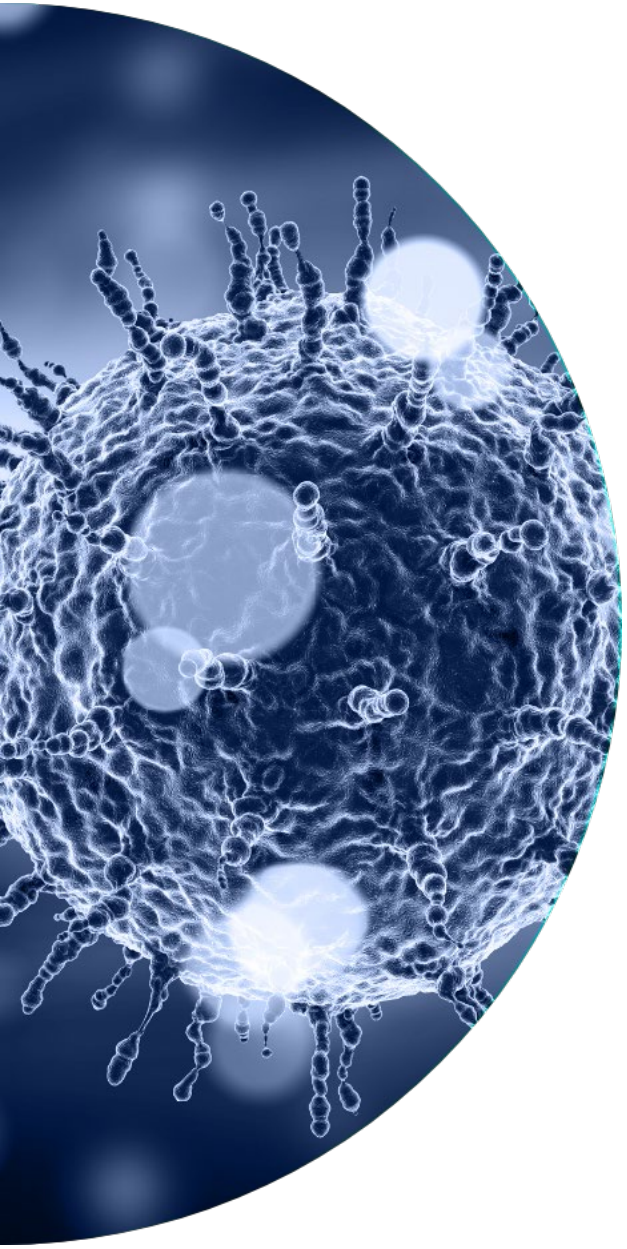


CANDEL THERAPEUTICS

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

Corporate Presentation | January 2025

NASDAQ: CADL

Forward Looking Statements

This Presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. 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; the therapeutic benefit of our programs, including the potential for our programs to extend patient survival; 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; our ability to continue as a going concern, 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; and developments and projections relating to our competitors or our industry. 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 Form 10-Q filed with the Securities and Exchange Commission on November 14, 2024.

Intratumoral immunotherapy: New frontier in cancer care

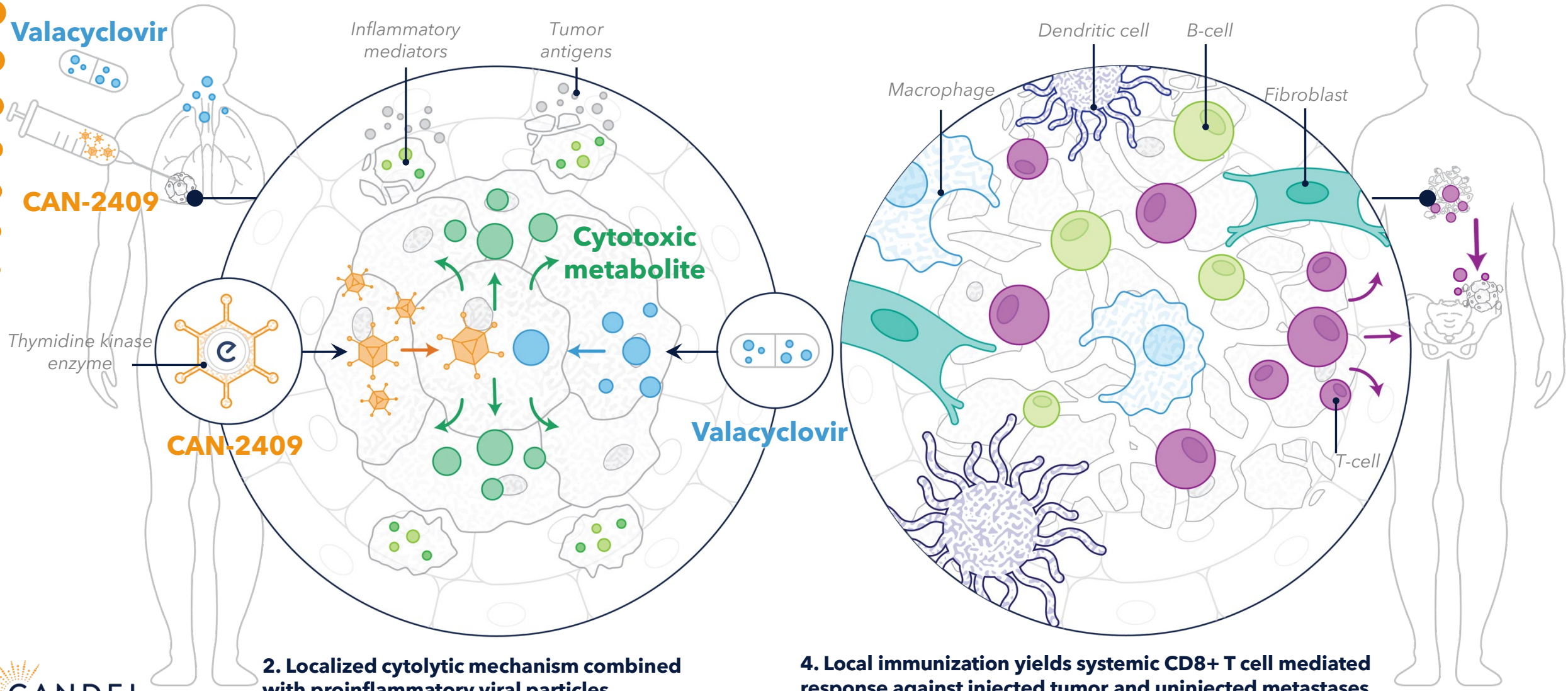
- Replimune ($REPL)
  - Receives Breakthrough Therapy Designation for RP1 and submits RP1 Biologics License Application to the FDA under the Accelerated Approval Pathway
- CG Oncology ($CGON)
  - Encouraging results for cretostimogene in BCG-unresponsive, high-risk non-muscle invasive bladder cancer Brought in $380M in first biotech IPO of 2024
- Johnson & Johnson ($JNJ)
  - Announced the creation of the Interventional Oncology (INTO) unit, focused on developing immunotherapies utilizing intratumoral delivery modalities, with minimum toxicity and increased efficacy
  - Recently initiated phase 1 clinical trial of JNJ-87704916, an oncolytic virus administered intratumorally, in relapsed or refractory metastatic NSCLC
- Candel Therapeutics ($CADL)
  - CAN-2409: Off-the-shelf pan-solid tumor therapy, individualized anti-cancer immune response
  - CAN-3110: Oncolytic HSV-1 designed for tumor-specific replication
  - enLIGHTEN™ Discovery Platform: Systematic, iterative HSV-based discovery platform leveraging human biology and advanced analytics

CAN-2409: Mechanism of action

Please visit https://vimeo.com/822135123

1. CAN-2409 locally administered combined with oral prodrug

3. CAN-2409 induces CD8+ cytotoxic T cells



2. Localized cytolytic mechanism combined with proinflammatory viral particles

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

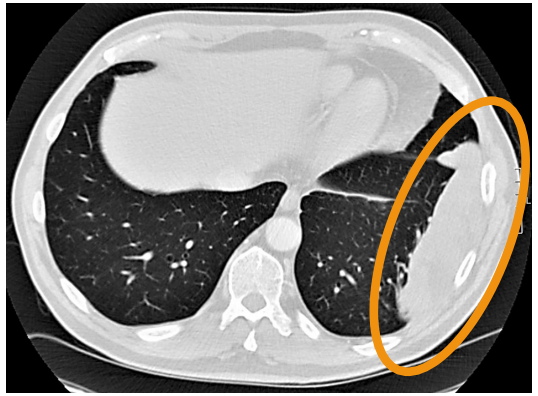
CANDEL THERAPEUTICS

CAN-2409 is an investigational product and its mechanism of action in humans has not been definitively established. This depiction of the CAN-2409 mechanism of action and the MoA video linked above are based on preclinical data and observations in clinical studies to date

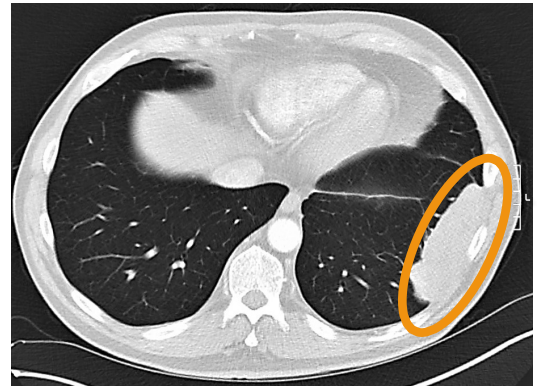
CAN-2409: Replication-defective adenoviral gene construct engineered for in situ vaccination against pan-solid tumors

- > 1,000 patients dosed
- Fast Track Designation in prostate cancer, non-small cell lung cancer (NSCLC), and pancreatic ductal adenocarcinoma (PDAC)
- Randomized controlled phase 3 clinical trial (n=745) in localized, intermediate-to-high-risk prostate cancer achieved primary endpoint (disease-free survival)
  - Conducted under Special Protocol Assessment (SPA)
- Proof of concept in patients with NSCLC and PDAC

- Monotherapy activity of CAN-2409 in NSCLC patient: Nearly 50% decrease in tumor volume in 3 weeks



Day 0
Tumor Dimensions: 148 x 40 x 82 mm
(10^{12} vp dose)



Day 22
Tumor Dimensions: 100 x 34 x 75 mm

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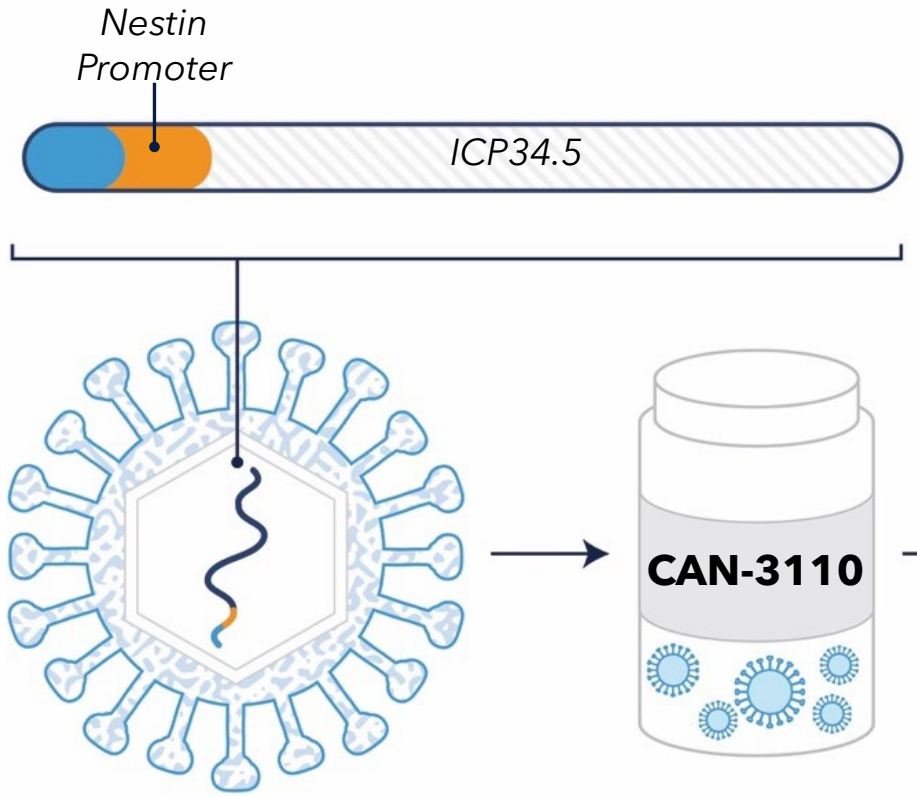
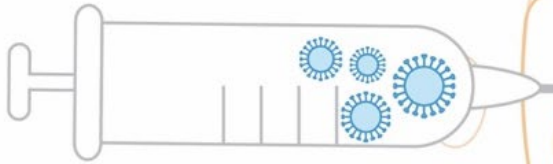
CAN-3110: Mechanism of action

Please visit https://vimeo.com/822133681





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

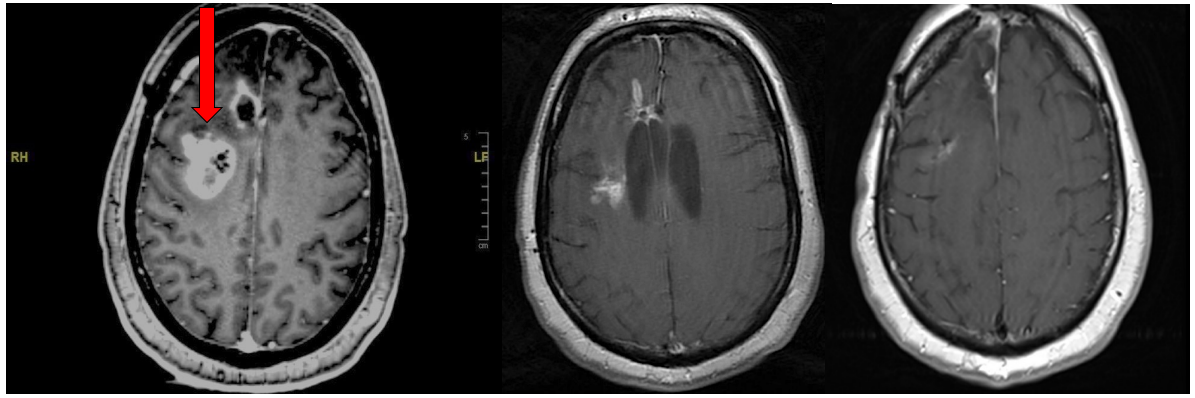
Virus expands in Nestin expressing tumor cells, causing oncolytic activity

CAN-3110 is an investigational product and its mechanism of action in humans has not been definitively established. This depiction of the CAN-3110 mechanism of action and the MoA video linked above are based on preclinical data and observations in clinical studies to date

CAN-3110: Replication-competent HSV-1 engineered to enhance selective killing of cancer cells while sparing healthy neighboring cells

- Proof of concept in patients with recurrent-high grade glioma (mostly glioblastoma)
- > 55 patients dosed
- Data published in Nature*
- Fast Track Designation and Orphan Drug Designation in recurrent high-grade glioma
- First cohort of patients treated with multiple injections of CAN-3110: 3/6 still alive after > 1 year (ongoing) (IOVC, Oct 2024)
- Antitumor activity of CAN-3110 in preclinical models of melanoma (SITC, Nov 2024)

Monotherapy activity of CAN-3110 in recurrent high-grade glioma: Clinical effect on injected tumor and uninjected tumor



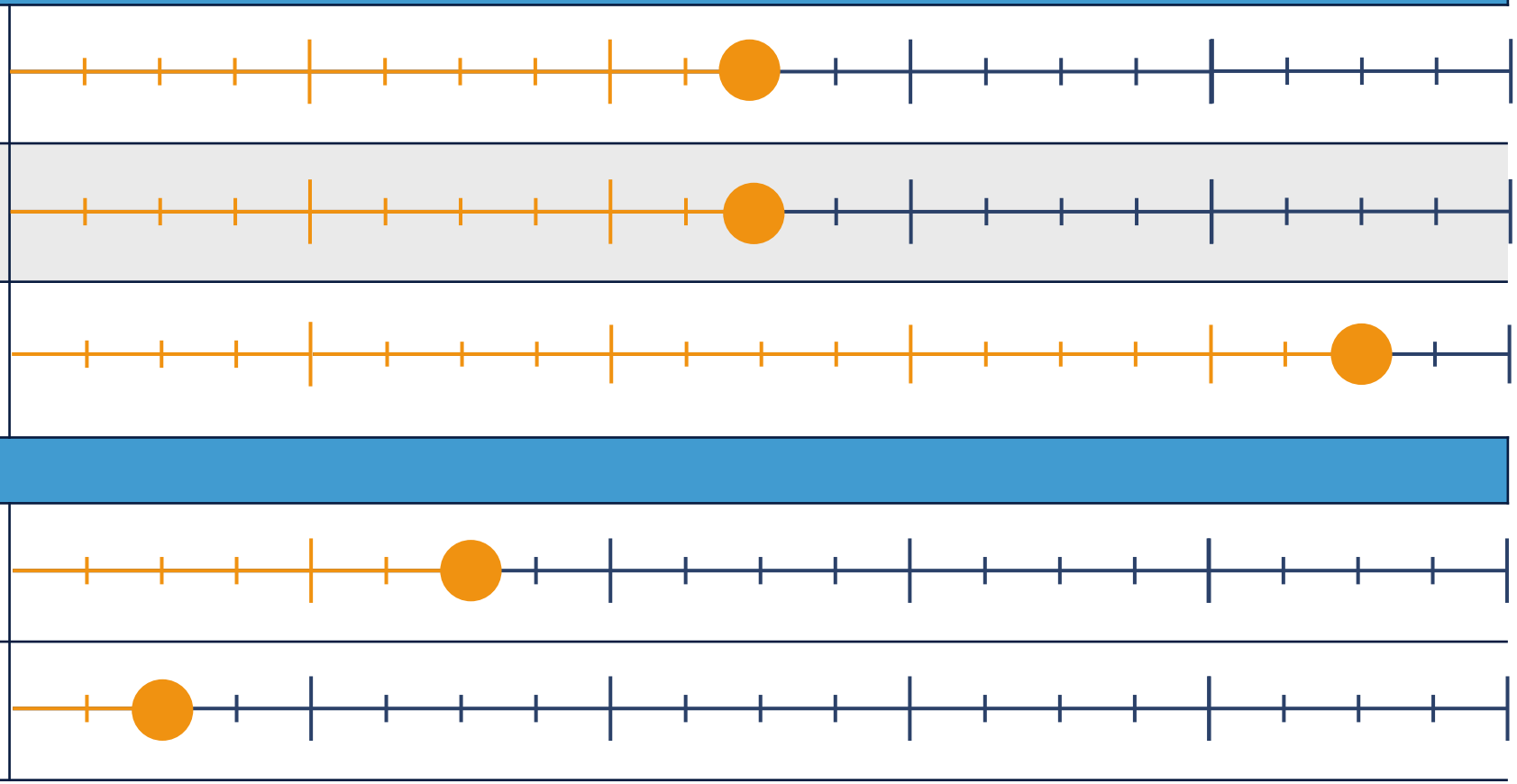
Day 0 | **Day 111**
Patient back to work | **Day 280**

