

Year in Review in GU Oncology – An Oncologist's perspective



BMUC

UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

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

Dr Simon Van Wambeke, medisch oncoloog ZAS



Prostaat

Blaas



Prostaat

Blaas



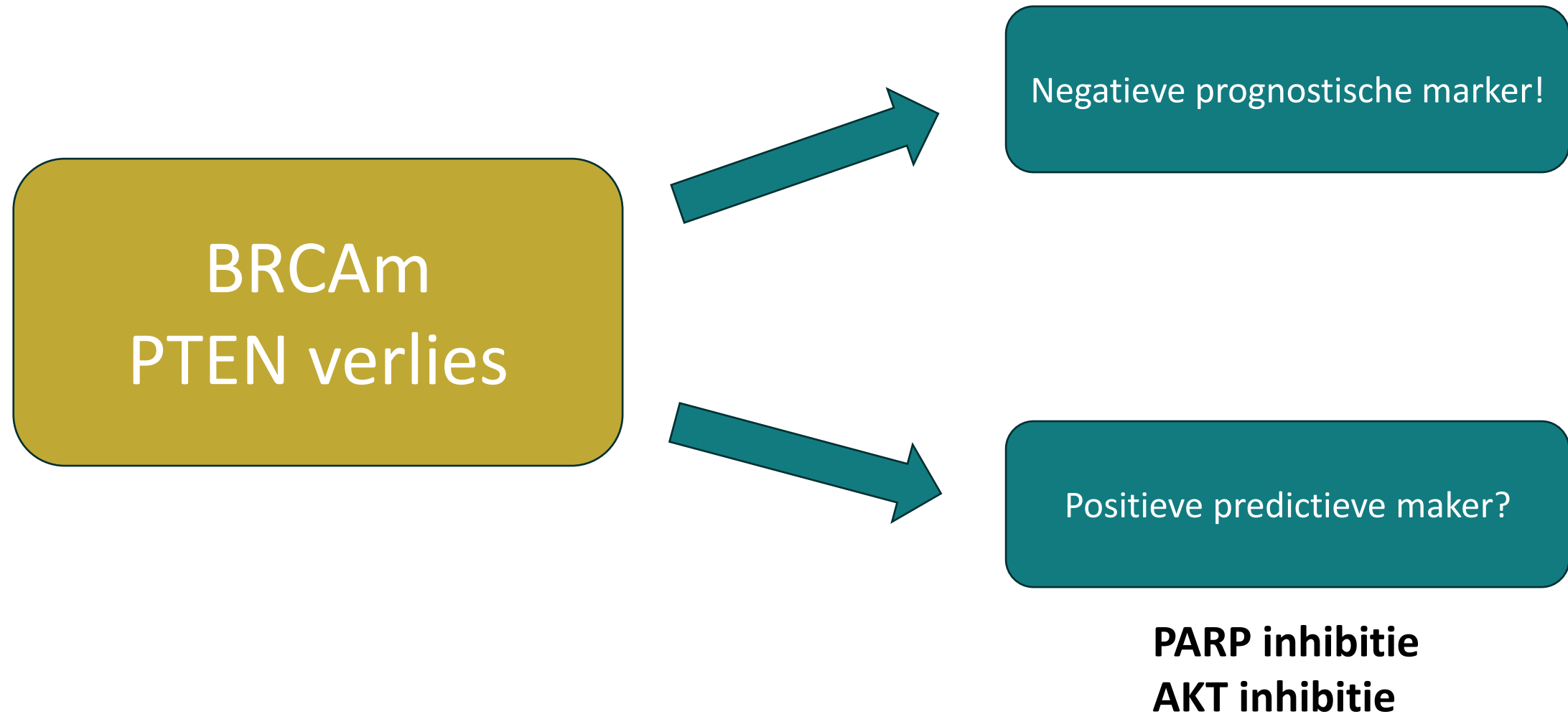
**Zijn we klaar voor biomarkergedreven
therapie in mHPSC?**

Waar plaatsen we Lu PSMA?



**Zijn we klaar voor biomarkergedreven
therapie in mHPSC?**

BRCAm, PTEN verlies

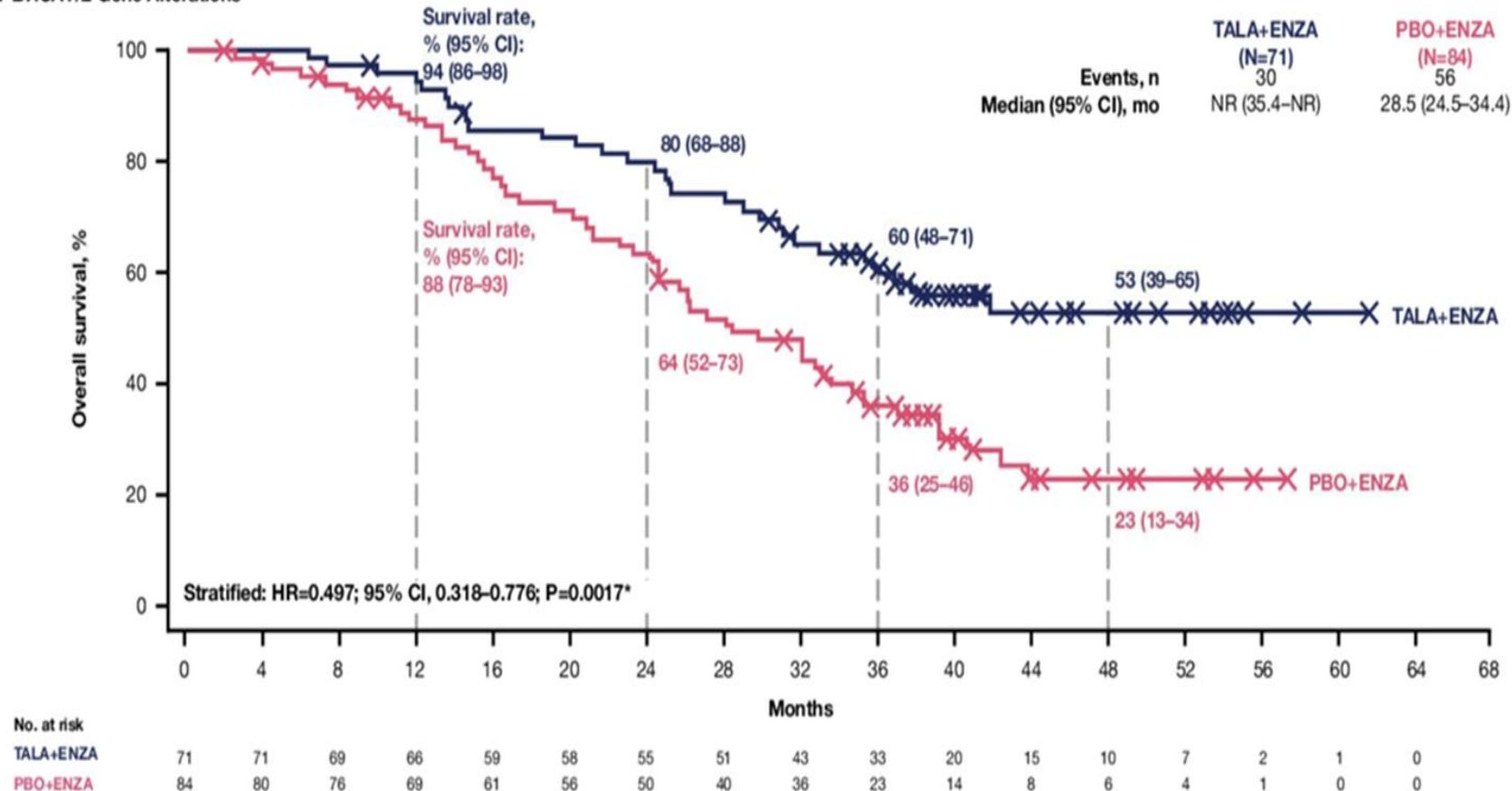


BRCAm 1L mCRPC



TALAPRO-2: ADT + ENZALUTAMIDE +/- TALAZOPARIB

B. BRCA1/2 Gene Alterations



BRCAm/HRRm mHSPC



AMPLITUDE

Key eligibility criteria

- mHSPC
- ECOG 0-2
- Alteration in ≥ 1 HRR gen
- Prior docetaxel allowed (16%)

