Phase 3, randomized, placebo-controlled clinical trial of CAN-2409+prodrug in combination with standard of care external beam radiation (EBRT) for newly diagnosed localized prostate cancer

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Disclosures

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Consulting Agreement/ Speakers Bureau with Candel Therapeutics, Teleflex, and Novartis

Learning Objectives

Attendees will learn about:

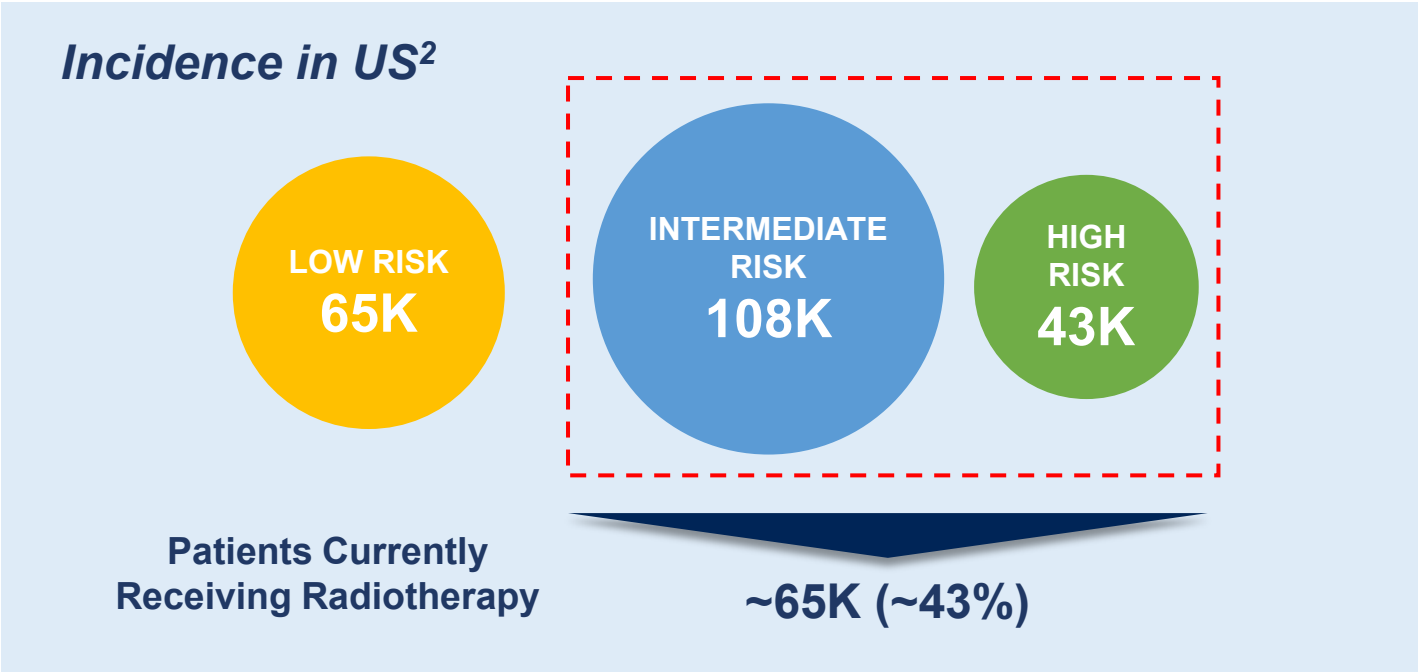
- Topline efficacy and safety results for the investigational agent CAN-2409 in combination with standard-of-care EBRT for newly diagnosed localized prostate cancer.

- CAN-2409 administration and how it fits into clinical practice.

- Potential of CAN-2409 as paradigm shift in the treatment of patients with intermediate-to-high-risk localized prostate cancer.