CANDEL THERAPEUTICS

*Ling AL et al. Nature 2023;623:157-166

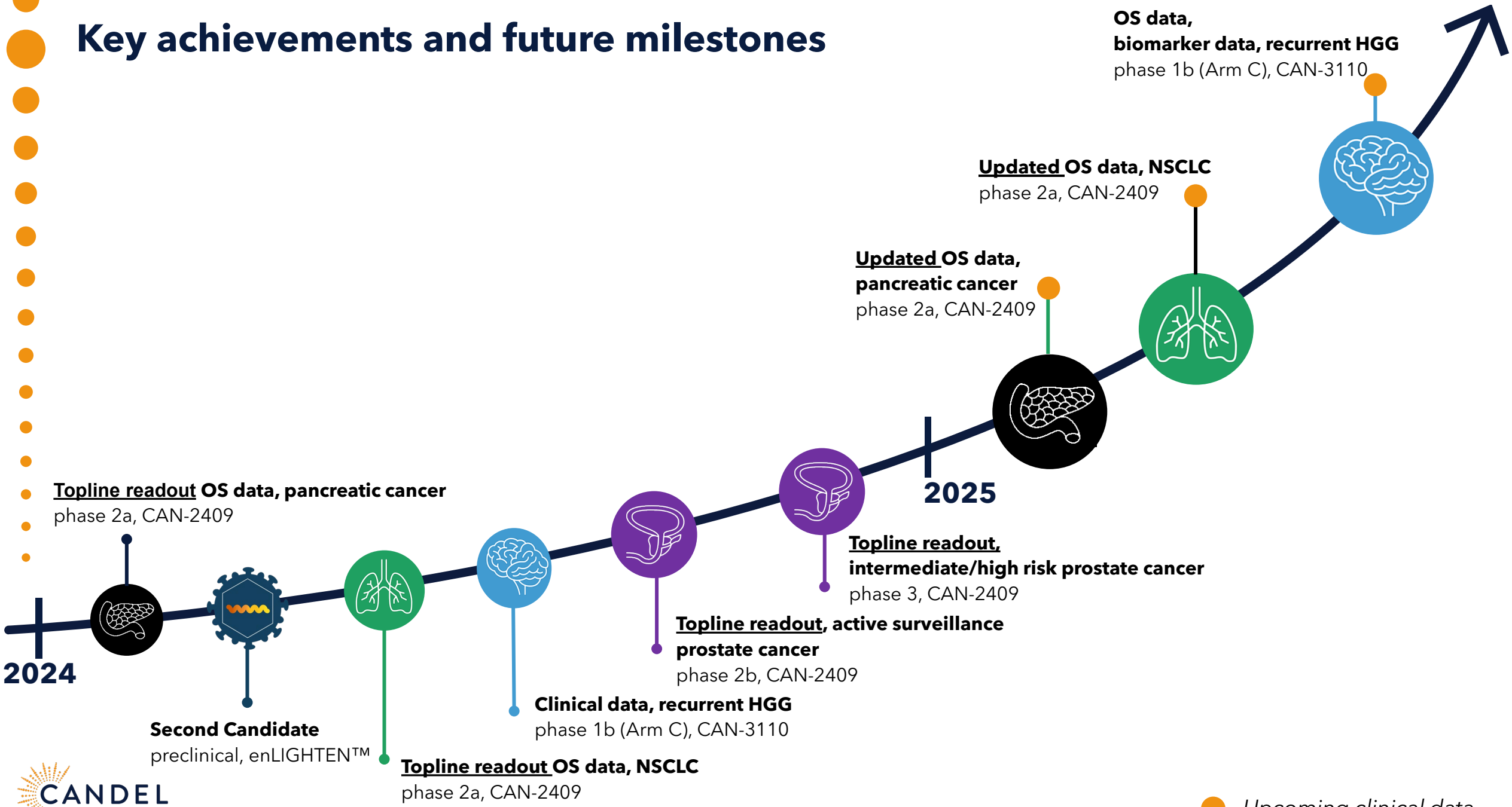
Pipeline focused on value creation

PROGRAM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	BLA Readiness
Adenovirus Platform						
CAN-2409 Pancreatic Cancer	*Borderline Resectable Pancreatic Adenocarcinoma, Fast Track Designation (FDA)*					
CAN-2409 Lung Cancer	*NSCLC + PD-1/PD-(L)1, Fast Track Designation (FDA)*					
CAN-2409 Prostate Cancer	*Localized, Intermediate/High Risk, Fast Track Designation (FDA), Special Protocol Assessment (FDA)*					
HSV Platform						
CAN-3110 Brain Cancer	*Recurrent High-Grade Glioma, Fast Track Designation (FDA)*					
enLIGHTEN™ Discovery Programs	*Solid Tumors*					



CANDEL THERAPEUTICS

Key achievements and future milestones



CANDEL THERAPEUTICS

Upcoming clinical data

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

Paul Peter Tak, MD, PhD, FMedSci

President & Chief Executive Officer

gsk · Flagship Pioneering · sitryx · Citryll

Francesca Barone, MD, PhD

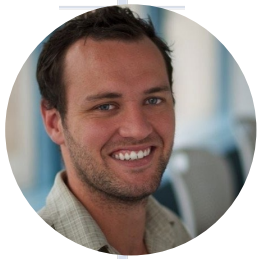
Chief Scientific Officer

Kintai Therapeutics · University of Birmingham

Seshu Tyagarajan, PhD, RAC

Chief Technical and Development Officer

Novartis · Roche · Biogen · Lilly



Charles Schoch, MBA, MSA, CPA

Interim Chief Financial Officer

Corbus Pharmaceuticals · pwc

Garrett Nichols, MD, MS

Chief Medical Officer

gsk · ViiV Healthcare · Chimerix · istari Oncology

Susan Stewart, JD

Chief Regulatory Officer

Tokai Medical Products · genzyme · Abbott

CANDEL THERAPEUTICS

Research Advisory Board of premier thought leaders

James Allison, Ph.D.
Chair of the Department of Immunology
MD Anderson Cancer Center
Director of the Parker Institute for Cancer Research
2018 Nobel Recipient

Edward Benz, M.D.
President and CEO Emeritus
Dana-Farber Cancer Institute

Henry Brem, M.D.
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Professor of Neurosurgery
Johns Hopkins University

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Yale Cancer Center

Philip Kantoff, M.D.
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Memorial Sloan Kettering Cancer Center

Gary Nabel, M.D., Ph.D.
Chief Innovation Officer of OPKO and
President/CEO of ModeX Therapeutics
Former CSO Sanofi

Padmanee Sharma, M.D., Ph.D.
Professor of Genitourinary Medical Oncology and Immunology
MD Anderson Cancer Center

CANDEL THERAPEUTICS

Candel at a glance

- CAN-2409: Off-the-shelf pan-solid tumor therapy, individualized anti-cancer immune response
  - Positive phase 3 randomized controlled clinical trial in localized, intermediate-to-high-risk prostate cancer
  - Proof of concept in PDAC and NSCLC
  - Fast Track Designation in NSCLC, pancreatic cancer, and prostate cancer
  - "Pipeline in a product" strategy advancing multiple programs in several large indications
  - Upcoming catalysts:
    - Final survival data in PDAC (Q1 2025)
    - Final survival and biomarker data in NSCLC (Q1 2025)

- CAN-3110: Oncolytic HSV-1 designed for tumor-specific replication
  - Proof of concept in patients with recurrent high-grade glioma published in *Nature*
  - Fast Track Designation, Orphan Drug Designation
  - Opportunity for creation of "pipeline in a product" by expansion into indications beyond brain cancers
  - Overall survival and immunological biomarker data, evaluating repeat dosing regimen of CAN-3110 (Q4 2025)

- Corporate Highlights
  - Very experienced Executive Team and strong scientific support from high-profile Research Advisory Board
  - Cash and cash equivalents of $102.9 million as of Dec 31, 2024 (unaudited) ; expected runway into Q1 2027
  - IP protection: CAN-2409 (2034, method of use); CAN-3110 (2036, composition of matter); 12 years data exclusivity
  - Low-cost manufacturing

CAN-2409

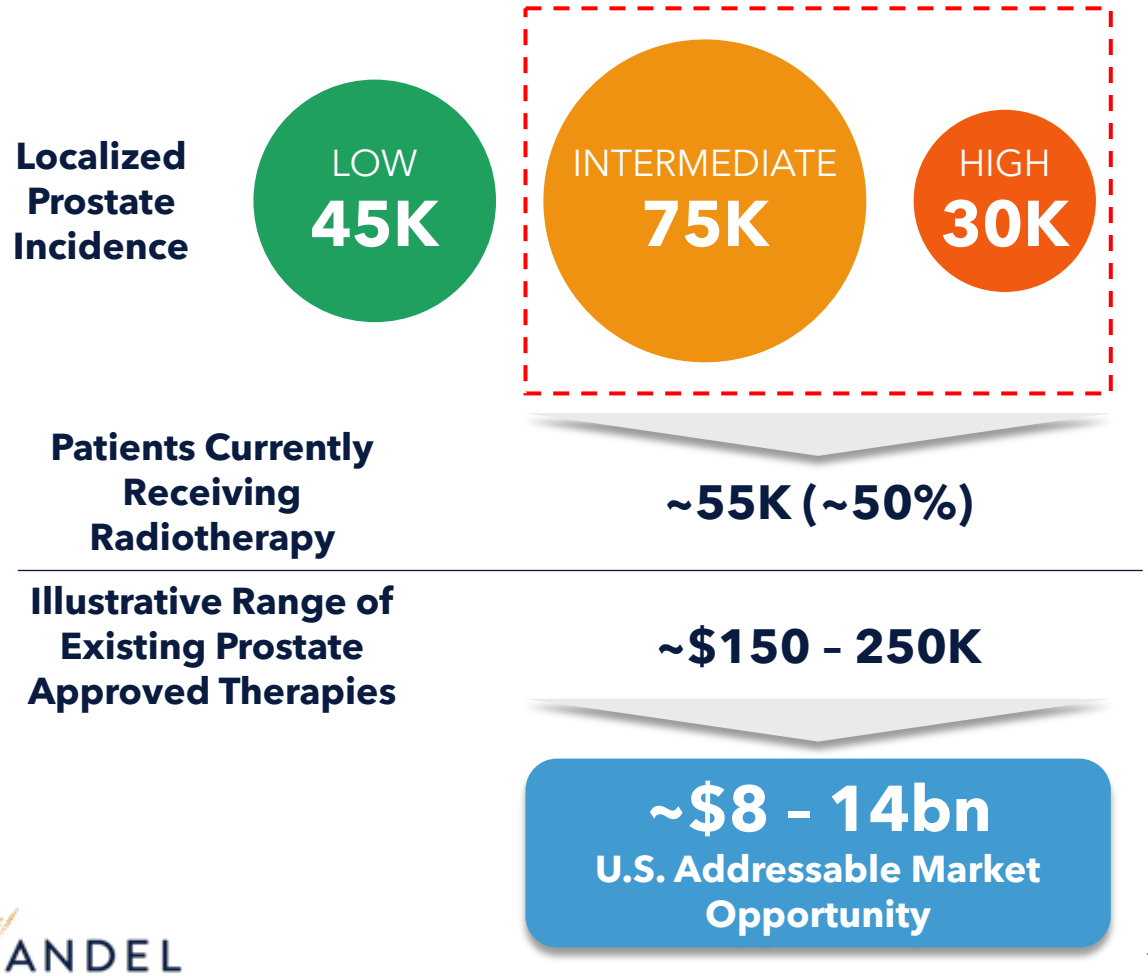
Off-the-shelf therapy, individualized cancer response

CANDEL THERAPEUTICS

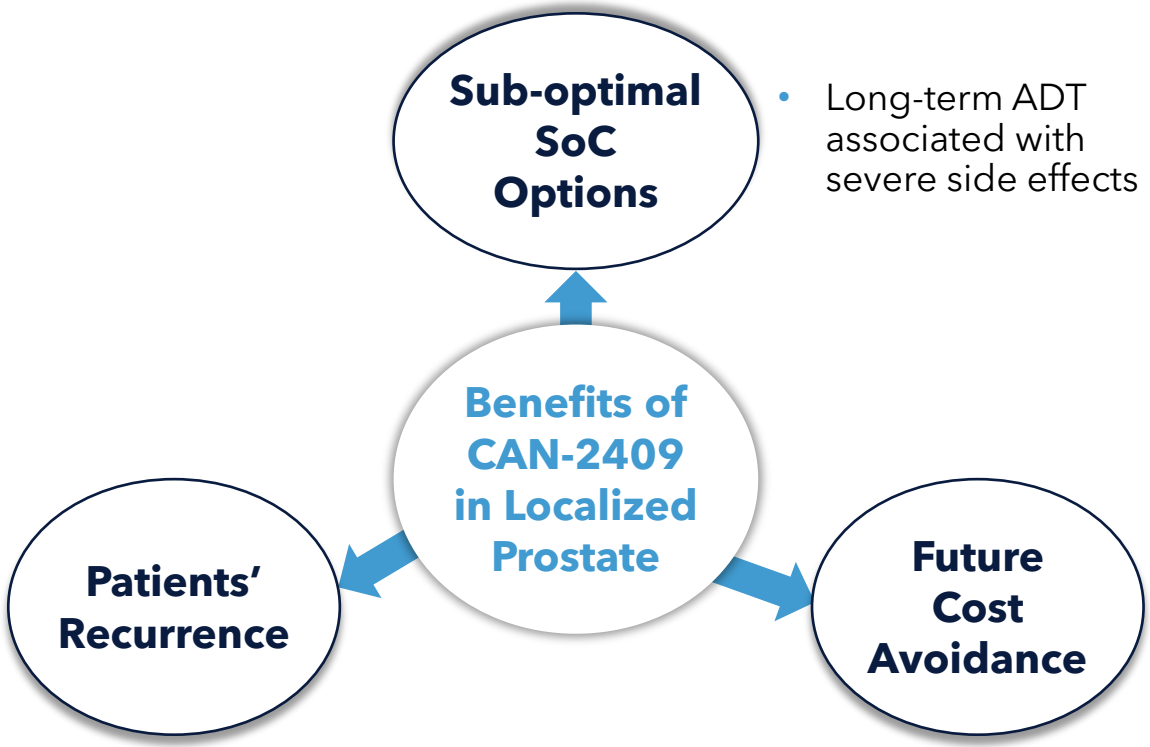
Candel is addressing a potential $10bn+ market with clear unmet need

The prostate cancer opportunity for CAN-2409

Substantial U.S. Addressable Market Opportunity



Clear Unmet Need for Patients



- Long-term ADT associated with severe side effects

- Recurrence in ~30% of patients post-radiotherapy, with ~50% high-risk patients
- Use of ADT or chemotherapy

- Costs of side effects related to ADT

Source: Globe Life Sciences (January 2021).

Target product profile for CAN-2409 in intermediate / high risk, localized prostate cancer

"Off-the-shelf" immunotherapy product designed to elicit a broad, potent immune response against solid tumors

Planned Indication	• Planned indication in newly diagnosed localized prostate cancer in patients with intermediate- to high-risk disease in conjunction with radiotherapy to prevent prostate cancer recurrence – NCCN(1) defined intermediate (at least one of: PSA 10 – 20ng/mL, Gleason score of 7, stage T2b/T2c) or patients with a single high-risk characteristic (one of: PSA >20ng/mL, Gleason score 8 – 10, stage T3a)
Administration	• Administered in combination with SoC external beam radiotherapy (EBRT) +/- short course of ADT (<6 months) • 3 courses of intraprostatic injections: 2mL total volume (2-6 weeks apart) – Each administration is performed in outpatient clinic (~20 minutes) – 14 days of valacyclovir orally following each injection course

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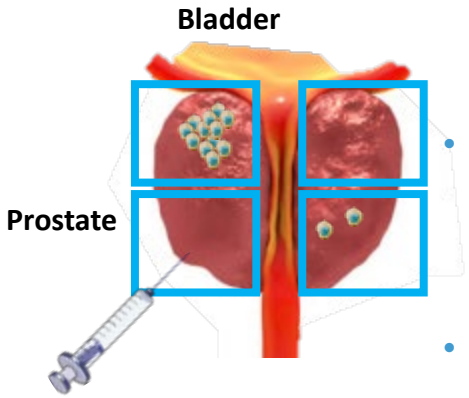
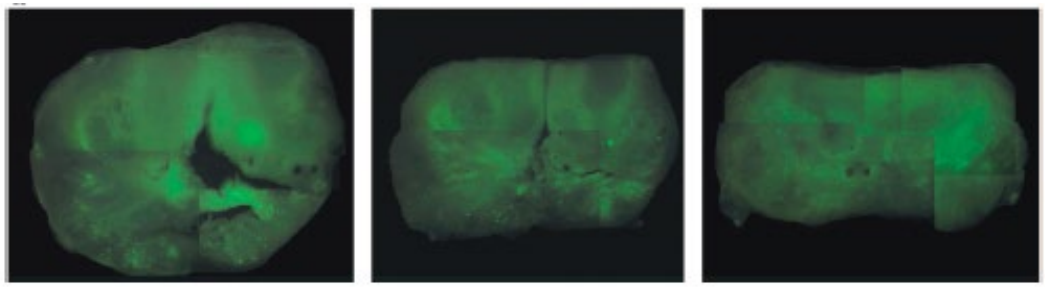
(1) National Comprehensive Cancer Network.

CAN-2409 is delivered in a routine and well-tolerated procedure

Standard urologic injection procedure



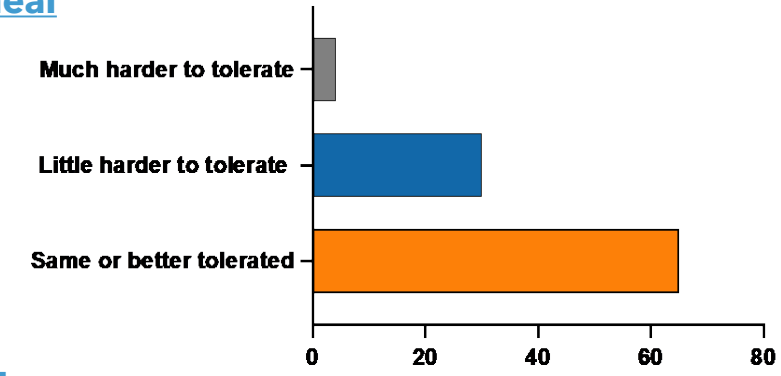
- Routine outpatient procedure (15 min, outpatient setting) performed by urologists or radiation oncologists
- Ultrasound guided injection (transrectal or transperineal) to 4 sites of prostate, one apical and one basal in each lobe
- A total volume of 2ml, 0.5ml in each of 4 quadrants of the prostate using a 10-22 G needle



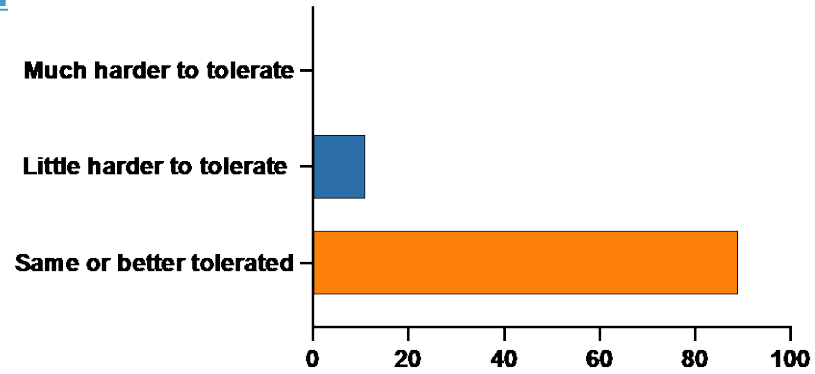
Distribution analysis of fluorescently labeled adenoviral vector in freshly resected prostate, demonstrating homogeneous distribution throughout the organ after 4 injections of virus (0.5ml) in each prostate quadrant.

