

What's new this year in uro-oncology ?

Medical oncology



BMUC

UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

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

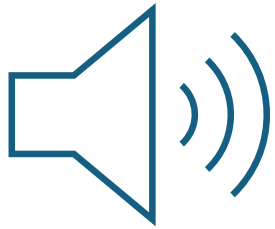
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11 DEC 2025

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Conflicts of interest



Speaker's fee

Astellas Pharma BV

BMS

Janssen

Servier



Advisory boards

Astellas Pharma BV

Pfizer

MSD

Servier



Prostate cancer

Prognostic and predictive markers



ADT + ARPI = backbone for M1 and very high-risk M0 patients



Prognostic marker

Who need treatment intensification ?



Predictive marker

Which treatment for intensification ?

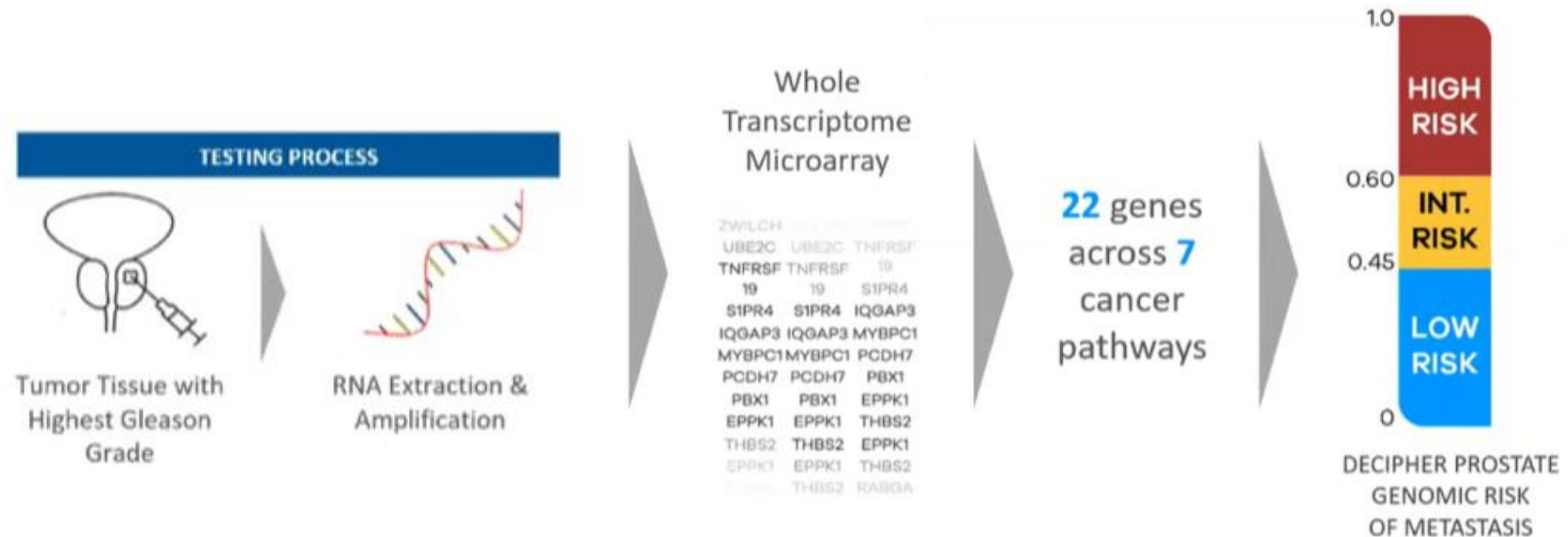
Treatment intensification

ADT + AAP @ 84 months	STAMPEDE high- risk M0	M1 low volume*	M1 high volume
Alive	79%	63%	34%
No relapse	72%	52%	29%
Deaths attributed to prostate cancer	50%	70%	82%



And **de-escalation** for low-risk patients : DE-ESCALATE EORTC phase III trial !

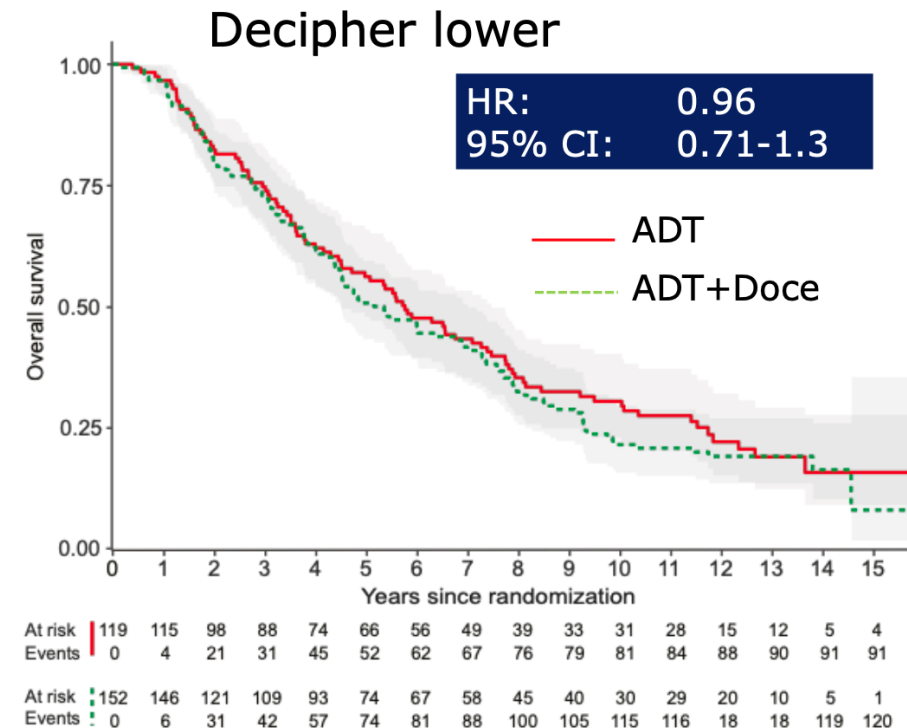
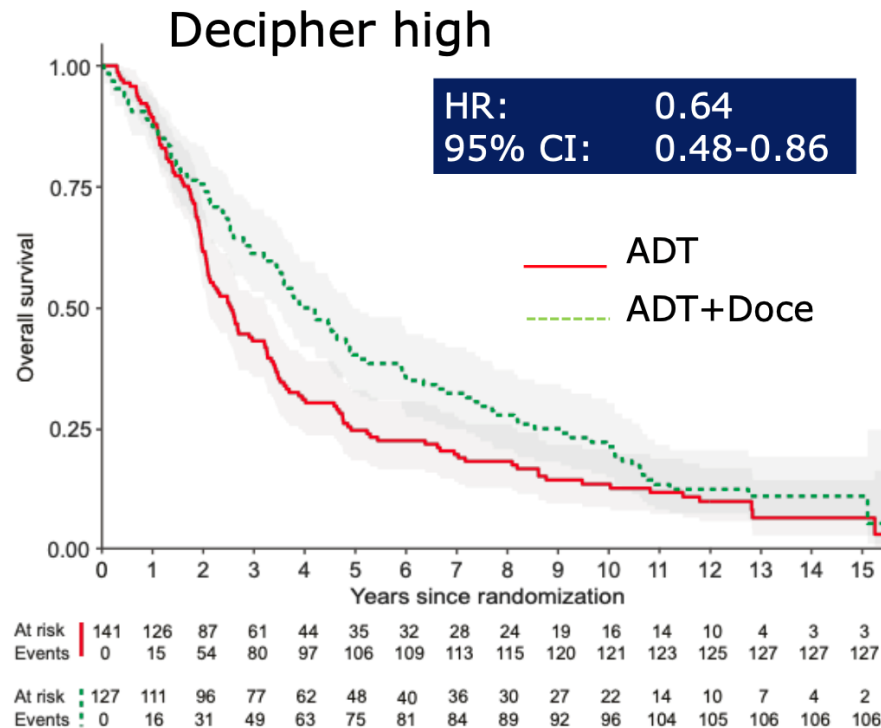
Decipher score



Localized disease : risk of metastasis and of prostate cancer mortality

Metastatic disease : risk of prostate cancer mortality

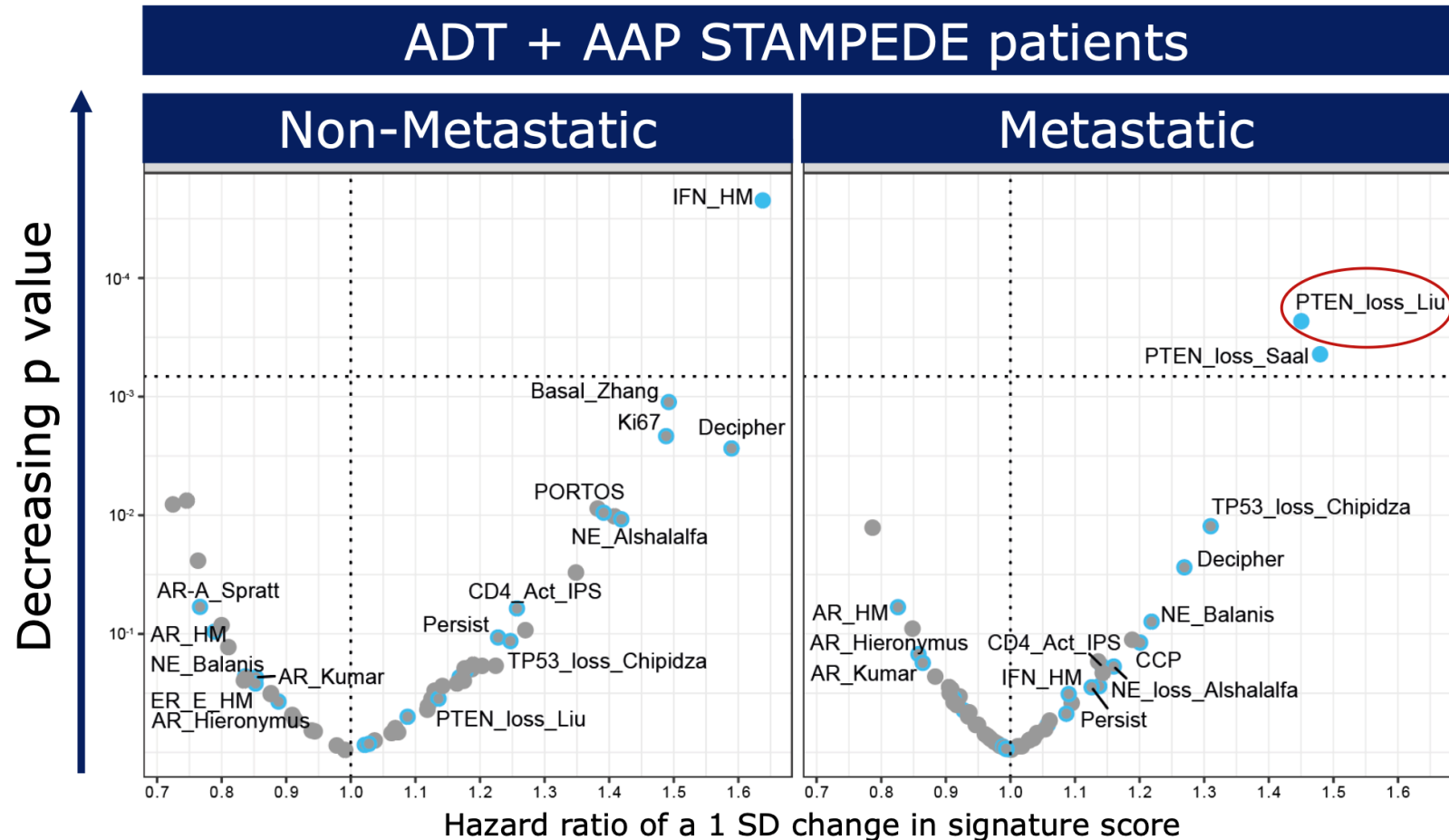
Decipher is predictive for docetaxel



High Decipher score identifies metastatic patients most likely to benefit from docetaxel
Biomarker-treatment interaction effect p value= 0.039*