Unmet need in localized prostate cancer

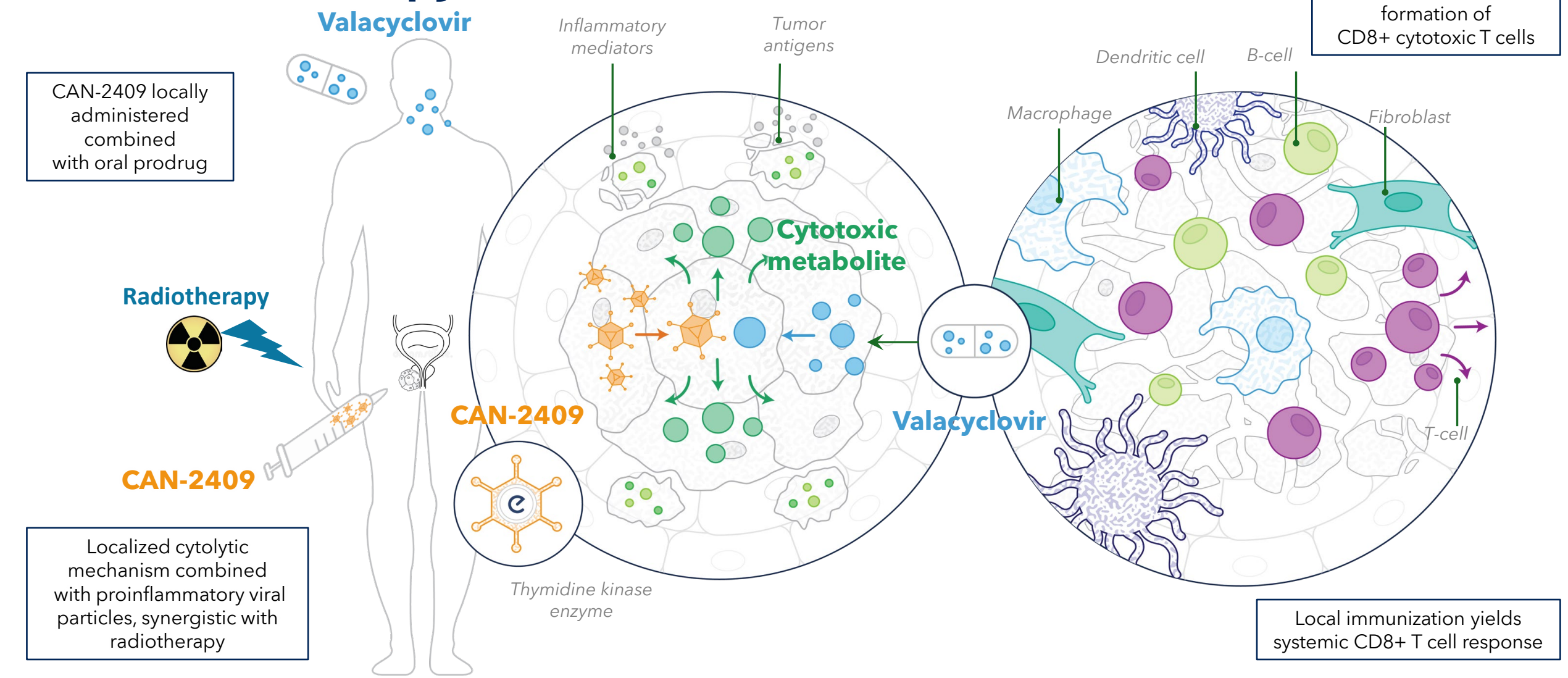
Global concern: approximately 1.4 million new cases of prostate cancer in 2020[1]



[1] WHO cancer fact sheet. February 3, 2022
[2] Globe Life Science Report, 2025 (data on file)

Ultimate goal of curative treatment is **prevention of cancer recurrence** while minimizing treatment related side effects and maintaining quality of life

CAN-2409 + prodrug: multimodal immunotherapy synergistic with radiotherapy



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

NCT01436968

N=745

Newly diagnosed, NCCN intermediate and 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*
- *Prostate cancer specific outcomes*
- *Overall survival*

