Neues aus der Uroonkologie
ASCO 2024

Christoph Lutz

Praxis für Hämatologie und Onkologie Koblenz

03.07.2024

Übersicht

1. Prostatakarzinom

2. Urothelkarzinom

2024 ASCO ANNUAL MEETING

EA8153: Cabazitaxel witH Abiraterone Versus Abiraterone Alone Randomized Trial for Extensive Disease Following Docetaxel: the CHAARTED2 Trial of the ECOG-ACRIN Cancer Research Group

Christos E. Kyriakopoulos[1], Yu-Hui Chen[2, 3], Robert Jeraj[1], Fenghai Duan[3, 4], Jun Luo[5], Emmanuel S. Antonarakis[6], Abhishek Tripathi[7], David Kosoff[1], Rohan Garje[8], Russell K. Pachynski[9], Rahul A. Parikh[10], Andrea L. Harzstark[11], Nabil Adra[12], Benjamin L. Maughan[13], Yousef Zakharia[8], Paul Corn[14], Glenn Liu[1], Michael A. Carducci[5]

[1]University of Wisconsin Carbone Cancer Center, Madison WI, [2]Dana-Farber Cancer Institute, Boston MA, [3]ECOG-ACRIN Biostatistics Center, Boston MA, [4]Brown University School of Public Health, Providence RI, [5]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore MD, [6]University of Minnesota Masonic Cancer Center, Minneapolis, MN, [7]City of Hope Comprehensive Cancer Center, Duarte, CA, [8]University of Iowa Holden Comprehensive Cancer Center, Iowa City IA, [9]Washington University Siteman Cancer Center, Saint Louis, MO, [10]University of Kansas Cancer Center, Westwood, KS, [11]Kaiser Permanente, San Francisco CA, [12]Indiana University Melvin and Bren Simon Cancer Center, Indianapolis IN, [13]University of Utah Huntsman Cancer Institute, Salt Lake City UT, [14]MD Anderson Cancer Center, Houston TX.

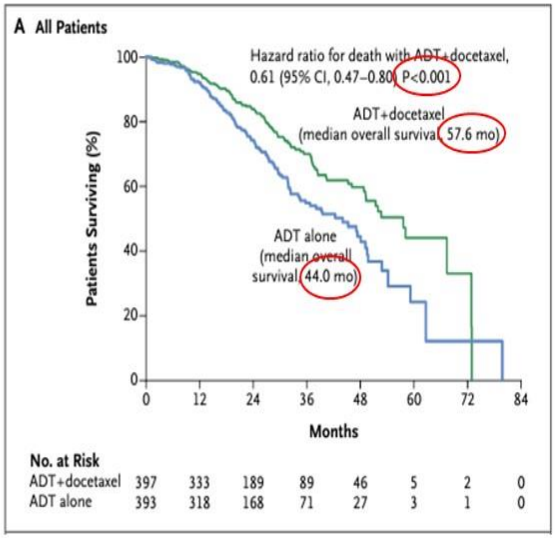
ECOG-ACRIN cancer research group

PRESENTED BY: Christos E. Kyriakopoulos, MD

E3805 (CHAARTED)

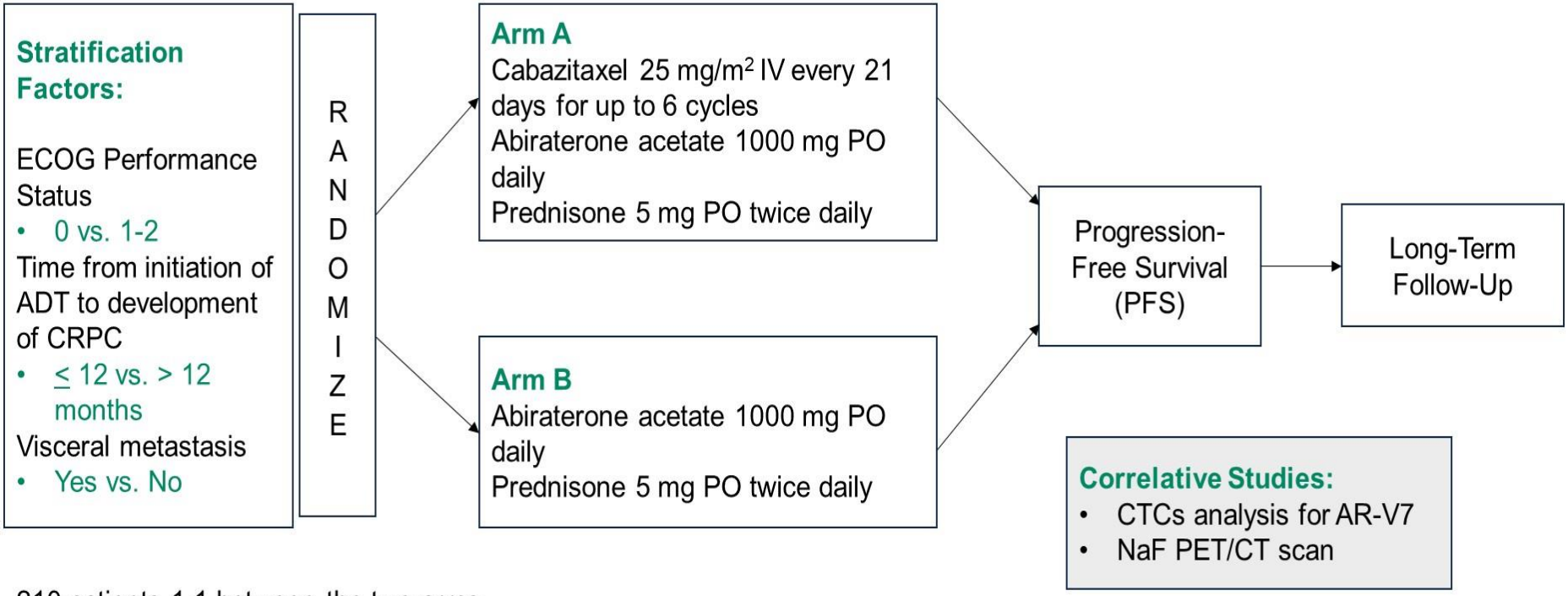
- Initial Report:
  - Addition of 6 cycles of docetaxel to ADT significantly prolonged OS compared to ADT alone in patient with mCSPC
  - **Primary Endpoint: OS 57.6 vs 44.0 months (p=0.0003)**

- Hypothesis:
  - Docetaxel would eradicate resistant clones already present at the time of diagnosis
  - Thus, would prolong response to ADT



Sweeney C et al. *N Engl J Med.* 2015 Aug 20;373(8):737-46

Study Schema – Randomized Phase II



210 patients 1:1 between the two arms
All patient continued ADT as per standard of care

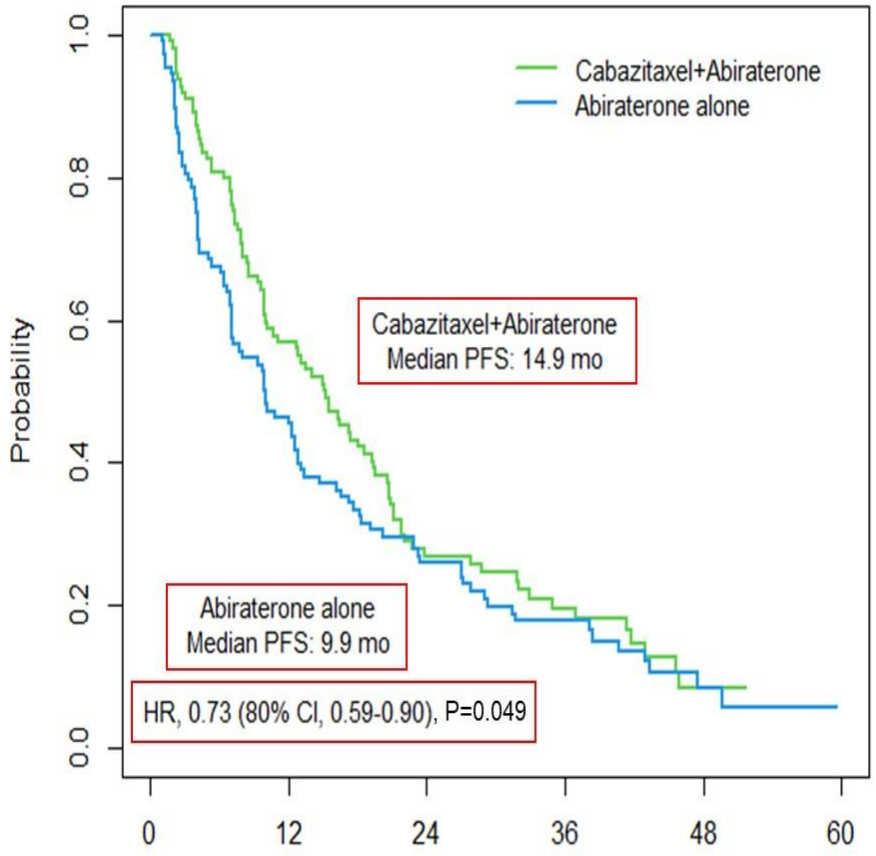
Einschlusskriterien: mCRPC; Docetaxel vorbehandelt für mHSPC
Auschlusskriterien: vorbehandelt wegen mCRPC, vorbehandelt mit ARPI

Patient Characteristics

	Cabazitaxel+Abiraterone (N=111)	Abiraterone alone (N=112)	Total (N=223)
Age (Median, Range)	63 (42-79)	66 (41-80)	64 (41-80)
ECOG PS (n, %)			
0	64 (57.7)	66 (58.9)	130 (58.3)
1	44 (39.6)	43 (38.4)	87 (39)
2	3 (2.7)	3 (2.7)	6 (2.7)
Gleason Score (n, %)			
< 7	3 (3.3)	4 (4.3)	7 (3.8)
7	15 (16.7)	9 (9.7)	24 (13.1)
8-10	72 (80)	80 (86)	152 (83.1)
Missing/Unknown	21	19	40
Baseline PSA (ng/mL)			
Median (Range)	13.5 (0.08-503.4)	13.3 (0.95-1020.4)	13.3 (0.8-1020.4)
Race (n, %)			
White	84 (80.8)	81 (75.7)	165 (78.2)
African-American	20 (19.2)	22 (20.6)	42 (19.9)
Other	0 (0)	4 (3.7)	4 (1.9)
Unknown/Missing	7	5	12

Primary Endpoint: PFS

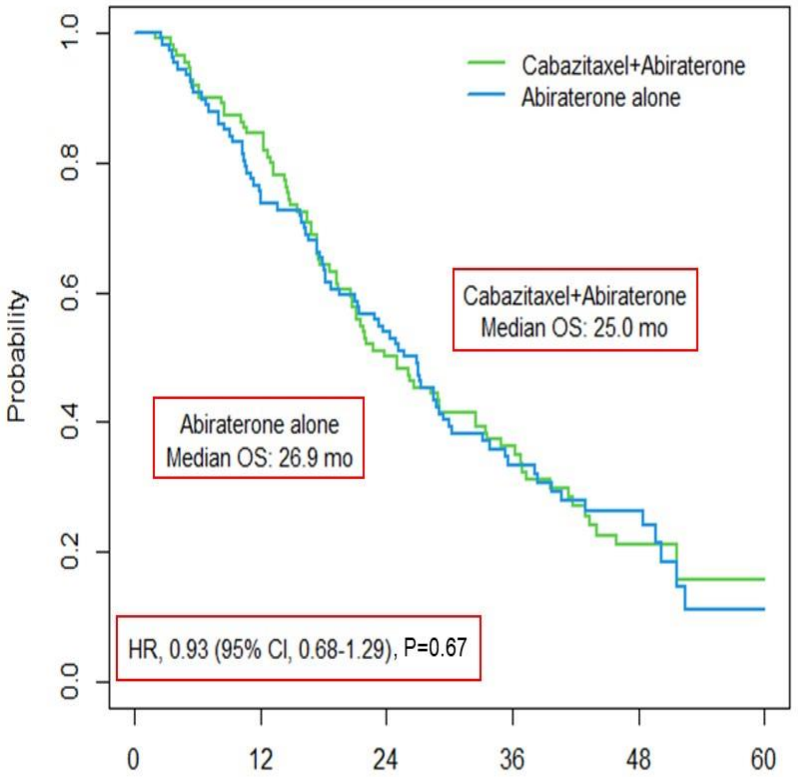
- **Median Follow-Up: 47.3 (0-61.2) months**
- **5 months difference in median PFS in favor of Cabazitaxel + Abiraterone (HR, 0.73)**



Number at Risk						
Cabazitaxel+Abiraterone	111	56	23	11	3	0
Abiraterone alone	112	45	22	12	3	0

Secondary Endpoints: Overall Survival

- No difference in Overall Survival between the two Arms (HR, 0.93)
- The study was underpowered for OS



Number at Risk						
Cabazitaxel+Abiraterone	111	92	53	32	11	1
Abiraterone alone	112	79	57	27	13	1

Secondary Endpoints: Safety

- Cabazitaxel overall well tolerated with more cytopenias
- Treatment related toxicities of at least 5% in any of the two arms

	Cabazitaxel+Abiraterone (N=109)				Abiraterone alone (N=108)				
	Grade				Grade				
	3	4	5	Total	3	4	5	Total	P-value
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Anemia	7 (6.4)	-	-	**7 (6.4)**	1 (0.9)	-	-	**1 (0.9)**	**0.07**
Fatigue	6 (5.5)	-	-	**6 (5.5)**	2 (1.9)	-	-	**2 (1.9)**	**0.28**
Neutrophil count decreased	5 (4.6)	6 (5.5)	-	**11 (10.1)**	-	-	-	**-**	**0.001**
White cell count decreased	6 (5.5)	3 (2.8)	-	**9 (8.3)**	-	-	-	**-**	**0.003**
Hypertension	11 (10.1)	-	-	**11 (10.1)**	12 (11.1)	-	-	**12 (11.1)**	**0.83**
WORST DEGREE	36 (33)	9 (8.3)	1 (0.9)	**46 (42.2)**	27 (25)	4 (3.7)	-	**31 (28.7)**	**0.047**

2024 ASCO ANNUAL MEETING

UHN Princess Margaret Cancer Centre

ABSTRACT LBA5002: A randomized, double-blind, placebo-controlled trial of metformin in reducing progression among men on expectant management for low-risk prostate cancer: The MAST (Metformin Active Surveillance Trial) study.

Neil E. Fleshner, Rui Miguel Bernardino, Katherine Lajkosz, Fred Saad, Jonathan Izawa, Darrel Drachenberg, Jeff W. Saranchuk, Simon Tanguay, Ricardo A. Rendon, Michael Leveridge, Bobby Shayegan, Adrian Fairey, Jessica Grace Cockburn, Doron Berlin, Robert James Hamilton, Tiiu Sildva, Rodney H. Breau, Patrick O. Richard, Laurence Klotz, Anthony M. Joshua

Prof. Anthony Joshua BSc(Med) MBBS PhD FRACP
Princess Margaret Cancer Centre, Toronto, Canada
Kinghorn Cancer Centre, St Vincents Hospital, Sydney, Australia

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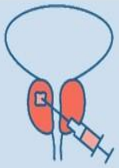
BACKGROUND: Management of Low-Risk PCa

	Watchful Waiting	Active Surveillance	Definitive Therapy
Strategy			
Patient Population			
Timeframe			
Considerations			

PRESENTED BY: Professor Anthony M.Joshua BSc (Med) (Hons) MBBS PhD (UToronto) FRACP

BACKGROUND: Rationale

BIOLOGICAL

- Importance of insulin, mTOR signaling[1]
- Overcomes NKX3.1 loss[2]
- Improved immune micro-environment[3]

EPIDEMIOLOGICAL

- Reduction of PCa mortality in diabetic men[4]
- Associated with less BCR[5]
- Improved OS in SEER[6]

CLINICAL

- Reduction of Ki67 in neoadjuvant trial[7]
- Improved OS with Abiraterone[8]
- Reduces progression and improves OS in HSPC[9]

1 White-Al Habeeb et al., 2016.2 Papachristodoulou et al., 2024. 3.Liu et al., 2018.4Margel et al., 2013. 5Zannella et al., 2013. 6 Scarton et al., 2022. Joshua et al., 2014 8 Wilson et al., 2022 9.Alghandour et al., 2021.7

PRESENTED BY: Professor Anthony M.Joshua BSc (Med) (Hons) MBBS PhD (UToronto) FRACP

Study Schema

PATIENT CHARACTERISTICS

- Newly diagnosed (≤ 12 mo)
- Low-risk prostate cancer including:
  - Gleason Score ≤ 6
  - ≤ 1/3 cores involved
  - <50% of any 1 core positive
- PSA ≤ 10 ng/ml

