

# ASCO Direct™

# Highlights Genitourinary

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UW/FHCC

# Faculty Disclosures

**I have no relevant financial relationship with any company (commercial interest) to disclose.**

# Long-Term Outcomes in EV-301: 24-Month Findings From the Phase 3 Trial of Enfortumab Vedotin vs Chemotherapy in Patients With Previously Treated Advanced Urothelial Carcinoma

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# Enfortumab Vedotin for Previously Treated Advanced Urothelial Carcinoma

- The 5-year relative survival rate for metastatic bladder cancer is  $\approx 8\%$ <sup>1</sup>
- Enfortumab vedotin (EV), an antibody–drug conjugate directed against Nectin-4, demonstrated overall survival (OS) and progression-free survival (PFS) benefit in patients with locally advanced or metastatic (la/m) urothelial carcinoma (UC) in the open-label, confirmatory phase 3 EV-301 trial (NCT03474107) at the prespecified interim analysis<sup>2</sup>

Efficacy and safety are presented for EV vs chemotherapy over a median follow-up period of  $\approx 2$  years

## Key eligibility criteria:

- Histologically/Cytologically confirmed UC
- Radiographic progression/relapse during or after PD-1/L1 treatment for advanced UC
- Prior platinum-containing regimen for advanced UC
- ECOG PS 0–1

1:1 randomization  
with stratification

## Enfortumab vedotin

(N=301)

1.25 mg/kg

on days 1, 8, and 15 of each 28-d cycle

## Preselected chemotherapy

(N=307)

Docetaxel 75 mg/m<sup>2</sup> or paclitaxel 175 mg/m<sup>2</sup> or  
vinflunine 320 mg/m<sup>2</sup>  
on day 1 of each 21-d cycle

## Primary end point: Overall survival

### Secondary end points:

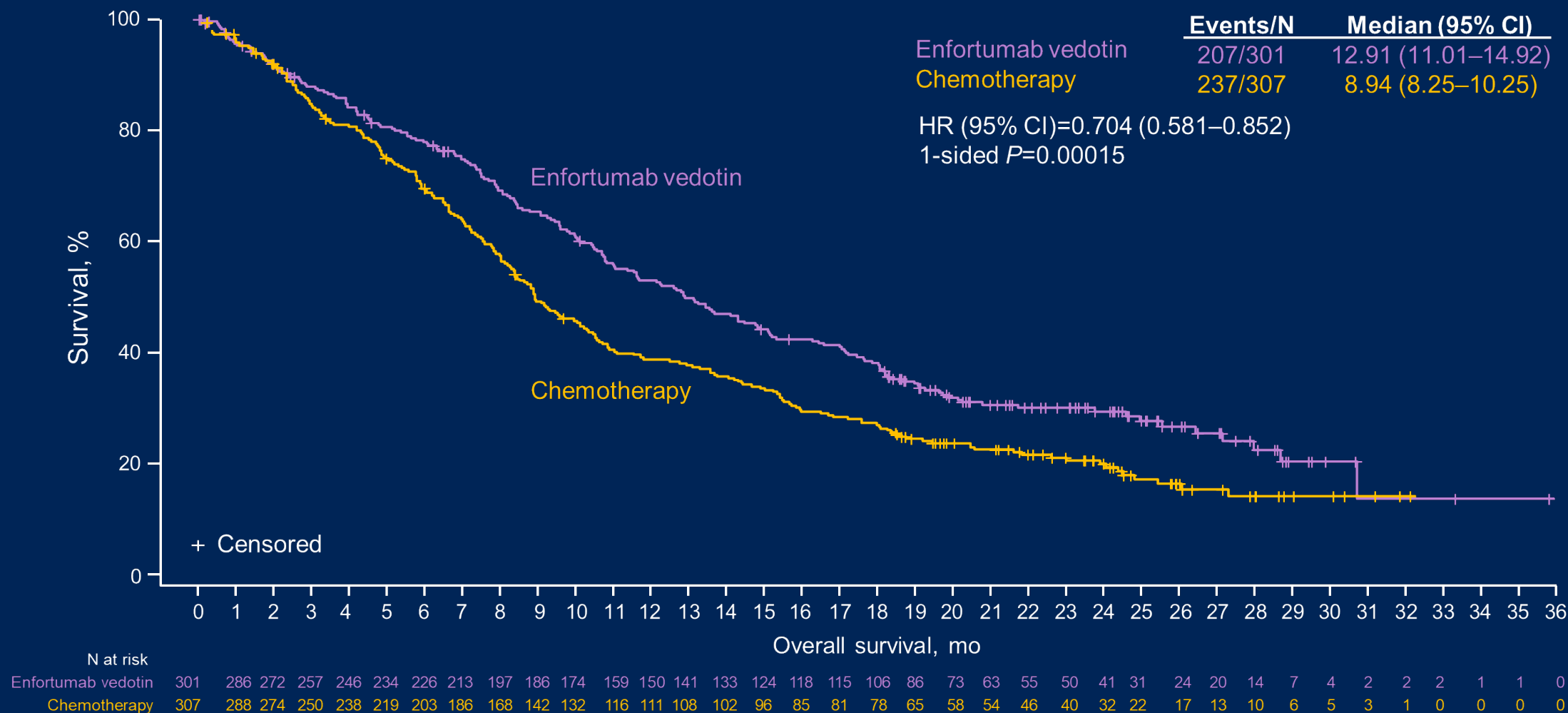
- Progression-free survival
  - Disease control rate
  - Overall response rate
  - Safety
- Investigator-assessed per RECIST v1.1

**Findings from the prespecified, event-driven OS analysis when 439 deaths occurred are presented**

ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; la/m, locally advanced or metastatic; OS, overall survival; PD-1/L1, programmed cell death protein-1/programmed death-ligand 1; RECIST, Response Evaluation Criteria In Solid Tumors; UC, urothelial carcinoma.

1. National Cancer Institute. <https://seer.cancer.gov/statfacts/html/urinb.html>. 2. Powles T, et al. *N Engl J Med*. 2021;384:1125-1135.

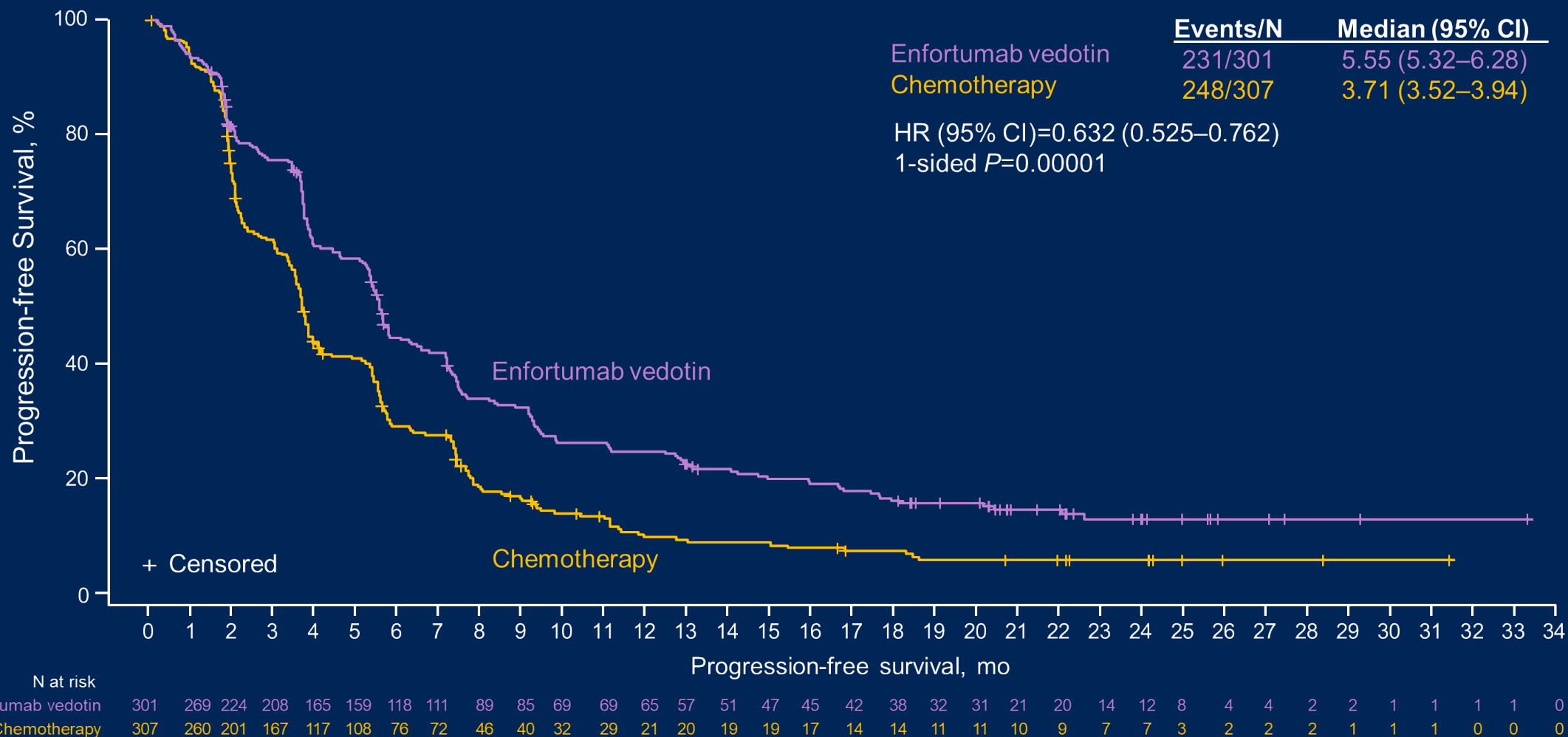
# Overall Survival



Data shown for intention-to-treat population.  
HR, hazard ratio.

