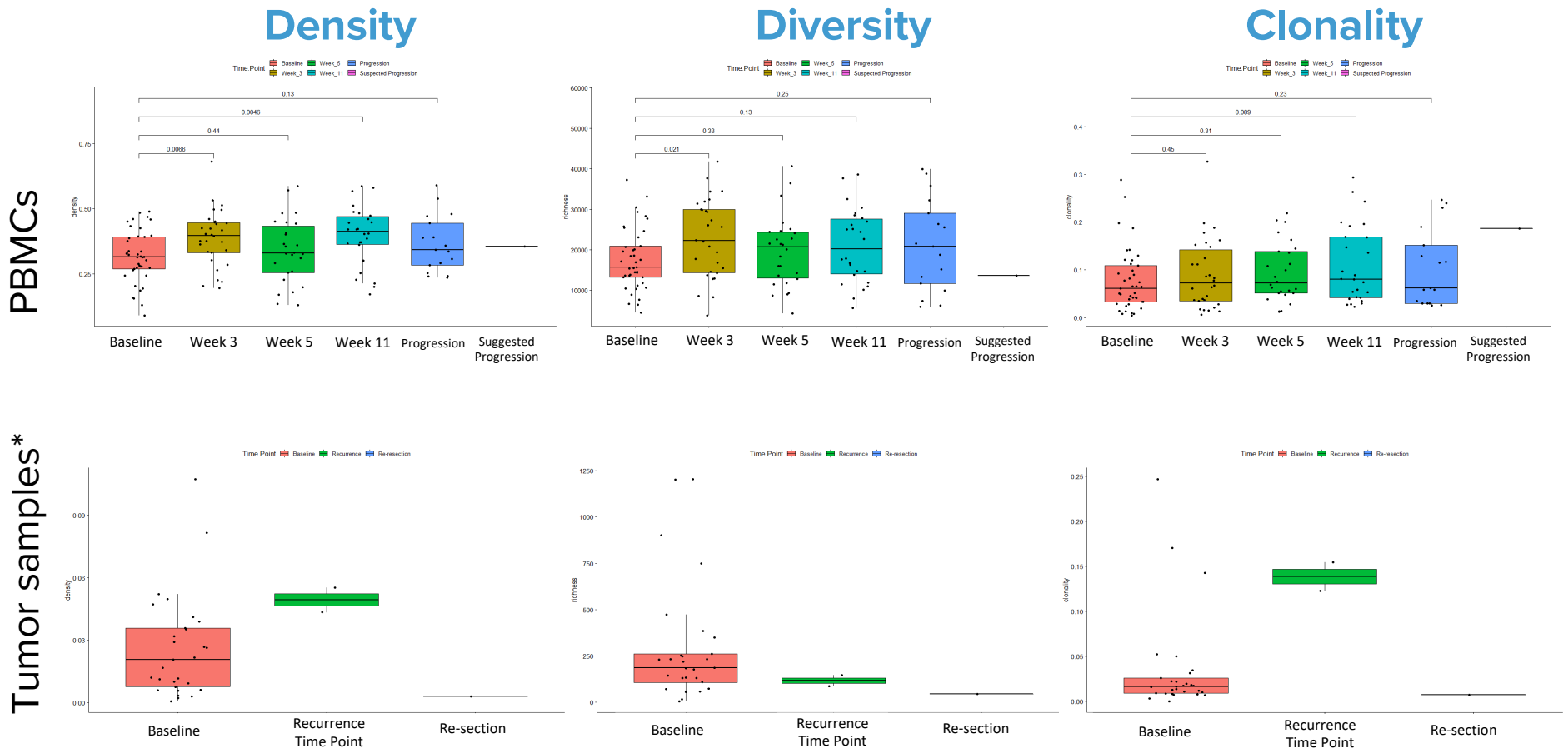
Decreased exhaustion



FDR adjusted p. value range (0.04 - 0.00095)

B= baseline
P= progression/off study

Combination of CAN-2409 and nivolumab results in expansion of TCR clone density, diversity and clonality



29 baseline tumors , 2 recurrences, 1 re-resection

Conclusions

- Combination of nivolumab and intratumoral CAN-2409 is well tolerated with no DLT observed and no added toxicity to standard of care
- Median overall survival appears comparable to historical standard of care outcomes; small patient number in different subgroups hampers conclusive outcome analysis
- Extensive longitudinal biomarker analysis supports CAN-2409 ability to activate systemic immune response, even after single administration
- Combination of CAN-2409 and nivolumab shows expansion of activated circulating CD4 and CD8 T cells and decreased exhaustion
- Preliminary analysis suggests ability of CAN-2409 and nivolumab to expand T cell repertoire density, diversity and clonality in the tumor tissue and in the peripheral blood

CAN-3110 in recurrent high-grade glioma

E. Antonio Chiocca, MD, PhD

CANDEL THERAPEUTICS

E. Antonio Chiocca, MD, PhD

Brigham and Women's Hospital & Harvard Medical School

Dr. E. Antonio Chiocca is the Chair of the BWH Department of Neurosurgery and is the Harvey Cushing Professor of Neurosurgery at Harvard Medical School. His research has focused on how viruses with specific gene mutations replicate selectively in tumors with a specific defect in a tumor suppressor pathway. Before joining BWH, Dr. Chiocca was Chairman of the Department of Neurosurgery at the Ohio State University Medical Center. He has more than 300 peer-reviewed publications. Currently, Dr. Chiocca serves as the lead investigator to Candel's phase 1 clinical trial studying the effects of CAN-3110 in recurrent malignant glioma.

Phase 1 clinical trial of CAN-3110 in recurrent high-grade glioma

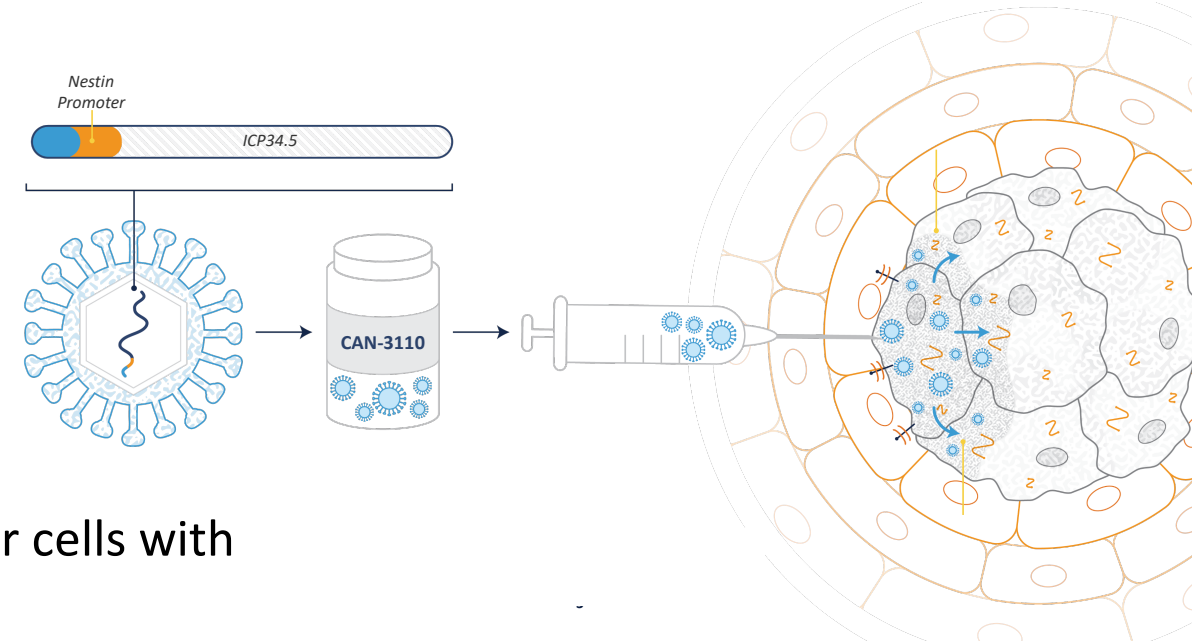
December 6, 2022

Department of Neurosurgery
Brigham and Women's Hospital
Founding Member, Mass General Brigham
HARVARD MEDICAL SCHOOL

CAN-3110: a conditional replication-competent oncolytic virus

HSV-1 engineered for immunogenic potency and specificity

- ICP34.5-null viruses have shown safety but replicate poorly
- CAN-3110: ICP34.5 expression under control of Nestin promoter
  - Nestin overexpressed in gliomas (and tumors outside the brain)
  - Improves replication
  - Provides tumor-specific oncolytic activity



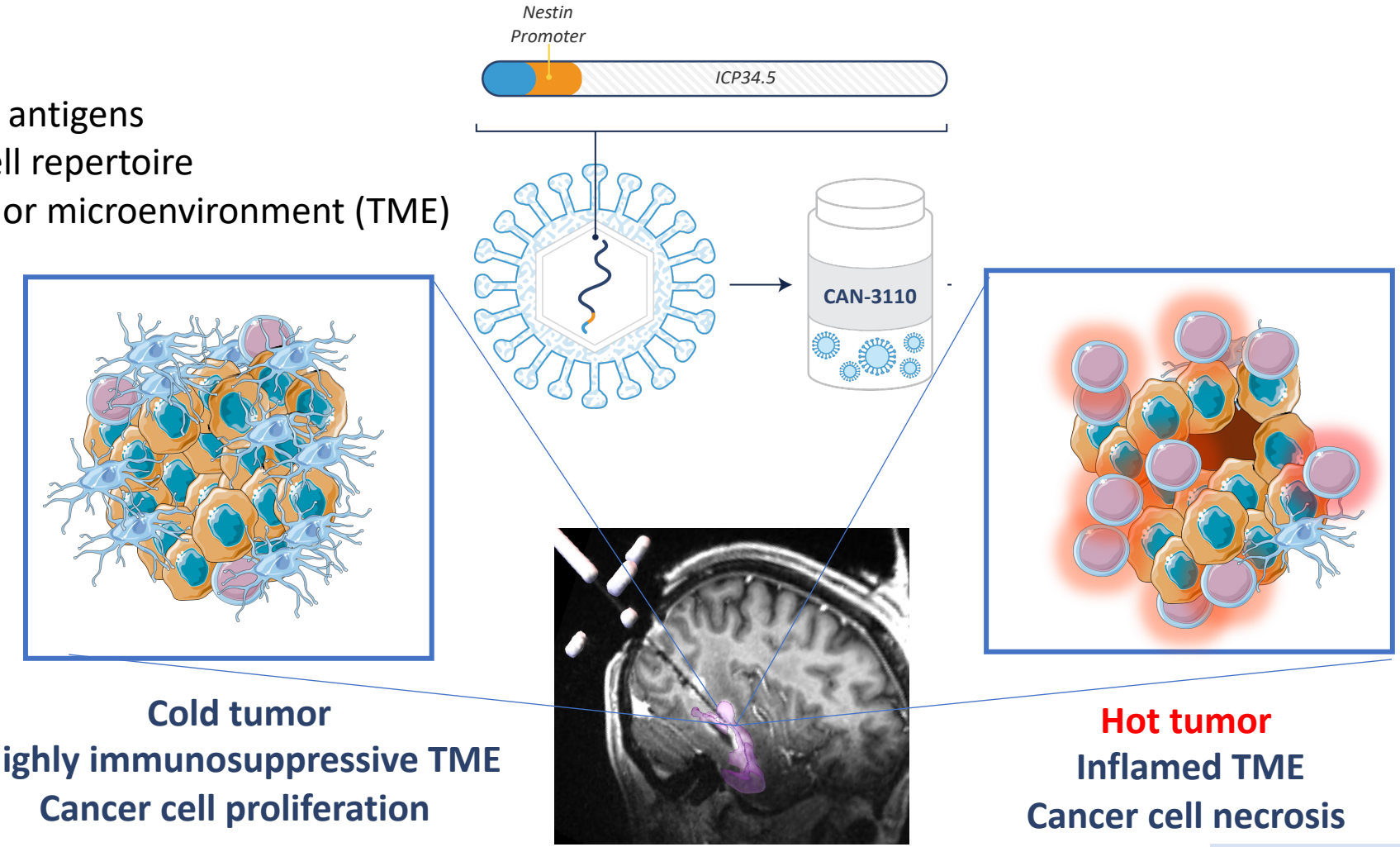
Designed for safety

- Disruption of ICP6 limits virus replication to dividing cells or cells with p16 tumor suppressor pathway defects
- Remains sensitive to anti-herpetic drugs
- Nestin provides tumor specificity

Department of Neurosurgery
Brigham and Women's Hospital
Founding Member, Mass General Brigham
HARVARD MEDICAL SCHOOL

CAN-3110 induces tumor cell death and reprograms the highly immunosuppressive microenvironment in high-grade glioma

Tumor cell death
Release of tumor antigens
Expansion of T cell repertoire
Activation of tumor microenvironment (TME)



Cold tumor
Highly immunosuppressive TME
Cancer cell proliferation

Hot tumor
Inflamed TME
Cancer cell necrosis

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Phase 1 clinical trial of CAN-3110 in recurrent high-grade glioma

Sponsor/PI: Dr. E. Antonio Chiocca (Brigham & Women's Hospital)

Patients with recurrent high-grade glioma

Lesions ≥ 1.0 cm

Arm A

Dose escalation (Cohort I-IX)
Single stereotactic injection of CAN-3110

3+3 dose escalation
1×10^6 to 1×10^{10} PFU in half-log increments
30 patients dosed