AAP + Niraparib + ADT

1:1 randomization

AAP + Placebo + ADT

Primary endpoint:

- rPFS by investigator
BRCAm -> HRRm

Key secondary endpoint:

- OS

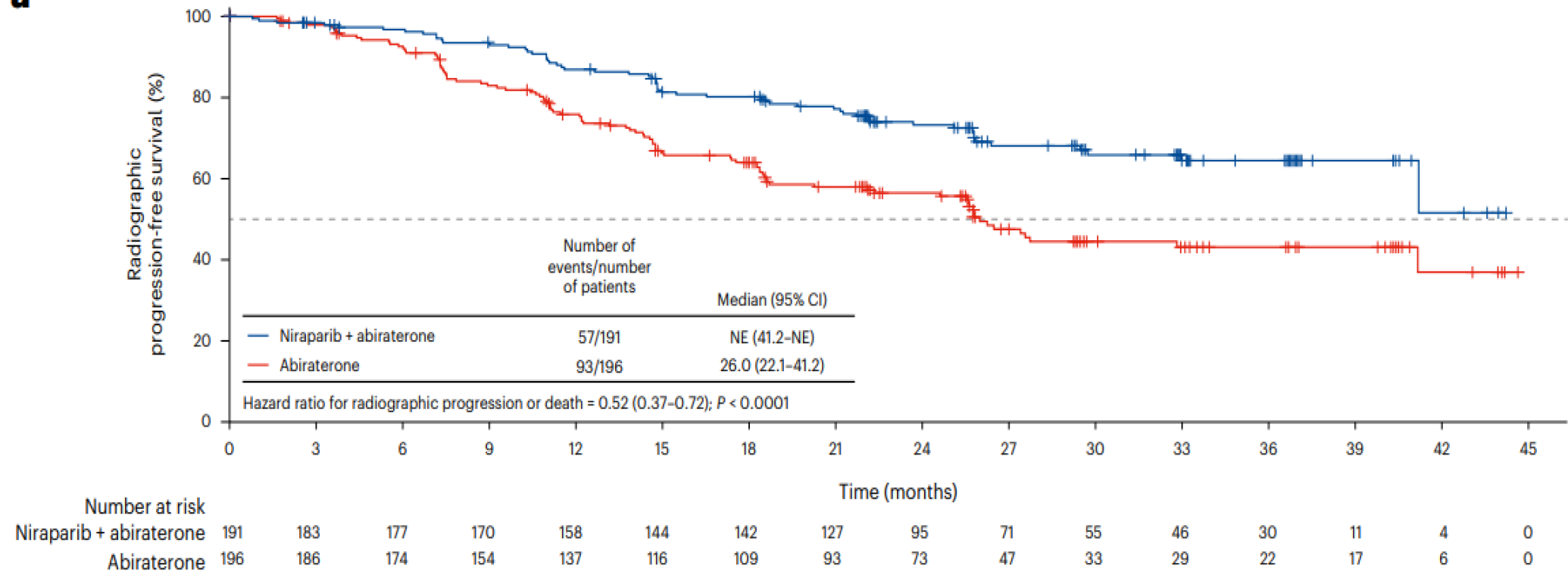
HRR testing (tumor, plasma of kiembaan): *BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, PALB2, RAD51B, RAD54L (geen ATM)*

56% BRCA 1/2

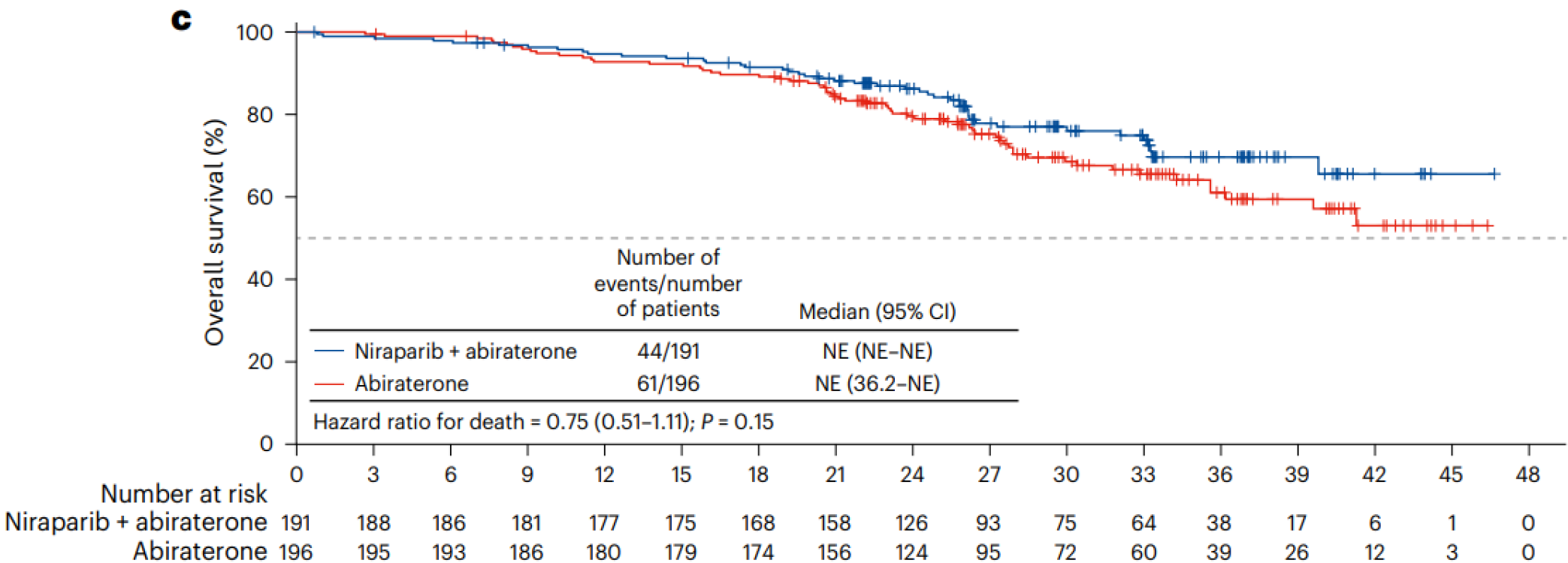
AMPLITUDE rPFS: BRCAm



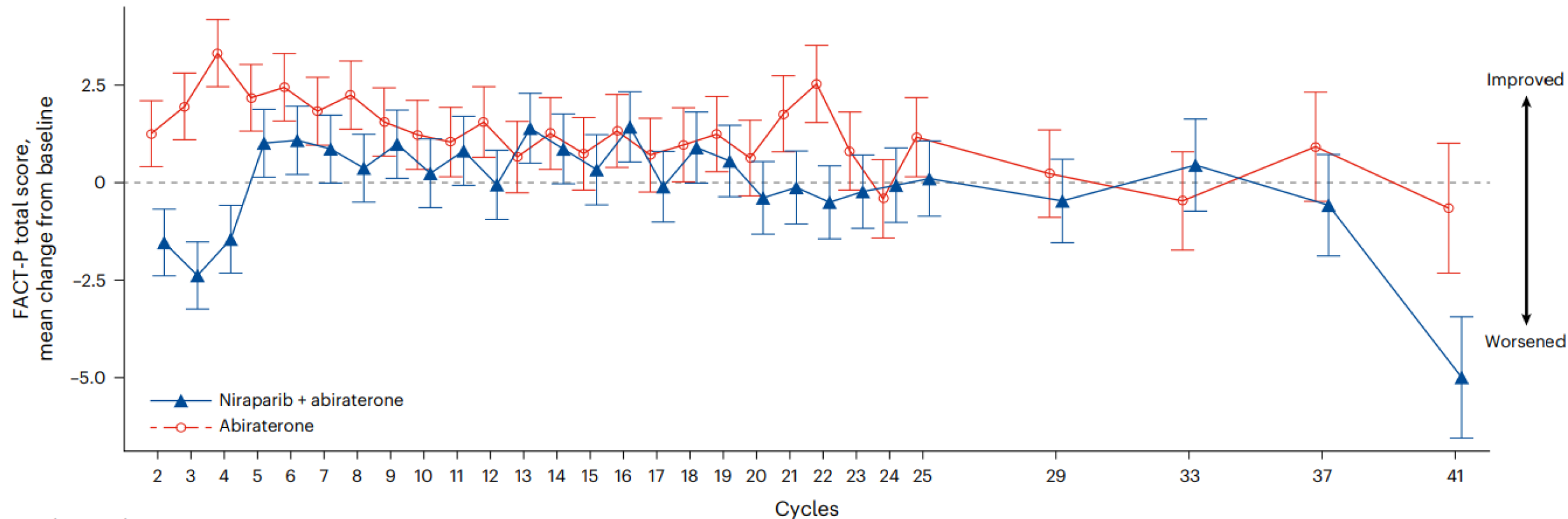
a



AMPLITUDE OS: BRCAm (50% maturiteit)