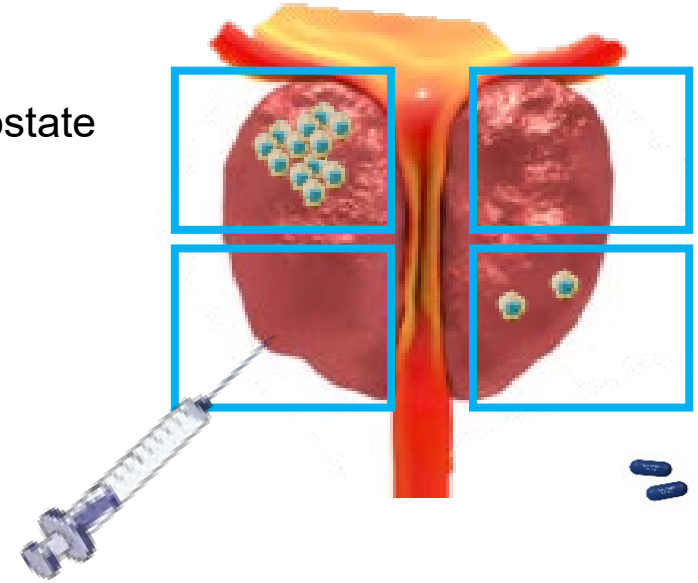
Conducted under agreement with FDA under Special Protocol Assessment

Randomization stratified by NCCN risk group and planned short course ADT (androgen deprivation therapy)

*Defined as local (biopsy), regional, metastatic disease or death due to any cause

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

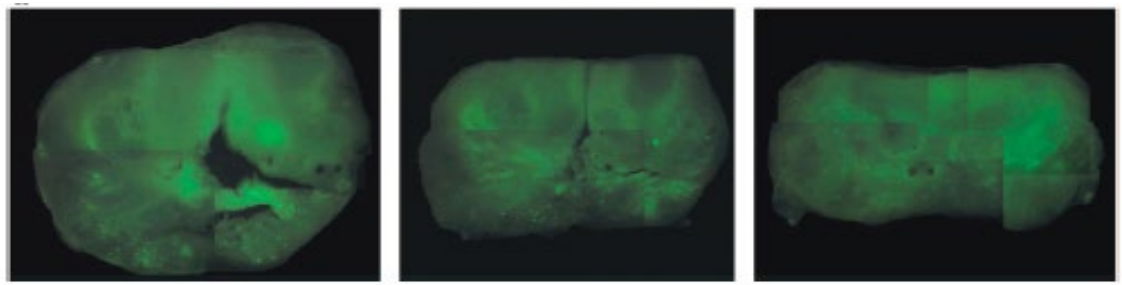
Standard urologic injection procedure



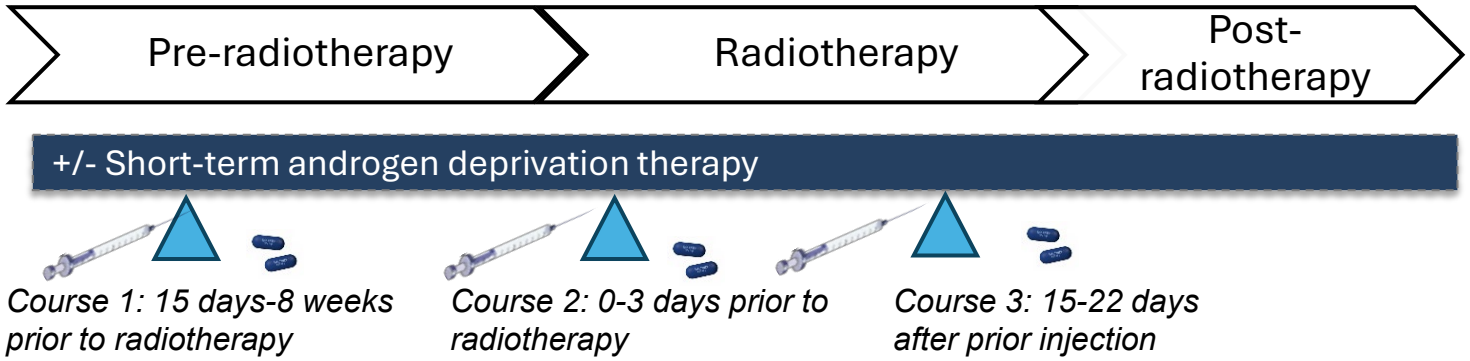
Prodrug (14 days of valacyclovir)

- **Ultrasound guided Injection (transrectal or transperineal)**
- **Performed by urologists or radiation oncologists in outpatient clinic**
- **A total volume of 2ml, 0.5ml in each of 4 quadrants of the prostate using a 20-22 G needle**