Data cutoff date: July 30, 2021

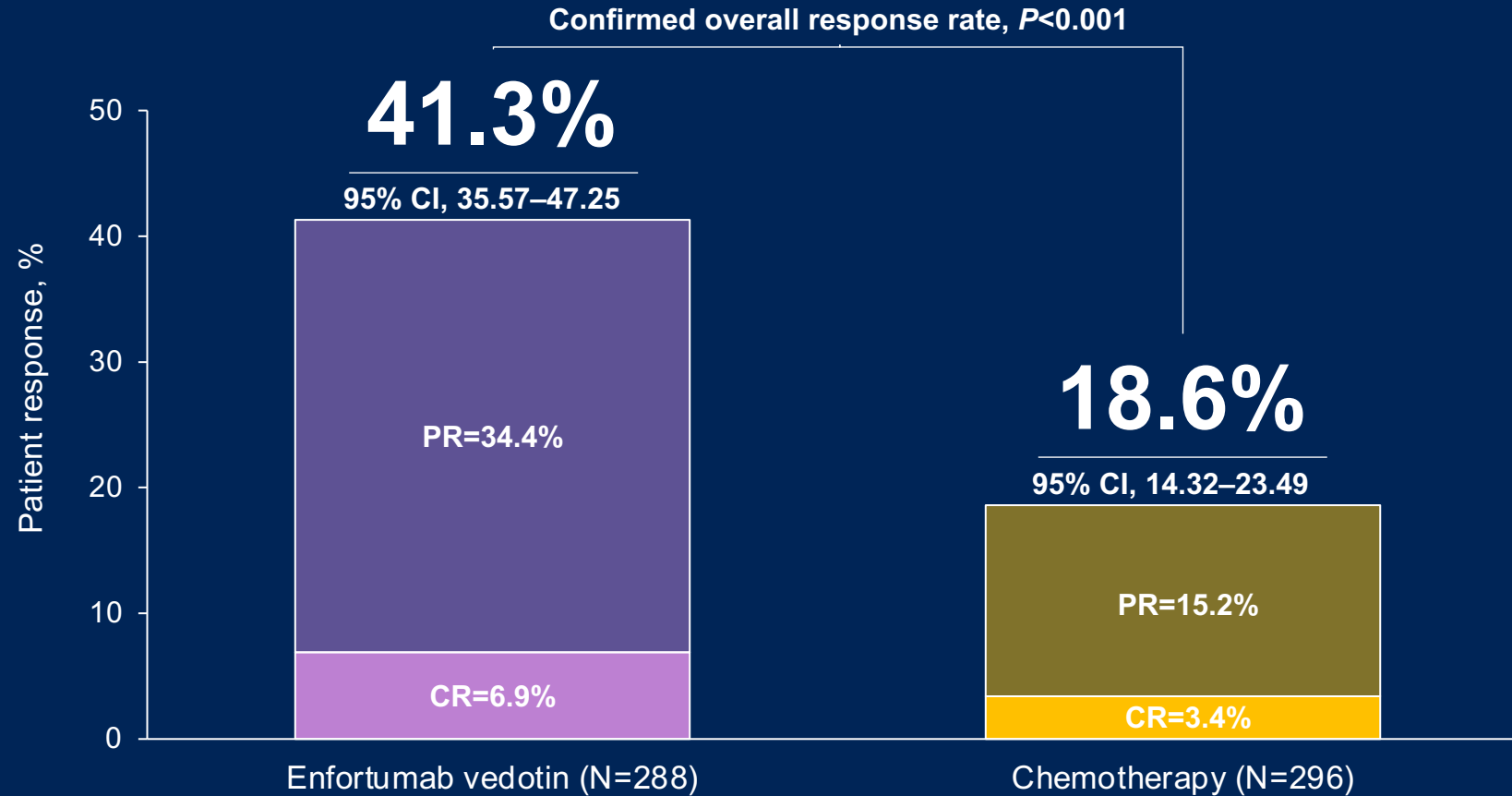
# Progression-Free Survival



Data shown for intention-to-treat population.  
 HR, hazard ratio.

Data cutoff date: July 30, 2021

# Investigator-Assessed Clinical Response



Disease control rate (95% CI),<sup>a</sup> %

71.9 (66.30–76.99)

53.4 (47.52–59.17)

$P < 0.001$

Response as assessed by investigator per RECIST version 1.1. Assessed in the response evaluable population.

CR, complete response; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors.

<sup>a</sup>Proportion of patients with best overall response of confirmed CR, PR, or SD ( $\geq 7$  wk); enfortumab vedotin vs chemotherapy.

# Safety/Tolerability

- Median (range) duration rates of treatment were 4.99 mo (0.5-29.9) for EV and 3.45 mo (0.2–26.4) for chemotherapy
- Rates of treatment-related adverse events (TRAEs; 93.9% vs 91.8%) and serious TRAEs (22.6% vs 23.4%) were comparable between EV and chemotherapy groups

Treatment-related adverse event, n (%)	Enfortumab vedotin (N=296)		Chemotherapy (N=291)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Alopecia	135 (45.6)	NR	108 (37.1)	NR
Peripheral sensory neuropathy	103 (34.8)	15 (5.1)	63 (21.6)	6 (2.1)
Pruritus	96 (32.4)	4 (1.4)	14 (4.8)	1 (0.3)
Fatigue	93 (31.4)	20 (6.8)	66 (22.7)	13 (4.5)
Decreased appetite	92 (31.1)	9 (3.0)	69 (23.7)	5 (1.7)
Diarrhea	74 (25.0)	10 (3.4)	49 (16.8)	5 (1.7)
Dysgeusia	73 (24.7)	NR	22 (7.6)	NR
Nausea	71 (24.0)	3 (1.0)	64 (22.0)	4 (1.4)
Maculopapular rash	50 (16.9)	22 (7.4)	5 (1.7)	NR
Anemia	34 (11.5)	8 (2.7)	63 (21.6)	23 (7.9)
Decreased neutrophil count	31 (10.5)	18 (6.1)	51 (17.5)	41 (14.1)
Neutropenia	20 (6.8)	14 (4.7)	25 (8.6)	18 (6.2)
Decreased white blood cell count	15 (5.1)	4 (1.4)	32 (11.0)	21 (7.2)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

NR, not reported; TRAE, treatment-related adverse event.

Occurring in ≥20% of patients in either treatment group or grade ≥3 TRAEs occurring in ≥5% of patients in either treatment group. Data shown for safety population.

Data cutoff date: July 30, 2021



# Adverse Events of Special Interest<sup>a</sup> (Safety Population)

Treatment-related adverse event, n (%)	Enfortumab vedotin (N=296)						Chemotherapy (N=291)					
	Grade						Grade					
	Any	1	2	3	4	5	Any	1	2	3	4	5
Rash	133 (44.9)	41 (13.9)	48 (16.2)	43 (14.5)	1 (0.3)	NR	28 (9.6)	21 (7.2)	6 (2.1)	1 (0.3)	0	NR
Severe cutaneous adverse reaction	60 (20.3)	20 (6.8)	25 (8.4)	14 (4.7)	1 (0.3)	NR	22 (7.6)	12 (4.1)	8 (2.7)	2 (0.7)	0	NR
Peripheral neuropathy	142 (48.0)	36 (12.2)	84 (28.4)	22 (7.4)	NR	NR	92 (31.6)	43 (14.8)	41 (14.1)	8 (2.7)	NR	NR
Peripheral neuropathy sensory events	135 (45.6)	35 (11.8)	82 (27.7)	18 (6.1)	NR	NR	89 (30.6)	42 (14.4)	39 (13.4)	8 (2.7)	NR	NR
Peripheral neuropathy motor events	23 (7.8)	6 (2.0)	11 (3.7)	6 (2.0)	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Dry eye	48 (16.2)	34 (11.5)	12 (4.1)	2 (0.7)	NR	NR	9 (3.1)	6 (2.1)	2 (0.7)	1 (0.3)	NR	NR
Blurred vision	13 (4.4)	11 (3.7)	2 (0.7)	0	NR	NR	6 (2.1)	5 (1.7)	0	1 (0.3)	NR	NR
Corneal disorders	2 (0.7)	2 (0.7)	NR	NR	NR	NR	0	0	NR	NR	NR	NR
Infusion-related reaction	27 (9.1)	12 (4.1)	11 (3.7)	4 (1.4)	NR	NR	14 (4.8)	7 (2.4)	7 (2.4)	0	NR	NR
Systemic infusion-related reaction event	24 (8.1)	11 (3.7)	9 (3.0)	4 (1.4)	NR	NR	9 (3.1)	4 (1.4)	5 (1.7)	0	NR	NR
Local infusion-related reaction event	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Infusion-site reaction	2 (0.7)	0	2 (0.7)	0	NR	NR	5 (1.7)	4 (1.4)	1 (0.3)	0	NR	NR
Extravasation-site reaction	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR
Hyperglycemia	20 (6.8)	3 (1.0)	4 (1.4)	12 (4.1)	0	1 (0.3)	1 (0.3)	0	1 (0.3)	0	0	0

MedDRA, Medical Dictionary for Regulatory Activities; NR, not reported.

<sup>a</sup>Adverse events of special interest to enfortumab vedotin. Events represent listings by preferred term and are sponsor-specific query/customized medical queries or standard MedDRA queries. Order of adverse events is as it appears in the Supplementary Appendix to the EV-301 primary publication (Powles, et al. *N Engl J Med.* 2021;384:1125-1135).