AMPLITUDE QoL

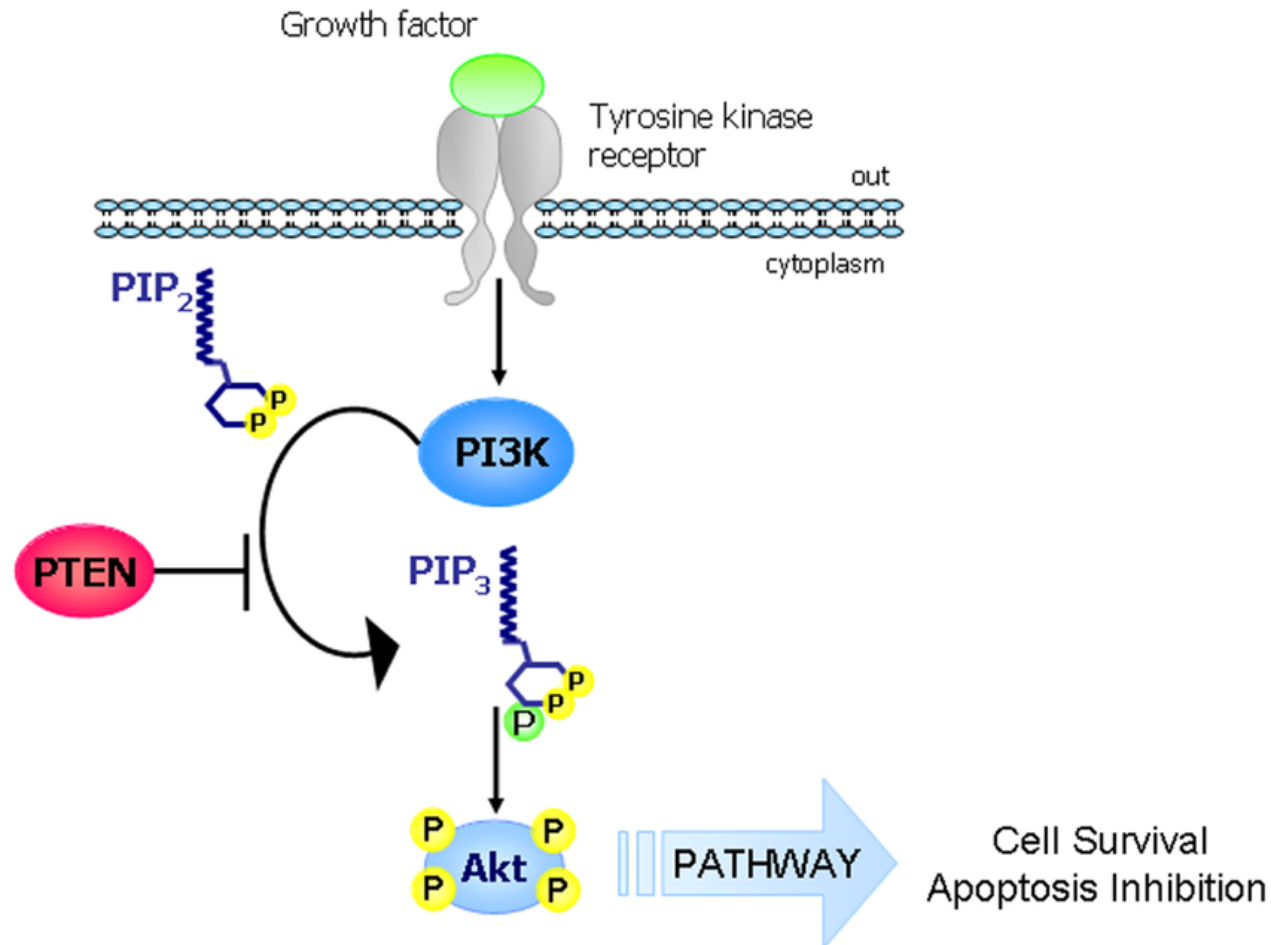


Number at risk

Niraparib + abiraterone	330	320	306	307	302	308	308	299	298	289	285	274	275	268	267	261	255	250	239	234	230	226	216	205				
Abiraterone	336	325	320	323	311	308	300	294	285	274	265	253	247	237	233	222	218	205	203	199	188	183	178	173				

146	108	83	53
127	91	68	45

Akt inhibatoren - PI3K pathway



AKT inhibitor in PTEN deficient mHSPC



CAPITELLO-281

Key eligibility criteria

- *De novo* mHSPC
- PTEN deficiency: $\geq 90\%$ of viable malignant cells with no specific cytoplasmic PTEN staining (IHC)
- No prior chemotherapy

AAP + Capivasertib 400 mg
4 days on, 3 days off + ADT

1:1 randomization

AAP + Placebo 4 days on, 3 days
off + ADT

Primary endpoint:

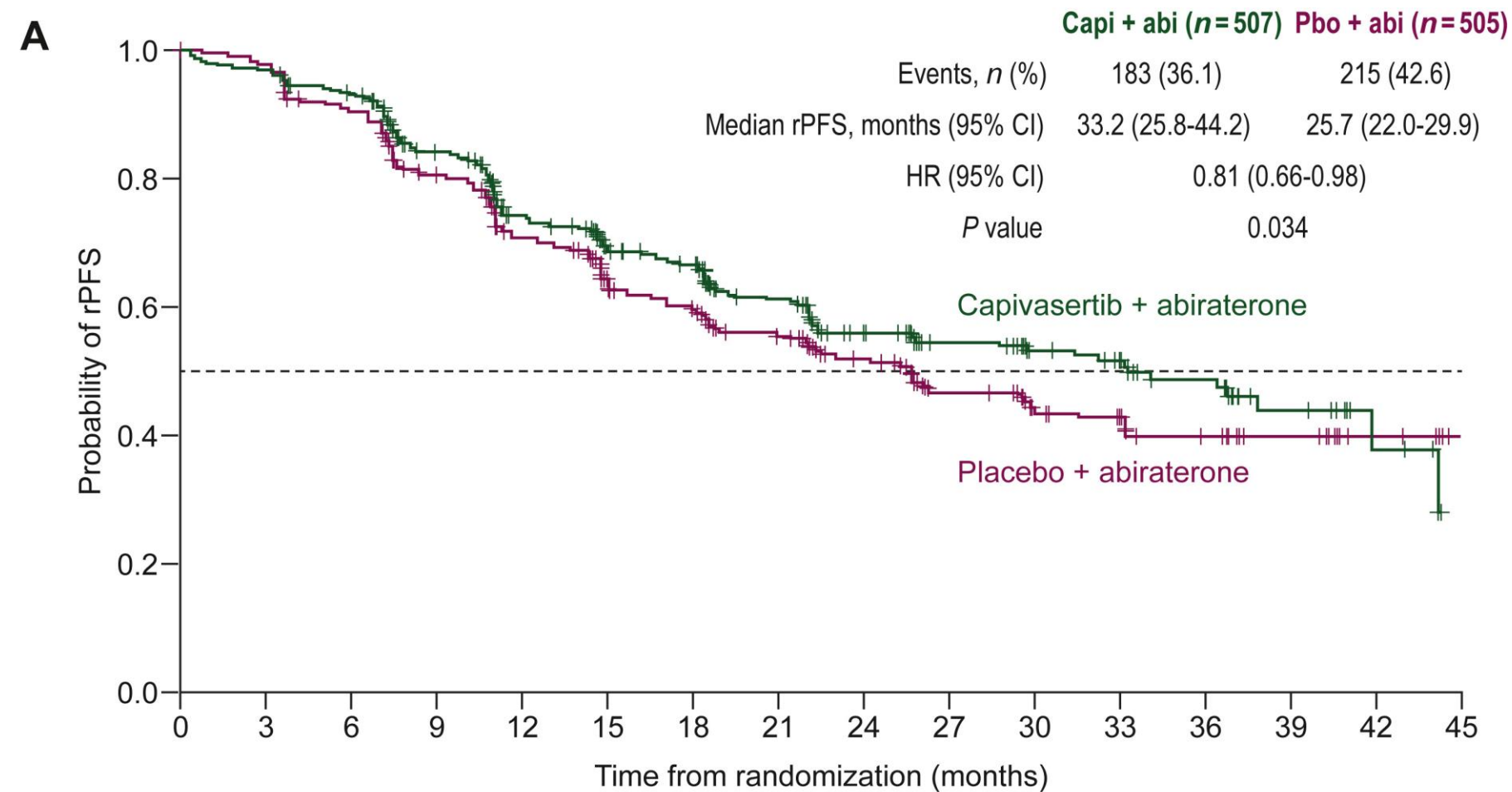
- rPFS by investigator (final analysis)

