

Yearly review, urological standpoint



YEAR IN REVIEW
IN GU ONCOLOGY
MEETING 2025

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Yearly review, urological standpoint



BMUC

UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

**YEAR IN REVIEW
IN GU ONCOLOGY
MEETING 2025**

No conflict of interest



Annual review in uro oncology

- Prostate cancer
- Bladder cancer
- Renal cancer



Annual review in uro oncology

- Prostate cancer Localized – Recurrent - Advanced
- Bladder cancer
- Renal cancer

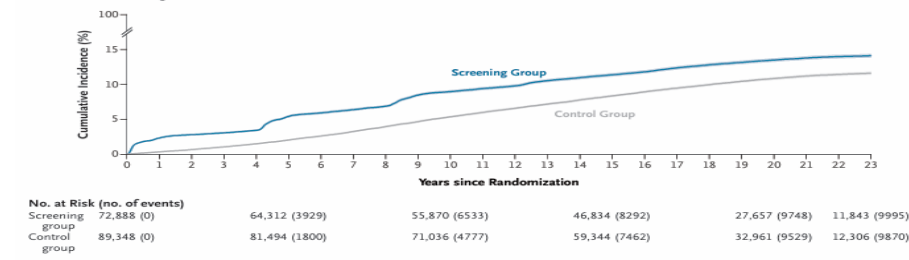
Prostate cancer – Localized disease - Screening



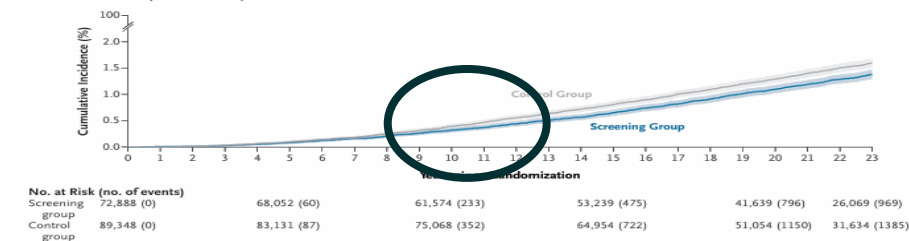
European Study of Prostate Cancer Screening — 23-Year Follow-up

Monique J. Roobol, Ph.D.,¹ Ivo I. de Vos, M.D.,¹ Marianne Månsson, Ph.D.,² Rebecka A. Godtman, M.D., Ph.D.,²
Kirsi M. Talala, Ph.D.,³ Elly den Hond, Ph.D.,⁴ Vera Nelen, M.D., Ph.D.,⁴ Arnaud Villers, M.D., Ph.D.,⁵
Gregoire Poinas, M.D.,⁶ Maciej Kwiatkowski, M.D., Ph.D.,⁷⁻⁹ Stephen Wyler, Ph.D., M.D.,^{7,8}
Franz Recker, M.D., Ph.D.,⁷ Donella Puliti, Ph.D.,¹⁰ Giuseppe Gorini, M.D., Ph.D.,¹⁰ Marco Zappa, Ph.D.,¹⁰
Alvaro Paez, M.D.,¹¹ Marcos Lujan, M.D.,¹² Chris H. Bangma, M.D., Ph.D.,¹ Teuvo Tammela, M.D., Ph.D.,^{13,14}
Fritz H. Schröder, M.D., Ph.D.,¹ Sebastiaan Remmers, Ph.D.,¹ Jonas Hugosson, M.D., Ph.D.,² and
Anssi Auvinen, M.D., Ph.D.,¹⁵ for the ERSPC Investigators*

A Prostate Cancer Diagnosis



B Prostate Cancer–Specific Mortality



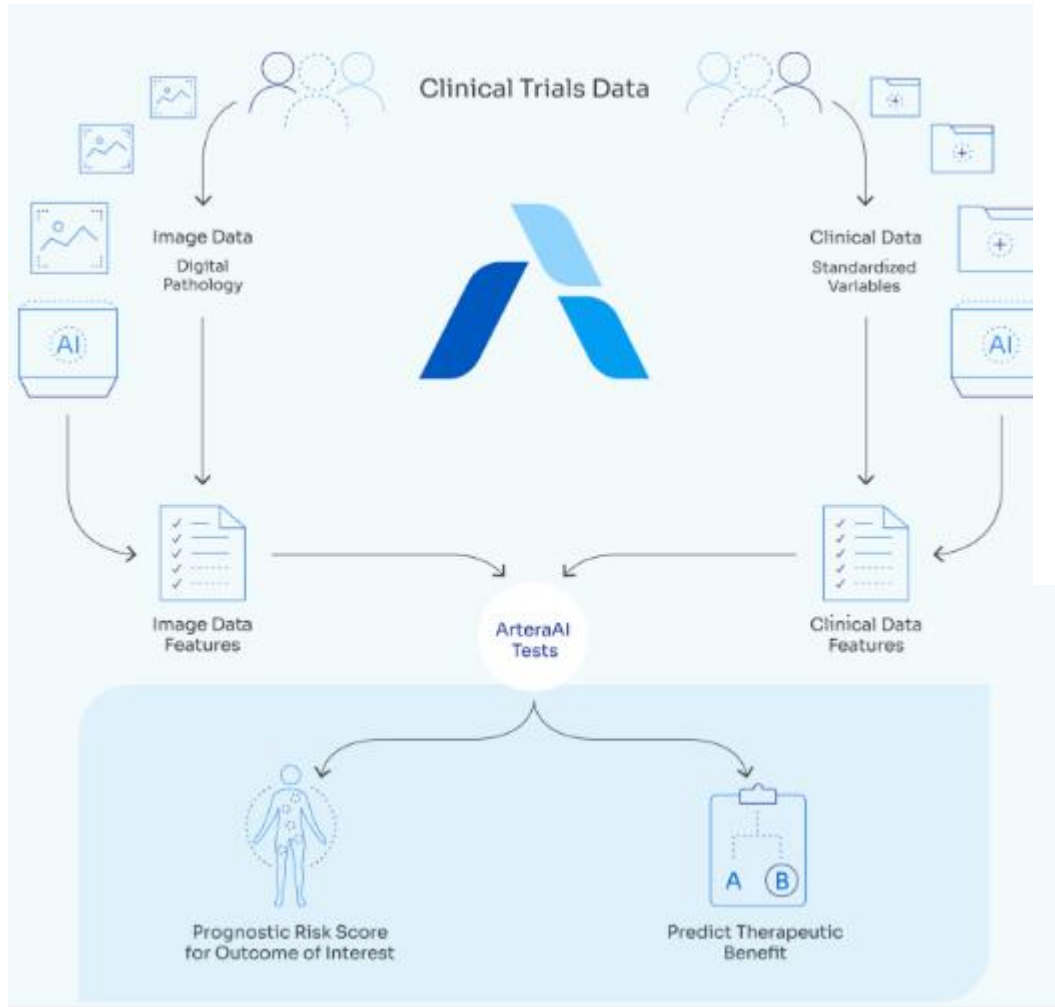
But

- 16% of significant PSA
- 24% of positive biopsies
- Doubling detection of low risk
- No risk-based screening

Table 2. Prostate Cancer Mortality According to Length of Follow-up.*

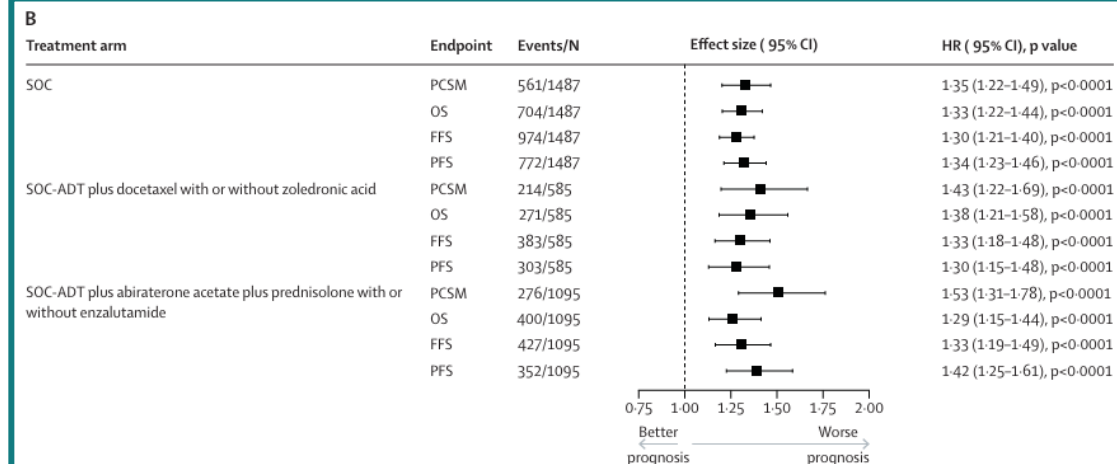
Length of Follow-up	Rate Ratio (95% CI)	Relative Risk Reduction	Absolute Risk Difference (95% CI)	No. Needed to Invite (95% CI)	No. Needed to Diagnose (95% CI)
		percent			
9 yr	0.83 (0.69–1.01)	17	0.05 (0.00–0.09)	1919 (903–14308)	73 (34–567)
11 yr	0.79 (0.67–0.93)	21	0.10 (0.03–0.15)	1041 (679–3486)	36 (22–118)
13 yr	0.80 (0.70–0.91)	20	0.12 (0.05–0.19)	803 (538–1927)	27 (18–62)
16 yr	0.82 (0.73–0.92)	18	0.16 (0.07–0.24)	628 (419–1481)	18 (12–45)
23 yr	0.87 (0.80–0.95)	13	0.22 (0.11–0.33)	456 (306–943)	12 (8–26)