Data cutoff date: July 30, 2021

# Conclusions

- After a median follow-up period of approximately 2 years, EV maintained a clinically meaningful and significant OS benefit versus chemotherapy consistent with findings from the primary efficacy results (which had occurred at the interim analysis)
  - PFS and ORR results were consistent with what was observed in the interim and final analysis
- Safety and tolerability of EV and chemotherapy were consistent with findings from the interim and final analysis
  - EV adverse events continued to be manageable and no new safety signals were observed
- These data showed continued survival benefit of EV versus chemotherapy, including a sustained magnitude of benefit, in patients with previously treated Ia/mUC

## **<sup>177</sup>Lu-PSMA-617 (LuPSMA) versus cabazitaxel in metastatic castration resistant prostate cancer (mCRPC) progressing after docetaxel: overall survival after median follow-up of 3 years**

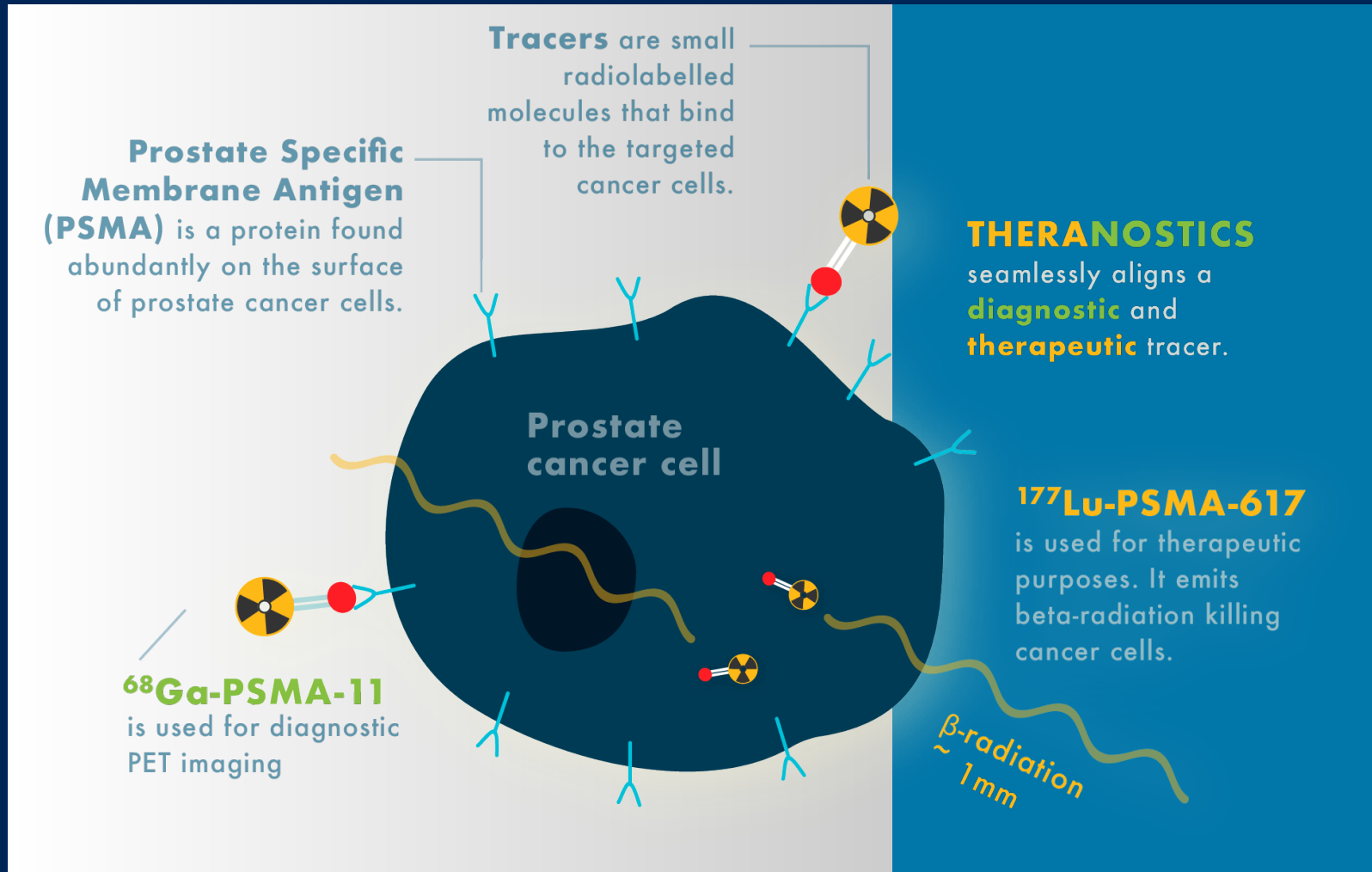
(TheraP ANZUP 1603)

Michael Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony Joshua, Jeffrey Goh, David Pattison, Hsiang Tan, Ian Kirkwood, Siobhan Ng, Roslyn Francis, Craig Gedye, Natalie Rutherford, Andrew Scott, Alison Zhang, Margaret McJannett, Martin Stockler, Scott Williams, Andrew Martin, Ian D. Davis, on behalf of the **TheraP Investigators**

TheraP is a partnership between ANZUP Cancer Trials Group and the Prostate Cancer Foundation of Australia (PCFA) in collaboration with the NHMRC Clinical Trials Centre (CTC) and the Australasian Radiopharmaceutical Trials Network (ARTnet) with support from the Australian Nuclear Science and Technology Organisation (ANSTO) and Endocyte Inc., a Novartis company

[Clinicaltrials.gov NCT03392428](https://clinicaltrials.gov/NCT03392428)

# $^{177}\text{Lu}$ -PSMA-617: $\uparrow$ OS and QoL in mCRPC<sup>1</sup>



<sup>1</sup> Sartor O et al, NEJM 2021; 385

# TheraP: First randomized trial of LuPSMA vs. cabazitaxel<sup>1</sup>

**50% MEN TREATED WITH CABAZITAXEL**  
 20mg/m<sup>2</sup> IV q3 weekly  
 Up to 10 cycles

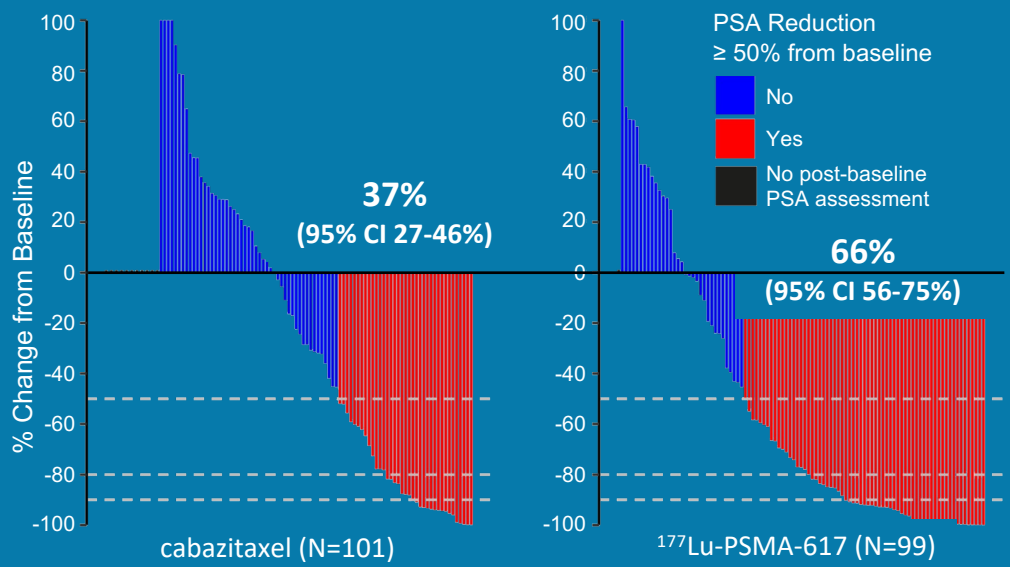
**50% MEN TREATED WITH <sup>177</sup>Lu-PSMA-617**  
 8.5 GBq IV q6 weekly  
 ↓ 0.5 GBq each cycle  
 Up to 6 cycles

## 1<sup>o</sup> endpoint

### PSA Reduction ≥ 50% from baseline



<sup>177</sup>Lu-PSMA-617: 29% (95% CI 16%-42%; p<0.0001) greater PSA50-RR



## 2<sup>o</sup> endpoints

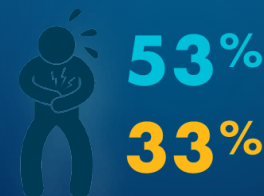
### Progression Free Survival at 12 months



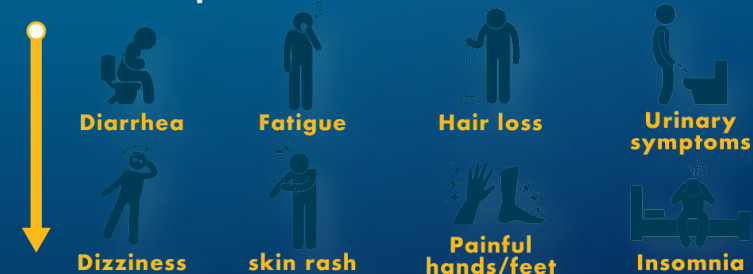
### Objective Response Rate on CT Scan (RECIST)