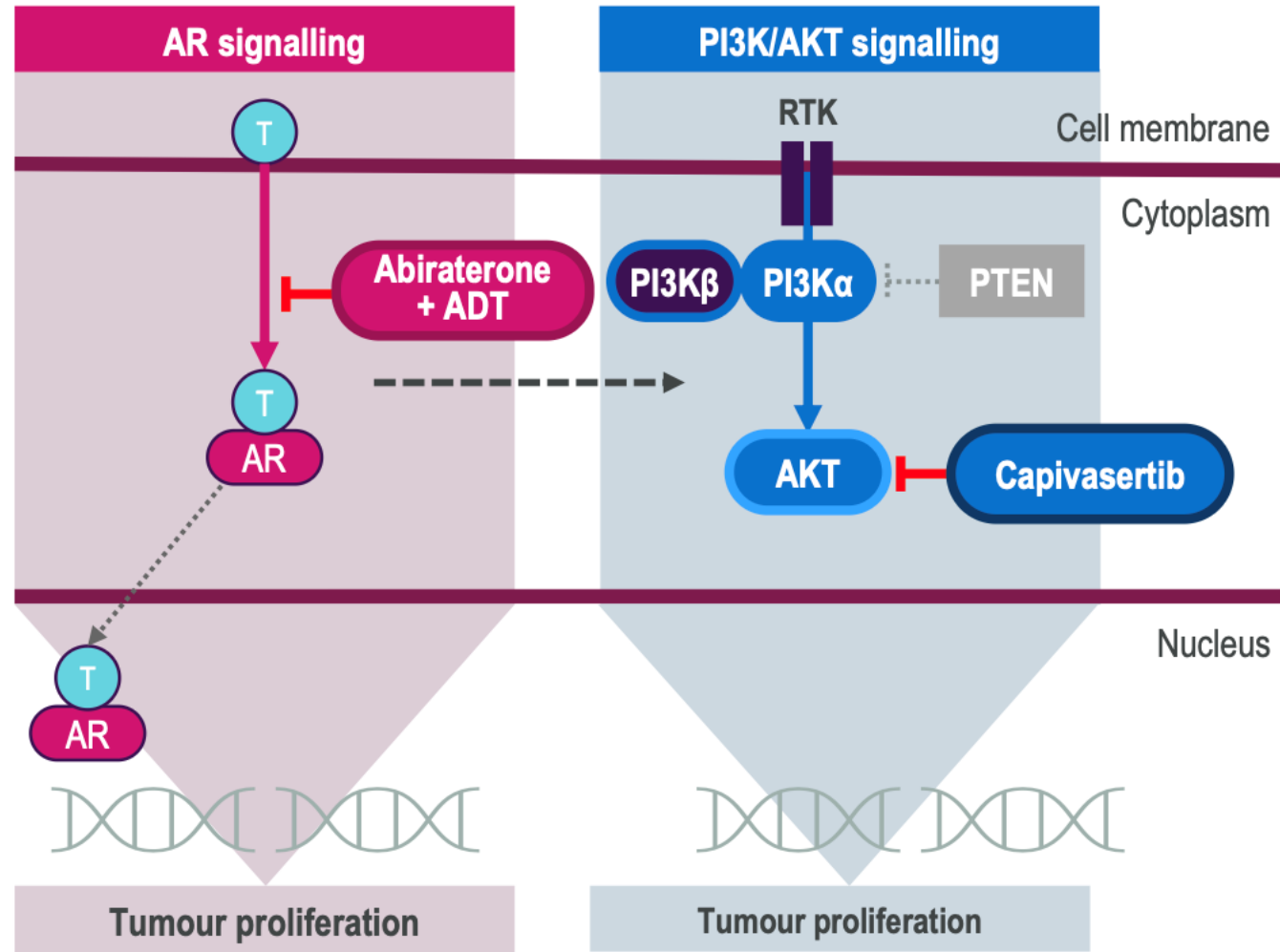
with Veracyte

Decipher is predictive for ADT + ARPI

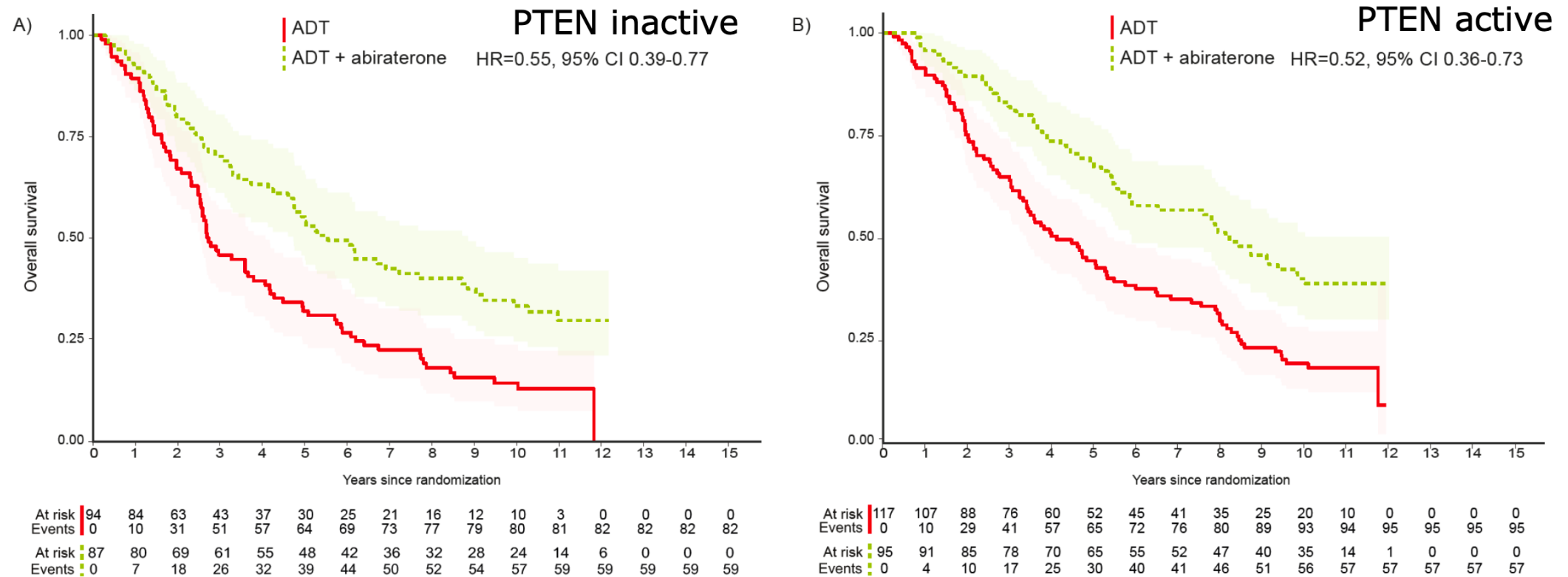


N=375

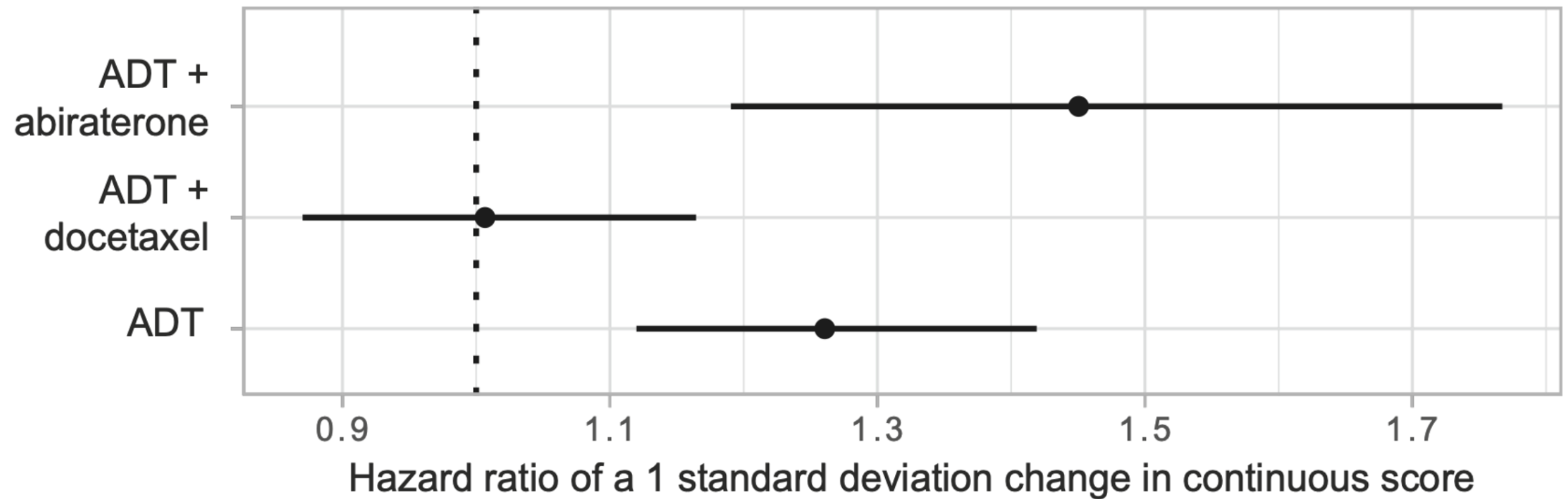
PTEN deficient cell



PTEN inactivation is prognostic

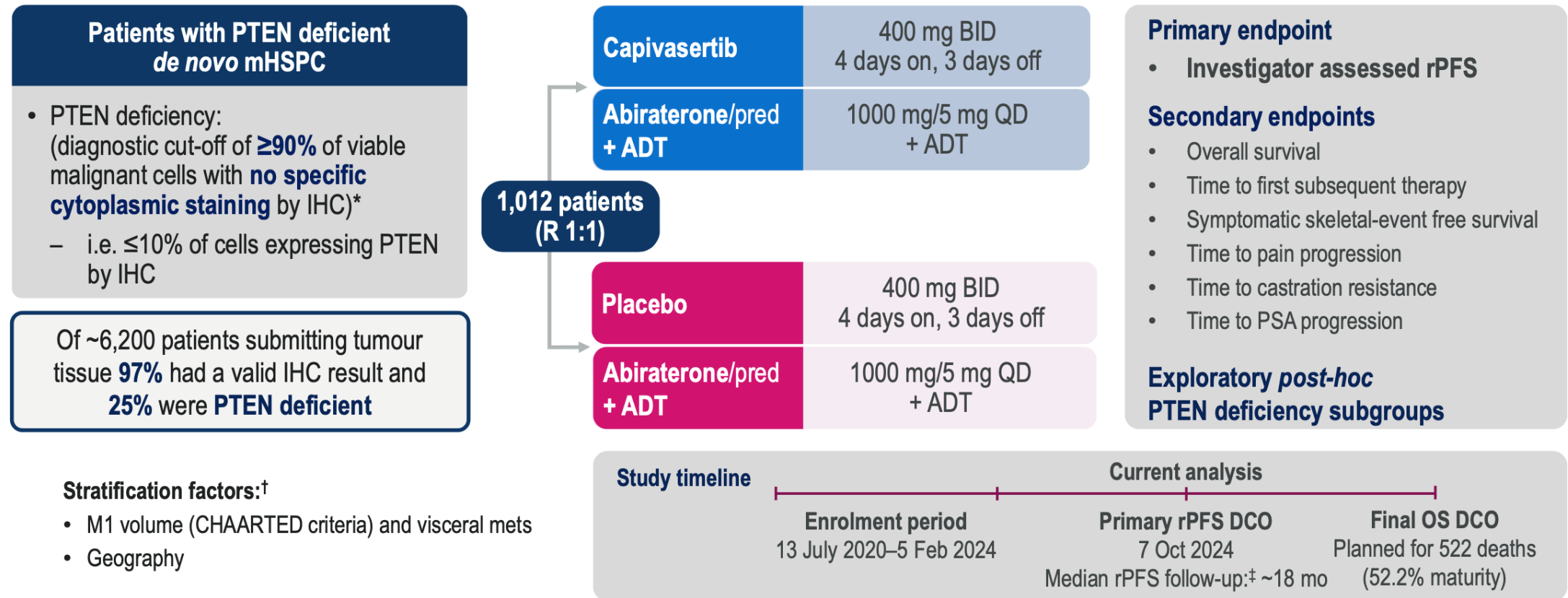


PTEN inactivation is predictive

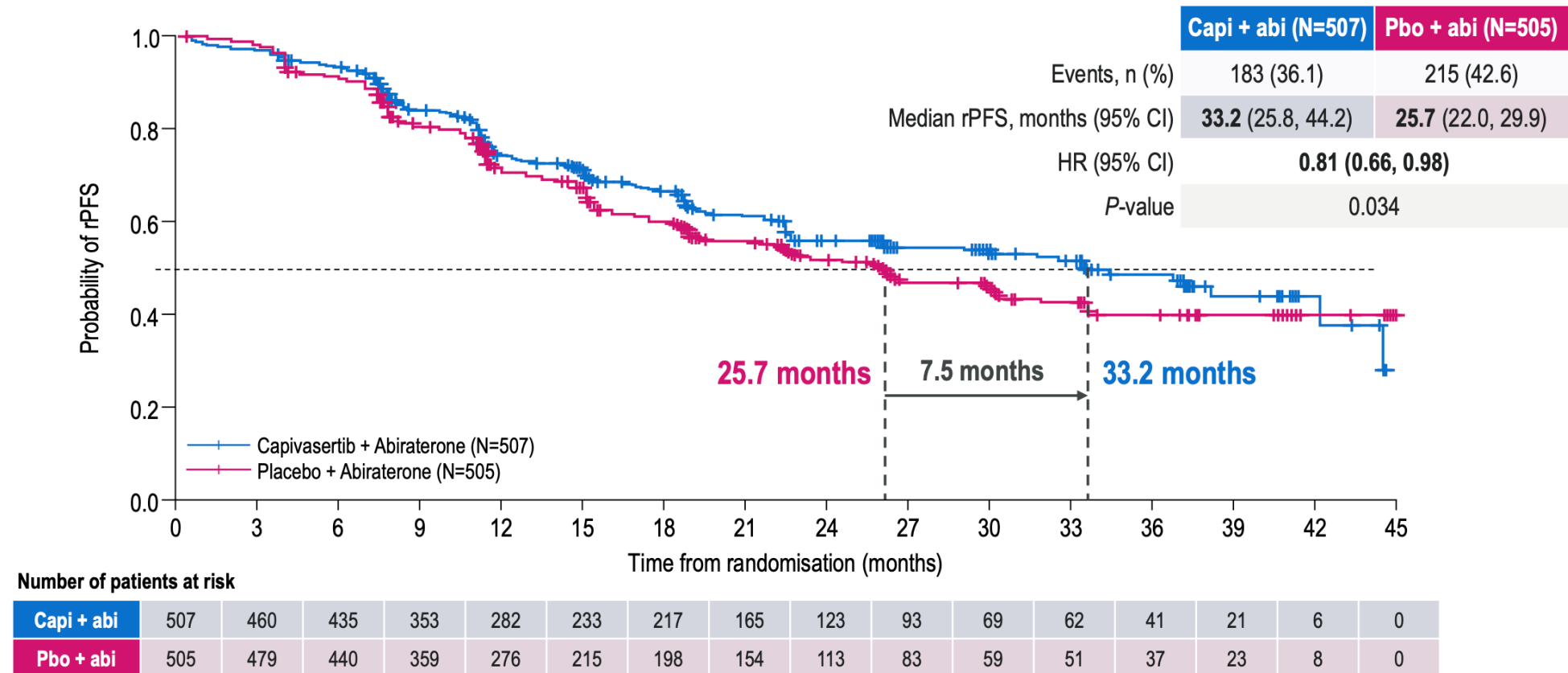


CAPItello-281 trial

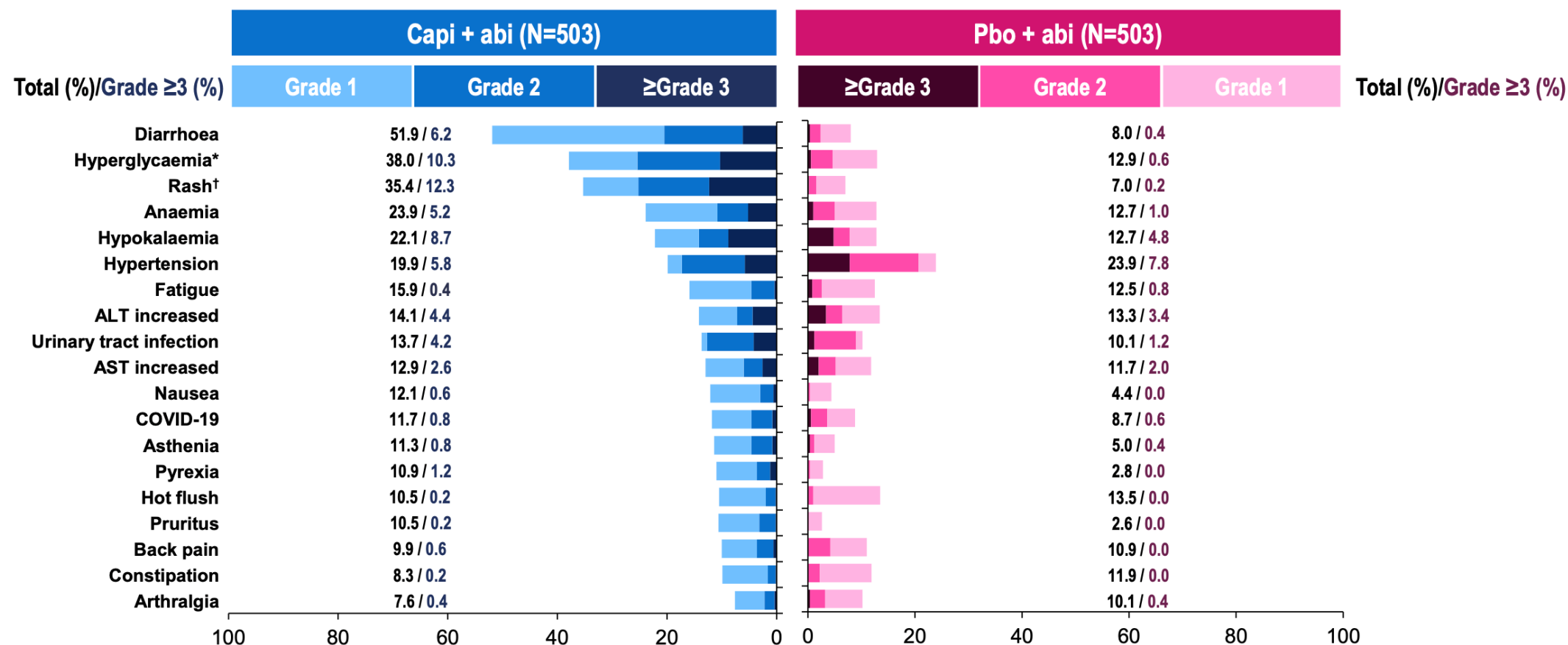
A global, multicentre, randomized, double-blind, Phase 3 study



Investigator-assessed rPFS



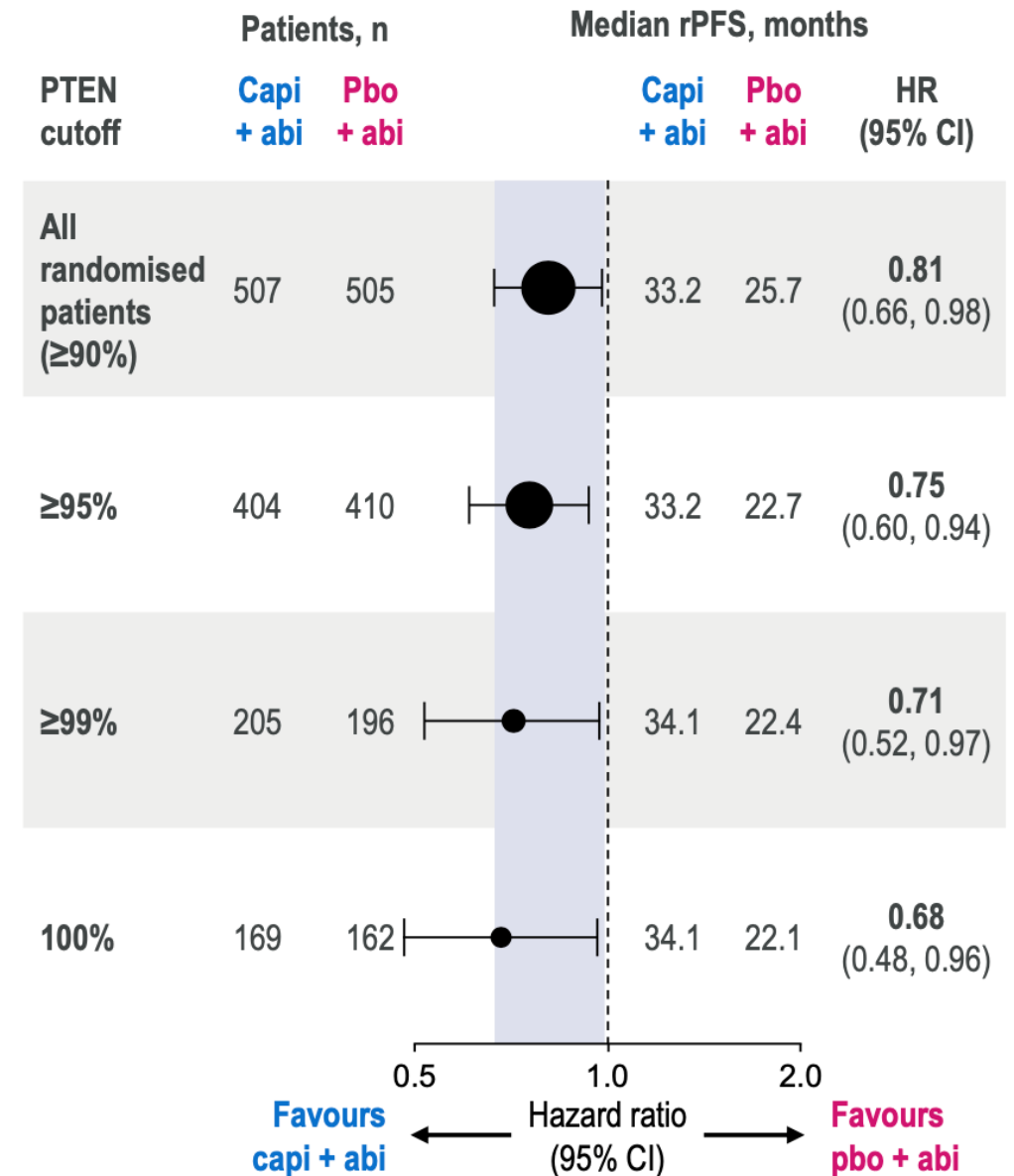
Toxicity



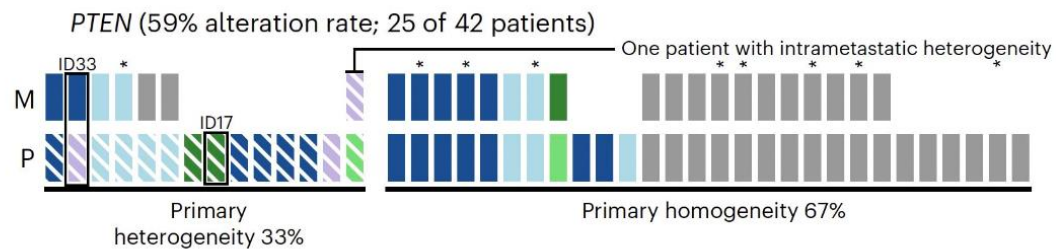
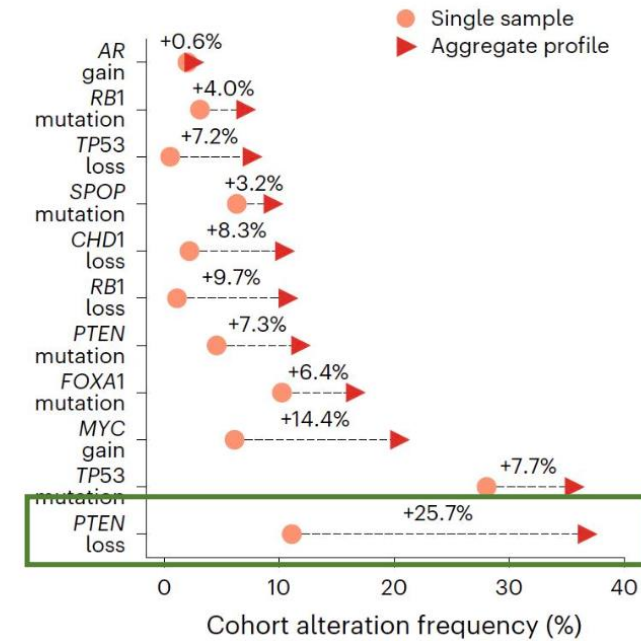
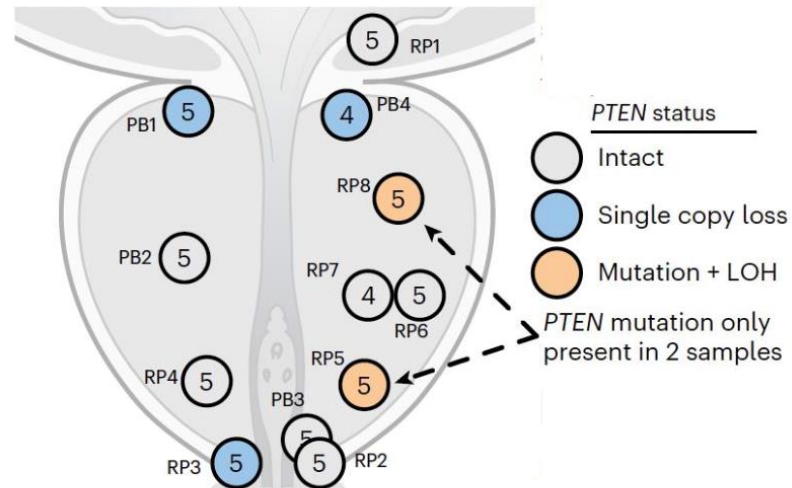
Diabetic ketoacidosis was reported in 6 patients (1.2%) in the capi + abi arm, and 0 patients in the pbo + abi arm.

PTEN subgroups

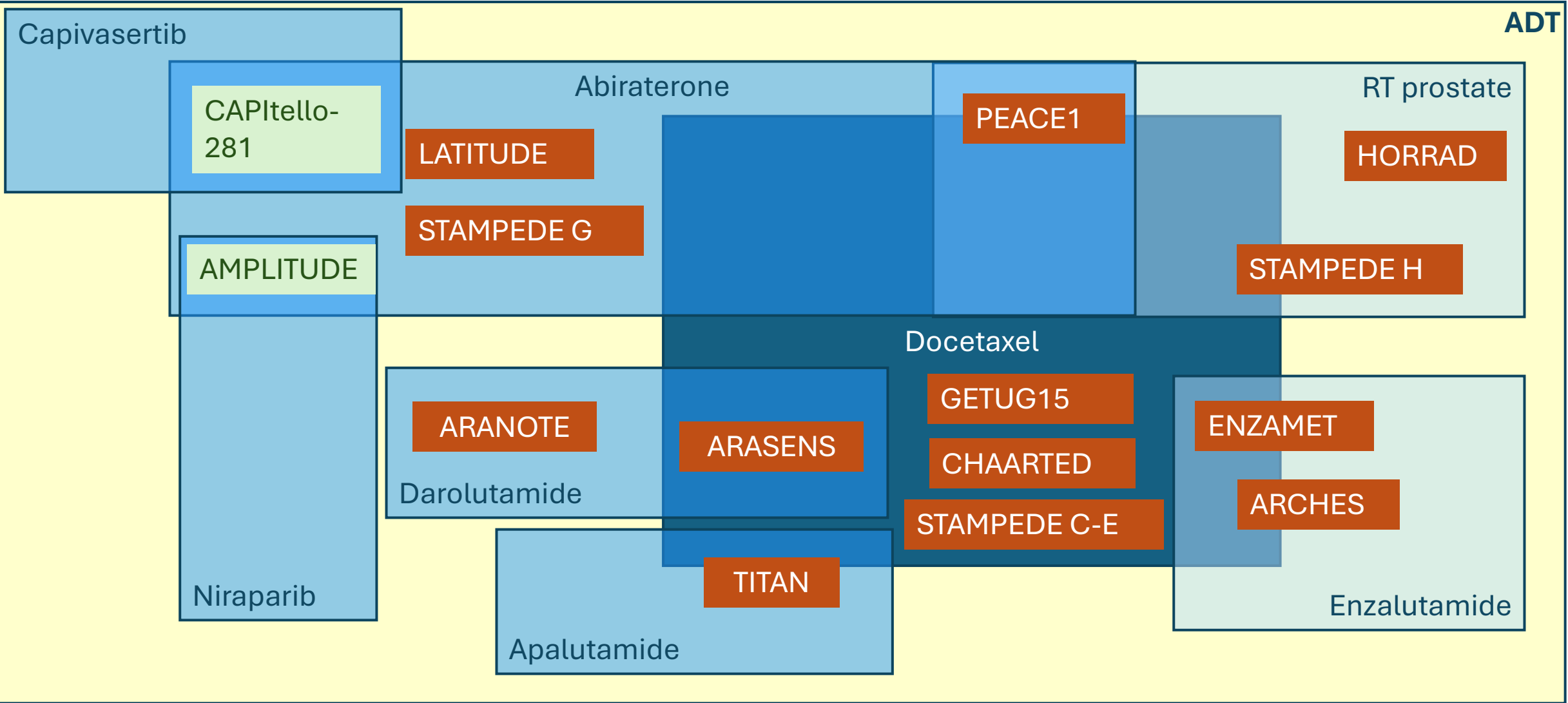
- Also for,
 - OS
 - Symptomatic skeletal events
 - Castration resistance