RANDOMIZE

1:1

ARM 1 (n=203)
Active Surveillance + Placebo

850 mg QD for 1 month followed by 850 mg BID for 35 months

ARM 2 (n=204)
Active Surveillance + Metformin

PRIMARY ENDPOINT

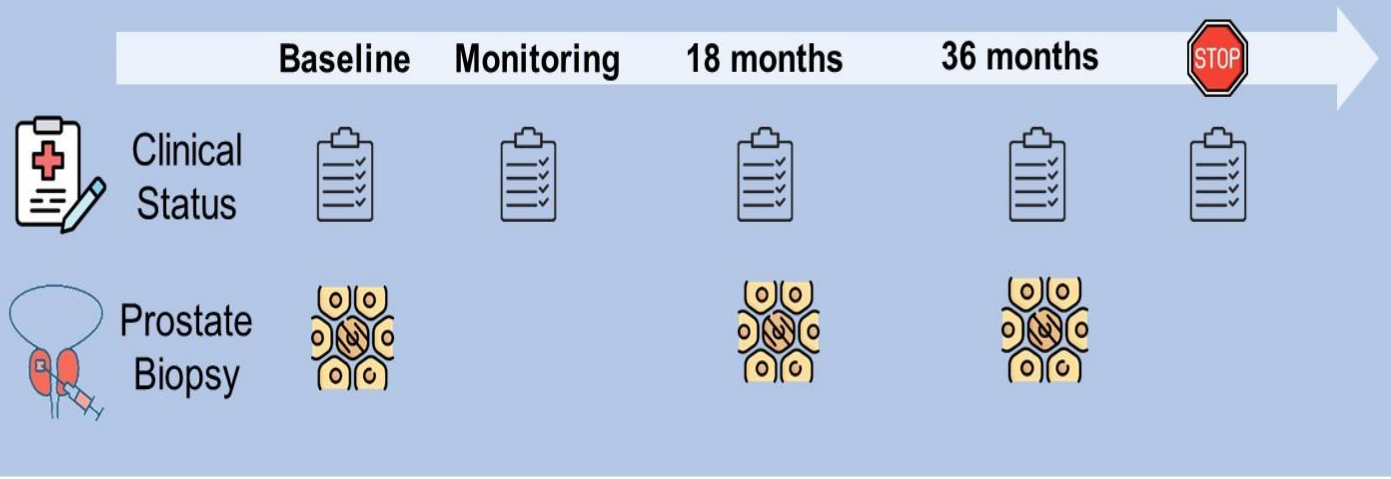
Time to Pathological Progression

Time to Definitive Therapy

Stratified by Centre

SPECIMEN & DATA COLLECTION

- Regular clinical monitoring
- 12-core prostate biopsy
- Dedicated site pathologist for all study biopsies
- Central pathology review of progression

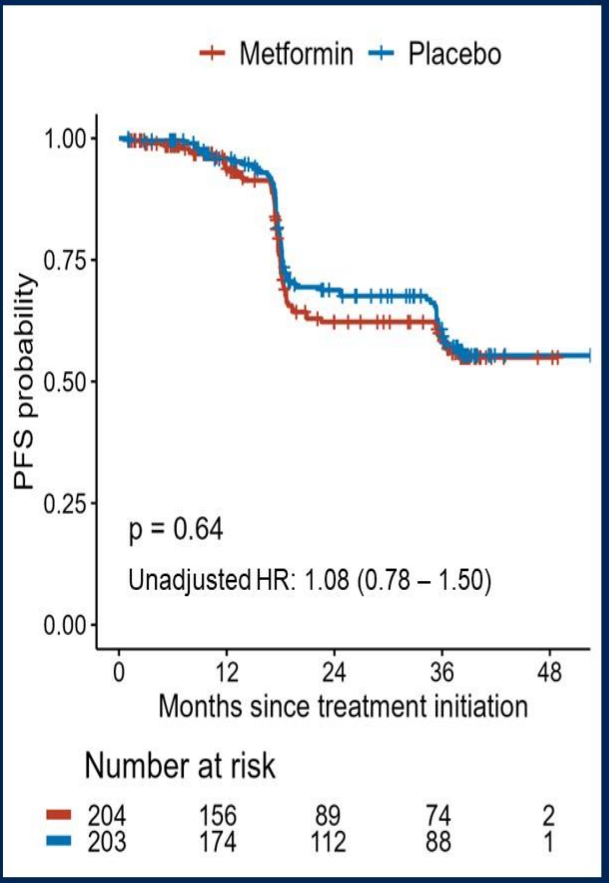


Baseline Demographics

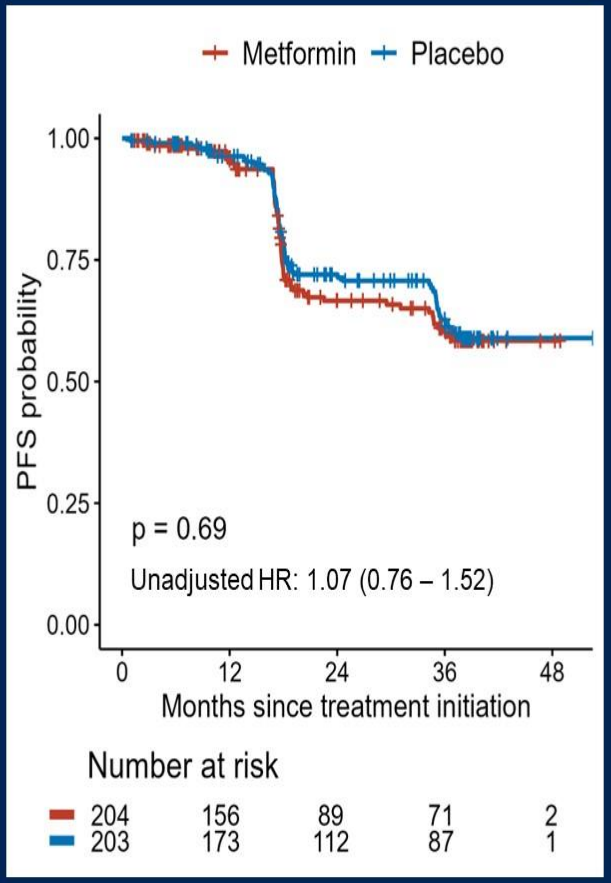
	Metformin (n=204)	Placebo (n=203)
Age		
Median (range)	62 (41 – 76)	63 (45 – 76)
Clinical Stage		
T1c (%)	189 (93.6)	185 (93.9)
T2a (%)	13 (6.4)	12 (6.1)
BMI		
Median (range)	27.4 (19.0 – 55.6)	27.7 (18.1 – 45.8)
PSA		
Median (range)	5.6 (0.8 – 31.4)	6.0 (0.4 – 16.1)
Positive Cores		
Median (range)	1 (0 – 7)	1 (0 – 6)
Tumour Volume		
Median (range)	43 (0 – 634)	44 (5.7 – 174)

Progression Free Survival

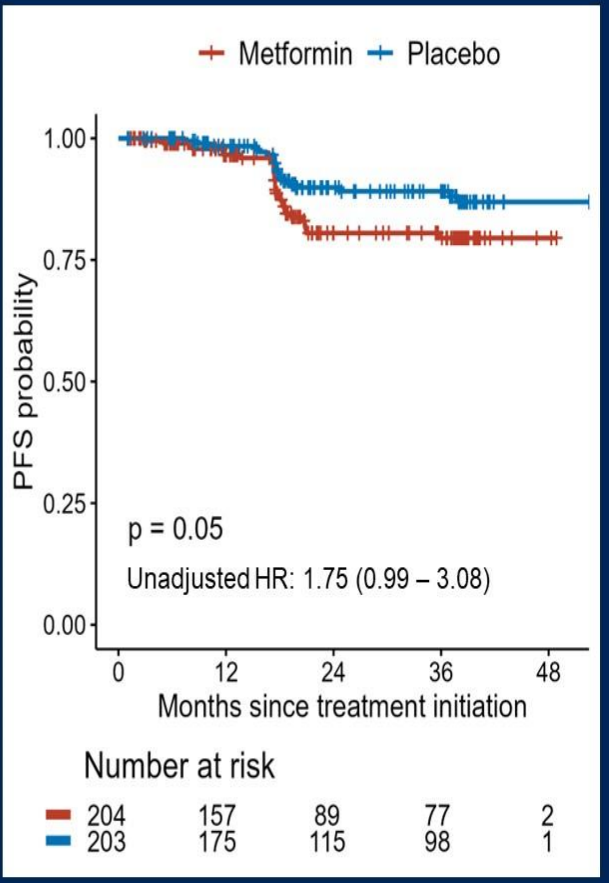
Therapeutic + Pathologic Progression



Pathologic Progression



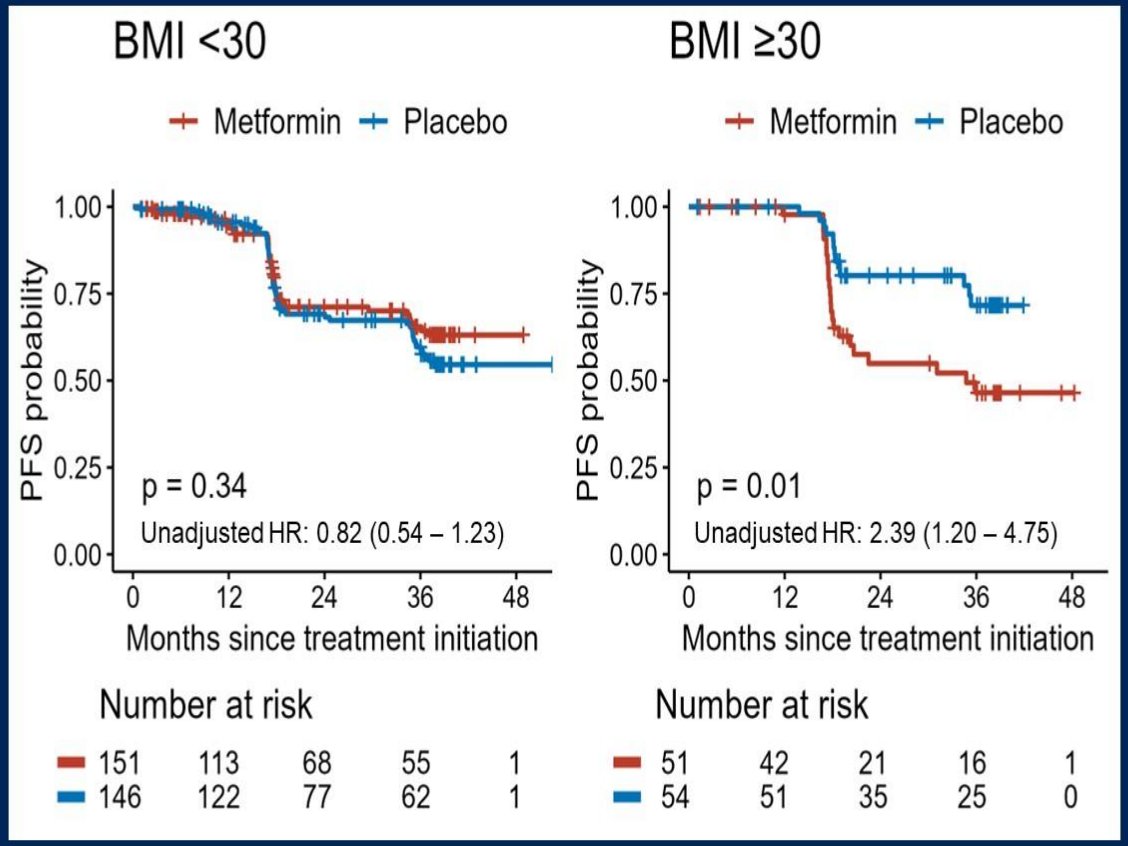
Therapeutic Progression



Pathological Progression Endpoints

	Metformin (n=62) (%)	Placebo (n=67) (%)	Log-rank p-value
% Cores Involved >33.3%	30 (48.4)	32 (47.8)	0.77
Max % Core Involvement ≥50%	28 (45.2)	30 (44.8)	0.78
Gleason ≥7	43 (69.4)	44 (65.7)	0.6
Gleason ≥8	8 (12.9)	3 (4.5)	0.082

BMI and Metformin with Pathologic Progression



Test for Interaction
Unadjusted p=0.012
Adjusted p=0.032

Toxicities

	Placebo		Metformin	
	Grade 1/2	Grade 3	Grade 1/2	Grade 3
Diarrhea	16 (8%)	0 (0%)	36 (18%)	2 (1%)
GI Symptoms *(i.e. nausea, bloating, pain)*	7 (3%)	0 (0%)	29 (14%)	5 (3%)
Fatigue	1 (0.5%)	0 (0%)	5 (3%)	0 (0%)
Hypoglycemia	0 (0%)	0 (0%)	1 (0.5%)	0 (0%)
Weight Loss	0 (0%)	0 (0%)	4 (2%)	0 (0%)
Decreased Appetite	0 (0%)	0 (0%)	6 (3%)	1 (0.5%)

Weight

	Placebo	Metformin
	n=165	n=148
Weight Change 12m	**0.6kg**	**-1.8kg**
	n=104	n=86
Weight Change 24m	**0.7kg**	**-1.4kg**

Key Takeaway Points

- Metformin use **does not** prevent progression of low-risk localized prostate cancer suitable for active surveillance
- Exploratory subgroup analyses indicate **potential detriment** to
  - Patients with high BMI at study entry
  - Patients with Grade group 4+ (Gleason 8+) at progression
- Further research is needed to understand the consequences of metformin on prostate cancer outcomes

2024 ASCO ANNUAL MEETING

MANCAN 2: A multicentre randomised controlled trial of self-help cognitive behavioural therapy (CBT) to manage hot flushes and night sweats (HFNS) in patients with prostate cancer receiving androgen deprivation therapy (ADT)

Simon J. Crabb, Alannah Morgan, Evgenia Stefanopoulou, Louisa Fleure, James Raftery, Gareth Owen Griffiths, Cherish Boxall, Sam Wilding, Theodora Nearchou, Sean Ewings, Jacqueline Nuttall, Zina Eminton, Emma Tilt, Roger Bacon, Jonathan Martin, Deborah Fenlon, Myra Hunter, Alison Richardson

Southampton Clinical Trials Unit, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; Turning Point, London, United Kingdom; Guys and St Thomas NHS Foundation Trust, London, United Kingdom; Prostate Cancer Support Organisation (PCaSO), Emsworth, United Kingdom; Department of Primary Care and Population Health, University College London, London, United Kingdom; Faculty of Medicine, Health and Life Sciences, Swansea University, Swansea, United Kingdom; Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom; School of Health Sciences, University of Southampton, Southampton, United Kingdom

SUPPORTED BY NIHR | National Institute for Health and Care Research

University of Southampton

University Hospital Southampton NHS Foundation Trust

UKCRC Registered Clinical Trials Units

Southampton Clinical Trials Unit

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Background

- Up to 80% of prostate cancer patients, who receive ADT, suffer HFNS which may impact quality of life and potentially ADT compliance[1]
- HFNS are associated with sleep disturbance, anxiety, low mood and cognitive impairment[2]
- Non-pharmacological mitigation options lack adequate prospective data[3]
- A prior, single centre, study found self-help CBT, delivered by a clinical psychologist, reduced HFNS impact due to ADT at 6 weeks[4]
- In breast cancer, CBT delivered by specialist nurses, improved HFNS impact at 6 months, in addition to sleep, anxiety and depression scores[5]

ADT, Androgen deprivation therapy; HFNS, hot flushes and night sweats; CBT, cognitive behavioural therapy; 1. Sharifi N, et al. JAMA. 2005;294(2):238-244; 2. Engstrom C. Am. J. Men's Health. 2008;2:122-132; 3. NICE guideline [NG131] https://www.nice.org.uk/guidance/ng131/chapter/Recommendations#people-having-hormone-therapy; 4. Stefanopoulou E, et al Psycho-Oncology. 2015;24:1159-66; 5. Fenlon D, et al. Psycho-Oncology. 2020;29:1514-1523

Trial design[1]

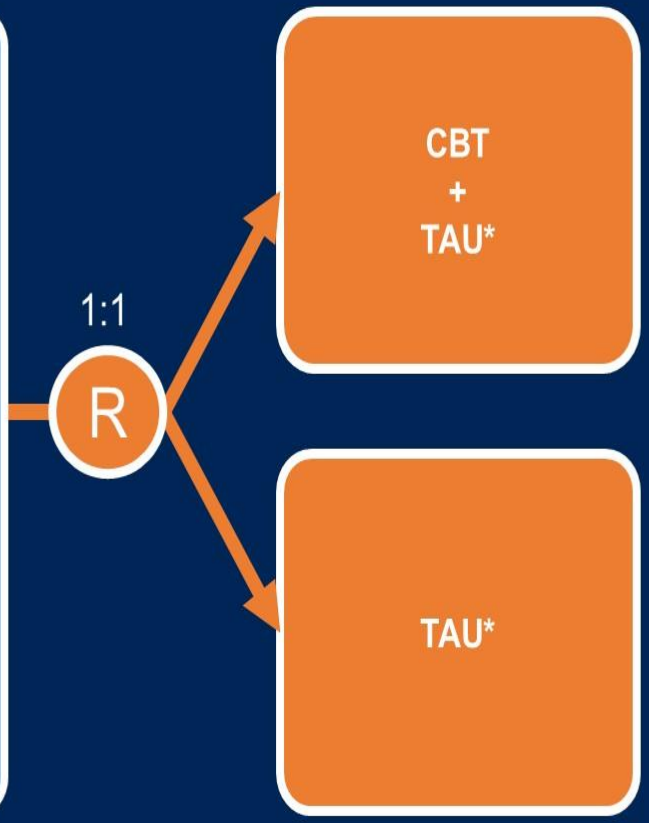
Patient population (summary)

Inclusion:

- Localised or advanced prostate cancer
- Curative or palliative treatment intent
- ≥ 6 months further continuous ADT planned
- Problematic hot flushes and night sweats (HFNS Problem Rating Scale ≥ 2)
- Able to participate in group sessions

Exclusion:

- Uncontrolled disease progression
- Receiving chemotherapy or multi fraction radiotherapy