### Troublesome Adverse Events Grade 3-4

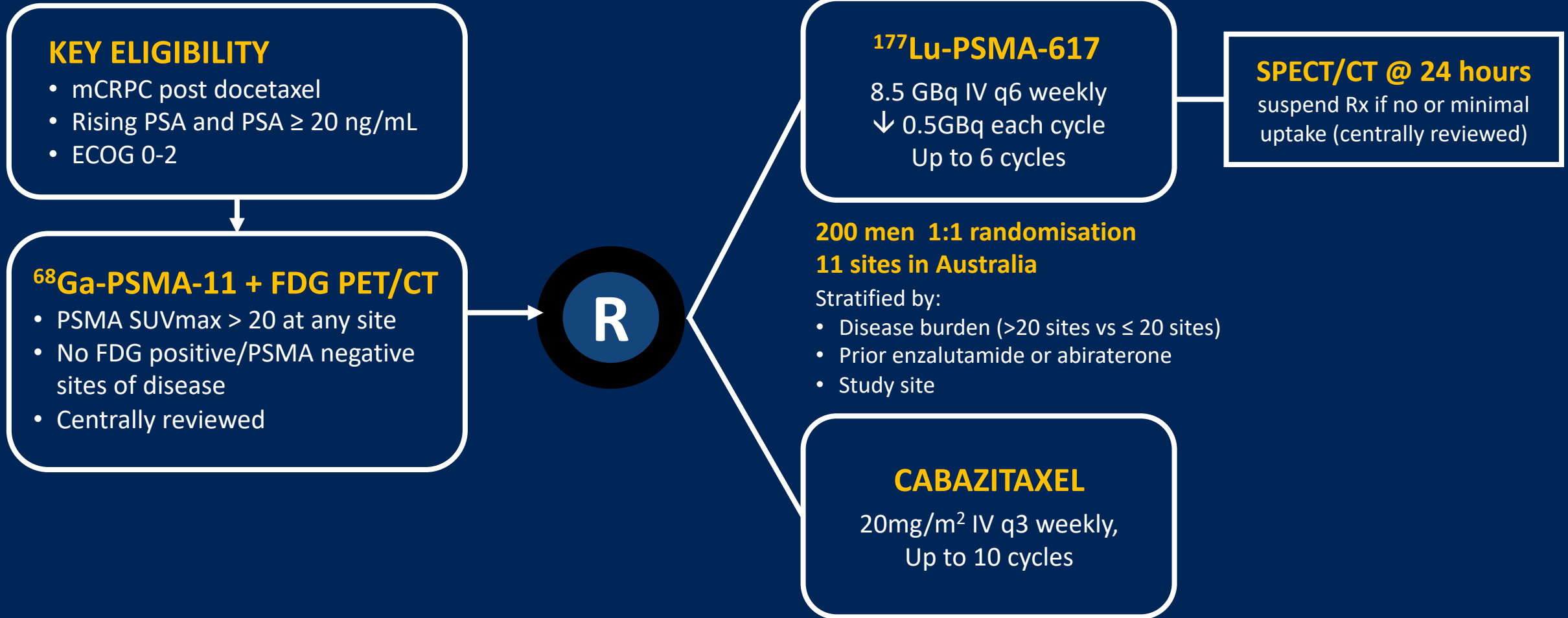


### Patient Reported Outcomes

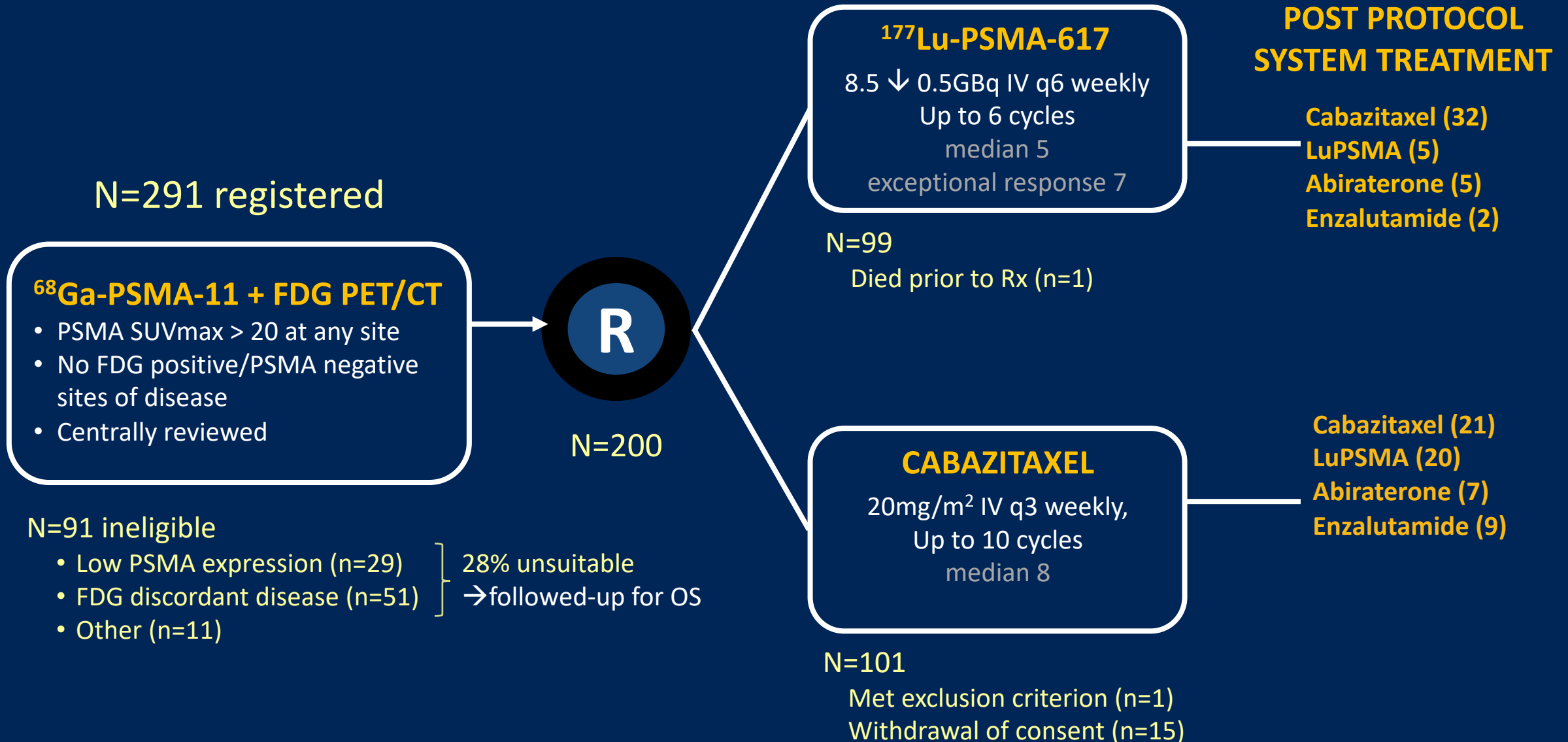


<sup>1</sup> Hofman MS et al, Lancet 2021; 397(10276)