CAN-2409 biodistribution analysis



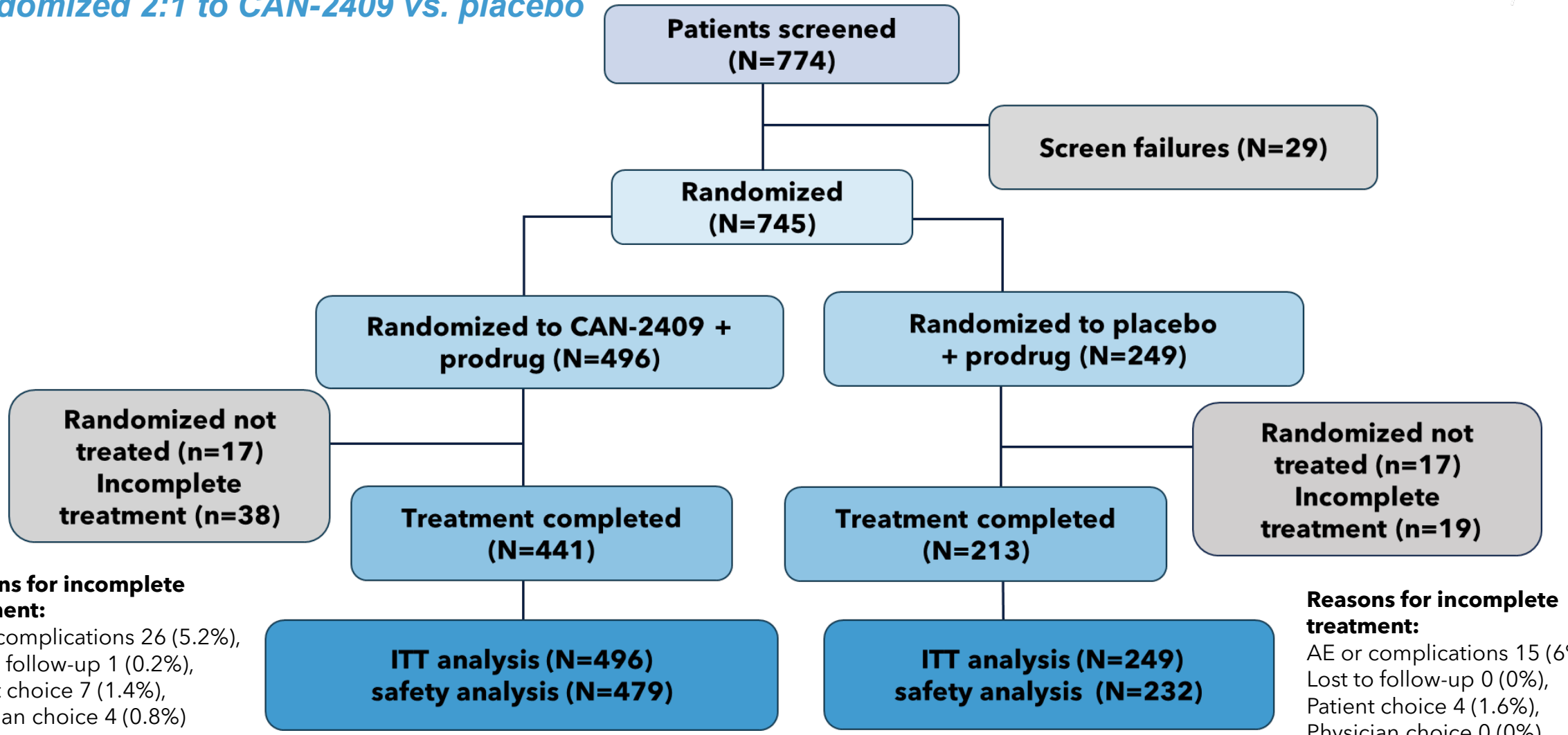
Images of fluorescently labeled adenoviral vector in freshly resected prostate, demonstrating homogeneous distribution throughout the organ after 4 injections of virus (0.5ml) in each prostate quadrant[2]



1 Aguilar L. 28th Annual Prostate Cancer Foundation, Scientific Retreat, October 2021
2. Rojas Martinez et al. Cancer Gene Ther. 2013 November; 20(11): 642–649.