Dose expansion (Cohort X)
1×10^9 PFU
12 patients

Arm B

Pre-administration of Cytoxan
+1 x 10^8 PFU
3 patients dosed
+ 1 x 10^9 PFU
6 patients dosed

BREAK THROUGH CANCER

Arm C*

Repeat dosing (up to 6)
+1 x 10^8 PFU x 6 doses
+ 1 x 10^9 PFU x 6 doses

Primary Endpoints
- Safety
- Determine maximum tolerated dose

Secondary Endpoints
- Immunological biomarkers
- MRI assessment of disease and progression free survival
- MRI alteration of permeability and flow at injection site

NCT03152318

*Break Through Cancer initiative

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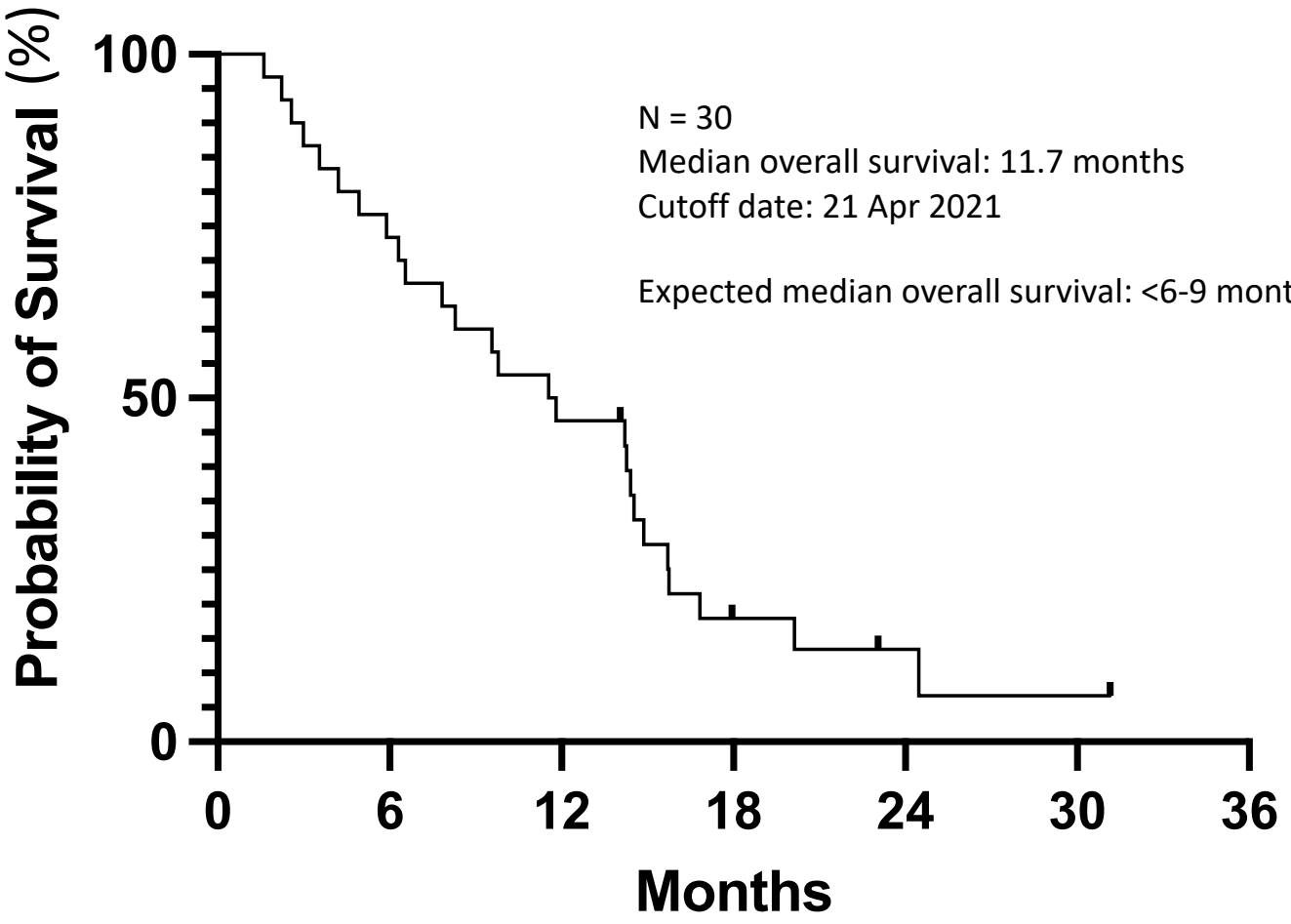
CAN-3110 related SAEs (arm A and B)

Cohort (arm)	Number of treated patients	Dose Level (pfu)	Number of patients with DLT	Number of patients with related SAE	Case #	Time (days)
1 (A)	3	$1x10^6$	0	0	NA	NA
2 (A)	3	$3x10^6$	0	0	NA	NA
3 (A)	3	$1x10^7$	0	0	NA	NA
4 (A)	3	$3x10^7$	0	0	NA	NA
5 (A), 1 (B)	6	$1x10^8$	0	0	NA	NA
6 (A)	3	$3x10^8$	0	0	NA	NA
7 (A), 10 (A), 2 (B)	21	$1x10^9$	0	1	046(IDHmut)	2
8 (A)	3	$3x10^9$	0	1	033(IDHmut)	16
9 (A)	6	$1x10^{10}$	0	0	NA	NA
TOTAL	50		0	2	Time range (days)→	2 to 16

DLT: dose limiting toxicity, SAE: serious adverse event

As of cutoff date 28 Jul 2022

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



N = 30
Median overall survival: 11.7 months
Cutoff date: 21 Apr 2021

Expected median overall survival: <6-9 months

<u>Update from SNO 2022</u>
N = 41
Median overall survival: 11.6 months
Data mature as of Oct 2022

EA Chiocca et al. Oral presentation. ASCO June 2021
A Ling et al. Oral presentation. SNO November 2022

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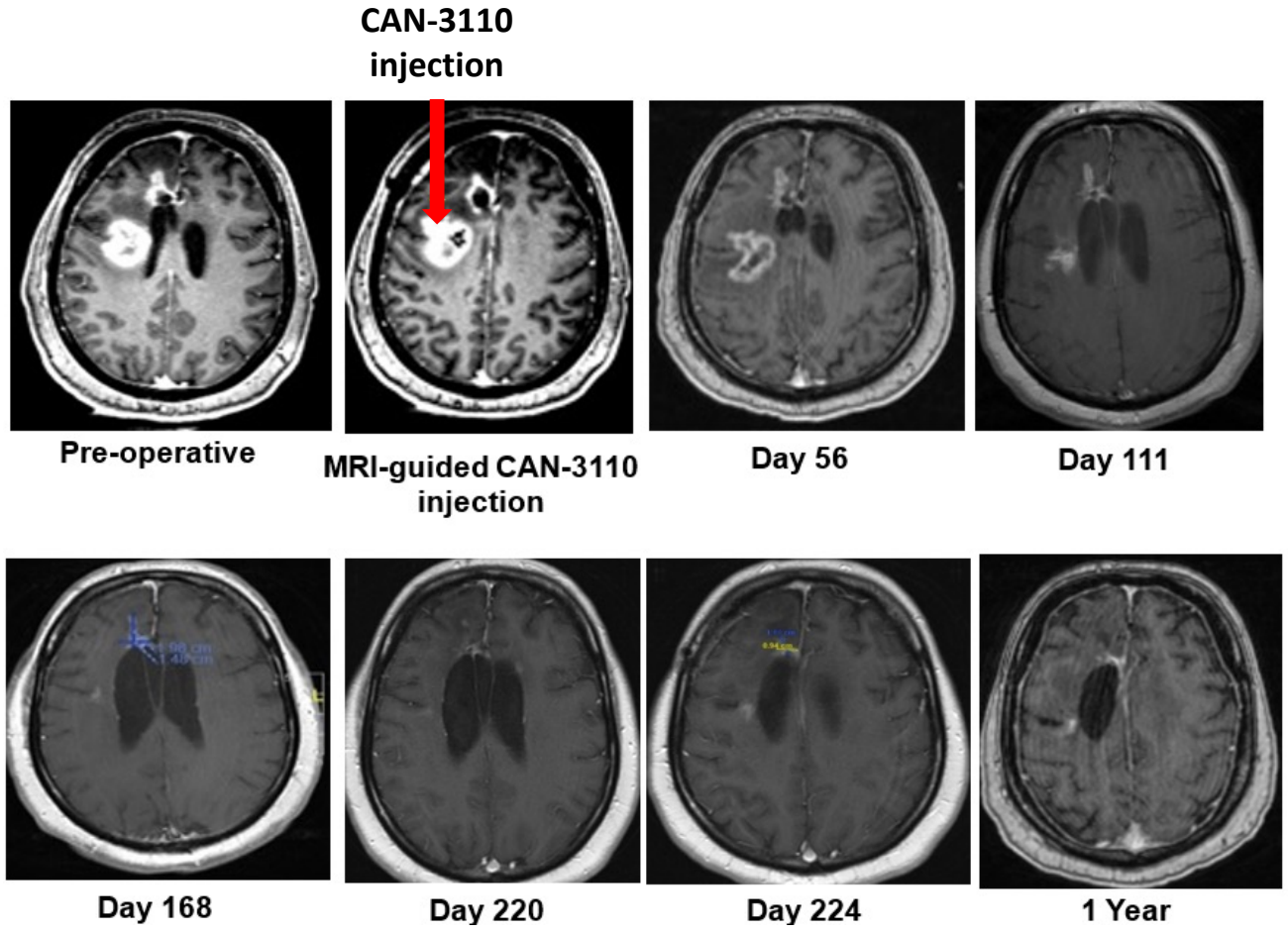
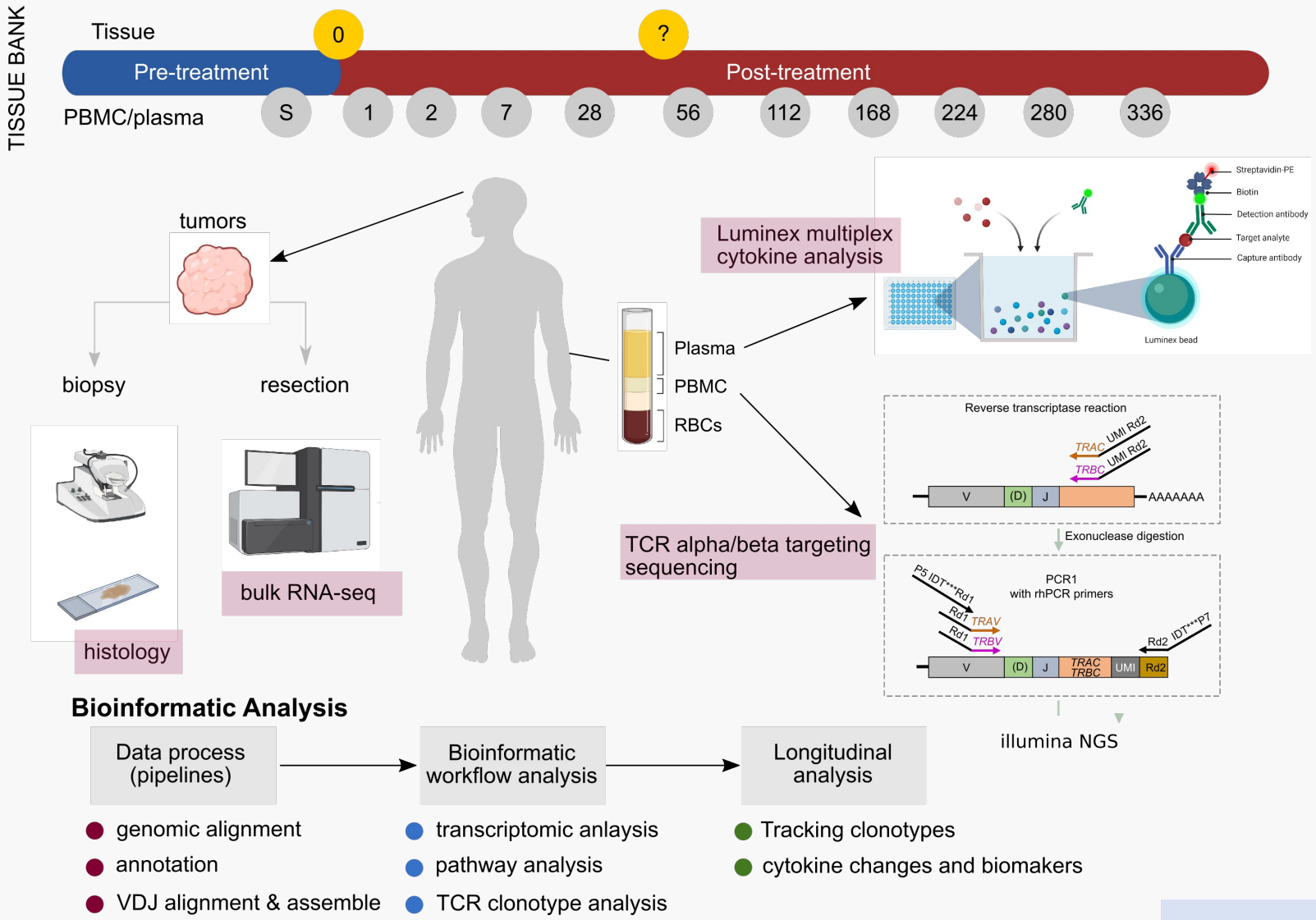
Complete response in injected and uninjected tumor without additional therapy following CAN-3110