Prostate cancer – Localized disease - Diagnostic

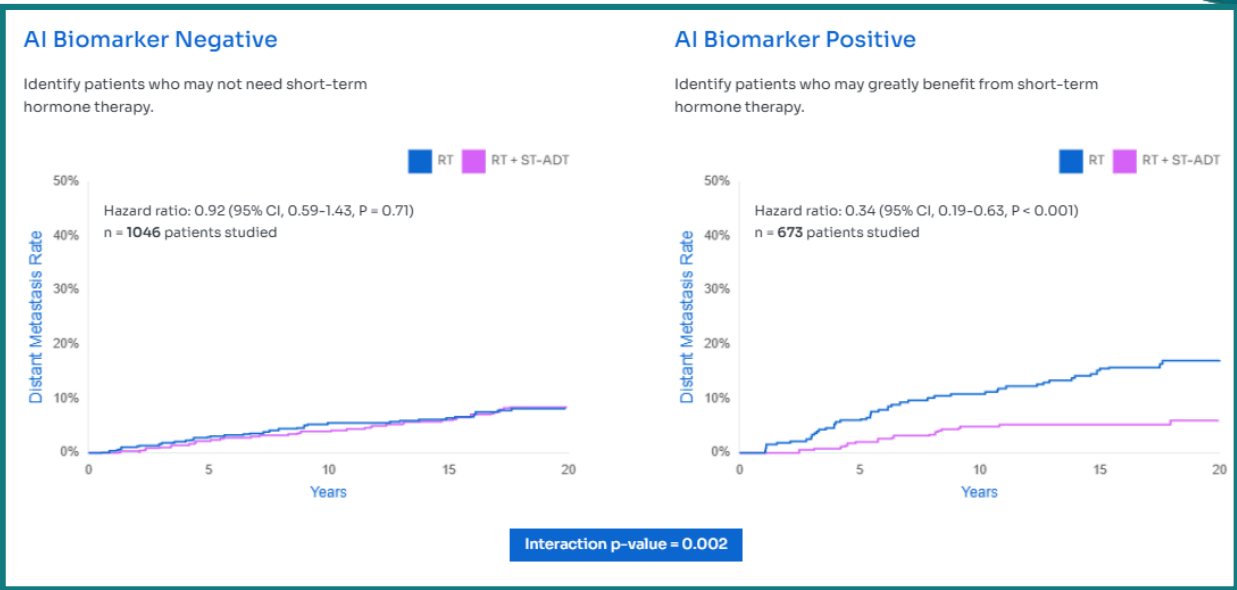
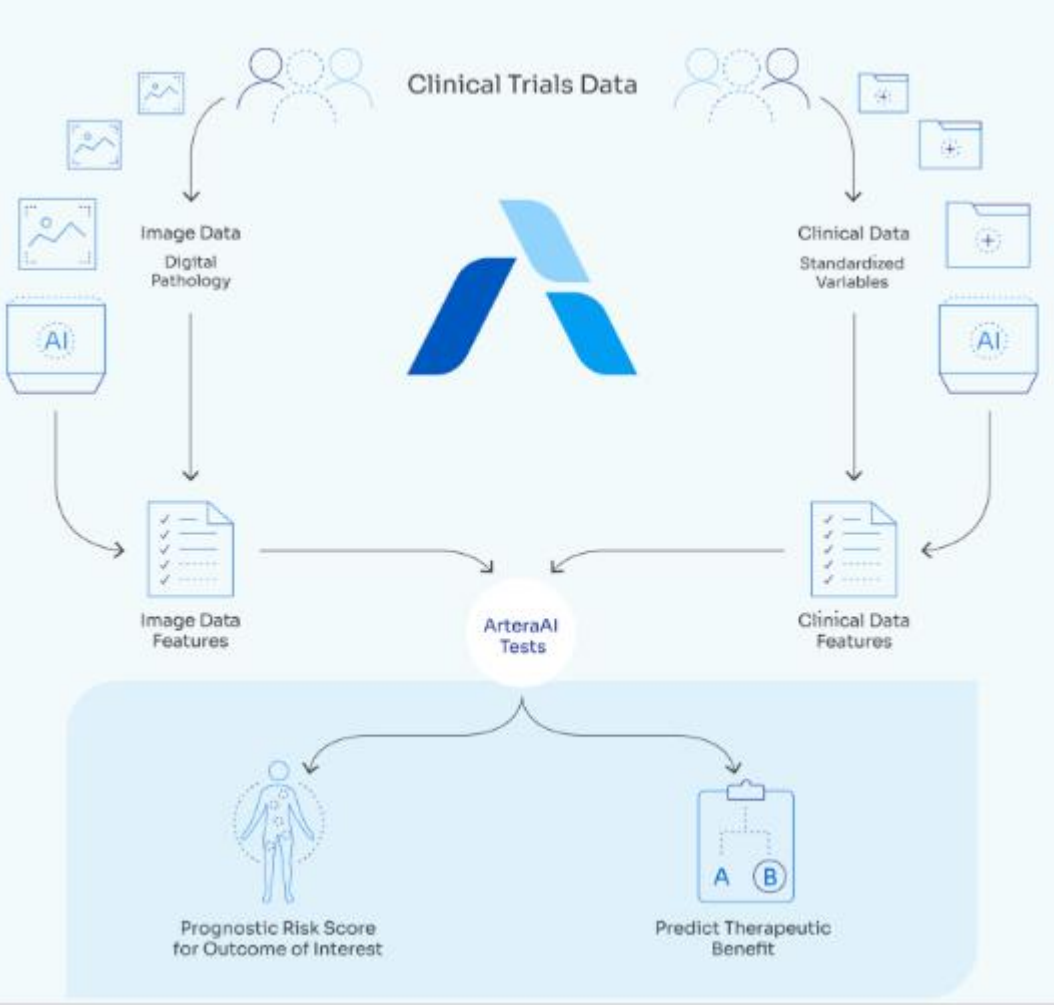


External validation of a digital pathology-based multimodal artificial intelligence-derived prognostic model in patients with advanced prostate cancer starting long-term androgen deprivation therapy: a post-hoc ancillary biomarker study of four phase 3 randomised controlled trials of the STAMPEDE platform protocol

Charles T A Parker, Larissa Mendes, Vinnie Y T Liu, Emily Grist, Songwan Joun, Rikiya Yamashita, Akinori Mitani, Emmalyn Chen, Marina A Parry, Ashwin Sachdeva, Laura Murphy, Huei-Chung Huang, Jacqueline Griffin, Douwe van der Wal, Tamara Todorovic, Sharanpreet Lall, Sara Santos Vidal, Miriam Goncalves, Suparna Thakali, Anna Wingate, Leila Zakka, Mick Brown, Daniel Wetterskog, Claire L Amos, Nafisah B Atako, Robert J Jones, William R Cross, Silke Gillesen, Chris C Parker, STAMPEDE collaborators*, Daniel M Berney, Phuoc T Tran, Daniel E Spratt, Matthew R Sydes, Mahesh K B Parmar, Noel W Clarke, Louise C Brown, Felix Y Feng, Andre Esteve, Nicholas D James, Gerhardt Attard



Prostate cancer – Localized disease - Diagnostic



NCCN Guidelines® Version 1.2025 Prostate Cancer

Principles of Risk Stratification and Biomarkers: Advanced Tools				
Category	Tool	Predictive	Prognostic	Prognostic Endpoint Trained For ^a
Gene Expression	22-gene genomic classifier (GC) (Decipher)	Not determined	Yes	DM
AI-Pathology	Multimodal artificial intelligence (MMAI) (ArteraAI Prostate)	Yes, for ST-ADT	Yes	DM, PCSM

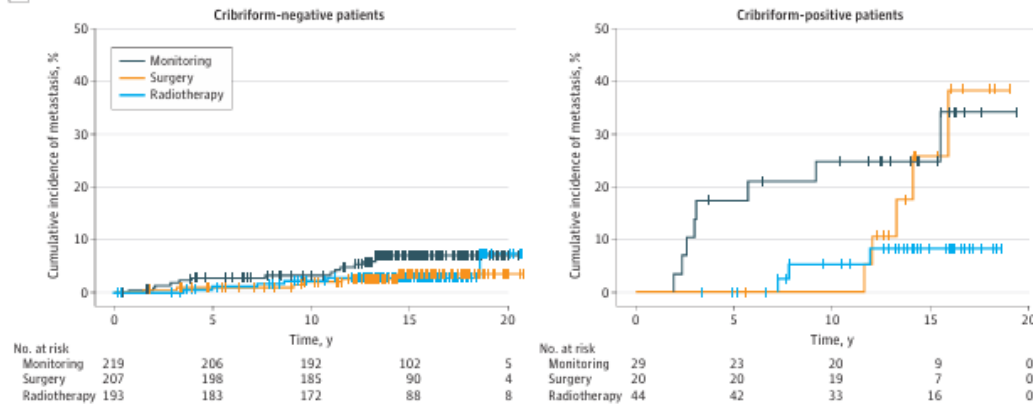
Prostate cancer – Localized disease – Active surveillance

JAMA Oncology | Brief Report

Active Monitoring, Surgery, and Radiotherapy for Cribriiform-Positive and Cribriiform-Negative Prostate Cancer A Secondary Analysis of the PROTECT Randomized Clinical Trial

Nikita Sushentsev, MD; Anne Y. Warren, MB BS; Richard Colling, MD; Clare Verrill, BM; Ekaterina Pazukhina, MSc; Oleg Blyuss, PhD; Tyler M. Seibert, MD; Tristan Barrett, MD; Ian G. Mills, PhD; Richard J. Bryant, MBChB;

B Cumulative incidence analysis



Treatment assigned

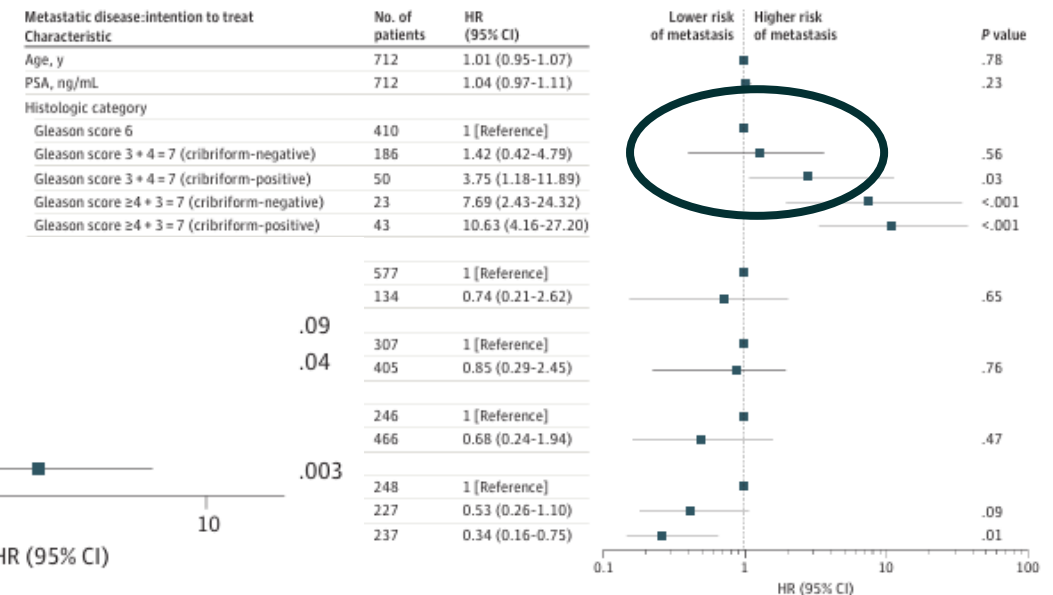
Active monitoring	248	1 [Reference]
Surgery	227	0.52 (0.25-1.08)
Radiotherapy with ADT	237	0.35 (0.16-0.78)

Cribriiform status

Cribriiform-negative	619	1 [Reference]
Cribriiform-positive	93	3.61 (1.60-8.11)

- 15 years results of MFS
- ITT population : 13.1% Cribriiform
 - HR 3.61 for apparition of metastasis
- 3+4 W/O cribriform = 3+3
- Slightly higher benefit from radiotherapy+ adt (!!underpowered)

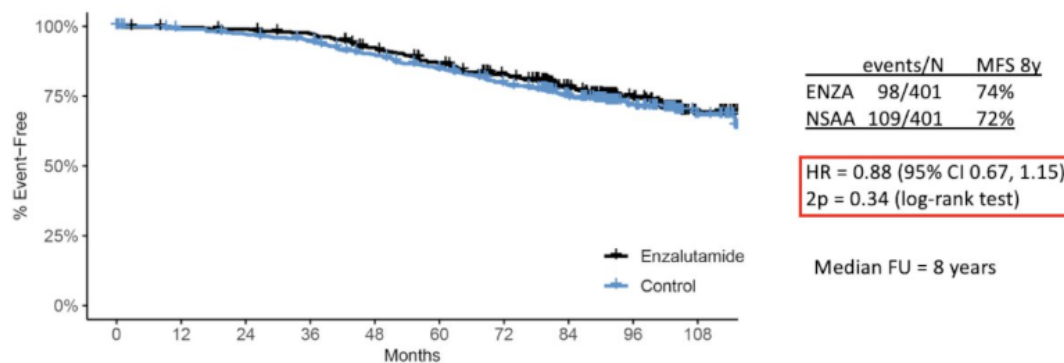
Figure 3. Subgroup Intention-to-Treat Analysis



Prostate cancer – Locally advanced – Hormonal intensification

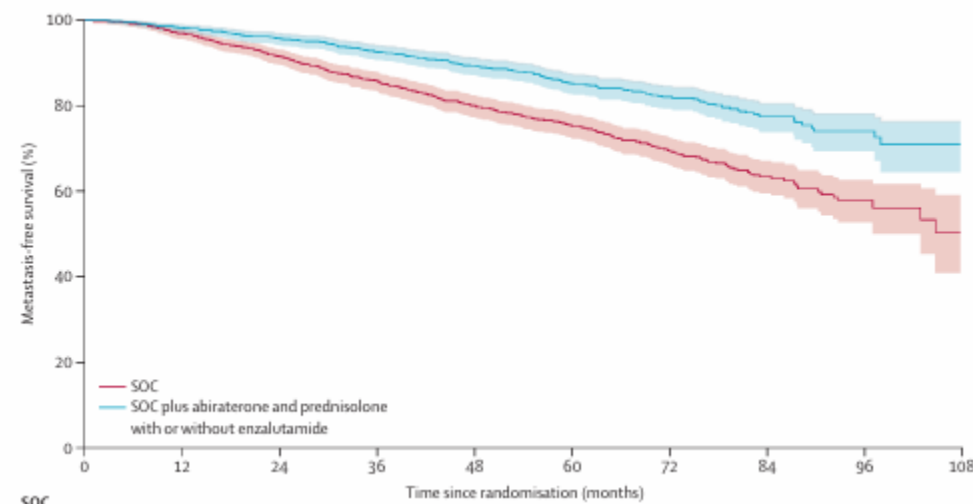
ENZARAD (ANZUP 1303): global, open-label, phase III trial (Mar 2014–Jun 2018)