Secondary endpoint:

- OS

25% of screened patients $\geq 90\%$ of viable malignant cells with no specific cytoplasmic PTEN staining

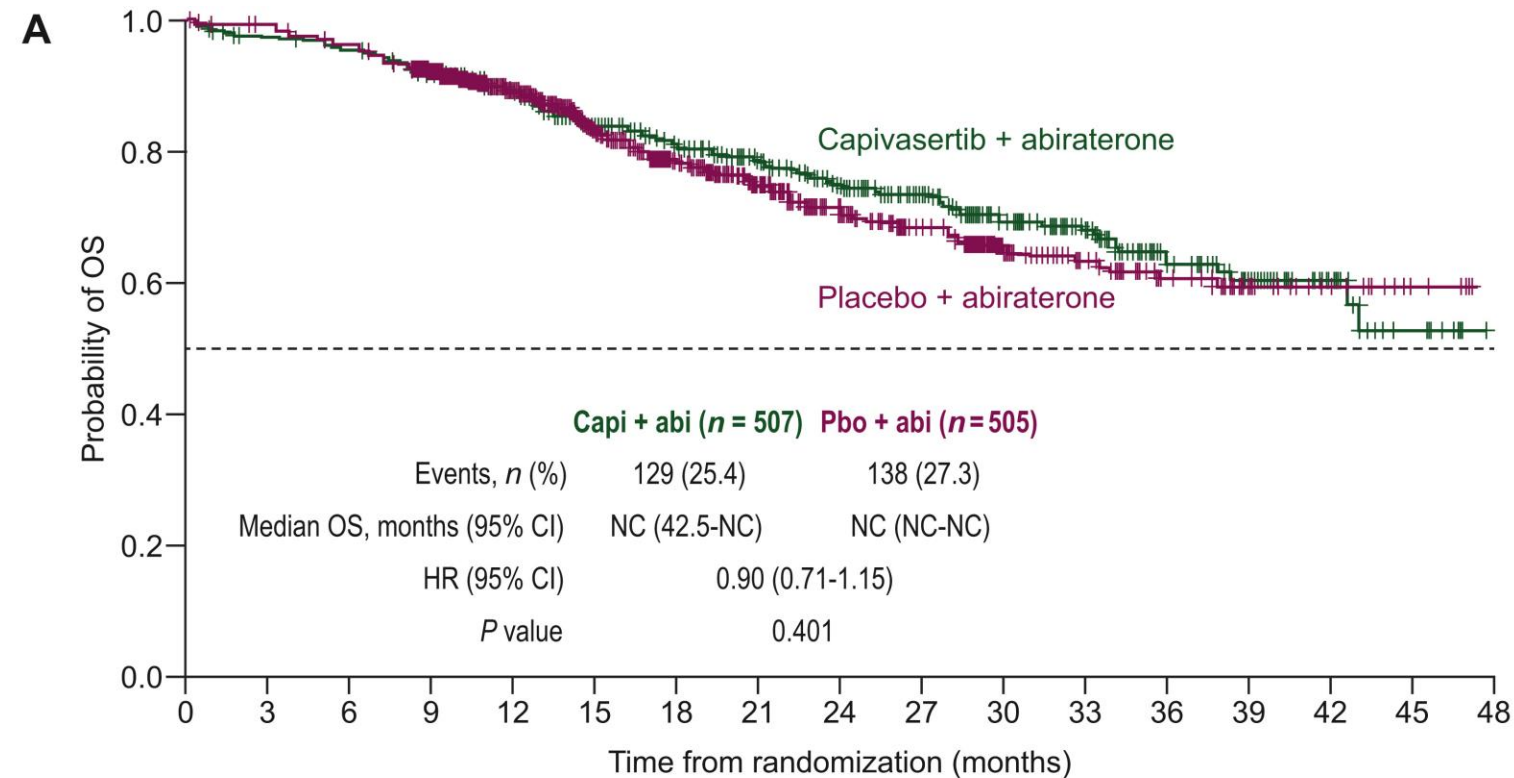
CAPITELLO: rPFS



Number of patients at risk

Capi + abi	507	460	435	353	282	233	217	165	123	93	69	62	41	21	6	0
Pbo + abi	505	479	440	359	276	215	198	154	113	83	59	51	37	23	8	0

CAPITELLO: OS (26% maturiteit)