Biomarker strategy



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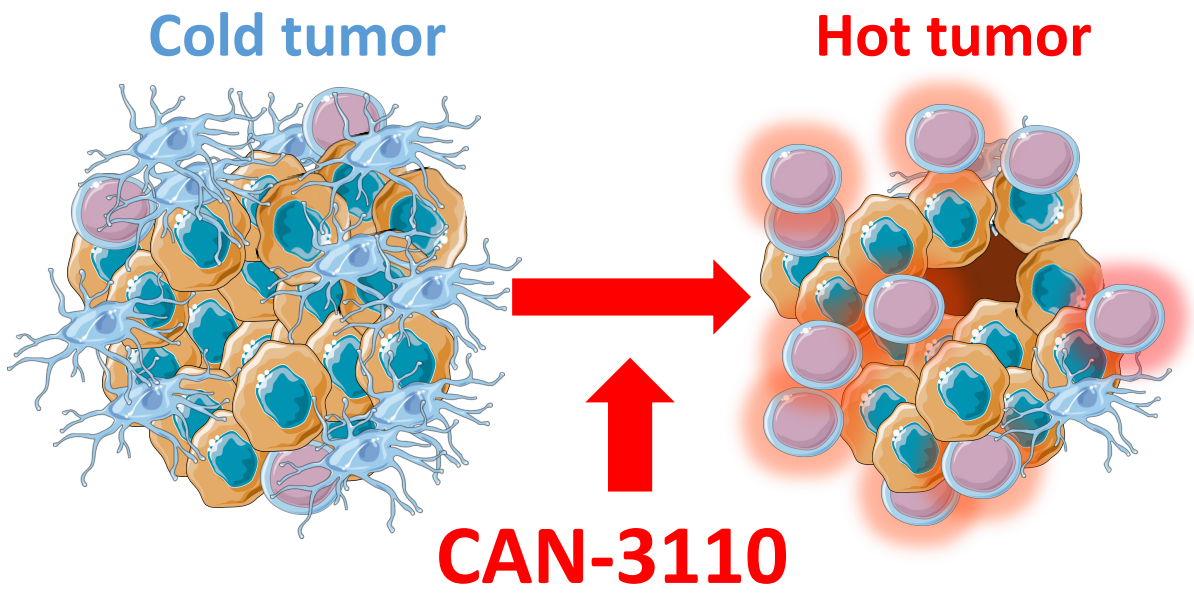
Scientific questions asked in this clinical trial

1. Is there post-injection evidence of CAN-3110 persistence and replication?

2. Is there post-injection evidence of increased CD8+, CD4+ T cells and B cells in glioblastoma multiforme (GBM)?



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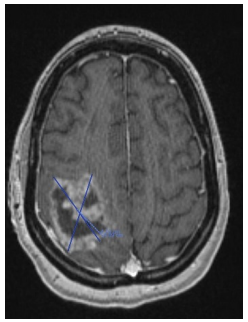
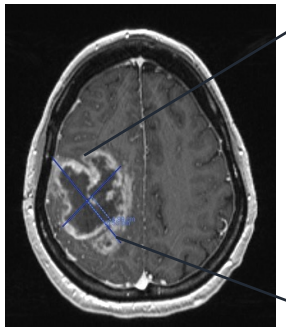
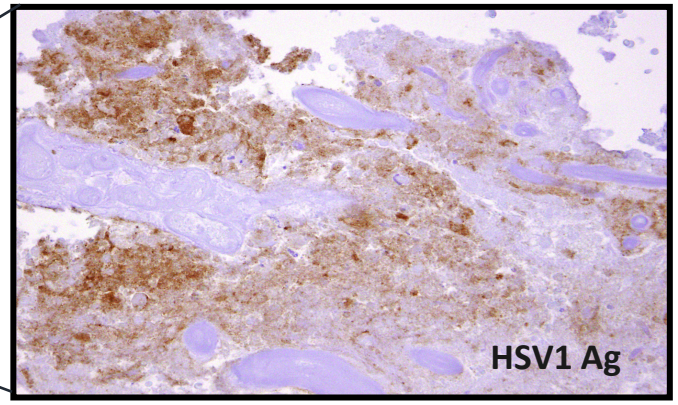
Persistent HSV antigen associated with T-cell infiltration in post-injection samples after CAN-3110 treatment

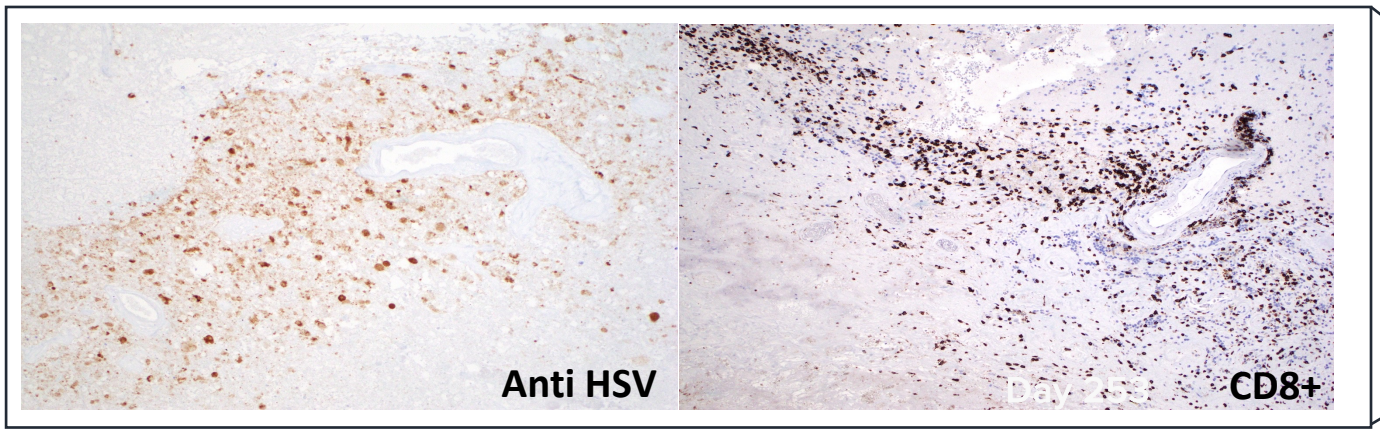
Patient A
(6 weeks post-HSV 10e6 pfus)



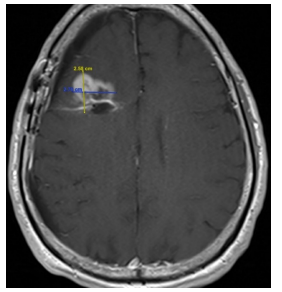




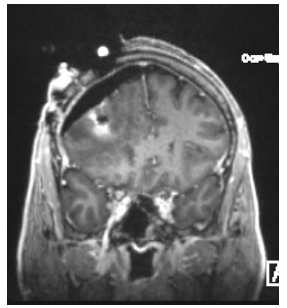
Patient B
(9 mo post-HSV 10e9 pfus)



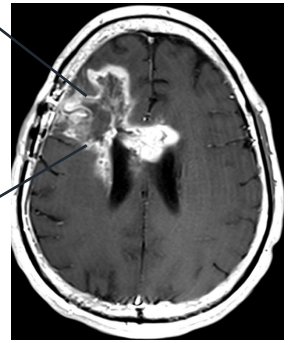
Preoperative



Intraoperative injection



Recurrence

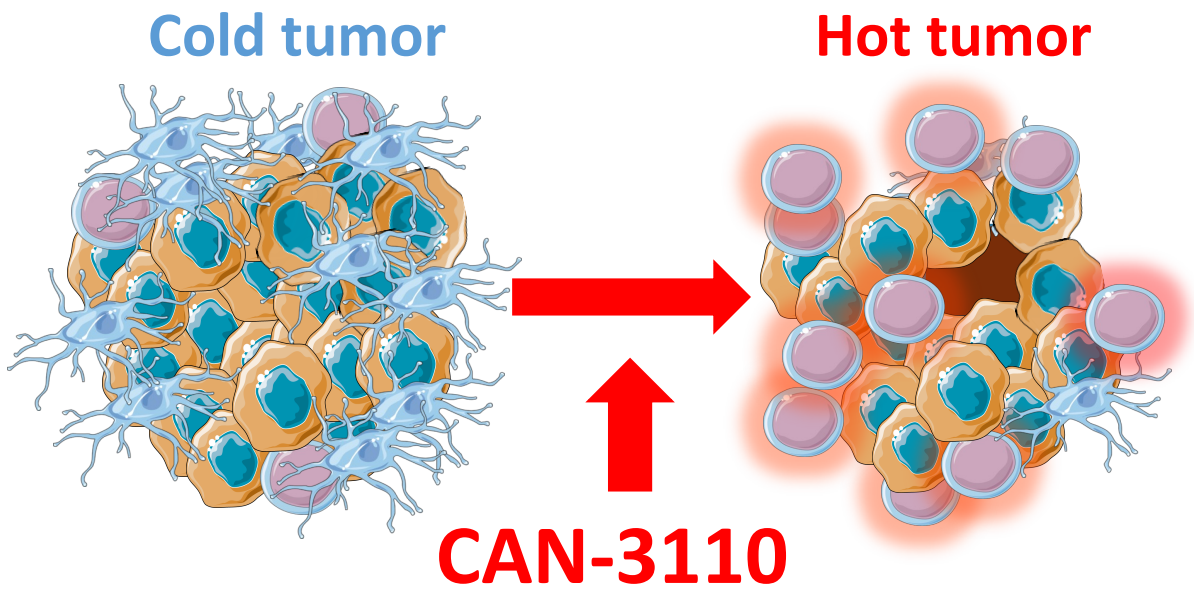


12/29 patients presented positive oHSV antigen in post-injection samples collected in a range of 24 to 801 days post treatment

Scientific questions asked in this clinical trial

1. Is there post-injection evidence of CAN-3110 persistence and replication?

2. Is there post-injection evidence of increased CD8+, CD4+ T cells and B cells GBM?



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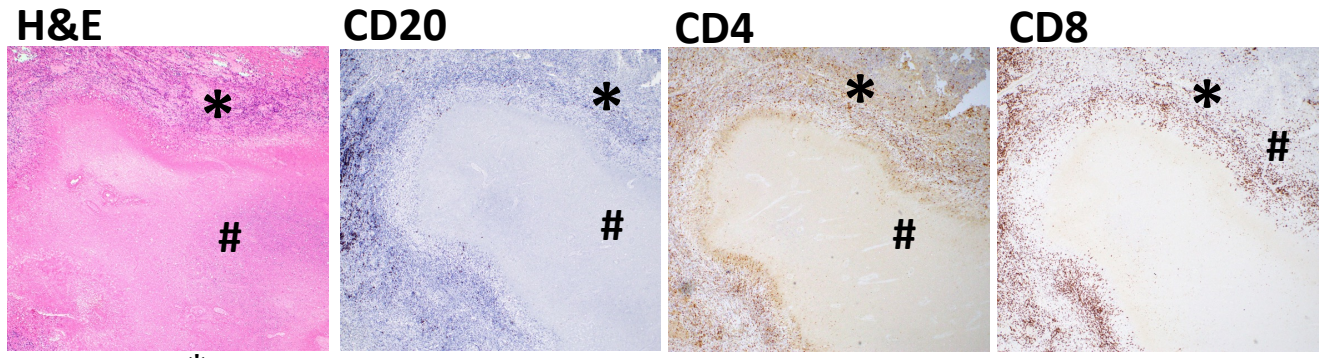
Evidence of increased T and B cell GBM infiltrates after CAN-3110

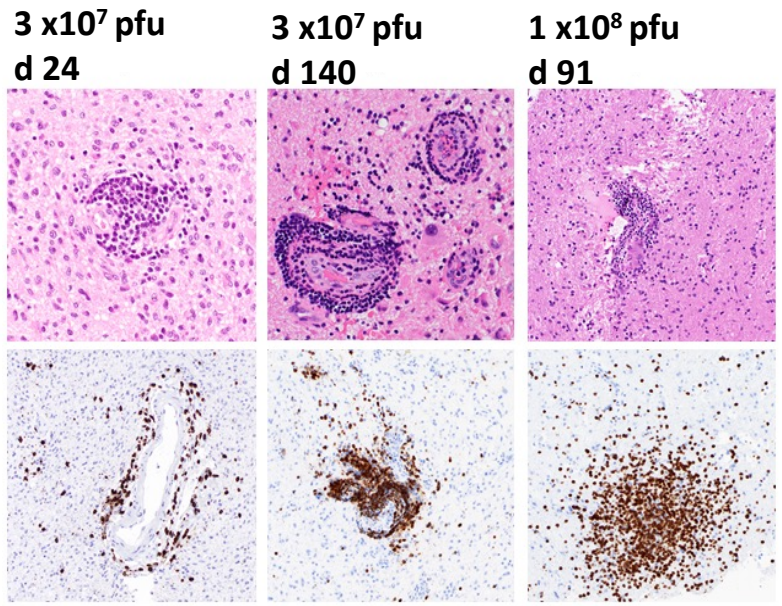
Post-injection necrotic tumor areas surrounded by T cells