Patient questionnaire substudy (n=32)[1]
"How did you tolerate the study procedure as compared to a prostate biopsy?"

Transperineal



Transrectal



> 2000 intraprostatic injections in phase 2/3 studies (40% transperineal; 56% transrectal; 4% not reported)

(1) Aguilar L. 28th Annual Prostate Cancer Foundation, Scientific Retreat, October 2021

Phase 3 clinical trial of CAN-2409 in patients with newly diagnosed, intermediate / high risk, localized prostate cancer

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

NCT01436968

N=745
Fully enrolled
Newly diagnosed, intermediate / high risk, localized prostate cancer

2:1
Randomization

CAN-2409 + Valacyclovir
(3 injection courses + radiotherapy, with or without short course ADT)

Placebo + Valacyclovir
(3 injection courses + radiotherapy, with or without short course ADT)

Primary Endpoints

- Disease-free survival (time to cancer recurrence or death due to any cause)

Key secondary endpoints

- PSA freedom from biochemical failure[1]
- Prostate cancer specific outcomes[2]
- Overall survival[3]

- *Randomization stratified by NCCN[4] risk group and planned short course ADT*

Conducted under agreement with FDA under Special Protocol Assessment

1) *Biochemical failure is defined using PSA nadir plus 2ng/ml definition.*
2) *Defined as time from date of randomization to prostate cancer recurrence or prostate cancer-related death.*
3) *Defined as time from date of randomization to date of death (all causes).*
4) *National Comprehensive Cancer Network.*

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Disease-free survival: primary endpoint to capture treatment effect in early localized prostate cancer

Disease-free survival (DFS)

Date of randomization to date of recurrence proven by biopsy, clinical or radiographic evidence of local or regional failure, distant metastases, or death from any cause

- Local failure: includes increase in tumor size by 50%, reappearance of palpable tumor or biopsy revealing adenocarcinoma of the prostate at least 2 years after randomization
- Regional failure: clinical recurrence with radiographic evidence of tumor in the pelvis
- Distant metastases: clinical recurrence with radiographic evidence of disease beyond the pelvis

- ***Endpoint validated by FDA with Special Protocol Assessment confirmed in 2019***
- ***Extensive market research with payers and key external experts confirmed that estimated DFS improvements would be clinically relevant***

Demographics/baseline characteristics of randomized patients

ITT population (N=745)	CAN-2409 + prodrug (N=496)	Placebo + prodrug (N=249)	Total (N=745)
Median age (yrs)	69	68	69
Race, n(%)			
White/Caucasian	385 (77.6)	206 (82.7)	591 (79.3)
Black/African American	93 (18.8)	28 (11.2)	121 (16.2)
Asian	3 (0.6)	1 (0.4)	4 (0.5)
Native Hawaiian or Pacific Islander	0 (0)	2 (0.8)	2 (0.3)
American Indian or Alaskan Native	1 (0.2)	1 (0.4)	2 (0.3)
Not reported	14 (2.8)	11 (4.4)	25 (3.4)
Ethnicity, n(%)			
Hispanic or Latino	37 (7.5)	34 (13.7)	71 (9.5)
Not Hispanic or Latino	377 (76.0)	175 (70.3)	552 (74.1)
Not reported	82 (16.5)	40 (16.1)	122 (16.4)
NCCN risk group, n(%)			
Intermediate	422 (85.1)	213 (85.5)	635 (85.2)
High	74 (14.9)	36 (14.5)	110 (14.8)
PSA ng/ml			
Median	6.815	6.500	6.700
Range	0.99 - 52.90	0.83 -63.30	0.83-63.30
Gleason score, n(%)			
< 7	19 (3.8)	5 (2.0)	24 (3.2)
7	417 (84.1)	217 (87.1)	634 (85.1)
> 7	60 (12.1)	27 (10.8)	87 (11.7)
ADT stratification, n(%)			
Planned ADT	244 (49.2)	122 (49.0)	366 (49.1)
No planned ADT	252 (50.8)	127 (51.0)	379 (50.9)

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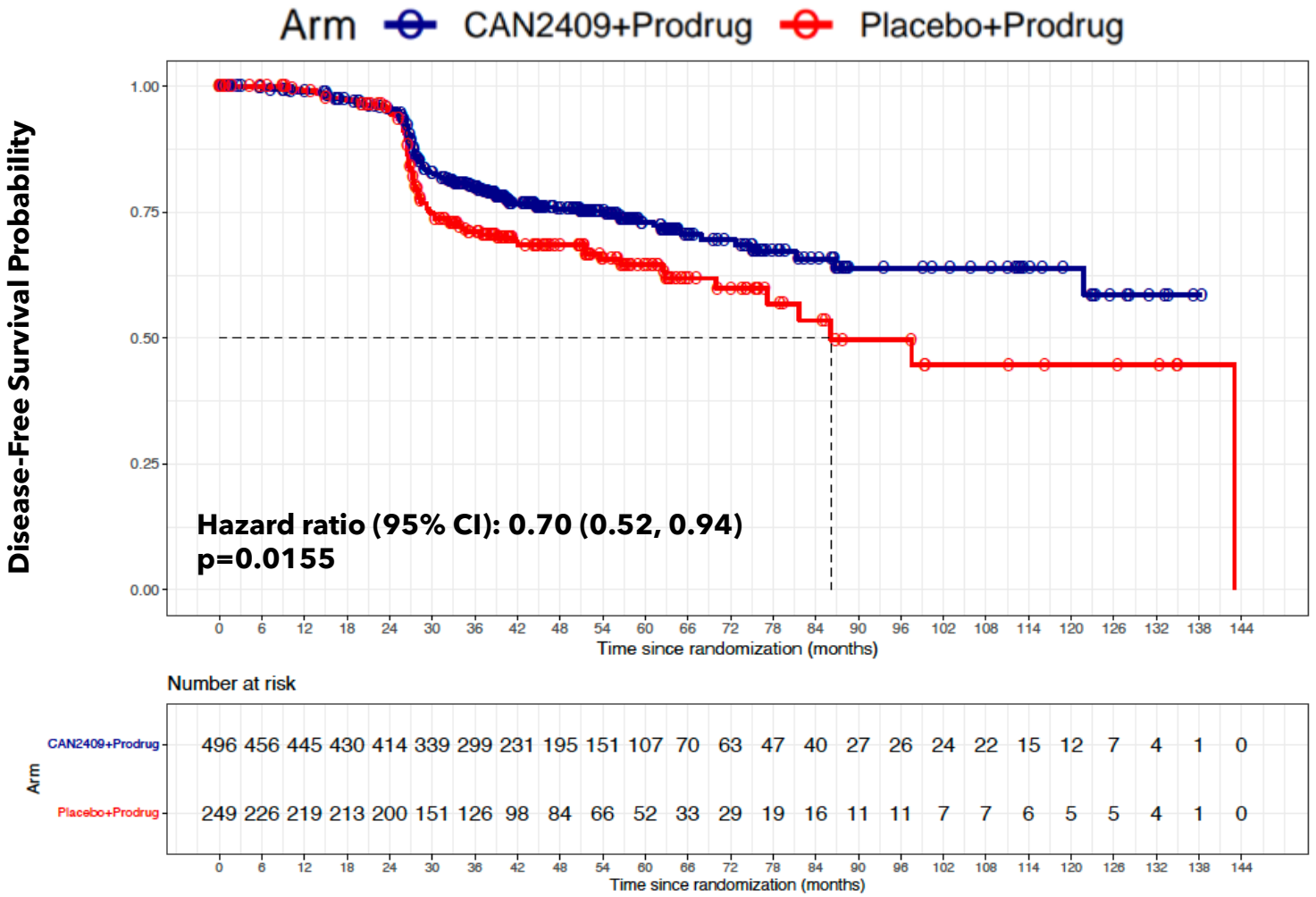
CAN-2409 significantly improved DFS in newly diagnosed, intermediate/high-risk prostate cancer (ITT, N=745): 30% decrease in disease recurrence



Note: Disease-free survival (DFS) represents time to cancer recurrence or death due to any cause

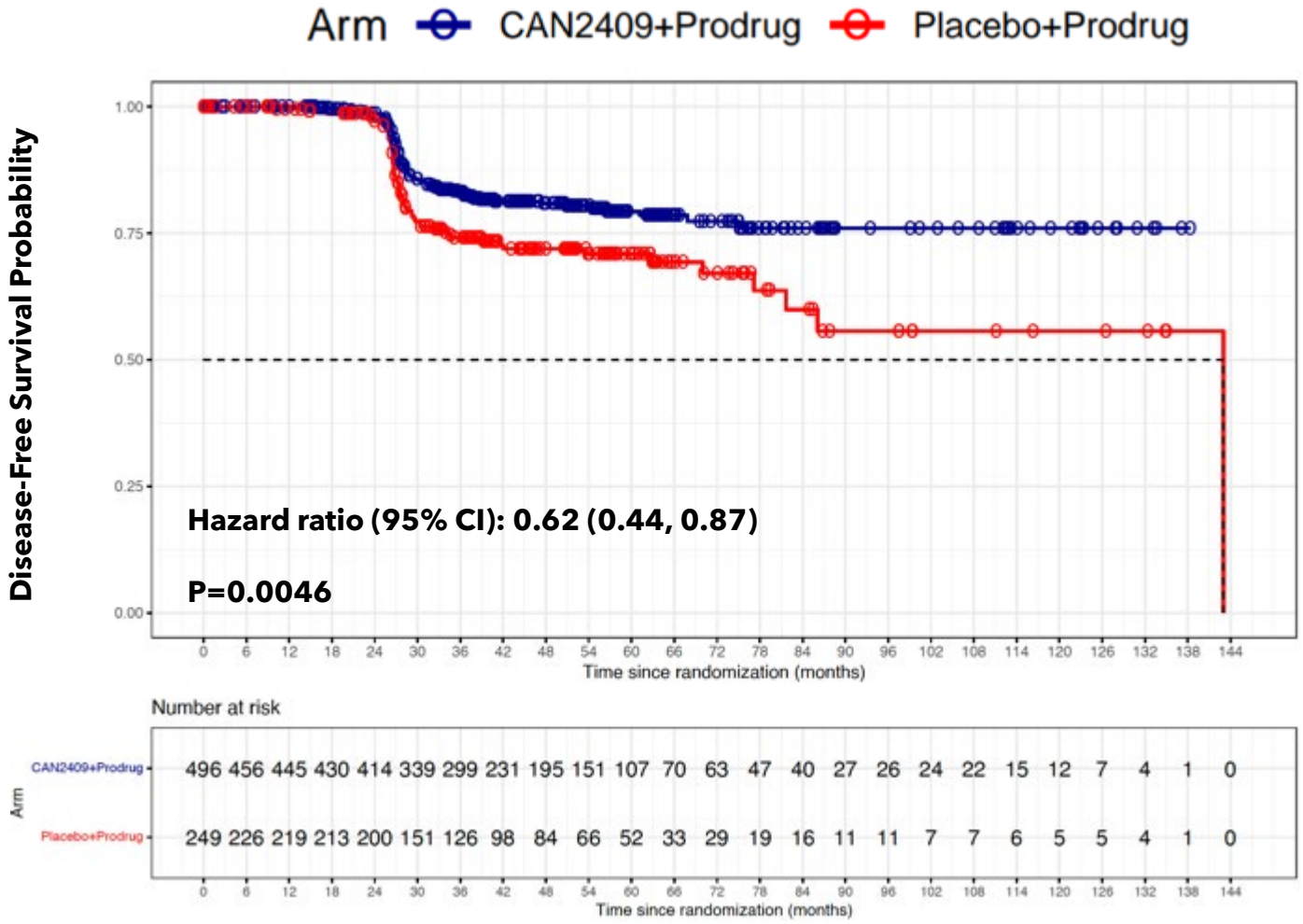
CAN-2409 improves DFS in key subgroups

	Subgroups	Number of patients	Hazard Ratio (95% CI)
	ITT:ITT	745	
Race	RACE:BLACK OR AFRICAN AMERICAN	121	
	RACE:UNKNOWN	25	
	RACE:WHITE	591	
Age	AGEGR1:< 65	190	
	AGEGR1:>= 65	555	
Ethnicity	ETHNIC:HISPANIC OR LATINO	71	
	ETHNIC:NOT HISPANIC OR LATINO	552	
	ETHNIC:UNKNOWN	122	
Severity	NCCN:High	110	
	NCCN:Intermediate	635	
ADT Usage	Actual ADT:No	358	
	Actual ADT:Yes	334	
Severity & ADT Usage	NCCN/Actual ADT:High, Yes	94	
	NCCN/Actual ADT:Intermediate, No	349	
	NCCN/Actual ADT:Intermediate, Yes	240	

← *FAVORS CAN-2409*

Descriptive, exploratory analysis; not statistically powered to detect differences between subgroups

CAN-2409 significantly improves prostate-specific outcomes (ITT, N=745): 38% risk reduction



(1) As per Globe Life Sciences (January 2021). Note: Disease-free survival (DFS) represents time to cancer recurrence or death due to any cause

CAN-2409: other key secondary endpoints

- Significant increase in the proportion of patients achieving a prostate-specific antigen (PSA) nadir of <0.2 ng/ml in the treatment arm compared to the placebo
  - 67.1% vs. 58.6%, respectively (p=0.0164)
- Freedom from PSA failure numerically lower in CAN-2409 treatment arm (HR 0.84)
- As expected*, overall survival was similar by treatment arm at 10 years
  - Only 2 deaths due to prostate cancer over 10+ years (one CAN-2409, one placebo)
  - 50 patients died due to other causes, unrelated to treatment

*Hamdy FC et al. N Engl J Med 2023;388:1547-1558

CAN-2409 significantly improves the rate of pathological complete response in 2 year biopsies compared to the placebo control arm

Pathological complete response was observed in 80.4% of the biopsies available at 2 years in the CAN-2409 arm compared to 63.6% in the placebo group

- 451 post-treatment biopsies centrally reviewed by at least 2 blinded independent readers
- 313 post-treatment biopsies available for review for the 2-year histologic analysis

	CAN-2409	Placebo
Total	214	99
Negative	172 (80.4%)	63 (63.6%)
Positive	42 (19.6%)	36 (36.4%)

Difference between arms chi-square test p= 0.0015

Biopsies available at 22-26 months from end of radiation date

CAN-2409 in combination with SoC radiation +/-ADT was generally well tolerated

Treatment related AEs >5% in either arm

Preferred term	CAN-2409+prodrug (N=479)	Placebo+prodrug (N=232)	Total (N=711)
Chills	160 (33.4)	20 (8.6)	180 (25.3)
Influenza-like illness	146 (30.5)	32 (13.8)	178 (25.0)
Fever	120 (25.1)	9 (3.9)	129 (18.1)
Fatigue	87 (18.2)	35 (15.1)	122 (17.2)
Urinary frequency	58 (12.1)	34 (14.7)	92 (12.9)
Nausea	53 (11.1)	19 (8.2)	72 (10.1)
Headache	45 (9.4)	12 (5.2)	57 (8.0)
Diarrhoea	30 (6.3)	18 (7.8)	48 (6.8)
Malaise	28 (5.8)	5 (2.2)	33 (4.6)
Vomiting	26 (5.4)	3 (1.3)	29 (4.1)
Urinary urgency	19 (4.0)	16 (6.9)	35 (4.9)
Urinary tract pain	18 (3.8)	14 (6.0)	32 (4.5)

Chills, fever, flu-like symptoms were commonly mild to moderate and self limited

Incidence of treatment related SAEs lower on CAN-2409

- 1.7% on CAN-2409 + SoC
- 2.2% on placebo + SoC

Incidence of SAEs lower on CAN-2409 arm

- 5.8% on CAN-2409 + SoC
- 7.3% on placebo + SoC

Incidence of treatment discontinuation due to AEs lower on CAN-2409 arm

- 5.4% on CAN-2409 + SoC
- 6.0% on placebo + SoC

Phase 3 clinical trial of CAN-2409 in intermediate-to-high risk, localized prostate cancer: primary endpoint achieved

Trial Design	• 745-patient randomized trial with treatment arm + placebo arm, focused on disease-free survival (DFS) primary endpoint and multiple secondary endpoints
Primary Endpoint	• Statistically significant and clinically meaningful improvement in DFS for CAN-2409 plus radiation therapy vs. radiation therapy alone. Hazard ratio 0.7, p=0.0155 in the intent to treat (ITT) analysis; median follow up time of 50.3 months
Secondary and Supplemental Endpoints	• Significant effect on prostate cancer-specific outcomes. Hazard ratio 0.62, p=0.0046 • Significant increase in the proportion of patients achieving a prostate-specific antigen (PSA) nadir of <0.2 ng/ml in the treatment arm compared to the placebo. 67.1% vs. 58.6%, p=0.0164 • Central, blinded evaluation of post-treatment biopsies: pathological complete response rate of 80.4% in the CAN-2409 treatment arm vs. 63.6% in the placebo control arm 2-yrs post-rdiation (p=0.0015)
Safety	• Compelling safety profile, with lower incidence of serious adverse events (SAEs) and treatment-related SAEs in active arm vs. control (5.8% vs. 7.3% and 1.7% vs. 2.2%, respectively)

CAN-2409: Pancreatic ductal adenocarcinoma opportunity

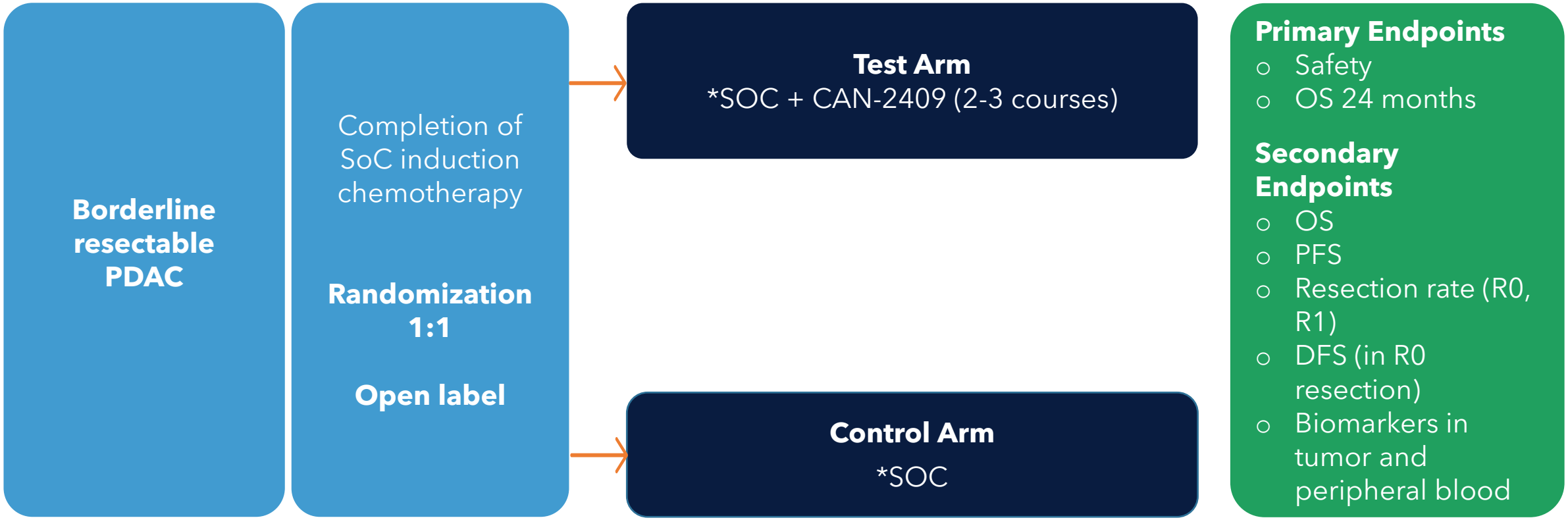
Incidence of pancreatic ductal adenocarcinoma in the US by risk level[1]