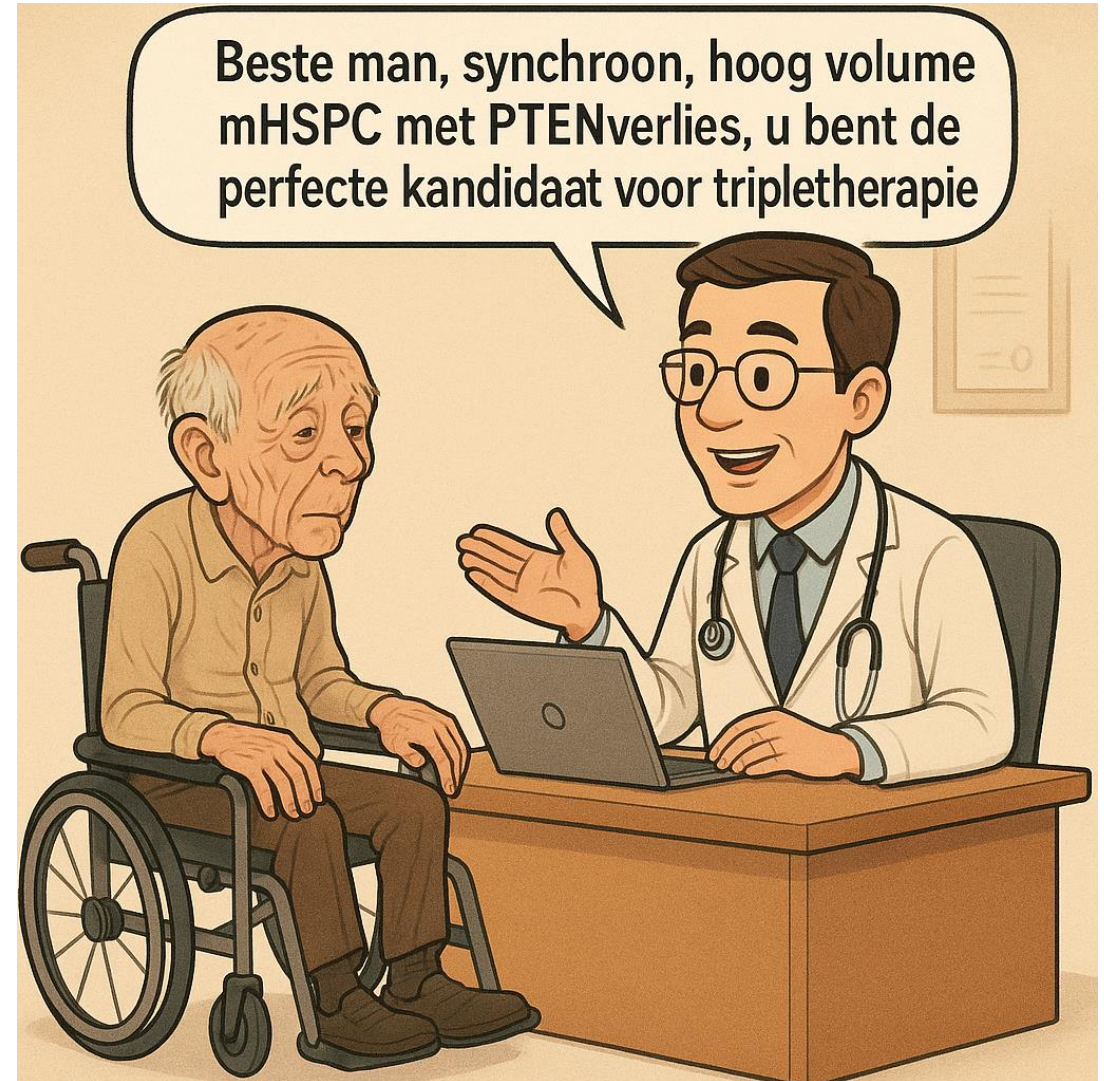
Number of patients at risk

Capi + abi	507	487	476	447	400	335	286	242	199	164	128	96	60	42	22	7	0
Pbo + abi	505	494	479	449	388	330	273	227	188	153	113	88	56	33	19	7	0

Is er nu al een bruikbare marker?



Leeftijd



STOPCAP IPD ARPI meta-analyse



Results: Data available

Eligible: 11 ARPI trials; 11,154 patients

Available: 7 trials; 7,778 patients (70%)

- 4 trials of androgen biosynthesis inhibitors; 4,685 patients (100%)
STAMPEDE (abi), LATITUDE (abi), PEACE-1 (abi), SWOG 1216 (ort)*
- 3 trials of “amides” ± abiraterone; 3,093 patients (48%)
ENZAMET (enz), TITAN (apa), STAMPEDE (abi + enza)

A photograph of a clinical trial data table. The table has multiple columns, including patient ID, treatment, and various outcome measures. The data is organized into rows, with some rows highlighted in blue and others in green. The table is displayed on a screen, and the text is somewhat blurred.

6

* Included in sensitivity analyses only

STOPCAP IPD ARPI meta-analyse



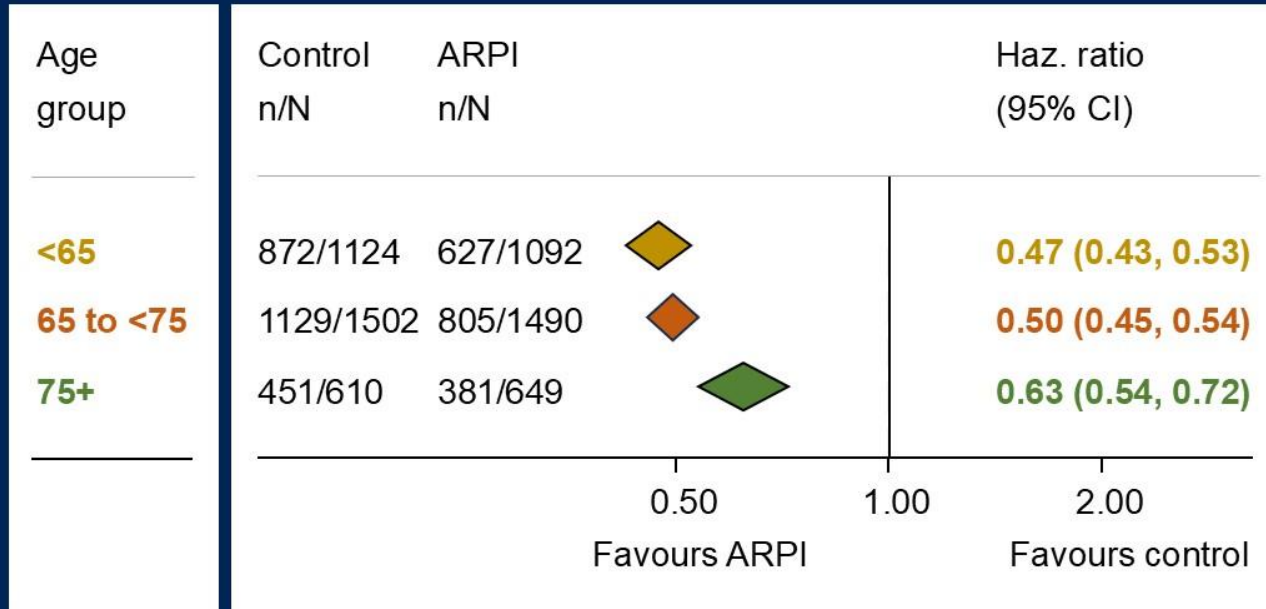
10

Effects of ARPIs on PFS by patient & tumour characteristics

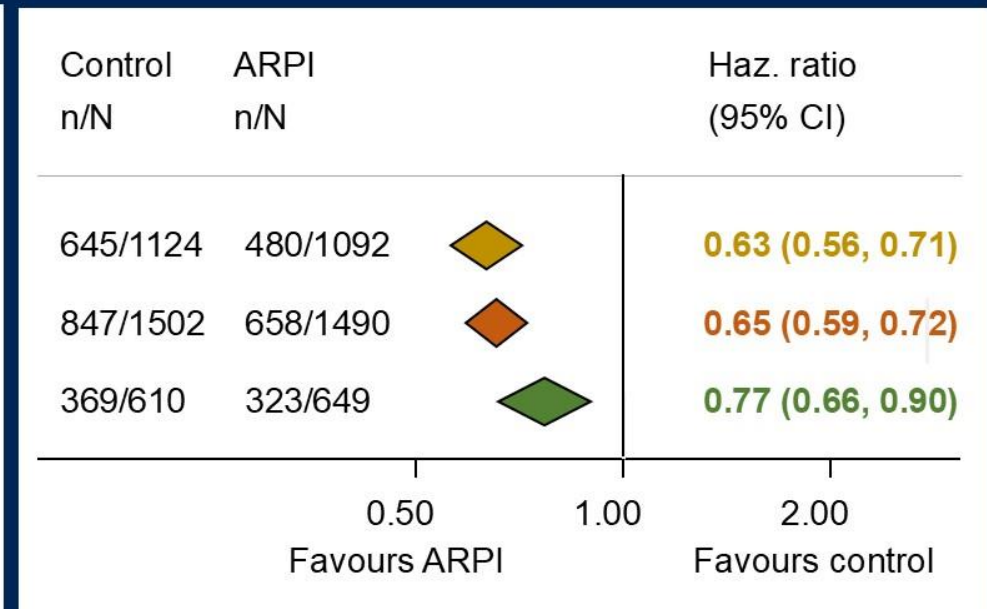
- No clear difference in the effects of ARPIs on PFS by
 - **Volume** of metastases
 - **Timing** of metastatic diagnosis
 - Clinical T-stage
 - Gleason sum score
 - Nodal involvement
 - Location of metastases
 - WHO performance status
 - BMI at randomisation
- Similar results for sensitivity analysis