 - PSA progression



PTEN heterogeneity



mHSPC : treatment options on top of ADT



Docetaxel : Gravis et al, Lancet Oncol, 2013,14 149-58; Sweeney et al, N Engl J Med, 2015, 373, 737-46; James et al, Lancet, 2016, 387, 1163-77
Abiraterone : Fizazi et al. N Engl J Med. 2017, 377, 352-60; James et al, N Engl J Med, 2017, 377, 338-51
Enzalutamide : Armstrong AJ et al. J Clin Oncol. 2019;37(32):2974–86. ; Davis et al, N Engl J Med, 2019, 381, 121-131
Apalutamide : Chi et al, N Engl J Med, 2019, 381, 13-24; Saad F et al. J Clin Oncol 2024;42:4271–81.
Darolutamide : Smith et al, N Engl J Med, 2022, 386, 1132-42

Radiothérapie : Parker et al, The Lancet, 2018, 392, 2353-66; Boevé et al, Eur Urol, 2019, 75, 410-18
Combo : PEACE1 Fizazi K, et al. Lancet 2022; 399(10336):1695–1707.
Niraparib : Attard G. et al Nat Med. 2025;
Capiwasertib : Fizazi et al. ESMO 2025
Lu-PSMA-617 : Tagawa et al ESMO 2025

Merci à Briec Sautois !