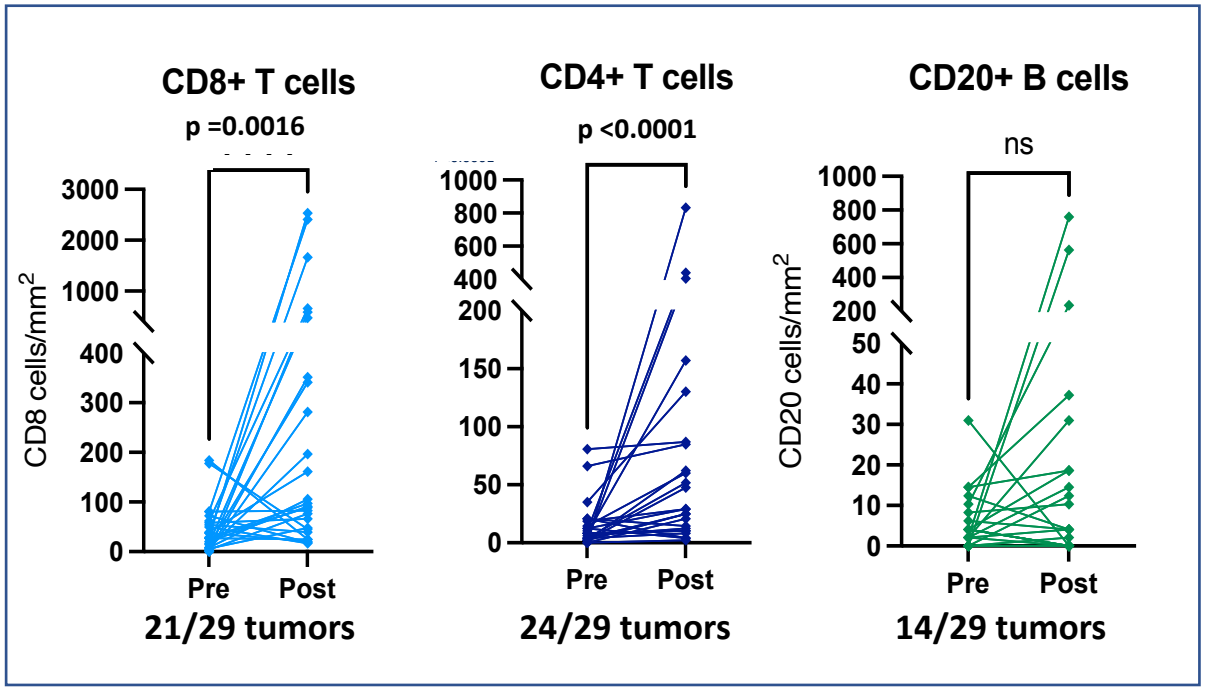


necrosis; * immune cell infiltrate

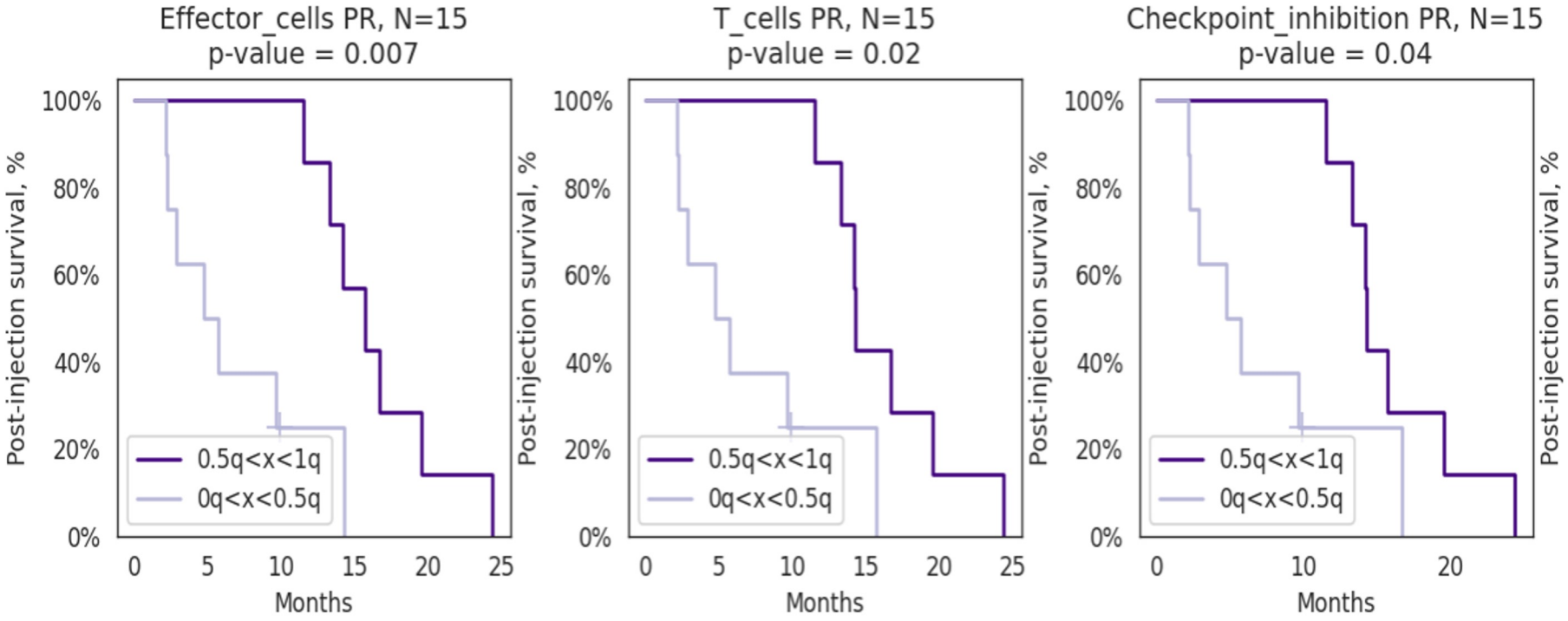
As of cutoff date 28 Jul 2022

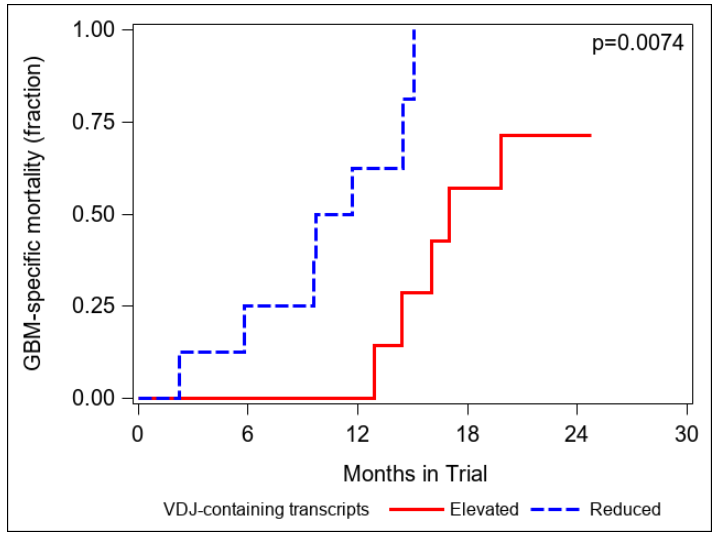
Perivascular tumor areas surrounded by T cells





CAN-3110 induces infiltration by effector T cells and changes to the T cell receptor repertoire associated with improved clinical survival





Subjects were divided into two groups by median immune signature score for each signature.
Statistical significance was calculated between the two groups using the log-rank test.

As of cutoff date
28 Jul 2022

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Conclusions

- Treatment with CAN-3110 is well tolerated, with no dose limiting toxicity observed
- Detection of HSV1 antigen and evidence of HSV1 replication in almost half of post treatment samples
- Significant increases in CD4+ and CD8+ T cells after CAN-3110 in the majority of post-CAN-3110 treatment samples with evidence for increased immune signatures and VDJ diversity in longer survivors after CAN-3110
- We are now evaluating whether multiple injections of CAN-3110 can fundamentally transform the treatment of high-grade glioma

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enLIGHTEN™ Discovery Platform

Francesca Barone, MD, PhD

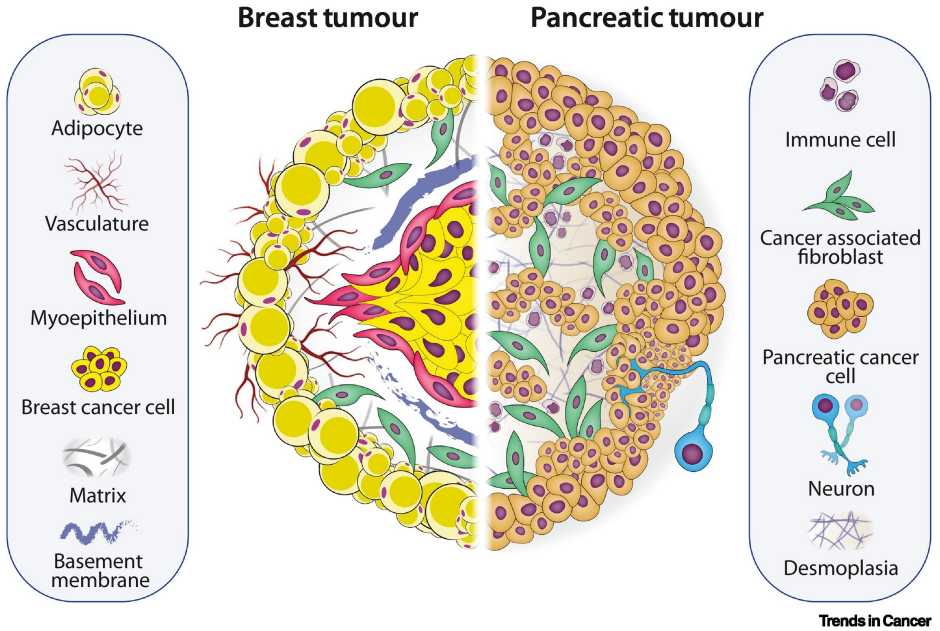
Francesca Barone, MD, PhD

Candel Therapeutics

Dr. Francesca Barone is the Chief Scientific Officer of Candel Therapeutics. At Candel, she leads scientific discovery, the development of their novel viral immunotherapies and biomarker strategy across their broad clinical portfolio. Dr. Barone previously served as Vice President and Head of Experimental Medicine at Flagship Pioneering's Kintai Therapeutics, now Senda Biosciences. She has extensive experience in designing experimental medicine clinical trials to support rigorous decision-making across various programs and indications. Prior to joining the industry, Dr. Barone held the academic position of Reader in Translational Rheumatology and Academic Director of Business Engagement for the College of Medical and Dental Sciences at the University of Birmingham. During her tenure, she was also the Director of the laboratories for immuno-phenotyping in the Institute of Translational Medicine.

Breaking down the barriers to cancer immunotherapy

Immunotherapy treatment failure arises from heterogeneous mechanisms present in diverse tumor microenvironments (TME) that are inadequately addressed by single-target therapies



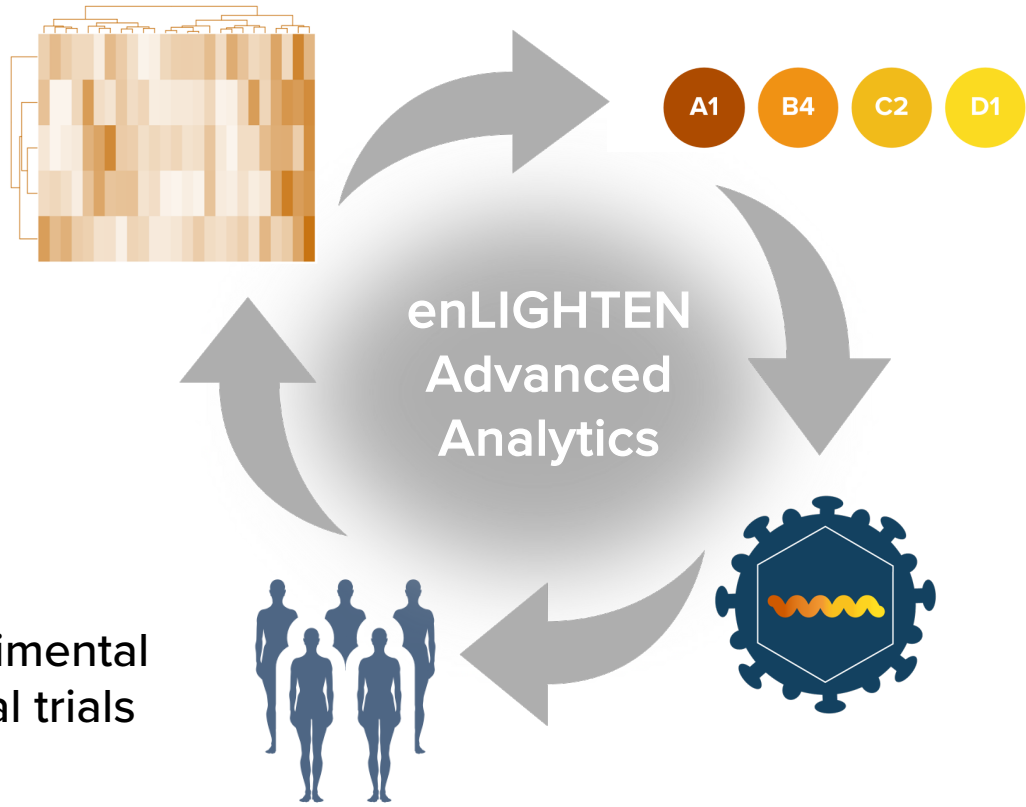
Carter E. et al. Trends in Cancer 2021; 11:1033-1046

Candel's multimodal approach: viral immunotherapies designed to target the heterogeneous mechanisms in the TME and overcome immunotherapy resistance