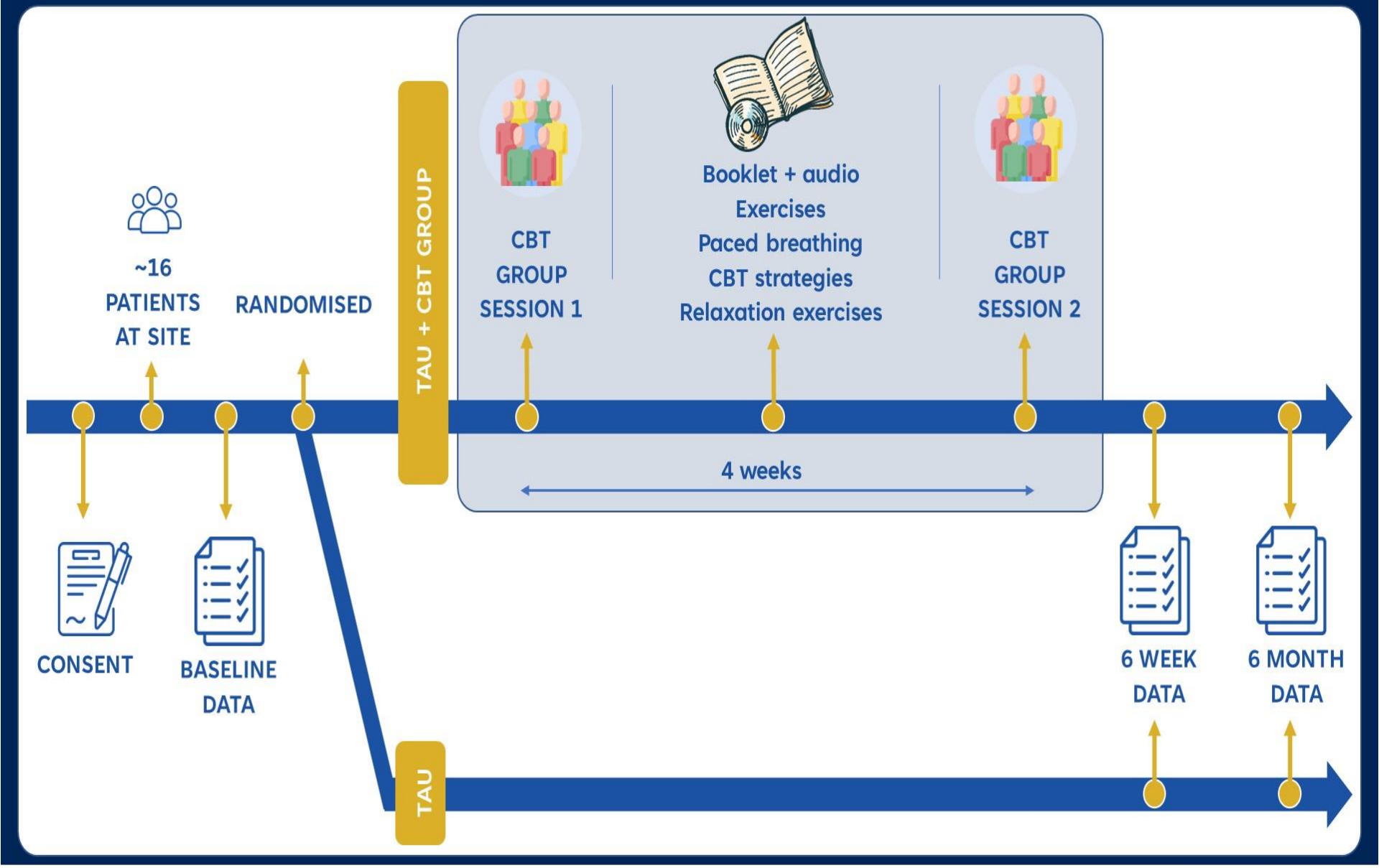
Primary endpoint

- HFNS Problem Rating Scale[2] at 6 months compared to baseline

Secondary endpoints**

- HFNS Rating Scale at 6 weeks
- HFNS frequency
- HFNS Beliefs and Behaviour subscales[3]
- Quality of life (EORTC QLQ C30)
- Anxiety (GAD7)
- Depressed mood (PHQ9)
- Work and Social Adjustment Scale (WSAS)
- Sleep (PSQI, item 6)
- ADT compliance
- Fidelity of CBT delivery

1. Crabb S, et al. Trials 2023;24(1):450. doi: 10.1186/s13063-023-07325-w; 2. Hunter M, et al. Climacteric. 2019;22:410-423; 3. Hunter M, et al. Maturitas. 2014;79:464-470; ADT, androgen deprivation therapy; HFNS, hot flushes and night sweats; CBT, cognitive behavioural therapy; TAU, treatment as usual; *Interventions to mitigate HFNS could include pharmaceuticals, herbal remedies, vitamin supplements, yoga and acupuncture; **Each endpoint assessed at 6 weeks and 6 months compared to baseline



Patient characteristics and workshop delivery

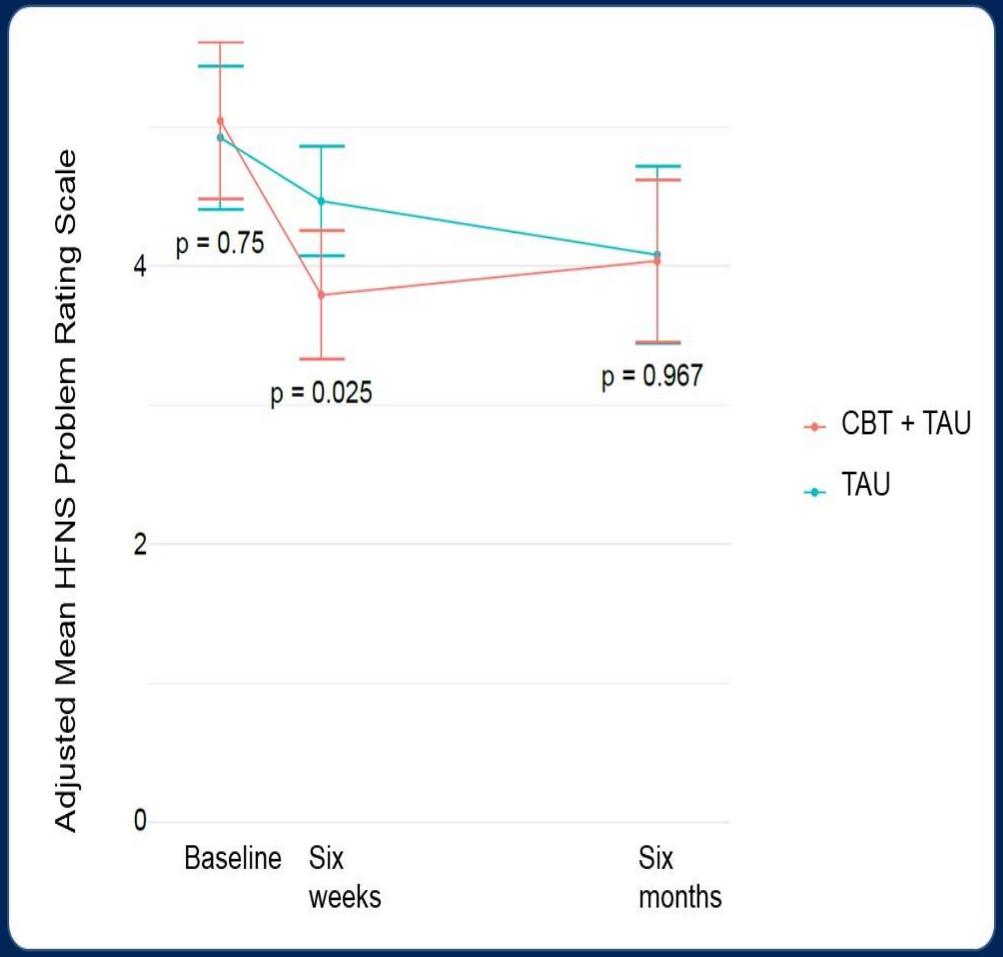
Recruited March 2022 to March 2023 from 9 centres

		Baseline TAU (n=81)		Baseline CBT + TAU (n=81)		6 months TAU (n=65)		6 months CBT + TAU (n=52)	
Age	Median (min, max)	71	(53, 85)	69	(47, 85)	71	(53, 85)	69	(52, 85)
Treatment intent	Curative Palliative	31 51	(38.8%) (61.7%)	30 51	(37.0%) (63.0%)	28 37	(43.1%) (56.9%)	16 36	(30.8%) (69.2%)
Time on ADT	< 1 year ≥ 1 year	41 40	(50.6%) (49.4%)	30 51	(37.0%) (63.0%)	35 30	(53.8%) (46.2%)	21 31	(40.4%) (59.6%)
Co-treatments*	ARTA** Bicalutamide Bisphosphonate	42 9 10	(51.9%) (11.1%) (12.3%)	40 10 7	(49.4%) (12.3%) (8.6%)	31 7 7	(47.7%) (10.8%) (10.8%)	27 6 5	(51.9% (11.5%) (9.6%)
HFNS treatment	None Drug based Non-drug based	72 6 3	(88.9%) (7.4%) (3.7%)	71 5 5	(87.7%) (6.2%) (6.2%)	57 5 3	(87.7%) (7.7%) (4.6%)	45 5 2	(86.5%) (9.6%) (3.8%)
Observation period started	Jan – Aug Sep – Dec	36 45	(44.4%) (55.6%)	37 44	(45.7%) (54.3%)	31 34	(47.7%) (52.3%)	23 29	(44.2%) (55.8%)
CBT workshop attendance	No One Both			22 20 39	(27.2%) (24.7%) (48.1%)			7 13 32	(13.5%) (25.0%) (61.5%)
Workshop delivery	Mean adherence								85%

TAU, treatment as usual; CBT, cognitive behavioural therapy; ADT, androgen deprivation therapy; HFNS, hot flushes and night sweats; *Options here are not mutually exclusive; **Androgen receptor targeted agent (included abiraterone and prednisolone, enzalutamide, darolutamide, apalutamide)

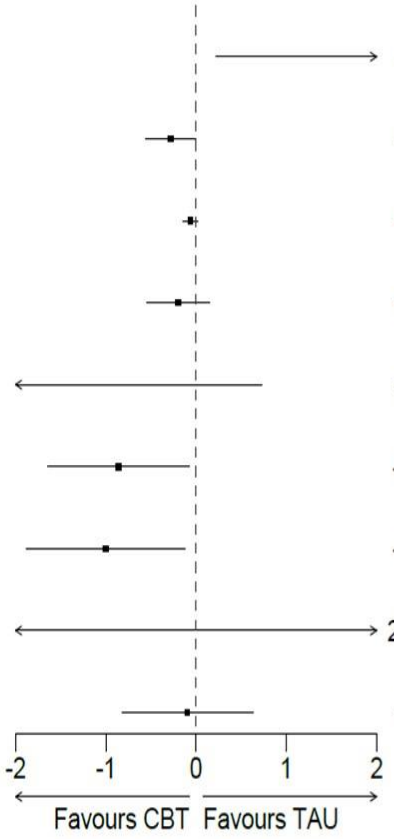
HFNS Problem Rating Scale

Mean score	CBT + TAU	TAU
Baseline	5.04	4.92
6 weeks	3.79	4.47
6 months	4.04	4.08



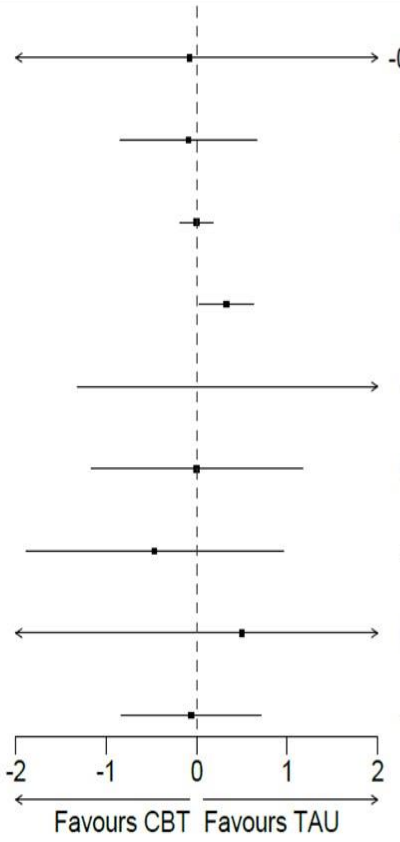
Secondary endpoints: 6 weeks

Endpoint	TAU	TAU + CBT	ES (95% CI)	p-value
Total HFNS frequency	66	58	5.20 (0.22 to 10.19)	0.043
HFNS social context and sleep subscale	66	57	-0.28 (-0.56 to 0.00)	0.055
HFNS calm and acceptance subscale	71	59	-0.06 (-0.14 to 0.02)	0.151
HFNS humour and openness subscale	68	58	-0.20 (-0.55 to 0.15)	0.269
QOL (EORTC QLQ-C30)	70	60	-3.70 (-8.14 to 0.73)	0.104
Anxiety (GAD7)	68	59	-0.86 (-1.64 to -0.08)	0.033
Depression (PHQ9)	67	60	-1.00 (-1.88 to -0.12)	0.027
Functional state (WSAS)	34	22	2.38 (-14.88 to 19.65)	0.803
Sleep (PSQI)	73	61	-0.10 (-0.82 to 0.63)	0.796



Secondary endpoints: 6 months

Endpoint	TAU	TAU + CBT	ES (95% CI)	p-value
Total HFNS frequency	58	50	-0.08 (-10.22 to 10.07)	0.988
HFNS social context and sleep subscale	62	50	-0.09 (-0.85 to 0.67)	0.853
HFNS calm and acceptance subscale	65	54	0.00 (-0.18 to 0.18)	1.000
HFNS humour and openness subscale	61	54	0.33 (0.03 to 0.63)	0.032
QOL (EORTC QLQ-C30)	65	54	4.17 (-1.32 to 9.66)	0.140
Anxiety (GAD7)	62	54	0.00 (-1.17 to 1.17)	1.000
Depression (PHQ9)	59	53	-0.47 (-1.89 to 0.96)	0.522
Functional state (WSAS)	32	17	0.50 (-3.65 to 4.66)	0.813
Sleep (PSQI)	65	54	-0.06 (-0.83 to 0.71)	0.882



Compliance with ADT at 6 months

TAU n=65		TAU + CBT n=51		p*
Compliant	Non-compliant	Compliant	Non-compliant	
56 (86.2%)	9 (13.8%)	51	0	0.006

* Fisher exact test; ** Due to zero cell counts, p-value is in comparison to TAU participants not attending any workshops

2024 ASCO ANNUAL MEETING

Health-related quality of life and pain in a phase 3 study of [^{177}Lu]Lu-PSMA-617 in taxane-naive patients with metastatic castration-resistant prostate cancer (PSMAfore)

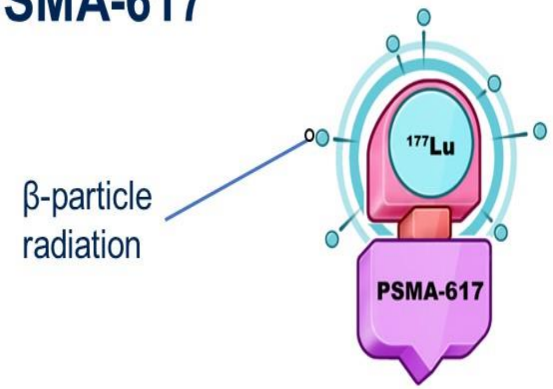
Presenter: Karim Fizazi

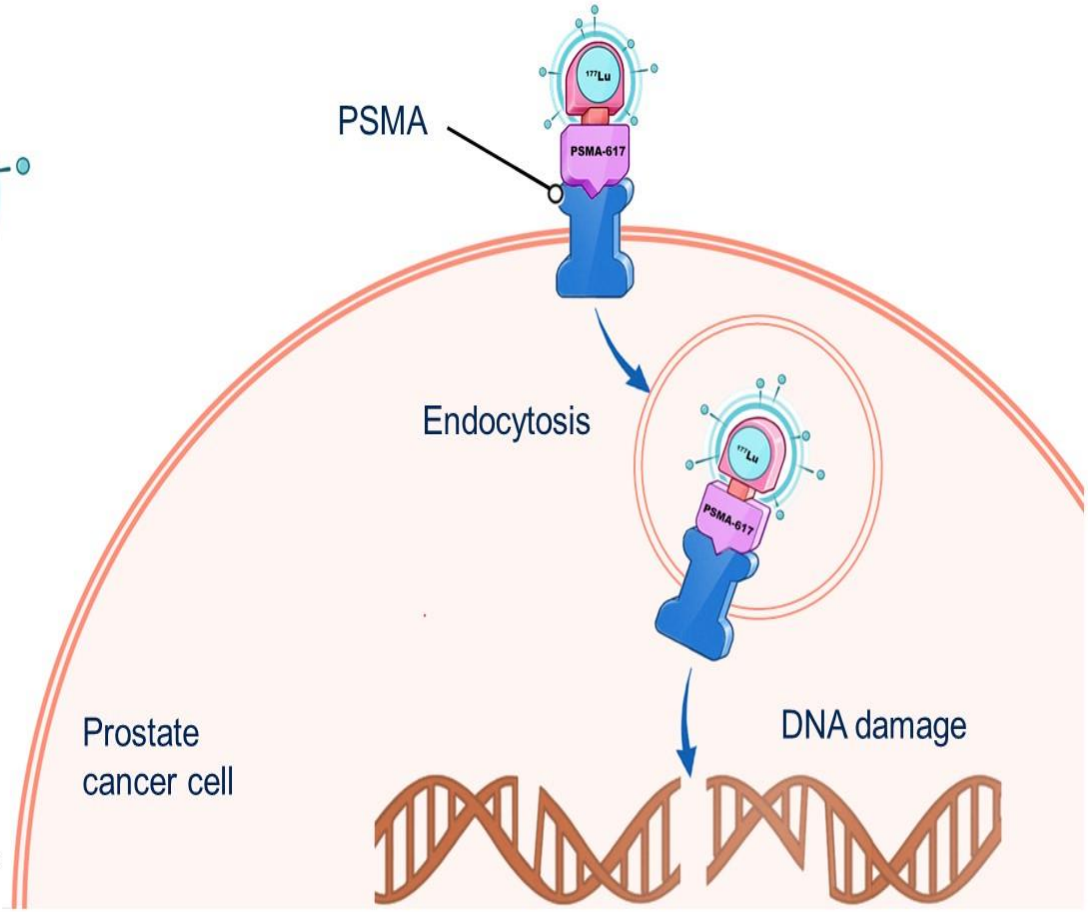
Gustave Roussy Institute, Paris-Saclay University, Villejuif, France