CONSORT diagram

Randomized 2:1 to CAN-2409 vs. placebo



Reasons for incomplete treatment:
AE or complications 26 (5.2%),
Lost to follow-up 1 (0.2%),
Patient choice 7 (1.4%),
Physician choice 4 (0.8%)

Reasons for incomplete treatment:
AE or complications 15 (6%),
Lost to follow-up 0 (0%),
Patient choice 4 (1.6%),
Physician choice 0 (0%)

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)

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

Treatment related AEs >5% in either arm

- Chills, fever, flu-like symptoms were commonly mild to moderate and self-limited
  - **>90% of fever, flu-like symptoms, chills and fatigue resolved within 24-72hrs**
- 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

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)

Radiation therapy regimen

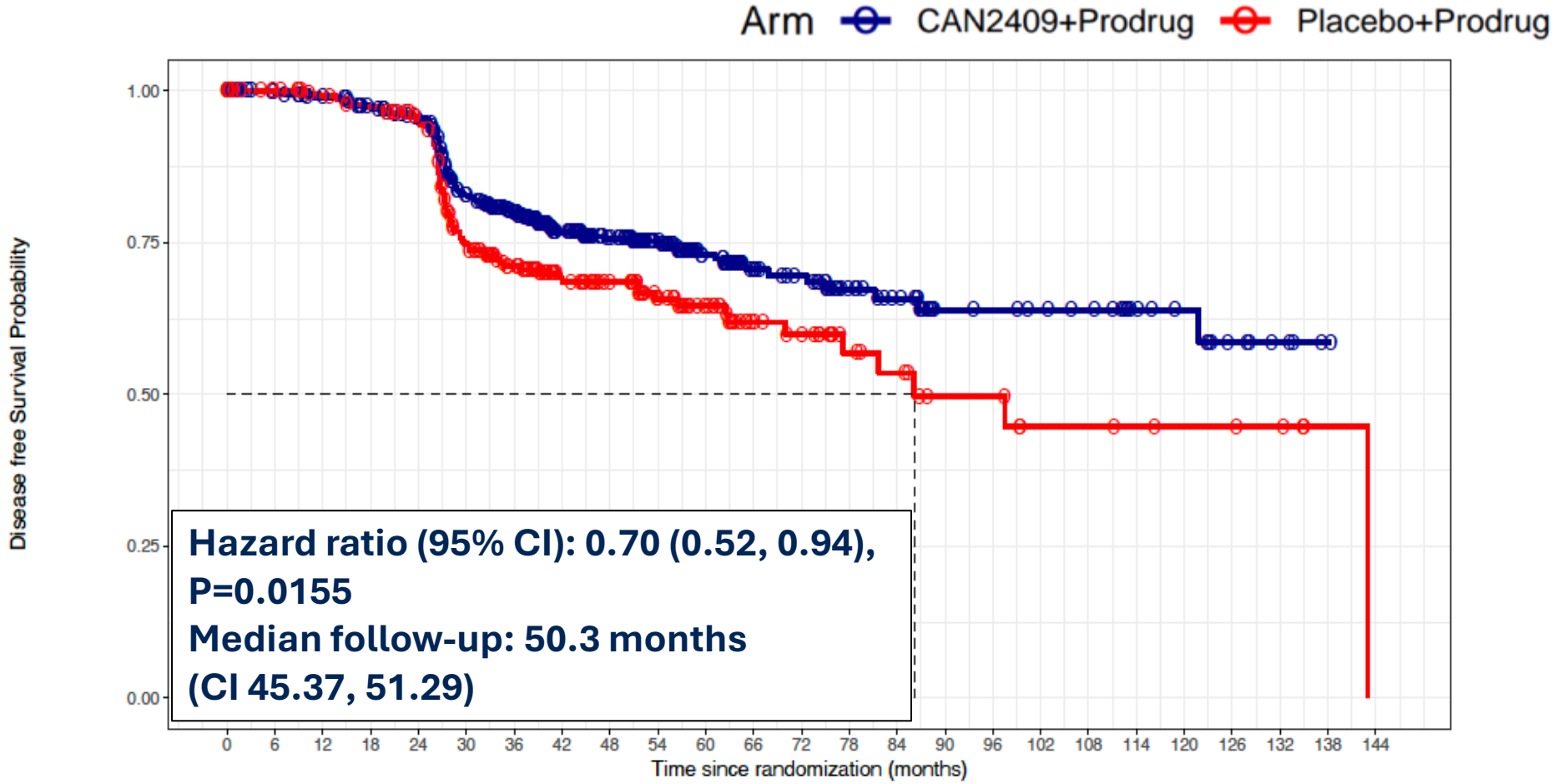
~25% received moderate hypofractionated XRT