CANDEL THERAPEUTICS

The enLIGHTEN Discovery Platform

Deconvolution of human tumor microenvironment properties



In silico selection and prioritization of multimodal payloads

Design of experimental medicine clinical trials

Integration into proprietary suite of HSV-1 vectors

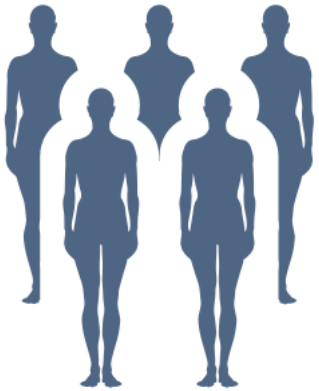
The first systematic, iterative HSV-based discovery platform leveraging human biology and advanced analytics to create new viral immunotherapies for solid tumors

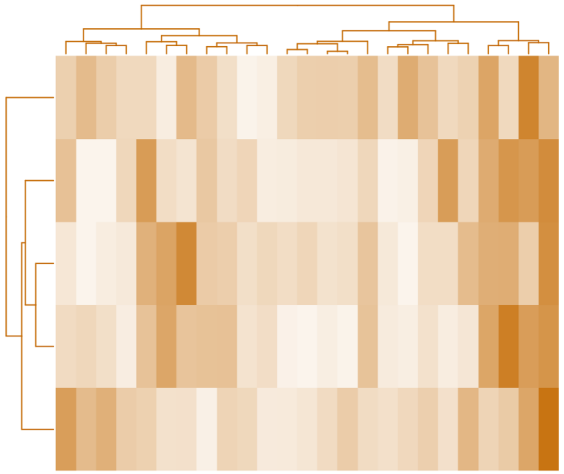
CANDEL THERAPEUTICS

enLIGHTEN is centered on human data for discovery

enLIGHTEN datasets are based on Candel's proprietary biomarker data and external datasets:

- Collaborations
- Publicly available datasets

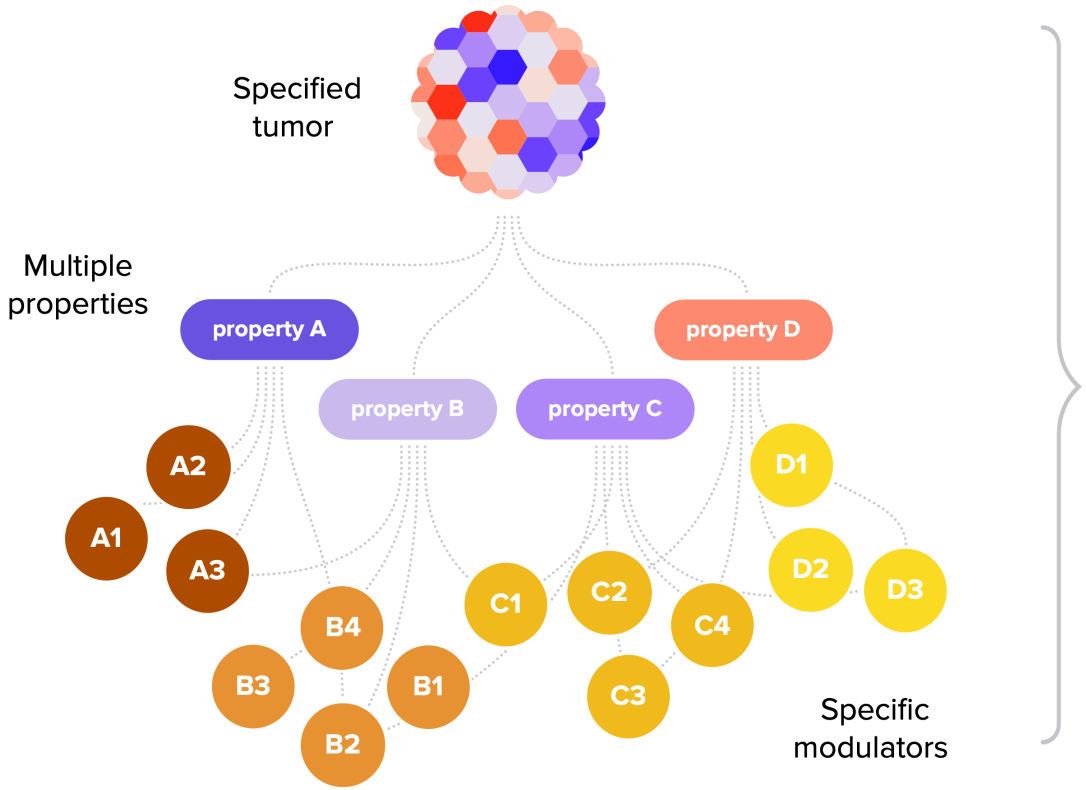




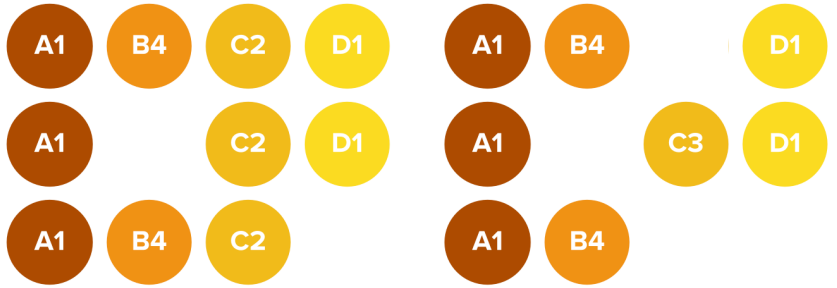
Opens the possibility to explore multiple indications and design tailored combination therapy

Overview of enLIGHTEN Advanced Analytics

Integrated computational approaches to design multimodal viral immunotherapies

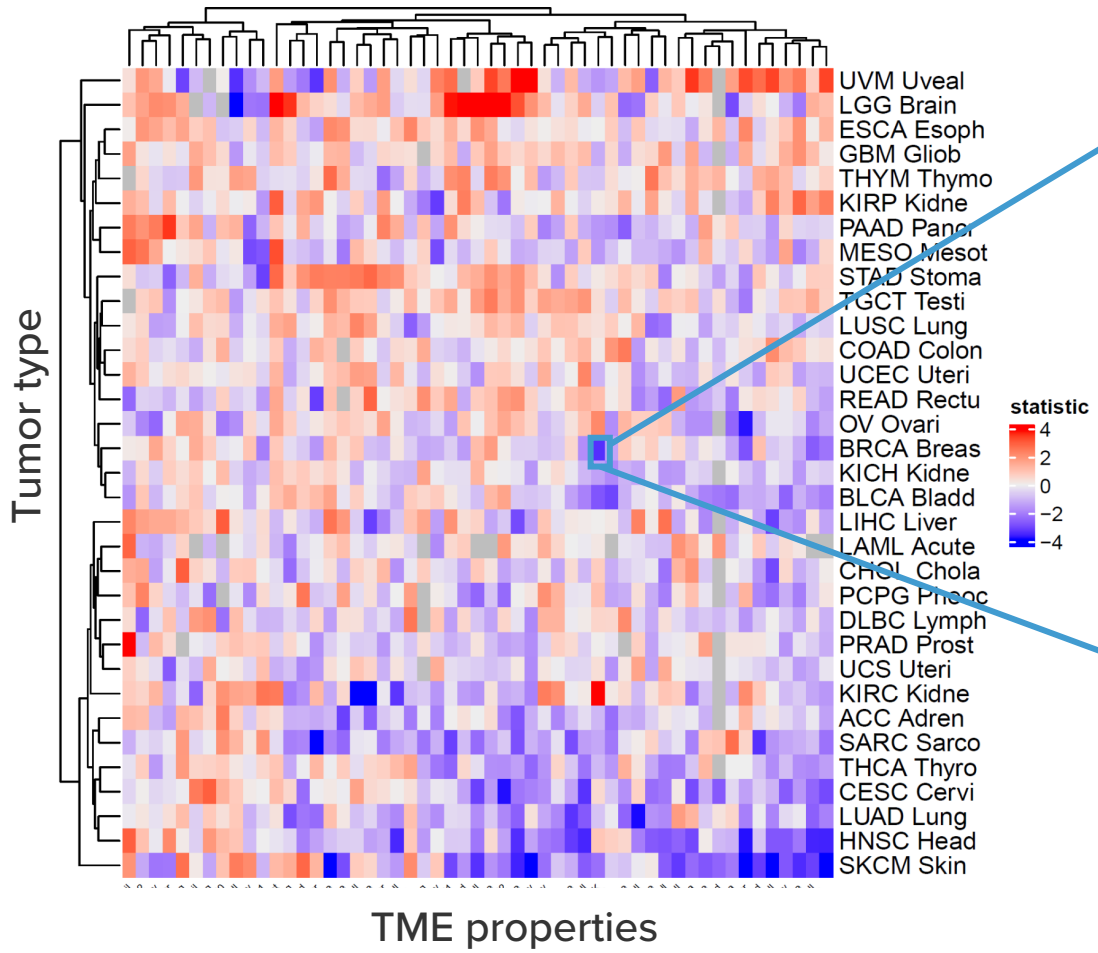


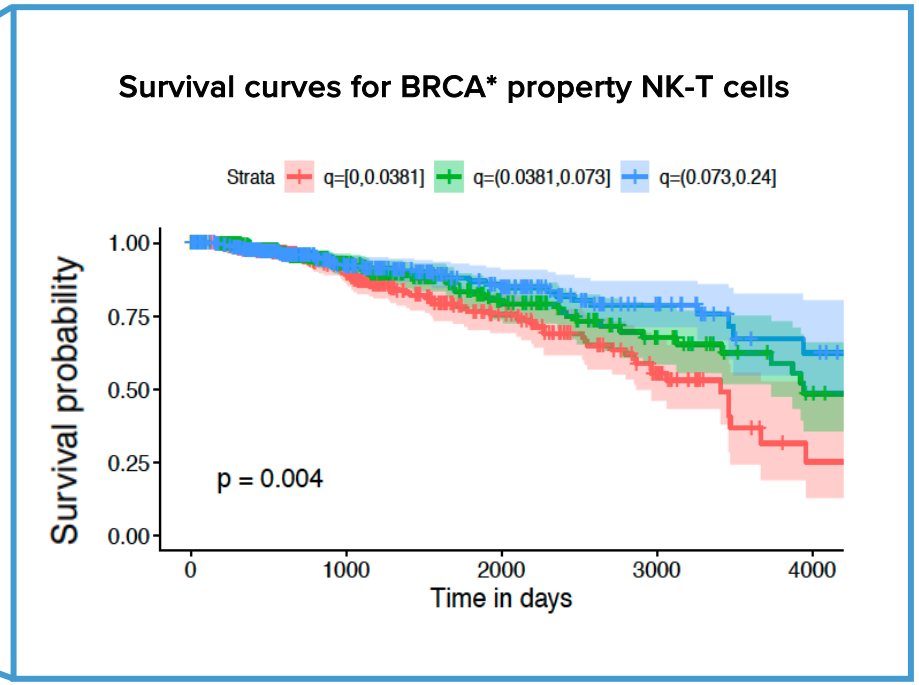
Selection of optimal modulator combination



Enables deconvolution of tumor properties and selection of property modulator combination

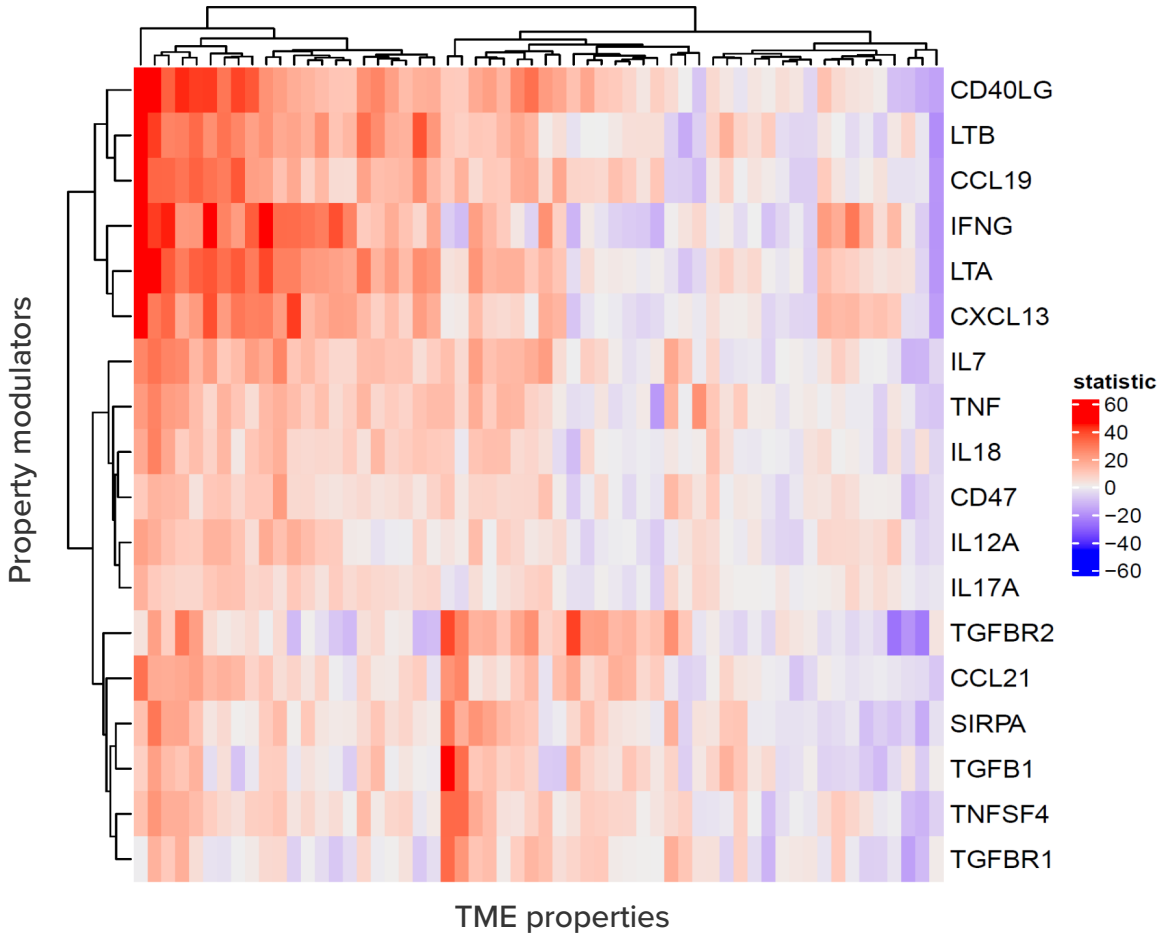
Application of enLIGHTEN Advanced Analytics to the Pan-Cancer Atlas