AMPLITUDE trial

Median follow-up: 30.8 months

Key inclusion criteria:

- mCSPC^a
- Alteration in ≥ 1 HRR eligible gene: BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, PALB2, RAD51B, RAD54L^b
- ECOG PS 0–2

Key exclusion criteria:

- Any prior
 - PARPi
 - ARPi other than AAP

Prior allowed treatments in mCSPC:

- ADT ≤ 6 months
- Docetaxel ≤ 6 cycles^c
- AAP ≤ 45 days
- Palliative RT

Randomised
1:1
(N=696)

Nira (200 mg QD)
+
AAP (1000 mg QD + 5 mg QD)
+
ADT
(n=348)

PBO
+
AAP (1000 mg QD + 5 mg QD)
+
ADT
(n=348)

Stratification factors:

- BRCA2 vs CDK12 vs all other alterations
- Prior docetaxel (yes vs no)
- Disease volume (high vs low)

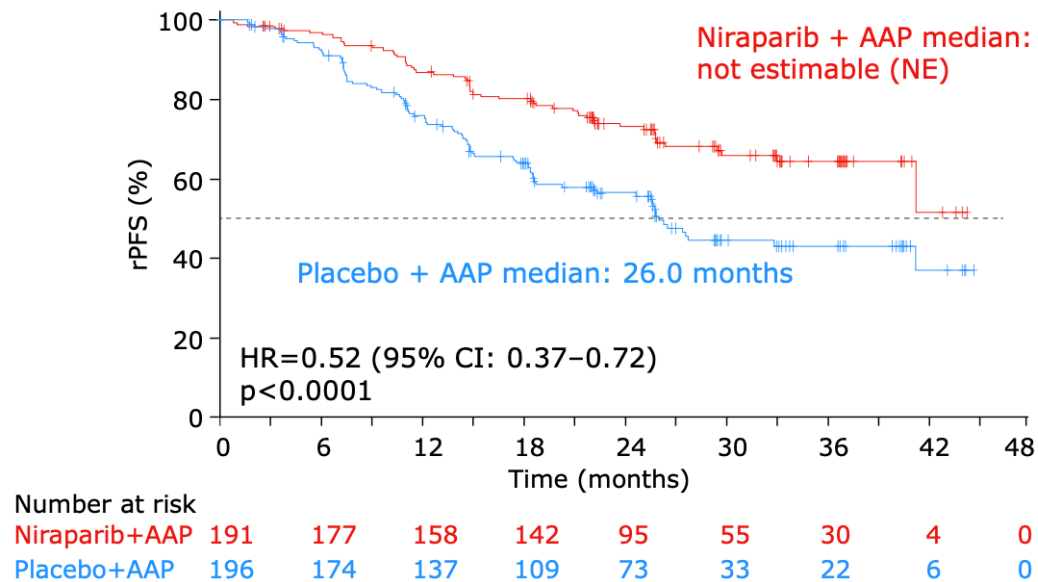
Primary end point
• rPFS by investigator review

Key secondary end points
• Time to symptomatic progression
• OS
• Safety

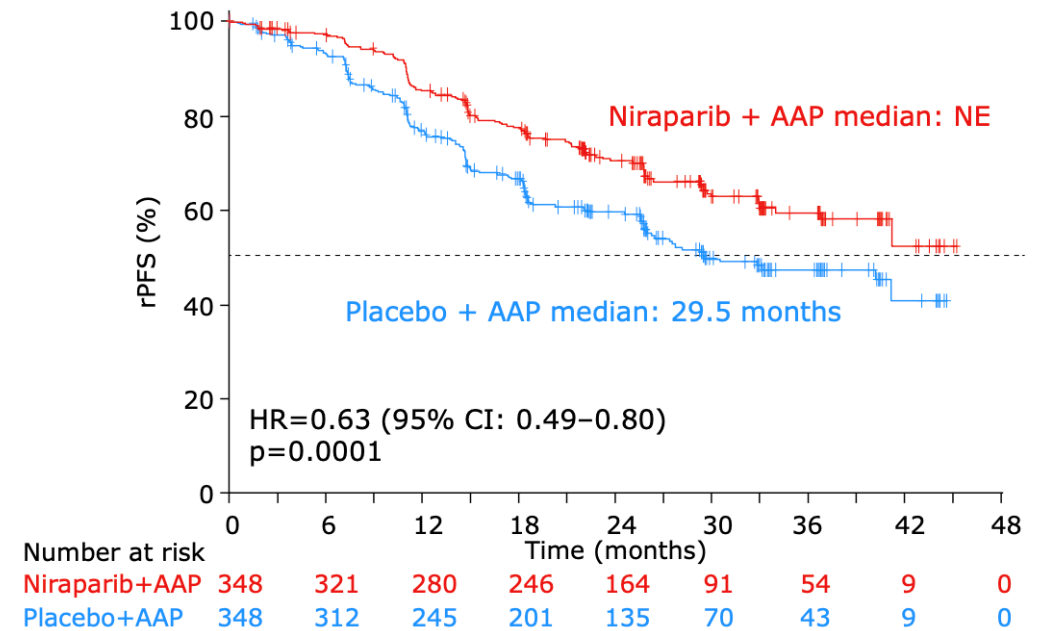
Clinical data cutoff: January 7, 2025

AMPLITUDE trial

BRCA sub-group



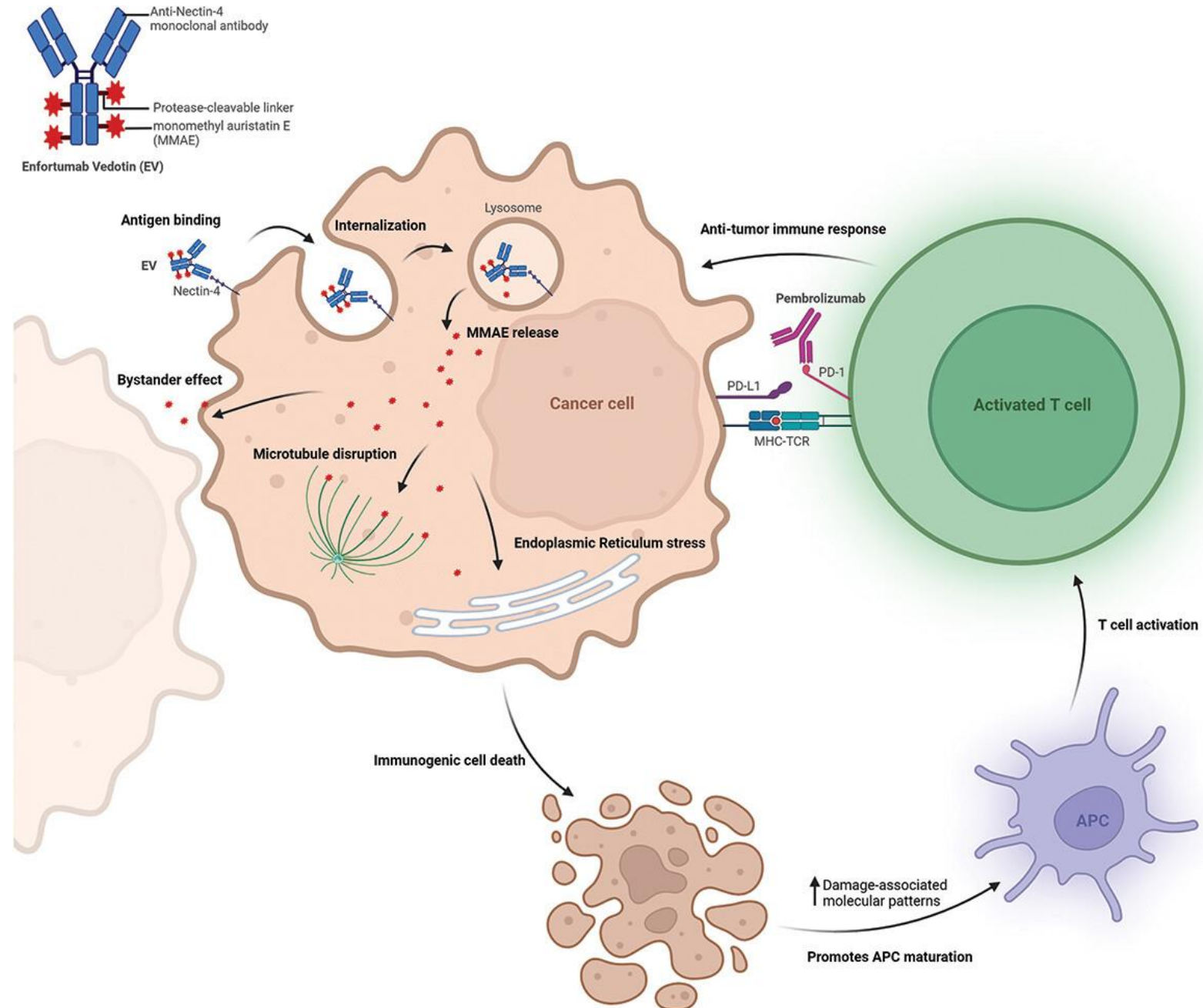
HRRm (ITT)



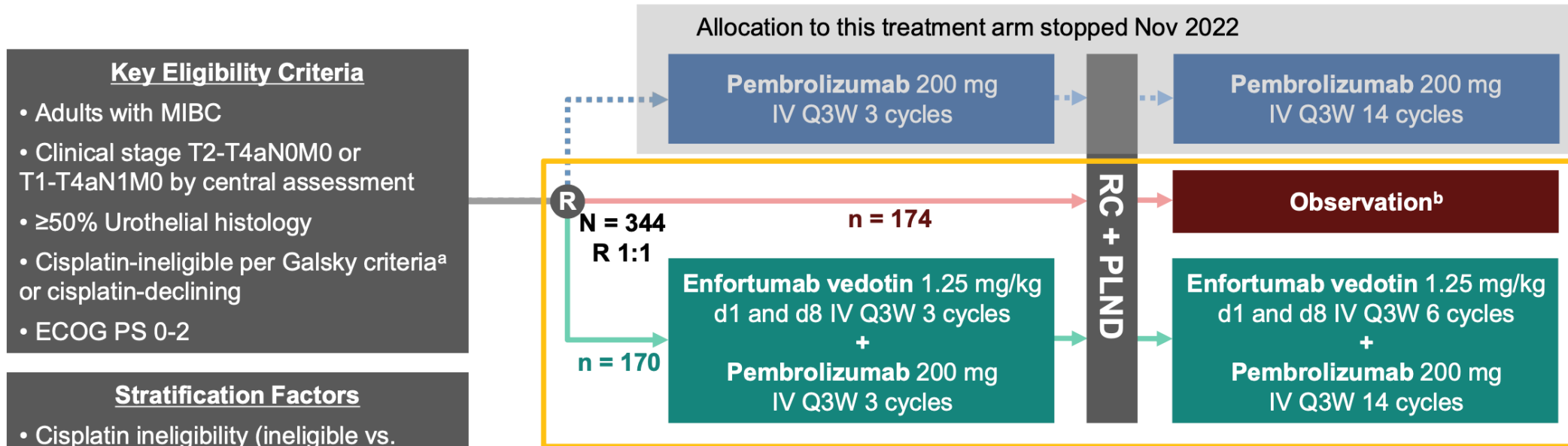


Urothelial cancer

Enfortumab vedotin (EV) + Pembrolizumab



Keynote-905/EV-303 trial



Primary endpoint: Event-free survival (EFS) by BICR

Key secondary endpoints: OS and pathological complete response (pCR; pT0N0, i.e. absence of viable tumor in examined tissue from surgery) by central pathologist review