Population	Design	Endpoints
- Localised and locally advanced PCa - High recurrence risk - Eligible for EBRT	R 1:1 N=802 ENZA 160 mg od for 24 mo + LHRH analogue for 24 mo + RT starting after 16 wk ± BT ± nodal RT Conventional NSAA for 6 mo + LHRH analogue for 24 mo + RT starting after 16 wk ± BT ± nodal RT	Primary - MFS based on conventional imaging (CT, MRI/bone scan, per ICECaP; lesions on PSMA-PET only are insufficient) by BICR Secondary - OS - PCa-specific survival - PSA PFS - clinical PFS - CRPC, HRQoL - AEs - Incremental cost-effectiveness



Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol

Gerhardt Attard, Laura Murphy, Noel W Clarke, William Cross, Robert J Jones, Christopher C Parker, Silke Gillessen, Adrian Cook, Chris Brawley, Claire L Amos, Nafisah Atako, Cheryl Pugh, Michelle Buckner, Simon Chowdhury, Zafar Malik, J Martin Russell, Clare Gilson, Hannah Rush, Jo Bowen, Anna Lydon, Ian Pedley, Joe M O'Sullivan, Alison Birtle, Joanna Gale, Narayanan Srihari, Carys Thomas, Jacob Tanguay, John Wagstaff, Prantik Das, Emma Gray, Mymoona Alzoube, Omi Parikh, Angus Robinson, Isabel Syndikus, James Wylie, Anjali Zarkar, George Thalmann, Johann S de Bono, David P Dearnaley*, Malcolm D Mason*, Duncan Gilbert, Ruth E Langley, Robin Millman, David Matheson, Matthew R Sydes†, Louise C Brown†, Mahesh K B Parmar†, Nicholas D James†, on behalf of the Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators‡



Prostate cancer – Locally advanced – Hormonal intensification



ENZARAD (ANZUP 1303): global, open-label, phase III trial
(Mar 2014-Jun 2018)

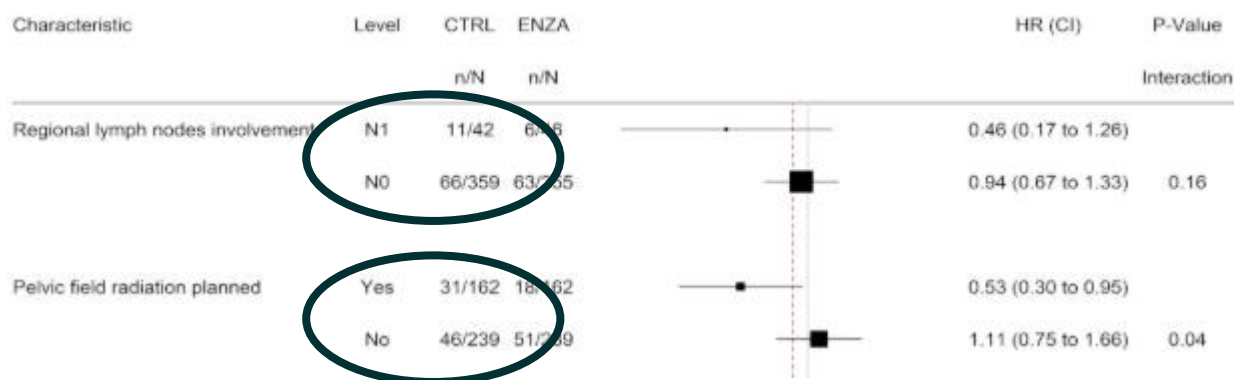
Population	Design	Endpoints
- Localised and locally advanced PCa - High recurrence risk - Eligible for EBRT	R 1:1 N=802 ENZA 160 mg od for 24 mo + LHRH analogue for 24 mo + RT starting after 16 wk ± BT ± nodal RT Conventional NSAA for 6 mo + LHRH analogue for 24 mo + RT starting after 16 wk ± BT ± nodal RT	Primary - MFS based on conventional imaging (CT, MRI/bone scan, per ICECaP; lesions on PSMA-PET only are insufficient) by BICR Secondary - OS - PCa-specific survival - PSA PFS - clinical PFS - CRPC, HRQoL - AEs - Incremental cost-effectiveness

?

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Prespecified subgroup analysis



	STAMPEDE (abiraterone)	ENZARAD (enzalutamide)
HR for MFS in cN1	0.49	0.43
HR for MFS in all patients	0.53 (p<0.0001)	0.88 (p=NS)
cN1	39%	11%
Median PSA	35	14
Clinical T3-4	92%	47%
Received radiation	82%	100%
Gleason 8-10	79%	89%

Prostate cancer – Locally advanced – Hormonal intensification



Offer IMRT/VMAT plus IGRT to the prostate in combination with long-term ADT and two years of abiraterone to cN0M0 patients with $\geq$ two high-risk factors (cT3-4, Gleason $\geq$ 8 or PSA $\geq$ 40 ng/mL).
Apalutamide?

Strong

cN1 conventional imaging	➔ ADT + Abiraterone/Apalutamide + pelvic irradiation	STRONG
cN1 PSMA PET scanner	➔ ADT + Abiraterone/Apalutamide + pelvic irradiation	Less strong
cN0 2 risks factors	➔ ADT + Abiraterone + pelvic irradiation	Less strong
cN0 <2 risks factors	➔ ADT + pelvic irradiation	

Prostate cancer – Recurrence – Treatment

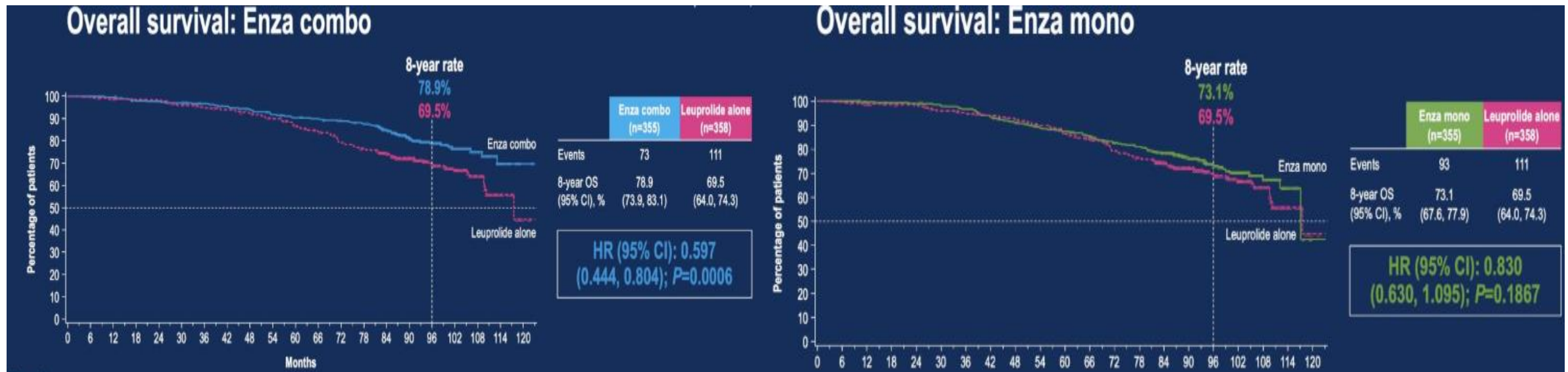


Improved Outcomes with Enzalutamide in Biochemically Recurrent Prostate Cancer

S.J. Freedland, M. de Almeida Luz, U. De Giorgi, M. Gleave, G.T. Gotto, C.M. Pieczonka, G.P. Haas, C.-S. Kim, M. Ramirez-Backhaus, A. Rannikko, J. Tarazi, S. Sridharan, J. Sugg, Y. Tang, R.F. Tutrone, Jr., B. Venugopal, A. Villers, H.H. Woo, F. Zohren, and N.D. Shore

Extended time to subsequent therapy

- Combo arm = Median time not reached at 8 years (HR 0.28; $p < 0.001$)
- Enza mono 84 vs 114 months (HR 0.45 ; $p < 0.001$)



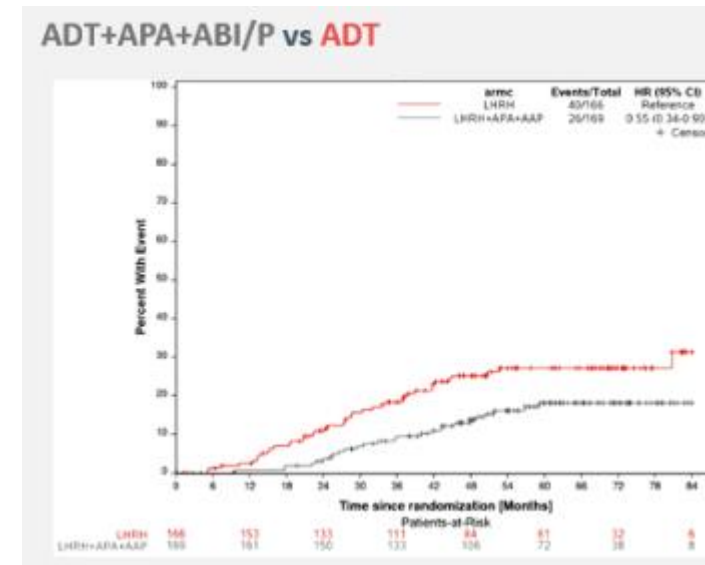
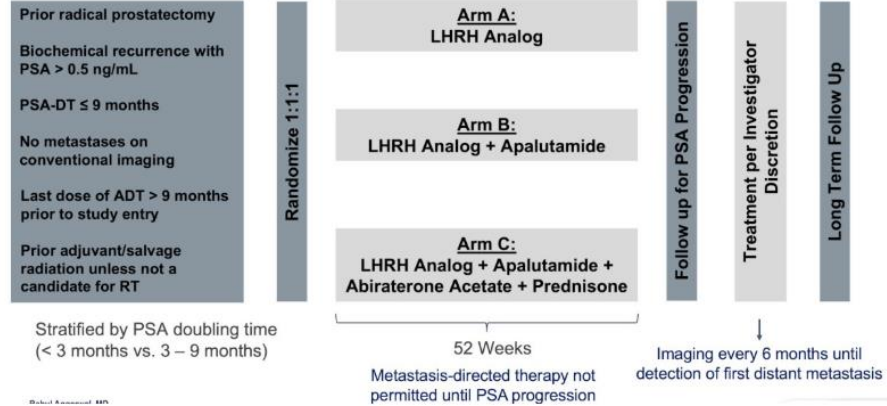
Prostate cancer – Recurrence – Treatment



PRESTO: A Phase III, Open-Label Study of Intensification of Androgen Blockade in Patients With High-Risk Biochemically Relapsed Castration-Sensitive Prostate Cancer (AFT-19)

Rahul Aggarwal¹, Glenn Heller², David W Hillman³, Han Xiao², Joel Picus⁴, Mary-Ellen Taplin⁵, Tanya Dorff⁶, Leonard Appleman⁷, Douglas Weckstein⁸, Akash Patnaik⁹, Alan Bryce¹⁰, Daniel Shevrin¹¹, James Mohler¹², Daniel Anderson¹³, Arpit Rao¹⁴, Scott Tagawa¹⁵, Alan Tan¹⁶, Susan Halabi¹⁷, Katharine Dooley³, Patrick O'Brien³, Ronald Chen¹⁸, Charles J Ryan¹⁹, Scott E Eggner⁹, Michael J Morris²; EORTC-55994 Study Group

Study Schema



Prostate cancer – Recurrence – Treatment



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Median PSA	5.2	1.8
Primary endpoint	MFS	PSA PFS Underpowered for MFS
First line treatment	PRT/RT	PRT
Stop treatment	At 36 w if PSA < 0.2 (90% of patients for median time of 20 months)	Every patients after 52 Weeks (median time of PSA PFS 24 months)
Imaging	Conventional	Conventional

Intensification si SOC for high risk BCR (PSA >1, PSADT <9 months, Normal Testosterone levels) but :

- PSMA pet positive patients? → *Intensification + SBRT = increased suspension treatment time; allowing monotherapy?*
- Low PSA, PSADT 6-9 months? → *Wait until PSMA PET positivity or higher PSA → Avoiding overtreatment?*
- Monotherapy ? → Cardiovascular patients? Older? Preservation of sexuality?