Co-authors: MJ Morris, N Shore, K Chi, M Crosby, J de Bono, K Herrmann, G Roubaud, J Nagarajah, M Fleming, B Lewis, L Nordquist, D Castellano, N Carnahan, S Ghebremariam, M Hertelendi, O Sartor,
on behalf of the PSMAfore Investigators

[^{177}Lu]Lu-PSMA-617 (^{177}Lu-PSMA-617): targeted radioligand therapy for PSMA-positive mCRPC

^{177}Lu-PSMA-617





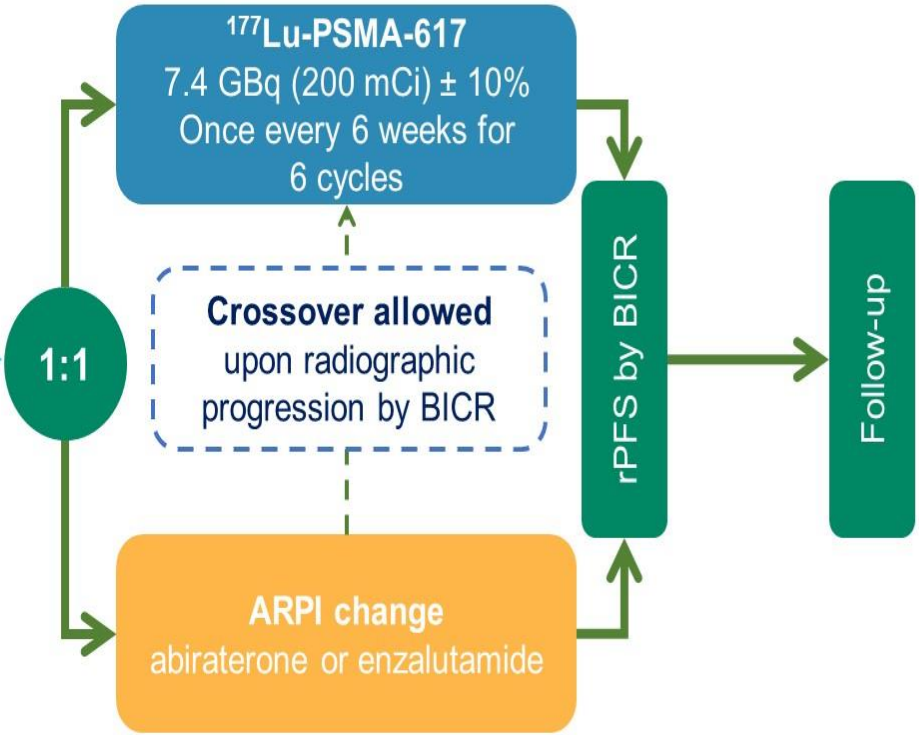
^{177}Lu-PSMA-617 plus SoC prolonged OS, rPFS and time to HRQoL/pain worsening in patients with advanced mCRPC (VISION)[1,2]

1. Sartor O, et al. *N Engl J Med* 2023;385:1091–1103. 2. Fizazi K, et al. *Lancet Oncol* 2023:24:597–610
HRQoL, health-related quality of life; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; PSMA, prostate-specific membrane antigen; rPFS, radiographic progression-free survival; SoC, standard of care

PSMAfore: a phase 3, randomized, open-label study

Eligible adults

- Confirmed progressive mCRPC
- ≥ 1 PSMA-positive metastatic lesion on [^{68}Ga]Ga-PSMA-11 PET/CT and no exclusionary PSMA-negative lesions
- Progressed once on previous second-generation ARPI
  - Candidates for change in ARPI
- Taxane-naive (except [neo]adjuvant > 12 months ago)
  - Not candidates for PARPi
- ECOG performance status 0–1



Stratification factors

- Prior ARPI setting (castration-resistant vs hormone-sensitive)
- BPI-SF worst pain intensity score (0–3 vs > 3)

ARPI, androgen receptor pathway inhibitor; BICR, blinded independent central review; BPI-SF, brief pain inventory – short form; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; mCRPC, metastatic castration-resistant prostate cancer; PARPi; Poly (ADP-ribose) polymerase (PARP) inhibitor; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; rPFS, radiographic progression-free survival

Second interim OS analysis

DCO: June 21, 2023
Median duration: 15.9 months

Baseline patient characteristics

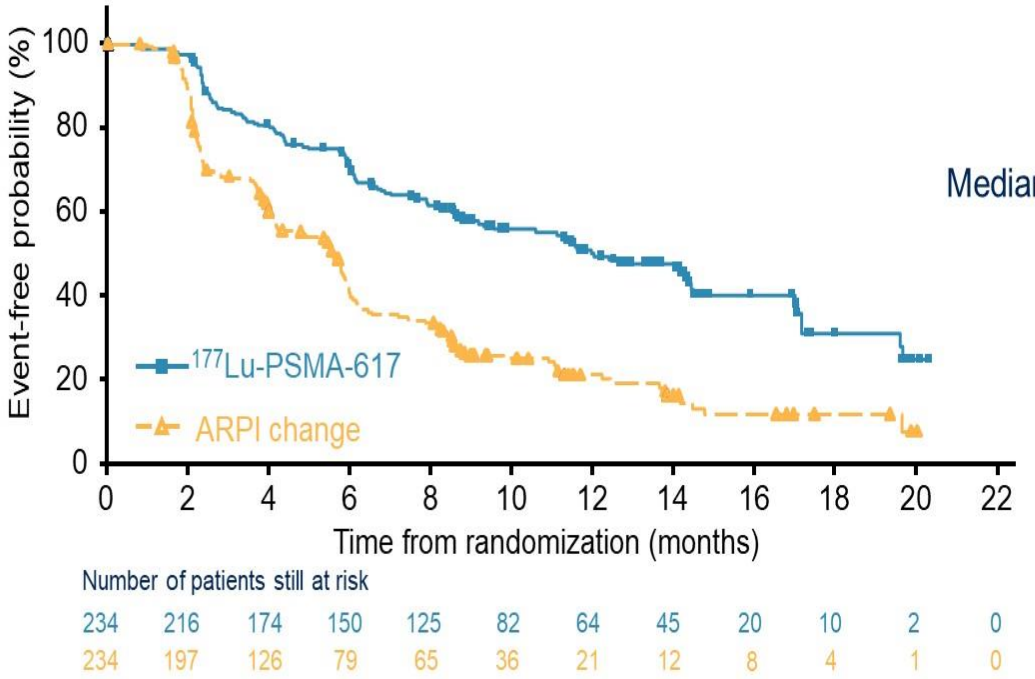
	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Age, median (range), years	71 (43–94)	72 (53–91)
White, n (%)	211 (90.2)	214 (91.5)
ECOG performance status, n (%)		
0	146 (62.4)	115 (49.1)
1	86 (36.8)	114 (48.7)
Gleason score 8–10, n (%)	136 (58.1)	107 (45.7)
PSA, median (range), µg/L	18.4 (0–1197)	14.9 (0–4224)
Hemoglobin, median (range), g/L	128.0 (88–155)	129.0 (88–156)
Alkaline phosphatase, median (range), IU/L	100.0 (36–1727)	103.5 (28–1319)
Site of disease, n (%)		
Liver	13 (5.6)	7 (3.0)
Lymph node	76 (32.5)	74 (31.6)
Bone	205 (87.6)	203 (86.8)
Prior ARPI, n (%)		
Abiraterone	119 (50.9)	130 (55.6)
Enzalutamide	94 (40.2)	84 (35.9)
Other	21 (9.0)	20 (8.5)

ARPI, androgen receptor pathway inhibitor; ECOG, Eastern Cooperative Oncology Group; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen

rPFS: the primary endpoint was met

Primary analysis[a] HR: 0.41 (95% CI: 0.29, 0.56); $p < 0.0001$

Second interim analysis[b] HR: 0.43 (95% CI: 0.33, 0.54)

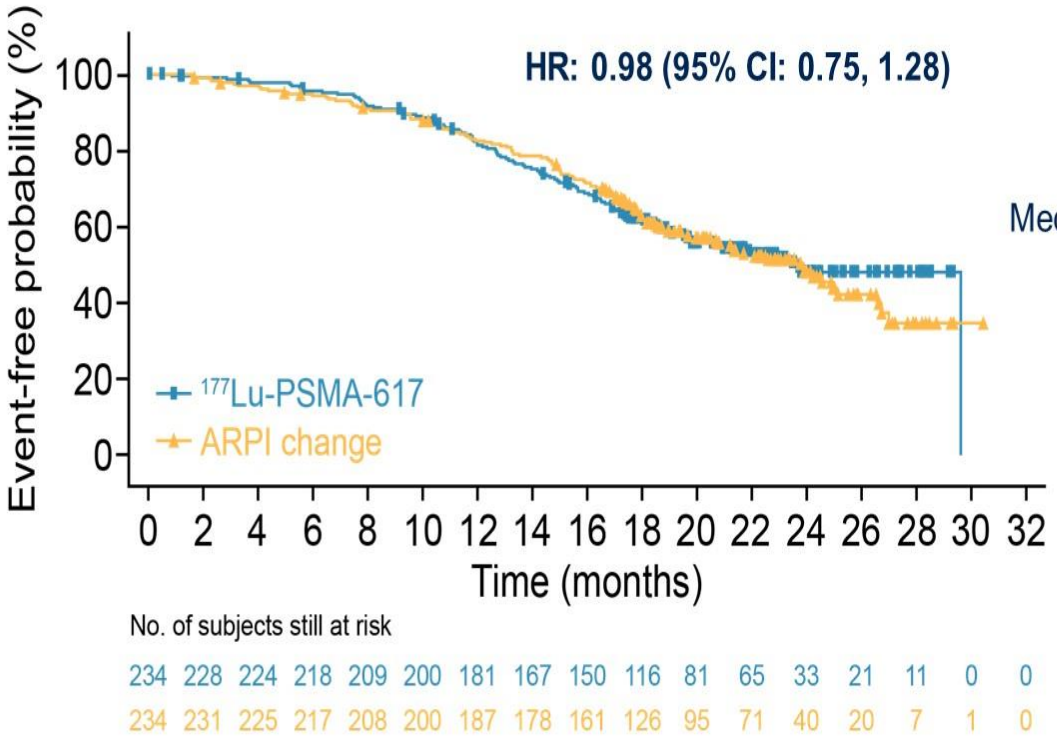


	177Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Events, n	115 (49.1%)	168 (71.8%)
Median, months (95% CI)	12.02 (9.30, 14.42)	5.59 (4.17, 5.95)

[a]Data cutoff October 2, 2022
[b]Data cutoff June 21, 2023
Previously presented at ESMO23
ARPI, androgen receptor pathway inhibitor; CI, confidence interval; HR, hazard ratio; PSMA, prostate-specific membrane antigen; rPFS, radiographic progression-free survival

OS: HR < 1 at third interim analysis with 73% information fraction

Intent-to-treat analysis



	177Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Events, n	104 (44.4%)	112 (47.9%)
Median, months (95% CI)	23.66 (19.75, NE)	23.85 (20.6, 26.55)

Crossover:

134/234 (57.3%) in ARPI change group
134/173 (77.5%) eligible patients

RPSFT crossover-adjusted OS analysis

- HR: 0.98 (95% CI: 0.76, 1.27)
- No difference versus the ITT analysis because RPSFT cannot adjust for crossover confounding in the context of overlapping ITT curves

ARPI, androgen receptor pathway inhibitor; CI, confidence interval; HR, hazard ratio; IF, information fraction; ITT, intent-to-treat ; NE, not evaluable; OS, overall survival; PSMA, prostate-specific membrane antigen; RPFST, rank-preserving structural failure time

Secondary and exploratory endpoints: patient-reported HRQoL and pain

Second interim analysis (DCO: June 21, 2023)

HRQoL

Prostate cancer-specific

Functional Assessment of Cancer Therapy-Prostate (FACT-P)

- Outputs include:
  - Total score
  - Subscales:
    - Physical well-being
    - Functional well-being
    - Emotional well-being
    - Social/family well-being

Generic

EuroQol 5-Dimension 5-Level (EQ-5D-5L)

- Outputs include:
  - Utility score

Chronic pain

Brief Pain Inventory – Short Form (BPI-SF)

- Outputs include time to worsening in:
  - Pain intensity
  - Pain severity (worst pain intensity)
  - Pain interference

BPI-SF, Brief Pain Inventory – Short Form; DCO, data cutoff; EQ-5D-5L, EuroQol-5 Dimension-5 Level; FACT-P, Functional Assessment of Cancer Therapy-Prostate; HRQoL, health-related quality of life

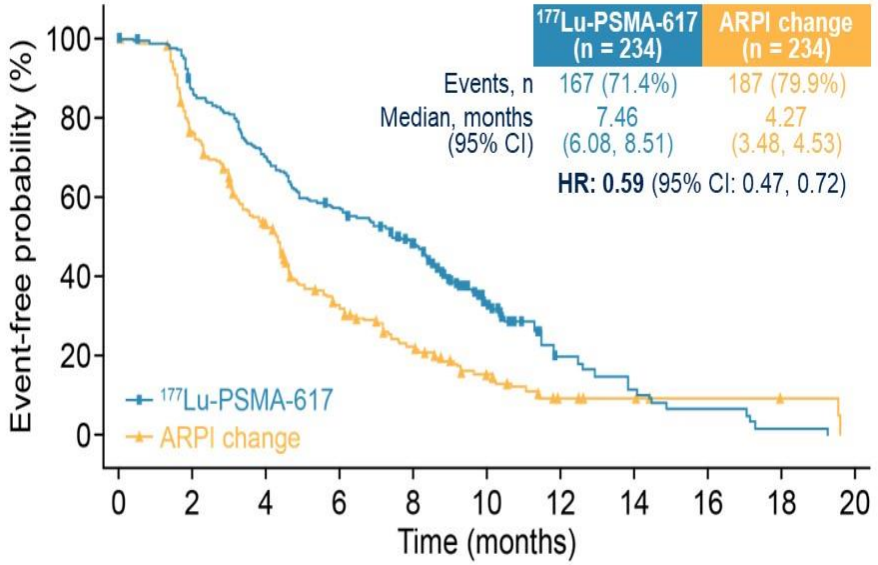
PRESENTED BY: Prof. Karim Fizazi

Time to HRQoL worsening at second interim analysis

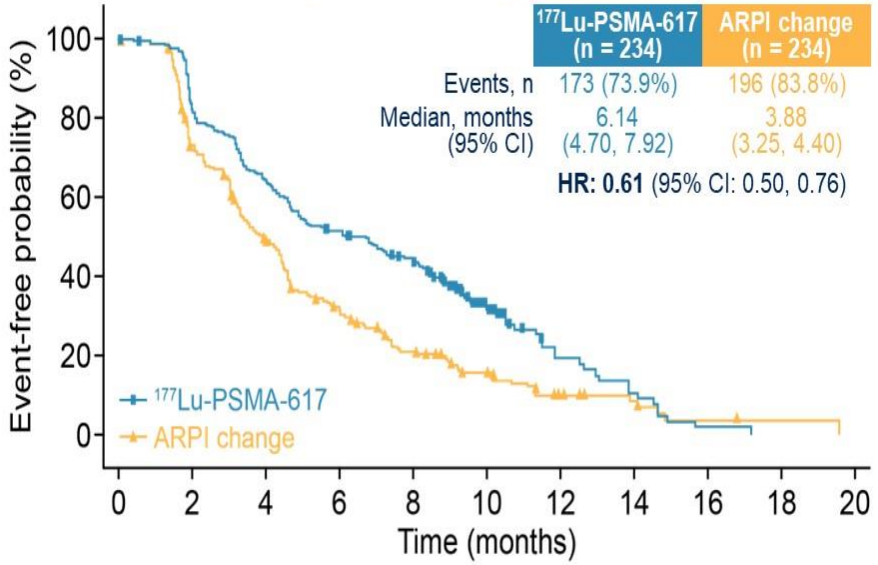
Prespecified analysis:

Composite time to worsening in FACT-P, EQ-5D-5L and BPI-SF including clinical progression and death

FACT-P total score[a]