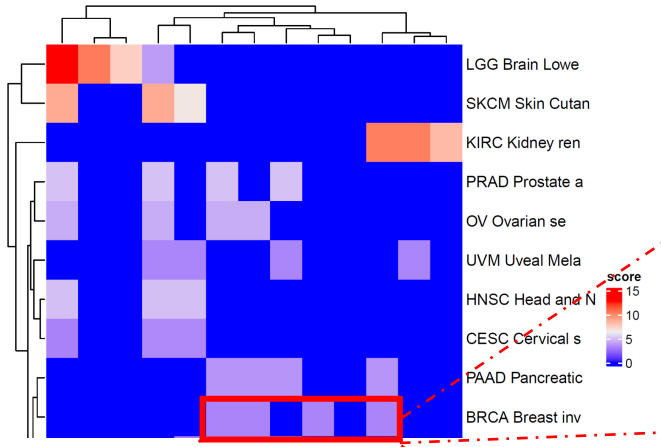


* BRCA: invasive breast cancer

Property modulators are selected in silico to design indication-specific payloads



Selection of optimal modulator combination



- A1 TNF family member
- B4 TNF family member 2
- C2 Macrophage function modulator
- D1 Anti inflammatory cytokine

In silico payload design

Establishment of single-gene mini-vector library

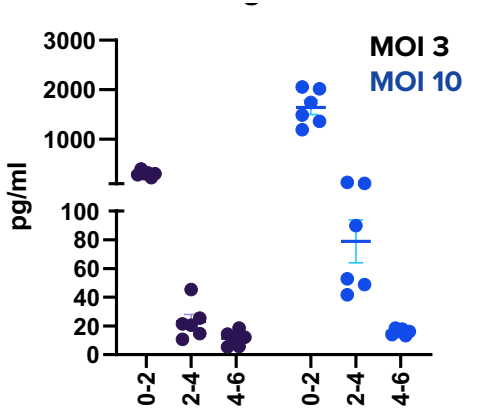
In silico selected modulators are encoded into mini vectors

Top modulator combination

Modulator encoding vectors

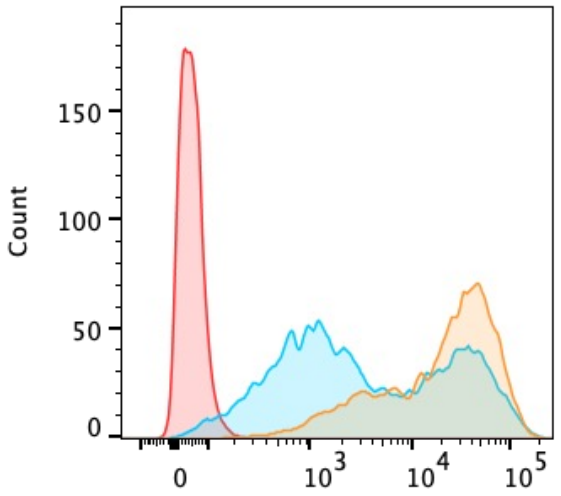
- 20+ mini-vectors encoded to date
- Expression of both secreted and cell surface molecules

Secreted modulator expression
(proinflammatory cytokine)



MOI multiplicity of infection

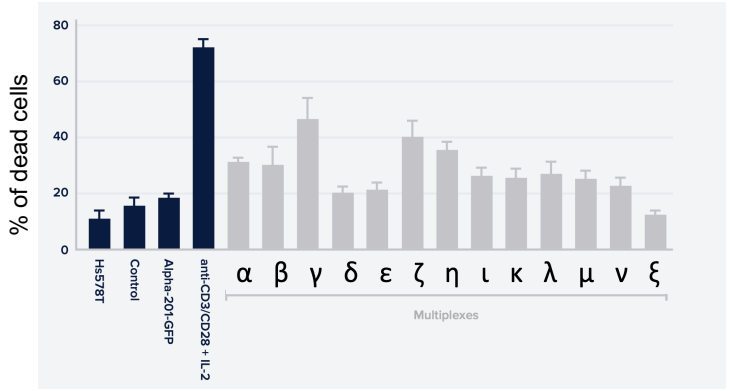
Cell-surface modulator expression
(TNF family member)



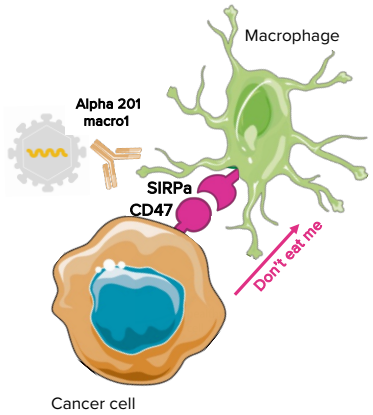
Alpha-201-GFP
Alpha-201-TNF family member MOI 3
Alpha-201-TNF family member MOI 10

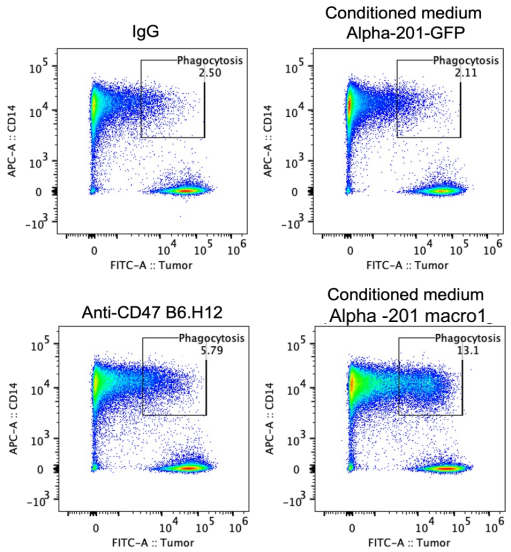
Robust pipeline of assays to test payload combinations