- Limited available treatment options for patients suffering from pancreatic cancer beyond resection when possible and chemotherapy
- Borderline resectable disease: median overall survival <18 months (with neoadjuvant chemoradiation and resection)[2]
- Metastatic disease: median overall survival ~11 months (with FOLFIRINOX)[3]
- Significant opportunity to improve response rates by teaching the immune system how to recognize cancer cells
- Pancreatic cancer therapy global market was estimated at $800 M in 2022 and is expected to grow to $3.5 B by 2028[4]

[1] *Park W et al. JAMA 2021;326:851–862*
[2] *Versteijne E et al. J Clin Onc 2020; 38:1763-1773*
[3] *Conroy T et al. NEJM 2011; 364:1817–1825*
[4] *Source: EvaluatePharma, accessed May 2023*

Randomized phase 2 clinical trial of CAN-2409 in borderline resectable pancreatic ductal adenocarcinoma (PDAC)

Reflecting v5/v6 of protocol (data collected to date reflects this design)



*SOC= Chemoradiation + Resection

Funded in part by NIH Grant R44 CA203336

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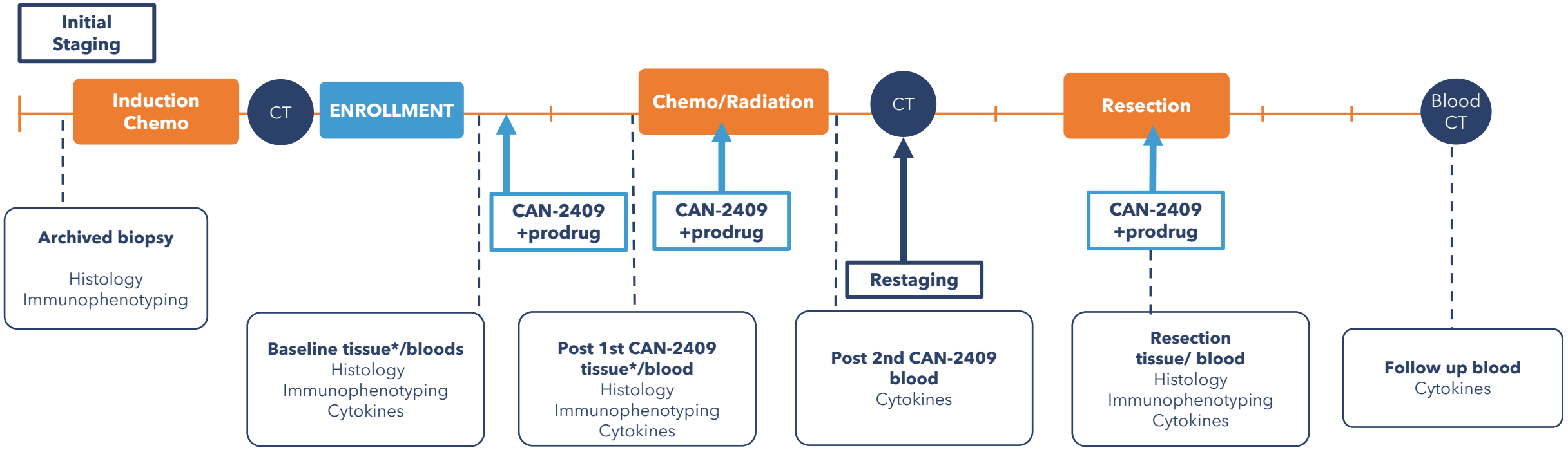
SOC treatment timeline in non-metastatic PDAC and timing of CAN-2409 injections

Through v5/v6 of protocol (data collected to date reflects this design)



Induction Chemo → At least two months of induction chemotherapy (e.g. 4 cycles of FOLFIRINOX based or 2 cycles of gemcitabine/nab-paclitaxel),

Chemo/Radiation → Such as capecitabine, 5-FU or gemcitabine concurrent with radiation over 3-5.5 weeks

*** If feasible**

Prodrug = valacyclovir or IV acyclovir

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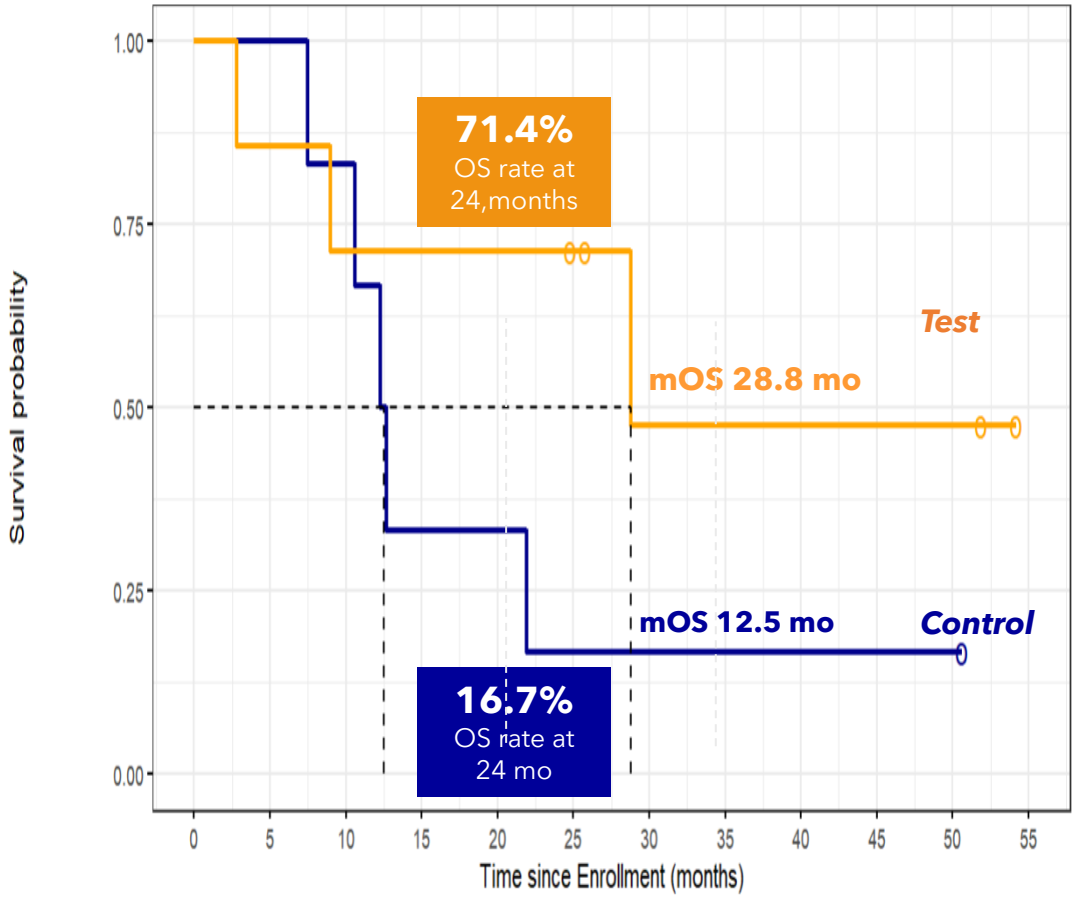
Overall survival in borderline resectable PDAC patients

Data as of 3/29/2024

PCN	Arm	Surgical result	pStage #	Date of last follow-up	OS mo (enrollment)	OS mo (diagnosis)	Alive (A) / Dead (D)
2022PIN	C	Unresected	IV	6/16/2020	10.6	17.2	D
2072PIN	C	Unresected	N/A*	11/13/2020	12.7	52.4	D
2092POS	C	Unresected	N/A*	7/23/2020	7.5	10.3	D
2052PLB	C	Resected	IIA	10/3/2020	12.3	16.9	D
2152PLB	C	Resected	IIB	9/25/2022	21.9	26.8	D
2112PLB	C	Resected	N/A*	3/28/2024	50.6+	54.8+	A
2102PLB	T	Unresected	IV	9/7/2020	9.0	13.7	D
2162PLB	T	Unresected	N/A*	6/9/2021	2.8	8.3	D
2042PIN	T	Unresected	IV	2/22/2024	54.2+	61.7+	A
2172PIN	T	Unresected	N/A*	1/14/2024	28.8	34.7	D
2082PLB	T	Resected	IA	2/26/2024	51.9+	57.0+	A
2182PLB	T	Resected	IB	3/04/2024	25.8+	32.3+	A
2192PIN	T	Resected	IA	3/20/2024	24.8+	30.3+	A

*Refer to slide with details on surgical status
pathologic tumor stage at resection

Time since enrollment

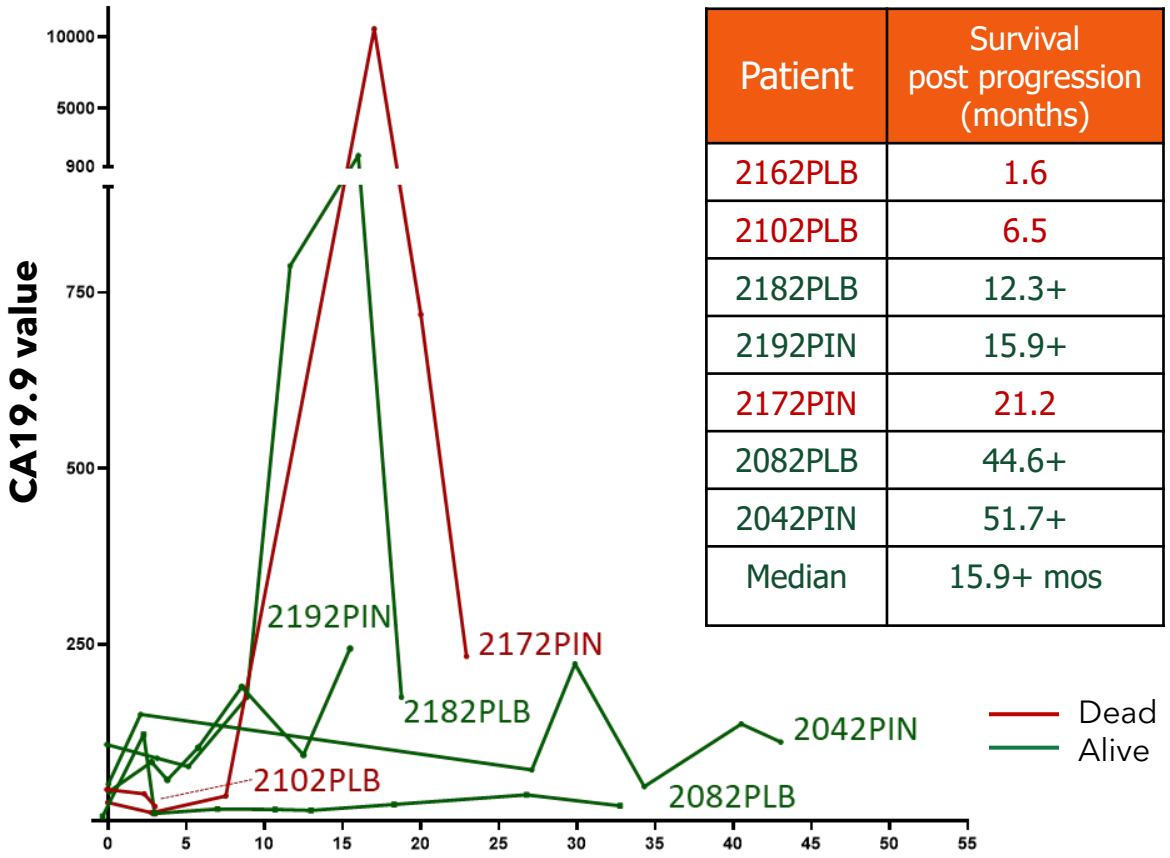


Censored = alive, still under follow-up

Arm: **C** = Control; **T** = Test (CAN-2409+prodrug)

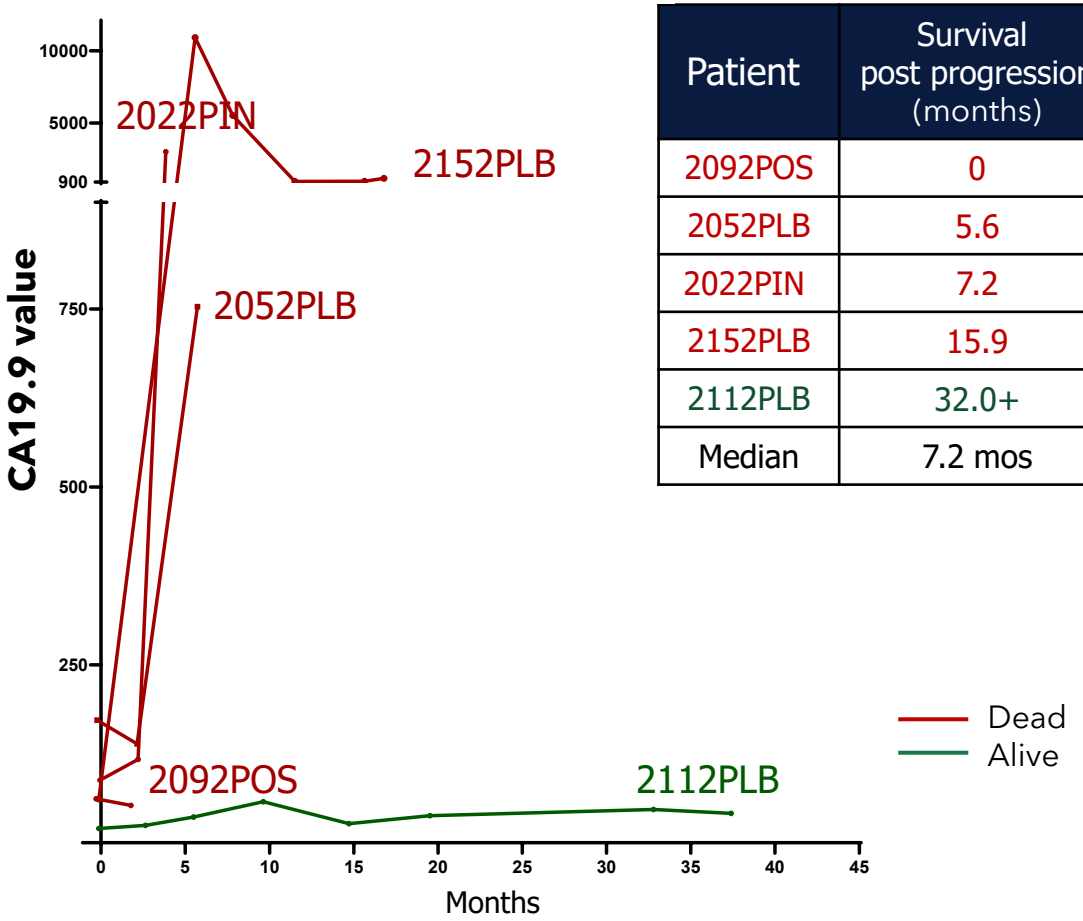
CA19-9 biomarker response associated with ongoing survival in CAN-2409 arm, but not in control arm, in patients with progressive disease

CAN-2409 arm



Patient	Survival post progression (months)
2162PLB	1.6
2102PLB	6.5
2182PLB	12.3+
2192PIN	15.9+
2172PIN	21.2
2082PLB	44.6+
2042PIN	51.7+
Median	15.9+ mos

Control arm

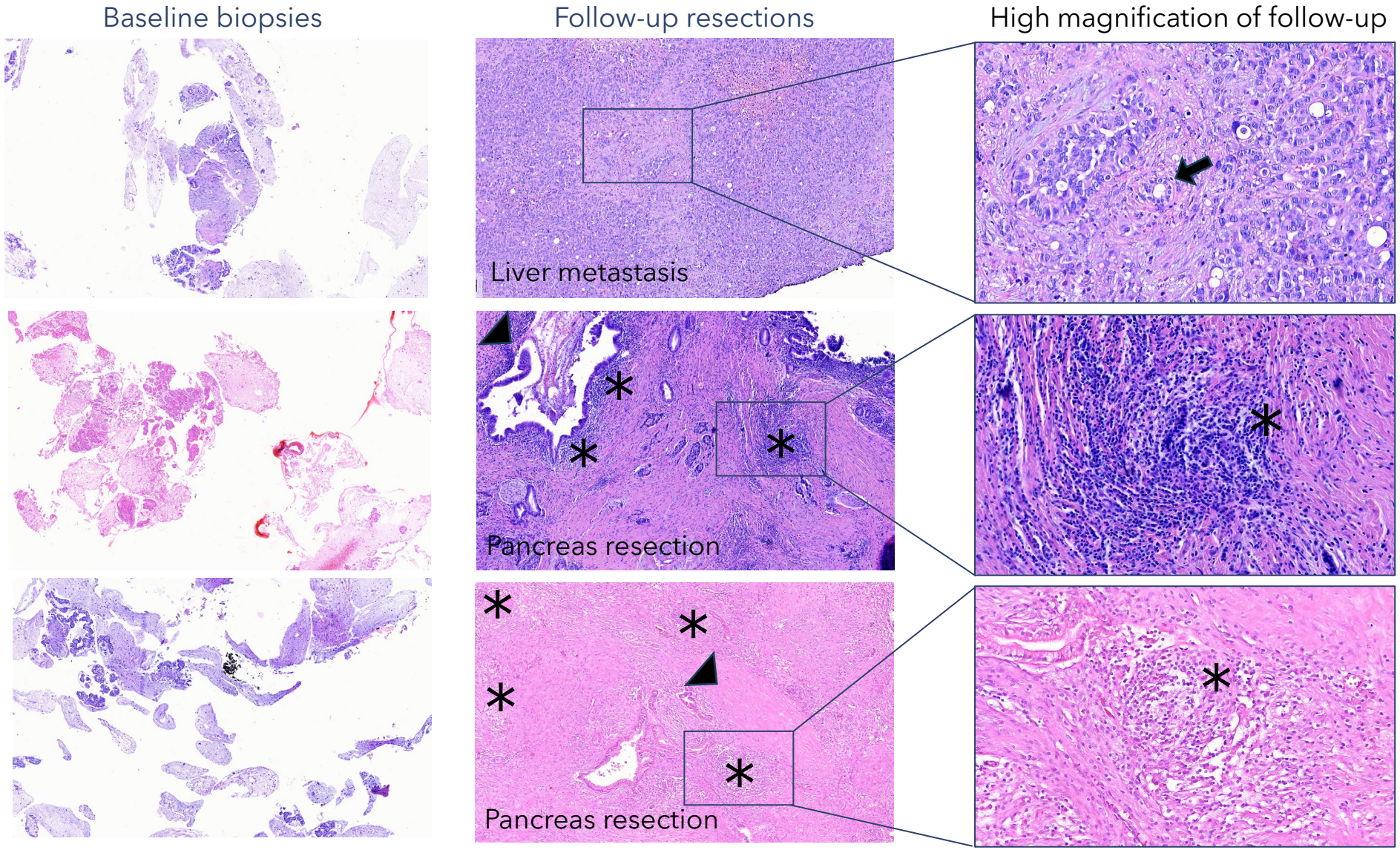


Patient	Survival post progression (months)
2092POS	0
2052PLB	5.6
2022PIN	7.2
2152PLB	15.9
2112PLB	32.0+
Median	7.2 mos