EQ-5D-5L utility score



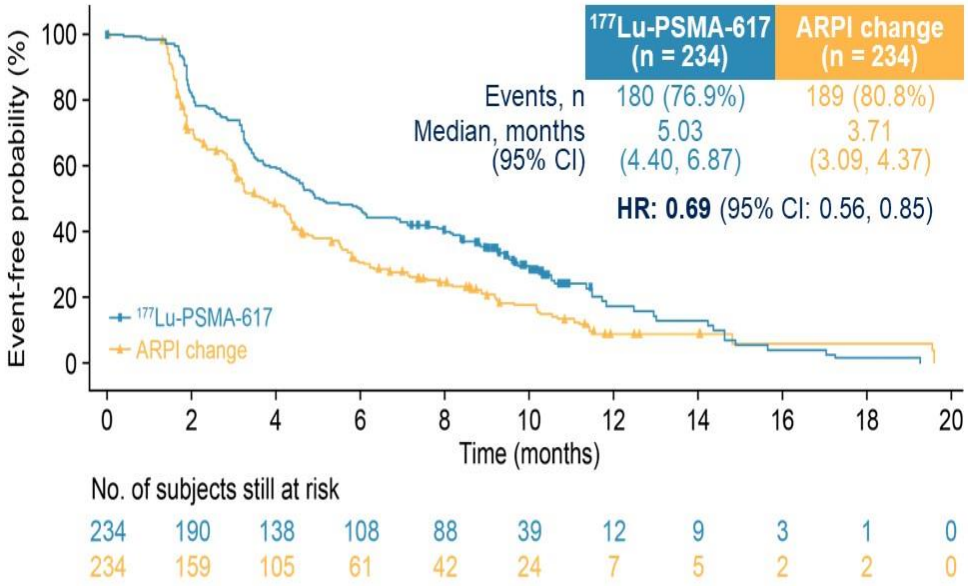
[a]Previously presented at ESMO23

Clinical progression was investigator-assessed as: cancer-related pain escalation, immediate need for new treatment, ECOG status deterioration or progression requiring treatment discontinuation

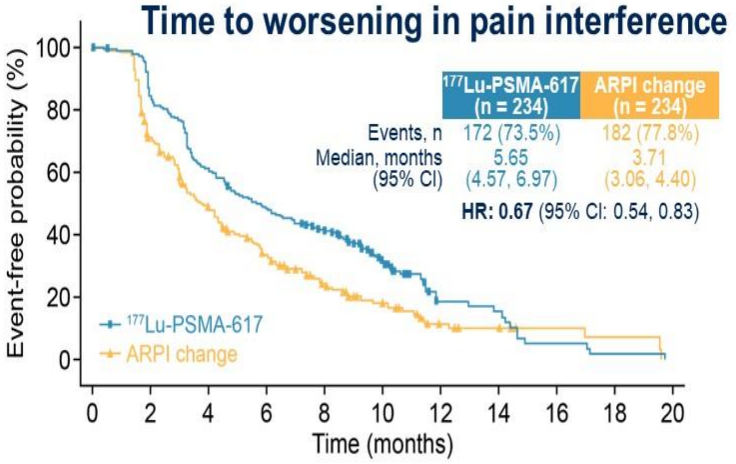
ARPI, androgen receptor pathway inhibitor; BPI-SF, Brief Pain Inventory – Short Form; CI, confidence interval; EQ-5D-5L, EuroQol-5 Dimension-5 Level; HR, hazard ratio; FACT-P, Functional Assessment of Cancer Therapy-Prostate; HRQoL, health-related quality of life; PSMA, prostate-specific membrane antigen

BPI-SF scales

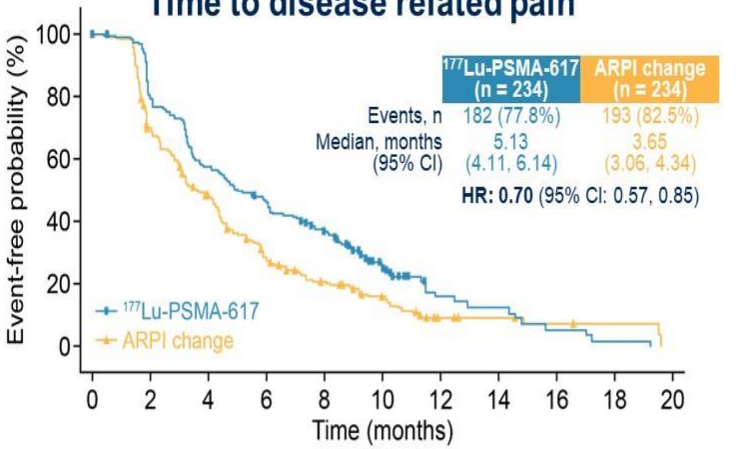
Time to worsening in pain intensity[a]



Time to worsening in pain interference



Time to disease related pain



[a]Previously presented at ESMO23

ARPI, androgen receptor pathway inhibitor; BPI-SF, Brief Pain Inventory – Short Form; CI, confidence interval; HR, hazard ratio; PSMA, prostate-specific membrane antigen

Treatment-emergent adverse events

AEs, n (%)	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Any	223 (98.2)	223 (96.1)
Grade 3–4	77 (33.9)	100 (43.1)
Serious	46 (20.3)	65 (28.0)
Treatment-related	7 (3.1)	5 (2.2)
Fatal[a] (grade 5)	4 (1.8)	5 (2.2)
Treatment-related	0	1 (0.4)
Leading to dose adjustment[b]	8 (3.5)	35 (15.1)
Leading to discontinuation[b]	13 (5.7)	12 (5.2)

[a]Fatal AEs included: COVID-19, cardiac arrest, intestinal ischemia, sepsis, cerebrovascular accident, coma, dyspnea, multiple organ dysfunction syndrome and treatment-related cerebrovascular accident
[b]AEs leading to dose adjustment or study treatment discontinuation included: dry mouth, thrombocytopenia, abdominal pain, acute kidney injury, anemia, back pain, neutropenia, platelet count decreased, sepsis, anaphylactic reaction, cerebrovascular accident, coma, dyspnea, fatigue, hepatic cytolysis, hyperaesthesia, spinal cord compression and tremor
Previously presented at ESMO23
AE, adverse event; ARPI, androgen receptor pathway inhibitor; PSMA, prostate-specific membrane antigen

Treatment-emergent adverse events in ≥ 10% of patients in either arm

AEs, n (%)	All grades		Grades 3–5	
	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Dry mouth	130 (57.3)	5 (2.2)	3 (1.3)	0
Asthenia	72 (31.7)	67 (28.9)	1 (0.4)	8 (3.4)
Nausea	71 (31.3)	28 (12.1)	0	1 (0.4)
Anemia	55 (24.2)	39 (16.8)	14 (6.2)	14 (6.0)
Fatigue	52 (22.9)	59 (25.4)	0	4 (1.7)
Constipation	50 (22.0)	31 (13.4)	1 (0.4)	0
Decreased appetite	48 (21.1)	42 (18.1)	0	1 (0.4)
Arthralgia	43 (18.9)	48 (20.7)	0	1 (0.4)
COVID-19	37 (16.3)	26 (11.2)	1 (0.4)	1 (0.4)
Diarrhea	37 (16.3)	20 (8.6)	0	1 (0.4)
Back pain	28 (12.3)	38 (16.4)	2 (0.9)	5 (2.2)
Vomiting	26 (11.5)	11 (4.7)	0	0
Peripheral edema	19 (8.4)	26 (11.2)	0	0
Weight loss	15 (6.6)	28 (12.1)	2 (0.9)	5 (2.2)

Previously presented at ESMO23
AE, adverse event; ARPI, androgen receptor pathway inhibitor; PSMA, prostate-specific membrane antigen

2024 ASCO ANNUAL MEETING

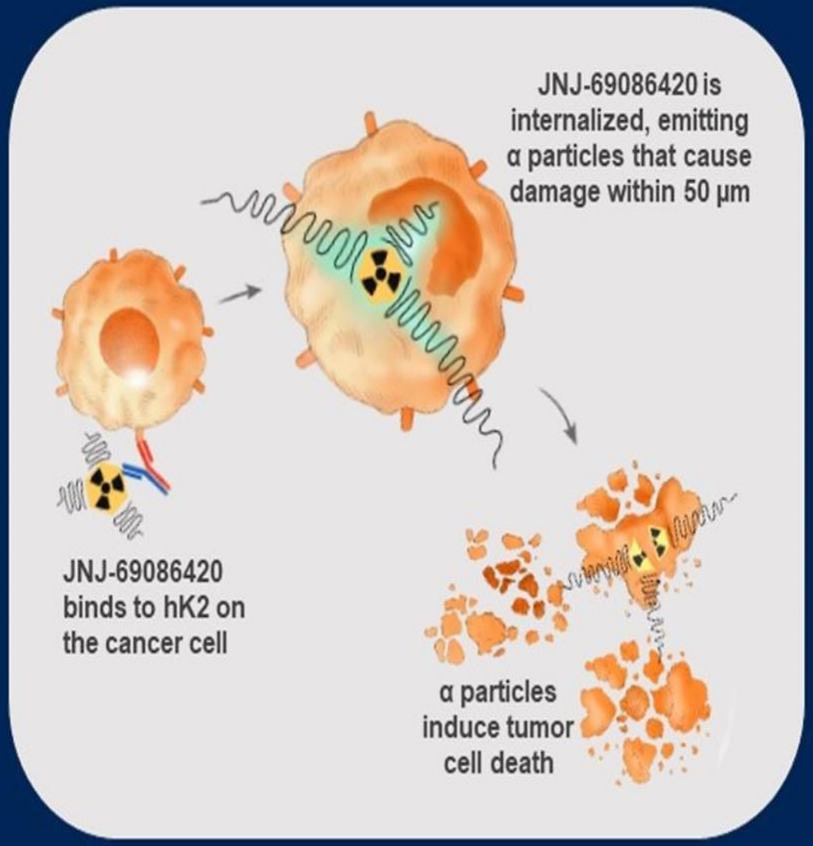
A Phase 1 Study of JNJ-69086420, an ^{225}Ac-Labeled Antibody Targeting Human Kallikrein 2 to Treat Metastatic Castration-Resistant Prostate Cancer

Michael J Morris, MD; Jeffrey Y C Wong, MD; Luke T Nordquist, MD; Russell Z Szmulewitz, MD; Neeraj Agarwal, MD; Edward F Attiyeh, MD; Steven Max, PhD; Chaitanya R Divgi, MD, MS; Daniel Patricia, RN, MLIS; Yu Cao, PhD; Xiang Li, PhD; Alex Yu, PhD; Karen Urtishak, PhD; Josh D Lauring, MD, PhD; A. Oliver Sartor, MD

PRESENTED BY: Michael J. Morris, MD

JNJ-69086420 is an hK2-Targeted, Humanized mAb Conjugated to ^{225}Ac

- hK2 is regulated by androgen receptor signaling, similar to PSA[1-3]
- hK2, encoded by *KLK2*, has high membranous expression in prostate cancer[4-7]
- hK2 exists in both a secreted and membrane-associated form[2,4,8]
- JNJ-69086420 preferentially binds to the membrane-associated form of hK2[4,5]
- JNJ-69086420 delivers α-particle radiation to prostate tumor cells[2]



1. Saedi MS, et al. *Int J Cancer*. 2001;94:558-563. 2. McDevitt MR, et al. *Nat Commun*. 2018;9(1):1629. 3. Lövgren J, et al. *Eur J Biochem*. 1999;262:781-789. 4. Thorek DL, et al. *Sci Transl Med*. 2016;8(367):367. 5. Morris MJ, et al. *J Clin Oncol*. 2022;40(6 suppl):TPS206. 6. Darson MF, et al. *Urology*. 1997;49:857-862. 7. Darson MF, et al. *Urology*. 1999;53(5):939-944. 8. Shen F, et al. *J Clin Oncol*. 2024;42(4 suppl):202.

Study Design

- NCT04644770: phase 1 first-in-human trial of JNJ-69086420 in mCRPC
- Key eligibility criteria
  - ≥1 prior ARPI
  - Prior chemotherapy allowed
  - No prior radiopharmaceutical therapy
  - No superscans
- Primary objectives
  - RP2D and safety

Data cutoff date: April 22, 2024.

Baseline Characteristics

Characteristic	All participants N = 75
Age, median (range), years	68 (46-84)
Prior cancer-related therapies	
Lines of prior therapy, median (range)	4 (0-12)
ARPI, n (%)	75 (100%)
≥2 ARPI, n (%)	40 (53%)
Any taxane-based chemotherapy, n (%)	49 (65%)
1 taxane-based chemotherapy, n (%)	28 (37%)
≥2 taxane-based chemotherapy, n (%)	21 (28%)
Primary RT, n (%)	17 (23%)
Palliative RT, n (%)	23 (31%)
No. courses RT, median (range)	1 (1-5)

Characteristic	All participants N = 75
PSA, median (range), µg/L	68.6 (0.4-2767.9)
Platelets, median (range), 10^9/L	222 (112-620)
Hemoglobin, median (range), g/dL	11.6 (7.7-15.7)
Extent of disease, n (%)	
Bone	66 (88%)
Soft tissue	36 (48%)
Visceral[a]	14 (19%)
Liver metastases	4 (5%)
Lymph node[b]	31 (41%)
Other	10 (13%)

[a]Includes lung, liver, adrenal, and central nervous system. [b]Includes pelvic and extra-pelvic.
Data cutoff date: April 22, 2024.

Safety | TEAEs of Interest

Adverse events	All participants N = 75	
	Any grade (%)	Grade ≥3 (%)
Any TEAE (in ≥20%)	96.0	61.3
Thrombocytopenia	58.7	17.3
Fatigue	53.3	1.3
Anemia	48.0	25.3
Decreased appetite	41.3	4.0
Nausea	40.0	2.7
Leukopenia	29.3	8.0
Vomiting	29.3	2.7
Cough	24.0	1.3
Dyspnea	24.0	0
Diarrhea	22.7	1.3
Hypertension	20.0	9.3
Dry mouth	20.0	0
Back pain	20.0	2.7
ILD[a]	6.7	5.3
Serious TEAE/TRAE (%)	32.0/16.0	
TEAE/TRAE leading to discontinuation (%)	14.7/12.0	
TEAE/TRAE leading to death[b] (%)	6.7/5.3	

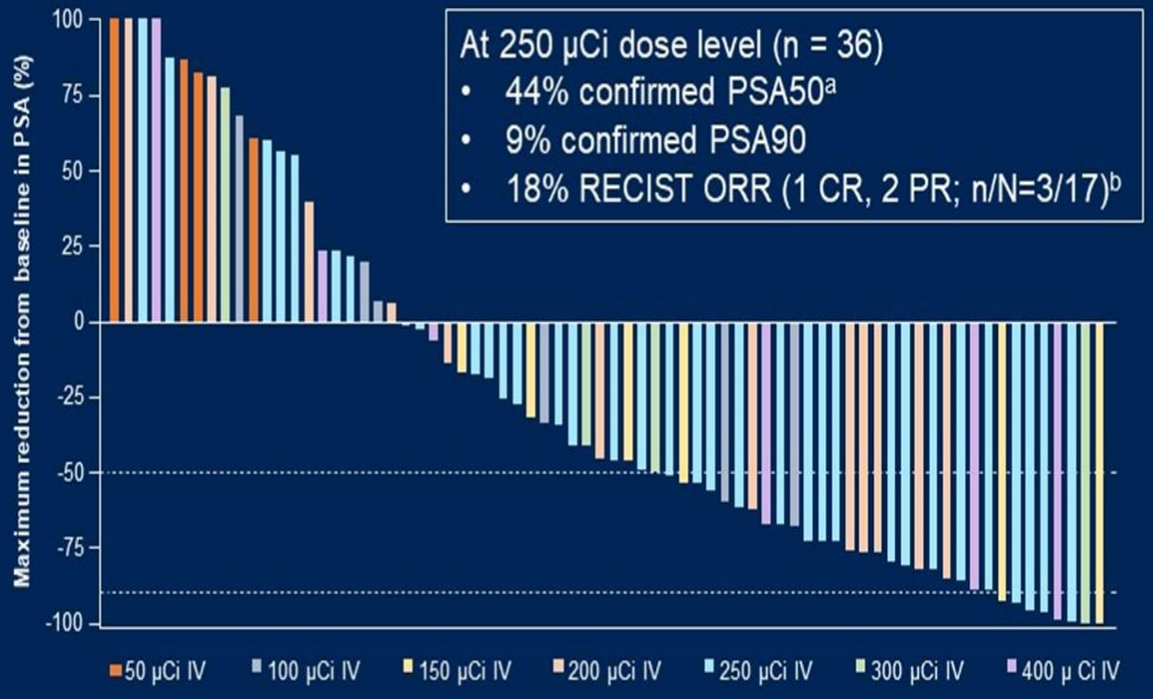
[a]ILD includes reports of pneumonitis, ground glass opacities, and acute hypoxic respiratory failure.
[b]ILD (n=2), respiratory failure (COVID-19, n=1), decreased appetite/hypotension (n=1).
Data cutoff date: April 22, 2024.