Other secondary endpoints include: Safety

Exploratory endpoints include: EFS by pCR status

Muscle invasive bladder cancer

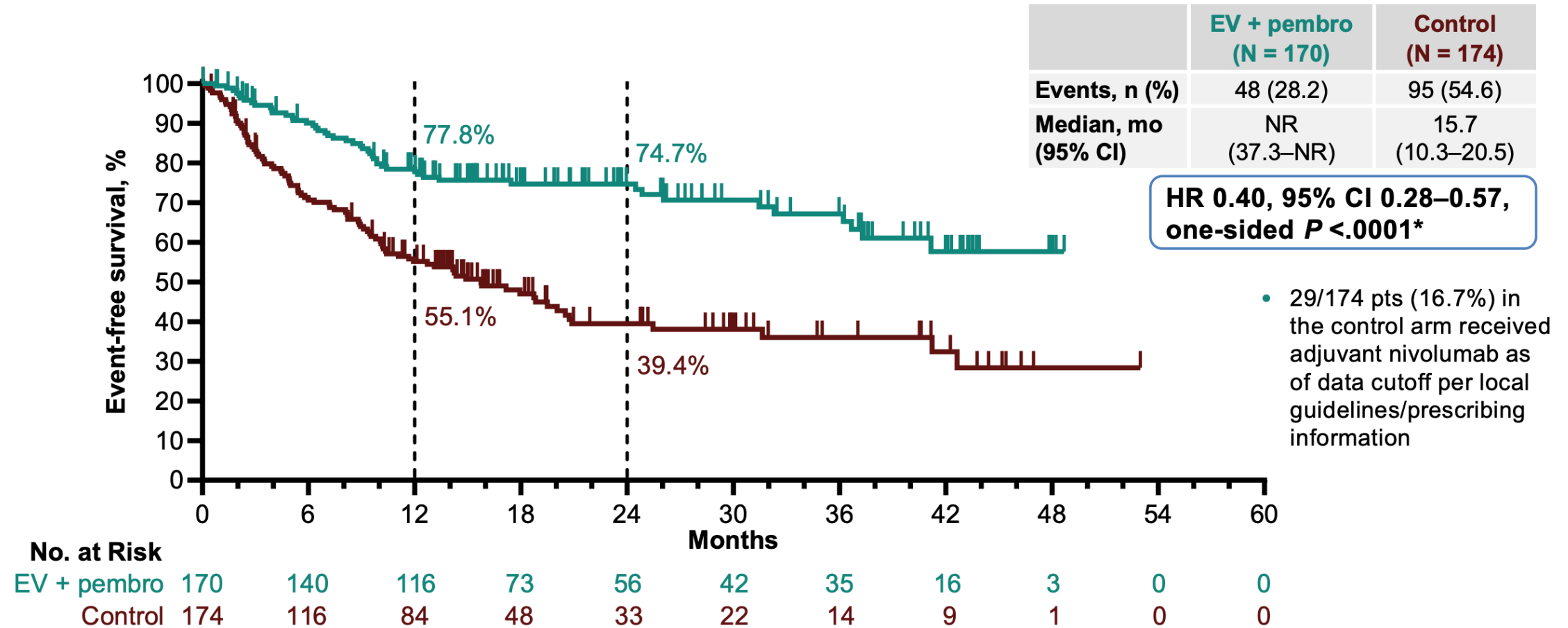
- About **half of patients** are ineligible for cisplatin
- Galsky criteria
 - Poor PS
 - Impaired renal function
 - Hearing loss
 - Peripheral neuropathy
 - NYHA class III heart failure



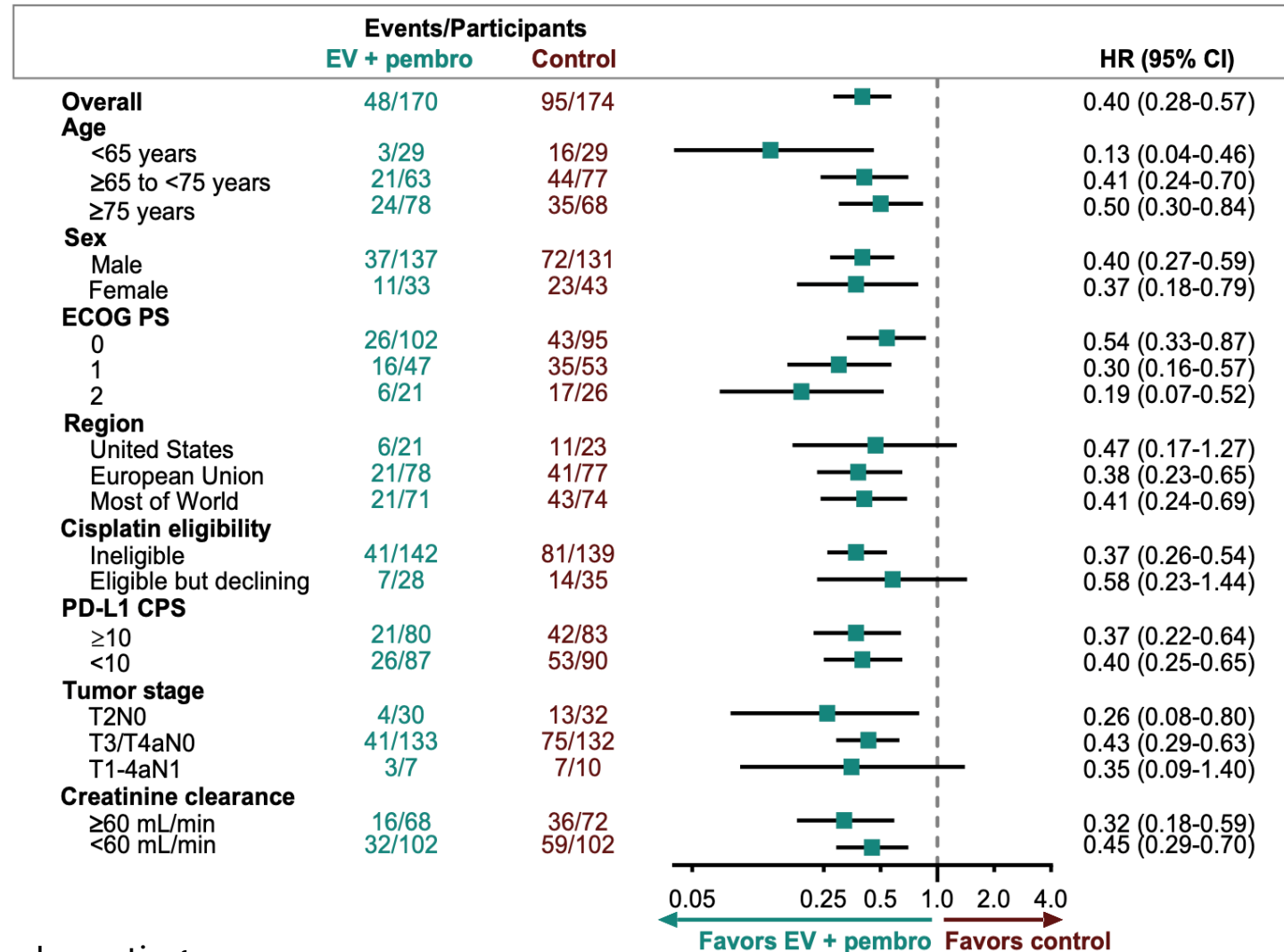
Baseline characteristics

Characteristic, n (%)	EV + pembro (N = 170)	Control (N = 174)
Median age (range), years	74.0 (47–87)	72.5 (46–87)
≥65 to <75 years	63 (37.1)	77 (44.3)
≥75 years	78 (45.9)	68 (39.1)
Male	137 (80.6)	131 (75.3)
ECOG PS		
0	102 (60.0)	95 (54.6)
1	47 (27.6)	53 (30.5)
2	21 (12.4)	26 (14.9)
Region		
United States	21 (12.4)	23 (13.2)
European Union	78 (45.9)	77 (44.3)
Most of World	71 (41.8)	74 (42.5)
Cisplatin eligibility status (per Galsky criteria)		
Ineligible	142 (83.5)	139 (79.9)
Eligible but declining	28 (16.5)	35 (20.1)
PD-L1 combined positive score (CPS) ≥10^a	80 (47.1)	83 (47.7)
Tumor stage at baseline (<i>centrally assessed using both pathology of TURBT specimen and imaging</i>) ^b		
T2N0	30 (17.6)	32 (18.4)
T3/T4aN0	133 (78.2)	132 (75.9)
T1-4aN1	7 (4.1)	10 (5.7)
Creatinine clearance		
≥60 mL/min	68 (40.0)	72 (41.4)
≥30 and <60 mL/min	102 (60.0)	101 (58.0)
<30 mL/min	0	1 (0.6)
Pure urothelial carcinoma histology	152 (89.4)	161 (92.5)

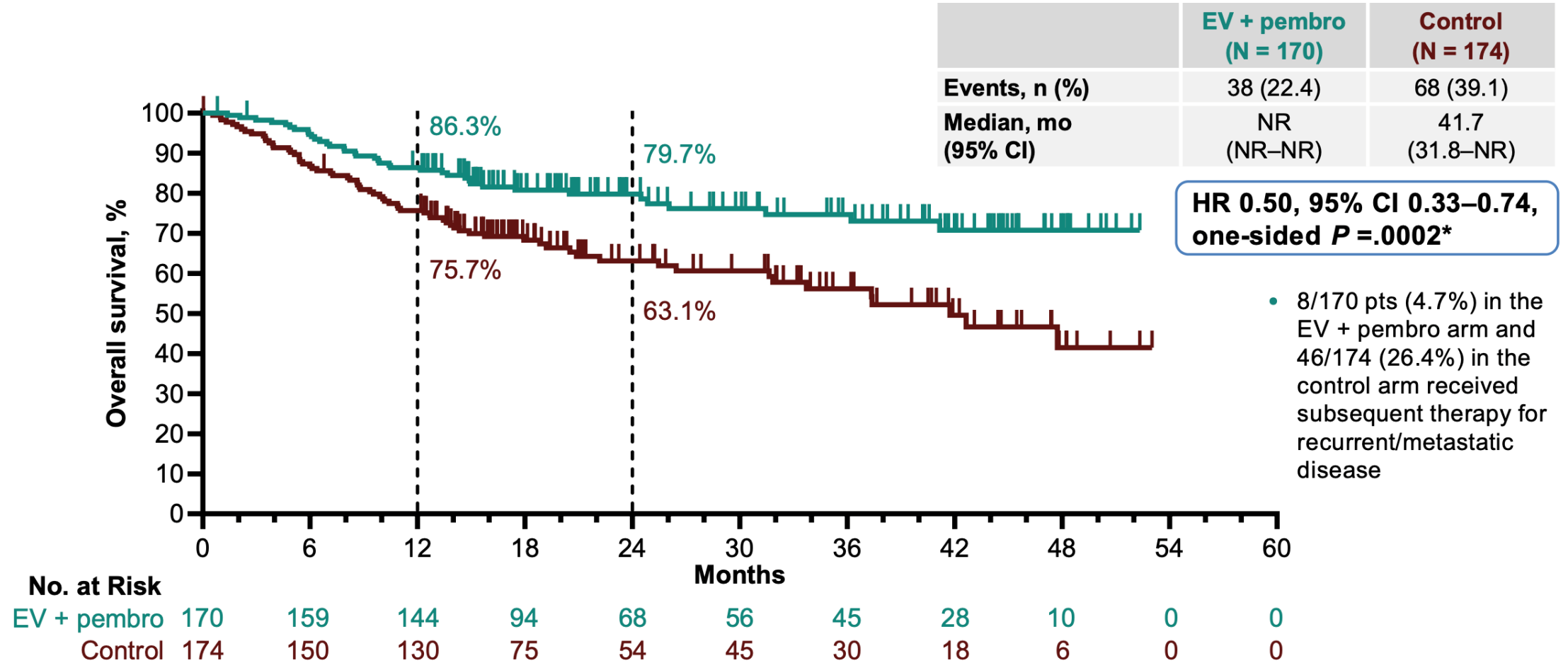
Primary endpoint : EFS



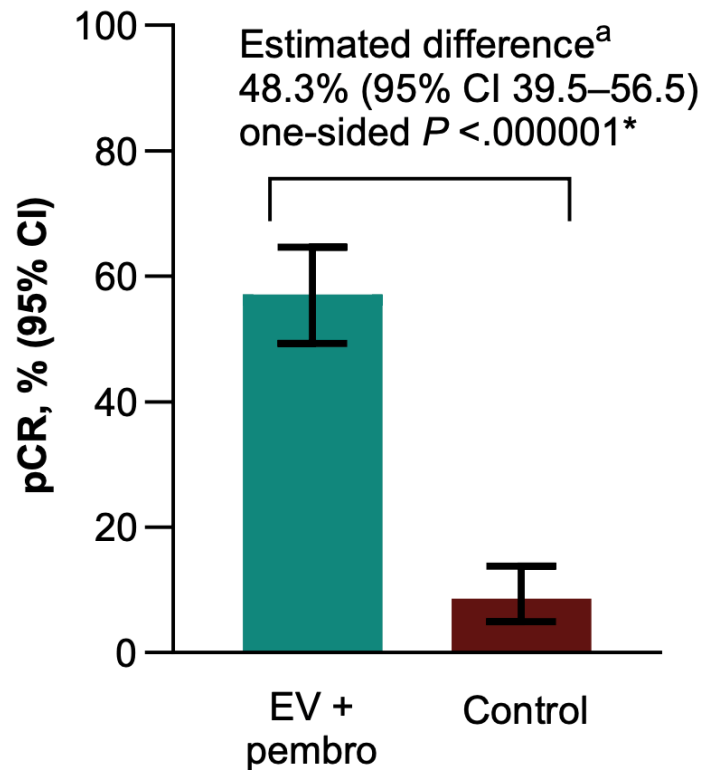
Subgroup analyses : EFS



Secondary endpoint : OS



Secondary endpoint : pCR

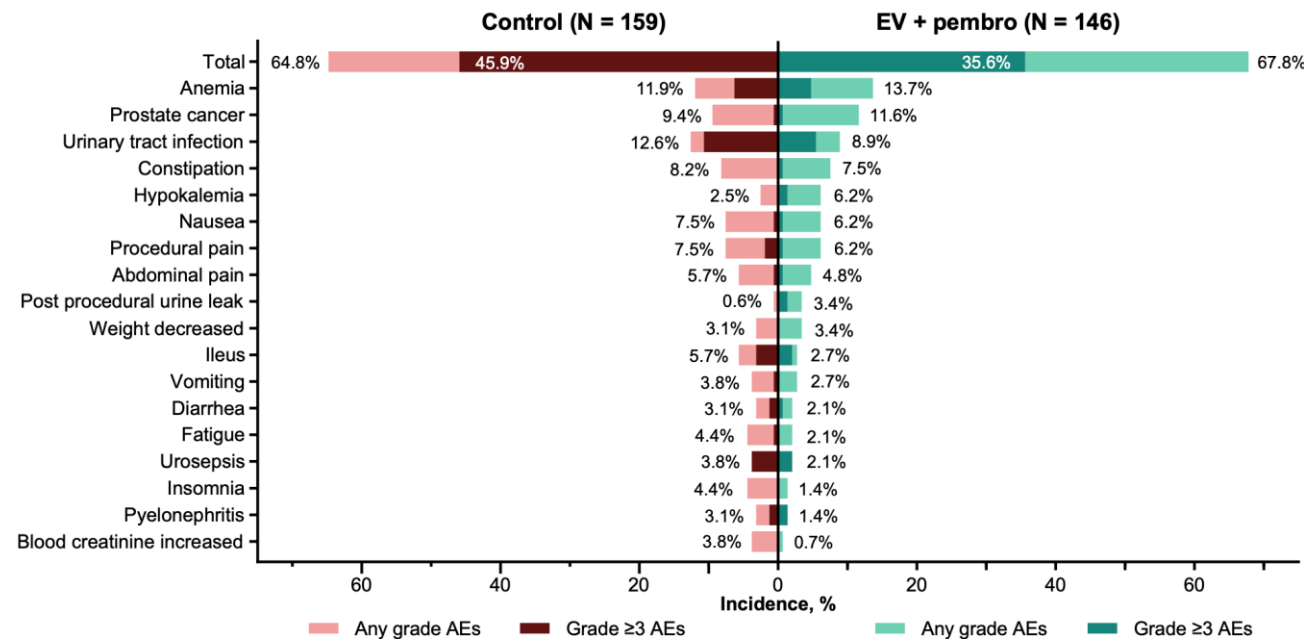


	EV + pembro (N = 170)	Control (N = 174)
pCR, n	97	15
pCR rate, % (95% CI)	57.1 (49.3–64.6)	8.6 (4.9–13.8)