- **CAN-2409 arm cases 2172, 2182 recurred, but CA19.9 (marker of tumor burden) responded to salvage chemo with ongoing survival**
- **Control arm cases 2022, 2152, 2052 recurred, but CA19.9 did not respond to salvage chemo and patients died**

CANDEL THERAPEUTICS

CAN-2409 induces formation of dense lymphocyte aggregates, disruption of tumor structures, and necrosis in PDAC



Arrows: cancer cell. Arrowheads: disrupted tumor structures and tumor necrosis. Asterisk: immune cells

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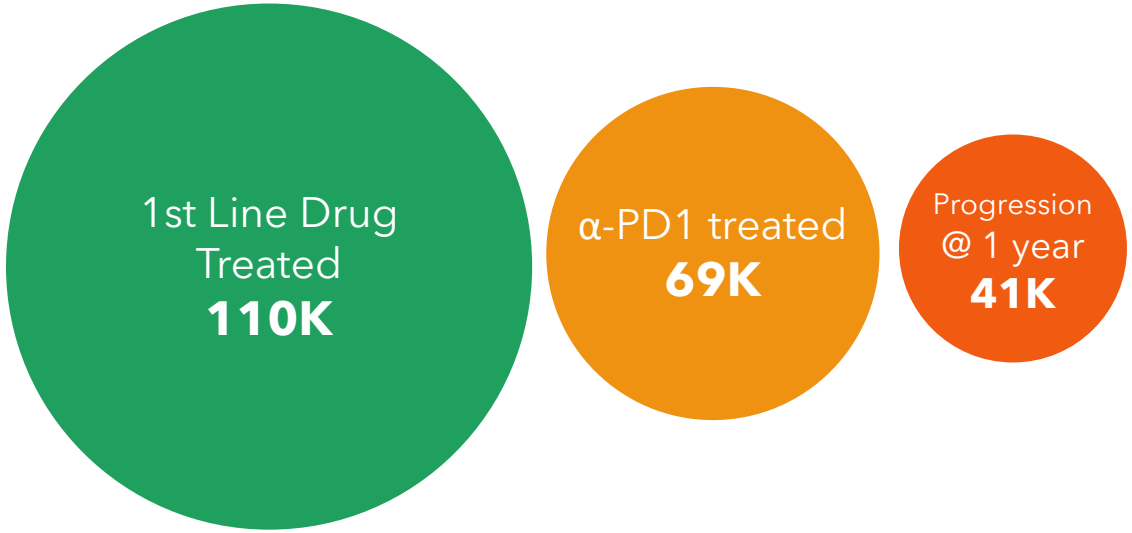
CANDEL THERAPEUTICS

Encouraging safety data, clinical activity and immunological changes after CAN-2409 in pancreatic cancer

- Notable improvements in estimated median overall survival of 28.8 months after experimental treatment with CAN-2409 versus only 12.5 months in control group
- At 24 months, survival rate was 71.4% in CAN-2409 treated patients versus only 16.7% in the control group after chemoradiation. At 36 months, estimated survival was 47.6% in the CAN-2409 group versus 16.7% in the control group
- Multiple injections of CAN-2409 were generally well tolerated, with no dose-limiting toxicities and no cases of pancreatitis
- In patients with progressive disease, there was a CA19-9 and survival response to salvage chemotherapy in the CAN-2409 arm but not in control arm
- CAN-2409 activates the immune response in the pancreatic tumor and peripheral blood

CAN-2409: Non-small cell lung cancer opportunity

Incident advanced NSCLC in the US[1]



- Lung cancer is the most commonly diagnosed cancer in the US with NSCLC representing over 80% of all lung cancer diagnoses[2]
- Majority of NSCLC patients without actionable mutations are treated with immune checkpoint inhibitors (ICI) as 1st line treatment
- After one year of ICI treatment, 60% of anti-PD1 treated patients will have progressive disease[3]
  - In ICI inadequate responders with SoC docetaxel[4]
    - **Median overall survival (mOS) <12 months**
- Significant opportunity to improve response to ICIs by teaching the immune system how to recognize the cancer cells
- NSCLC cancer therapy global market was estimated at $32B in 2023 and is expected to grow to $52B by 2028[5]

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

Upside to this target population as ~25% of patients treated in the 2L setting receive an anti-PD-1/L1

[1] SEER Cancer Statistics Factsheets, accessed Mar 2024
[2] American Cancer Society Website, accessed Mar 2024
[3] Gandi L et al. NEJM 2018; 378:2078-92
[4] Reckamp K et al. J Clin Onc 2022;40:2295-2306
[5] EvaluatePharma, accessed May 2023

Ongoing phase 2 clinical trial of CAN-2409 + continued ICI in stage III/IV NSCLC patients with an inadequate response to ICI

Stage III/IV non-resectable NSCLC with inadequate response to ICI

N=80
(40 per cohort)

Cohort 1
Stable Disease (after >18 wks ICI)

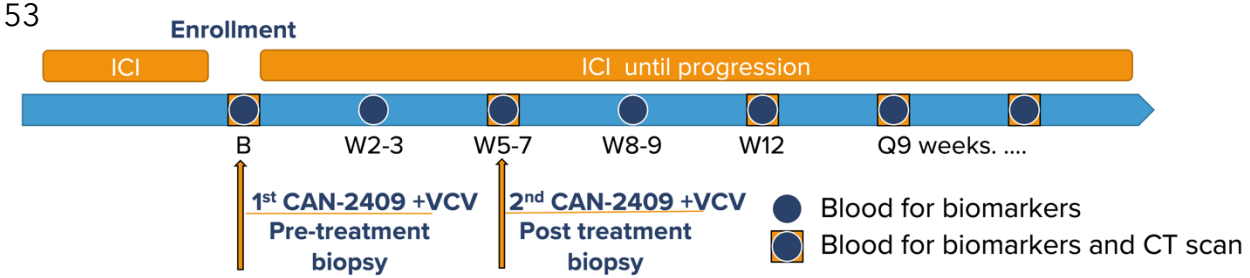
Cohort 2
Progressive Disease (after >18 wks ICI)

CAN-2409 and valacyclovir (2 courses) with continued standard of care: Anti-PD-1/PD-L1 +/- chemotherapy

Primary Endpoints
- Response by RECIST criteria
- Disease control rate

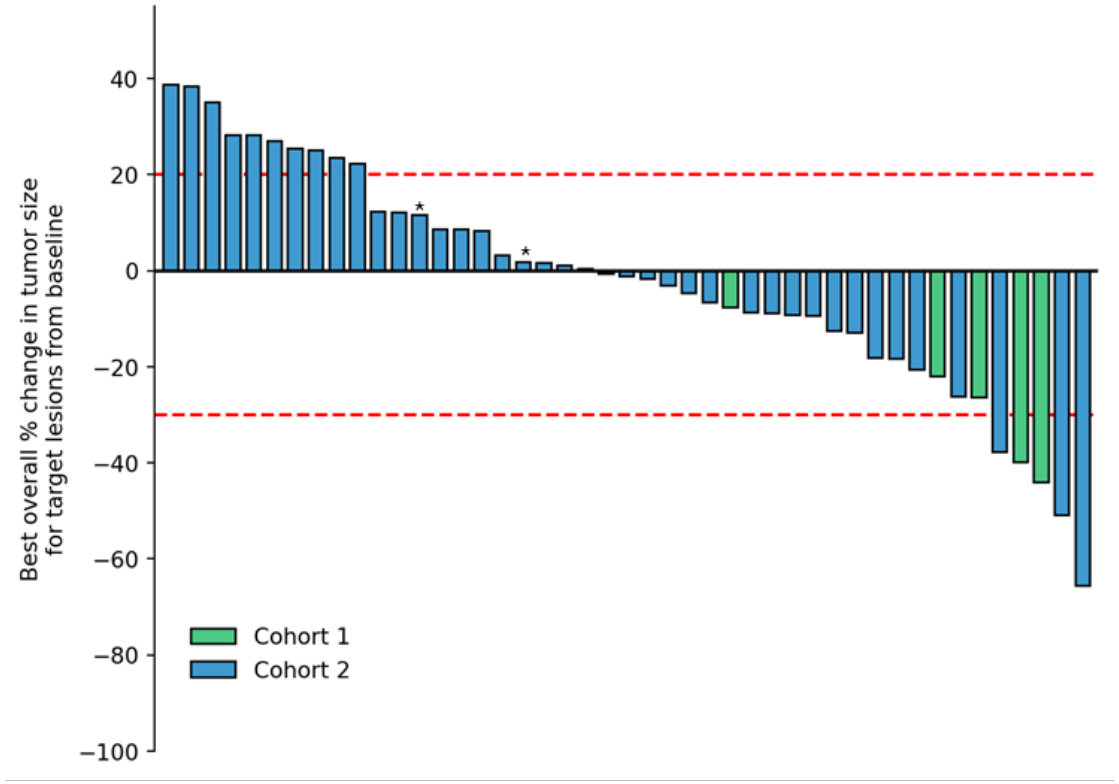
Secondary Endpoints
- Progression-free survival
- Overall survival
- Quality of life
- Immunological biomarkers
- Response by iRECIST and itRECIST (Exploratory)

NCT04495153



Evidence that CAN-2409 can control disease

Most patients entering clinical trial with progressive disease despite ICI treatment achieved disease control after administration of CAN-2409



Cohort	PR	SD	PD	N	ORR	DCR	DoR for PR[2]	SD duration[2]
1	2	3	0	5	40%	100%	11.6 mo (10.4+ to 12.8+)	6.2 mo (2.8+ to 16.7)
2	3	25	12	40	8%	70%	6.1 mo (2.8 to 16.3)	3.8 mo (0+ to 14.5)
Total	5	28	12	45	13%	N/A		

[1] An additional evaluable patient in Cohort 2 had pending central read at time of data snapshot
[2] Median (range) for DoR and SD duration
+ Indicates response was ongoing at date of last follow up

* PD due to presence of new lesion

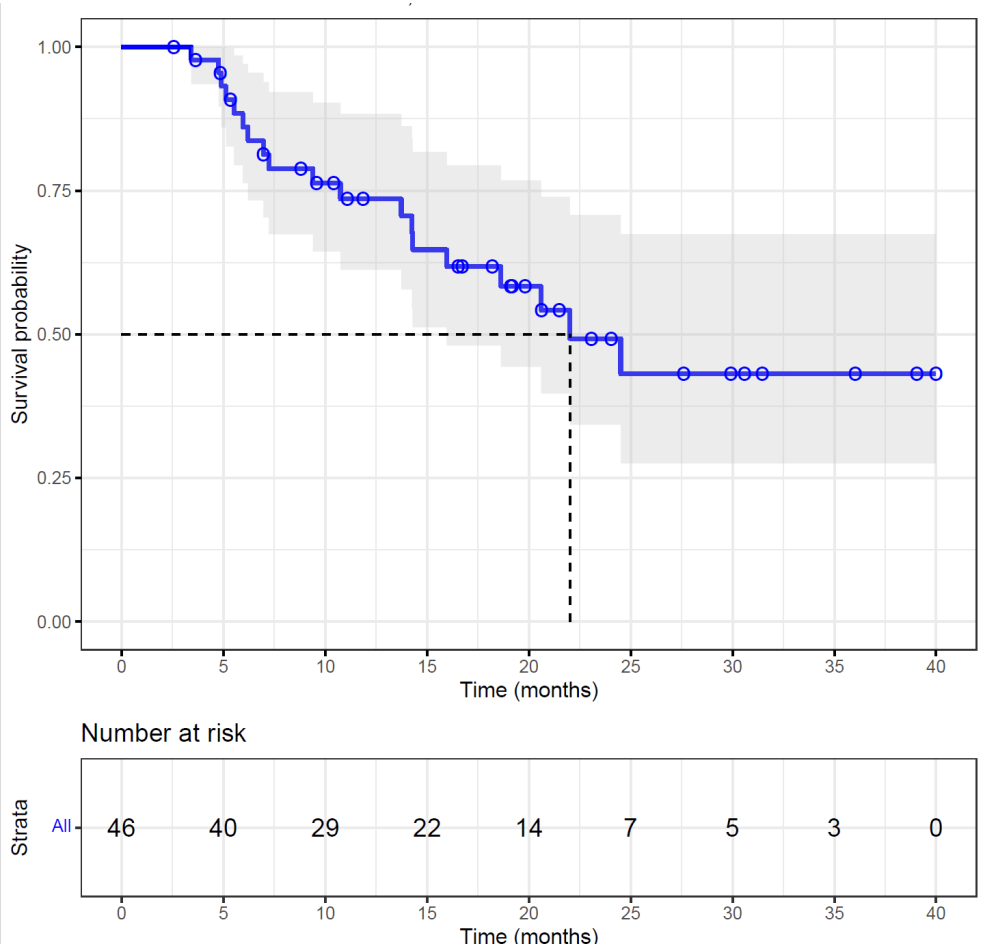
Data shown based on blinded independent central review (BICR) of radiographic data per RECIST 1.1 in evaluable patients. Note: one patient in cohort 2 (MU-008) was pending central read at the time of data cutoff

Evaluable patients are those who received 2 courses of CAN-2409 + prodrug (valacyclovir) and completed the 12-week treatment window

PR: partial response, SD: stable disease, PD: progressive disease, ORR: objective response rate, DCR: disease control rate, DoR: duration of response

mOS of 22.0 months after CAN-2409 treatment in NSCLC patients with an inadequate response to immune checkpoint inhibitors (cohort 1 and cohort 2)

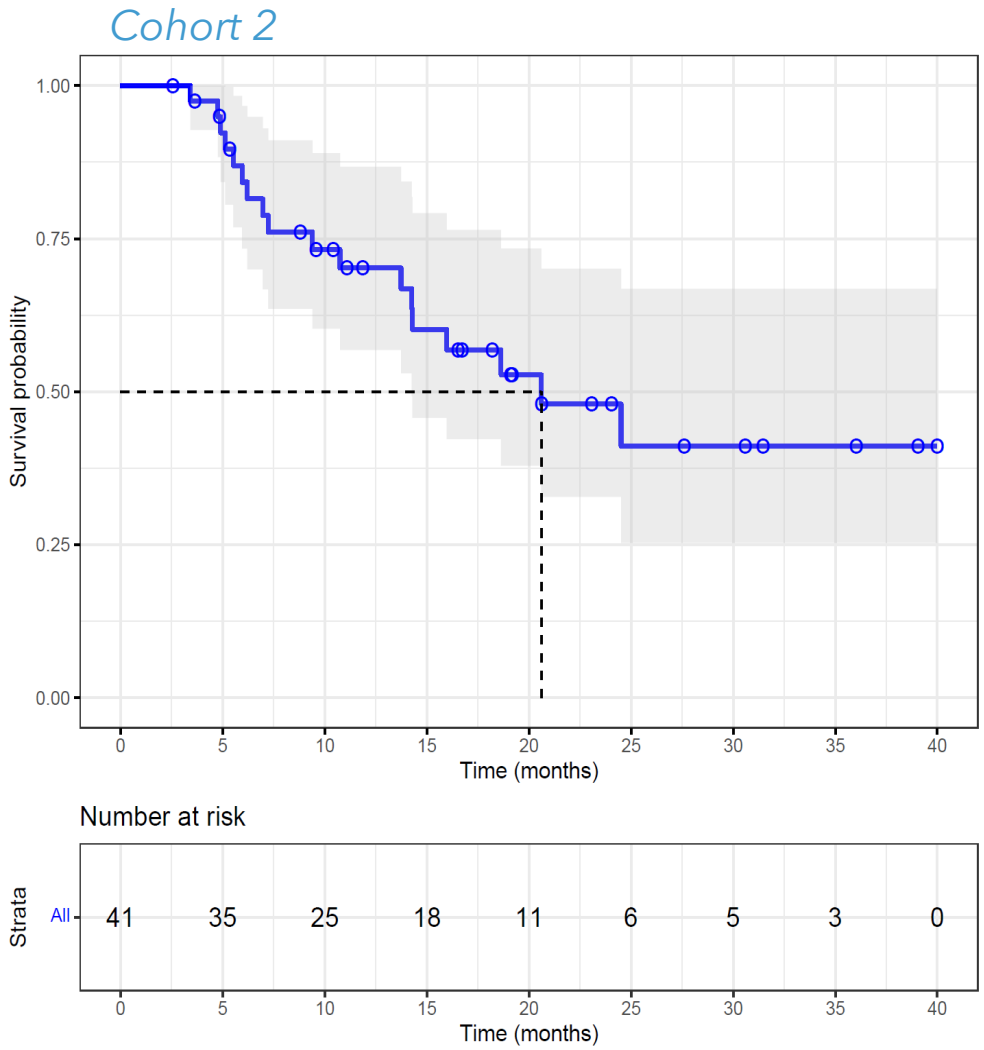
Cohort 1 + Cohort 2



Median overall survival: 22.0 mos (14.3, NA)
Median follow-up: 20.6 mos

Data cutoff 1 April 2024

mOS of 20.6 months after CAN-2409 treatment in NSCLC patients with progressive disease despite immune checkpoint inhibitor (cohort 2)



Median overall survival: 20.6 mos (13.7, NA)
Median follow-up: 20.6 mos

mOS in this population is <12 months using SoC

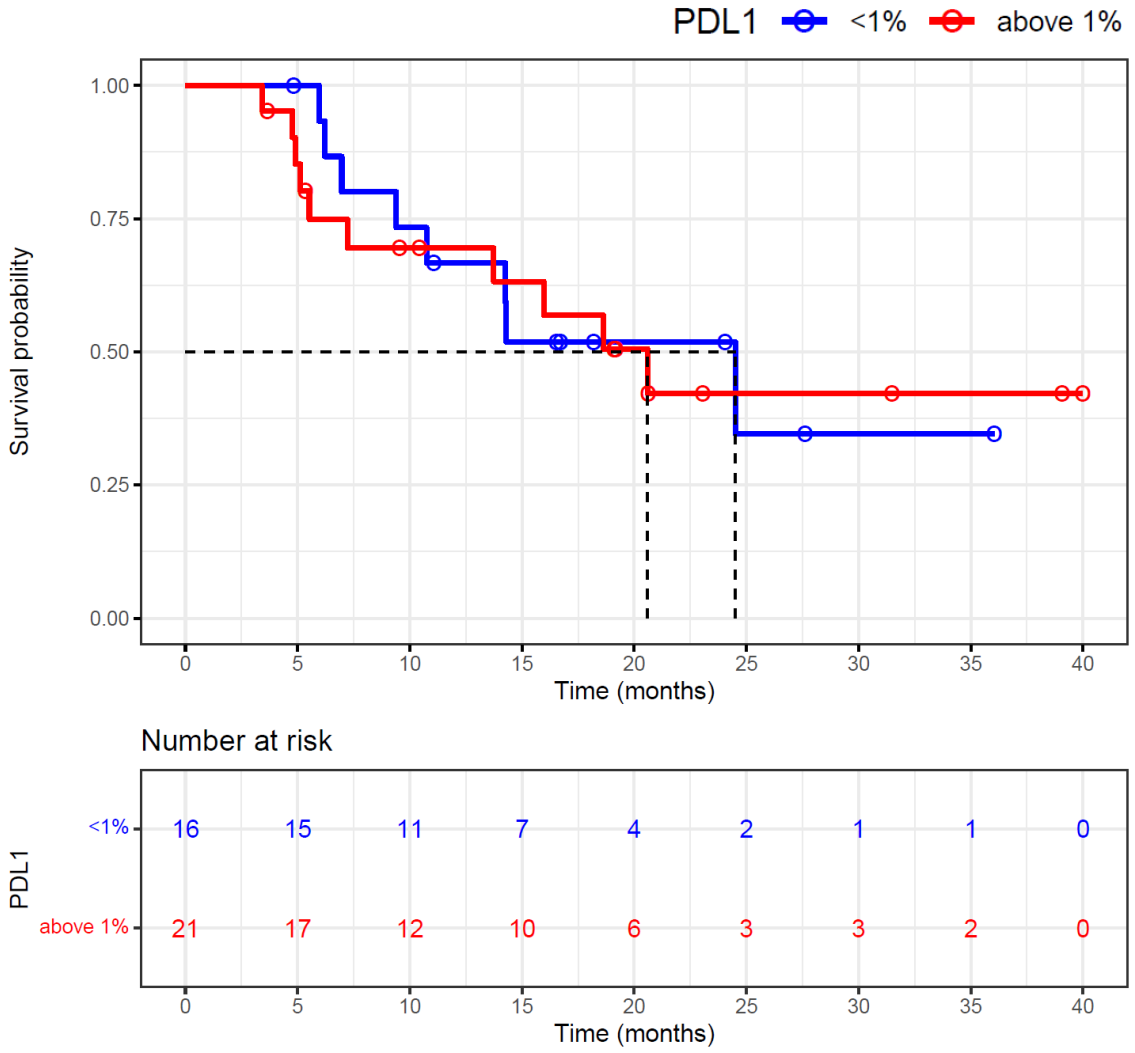
Reckamp K et al. J Clin Onc 2022;40:2295-2306