Multicellular tumor killing assays

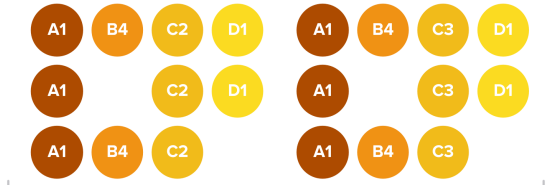


Phagocytosis assay



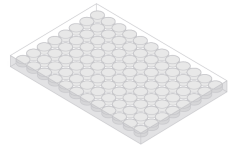


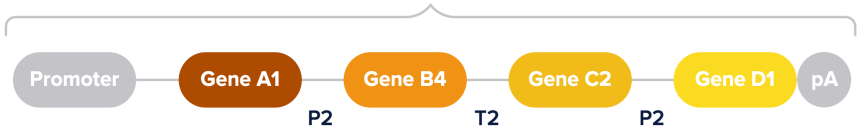
In silico predictions



Mini-vector library

Supervised multiplex

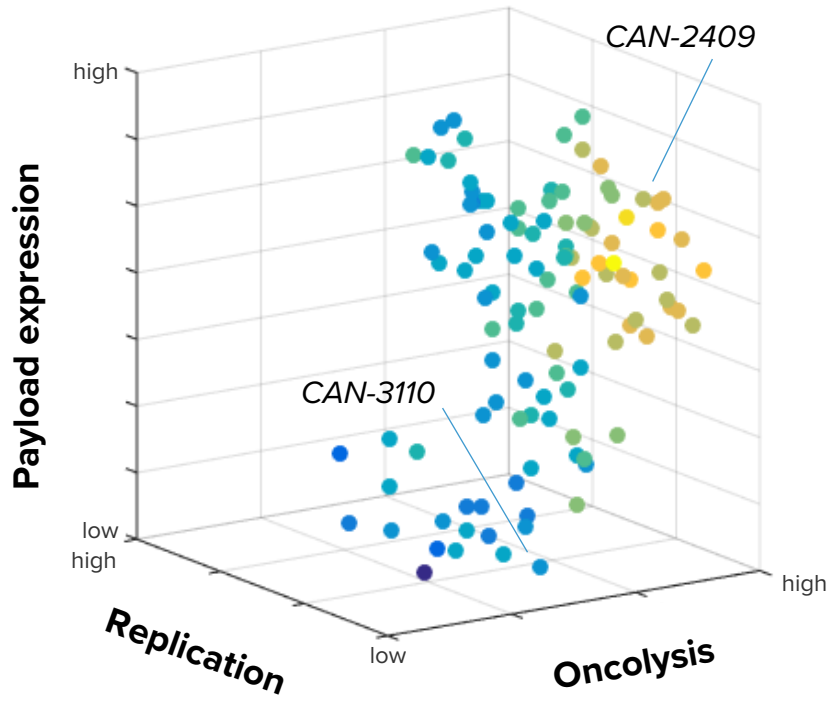


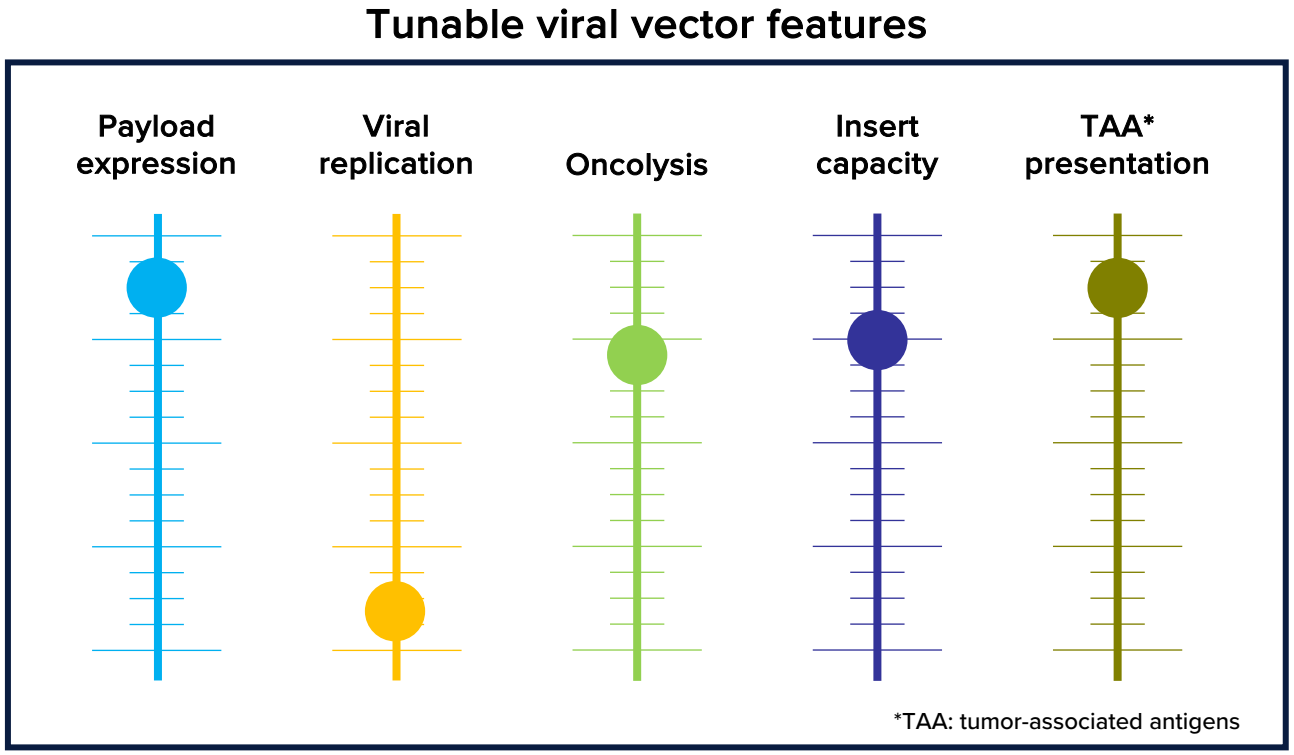


Development candidate : HSV-1 vector encoding nominated multimodal payload

CANDEL THERAPEUTICS

HSV platform provides a flexible delivery system for tumor-specific modulators

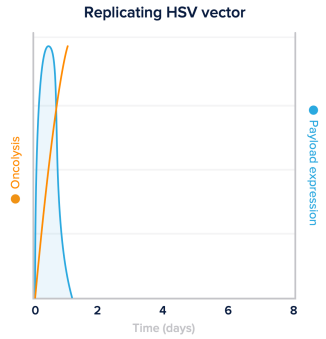


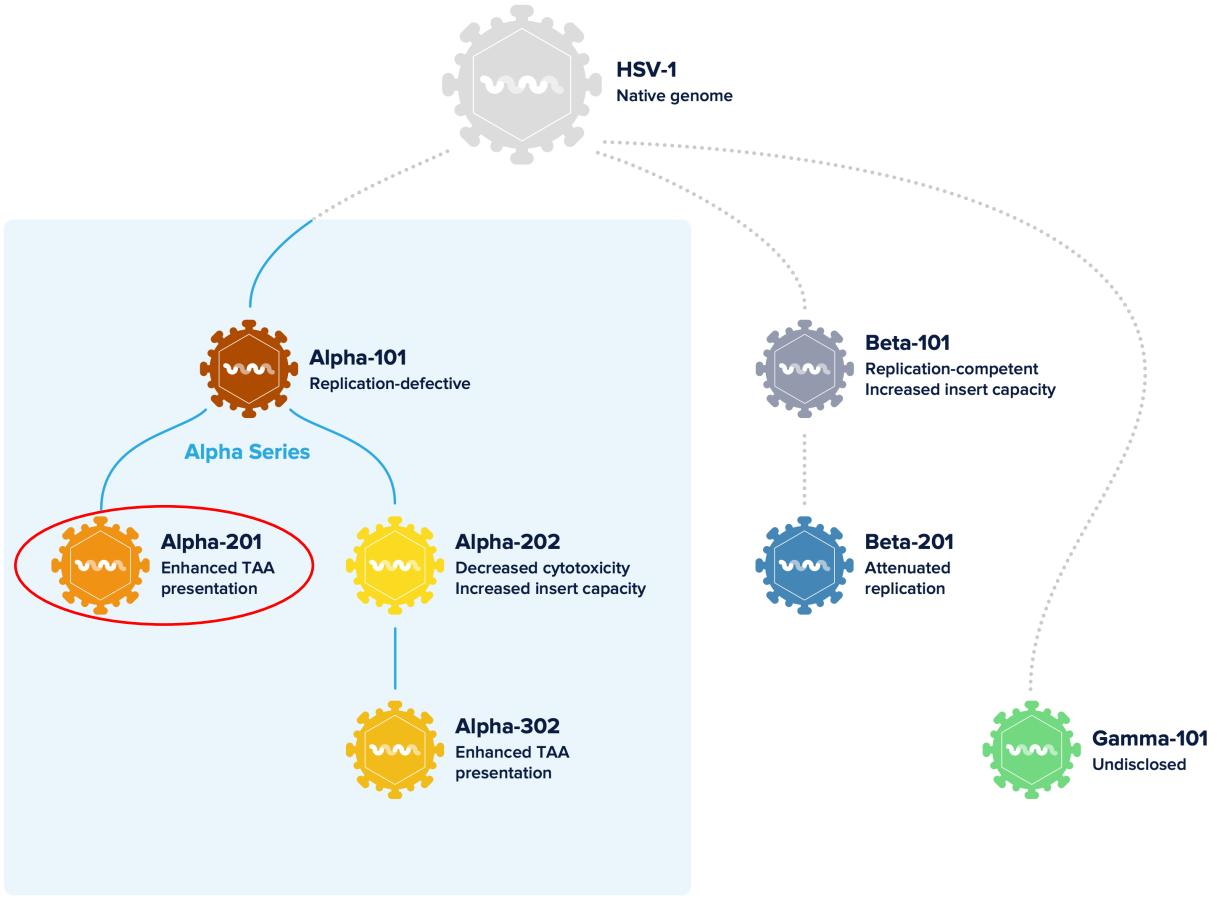


The suite of proprietary, engineered enLIGHTEN HSV-1 vectors allows for the delivery of multiple investigational immune-modulating gene products to tumors leveraging the immunogenic properties of a viral infection

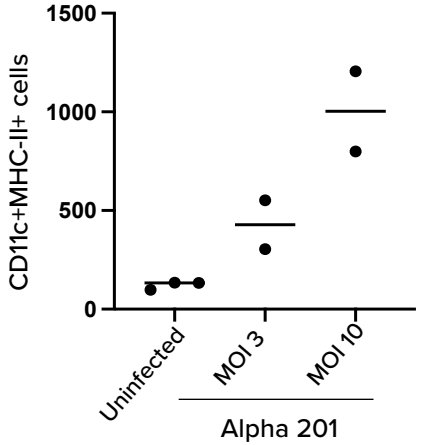
CANDEL THERAPEUTICS

Candel Alpha series: Engineered for delayed oncolysis to support sustained payload expression

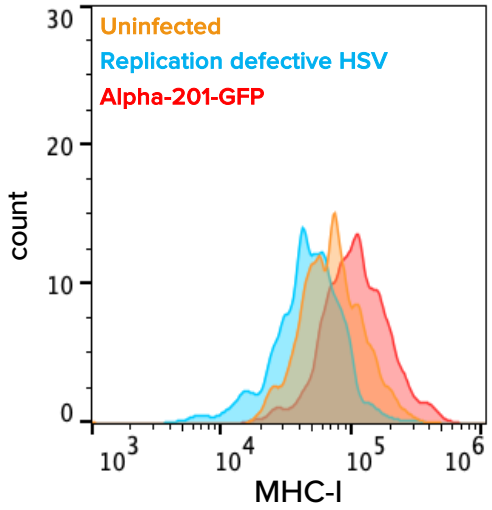




Expansion of APCs



Regulation of MHC-I expression



Alpha-201: first vector selected for enhanced immunostimulatory activity coupled with sustained payload expression and regulated oncolysis

Experiments performed in PBMCs: cancer cells cocultures

enLIGHTEN platform partnership with UPenn: Example of enLIGHTEN discovery platform application

Evaluation of a potential combination immunotherapy using tailored HSV-1 based viruses to deliver payloads that could enhance the activity of CAR-T cells

Features of Successful Drug Development*	Challenge for CAR-T Cells in Solid Tumors	Solution via HSV-1-Based OV
Exposure at the Site of Action	Insufficient CAR-T ingress	Features of the vector itself plus encoded factors turn cold tumors hot
Target binding / engagement	Antigenic heterogeneity	Expose TAAs* via oncolysis
		Encode factors to engage CAR-T cells
Expression of pharmacological activity	Suppressive TME	Encode cytokines to stimulate and activate CAR-T cells
		Encode inhibitors of key suppressive factors

TAAs: tumor associated antigens
OV: oncolytic virus

*Morgan P. et al. Drug Discovery Today 2012;17: 419-424

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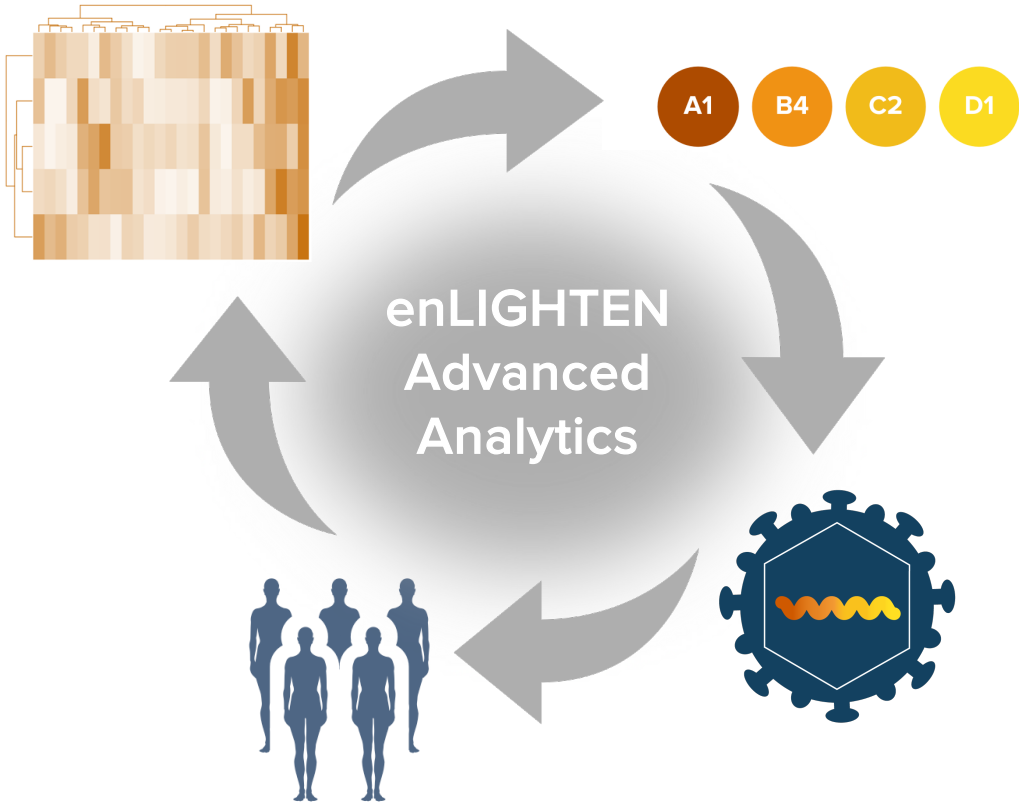
enLIGHTEN: Viral immunotherapy by design

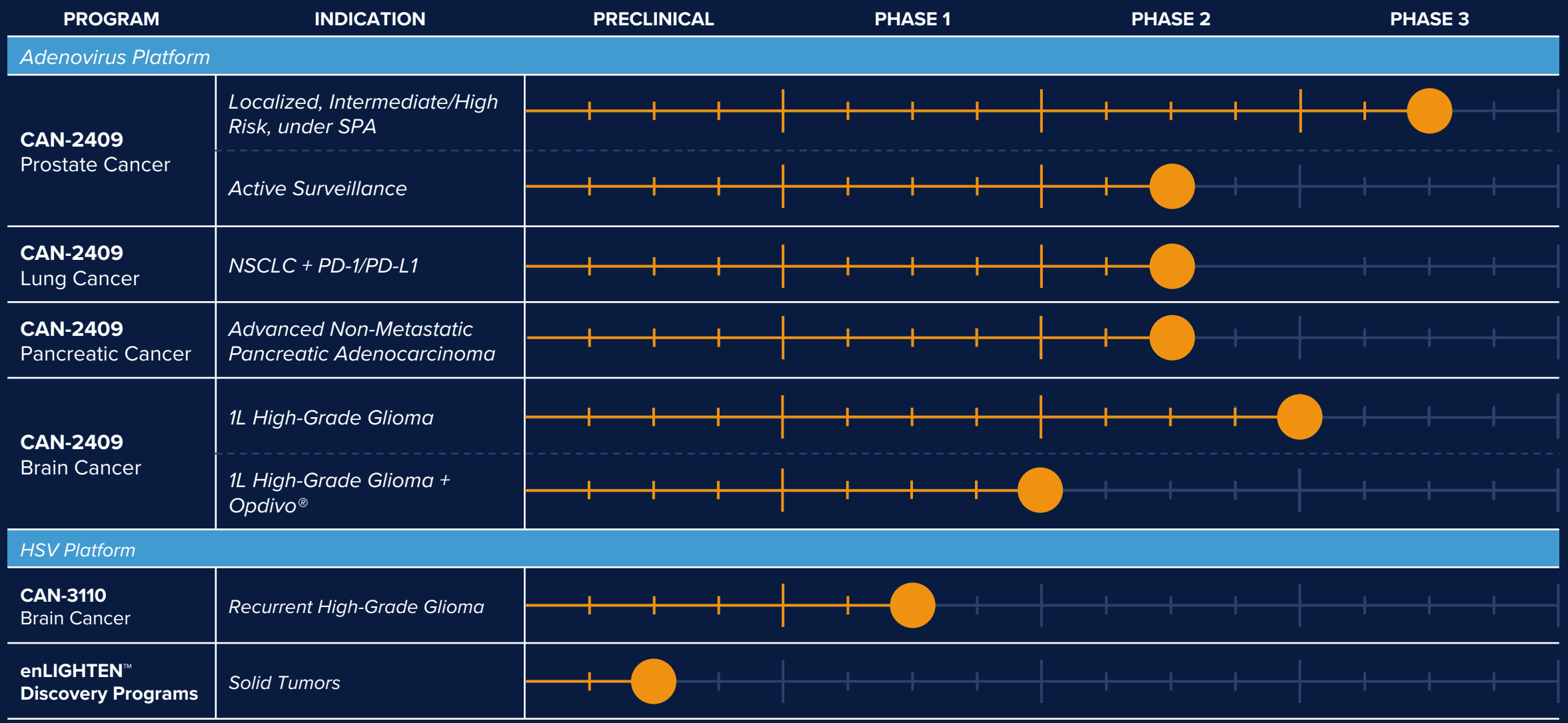
- Strong focus on human biology to increase probability of success
- Data-driven approach using advanced analytics to de-risk multimodal payload design
- Suite of proprietary, engineered HSV-1 vectors to enable fast translation to clinic
- Rapid and iterative approach
- Flexibility to design assets for monotherapy or combination therapy
- Opportunity to create value through partnerships