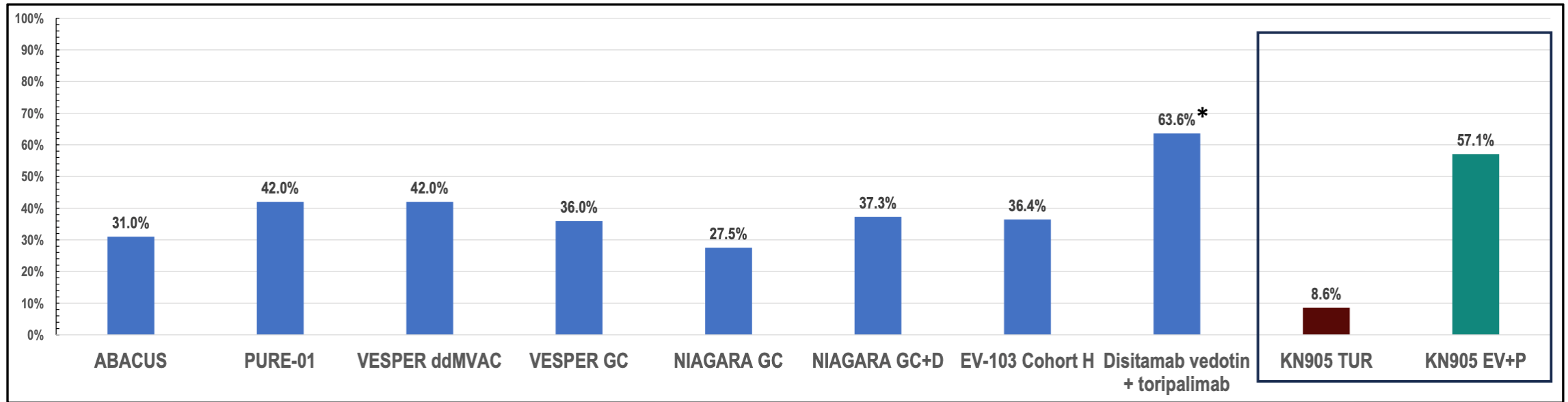
- **pCR:** absence of viable tumor (pT0N0) in examined tissue from RC + PLND
- Pts who did not undergo surgery, including those with clinical complete response after neoadjuvant therapy, were considered non-responders

Surgery was feasible after EV + P

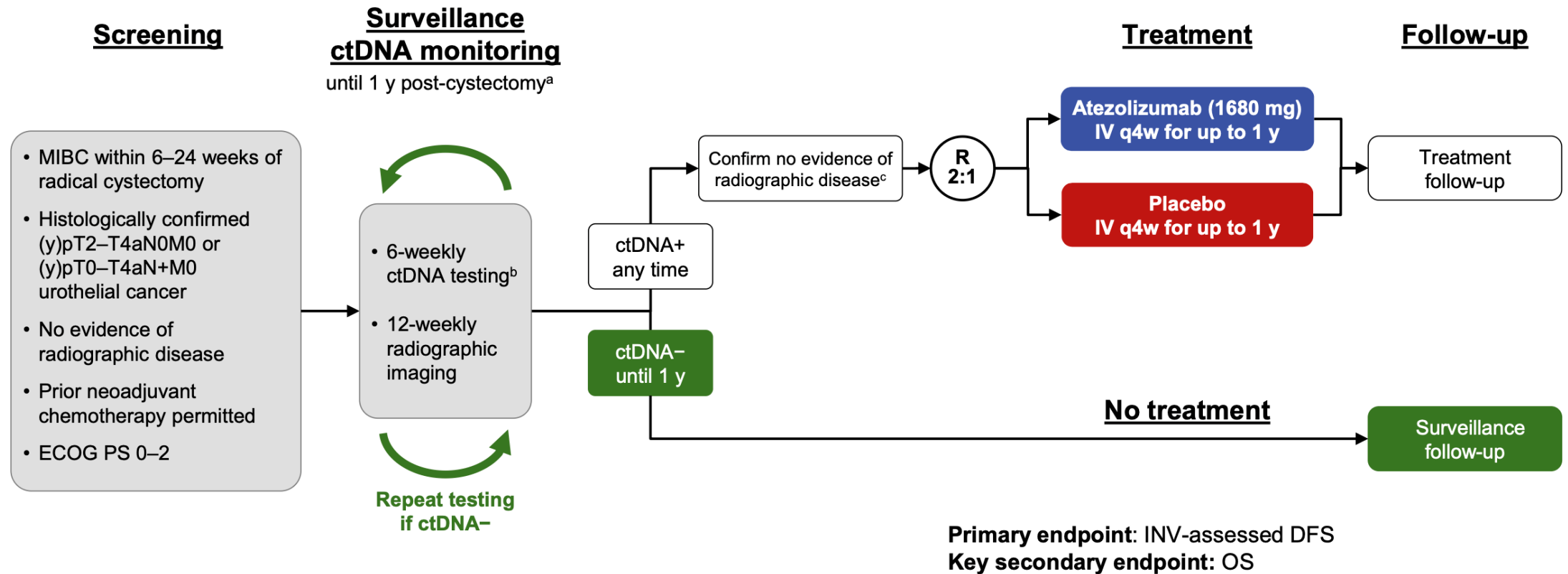
- 87.6% of patients underwent surgery
- Grade 5 events during surgery phase were low
 - 2.7% in EV + P versus 5.7% in control



Pathological response rate

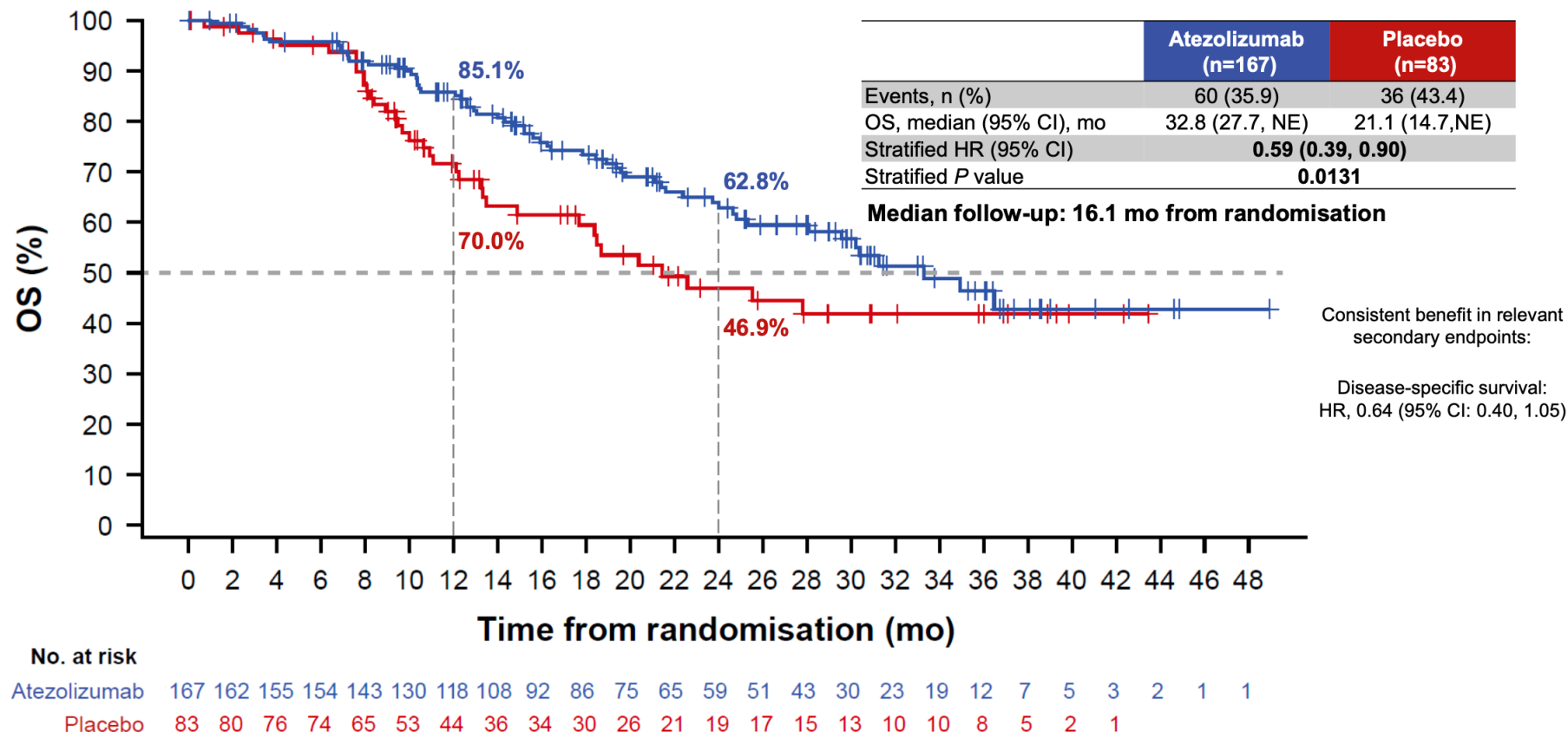


Adjuvant phase after pCR ?

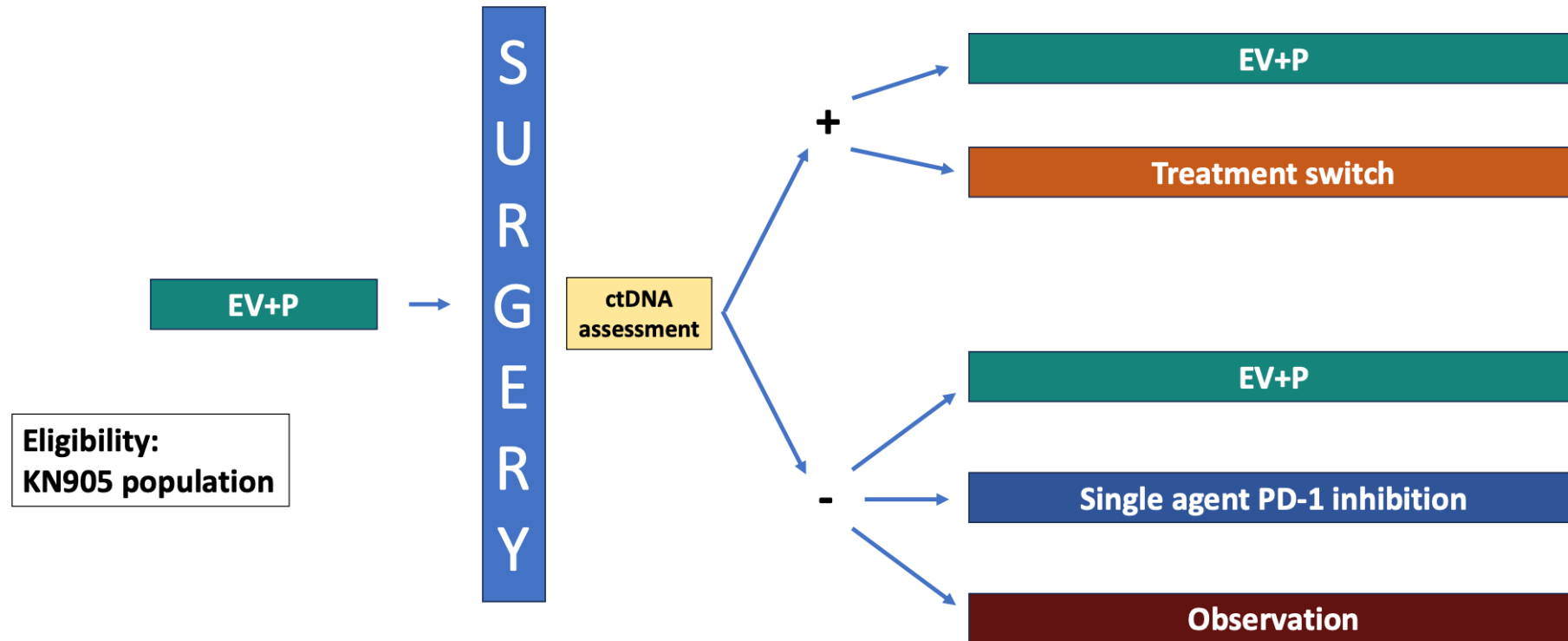


Adjuvant phase after pCR ?