Data cutoff 1 April 2024

Improved mOS after CAN-2409 treatment is independent of PD-L1 status

PD-L1 status for Cohort 2 evaluable patients

PDL1 Subgroup	Number of patients	Median OS (month)
<1%	16	24.5 (7.0, NA)
>=1%	21	20.6 (5.5, NA)

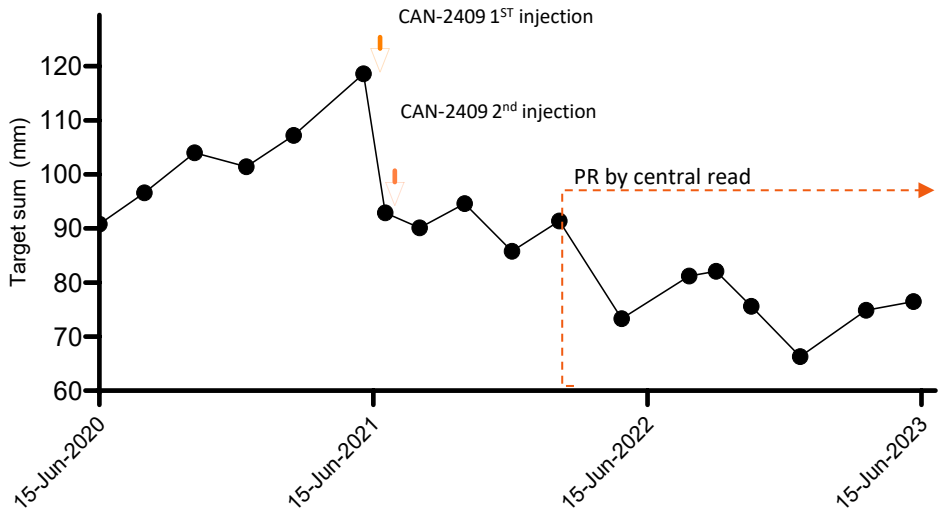


Data cutoff 1 April 2024

Partial response in extended lung mass with durable post-treatment tumor regression after CAN-2409 treatment (>30 months, ongoing)

PA-003 (Cohort 1)

73M, Stage III non-squamous NSCLC diagnosed Jan'20
PD-L1<1%
Initial therapy: pembro + carbo + pemetrexed Feb'20
Maintenance: pembro + pemetrexed from Jun'20 which continued on-trial
OS 29.9 mo. (ongoing as of LFV, Dec2023)

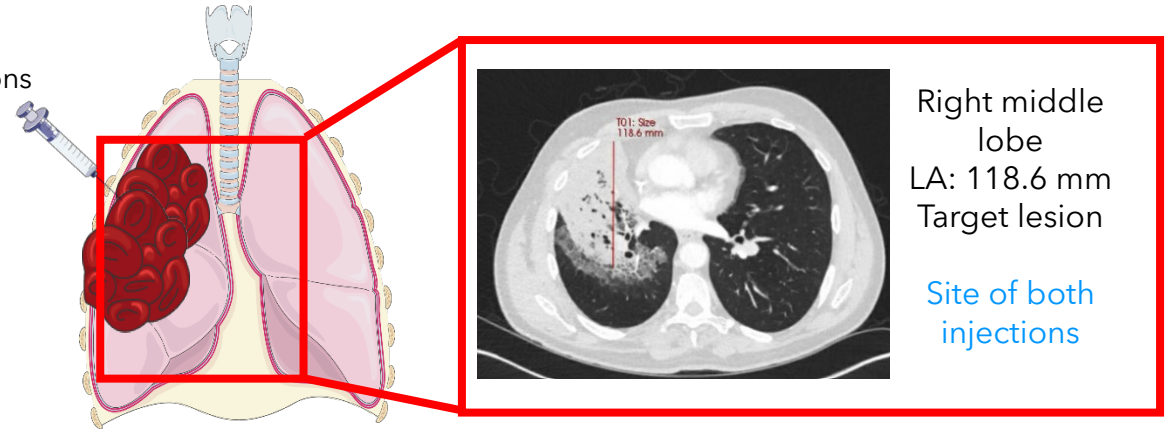


Legend
RECIST target lesions (red)
LN = lymph node; LA = long axis; SA = short axis

LFV: last follow up visit

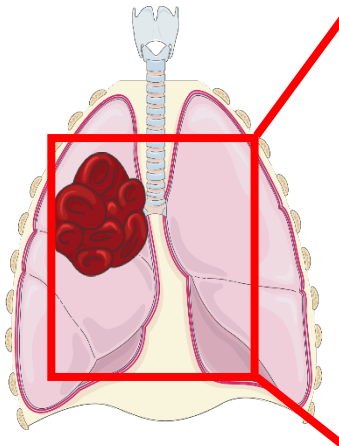
Baseline

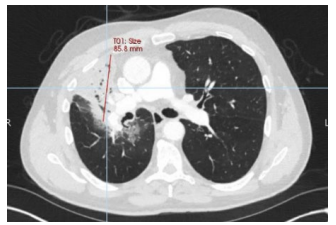
Both injections



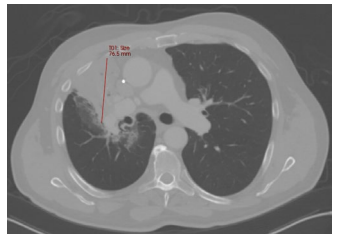
Right middle lobe
LA: 118.6 mm
Target lesion

Site of both injections





6 Months
LA: 85.8 mm
Target lesion



24 Months
LA: 76.5 mm
Target lesion

Schematics to show general lesion injection orientation; not to scale

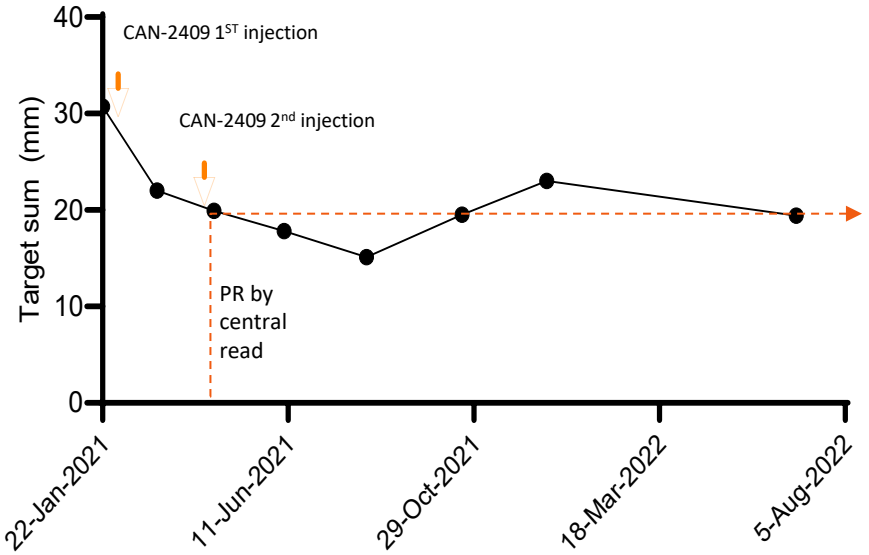
Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 April 2024.

Local injection induces systemic anti-tumor activity

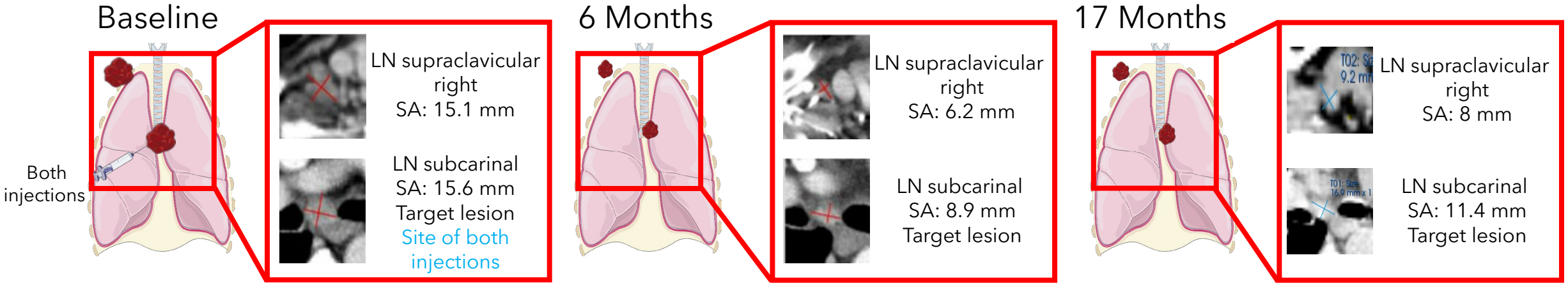
Evidence of abscopal effect, survival > 30 months (ongoing) after CAN-2409 treatment

NY-007 (Cohort 2)

74M, Stage IV non-squamous NSCLC diagnosed Feb'19
PD-L1 <1%
Initial therapy: cisplatin/etoposide Feb-Jul'19
Maintenance: nivolumab from Sep'19, continued on-study
OS 36.0 mo. (ongoing as of LFVJan2024)



Legend
RECIST target lesions (red)
LN = lymph node; LA = long axis; SA = short axis

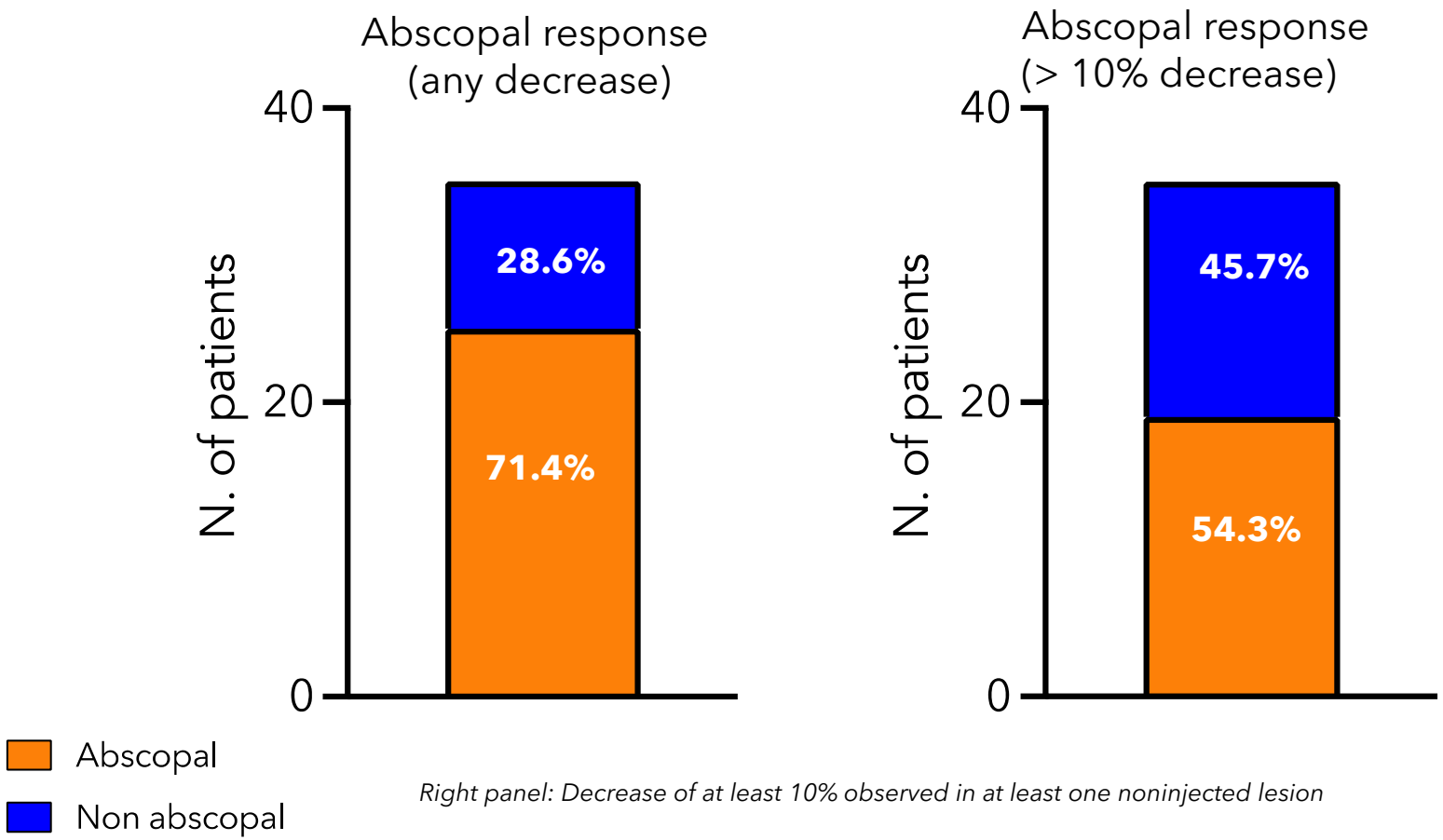


Schematics to show general lesion injection orientation; not to scale

Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 April 2024.

Local injection induces systemic anti-tumor activity

Regression of uninjected lesions in about two-thirds of evaluable patients presenting with multiple lesions

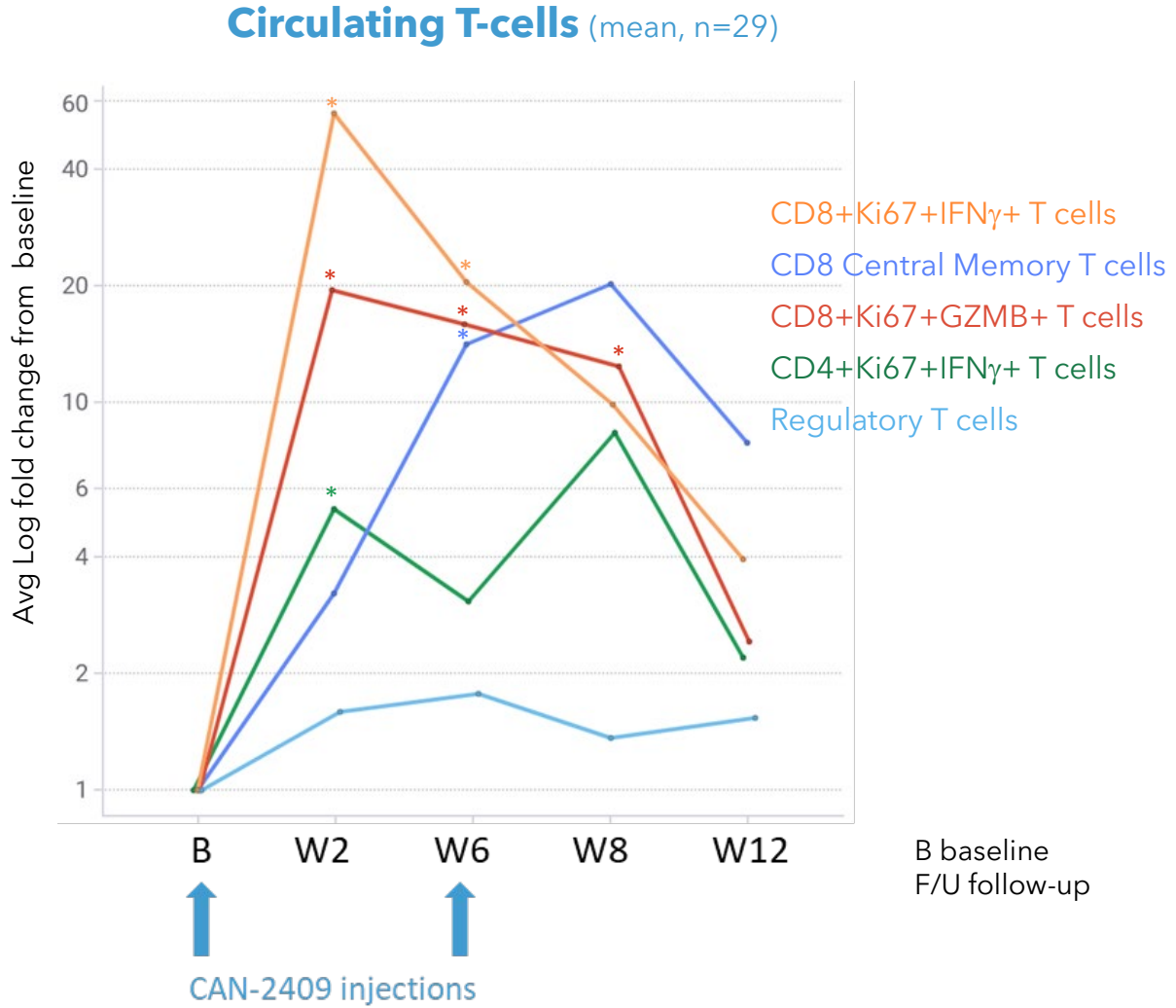


Right panel: Decrease of at least 10% observed in at least one noninjected lesion

- Systemic response or abscopal response (decrease of non injected lesions) was measured on all evaluable patients with at least 1 non-injected lesion (n=35)
- Abscopal response associated with improved survival

Data cutoff 1 April 2024

CAN-2409 induces significant increase in circulating T helper and cytotoxic T cells