Candel Therapeutics

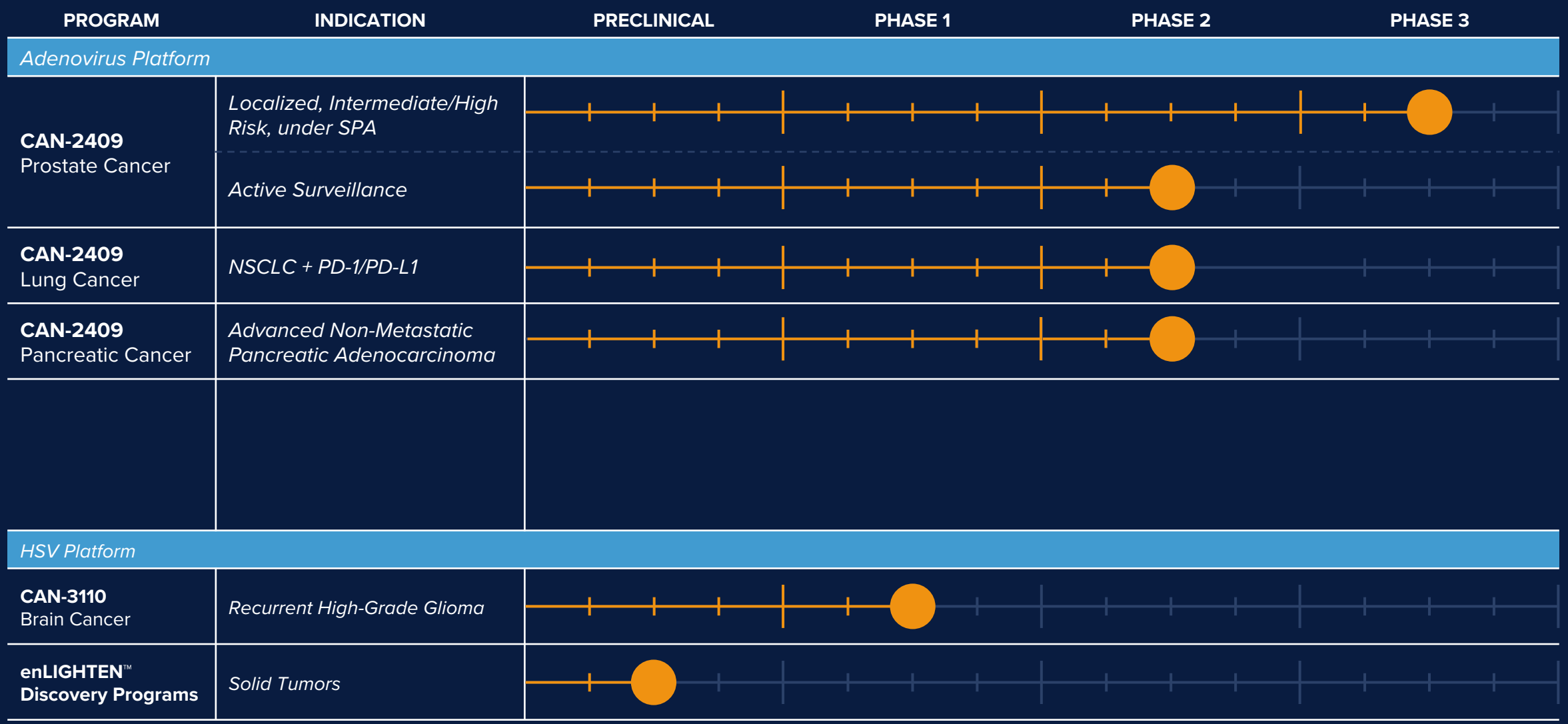
Paul Peter Tak, MD, PhD, FMedSci

Clinical pipeline focused on value creation



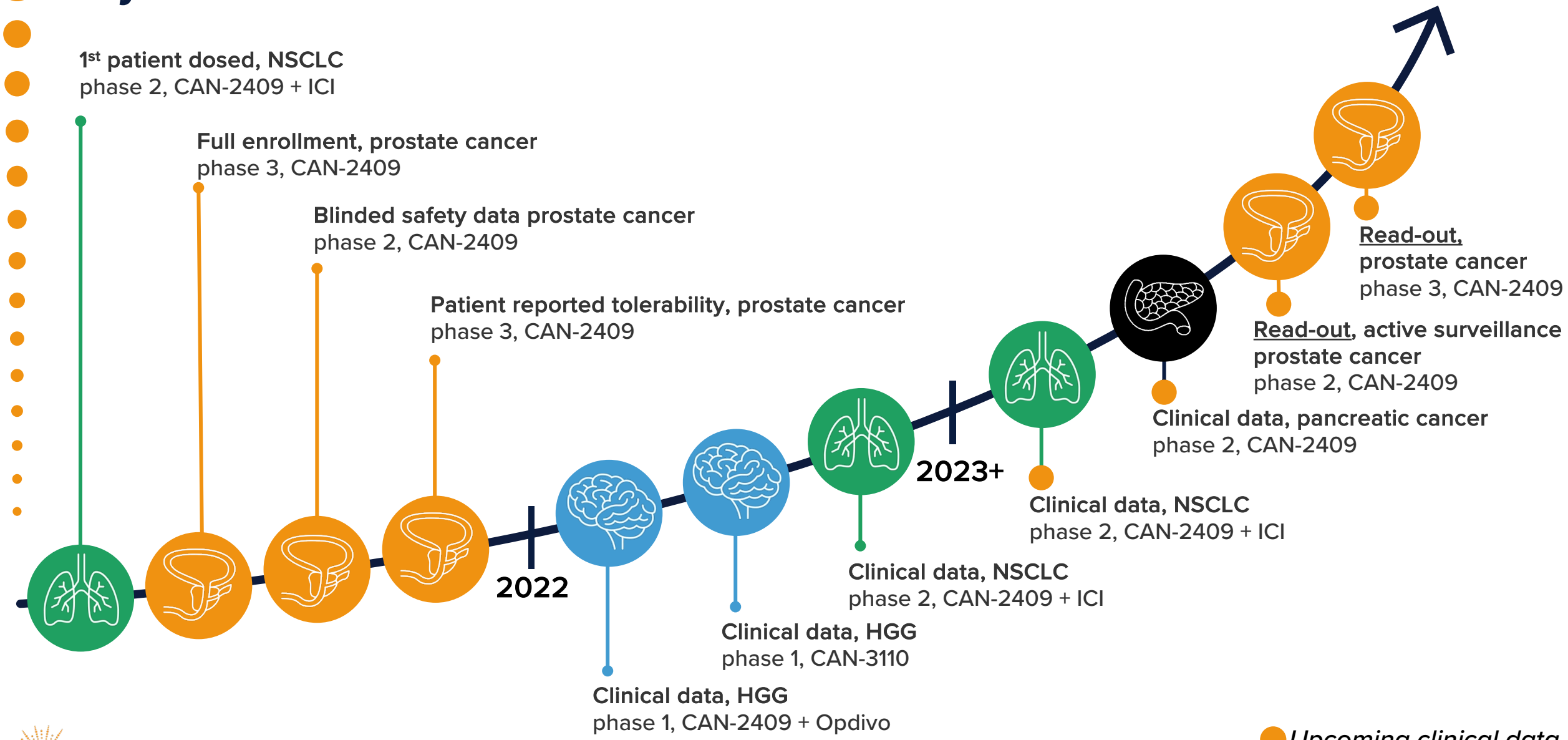
SPA – special protocol assessment

Clinical pipeline focused on value creation



SPA – special protocol assessment

Key achievements and future milestones



Upcoming clinical data

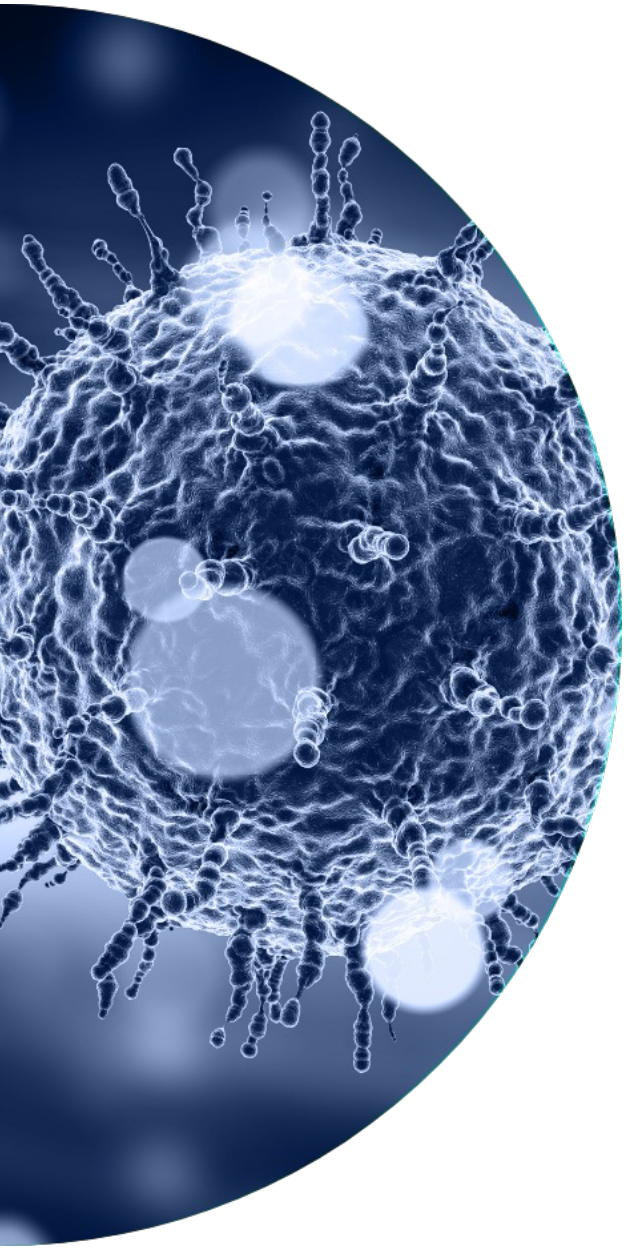
R&D Day Highlights I

- CAN-2409 NSCLC phase 2 data
  - Favorable safety/tolerability profile in comparison to SoC 2L options
  - Consistent induction of local and systemic cytotoxic T cell response
  - Robust evidence of local and systemic anti-tumor activity
  - Additional data in Q3 2023
- CAN-2409 HGG in combination with nivolumab phase 1
  - Combination is well tolerated with no DLT observed and no added toxicity to standard of care
  - mOS appears comparable to historical standard of care outcomes
  - Biomarker analysis demonstrates induction of systemic immune response after single administration
- CAN-2409 pancreas
  - Ongoing phase 2 clinical trial, preliminary data Q4 2023
- CAN-2409 prostate
  - Phase 3 in localized intermediate/high-risk prostate cancer expected to read out in Q4 2024
  - Phase 2 in active surveillance, localized prostate cancer expected to read out in Q4 2023

R&D Day Highlights II

- CAN-3110 recurrent HGG phase 1
  - Treatment with CAN-3110 is well tolerated, with no dose limiting toxicity observed
  - mOS of 11.6 months with a single dose of CAN-3110
  - Persistent HSV-1 antigen and HSV-1 replication consistent with mechanism of action
  - Robust evidence of immune activation
  - Evaluation of repeat dosing of CAN-3110 initiated
- enLIGHTEN
  - Established discovery engine to generate novel viral immunotherapies targeting the TME
- Company
  - Significant unmet need and commercial opportunity for each selected indication
  - In HGG, portfolio decision to prioritize CAN-3110 and not pursue phase 3 clinical trial of CAN-2409
  - Strong scientific support from high-profile Research Advisory Board
  - Cash and cash equivalents of $77.2M as of September 30, 2022, with runway into Q1 2024

Q&A



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Thank You

Candel's Virtual R&D Day | December 6, 2022

NASDAQ: CADL

List of abbreviations

2L	Second line
ADT	Androgen deprivation therapy
AE	Adverse event
BRCA	Breast cancer gene
BTC	Break Through Cancer
CAIX	Hypoxia-regulated carbonic anhydrase IX
CAR-T	Chimeric antigen receptor
CEA	Carcinoembryonic antigen
CIMAC-CIDC	Cancer Immune Monitoring and Analysis Centers
CLDN18.2	Claudin18.2
CTC	Common Terminology Criteria
CTLA-4	Cytotoxic T-lymphocyte–associated antigen 4
DCR	Disease control rate
DLT	Dose-limiting toxicity
DoR	Duration of response
ECOG	Eastern Cooperative Oncology Group
EGFR	Epidermal growth factor
EGJC	Esophagogastric Junction Cancer
F/U	Follow up
FDA	U.S. Food and Drug Administration
GBM	Glioblastoma multiforme
GD2	Disialoganglioside
GFP	Green fluorescent protein
Gr3	CTC Grade 3
GTR	Gross total resection
HER2	Human epidermal growth factor receptor 2
HGG	High-grade glioma
HNSCC	Head and neck squamous cell carcinoma
HPIV	Human parainfluenza virus
HPV	Human papillomavirus
HSV	Herpes simplex virus
ICI	Immune checkpoint inhibitor
IFN	Interferon
JHU	Johns Hopkins University
KPS	Karnofsky Performance Scale
LA	Long axis
LN	Lymph node
MGMT	O6-methylguanine-DNA methyl-transferase
mOS	Median overall survival
mPFS	Median progression free survival
MSKCC	Memorial Sloan Kettering
MSLN	Mesothelin
NCCN	National Comprehensive Cancer Network
NDV	Newcastle Disease Virus
NK cell	Natural killer cell
NSCLC	Non-small cell lung cancer
ORR	Overall response rate
OS	Overall survival
OV	Oncolytic virus
PD1	Progressive disease
PD1	Programmed cell death protein 1
PFS	Progression free survival
PR	Partial response
RNA	Ribonucleic acid
SA	Short axis
SD	Stable disease
SoC	Standard of care
SPA	Special protocol assessment
STR	Subtotal resection
TAAs	Tumor associated antigens
TCR	T-cell receptor
TIL	Tumor-infiltrating lymphocyte
TME	Tumor microenvironment
TMZ	Temozolomide
TNF	Tumor necrosis factor
TRAE	Treatment-related adverse event
VDJ	Variability, diversity, and joining
WT	Wild type

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