Prostate cancer – MHSPC – Oligometastatic



Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

Christopher C Parker, Nicholas D James, Christopher D Brawley, Noel W Clarke, Alex P Hoyle, Adnan Ali, Alastair W S Ritchie, Gerhardt Attard, Simon Chowdhury, William Cross, David P Dearnaley, Silke Gillesen, Clare Gilson, Robert J Jones, Ruth E Langley, Zafar I Malik, Malcolm D Mason, David Matheson, Robin Millman, J Martin Russell, George N Thalmann, Claire L Amos, Roberto Alonzi, Amit Bahl, Alison Birtle, Omar Din, Hassan Douis, Chinnamani Eswar, Joanna Gale, Melissa R Gannon, Sai Jonnada, Sara Khaksar, Jason F Lester, Joe M O'Sullivan, Omi A Parikh, Ian D Pedley, Delia M Pudney, Denise J Sheehan, Narayanan Nair Srihari, Anna T H Tran, Mahesh K B Parmar*, Matthew R Sydes*, on behalf of the Systemic Therapy for Advanced or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators†

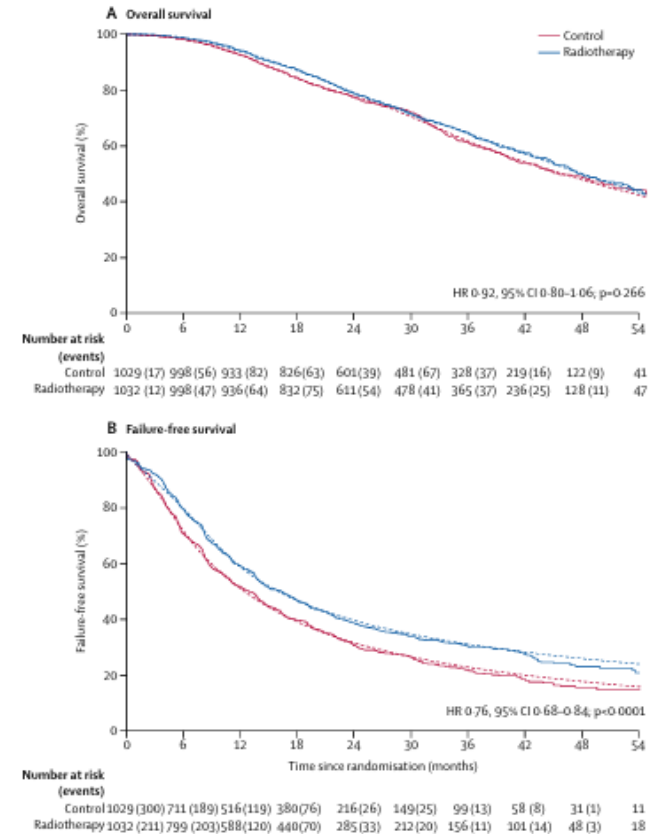
Overall survival

All patients	0.92 (0.80–1.06)	62%	65%	41.6	42.5	1.0 (–0.6 to 2.5)
Low metastatic burden	0.68 (0.52–0.90)	73%	81%	45.4	49.1	3.6 (1.0 to 6.2)
High metastatic burden	1.07 (0.90–1.28)	54%	53%	38.8	37.6	–1.2 (–3.5 to 1.1)

2018 SOC = ADT + prostate radiotherapy

but

- No IGRT
- 18% of docetaxel
- No PSMA

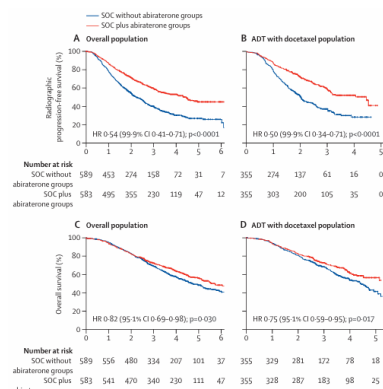


Prostate cancer – MHSPC – Oligometastatic



Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design

Karim Fizazi, Stéphanie Foulon, Joan Carles, Guilhem Roubaud, Ray McDermott, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacsó, Gwenaëlle Gravis, Fabio Calabro, Jean-François Berdah, Ali Hasbini, Marlon Silva, Antoine Thierry-Vuillemin, Igor Latorzeff, Loïc Mourey, Brigitte Laguerre, Sophie Abadie-Lacourtoisie, Etienne Martin, Claude El Kouri, Anne Escande, Alvar Rosello, Nicolas Magne, Friederike Schlurmann, Frank Priou, Marie-Eve Chand-Fouche, Salvador Villà Freixa, Muhammad Jamaluddin, Isabelle Rieger, Alberto Bossi, on behalf of the PEACE-1 investigators*



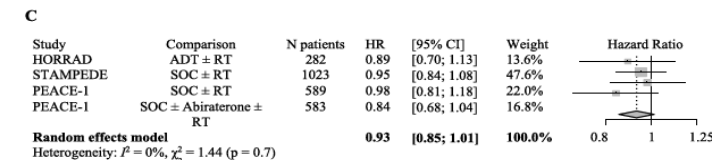
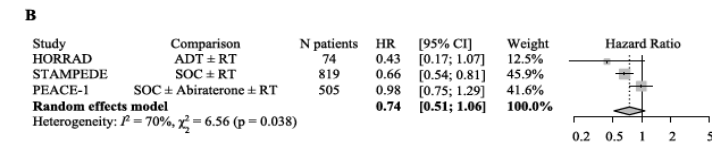
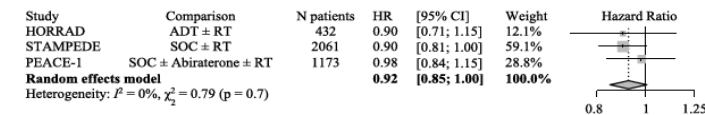
2022 SOC = ADT + Abiraterone +/- prostate radiotherapy

But

- No IGRT,
- +/- docetaxel
- No PSMA

Prostate radiotherapy in patients with metastatic hormone-sensitive prostate cancer: A systematic review and meta-analysis of randomised controlled trials

Navid Roessler^{a,b}, Marcin Miszczyk^{a,c,*}, Alessandro Dematteis^{a,d}, Fabio Zattoni^{e,f}, Tamás Fazekas^{a,g,h}, Filippo Carletti^e, Giuseppe Reitanoⁱ, Akihiro Matsukawa^{a,i}, Ahmed R. Alfarhan^{a,j}, Angelo Cormio^{a,k}, Abdulrahman S. Alqahtani^{a,l}, Timo F.W. Soeterik^m, Giulia Marvaso^{n,o}, Giorgio Gandaglia^p, Péter Nyirády^q, Paweł Rajwa^{a,q,r}, Łukasz Nyk^s, Peter Soo Palencia^t, Michael S. Leapman^u, Barbara A. Jereczek-Fossa^{a,o}, Shahrokh F. Shariat^{a,g,u,v,w,x,y}



2025 SOC = ???

But

- rPFS improved
- No OS in HORRAD and PEACE-1
- APCCC consensus

Prostate cancer – MHSPC – Oligometastatic



Best Systemic Therapy With or Without Radical Prostatectomy in the Management of Men With Oligometastatic Prostate Cancer: The RAMPP Randomised Controlled Trial

Markus Graefen^{a,†}, Fabian Falkenbach^{a,b,†,*}, Tobias Maurer^{a,c}, Lars Budäus^{a,c}, Derya Tilki^{a,c,k}, Pierre I. Karakiewicz^b, Markus Aly^d, Peter Wiklund^d, Klaus Brasso^e, Andreas Røder^e, Mads H. Poulsen^f, Martin Schostak^{g,h}, Christiane Görtzen^a, Anke Renter^a, Gunhild von Amsberg^{a,i}, Alexander Haese^a, Hans Heinzer^a, Georg Salomon^a, Thomas Steuber^{a,c}, Burkhard Beyer^j

Initial best systemic therapy, n (%)

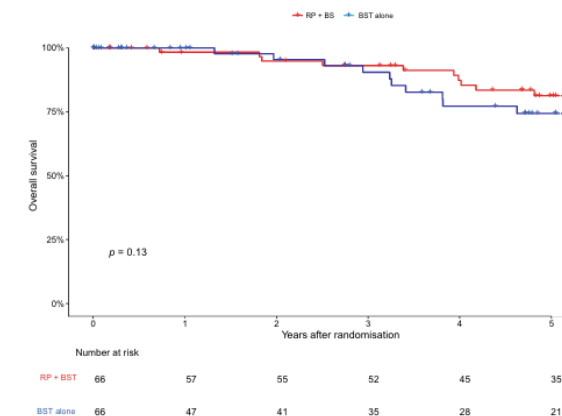
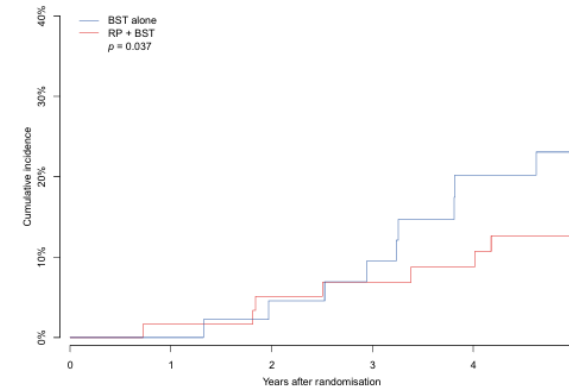
ADT alone	56 (85)	42 (64)
ADT + chemotherapy	3 (5)	7 (11)
ADT + androgen receptor pathway inhibitor	0 (0)	4 (6)
Started after 3 mo/data not available	7 (11)	13 (20)

Adverse events, n (%)

Serious adverse events, n (%)

Surgery-specific complications overall, n (%)

Clavien-Dindo grade <III	19 (29)	–
Clavien-Dindo grade ≥III	9 (14)	–
Bowel injury	1 (2)	–
Bleeding	3 (5)	–
Anastomotic leakage	3 (5)	–
Lymphocele	2 (3)	–
Thromboembolic/cardiac event	0	–
Impaired wound healing	0	–



Prostate cancer – MHSPC – Oligometastatic



	Patients with low-volume metastatic disease		Overall study population	
	Standard of care with or without abiraterone (n=200)	Standard of care plus radiotherapy with or without abiraterone (n=198)	Standard of care with or without abiraterone (n=458)	Standard of care plus radiotherapy with or without abiraterone (n=451)
Missing data	53/253 (20.9%)	54/252 (21.4%)	130/588 (22.1%)	133/584 (22.8%)
Total events	52 (26.0%)	22 (11.1%)	102 (22.3%)	55 (12.2%)
Urinary catheter	9 (4.5%)	7 (3.5%)	22 (4.8%)	23 (5.1%)
Suprapubic catheter	0	0	0	2 (0.4%)
Double J ureteric stent	13 (6.5%)	12 (6.1%)	28 (6.1%)	20 (4.4%)
Nephrostomy	2 (1.0%)	1 (0.5%)	6 (1.3%)	5 (1.1%)
Prostate radiotherapy	17 (8.5%)	0	27 (5.9%)	1 (0.2%)
Transurethral resection of the prostate	10 (5.0%)	1 (0.5%)	18 (3.9%)	2 (0.4%)
Radical prostatectomy	1 (0.5%)	1 (0.5%)	1 (0.2%)	2 (0.4%)

Diarrhoea

113 (18.7%)

14 (2.3%)

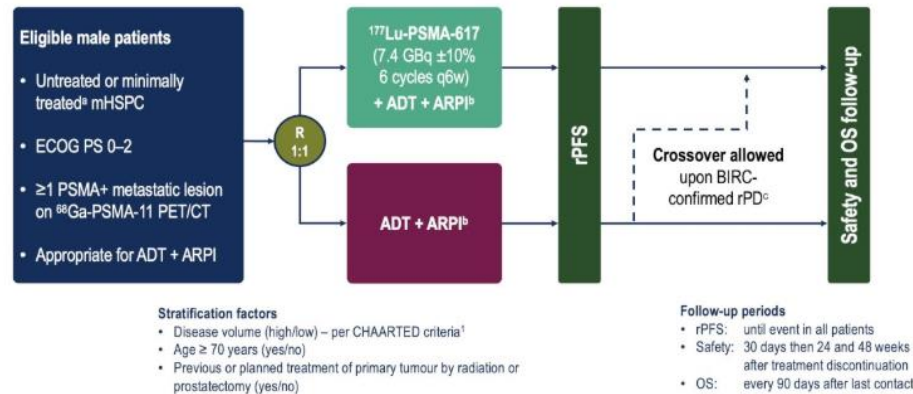
172 (30.7%)

1 (0.2%)

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of ≥7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by an increase in frequency and/or loose or watery bowel movements.					