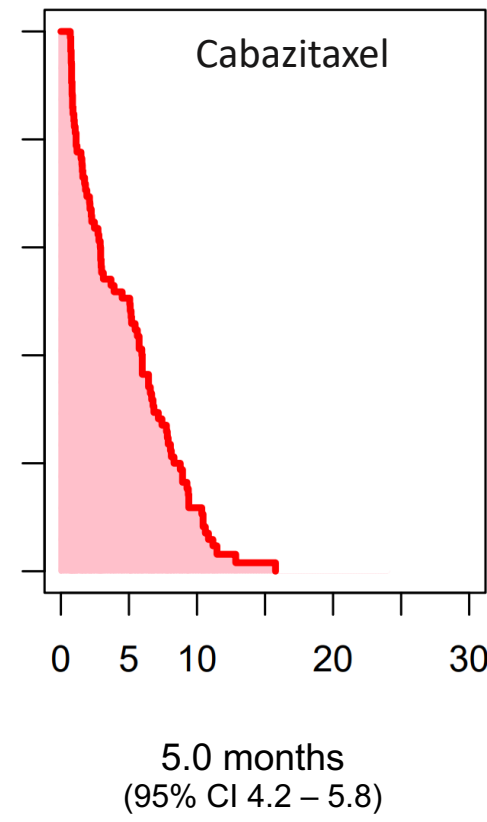
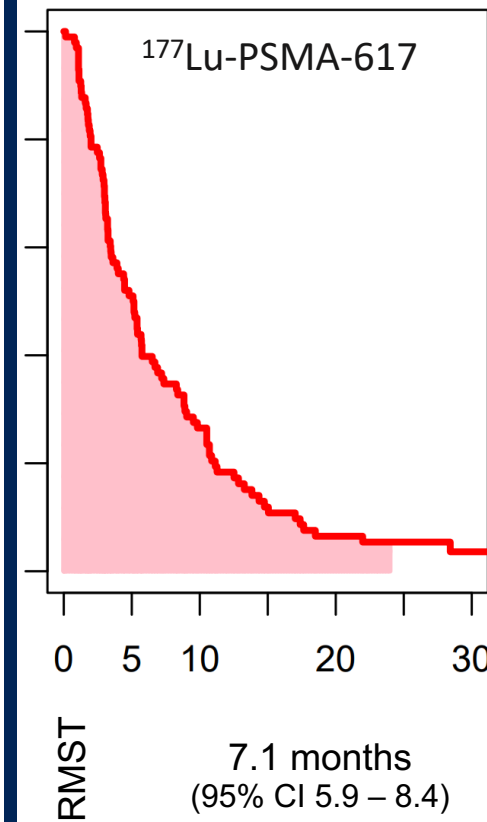
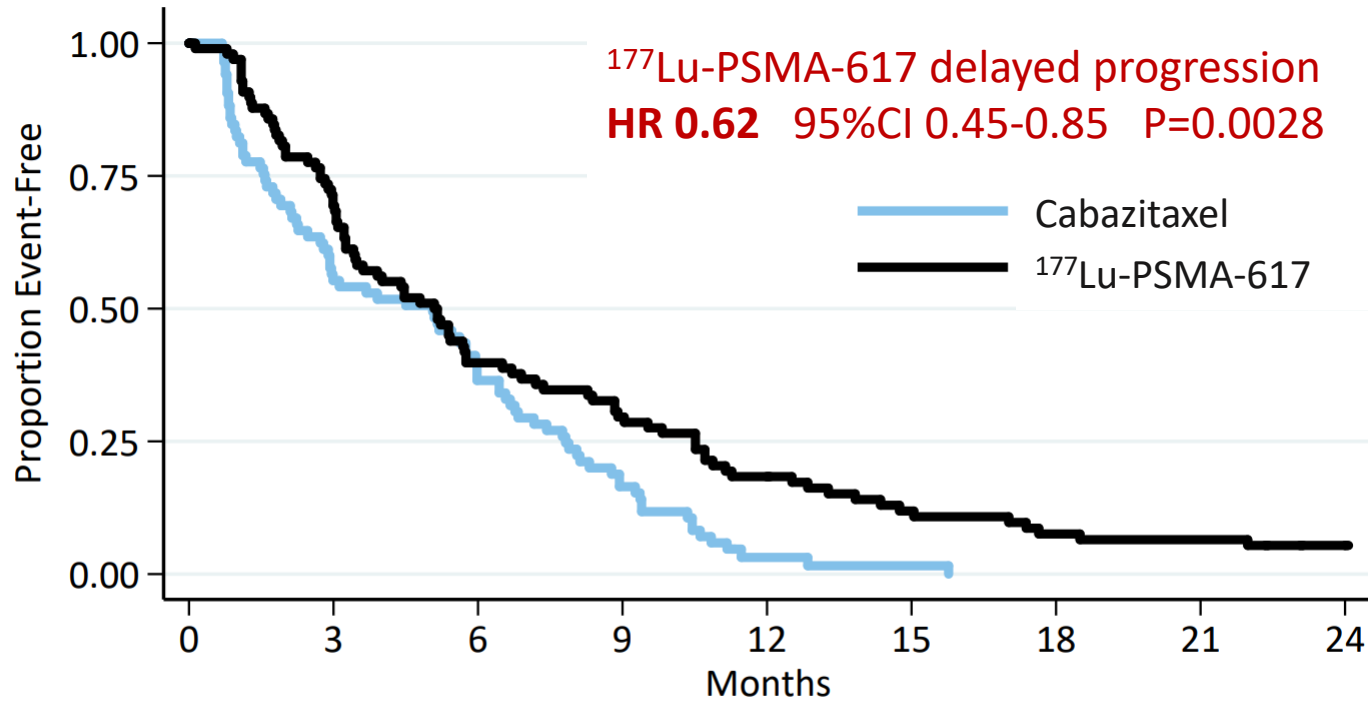
# TheraP Trial Schema



# Aim: report secondary endpoint of OS



# Progression Free Survival (PSA and radiographic)



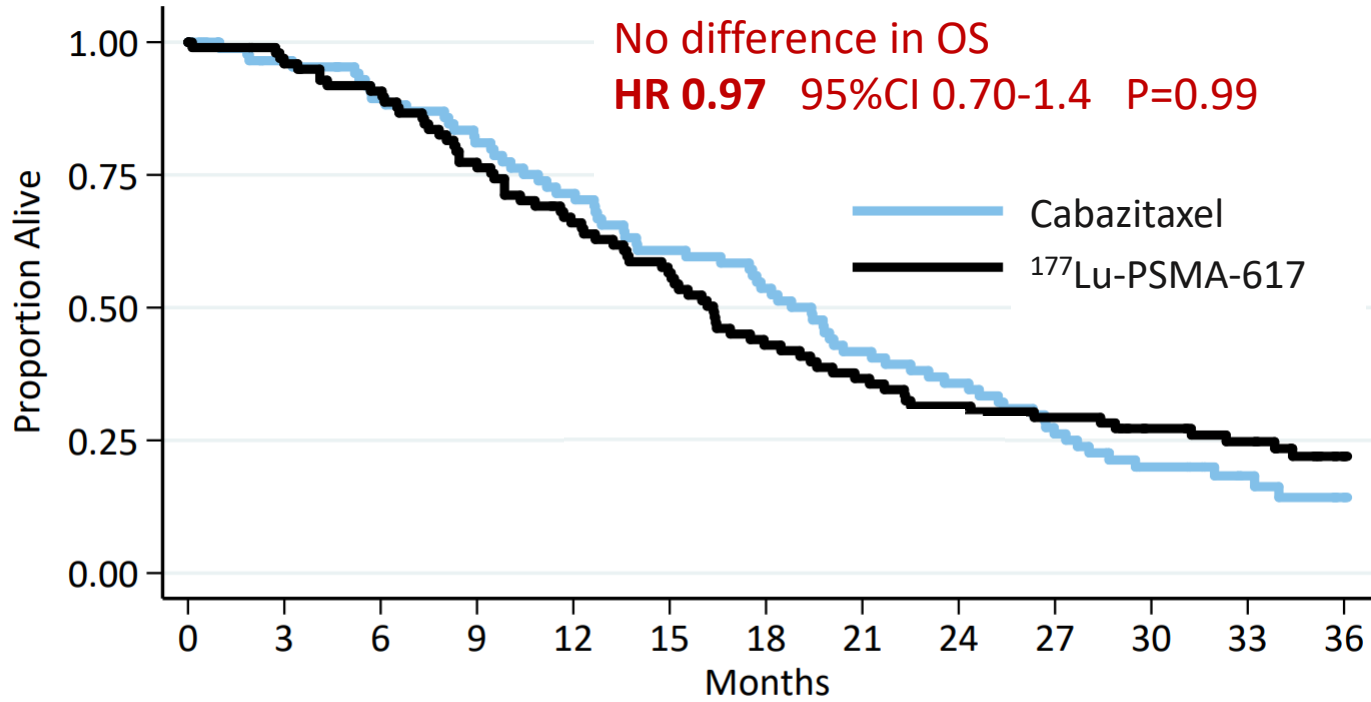
Number at risk

	0	3	6	9	12	15	18	21	24
Cabazitaxel	101	47	31	14	2	1	0	0	0
Lu-PSMA	99	68	39	29	17	11	7	6	3

- Treatment effect not constant with respect to time → restricted mean survival time (RMST)
- 177 progression events. Cut-off 31 DEC 2020 for non-OS endpoints.
- Similar HR for rPFS (0.65) and PSA-PFS (0.60), and in per-protocol sensitivity analyses