EBRT, n (%)	CAN-2409	Placebo	Total
Received RT	479 (100)	232 (100)	711 (100)
Conventional RT (~78Gy in 2 Gy fractions)	341 (71.2%)	174 (75%)	515 (72.4%)
Moderate hypofractionated (60 Gy in 3 Gy fractions)	123 (25.7%)	54 (23.3%)	177 (24.9%)
Unknown	15 (3.1%)	4(1.7%)	19(2.7%)

- Protocol amended in 2019 to allow moderate hypofractionated regimen

- Both XRT regimens were well tolerated
  - No significant differences in safety profile
  - Grade ≥3 treatment related AEs were similar on CAN-2409 and PBO arms with both hypofractionated (1.6% vs 1.9%) and standard EBRT (1.8% vs. 1.1%), respectively

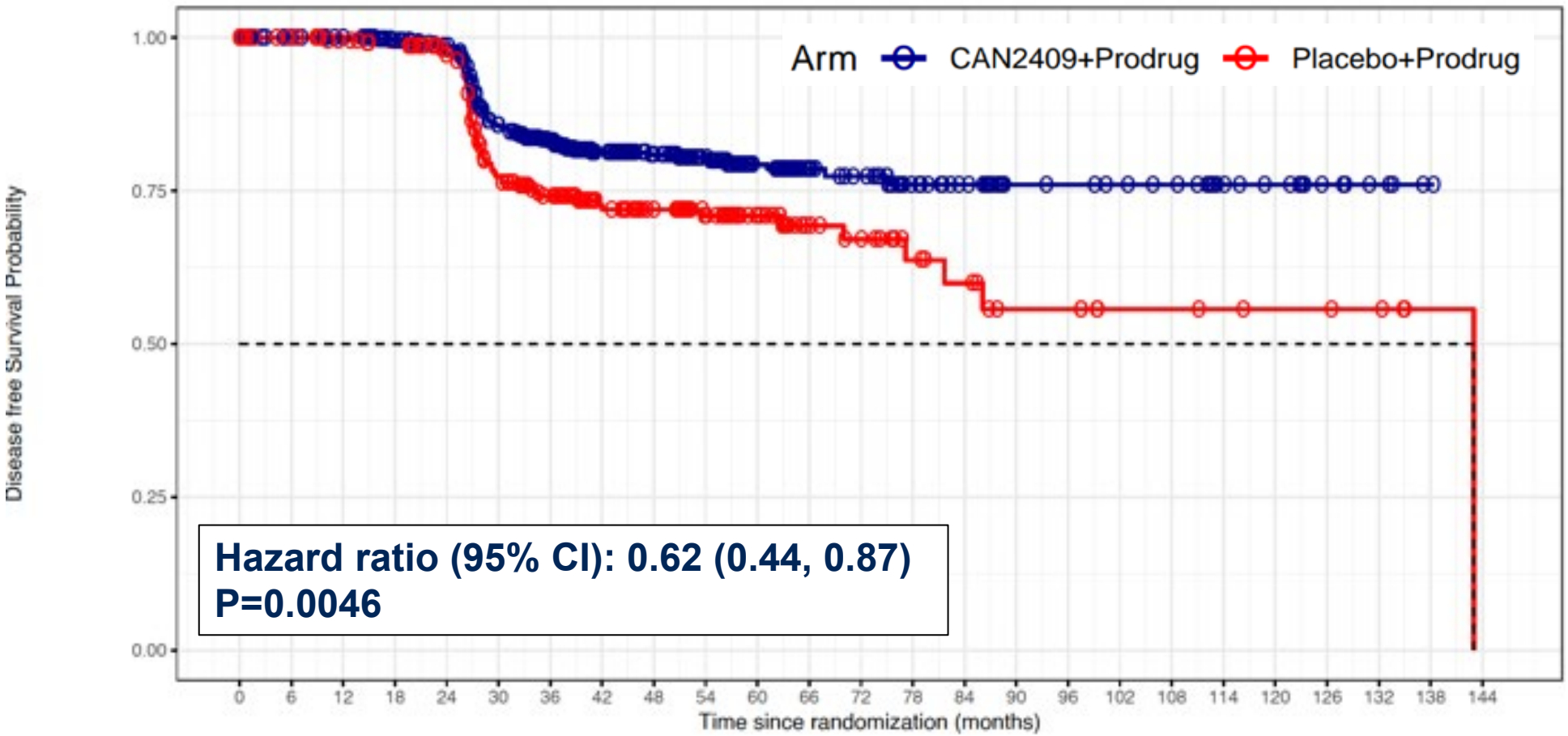
CAN-2409 significantly improves disease-free survival (DFS) in newly diagnosed, intermediate/high-risk prostate cancer