- Improved PFS
- Improved urological adverse event?
- Not clear OS improvement
- Toxicity
- Future : Prostate + metastasis?
- Prostatectomy in this setting?

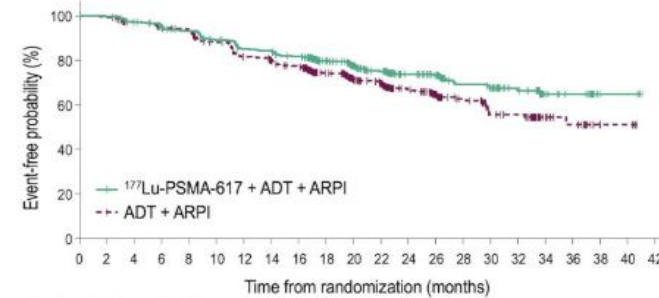
Prostate cancer – MHSPC – RLT



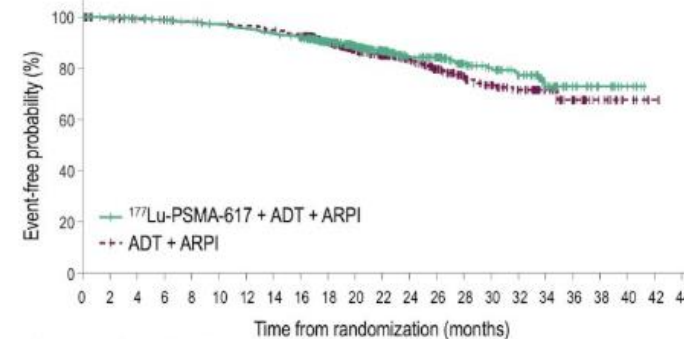
		HR (95% CI)	177Lu-PSMA-617 + ADT + ARPI	ADT + ARPI
All patients		0.72 (0.58, 0.90)	139/572 (24.3)	172/572 (30.1)
Tumour volume ^a	High	0.72 (0.56, 0.92)	116/389 (29.8)	144/390 (36.9)
	Low	0.73 (0.42, 1.27)	23/183 (12.6)	28/182 (15.4)
Age	< 70 years	0.68 (0.50, 0.92)	75/326 (23.0)	99/326 (30.4)
	≥ 70 years	0.78 (0.56, 1.10)	64/246 (26.0)	73/246 (29.7)
mHSPC ^b	De novo ^c	0.74 (0.54, 1.01)	74/298 (24.8)	89/274 (32.5)
	Recurrent	0.74 (0.53, 1.04)	60/249 (24.1)	77/274 (28.1)
Previous/planned treatment to primary tumour ^d	Yes	0.75 (0.46, 1.22)	31/156 (19.9)	35/155 (22.6)
	No	0.71 (0.55, 0.92)	108/416 (26.0)	137/417 (32.9)
Initial Gleason score	< 8	0.54 (0.33, 0.88)	29/152 (19.1)	39/134 (29.1)
	≥ 8	0.76 (0.58, 0.99)	99/389 (25.4)	122/406 (30.0)
Baseline LDH level	≤ 260 IU/L	0.69 (0.53, 0.89)	104/471 (22.1)	143/489 (29.2)
	> 260 IU/L	0.61 (0.30, 1.26)	20/37 (54.1)	18/33 (54.5)
Baseline PSA level	< Median	0.85 (0.62, 1.16)	73/279 (26.2)	83/287 (28.9)
	$\geq$ Median	0.60 (0.44, 0.83)	63/284 (22.2)	89/283 (31.4)
ECOG performance status	0	0.78 (0.59, 1.03)	92/397 (23.2)	107/407 (26.3)
	1-2	0.63 (0.43, 0.92)	47/175 (26.9)	64/162 (39.5)

Favours 177Lu-PSMA-617 + ADT + ARPI ← HR (95% CI)

rPFS by BIRC – the primary endpoint was met



	177Lu-PSMA-617 + ADT + ARPI (N = 572)	ADT + ARPI (N = 572)
Events – n (%)	139 (24.3)	172 (30.1)
rPD	112 (19.6)	152 (26.6)
Death without rPD	27 (4.7)	20 (3.5)
HR (95% CI)	0.72 (0.58, 0.90)	
p value	0.002 ^a	
Median rPFS (95% CI) – months	NR (NE, NE)	NR (29.7, NE)



	177Lu-PSMA-617 + ADT + ARPI (N = 572)	ADT + ARPI (N = 572)
Events – n (%)	85 (14.9)	99 (17.3)
Censored – n (%)	487 (85.1)	473 (82.7)
HR (95% CI)	0.84 (0.63, 1.13)	
p value	0.125 ^a	
Median OS (95% CI) – months	NR (NE, NE)	NR (NE, NE)

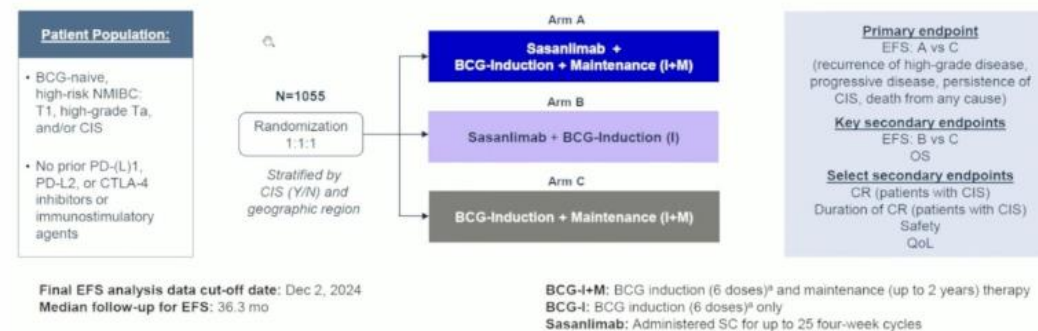
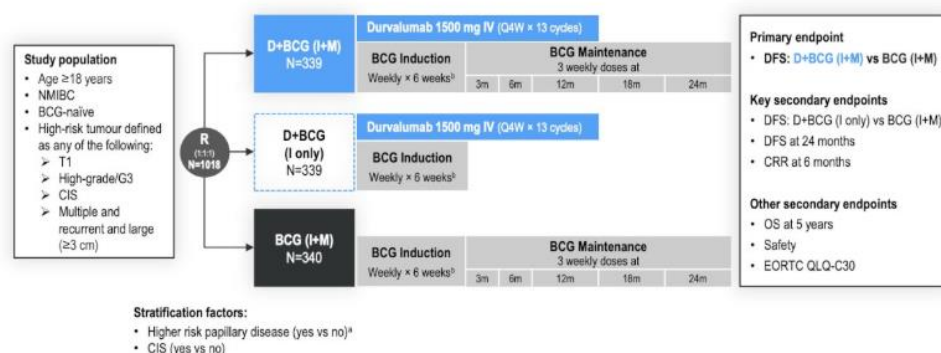
- Need for clearer signal or OS → not for all commers
- Need for reliable predictive marker



Annual review in uro oncology

- Prostate cancer
- **Bladder cancer NMIBC - MIBC**
- Renal cancer

Bladder cancer – NMIBC – High risk



Histological classification, n (%)

	Arm A	Arm B	Arm C
UC	339 (96.3)	346 (98.3)	332 (94.6)
UC with squamous differentiation	6 (1.7)	2 (0.6)	8 (2.3)
UC with glandular differentiation	2 (0.6)	4 (1.1)	3 (0.9)
UC with variant histology	4 (1.1)	0	6 (1.7)
Other	1 (0.3)	0	2 (0.6)

Worst T stage, n (%)

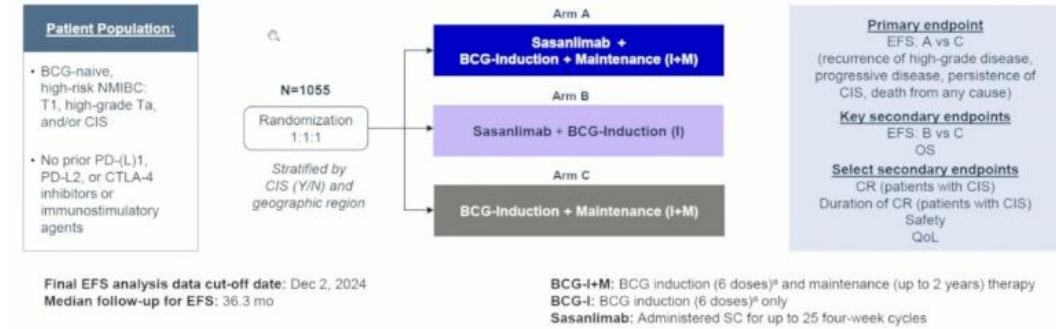
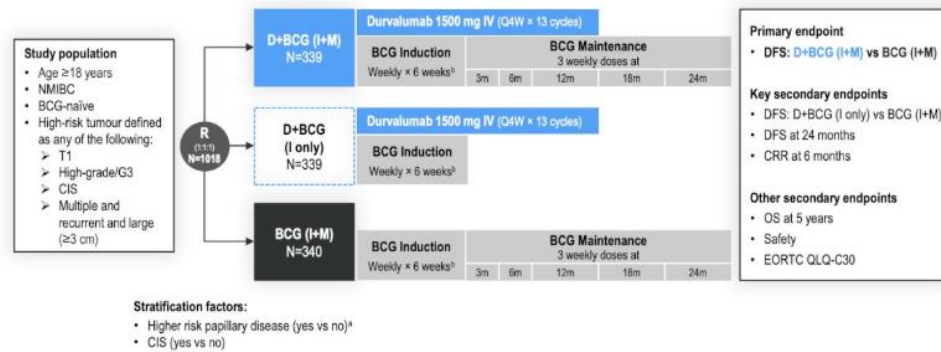
	Arm A	Arm B	Arm C
CIS	52 (14.8)	42 (11.9)	50 (14.2)
Ta	96 (27.3)	136 (38.6)	107 (30.5)
T1	204 (58.0)	174 (49.4)	194 (55.3)

Smoking history, n (%)