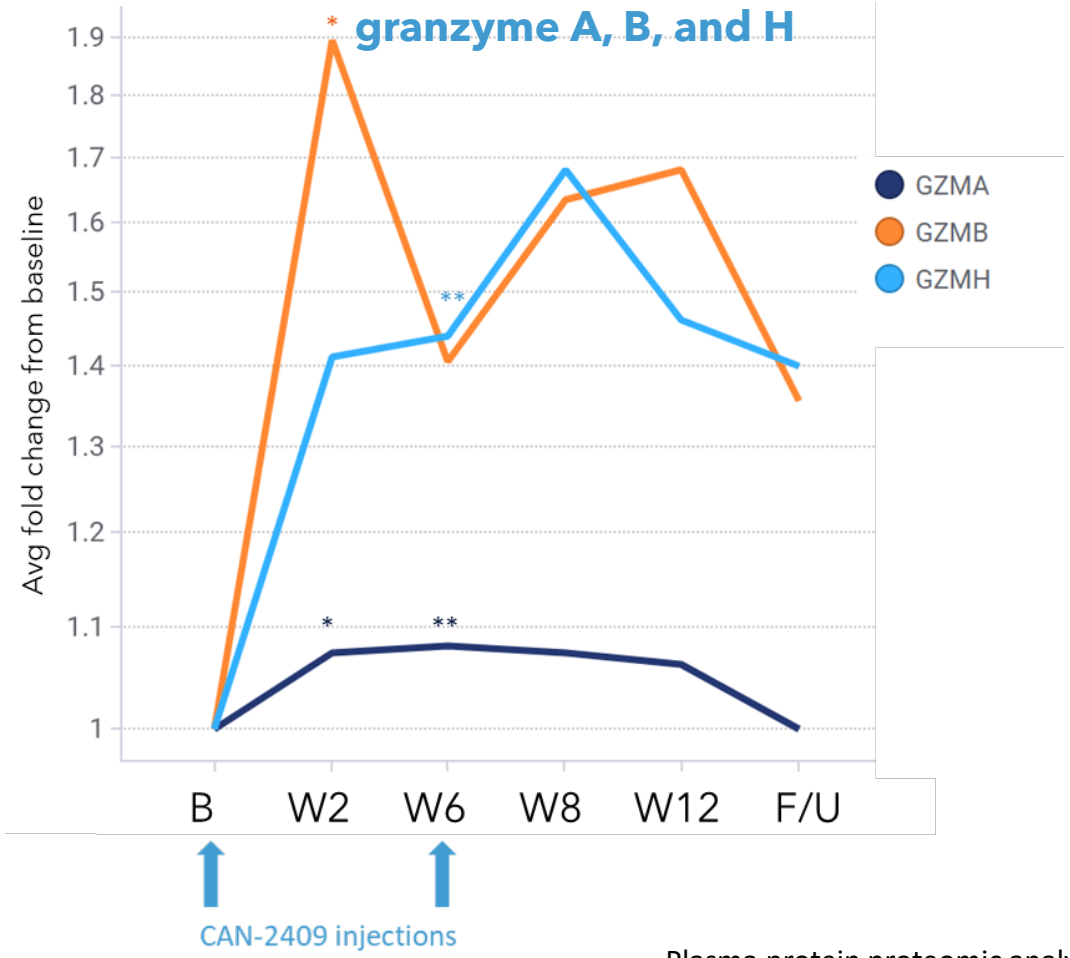


*Indicates significant change from baseline (t test p<0.05)
Flow cytometry analysis on cohort 2 patients

Data cutoff 1 April 2024

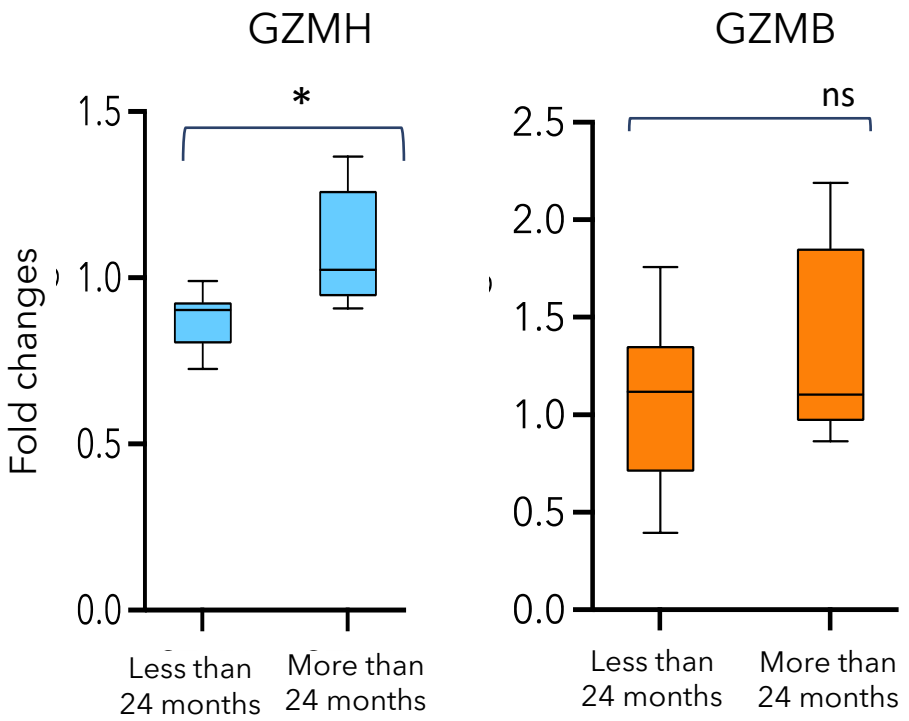
Immune activation after 2nd CAN-2409 administration is associated with prolonged survival

CAN-2409 induces significant increase in circulating inflammatory mediators including granzyme A, B, and H



*p<0.05; **p<0.005

Higher levels of GZMH after 2nd injection of CAN-2409 associated with survival (24 months)

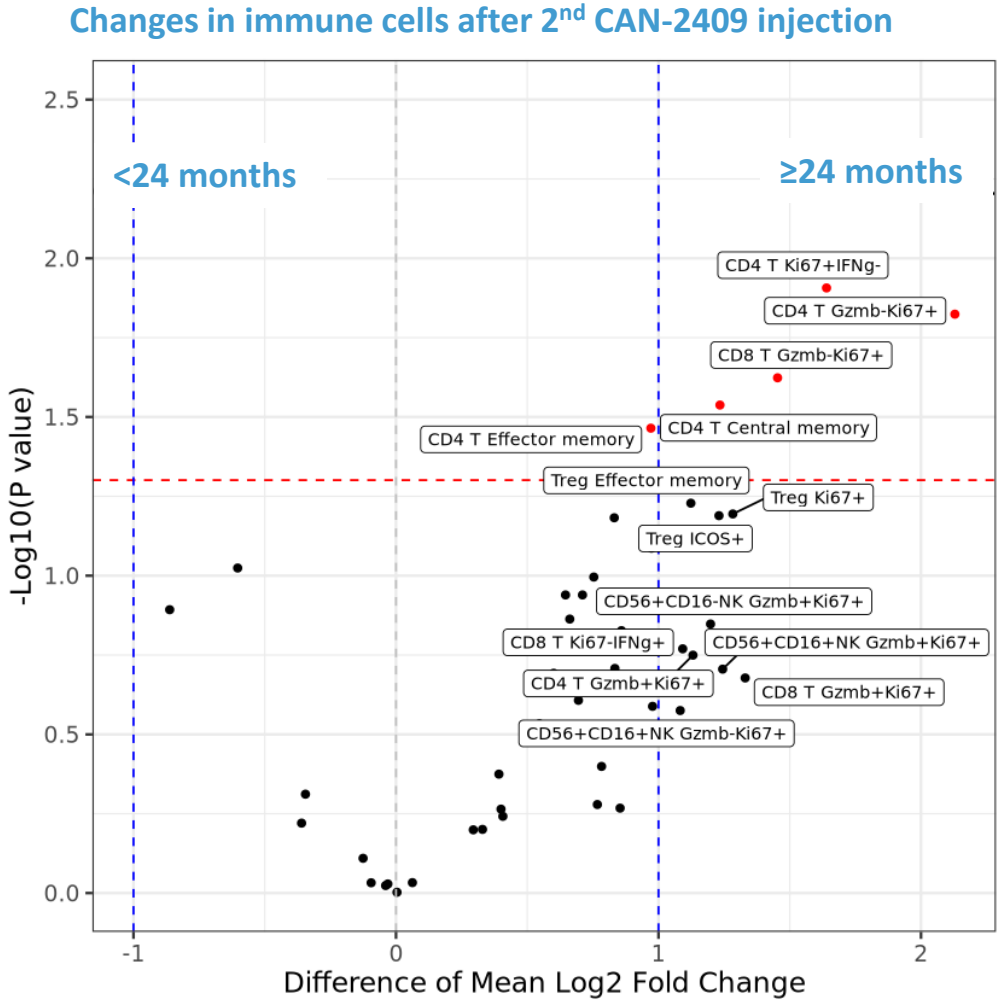


*p<0.05; **p<0.005

Plasma protein proteomic analysis measured by OLINK immuno-oncology panel

Data cutoff 1 April 2024

Immune activation after 2nd CAN-2409 administration is associated with prolonged survival



Multiparameter flow cytometry
Fold changes between 1st and 2nd injection in short (< 24 months; n=9) and long (> 24 months; n=4) survivors
Cohort 2 patients

Data cutoff 1 April 2024

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

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

- 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)

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

Systemic immunotherapy delivered intratumorally

- Intra-tissue injection is a proven strategy for in situ vaccination
- Optimal benefit/risk by minimizing 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 better tolerated 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

Encouraging safety data, clinical activity and immunological changes after CAN-2409 in NSCLC

- Experimental treatment of CAN-2409 + valacyclovir in NSCLC patients with an inadequate response to ICI is feasible and well tolerated, and results in median overall survival (mOS) of 22.0 months after only two administrations.
- We observed mOS of 20.6 months in patients with progressive disease at baseline, exceeding mOS reported in this population using standard of care chemotherapy (1, 2).
- While 90% of the patients had stage IV disease, an abscopal effect was observed in more than 70% of the patients presenting with at least one uninjected lesion; this implies that only one or two tumors need to be injected to teach the immune cells how to recognize the patient's tumor and induce systemic and durable anti-tumor immunity.

[1] *Reckamp K et al. J Clin Onc 2022;40:2295-2306*

[2] *Garon EB et al. Lancet. 2014;384:665-73*

CAN-3110

Oncolytic virus with tumor-specificity

CANDEL THERAPEUTICS

CAN-3110: High-grade glioma opportunity

Prevalence of glioblastoma in the US[1]

- Glioblastoma, the most common form of high-grade glioma, is a rare and often deadly cancer
- Fewer than 10% of patients survive > 5 years past initial diagnosis[2]
- Median overall survival < 6-9 months in recurrent high-grade glioma[3]
- Current standard of care includes surgical resection with few available therapeutic options
- Significant opportunity to improve survival by teaching the immune system how to recognize the cancer cells and turn 'cold tumors' into 'hot tumors'

1 Miller KD et al. CA Cancer J Clin 2021;71:381-406
2 Stupp R et al. Lancet Oncol. 2009;10:459-466
[3] vanLinde MC et al. J Neuro Onc 2017;135:183–192

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

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

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
11 patients dosed

Arm B

Pre-Administration of Cytoxan
3×10^8 PFU
6×10^9 PFU
9 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
12 patients targeted

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

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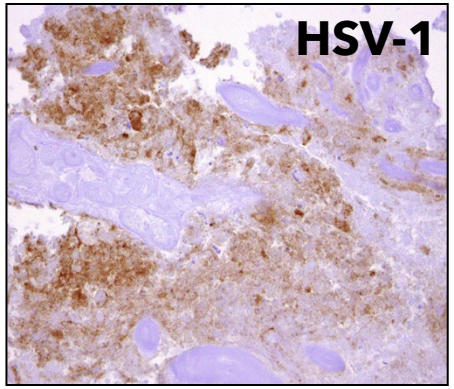
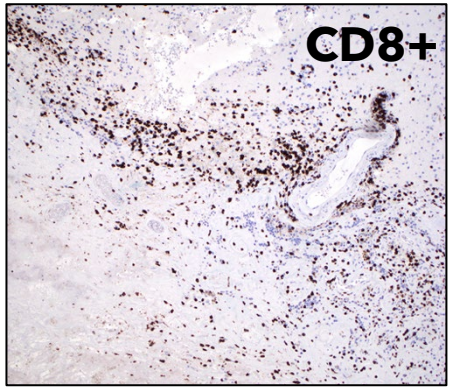
CAN-3110 treatment in patients with recurrent high-grade glioma

Persistent HSV antigen expression in injected tumors as well as uninjected tumors associated with CD8+ T cell infiltration after single CAN-3110 injection

injected lesion

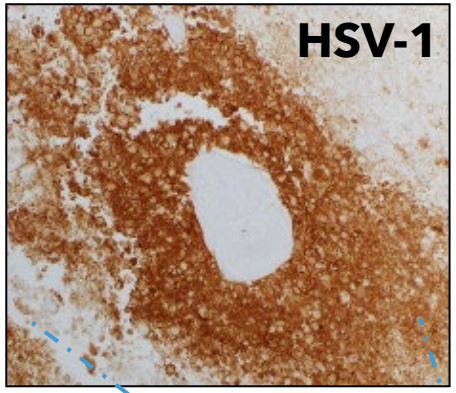


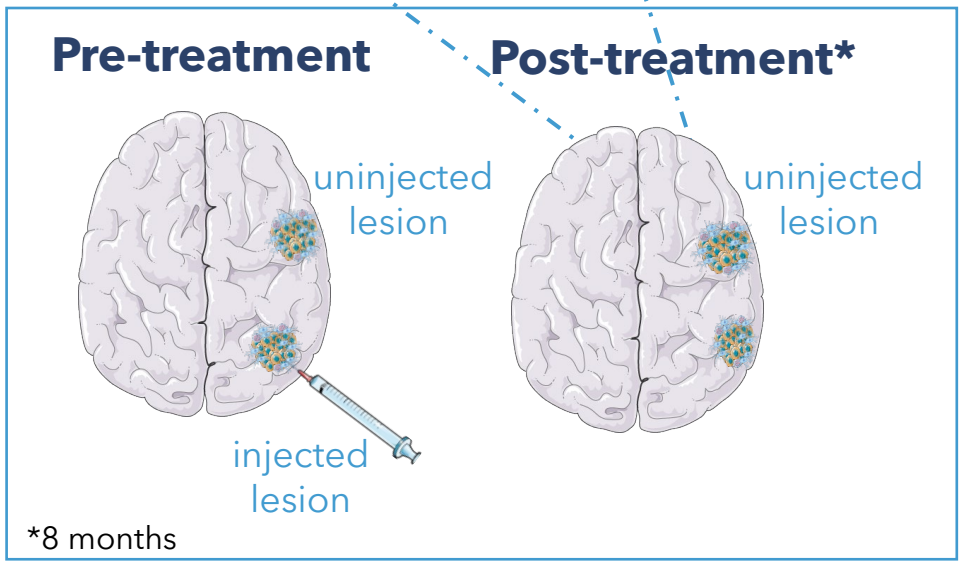
HSV1 antigen 6 weeks after injection of $1x10^6$ pfu
1.79×10^6 copies of viral DNA/mg
2.97×10^5 copies of viral RNA transcript (ICP22)/mg



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

uninjected lesion

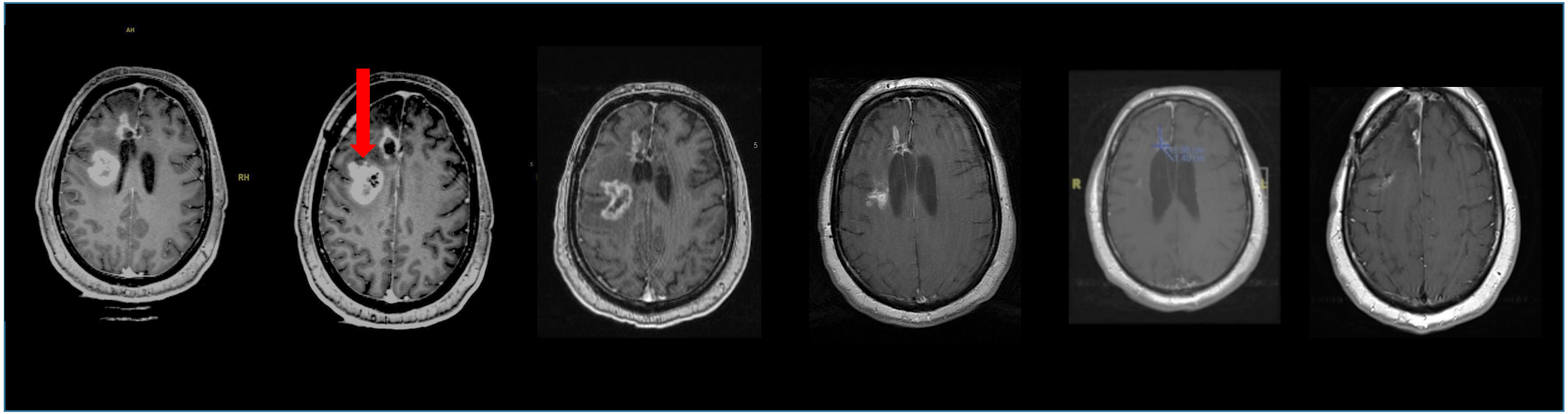




Ling AL et al. Nature 2023;623:157-166

Monotherapy activity of CAN-3110 in recurrent high-grade glioma (arm A)

Clinical effect on injected tumor and uninjected tumor



Baseline	Day 0	Day 56	Day 111	Day 168	Day 280
	Black hole within tumor image is injection site 10^6 PFU dose	Reduction in contrast area with no additional treatment	Patient back to work		

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

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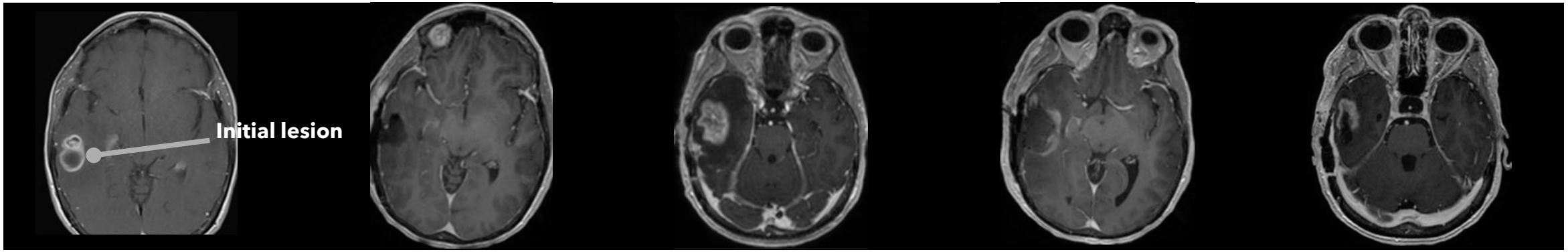
Ling AL et al. Nature 2023;623:157-166

Durable response for 2 years after CAN-3110 in recurrent high-grade glioma (arm A)