Effects of ARPIs by age group

PFS



OS



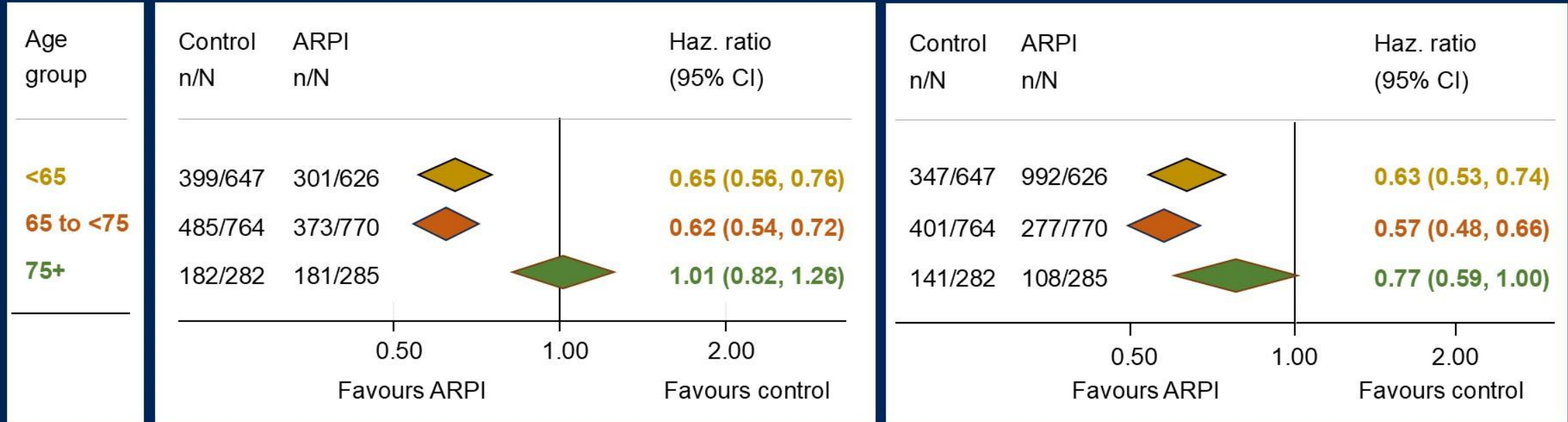
75+ vs <65: Interaction HR=1.32, p=0.003
Heterogeneity p=0.055

Interaction HR=1.22, p=0.052
Heterogeneity p=0.16

Effects of ARPIs by age group: **abiraterone trials**

OS

PCSS*



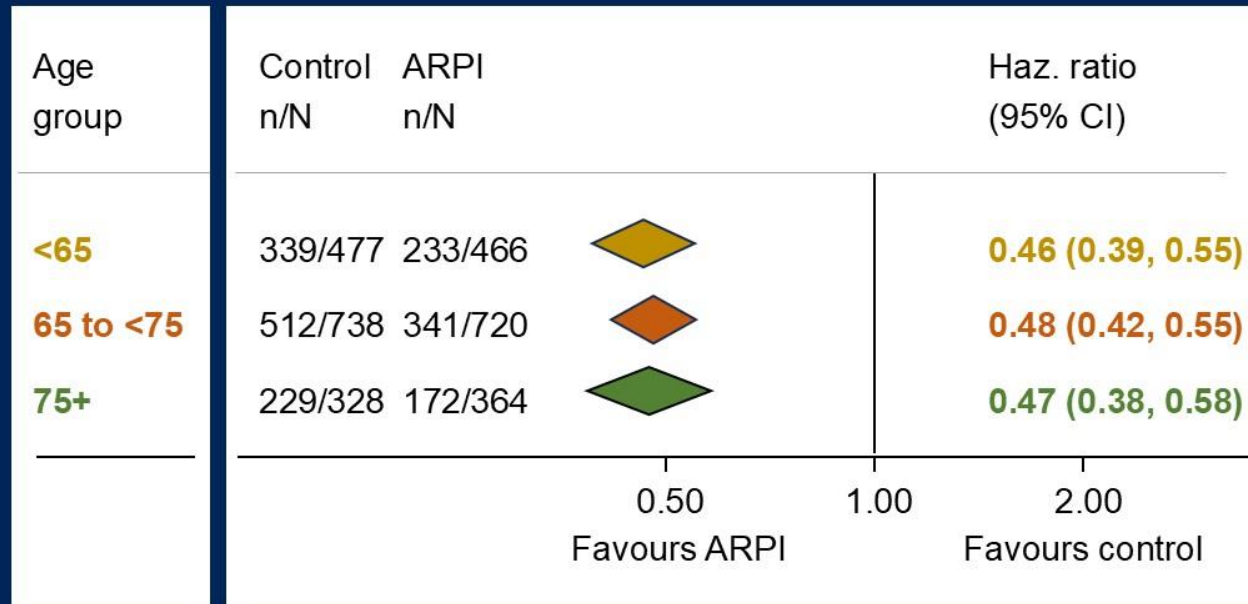
75+ vs <65: Interaction HR=1.56, p=0.001