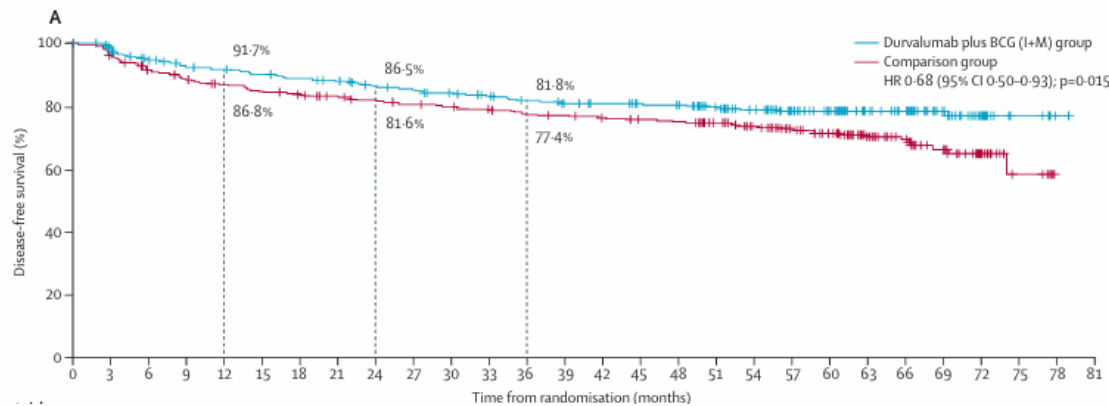
	Arm A	Arm B	Arm C
Never smoker	127 (36.1)	108 (30.7)	126 (35.9)
Current smoker	71 (20.2)	70 (19.9)	54 (15.4)
Former smoker	154 (43.8)	174 (49.4)	171 (48.7)

Smoking status	Arm A	Arm B	Arm C
Current	62 (18%)	60 (18%)	63 (19%)
Former	175 (52%)	182 (54%)	173 (51%)
Never	102 (30%)	97 (29%)	104 (31%)
Carcinoma in situ*			
Yes	125 (37%)	125 (37%)	125 (37%)
No	214 (63%)	214 (63%)	215 (63%)
Papillary disease only			
Yes	217 (64%)	222 (65%)	220 (65%)
No	122 (36%)	117 (35%)	120 (35%)
T1 disease†	195 (58%)	191 (56%)	211 (62%)
Ta disease†	112 (33%)	114 (34%)	99 (29%)

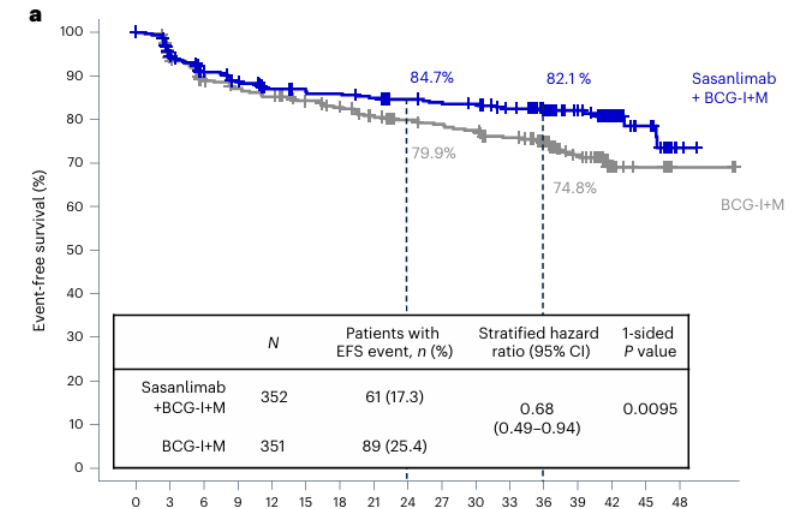
Bladder cancer – NMIBC – High risk



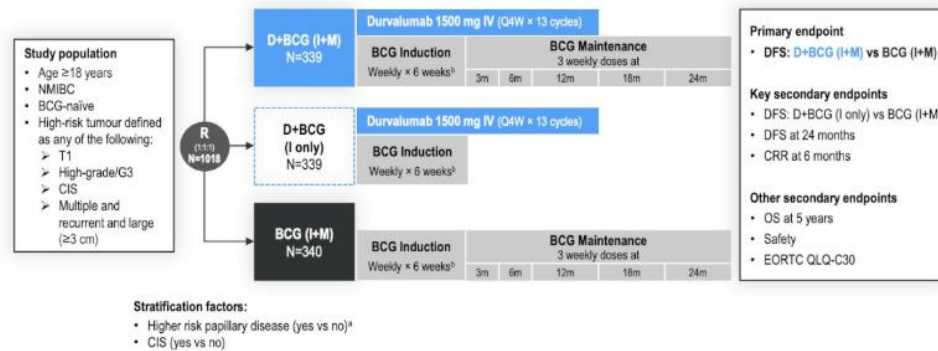
DFS : HG recurrence, cis persistence, progression or death



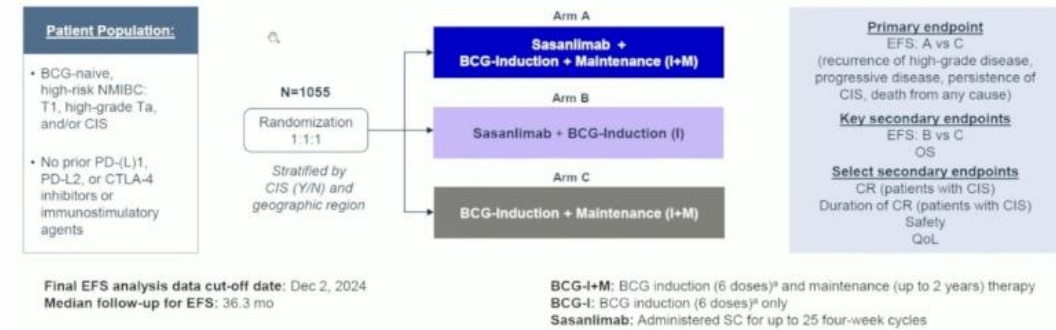
EFS : HG rec, T1, progression or metastasis



Bladder cancer – NMIBC – High risk

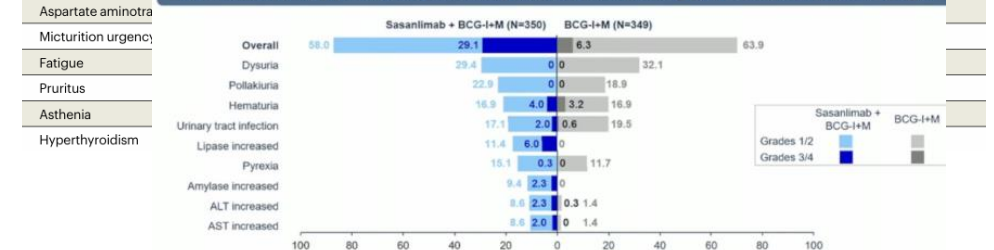


	Durvalumab plus BCG induction and maintenance group (n=336)	Durvalumab plus BCG induction group (n=337)	Comparison group (n=339)
Adverse events of any cause			
Any grade	325 (97%)	322 (96%)	307 (91%)
Maximum grade 3 or 4*	113 (34%)	90 (27%)	56 (17%)
Serious adverse event	108 (32%)	82 (24%)	63 (19%)
Leading to death	0 (2%)	4 (1%)	4 (1%)
Discontinuation of study treatment	105 (31%)	65 (19%)	68 (20%)
Discontinuation of durvalumab	60 (18%)	54 (16%)	–
Discontinuation of BCG	70 (21%)	22 (7%)	68 (20%)
Treatment-related adverse events†			
Any grade	298 (89%)	269 (80%)	245 (72%)
Maximum grade 3 or 4*	71 (21%)	52 (15%)	13 (4%)
Serious adverse event	45 (13%)	38 (11%)	13 (4%)
Leading to death	0	0	0
Discontinuation of study treatment	92 (27%)	54 (16%)	56 (17%)
Discontinuation of study treatment, related to durvalumab	54 (16%)	44 (13%)	1 (<1%)‡
Discontinuation of study treatment, related to BCG	55 (16%)	15 (4%)	55 (16%)
Discontinuation of durvalumab, related to durvalumab	50 (15%)	42 (12%)	0
Discontinuation of BCG, related to BCG	51 (15%)	14 (4%)	55 (16%)

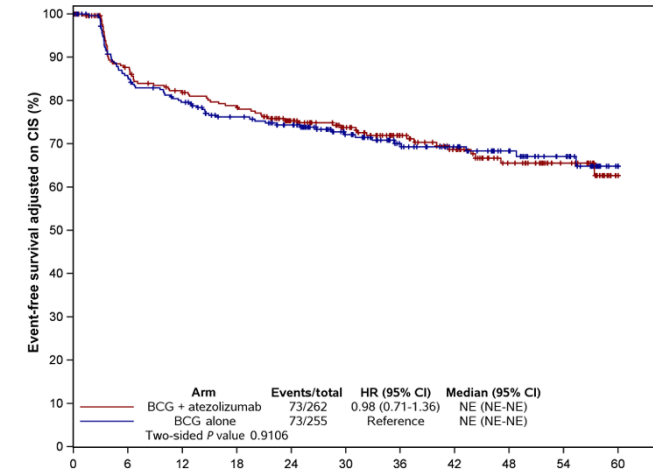
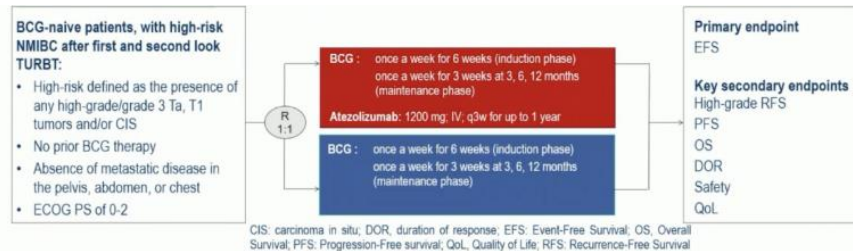


	Sasanlimab + BCG-I+M (N=350)		Sasanlimab + BCG-I (N=348)		BCG-I+M (N=349)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Patients with any event, n (%)	305 (87.1)	102 (29.1)	275 (79.0)	76 (21.8)	245 (70.2)	22 (6.3)
Dysuria	103 (29.4)	0	46 (13.2)	0	112 (32.1)	0
Pollakiuria	80 (22.9)	0	27 (7.8)	0	66 (18.9)	0
Hematuria	73 (20.9)	14 (4.0)	31 (8.9)	5 (1.4)	70 (20.1)	11 (3.2)
Urinary tract infection	67 (19.1)	7 (2.0)	28 (8.0)	2 (0.6)	70 (20.1)	2 (0.6)
Lipase increased	61 (17.4)	21 (6.0)	42 (12.1)	5 (1.4)	0	0
Pyrexia	54 (15.4)	1 (0.3)	35 (10.1)	0	41 (11.7)	0
Hypothyroidism	50 (14.3)	2 (0.6)	44 (12.6)	0	0	0
Amylase increased	41 (11.7)	8 (2.3)	33 (9.5)	3 (0.9)	0	0
Alanine aminotransferase increased	38 (10.9)	8 (2.3)	24 (6.9)	2 (0.6)	6 (1.7)	1 (0.3)

The observed safety profile was consistent with the known safety profile for each individual agent



Bladder cancer – NMIBC – High risk



	Total (N = 517)	BCG (N = 255)	BCG + atezolizumab (N = 262)
Age (years), mean (range)	67.4 (29.0-91.0)	67.0 (29.0-91.0)	67.7 (36.0-88.0)
Sex, n (%)			
Male	442 (85.5)	221 (86.7)	221 (84.4)
Female	75 (14.5)	34 (13.3)	41 (15.6)
ECOG PS, n (%) ^a			
0	453 (88.6)	227 (90.1)	226 (87.3)
1	54 (10.6)	22 (8.7)	32 (12.4)
2	4 (0.8)	3 (1.2)	1 (0.4)
High-risk feature, n (%) ^{b,c}			
Ta high-grade/grade 3	110 (21.3)	57 (22.4)	53 (20.2)
T1	204 (39.5)	102 (40.0)	102 (38.9)
CIS	202 (39.1)	96 (37.6)	106 (40.5)
Smoking habits, n (%) ^d			
Nonconsumer	98 (19.0)	59 (23.2)	39 (14.9)
Former consumer	330 (64.0)	157 (61.8)	173 (66.0)
Current consumer	88 (17.1)	38 (15.0)	50 (19.1)
Prior bladder instillations, n (%)			
No	497 (96.1)	250 (98.0)	247 (94.3)
Yes	20 (3.9)	5 (2.0)	15 (5.7)