- Persistent G3/G4 thrombocytopenia on fixed dosing schedule at cumulative doses ≥500 µCi
- Only 1/26 (3.8%) G3 thrombocytopenia without recovery following a single 250-400 µCi dose

- Overall, 6.7% of patients had ILD, including 2 fatal cases
  - All ILD associated with cumulative doses ≥600 µCi
  - No ILD associated with cumulative dose cohorts ≤500 µCi

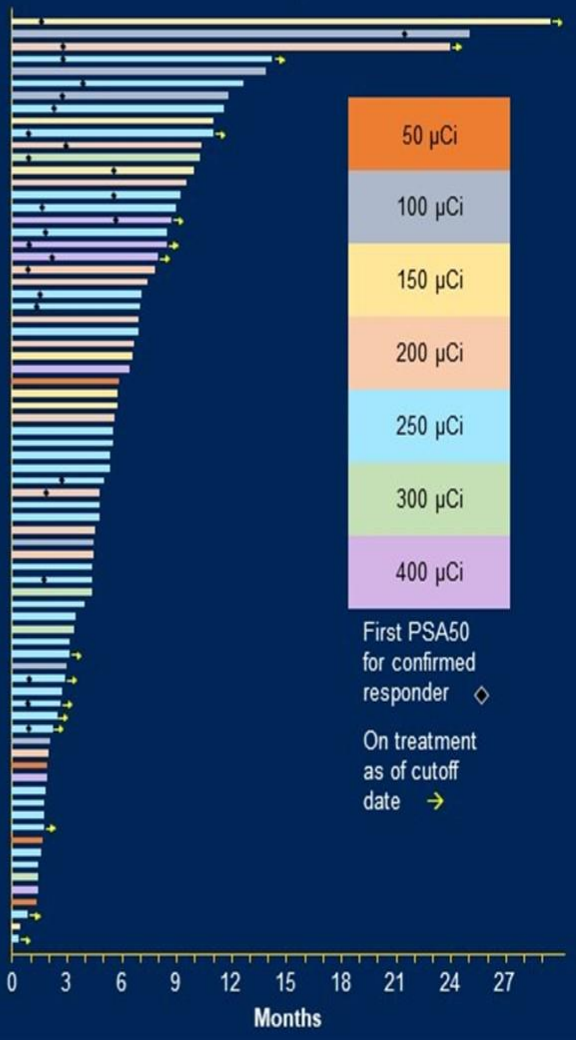
JNJ-69086420 Induces Deep and Durable PSA Responses

All cohorts (N = 75)



At 250 µCi dose level (n = 36)
- 44% confirmed PSA50[a]
- 9% confirmed PSA90
- 18% RECIST ORR (1 CR, 2 PR; n/N=3/17)[b]

All cohorts (N = 75)



[a]Confirmed by another reduction 3 weeks or later. N = 32 subjects who were on treatment for ≥12 weeks or discontinued treatment or achieved any PSA50. [b]N = 17 with measurable disease at baseline and at least 1 post-baseline assessment or off study. Confirmed ORR based on RECIST, without evidence of bone progression based on PCWG3.

Data cutoff date: April 22, 2024.

PRESENTED BY: Michael J. Morris, MD

2024 ASCO ANNUAL MEETING

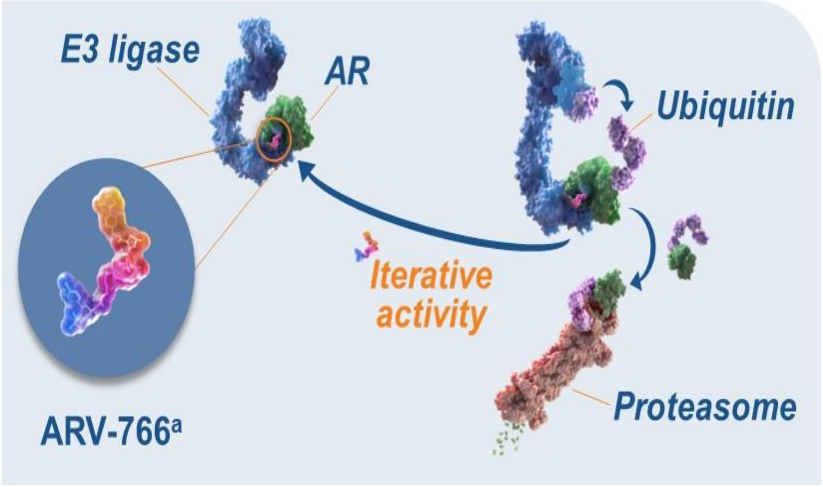
ARV-766, a PROteolysis TArgeting Chimera (PROTAC) Androgen Receptor Degrader, in Metastatic Castration-Resistant Prostate Cancer: Initial Results of a Phase 1/2 Study

Daniel P Petrylak[1], Meredith McKean[2], Joshua M Lang[3], Xin Gao[4], Robert Dreicer[5], Daniel M Geynisman[6], Tyler F Stewart[7], Mitul Gandhi[8], Leonard J Appleman[9], Tanya Dorff[10], Gurkamal Chatta[11], Ronald F Tutrone[12], Jose De La Cerda III[13], Elmer Berghorn[14], Jiachang Gong[14], Tinghui Yu[14], Erin Dominy[14], Edward Chan[14], Neal D Shore[15]

[1]Smilow Cancer Hospital, Yale School of Medicine, New Haven, CT; [2]Sarah Cannon Research Institute, Nashville, TN; [3]Carbone Cancer Center, University of Wisconsin-Madison, Madison, WI; [4]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [5]University of Virginia Comprehensive Cancer Center, Charlottesville, VA; [6]Fox Chase Cancer Center, Philadelphia, PA; [7]UC San Diego Health, La Jolla, CA; [8]Virginia Cancer Specialists, Gainesville, VA; [9]University of Pittsburgh Medical Center, Pittsburgh, PA; [10]City of Hope Comprehensive Cancer Center, Duarte, CA; [11]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [12]United Urology Group, Towson, MD; [13]Urology San Antonio, San Antonio, TX; [14]Arvinas Operations, Inc., New Haven, CT; [15]Carolina Urologic Research Center, Myrtle Beach, SC

Background

- Patients with mCRPC inevitably develop resistance to available therapies, including ARPIs, and experience disease progression[1]
- ≈20%–25% of men with mCRPC will develop mutations in the *AR* LBD (amino acids 671–920)
  - L702H, H875Y, and T878A are the most common *AR* mutations and are associated with poor prognosis[2–4]
- ARV-766 is a novel, potent, oral PROTAC AR degrader that targets wild-type *AR* and clinically relevant *AR* LBD mutants, including *AR* L702H, H875Y, and T878A



[a]General PROTAC protein degrader is shown.

AR=androgen receptor; ARPI=androgen receptor pathway inhibitor; LBD=ligand-binding domain; mCRPC=metastatic castration-resistant prostate cancer; PROTAC=PROteolysis TArgeting Chimera.

1. Boudadi K and Antonarakis ES. *Clin Med Insights Oncol*. 2016;10(Suppl 1):1-9.
2. Snaterse G, et al. Prostate Cancer Prostatic Dis. 2023;26(2):293-301.
3. Lallous N, et al. Genome Biol. 2016;17:10.
4. Shiota M, et al. Endocr Relat Cancer. 2022;29(10):R143-R155.

ARV-766 Monotherapy: Study Design[a] (NCT05067140)

Phase 1 dose escalation (part A)	Phase 2 cohort expansion (part B)
Key eligibility criteria • Progressive mCRPC • Ongoing ADT • ≥2 prior systemic therapies (including ≥1 ARPI)	**Key eligibility criteria** • Progressive mCRPC • Ongoing ADT • 1–3 prior ARPIs • ≤2 prior chemotherapy regimens
Treatment • Ascending doses of ARV-766 (20–500 mg orally QD)	**Treatment** • ARV-766 100 mg or 300 mg orally QD (1:1 randomization)
Primary objective • Safety and tolerability of ARV-766 to select RP2Ds	**Primary objective** • Evaluate the antitumor activity of ARV-766

- Safety was evaluated in all patients treated with ARV-766 across the phase 1/2 study
- For this analysis, antitumor activity[b] was assessed in the subgroup of patients with *AR* LBD mutations
- Data cutoff date for this analysis: April 15, 2024

[a]Parts C and D of this study are assessing ARV-766 in combination with abiraterone.
[b]PSA declines were evaluated in patients with ≥1 month of PSA follow-up; response per PCWG3/RECIST was evaluated in patients with measurable disease at baseline and ≥1 on-treatment scan.
ADT=androgen deprivation therapy; AR=androgen receptor; ARPI=androgen receptor pathway inhibitor; LBD=ligand-binding domain; mCRPC=metastatic castration-resistant prostate cancer; PCWG3=Prostate Cancer Working Group 3; PSA=prostate-specific antigen; QD=once daily; RECIST=Response Evaluation Criteria in Solid Tumors; RP2D=recommended phase 2 dose.

ARV-766 Monotherapy: Patient Baseline Characteristics[a]

Parameter	Total (N=123)	*AR* LBD Mutations (n=53)
Median age (range), y	72 (47–88)	72 (47–88)
ECOG performance status, n (%)		
0	70 (57)	24 (45)
1	53 (43)	29 (55)
Visceral disease, n (%)	28 (23)	14 (26)
Prior lines of therapy, median (range)	4 (1–10)	4 (1–10)
Prior ARPI, n (%)	123 (100)	53 (100)
Abiraterone alone	36 (29)	19 (36)
Enzalutamide, apalutamide, or darolutamide alone	31 (25)	5 (9)
≥2 ARPIs	56 (46)	29 (55)
Prior taxane, n (%)	69 (56)	31 (58)
Docetaxel alone	48 (39)	20 (38)
Cabazitaxel alone	1 (1)	1 (2)
Docetaxel and cabazitaxel	20 (16)	10 (19)

[a]Includes all patients treated with ARV-766 across the phase 1/2 study

AR=androgen receptor; ARPI=androgen receptor pathway inhibitors; ECOG=Eastern Cooperative Oncology Group; LBD=ligand-binding domain.

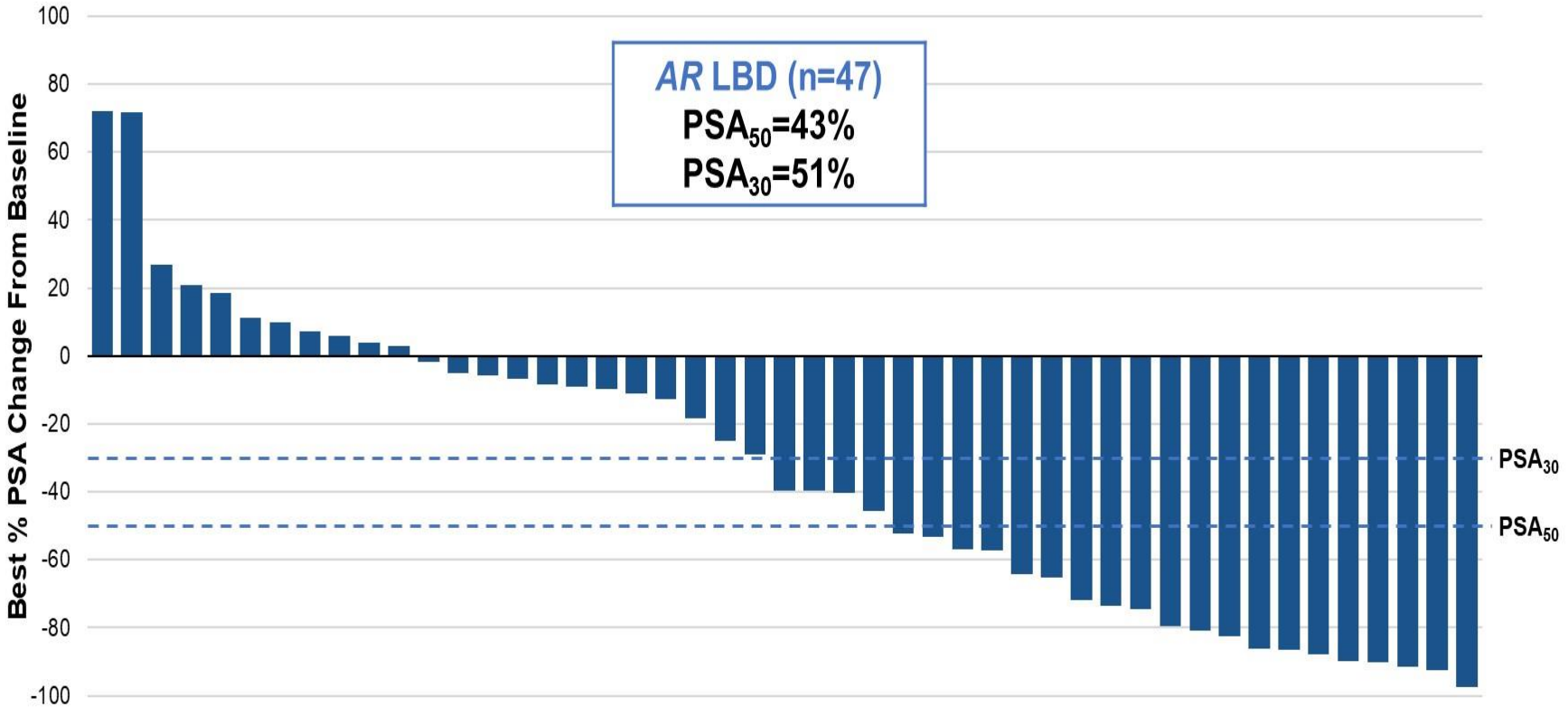
ARV-766 Monotherapy: Safety

- There were no DLTs, and an MTD was not reached in phase 1 (part A)
- Across all 123 phase 1/2 patients:
  - 118 (96%) had ≥1 any grade TEAE
    - 46 (37%) had a grade 3/4 TEAE
    - 3 (2%) had a grade 5 TEAE[a]
  - 9 (7%) had TEAEs that led to dose reduction of ARV-766
  - 10 (8%) had TEAEs that led to discontinuations of ARV-766

TRAEs in ≥10% of patients, n (%)	Total (N=123)			
	Total	Grade 1	Grade 2	Grade 3
Fatigue	41 (33)	26 (21)	12 (10)	3 (2)
Nausea	25 (20)	16 (13)	8 (7)	1 (1)
Diarrhea	19 (15)	13 (11)	5 (4)	1 (1)
Increased blood creatinine	18 (15)	14 (11)	4 (3)	0
Alopecia	17 (14)	14 (11)	3 (2)	NA
Decreased appetite	13 (11)	4 (3)	9 (7)	0

[a]Grade 5 TEAEs were death (unknown cause), brain stem stroke, and malignant neoplasm progression (n=1 each).
DLT=dose-limiting toxicity; MTD=maximum tolerated dose; NA=not applicable; TEAE=treatment-emergent adverse event; TRAE=treatment-related adverse event.

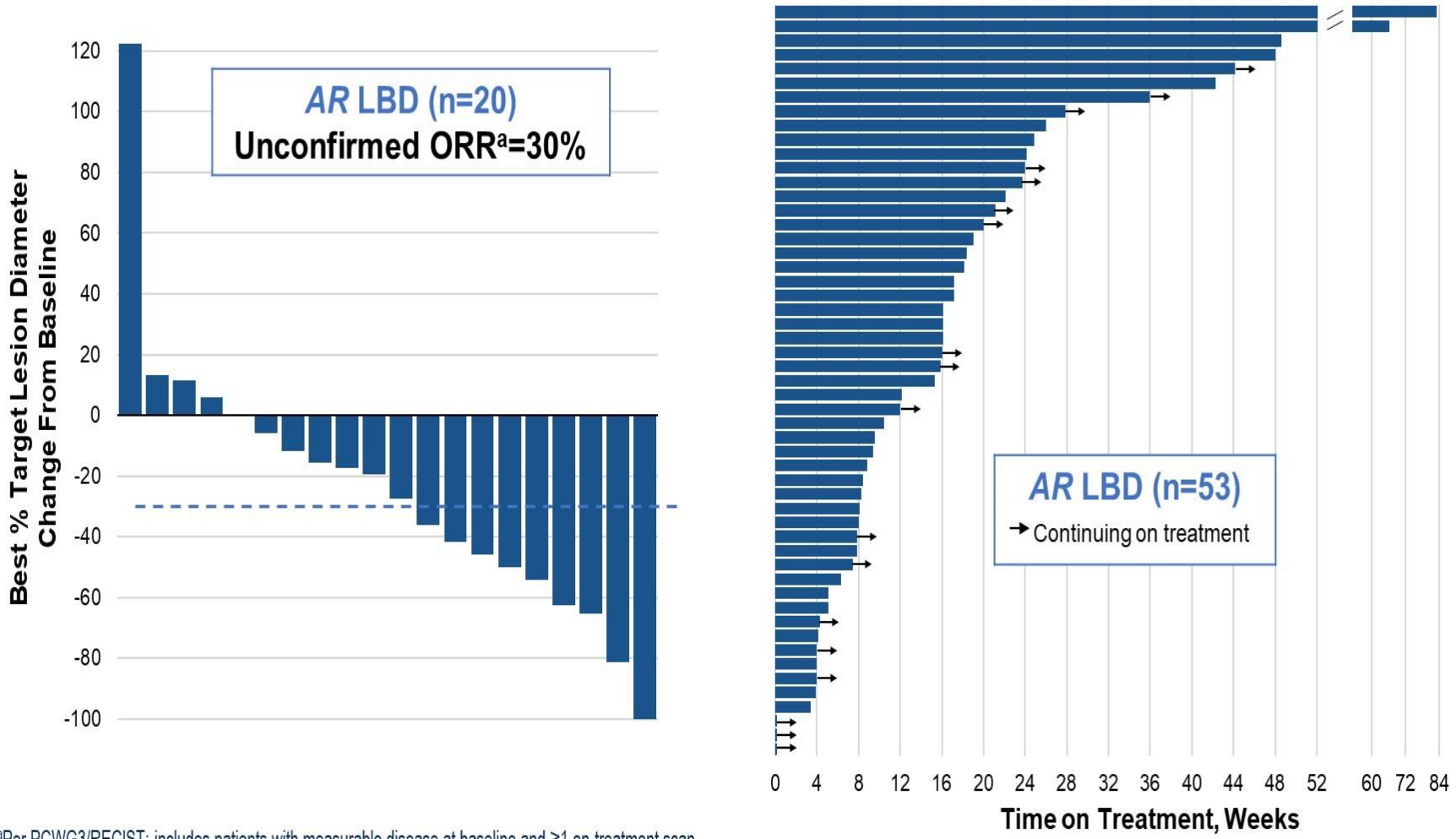
ARV-766 Monotherapy: Best Declines in PSA in Patients With *AR* LBD Mutations[a]



[a]Includes patients with ≥1 month of PSA follow-up.