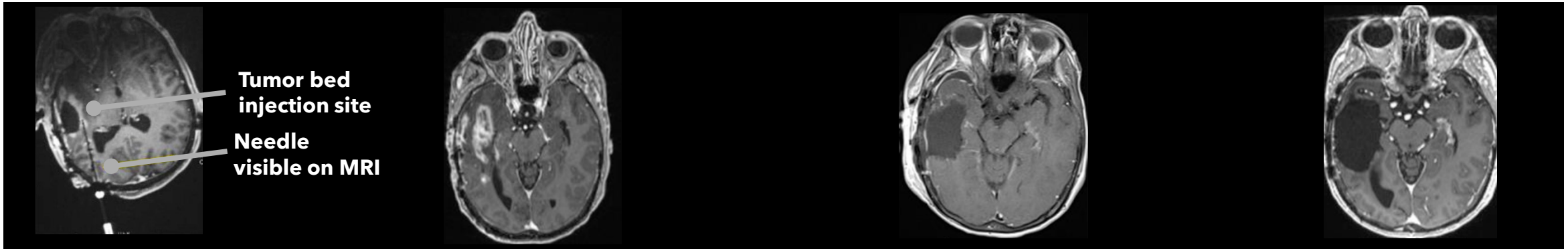
Day -262
Initial presentation

Day -259
Initial resection

Day -47
Tumor recurrence

Day -30
2nd subtotal resection

Day -14
Rapid progression



Day 0
CAN-3110 Injection

Day 91
Tumor recurrence with TIL

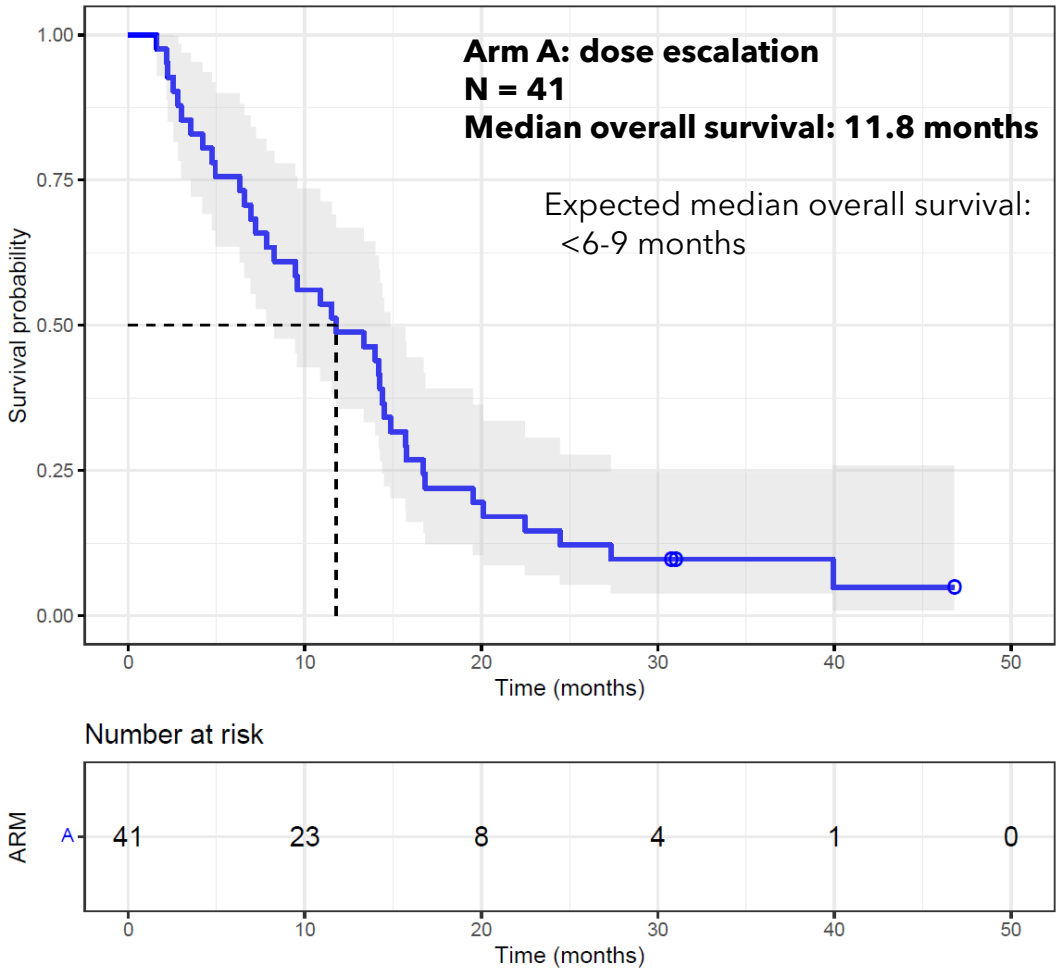
Day 96
After resection, histology shows TILs

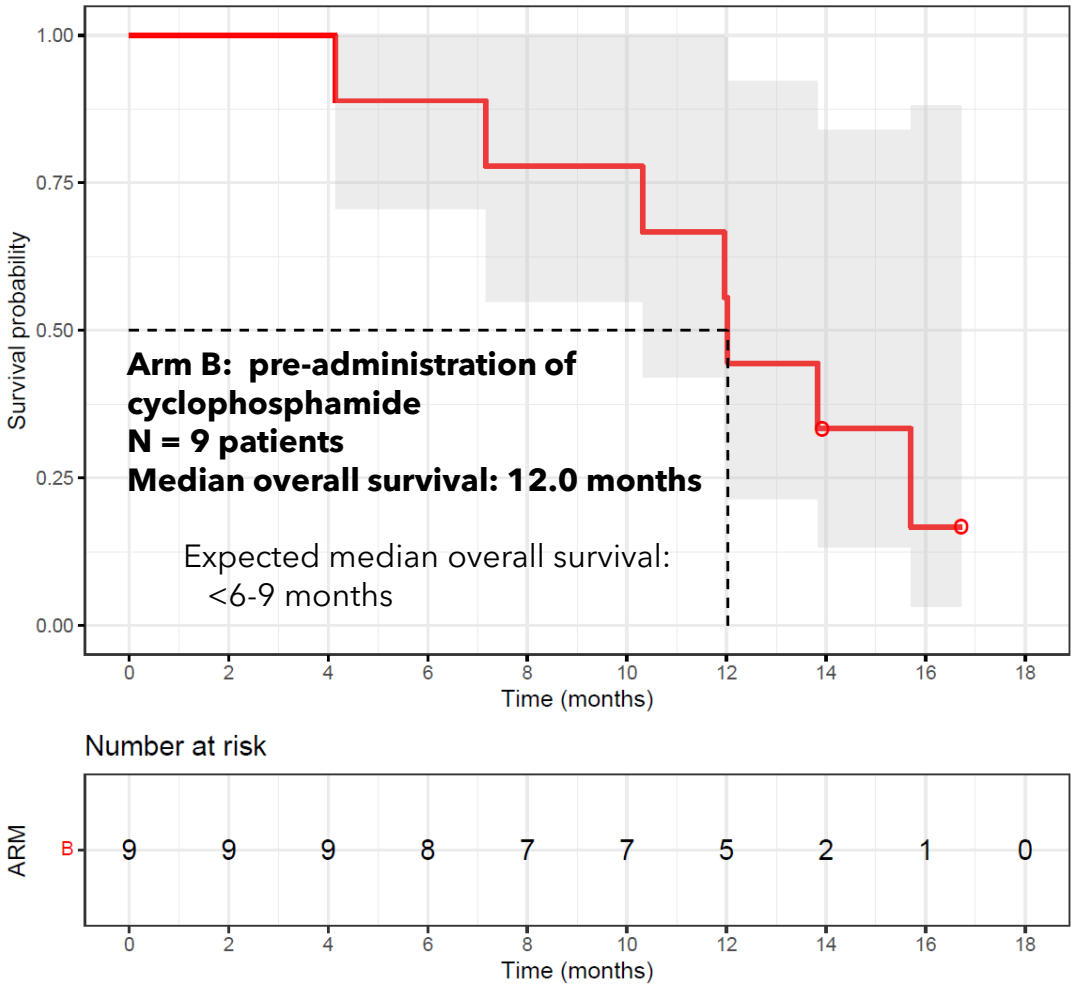
Day 630
No visible tumor

61 YOF, IDH wild-type, MGMT methylated glioblastoma, right temporal lesion initially treated with surgery, chemoradiation and temozolomide
CAN-3110 dose: 10^8 PFUs. Patient passed away as passenger in a motor vehicle accident on day 717.

Ling AL et al. Nature 2023;623:157-166

Encouraging overall survival in recurrent high-grade glioma after single injection of CAN-3110



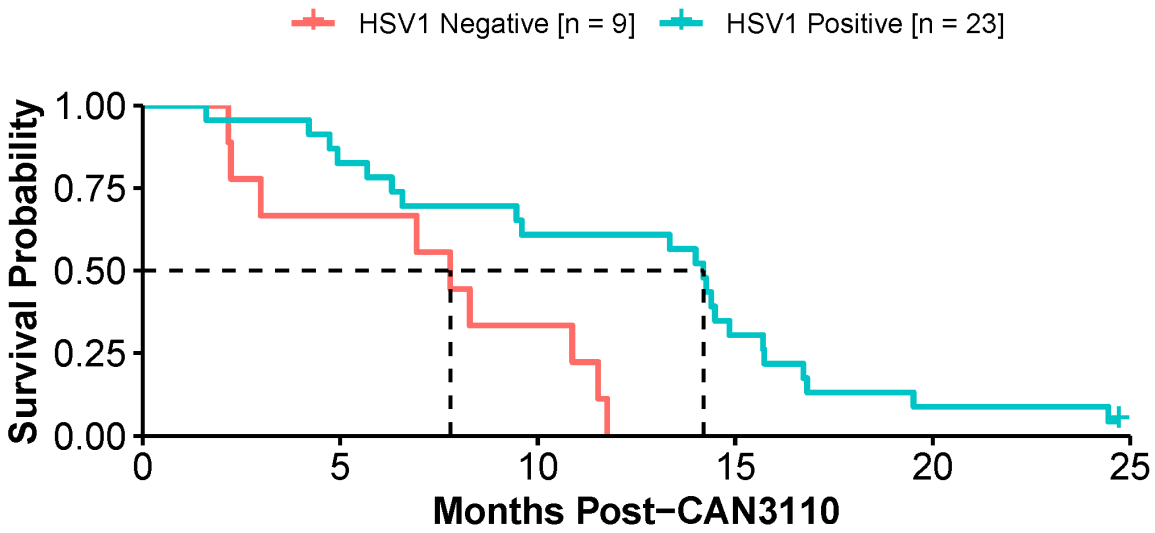


- 41 unique patients were dosed; one patient was treated twice, in cohort IX and X
- A total of 50 unique patients

Note: As of cutoff date, 20 Apr 2023.

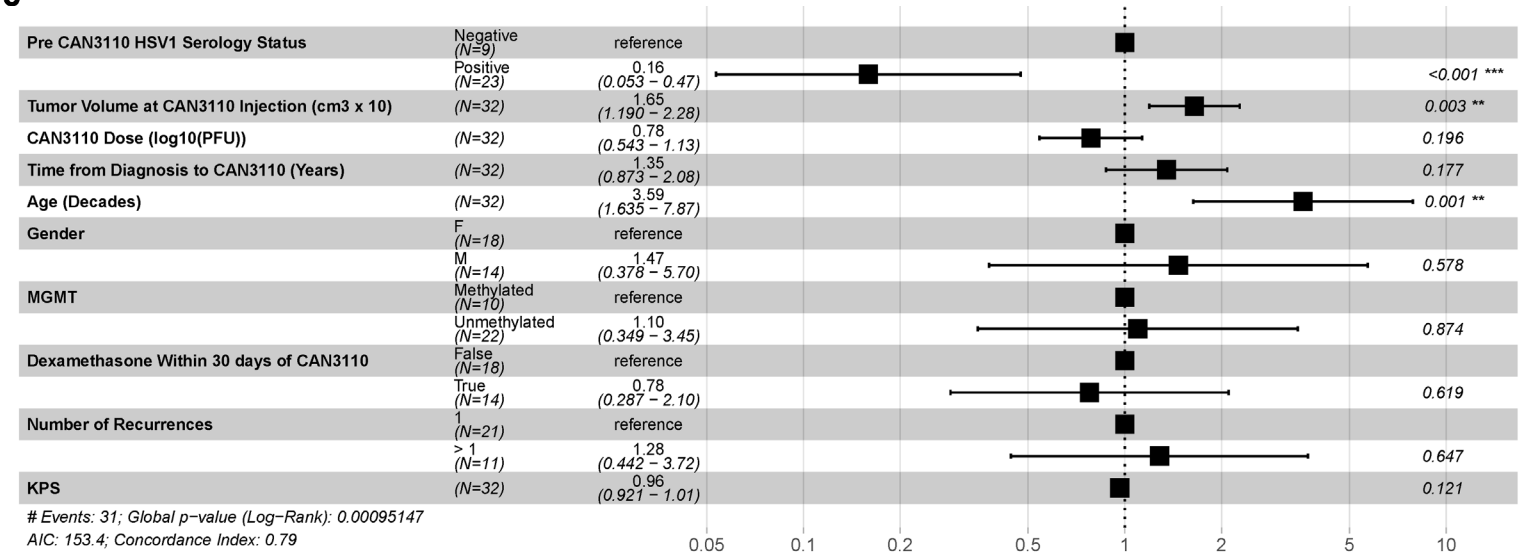
Barone F et al. ASGCT 2023 Abstract 2893

Prolonged survival after CAN-3110 treatment is associated with HSV1 seropositivity



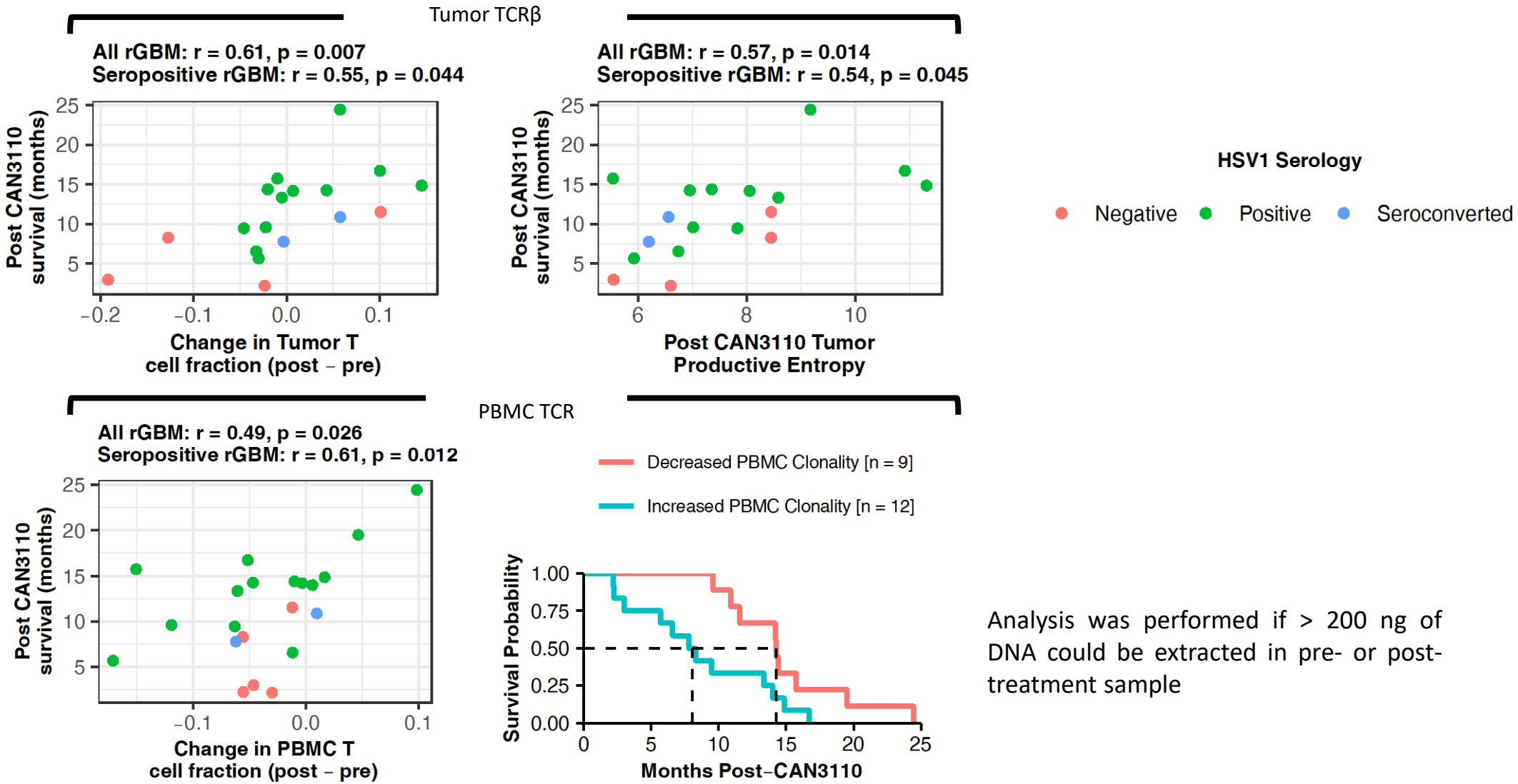
HSV2 serology status is not associated with survival

COxPH Hazard Ratios



Ling AL et al. Nature 2023;623:157-166

Changes in T cell fractions and TCRβ diversity correlate with survival after CAN-3110 treatment



Analysis was performed if > 200 ng of DNA could be extracted in pre- or post-treatment sample

Ling AL et al. Nature 2023;623:157-166

Overall survival data after repeated administration of CAN-3110 in recurrent glioblastoma, suggesting a long tail of survival

mOS 12.3 (C.I 5.6-18.7)

Patient	Age	Sex	MTMG status	#injections	OS in months	Status
1	54	M	unmet	4	12.3	D
2	66	F	unmet	6	18.7	A
3	75	F	meth	6	9.1	D
4	64	M	unmet	5	13.0	A
5	61	F	unmet	4	12.2	A
6	69	F	unmet	4	5.6	D

MTMG = O6-methylguanine-DNA methyltransferase
methylation status: unmet=unmethylated, meth=methylated

Up to 6 injections of 1x10^8 pfu CAN-3110
Data cutoff October 24th 2024

CANDEL THERAPEUTICS

EA Chiocca. 16th Annual International Oncolytic Virotherapy Conference Oct. 2024

Encouraging safety data, clinical activity and immunological changes after CAN-3110 in recurrent high-grade glioma (glioblastoma)

- Monotherapy treatment with CAN-3110 in rHGG is well tolerated and associated with doubling of expected median overall survival
- Immunological changes in the tumor microenvironment are associated with improved survival and HSV1 seropositivity
- First six patients have been dosed in cohort C (fully funded by the Break Through Cancer foundation)
- Repeated injections of CAN-3110 (up to six) feasible and well tolerated
- 3 out of 6 patients still alive after more than one year after repeated administration of CAN-3110.
- Near absence of tumor cells alongside dense lymphocyte infiltrates in biopsies obtained after repeated CAN-3110 administration

Candel at a glance

- CAN-2409: Off-the-shelf pan-solid tumor therapy, individualized anti-cancer immune response
  - Positive phase 3 randomized controlled clinical trial in localized, intermediate-to-high-risk prostate cancer
  - Proof of concept in PDAC and NSCLC
  - Fast Track Designation in NSCLC, pancreatic cancer, and prostate cancer
  - "Pipeline in a product" strategy advancing multiple programs in several large indications
  - Upcoming catalysts:
    - Final survival data in PDAC (Q1 2025)
    - Final survival and biomarker data in NSCLC (Q1 2025)

- CAN-3110: Oncolytic HSV-1 designed for tumor-specific replication
  - Proof of concept in patients with recurrent high-grade glioma published in *Nature*
  - Fast Track Designation, Orphan Drug Designation
  - Opportunity for creation of "pipeline in a product" by expansion into indications beyond brain cancers
  - Overall survival and immunological biomarker data, evaluating repeat dosing regimen of CAN-3110 (Q4 2025)

- Corporate Highlights
  - Very experienced Executive Team and strong scientific support from high-profile Research Advisory Board
  - Cash and cash equivalents of $102.9 million as of Dec 31, 2024 (unaudited) ; expected runway into Q1 2027
  - IP protection: CAN-2409 (2034, method of use); CAN-3110 (2036, composition of matter); 12 years data exclusivity
  - Low-cost manufacturing