Events, n (%)	BCG (N = 250)	BCG + atezolizumab (N = 255)
Any AEs	235 (94.0)	252 (98.8)
Grade ≥3 AEs	59 (23.6)	102 (40.0)
Serious AEs	53 (21.2)	97 (38.0)
Any TRAEs	189 (75.6)	240 (94.1)
Grade ≥3 TRAEs	22 (8.8)	58 (22.7)
Serious TRAEs	21 (8.4)	60 (23.5)
TRAEs leading to dose interruption	19 (7.6)	47 (18.4)
TRAEs leading to withdrawal	22 (8.8)	73 (28.6)
BCG withdrawal only	22 (8.8)	32 (12.5)
Atezolizumab withdrawal only	0 (0.0)	41 (16.1)
BCG + atezolizumab	0 (0.0)	8 (3.1)

EFS : **LG**-HG recurrence, progression, death

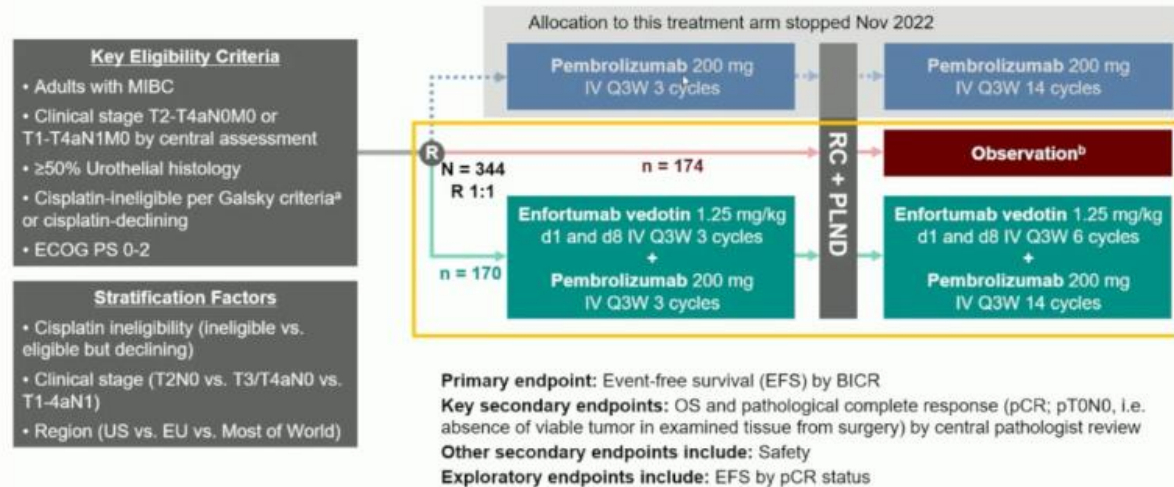
Bladder cancer – NMIBC – High risk



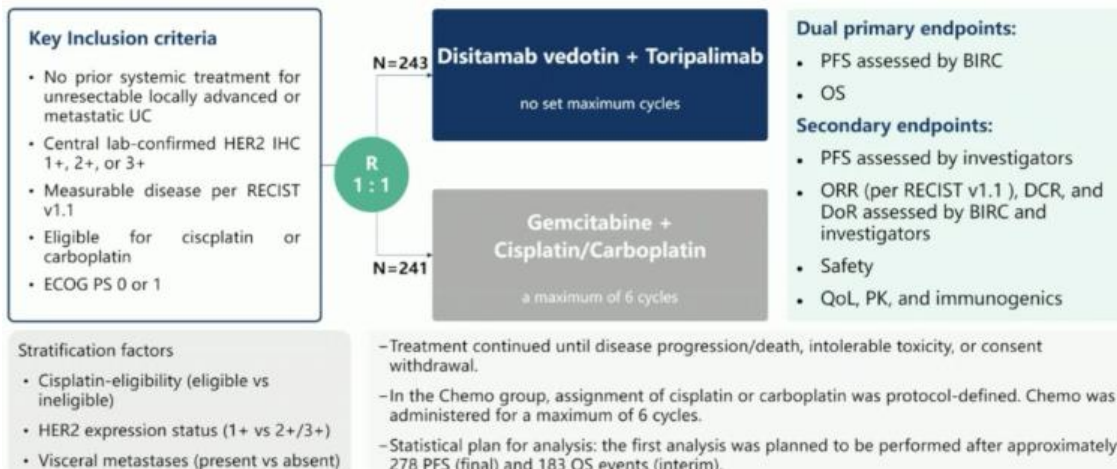
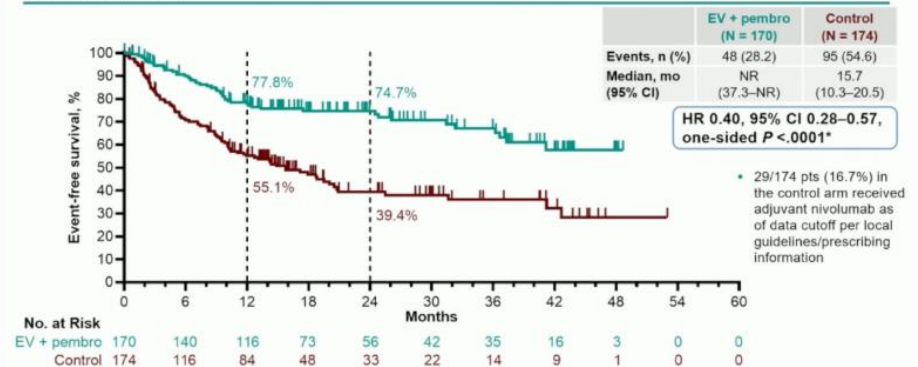
Systemic treatment standard of care for localized disease?

- AE's
- Logistic
- Risk of overtreatment
- Need for prognostic/predictive marker
 - Ct/utDNA?
 - EAU very high risk population?

Bladder cancer – MIBC – Neoadj/periop

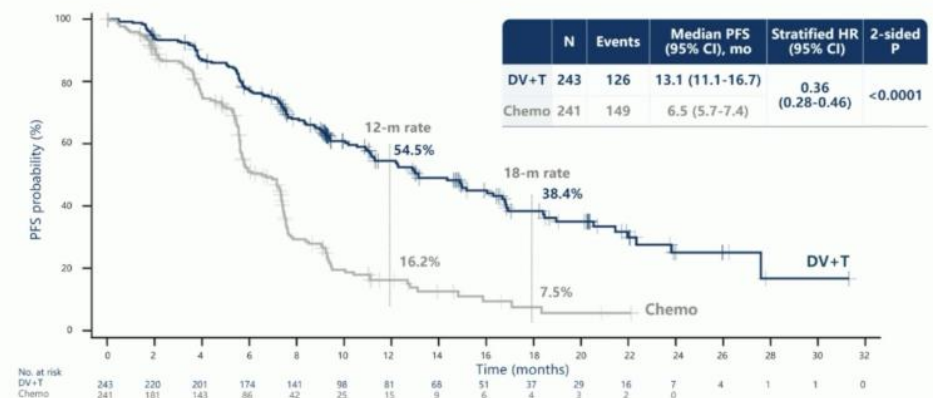


Primary Endpoint: EFS^a by BICR ITT Population



Progression-free Survival according to BIRC

Clinically meaningful reduction in the risk of progression or death by 64% with DV+T

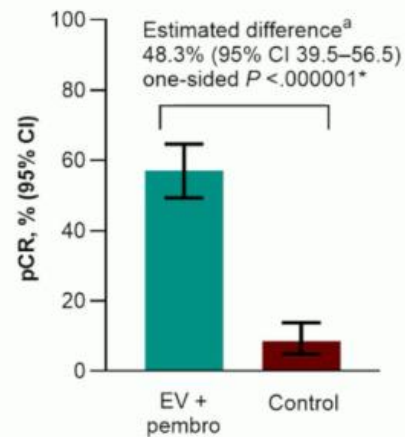


Bladder cancer – MIBC – Neoadj/periop



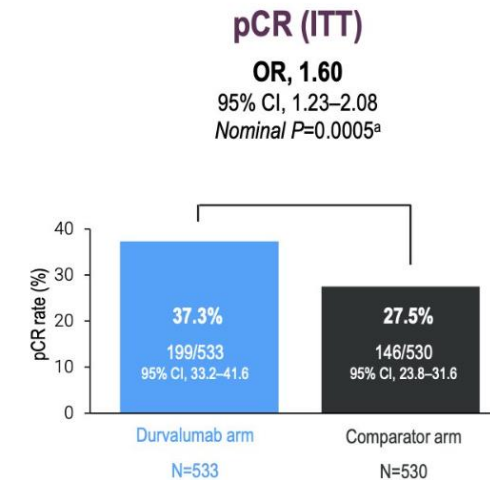
	BLASST-1 NCT03294304	AURA NCT03674424	NCT02989584	HCRN GU 14-188 NCT02365766	HCRN GU 1657 NCT03558087	NIAGARA NCT03732677	VESPER NCT01812369	COXEN NCT02177695
Year	2020	2021	2022	2023	2023	2024	2021	2021
Design	Phase II single arm	Phase II randomized double cohort	Phase II single arm	Phase II single arm double cohort	Phase II single arm	Phase III	Phase III	Phase II randomized
Treatment	GC 4x + nivolumab	GC 4x + avelumab MVAC 4x + avelumab	GC 4x + atezolizumab	GC 4x + pembrolizumab	GC 4x + nivolumab	GC 4x + durvalumab	MVAC 6x GC 4x	MVAC 4x GC 4x
Cisplatin eligibility	50ml/min/1.73 m ²	60ml/min/1.73m ²	60ml/min/1.73 m ²	60ml/min/1.73m ²	60ml/min/1.73m ²	>40ml/min/1.73m ²	50ml/min/1.73m ²	60ml/min/1.73m ²
n	41	28	28	39	42	76	248	245
Tumour char.								
cT2%	90	?	?	79.5	42.9	57	40.3	90
>cT2%	10	cT4 7%	cT4 7%	20.5	57.1	43	59.7	9.6
ypT								
ypT0%	49	50	54	41	41	cCR*43%	37.3	42
<ypT2%	65.8	57	64	28.1	54	No 51%	49.7	36
						0	63	49
						7%*	55	48

	ABACUS NCT02662309	PURE-01 NCT02736266	AURA NCT03674424	HCRN GU 14-188 NCT02365766	EV 103 NCT03288545	NURE-Combo NCT04876313	SUNRISE 4 NCT04919512	SURE 01 NCT05226117	RC 48 C017 NCT05297552	SURE 02 NCT05535218
Year	2022	2022	2022	2023	2023	2024	2024	2024	2024	2025
Design	Phase II single arm	Phase II single arm	Phase II randomized double cohort	Phase II single arm double cohort	Phase II single arm	Phase II single arm	Phase 2 randomized	Phase 2 single arm	Phase 2 single arm	Phase 2 single arm
Treatment	Atezolizumab X2	Pembrolizumab x3	Avelumab x4	Pembrolizumab x5	Enfortumab Vedotin x3	Nivolumab + Paclitaxel x4	TAR 200 TAR 200 + Cetrelumab	Sacituzumab goxitecan x4	Disitamab vedotin + toripalimab x 6	Sacituzumab goxitecan + Pembrolizumab X4
Cisplatin eligibility	Ineligible or refusing	Eligible 92%	<60ml/min/1.73m ²	<60ml/min/1.73m ²	Ineligible	<60ml/min/1.73m ² or refusing	Ineligible or refusing	Ineligible or refusing	/	<60ml/min/1.73m ² or refusing
n	95	155	28	31	22	31	53	31	25	29****
Tumour char.										
cT2%	74	48.4	?	40	68.2	45.2	75**	83**	72	38.6
>cT2%	26	51.6	?	60	31.8	57.8*	25**	17**	28	61.4*****
ypT										
ypT0%	31	36.8	18	41	36.4	38	42	23	44***	62.1 (18/29)
<ypT2%	39	53.6	21	53	50	72	60	35	48	75.9 (22/29)
										/