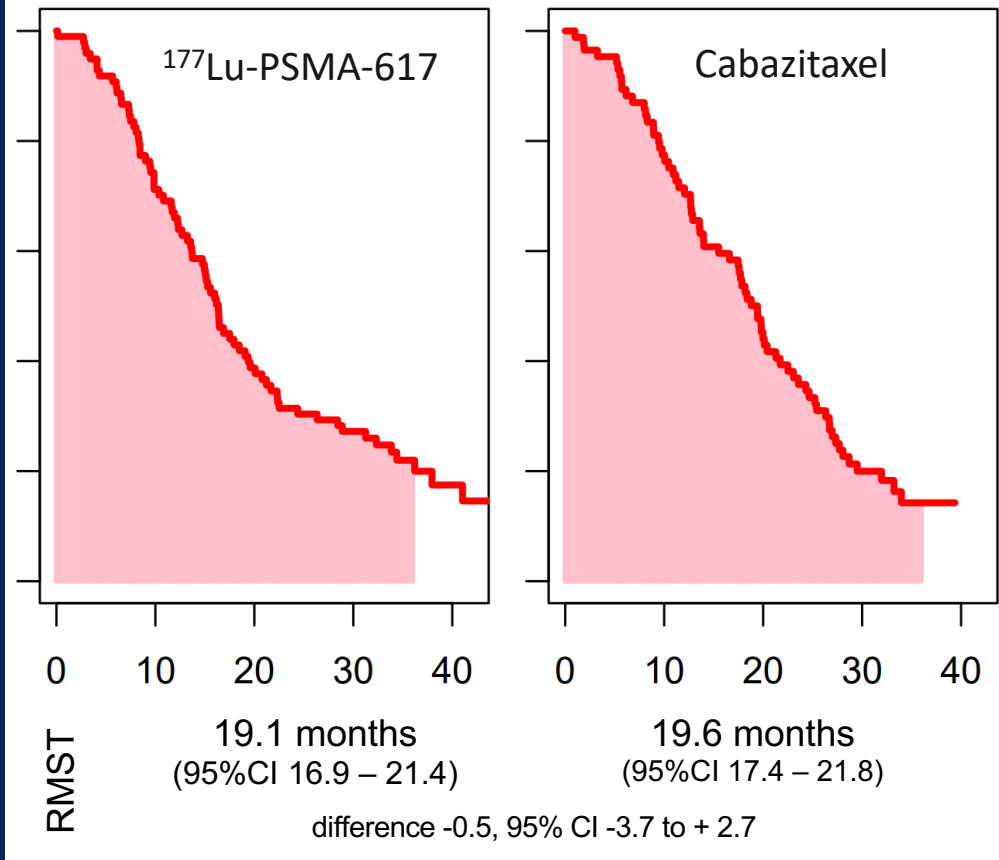


# Overall survival (ITT)



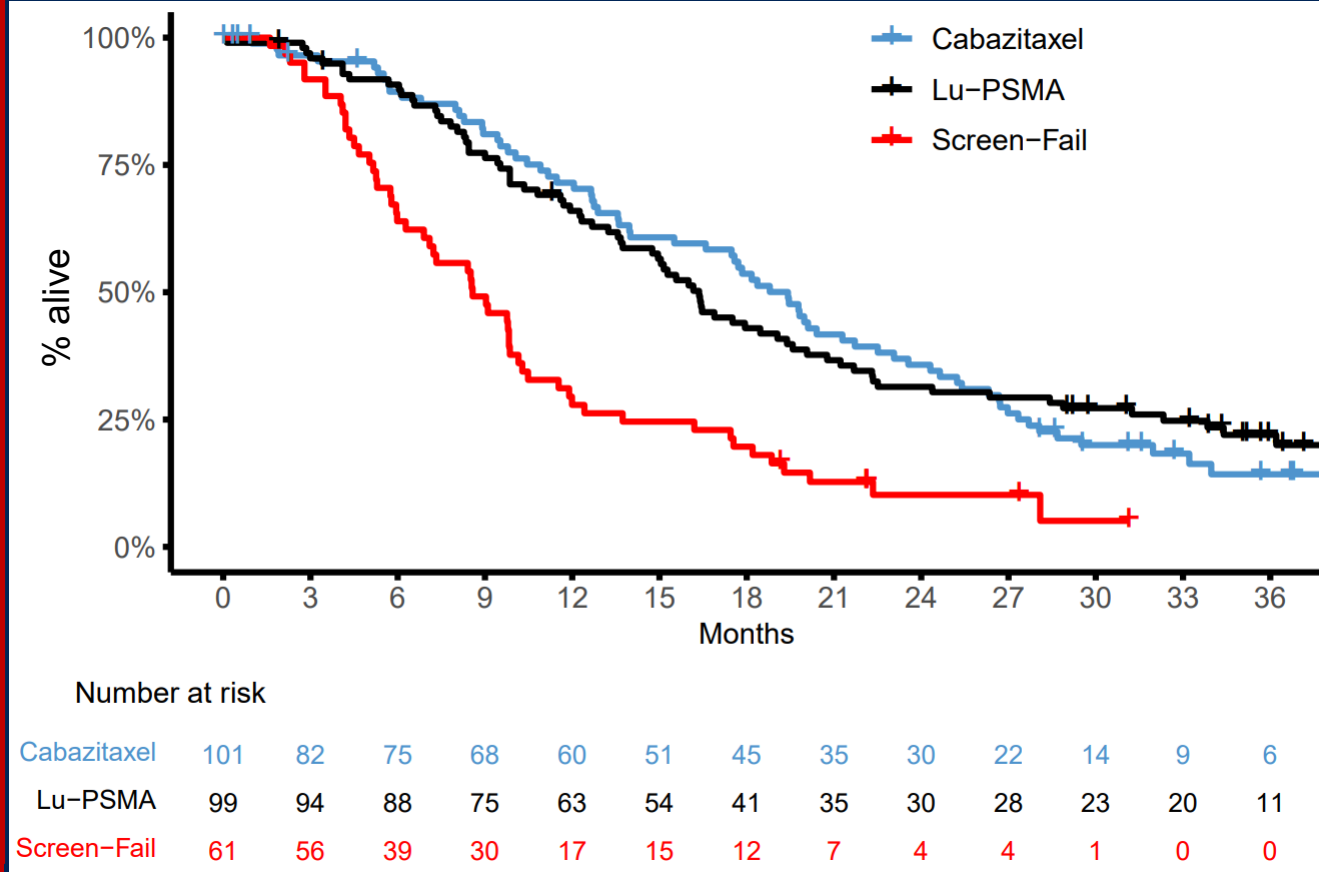
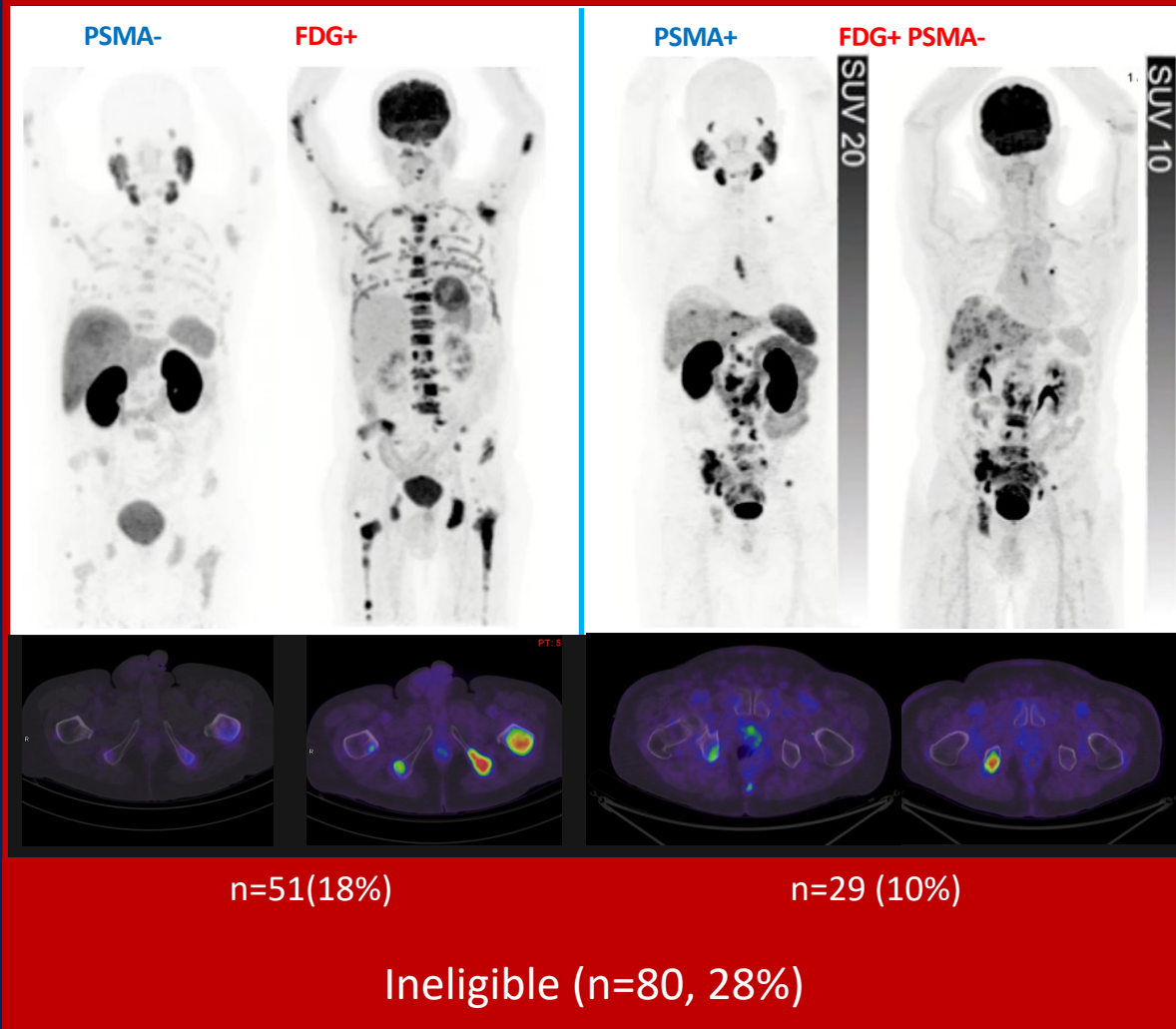
Number at risk

	0	3	6	9	12	15	18	21	24	27	30	33	36
Cabazitaxel	101	82	75	68	60	51	45	35	30	22	14	9	6
Lu-PSMA	99	94	88	75	63	54	41	35	30	28	23	20	11



- Cut-off 31 DEC 2021 for OS
- At 36 months follow-up, death reported in 147/200; 70/101 assigned cabazitaxel vs. 77/99 assigned LuPSMA
- Per-protocol analysis: no difference in OS
- No additional safety signals with longer follow-up.