OS in patients who tested ctDNA+



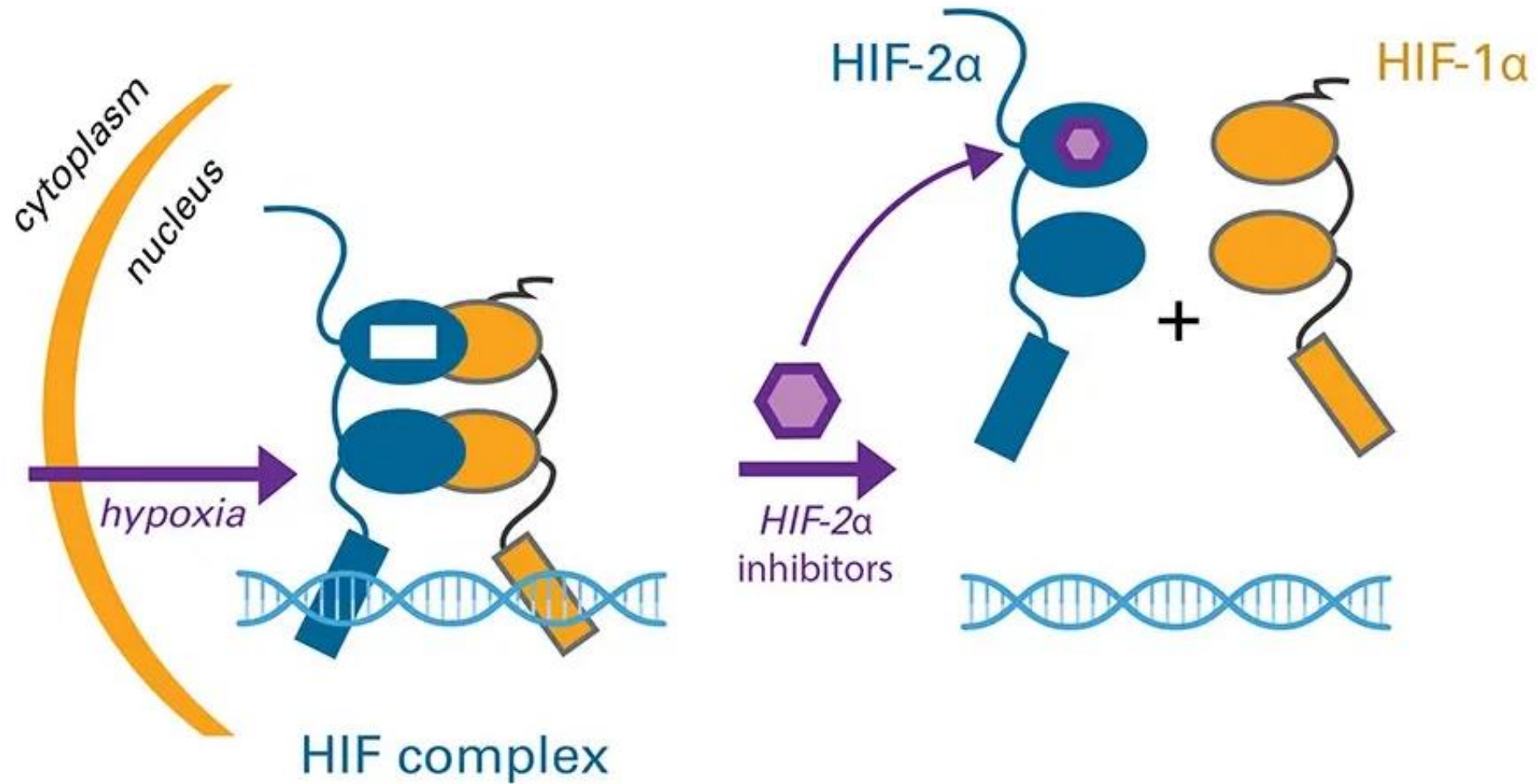
Perspective





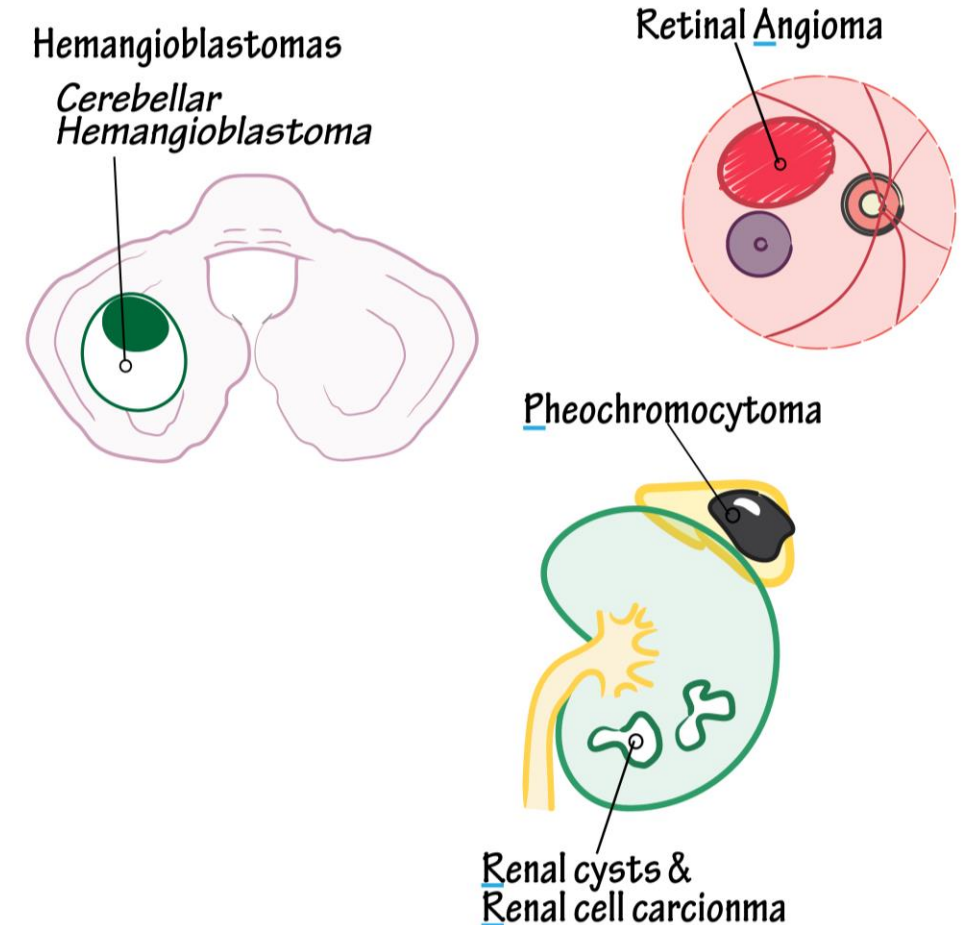
Kidney cancer

Belzutifan



Von-Hippel Lindau disease

- **VHL gene mutation**
- Autosomal dominant
- Life expectancy
 - 60 years in female
 - 67 years in male
- Main cause of death
 - CNS hemangioblastomas



LITESPARK-004

Key Eligibility Criteria

- Diagnosis of VHL disease, based on germline alteration
- ≥ 1 measurable RCC tumor
- No RCC tumor or other VHL tumor that necessitates immediate surgery^a
- No prior systemic anticancer therapy
- No metastatic disease
- ECOG PS 0 or 1

N = 61

Belzutifan
120 mg orally once daily^b

Tumor Assessments

- At screening and every 12 weeks for a minimum of 3 years, then every 24 weeks thereafter

End Points

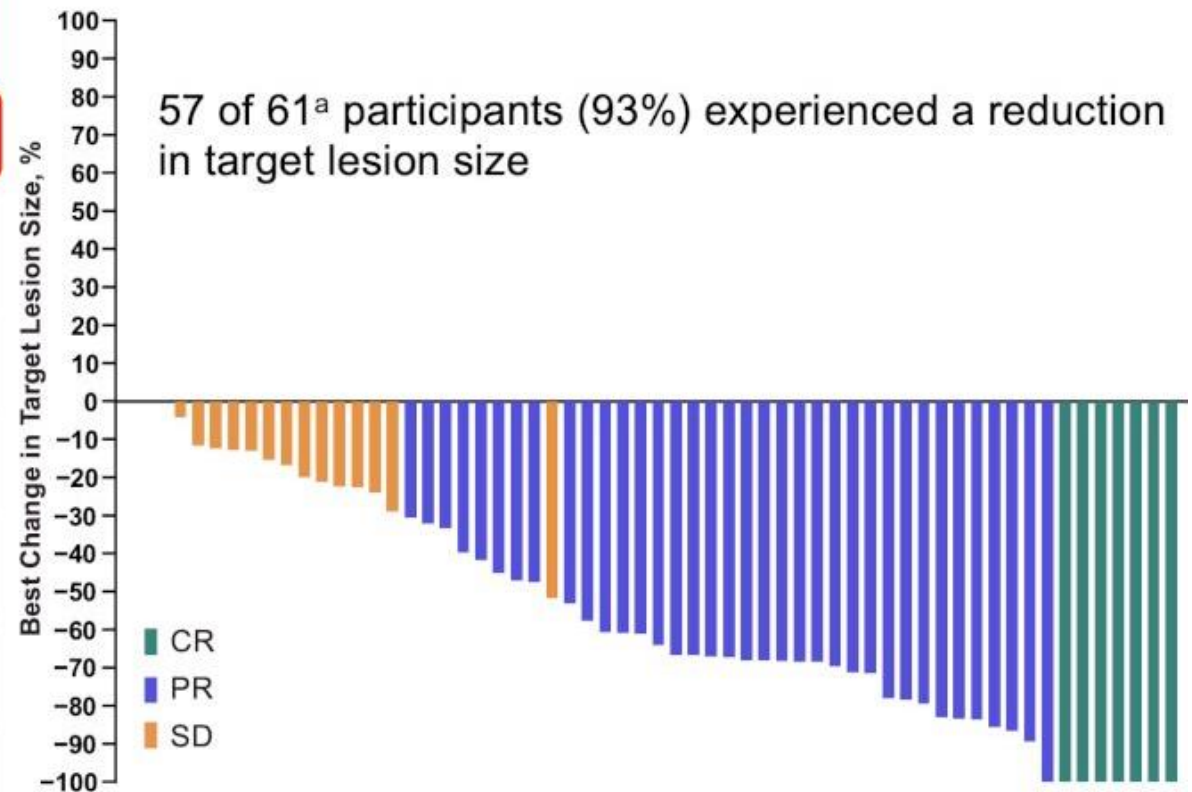
- Primary: ORR in VHL disease–associated RCC per RECIST v1.1 by IRC
- Secondary: ORR in other VHL disease–associated neoplasms; DOR; TTR per RECIST v1.1 by IRC; and safety

Baseline characteristics

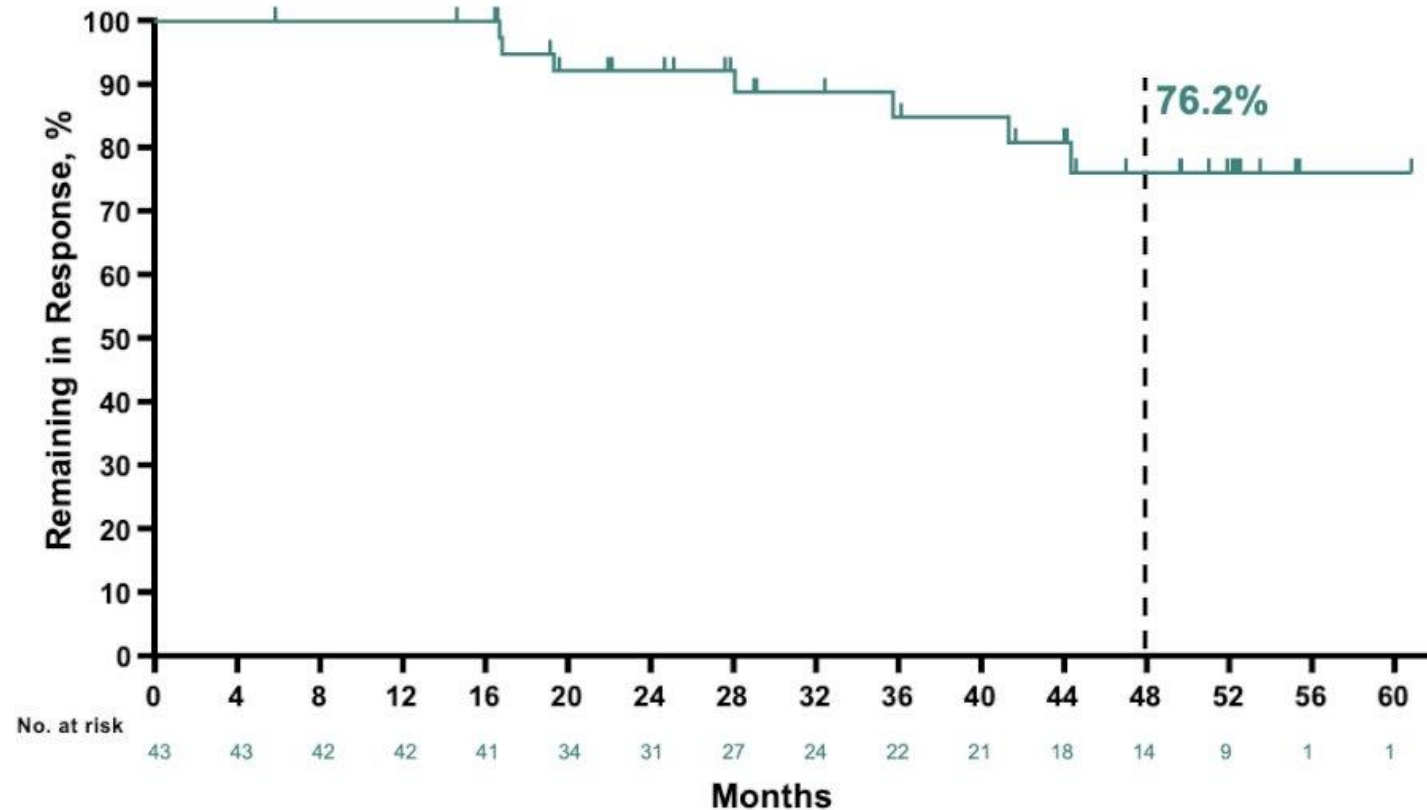
	N = 61		N = 61
Age, median (range), years	41 (19-66)	Prior VHL disease–related surgical procedures,^c n (%)	
Sex, n (%)		No. of participants who had ≥1 prior surgical procedure	59 (97)
Male	32 (52)	RCC	47 (77)
Female	29 (48)	Pancreatic lesions (serous cystadenoma + pNET)	9 (15)
ECOG PS, n (%)		CNS hemangioblastoma	46 (75)
0	50 (82)	Retinal hemangioblastoma	26 (43)
1	10 (16)	Size of target lesions,^d median (range), mm	
2 ^a	1 (2)	RCC	22 (10-43)
No. of participants with non-RCC neoplasms^b per IRC, n (%)		CNS hemangioblastoma	17 (10-87)
pNET	20 (33)	pNET	19 (10-52)
CNS hemangioblastoma	50 (82)	VHL alteration, n (%)	
Retinal hemangioblastoma	14 (23)	Deletion	18 (30)
		Mutation	43 (70)