	EV + pembro (N = 170)	Control (N = 174)
pCR, n	97	15
pCR rate, % (95% CI)	57.1 (49.3–64.6)	8.6 (4.9–13.8)

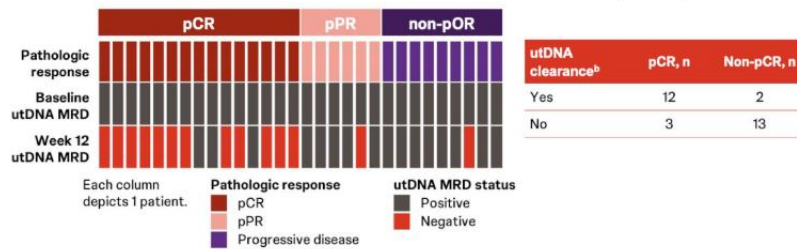
- pCR: absence of viable tumor (pT0N0) in examined tissue from RC + PLND
- Pts who did not undergo surgery, including those with clinical complete response after neoadjuvant therapy, were considered non-responders



Bladder cancer – MIBC – Neoadj/periop

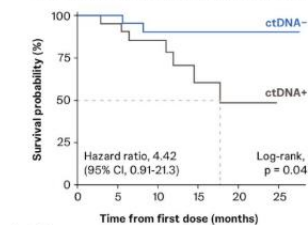


utDNA clearance at Week 12^{a,b} and pathologic response in patients that were utDNA+ at baseline and had matched week 12 utDNA results (N = 30)



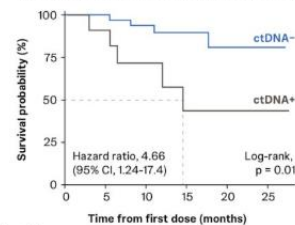
ctDNA negative status at baseline and week 12 was associated with longer recurrence-free survival:

RFS by baseline ctDNA MRD status^a (N = 44)

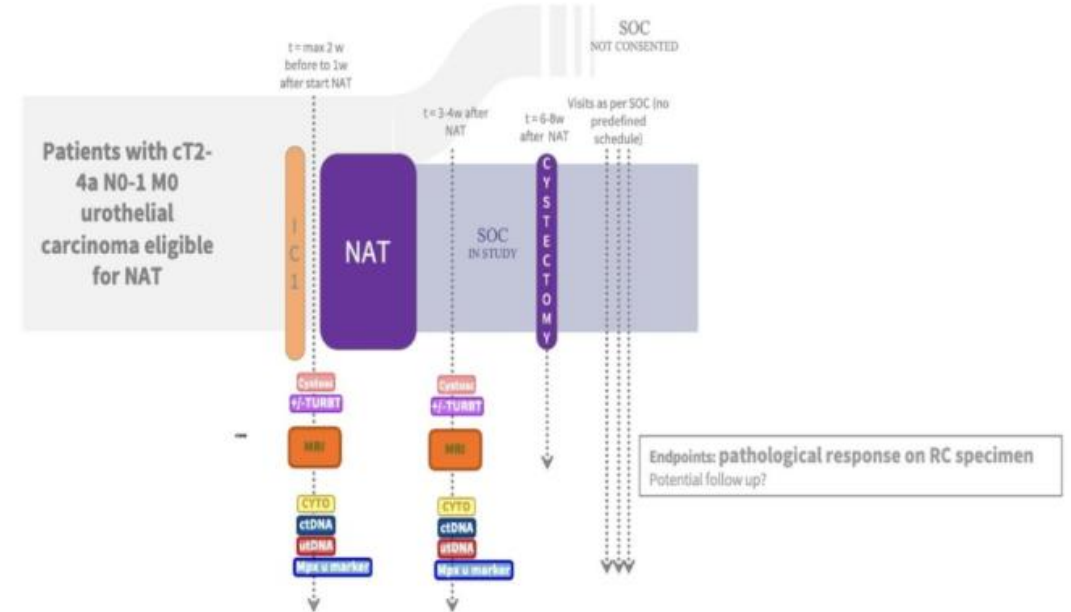


No. at risk:	22	22	17	11	5	2
ctDNA-	22	20	14	6	4	0
ctDNA+						

RFS by Week 12 ctDNA MRD status^a (N = 44)

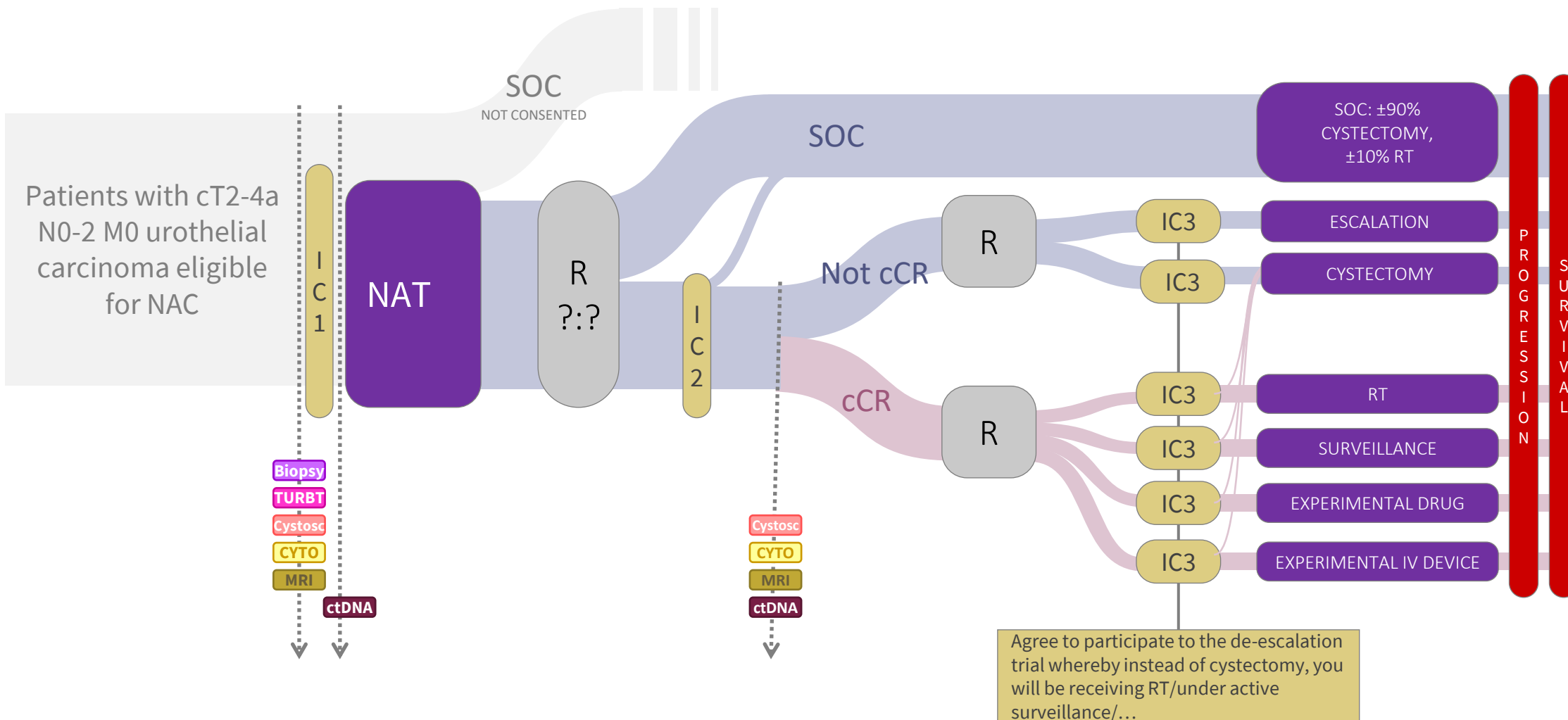


No. at risk:	32	32	25	14	7	1
ctDNA-	32	30	25	14	7	1
ctDNA+						



Stage 2: TWiCs, conditional on stage 1

De-escalation and Escalation

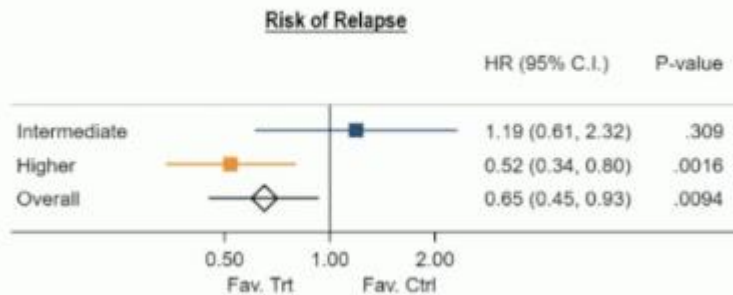
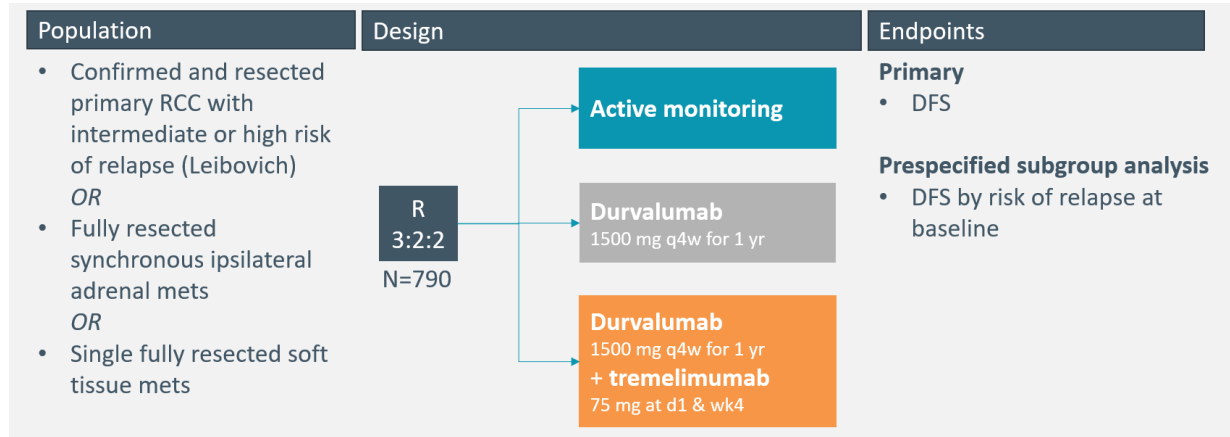




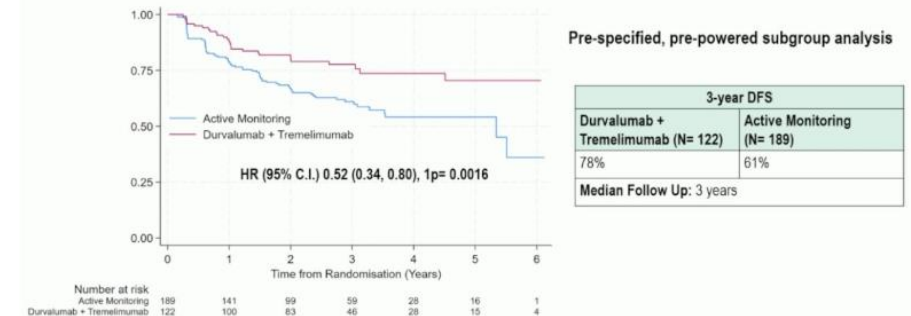
Annual review in uro oncology

- Prostate cancer
- Bladder cancer
- **Renal cancer**

Bladder cancer – RCC - Adjuvant



RAMPART DFS in the Higher Risk Population – ITT



RAMPART DFS in the Intermediate Risk Population - ITT