CAN-2409 results in **30% improvement in DFS** (includes death from any cause) compared to SoC (ITT*, n=745)

**intent to treat population*

CAN-2409 significantly improves prostate cancer-specific DFS



Highly significant 38% reduction in risk for prostate cancer recurrence or prostate cancer-related death (ITT*, n=745)

**intent to treat population*

Prostate-specific outcomes stratified by use of short-term androgen deprivation therapy (ADT) or radiation regimen

Use of ADT	Risk Category	N events/ patients	Prostate specific HR with CAN-2409
No Androgen deprivation therapy	- Intermediate (overall)	86/349	**HR = 0.56 95% CI 0.37, 0.86**
	Intermediate Favorable	44/188	**HR = 0.49 95% CI 0.27, 0.90**
	Intermediate Unfavorable	42/161	**HR = 0.66 95% CI 0.36, 1.23**
	High risk	5/9	Cannot be estimated
Androgen deprivation therapy	**Intermediate (overall)**	32/240	**HR = 0.69 95% CI 0.34 – 1.39**
	Intermediate Favorable	3/31	**HR = 0.64 95% CI 0.06, 7.05**
	Intermediate Unfavorable	29/209	**HR = 0.68 95% CI 0.32, 1.42**
	High risk	21/94	**HR = 0.69 95% CI 0.29 – 1.67**

PrCa specific-DFS outcomes by RT regimen:

- **Mod-hypofractionated EBRT:**
  - Events: 52/177
  - HR= 0.52 (CI: 0.30-0.93)
- **Conventional EBRT:**
  - Events: 136/515
  - HR=0.76 (CI: 0.53-1.07)

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)
- As expected*, overall survival was similar by treatment arm in this time frame (median follow up 50 months)
  - Only 2 deaths due to prostate cancer (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

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

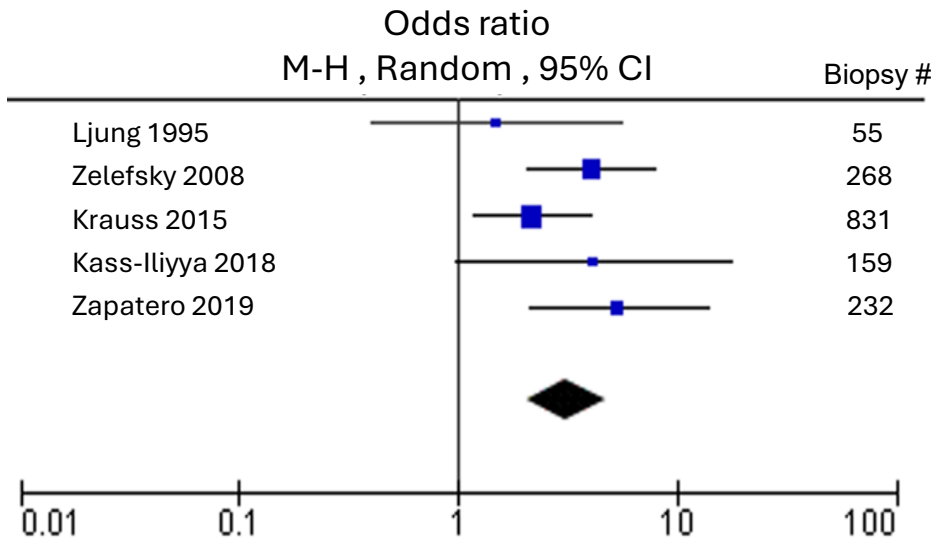
***Significant difference between arms, chi-square test p= 0.0015**