AR=androgen receptor; LBD=ligand-binding domain; PSA=prostate-specific antigen; PSA_{30}=best PSA declines ≥30%; PSA_{50}=best PSA declines ≥50%.

ARV-766 Monotherapy: Tumor Response and Treatment Duration in Patients With *AR* LBD Mutations



[a]Per PCWG3/RECIST; includes patients with measurable disease at baseline and ≥1 on-treatment scan.

AR=androgen receptor; LBD=ligand-binding domain; ORR=objective response rate; PCWG3=Prostate Cancer Working Group 3; RECIST=Response Evaluation Criteria in Solid Tumors.

1. Prostatakarzinom

2. Urothelkarzinom

2024 ASCO ANNUAL MEETING

UniSR Università Vita-Salute San Raffaele

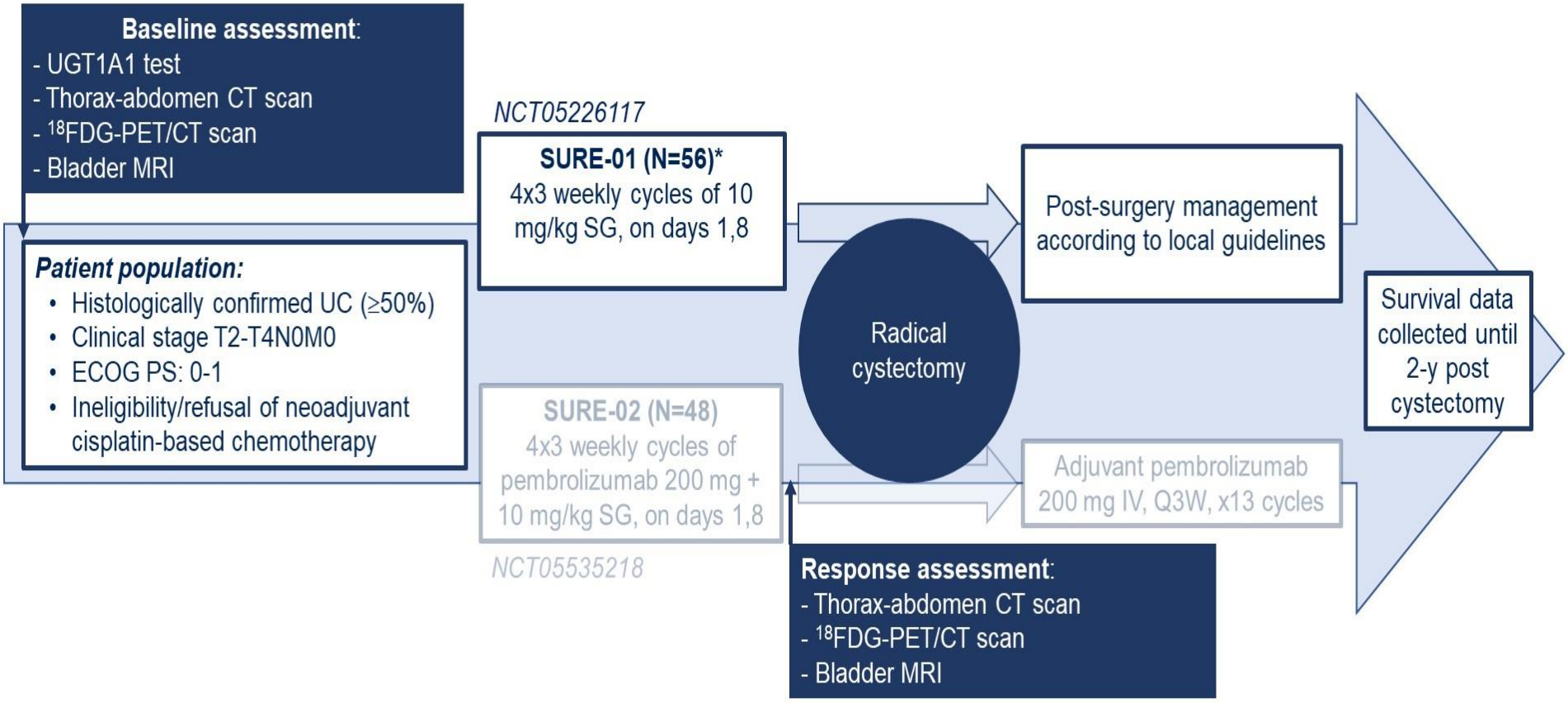
I.R.C.C.S. Ospedale San Raffaele
Gruppo San Donato

LBA4517: Preoperative sacituzumab govitecan in patients with muscle-invasive urothelial bladder cancer: Interim results of the SURE-01 study

Antonio Cigliola,[1] Marco Moschini,[2] Valentina Tateo,[1] Chiara Mercinelli,[1] Damiano Alfio Patanè,[1] Emanuele Crupi,[1] Renzo Colombo,[2] Vincenzo Scattoni,[2] Maurizio Colecchia,[3,4] Giorgio Brembilla,[5] Francesco Montorsi,[2,3] Andrea Necchi[1,3]

[1]Department of Medical Oncology, IRCCS San Raffaele Hospital, Milan, Italy; [2]Department of Urology, IRCCS San Raffaele Hospital, Milan, Italy; [3]Vita-Salute San Raffaele University, Milan, Italy; [4]Department of Pathology, IRCCS San Raffaele Hospital, Milan, Italy; [5]Department of Radiology, IRCCS San Raffaele Hospital, Milan, Italy

SURE trial platform



Primary Endpoint: ypT0N0 rate; ***Secondary Endpoints***: ypT≤1N0 rate, EFS, OS, QoL, Safety (CTCAE v.5.0)

*Statistical considerations: ypT0N0 ≤ 20% (H0) and ≥35% (H1); single-stage A'Hern's design: N=56 patients, with 80% power and a one-sided α = 5%.

Safety: Treatment Related Adverse Events

Safety population: patients who received at least 1 cycle of SG (N=21)

TRAE		Any Grade N (%)	Grade 1 N (%)	Grade 2 N (%)	Grade 3 N (%)	Grade 4 N (%)	Grade 5 N (%)
	Overall	**17 (81.0)**	**15 (71.4)**	**6 (28.6)**	**7 (33.3)**	**4 (19.1)**	**1 (4.8)**
Hematological	Anemia	9 (42.8)	8 (38.1)	0	1 (4.8)	0	0
	Neutropenia	7 (33.3)	0	0	3 (9.5)	4 (19.1)	0
	Thrombocytopenia	1 (4.8)	0	1 (4.8)	0	0	0
Gastrointestinal	Diarrhea	9 (42.9)	3 (14.3)	1 (4.8)	5 (23.9)	0	0
	Nausea	3 (14.3)	3 (14.3)	0	0	0	0
	Vomiting	1 (4.8)	1 (4.8)	0	0	0	0
Dermatological	Alopecia	8 (38.1)	5 (23.9)	3 (14.3)	0	0	0
	Cutaneous	1 (4.8)	1 (4.8)	0	0	0	0
Urinary	Hematuria	1 (4.8)	1 (4.8)	0	0	0	0
	UTI	1 (4.8)	1 (4.8)	0	0	0	0
	Creatinine increase	2 (9.5)	0	0	2 (9.5)	0	0
Other	Sepsis	3 (14.3)	0	0	0	2 (9.5)	1 (4.8)
	Fatigue	6 (28.6)	6 (28.6)	0	0	0	0

Abbreviations: SG: sacituzumab govitecan; TRAE: treatment-related adverse events; UTI: urinary tract infections

N: number of patients

Safety: Treatment Related Adverse Events leading to dose modification or discontinuation

TRAEs	ITT population N (%)	SG 10 mg/kg N (%)	SG 7.5 mg/kg* N (%)
• TRAEs leading to SG interruption:	4 (19.0)	4 (19.0)	0
• Sepsis (G3)	1 (4.8)	1 (4.8)	0
• Neutropenia (G3)	2 (9.5)	2 (9.5)	0
• Neutropenia (G4)	1 (4.8)	1 (4.8)	0
• TRAEs leading to dose reduction:	7 (33.3)	6 (28.6)	1 (4.8)
• Anemia (G3)	1 (4.8)	1 (4.8)	0
• Diarrhea (G3)	1 (4.8)	1 (4.8)	0
• Neutropenia (G3)	5 (23.9)	4 (19.0)	1 (4.8)
• TRAEs leading to SG discontinuation:	1 (4.8)	1 (4.8)	0
• Sepsis (G5)	1 (4.8)	1 (4.8)	0

*and Peg-GCSF support

- 3 patients died after treatment discontinuation at C1D8:
  - One death due to sepsis following G4 neutropenia + G3 diarrhea
  - Two due to non-treatment-related complications (CNS deterioration for unknown reason and disease-progression, respectively)
- Grade 3-4 TRAEs were more common in patients with homozygous or heterozygous UGT1A1*28 polymorphisms (5/8; **62.5%**) vs wild-type status (2/10; **20%**)

Results (N=21)

- 18/21 patients completed all 4 cycles of neoadjuvant SG and underwent surgery
- 11 pts underwent RC and 7 refused to undergo RC after the evidence of clinical CR (N=6) or due to patient decision (N=1), then received reTURBT
- Median duration of neoadjuvant treatment: 11.7 weeks (range: 0.4–16.4)
- Median time from end of SG to surgery: 6.9 weeks (range: 4.3–9.9)

Median follow-up: 7.1 months

Outcome	N (%)
Total N=11 RC-evaluable patients	
• ypT0N0 (95%CI)	4 (36.4; 14.9–64.8)
• ypT≤1N0 (95%CI)	5 (45.4; 21.2–72.0)
Total N=21 ITT patients	
• **ypT0N0-x (95%CI)**	**10 (47.6; 28.3–67.6)**
• ypT≤1N0-x	11 (52.4)
• ypT2Nx[a]	1 (4.7)
• ypT3-4N0[b]	3 (14.3)
• $ypT_{any}N+$[b]	3 (14.3)
Relapse/progression during or post-SG	1 (4.7)

[a]This patient refused to undergo RC despite the evidence of residual disease: He underwent reTURBT > chemoRT

[b]All these patients had ctDNA negative test post-RC. None of them have relapsed.

Responses assessed with reTURBT

Our definition of cCR

Patient ID	VI-RADS post-therapy[1]	Cystoscopy	ctDNA post-therapy	Pathological findings (reTURBT)	Clinical CR	
11	0	Neg	Neg	ypT0Nx	✓	Observation
13	0	Neg	Neg	ypT0Nx	✓	
16	0	Neg	Neg	ypT0Nx	✓	
17	0	Neg	Neg	ypT0Nx	✓	
19	0	Neg	Neg	ypT0Nx	✓	
20	0	Neg	Neg	ypT0Nx	✓	
21	5	Pos	Pos (MTM/mL: 0.32)	ypT2Nx	✗	ChemoRT

1. Necchi A, et al. *BJU Int*. 2024 Feb;133(2):214-222

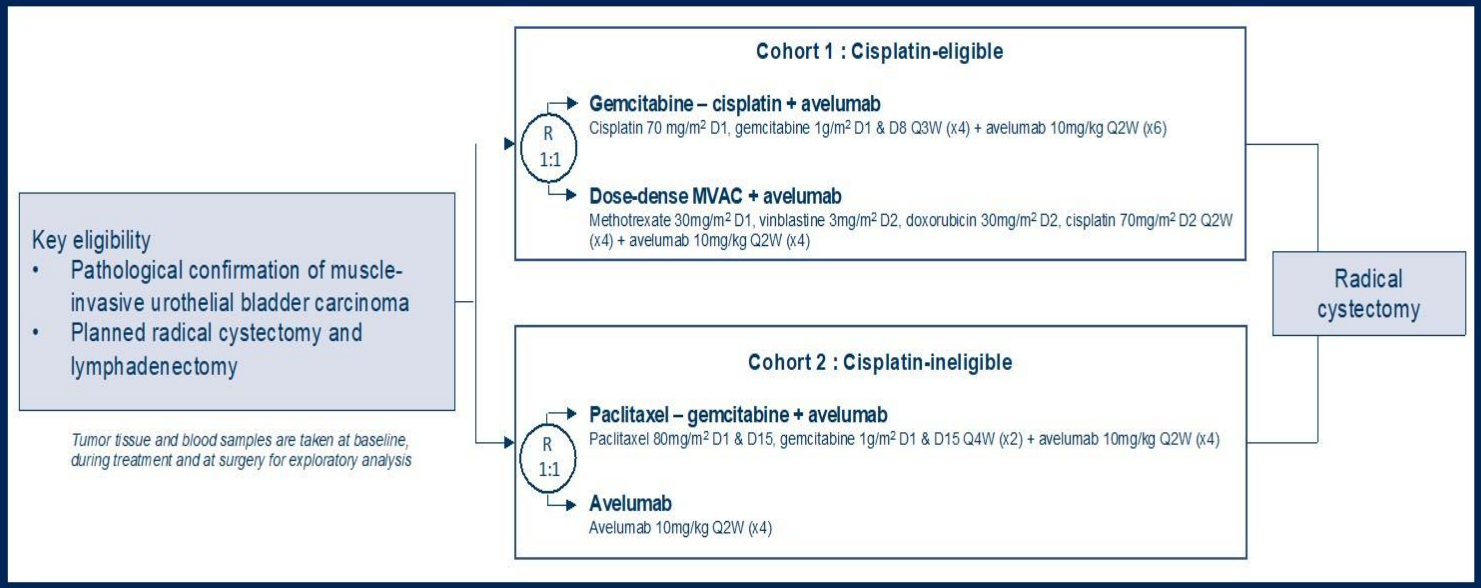
2024 ASCO ANNUAL MEETING

Avelumab as neoadjuvant therapy in patients with muscle-invasive urothelial carcinoma: Survival data from AURA trial - Oncodistinct 004.

Jeremy Blanc, Aurélien Carnot, Philippe Barthelemy, Vinciane Casert, Lionel Staudacher, Jan Van den Brande, Brieuc Sautois, Vincent Vanhaudenarde, Emmanuel Seront, Veronique Debien, Lieveke Ameye, Nuria Kotecki, Jean Christophe Fantoni, Thibault Tricard, Thierry Andre Roumeguere, Ahmad Awada & **Nieves Martinez Chanza**.

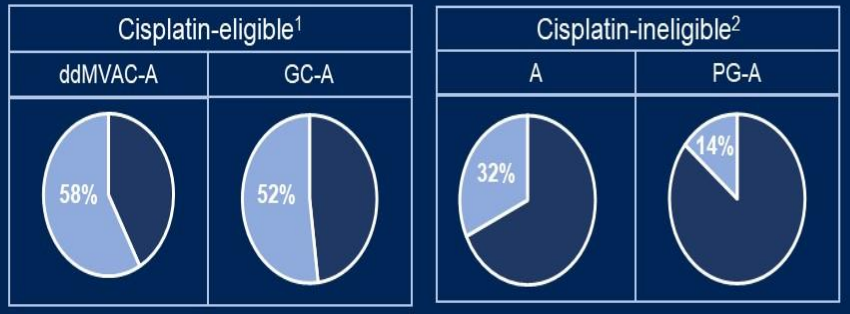
PRESENTED BY: Jeremy Blanc, MD, PhD student

AURA : a multi-centric non comparative randomized phase II trial investigating neoadjuvant avelumab alone or in combination with chemotherapy



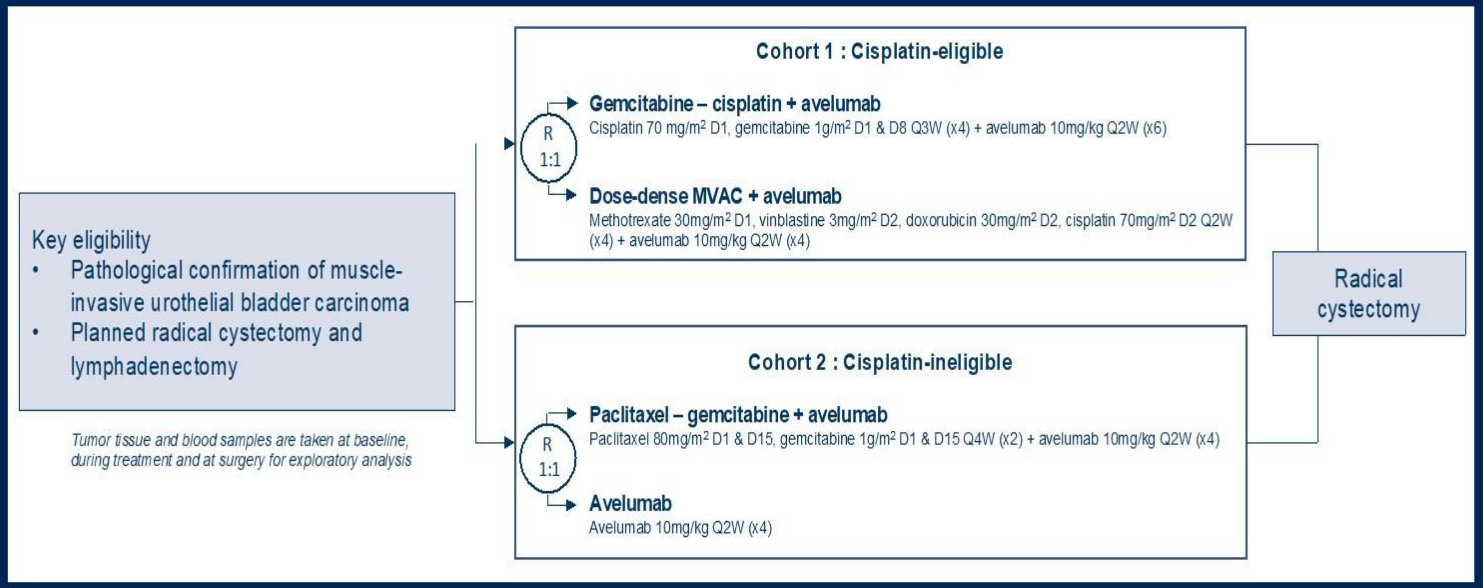
Primary Endpoint:

- Proportion of patients achieving a pathological complete response (pCR) ypT0/TisN0



[1]Martinez Chanza N et al. ,ESMO 2021; [2]Martinez Chanza N et al., ASCO 2022

AURA : a multi-centric non comparative randomized phase II trial investigating neoadjuvant avelumab alone or in combination with chemotherapy



Primary Endpoint:

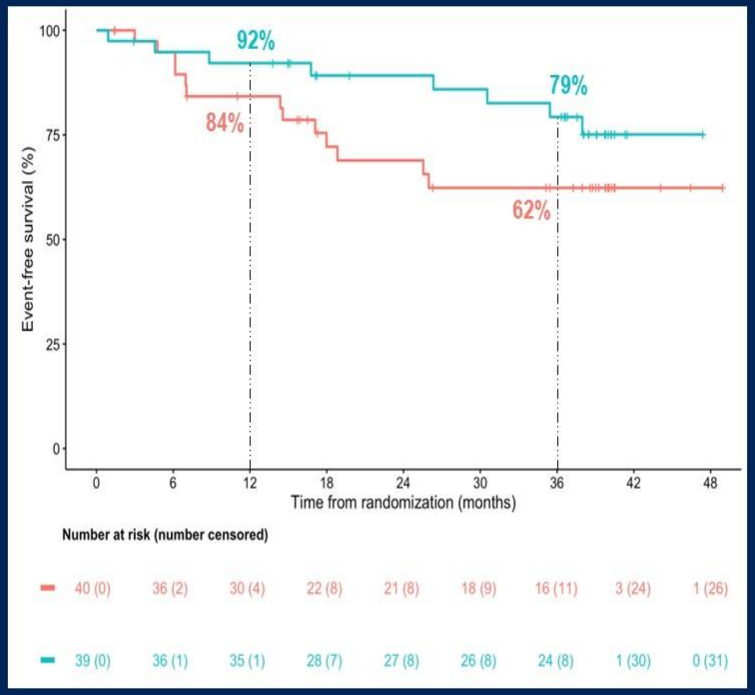
- Proportion of patients achieving a pathological complete response (pCR) ypT0/TisN0

Secondary Endpoints:

- Proportion of patients achieving <ypT2N0
- Safety (CTCAE v4)
- Event-free survival (EFS) and overall survival (OS) at 12 and 36 months

Survival in the **cisplatin-eligible** cohort

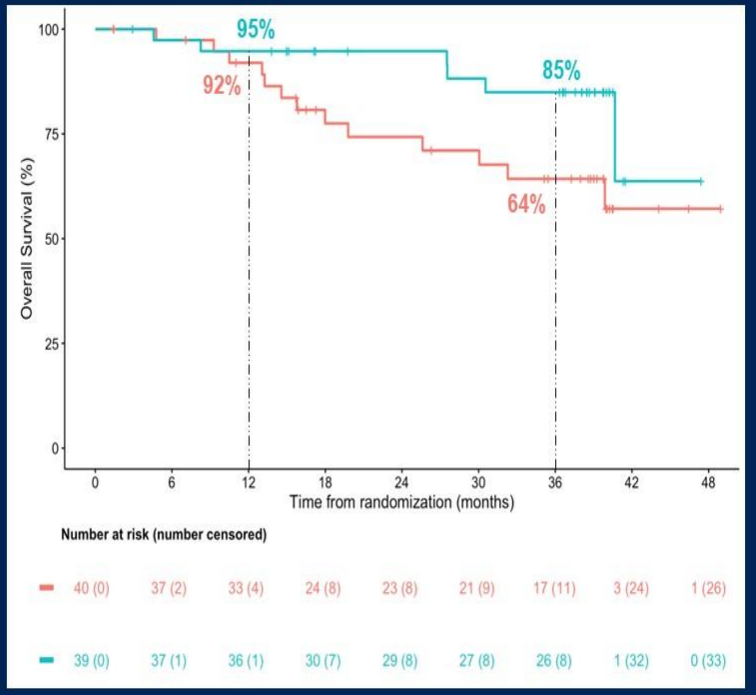
Event-free survival



ddMVAC-A

GC-A

Overall survival

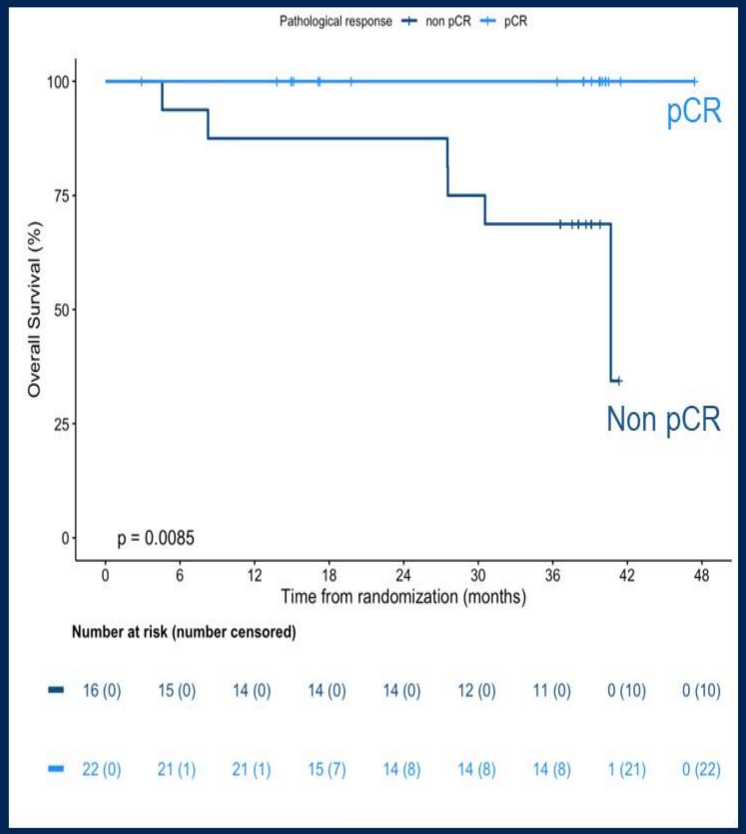


12-month EFS	92% ddMVAC-A 84% GC-A
Preliminary 36-month EFS	79% ddMVAC-A 62% GC-A

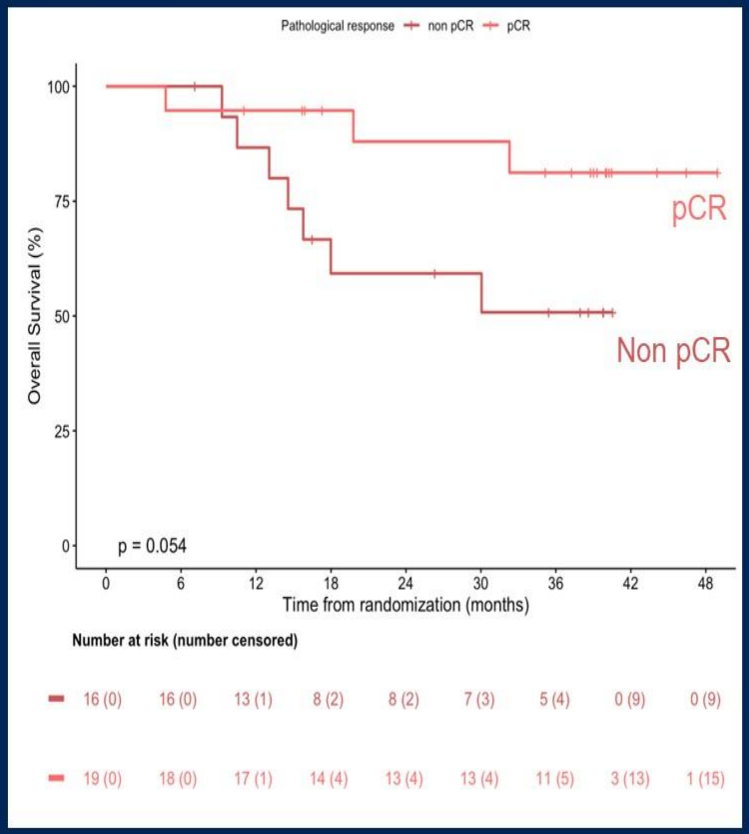
12-month OS	95% ddMVAC-A 92% GC-A
Preliminary 36-month OS	85% ddMVAC-A 64% GC-A

Overall survival in the **cisplatin-eligible** cohort according to pCR

ddMVAC-A arm



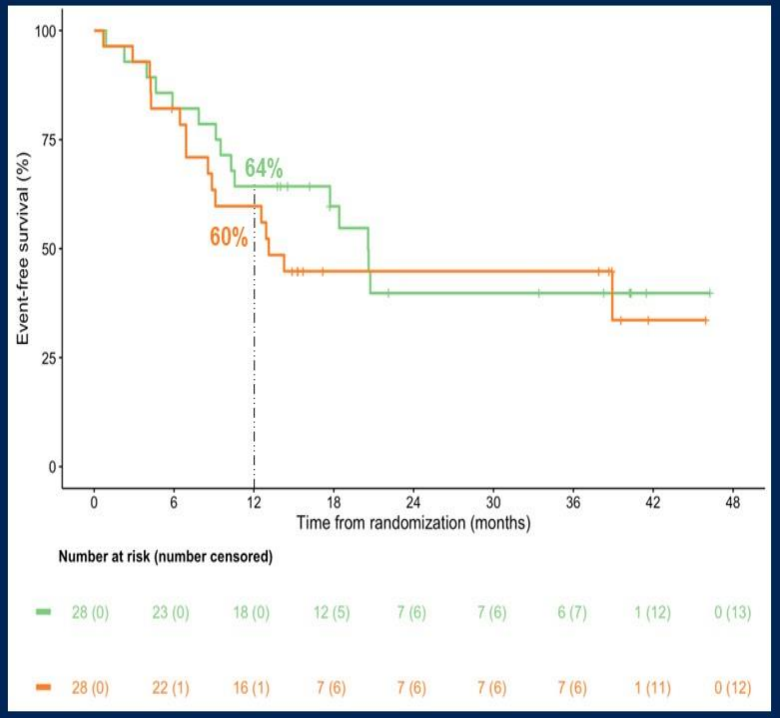
GC-A arm



Achieving a **pCR** is associated with **longer overall survival**

Survival in the **cisplatin-ineligible** cohort

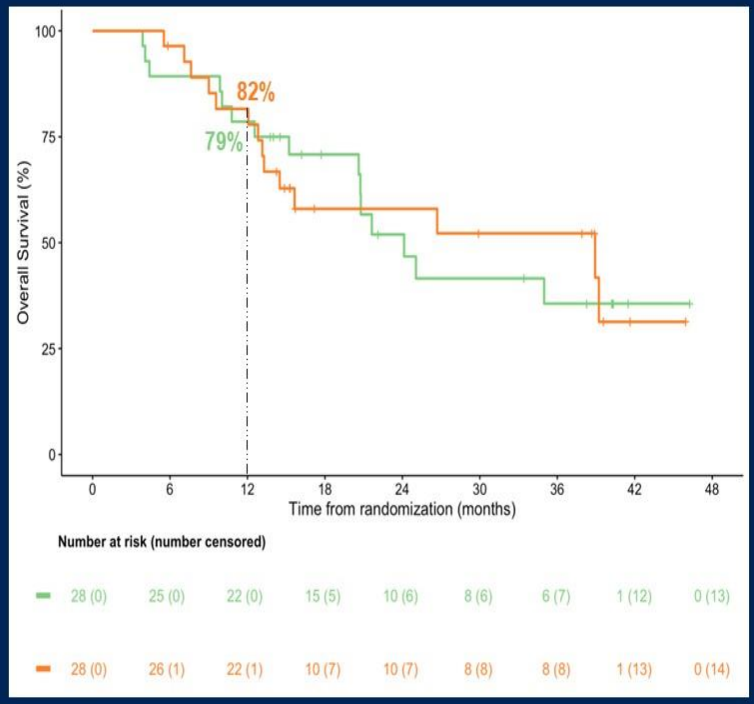
Event-free survival



PG-A

A

Overall survival

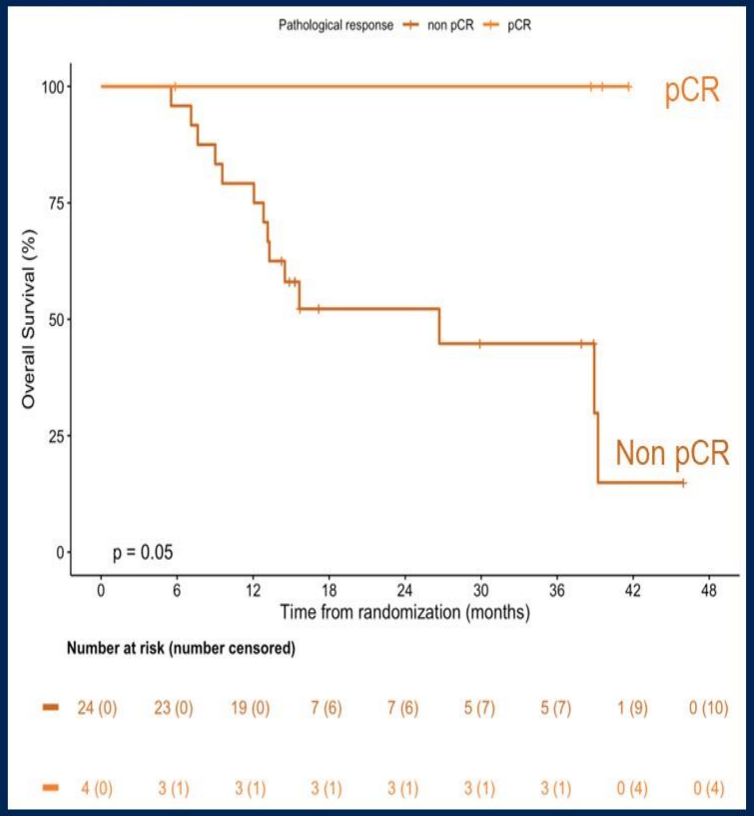


12-month EFS	64% A 60% PG-A

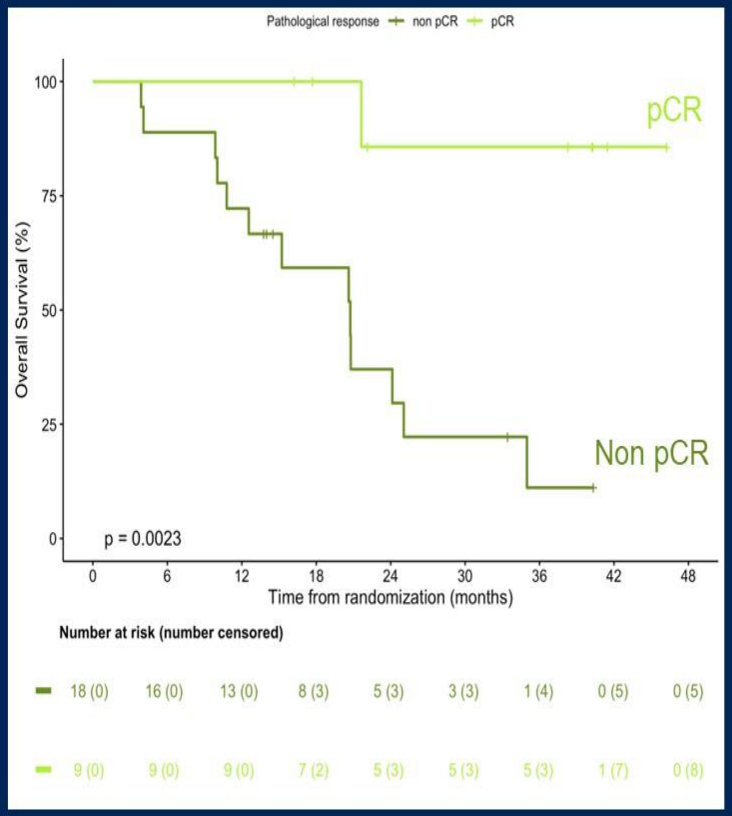
12-month OS	79% A 82% PG-A

Overall survival in the **cisplatin-ineligible** cohort according to pCR

PG-A arm



A arm



Achieving a **pCR** is associated with **longer overall survival**

Conclusions

- Cisplatin-eligible cohort :
  - **High EFS and OS rates** are achieved at 12 months and 36 months in patients treated with neoadjuvant avelumab in combination with cisplatin-based chemotherapies, especially in patients treated with **ddMVAC-A**
- Cisplatin-ineligible cohort :
  - Lower survival outcomes are achieved at 12 months, with **no additional benefit of PG-A**
  - **Longer follow-up** is needed for 36-month survival analysis
- Achieving a **pCR** is correlated with **better survival outcomes** for each treatment arm
- Further investigation through **phase III** trial is essential to validate our findings including **biomarker** identification for optimizing muscle-invasive bladder cancer care and patients' selection