Interaction HR=1.23, p=0.19

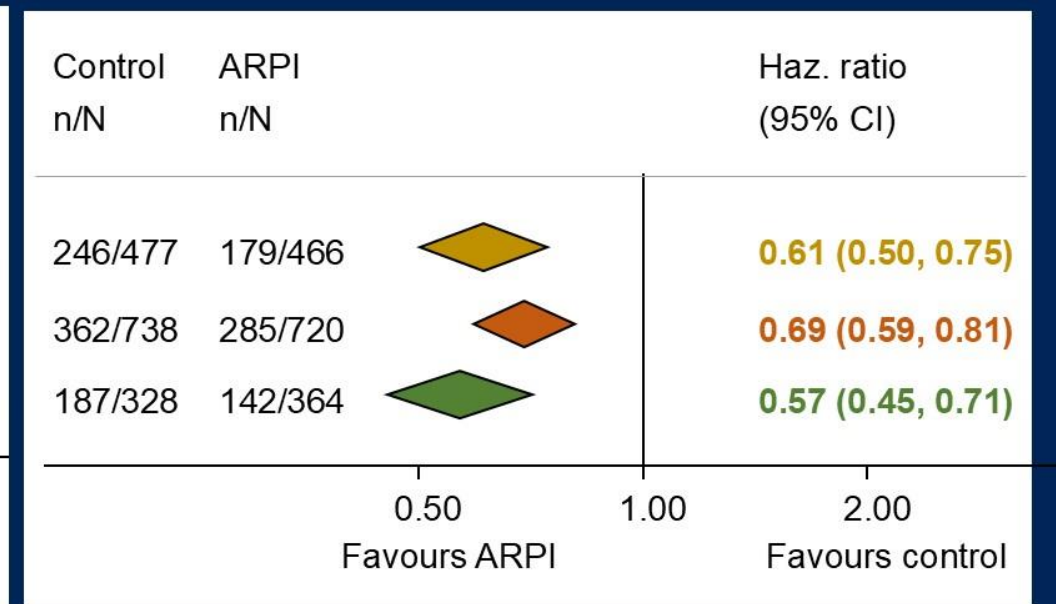
*PCSS=prostate cancer-specific survival

Effects of ARPIs by age subgroup: “amide” trials

PFS



OS



75+ vs <65: Interaction HR=1.02, p=0.88

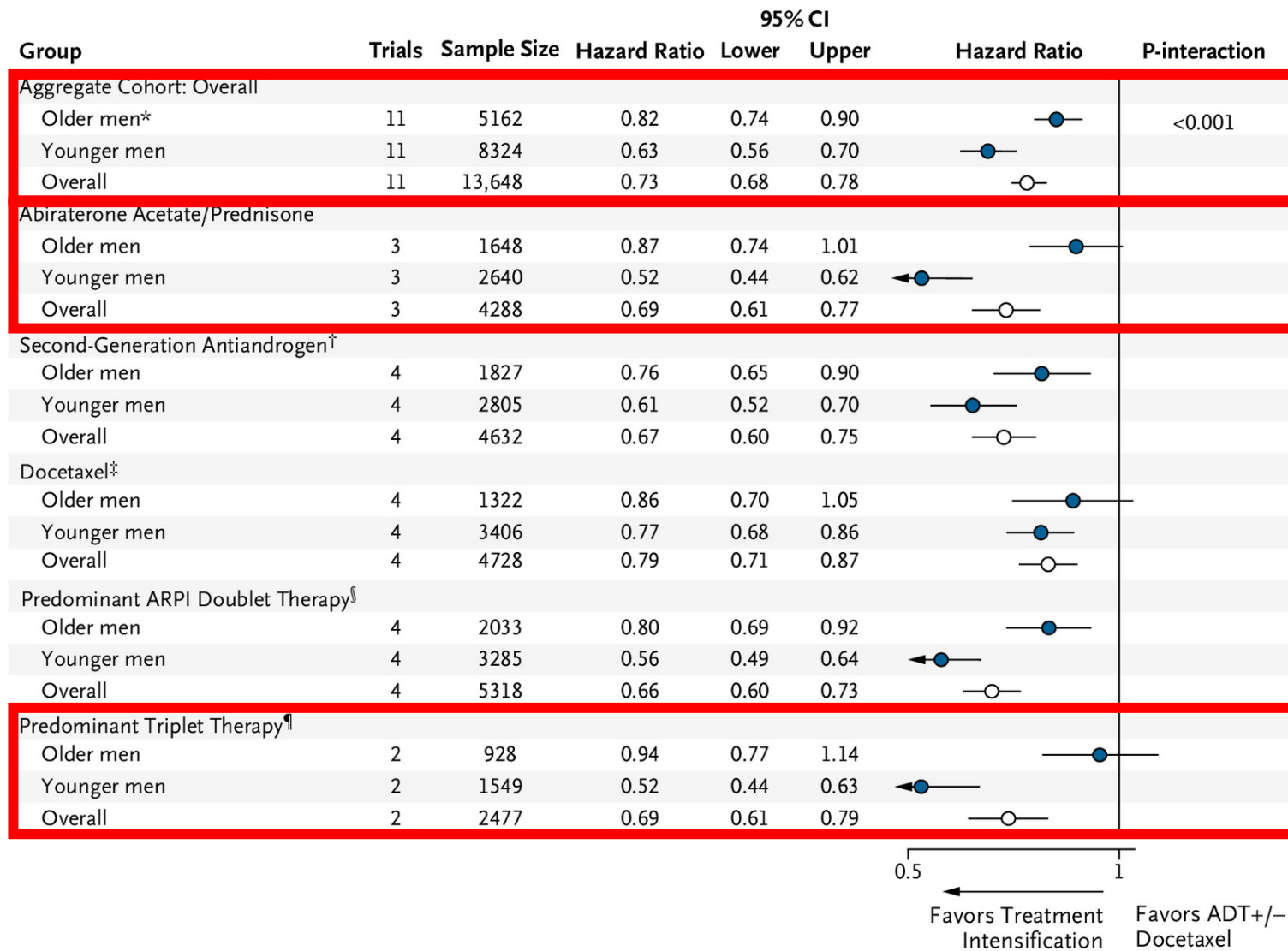
Interaction HR=0.93, p=0.61

Note: 48% available data at present

Meta-analyse NEJM Evidence

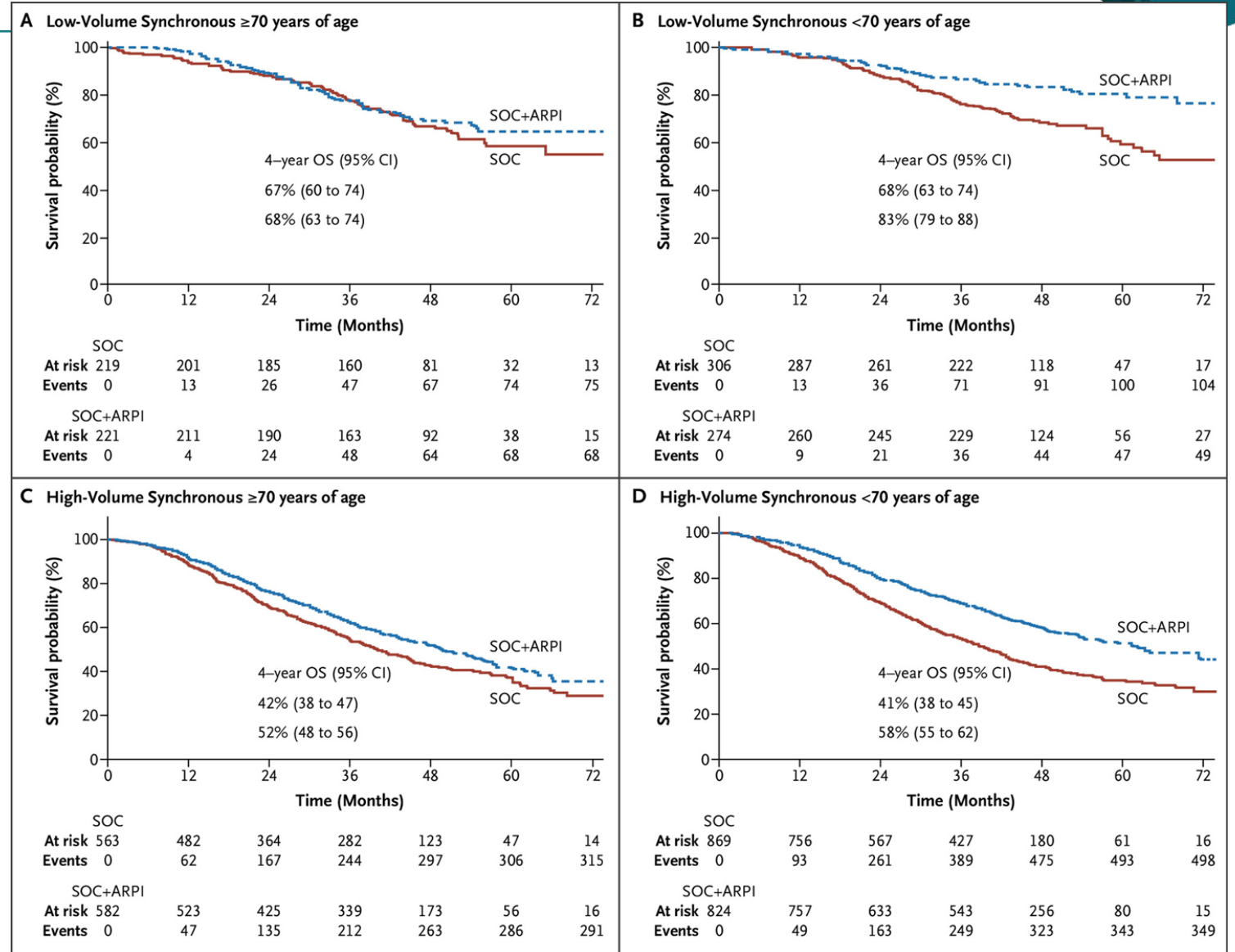


Overall Survival



Meta-analyse NEJM Evidence

- IPD meta-analysis:
TITAN, ARASENS, LATITUDE





**Zijn we klaar voor biomarkergedreven
therapie in mHPSC?**

Waar plaatsen we Lu PSMA?



Waar plaatsen we Lu PSMA?