ORR in RCC

	RCC N = 61
ORR, % (95% CI)	70 (57-81)
Best response n (%)	
CR	7 (11)
PR	36 (59)
SD	17 (28)
PD	0
NE ^a	1 (2)



Duration of response for RCC

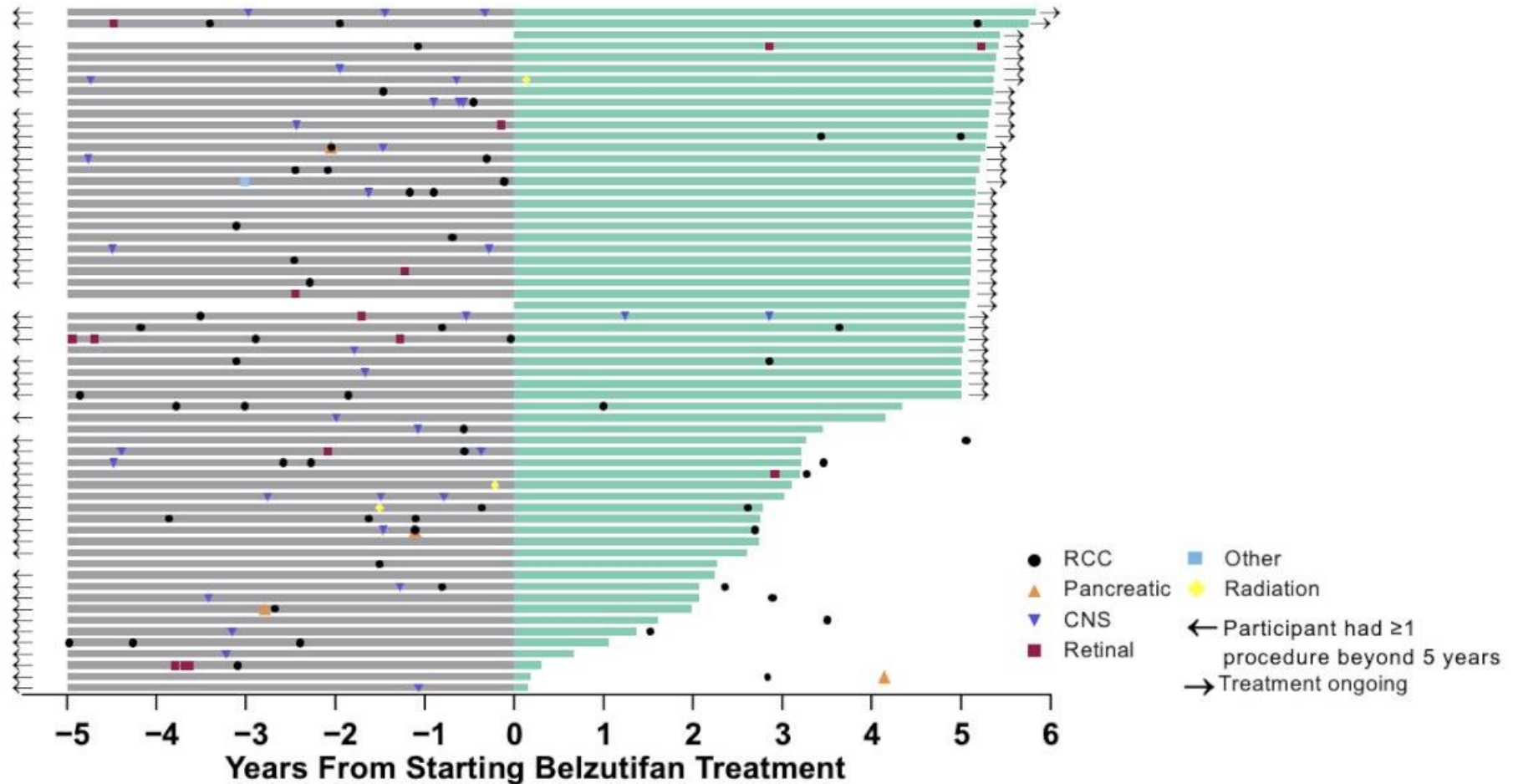


But also for CNS hemangioblastomas (81.5%), retinal hemangioblastomas (94.1%) and pNETs (91.5%)

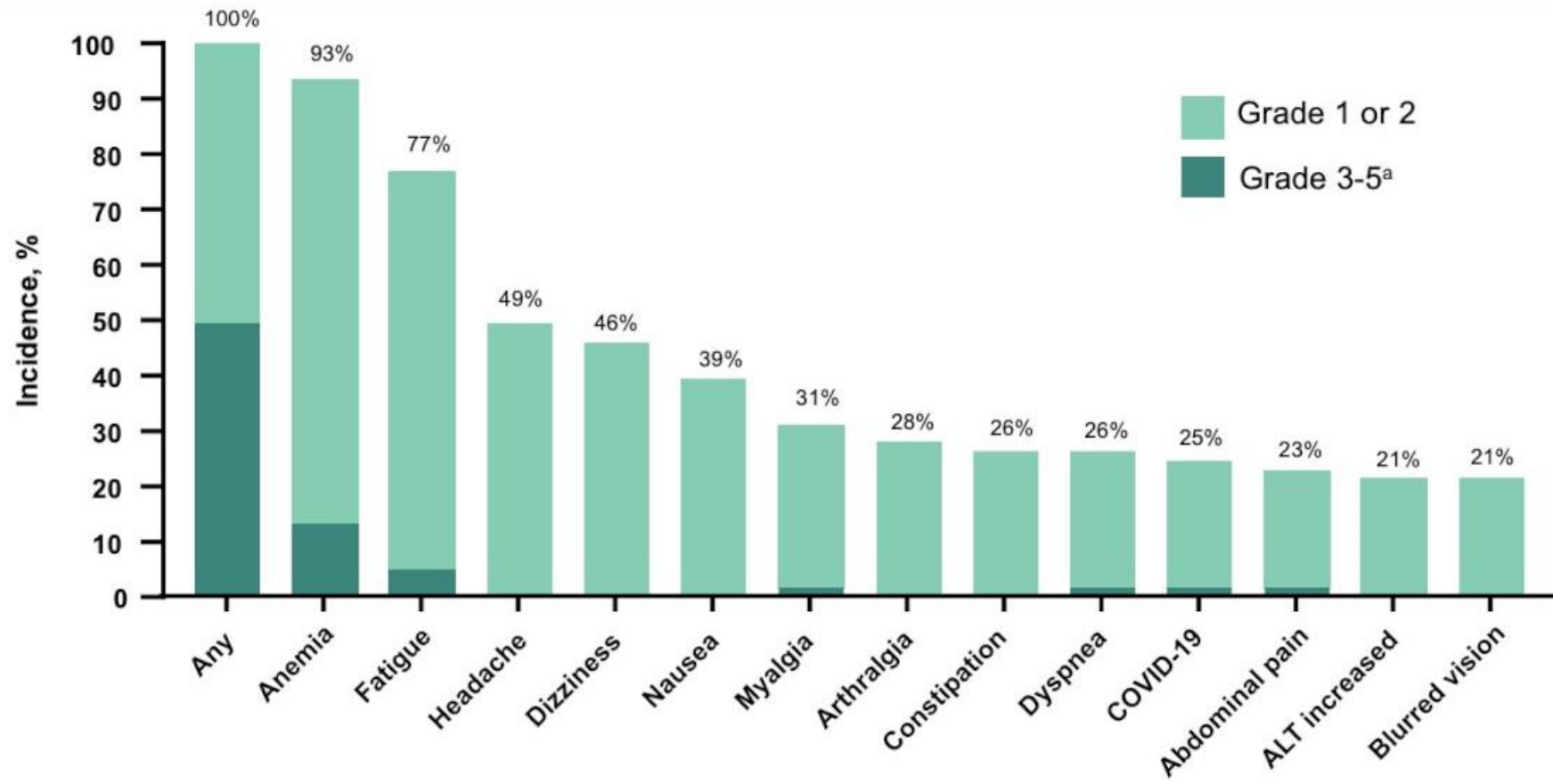
Responses in retinal hemangioblastomas

	Retinal hemangioblastoma n = 14
Participants with retinal hemangioblastoma at baseline, n	14
Improved	14 (100)
Stable	0
Progressed	0
NE/NA	0
Response rate, % (95% CI)	100 (77-100)
DOR, median (range), months	NR (8.5-61.0+)
TTR, median (range), months	2.8 (2.5-10.8)
Eyes assessed at baseline, n	18
Improved	18 (100)
Stable	0
Progressed	0
NE/NA	0
Response rate, % (95% CI)	100 (82-100)

VHL-disease related procedures



Adverse events with incidence $\geq 20\%$



LITESPARK-022 trial

POSITIVE

Study design

Key Eligibility Criteria

- Histologically or cytologically confirmed RCC with clear cell component
 - Intermediate-high risk RCC
 - pT2, grade 4 or sarcomatoid, N0, M0
 - pT3, any grade, N0, M0
 - High risk RCC
 - pT4, any grade, N0, M0
 - pT any stage/grade, N+, M0
 - M1 NED^a
- No prior systemic therapy
- BICR-verified tumor free (CT or MRI of the brain, chest, abdomen, and pelvis and bone imaging)

Stratification

- Intermediate-high risk vs high risk vs M1 NED
- Tumor grade 1 or 2 vs tumor grade 3 or 4

R^b (1:1)
N ≈ 1600

Belzutifan
120 mg oral QD
54 weeks^c
+
Pembrolizumab
400 mg IV Q6W
9 cycles^c

Placebo oral QD
54 weeks^c
+
Pembrolizumab
400 mg IV Q6W
9 cycles^c

Follow-up

- Years 1-2: Q12W
- Years 3-5: Q16W
- Years 6+: Q24W
- Efficacy and PROs
- Safety: 30 days after treatment cessation (or 90 days for serious AEs)

End Points

- Primary: DFS
- Secondary: OS, safety and tolerability, DRSS, PROs

LITESPARK-011 trial

POSITIVE

Key eligibility criteria

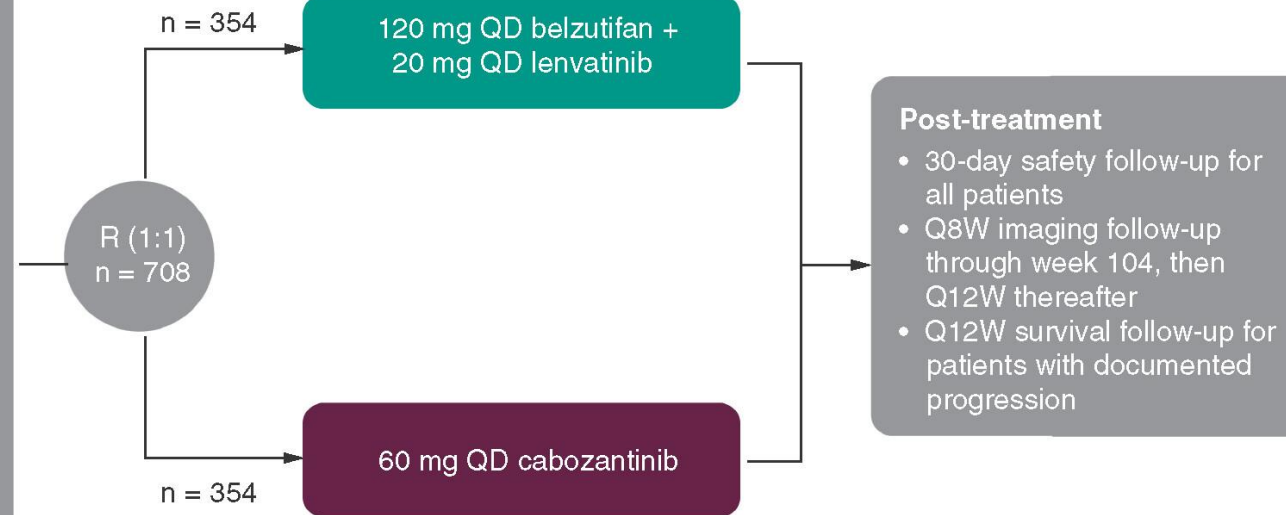
- Advanced or metastatic RCC with clear cell component
- Disease progression after first- or second line anti-PD-1/PD-L1 therapy or as neoadjuvant/adjuvant treatment with progression on or within 6 months of last dose
 - Therapy immediately preceding must be anti-PD-1/PD-L1
- Received ≤ 2 prior systemic therapies^a
- Measurable disease per RECIST v1.1
- KPS score $\geq 70\%$

Stratification

- IMDC prognostic scores (0 vs 1–2 vs 3–6)
- Line of treatment in which anti-PD-1/PD-L1 therapy was given (1 [adjuvant, neoadjuvant/adjuvant, or first-line] vs 2 [second-line])
- Geographic region (North America vs Western Europe vs ROW)

Assessments

- Q8W first 104 weeks and then Q12W thereafter



Post-treatment

- 30-day safety follow-up for all patients
- Q8W imaging follow-up through week 104, then Q12W thereafter
- Q12W survival follow-up for patients with documented progression

End points

- Primary: PFS, OS
- Secondary: ORR, DOR, safety and tolerability

Any
question ?

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