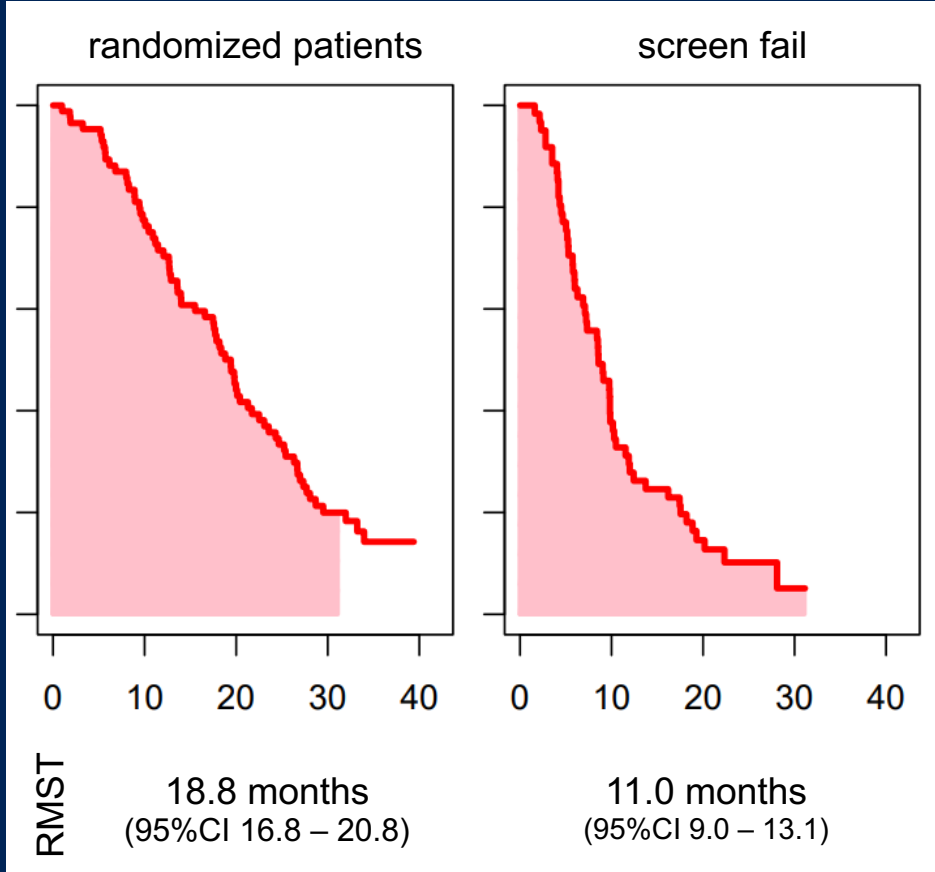
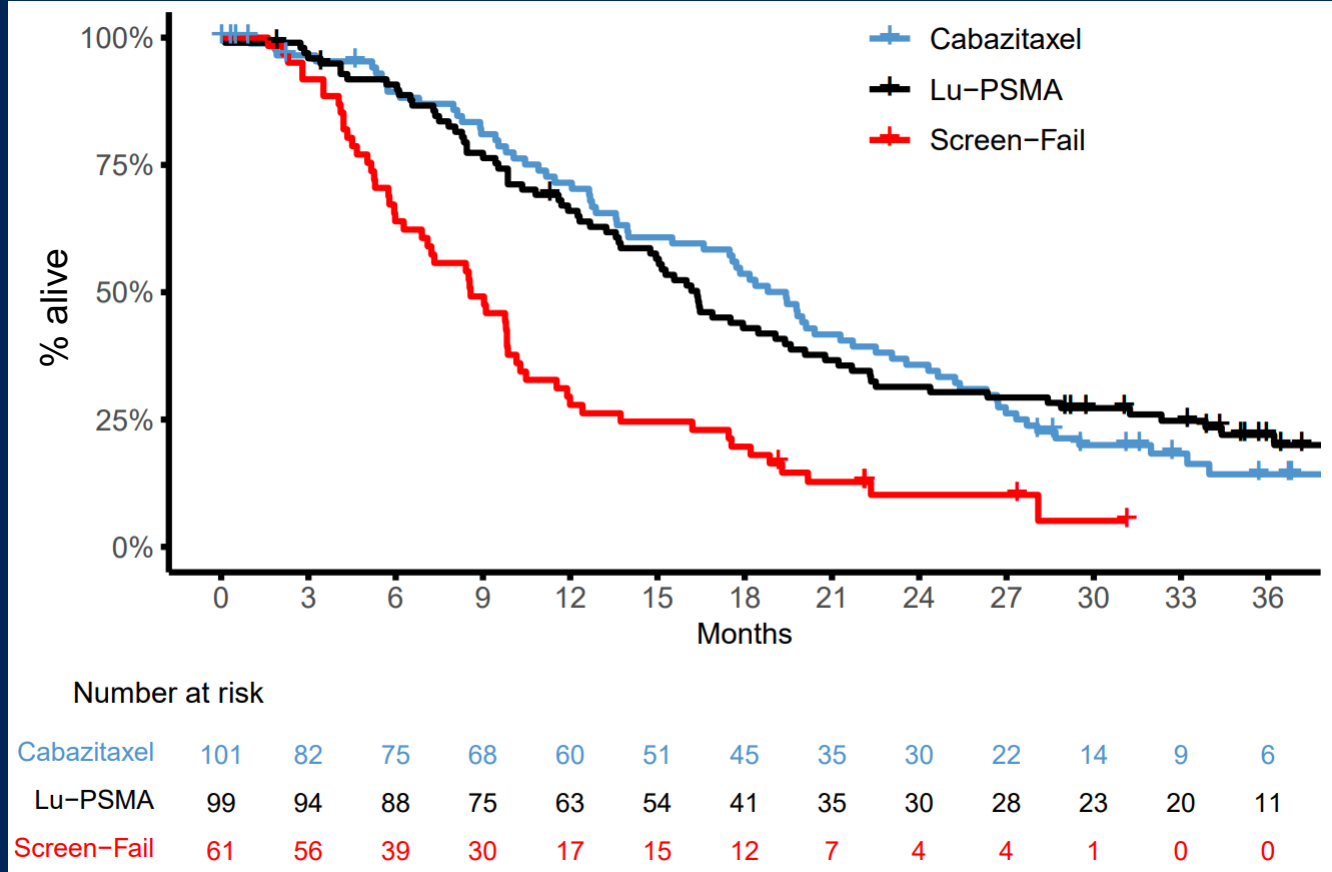
# OS of PSMA/FDG PET Screen Failures



Next line of treatment: cabazitaxel 29 (48%), enzalutamide 4 (7%), LuPSMA 3 (5%), carboplatin 3 (5%), other 3 (5%), mitoxantrone 1 (2%)

Patients met other TheraP trial eligibility criteria.  
61 of 80 consented for follow-up

# OS of PSMA/FDG PET Screen Failure



Next line of treatment: cabazitaxel 29 (48%), enzalutamide 4 (7%), LuPSMA 3 (5%), carboplatin 3 (5%), other 3 (5%), mitoxantrone 1 (2%)

# Discussion

## Strengths

Prospective, randomized,  
multi-center

3 years follow-up

Active control arm<sup>1</sup>  
(vs. VISION)

## Limitations

Post protocol  
cross-over  
confounds OS

Withdrawal post  
randomization in  
cabazitaxel arm

OS a 2<sup>o</sup> endpoint  
(underpowered)

## Clinical Implications

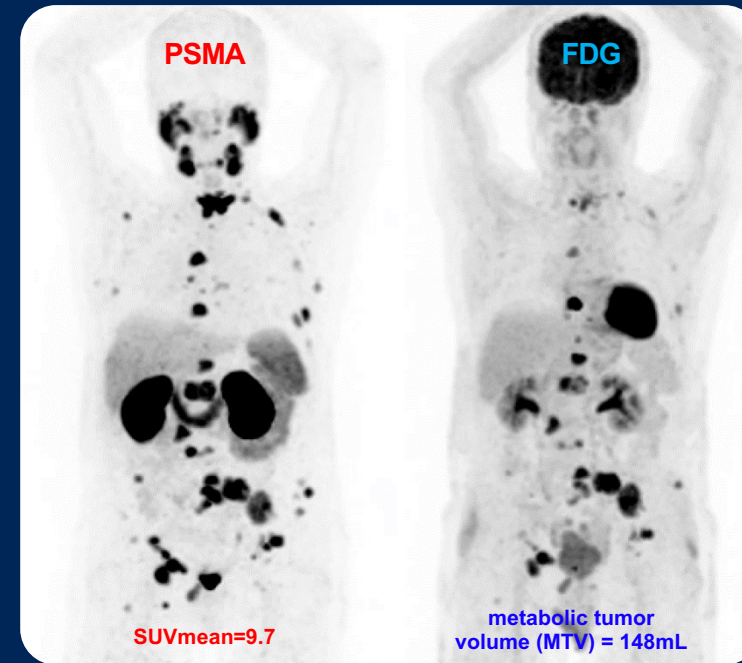
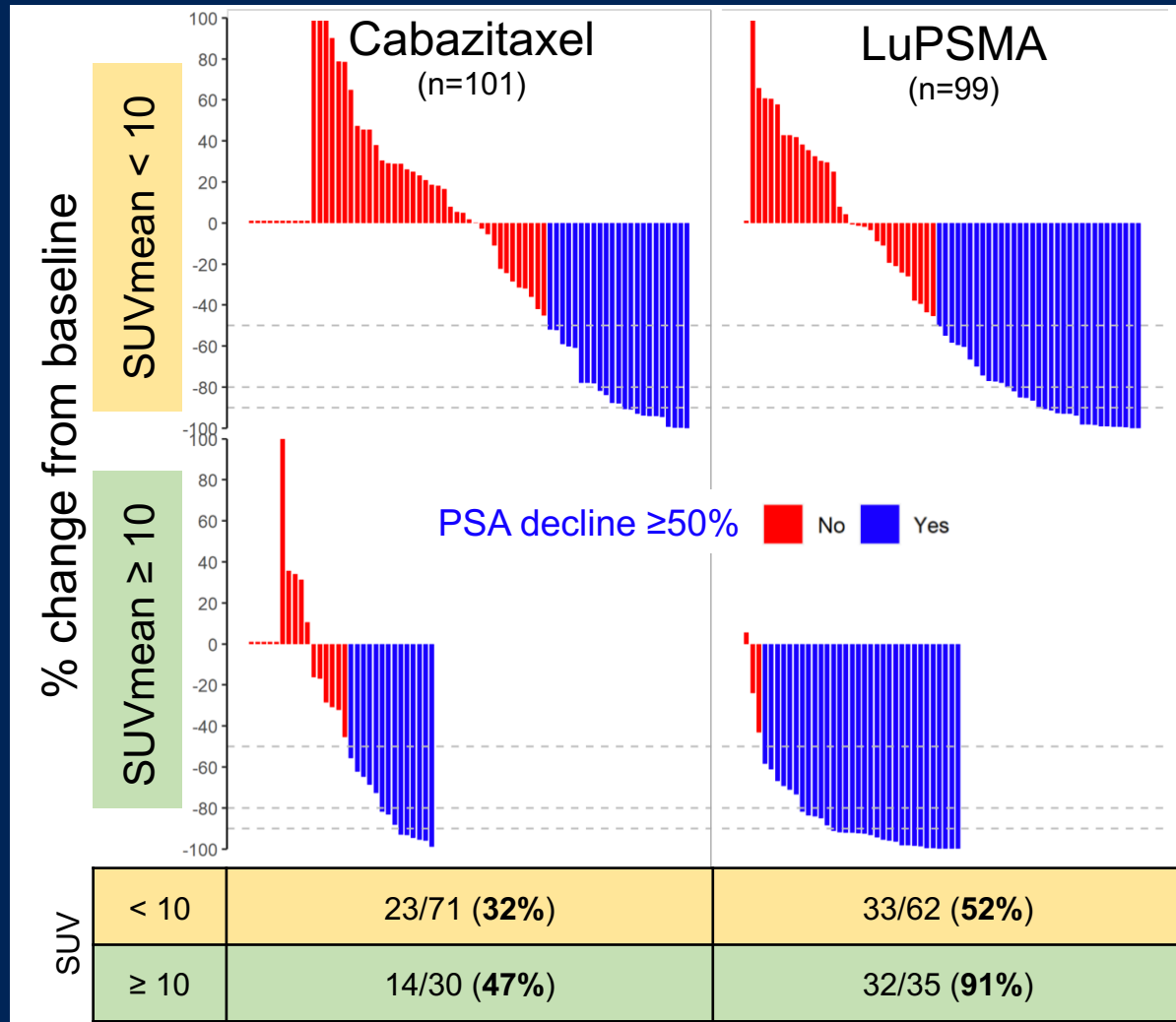
LuPSMA: >greater activity  
PSA50-RR, RECIST,  
rPFS, PSA-PFS