Positive biopsies ≥ 2 years after radiotherapy are predictive of metastases and cancer-related mortality after long-term follow up

Patients with a positive prostate biopsy ≥ 2 years after radiotherapy because of localized cancer had:

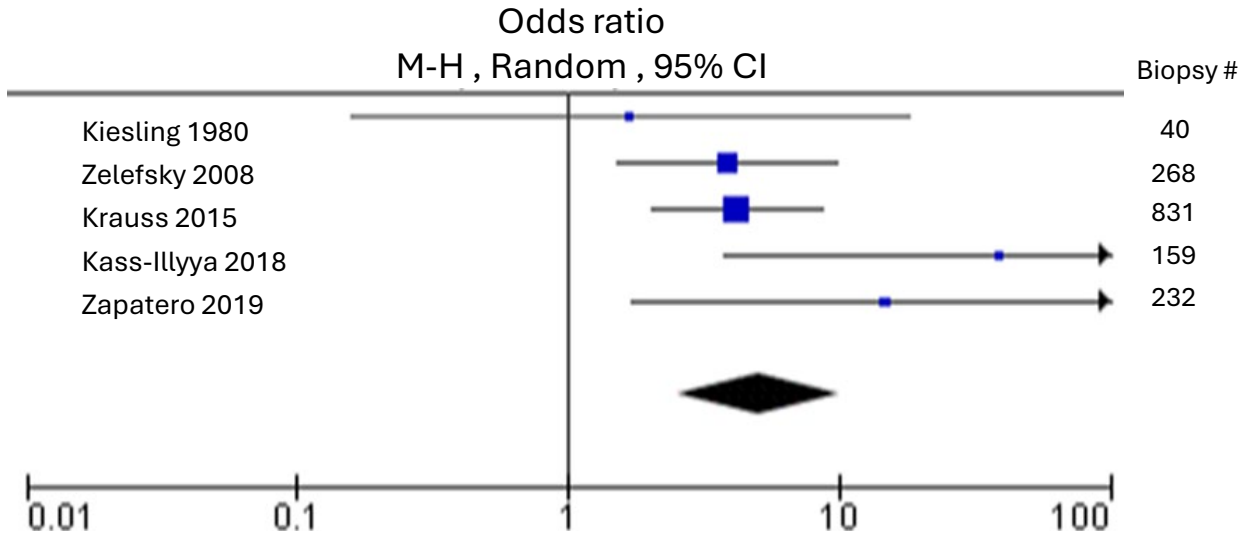
- 10-fold higher odds of developing biochemical failure (P < 0.00001)
- 3-fold higher odds of developing distant metastasis (P < 0.00001)
- 5-fold higher odds of dying from their prostate cancer (P < 0.00001)

Risk of developing distant metastasis



Total HR 3.12 [2.06, 4.73]*

Risk of prostate cancer mortality



Total HR 5.07 [2.57, 10]*

* Weighted risk across studies, represented Forrest plots for metastasis-free survival and cancer mortality

Singh S et al. Prostate Cancer Prostatic Dis 2021;24:612-622

Concluding remarks

- CAN-2409 significantly improved disease-free survival in patients with localized, intermediate-to-high-risk prostate cancer treated with standard-of-care EBRT with curative intent (HR 0.70; p = 0.0155)
- CAN-2409 significantly improved prostate cancer-specific outcomes (HR 0.62; p = 0.0046)
- CAN-2409 significantly increased the proportion of patients achieving a PSA nadir of < 0.2 ng/ml compared to placebo (67.1% vs. 58.6%; p = 0.0164)
- CAN-2409 significantly improved the rate of pathological complete response in 2-year biopsies compared to the placebo control arm (80.4% vs. 63.6%; p = 0.0015)
- CAN-2409 was safe and well-tolerated
- CAN-2409 immunotherapy could represent the first new therapy for men with localized prostate cancer who seek cure in over 20 years

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