Similar OS to  
cabazitaxel, a life  
prolonging treatment<sup>1</sup>

Fewer AEs, better patient  
reported outcomes

<sup>1</sup> de Wit R et al, NEJM 2019; 381

# Discussion: PSMA as predictive biomarker<sup>1</sup> (PSA50-RR)<sup>21</sup>



## Odds of PSA50-RR to LuPSMA vs cabazitaxel

	OR (95% CI)
PSMA SUVmean < 10	2.2 (1.1 – 4.5)
PSMA SUVmean ≥ 10	12.2 (3.4 - 59)

P=0.03

Further analysis to be performed including OS

<sup>1</sup>Buteau J et al, ASCO GU 2022. doi:10.1200/JCO.2022.40.6\_suppl.010

# Conclusion

The TheraP data support the choice of <sup>177</sup>Lu-PSMA-617 over cabazitaxel for patients with PSMA-positive, progressive mCRPC after docetaxel and androgen-receptor pathway inhibitor, on the basis of its higher PSA response rate, greater PFS benefit, QoL benefits, favorable safety profile and dosing schedule, and similar survival outcomes.

Survival was considerably shorter for patients excluded on PSMA/FDG-PET with either low PSMA-expression, or discordant disease.

# Acknowledgements

All slides can be downloaded at:  
[www.anzup.org.au/therap](http://www.anzup.org.au/therap)

## We thank:

- Patients and support network
- Principal and co-investigators
- Study coordinators
- Nurses
- Radiopharmacists/chemists
- Nuclear medicine technologists
- Clinical research associates
- Data managers

## Industry support:

- PSMA-617 supply and financial support: Endocyte Inc., a Novartis company
- Lutetium-177 no carrier added supplied from Australian Nuclear Science and Technology Organisation (ANSTO)

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  - Movember
  - It's a Bloke Thing Foundation
  - Can4Cancer
- Cancer Australia (ANZUP infrastructure support)
- M Hofman: Peter MacCallum Foundation, Prostate Cancer Foundation (PCF) NHMRC Investigator Grant

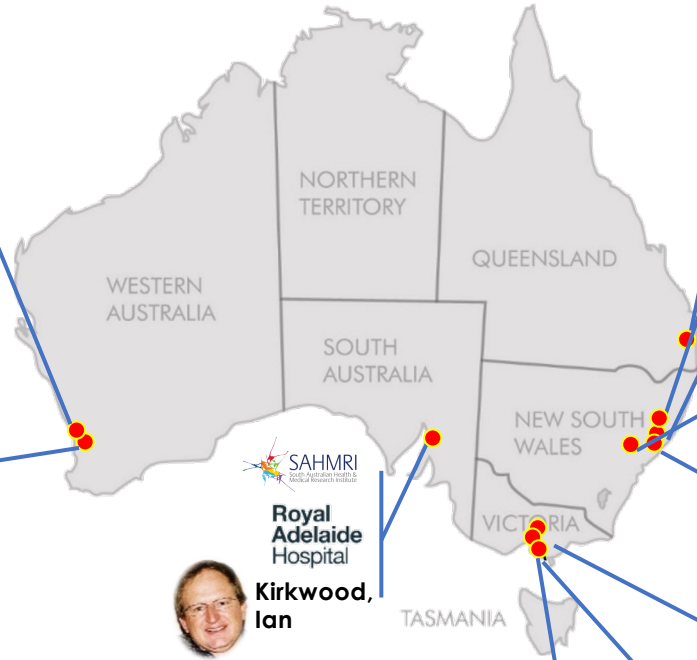


## Study designed and conducted by ANZUP in collaboration with:

- NHMRC Clinical Trials Centre at the University of Sydney
- Australasian Radiopharmaceutical Trials Network (ARTnet)



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**THE UNIVERSITY OF MELBOURNE**

**Australasian Radiopharmaceutical Trials network**

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**ANZUP**  
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# Abstract #198: Racial Concordance and Trust in Health Communications: A Randomized Trial of Videos about Prostate Cancer

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## Background

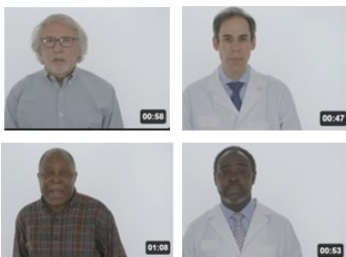
- Black men are at higher risk of prostate cancer and develop more aggressive disease compared to White men.
- The Internet is a popular source of health information; however, Black adults are underrepresented in online content about prostate cancer.

## Objective

- To evaluate the association between racial representation in online content about prostate cancer and trust in the content.
- A secondary objective was to identify additional attributes that influence trust in online content

## Methods

- Randomized trial n=2904 U.S. adults age ≥40
- Randomized to view 1 of 8 online videos with an equivalent script about either prostate cancer screening or clinical trials presented by 1 of 4 different presenters: Black physician, Black patient, White physician, or White patient



- Logistic regression was used to compare trust in the videos, based upon the characteristics of the speaker and topic

**Conclusions:**  
 Racial concordance is significantly associated with trust in prostate cancer information among Black adults. Additionally, health information is considered more trustworthy when delivered by a physician vs. a patient.

Supported by a Department of Defense Health Disparity Research Award  
 For more information, contact: stacyloeb@gmail.com

## Results:

### 1. Demographics of the Study Population

	Black adults (n=1703)	White adults (n=1201)
Age (Mean, SD)	55.5 (11.0)	63.0 (11.81)
Gender (#, %)		
Male	901 (52.9%)	900 (74.9%)
Female	802 (47.1%)	301 (25.1%)
Ethnicity (#, %)		
Hispanic	115 (6.8%)	3 (0.25%)
Non-Hispanic	1582 (92.9%)	1195 (99.5%)

### 2. Trust in Prostate Cancer Videos Among Black and White Adults

	Black Adults (N = 1703)			White Adults (N = 1201)		
	Low Trust n (%)	High Trust n (%)	p value	Low Trust n (%)	High Trust n (%)	p value
Race of speaker			0.0002			0.24
Black	230 (42.9)	615 (52.7)		139 (46.8)	461 (51.0)	
White	306 (57.1)	552 (47.3)		158 (53.2)	443 (49.0)	
Speaker Qualification			0.0006			0.01
Doctor	235 (43.8)	618 (53.0)		128 (43.1)	470 (52.0)	
Patient	301 (56.2)	549 (47.0)		169 (56.9)	434 (48.0)	
Topic of video			0.06			0.002
Screening	251 (46.8)	605 (51.8)		126 (42.4)	477 (52.8)	
Clinical Trial	285 (53.2)	562 (48.2)		171 (57.6)	427 (47.2)	

### 3. Multivariable Analysis for Trust in Prostate Cancer Videos

	Black adults (n=1703) Adjusted OR (95% CI), p-value	White adults (n=1201) Adjusted OR (95% CI), p-value
Black vs White Speaker	1.49 (1.21, 1.83), p<0.001	1.19 (0.91, 1.54), p=0.21
Patient vs Doctor	0.69 (0.56, 0.85), p<0.001	0.70 (0.54, 0.91), p=0.008
Clinical Trials vs Screening	0.81 (0.66, 0.99), p=0.04	0.66 (0.54, 0.91), p=0.002