PSMAAddition



Key eligibility criteria

- mHSPC
- ≥ 1 PSMA-positive metastatic lesion on [68Ga]Ga-PSMA-11 PET/CT
- ECOG: 0-2

^{177}Lu -PSMA-617 7.4 GBq (200 mCi) $\pm$ 10% every 6 weeks for 6 cycles + ADT + ARPI

1:1 randomization

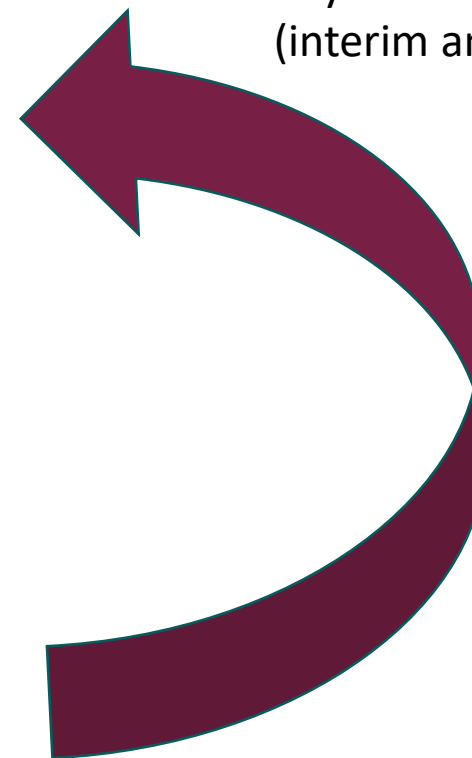
ADT + ARPI

Primary endpoint: rPFS by BICR
(interim analysis: 74% mat)

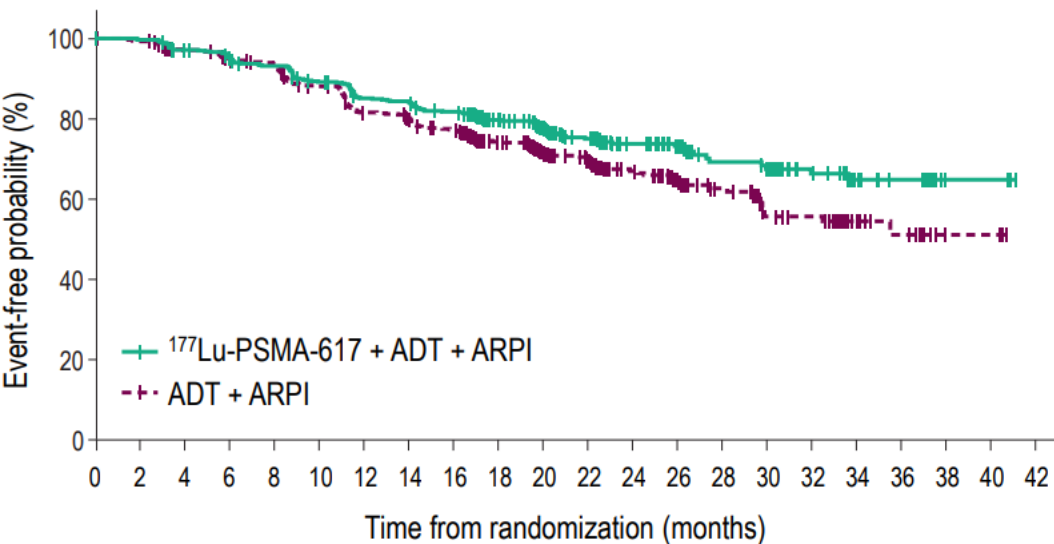
Key secondary endpoint: OS
(interim analysis: 47% mat)

Upon BICR progression, control patients were allowed to cross over to Lu PSMA

- 16% of control arm
- 60% of rPD



PSMAddition: rPFS (74% maturiteit)



Number of patients still at risk

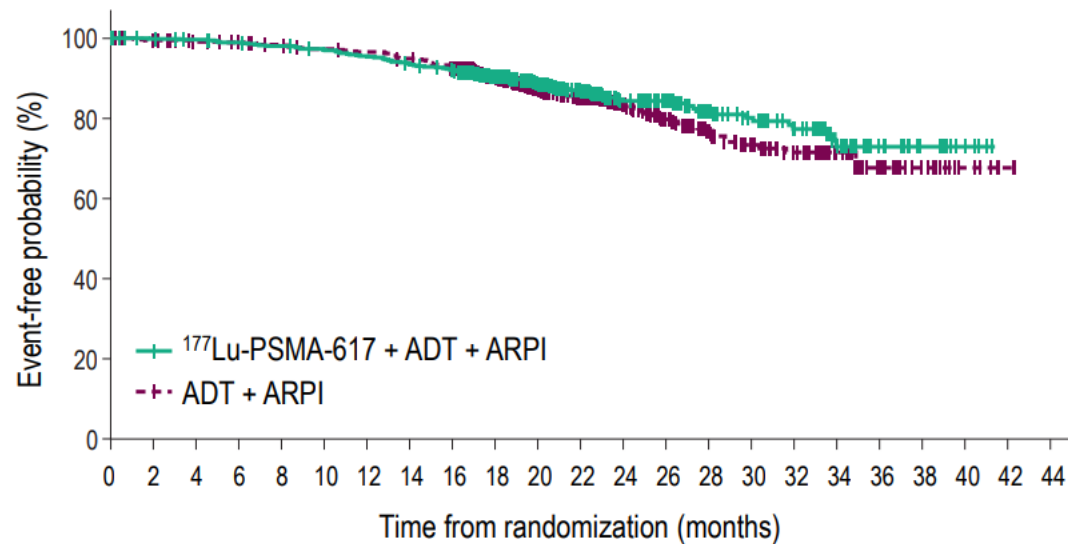
572	558	539	524	512	485	458	452	436	337	252	212	153	134	79	73	59	23	18	3	3	0
572	550	527	507	495	461	424	408	391	304	225	195	134	99	74	50	47	19	15	4	4	0

	¹⁷⁷ Lu-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)

^a Significance threshold at rPFS IA2: 0.009 (one-sided; stratified log-rank test); information fraction, 74.4%
CI, confidence interval; IA, interim analysis; NE, not estimable; NR, not reached



PSMAddition: OS (47% maturiteit)



Number of patients still at risk

572	566	562	556	550	543	533	521	512	424	336	267	195	174	109	94	78	45	27	12	5	0	0
572	561	551	547	539	531	526	516	501	432	315	268	196	159	118	91	72	46	28	16	7	2	0

	¹⁷⁷ Lu-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)

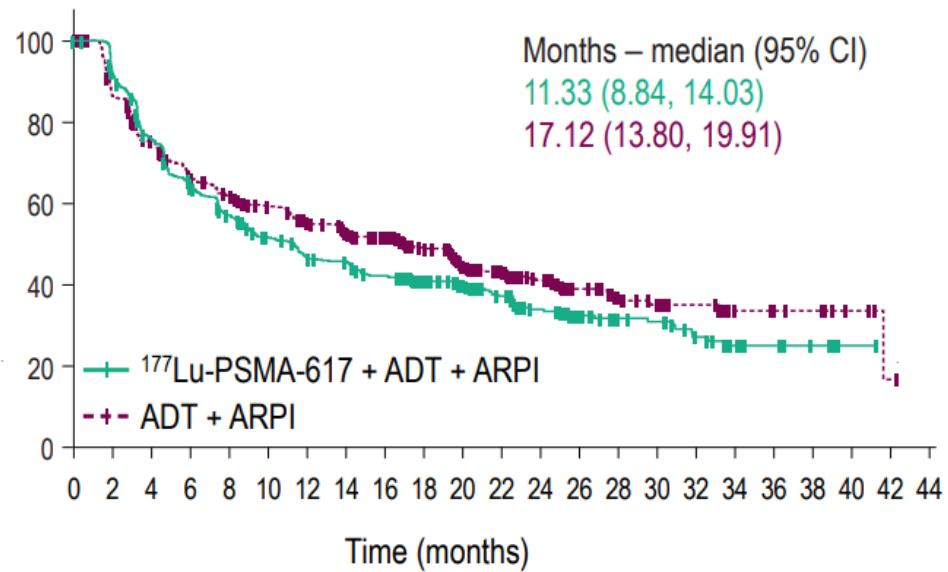
^a Significance threshold at OS IA1: 0.0011 (one-sided; stratified log-rank test); information fraction, 47.3%

PSMAddition: HRQoL



FACT-P total score^a

HR: 1.14 (95% CI: 0.98, 1.33)



Number of patients still at risk

572	509	415	351	305	269	241	234	212	165	124	101	73	54	39	37	28	14	9	6	1	0	0
572	477	410	356	327	304	276	254	239	188	133	117	86	63	44	35	25	12	10	8	4	1	0

Canadian Cancer Trials Group (CCTG) Study PR.21 (Fase II)



Key eligibility criteria

- mCRPC: chemo-naïef, post-ARPI
- PSMA positief (uptake>lever)
- ECOG 0-2

1:1 randomization

^{177}Lu -PSMA-167 7.4GBq (+-10%) elke 6 w x 6

Docetaxel 75mg/m² elke 3 w x 12

progressie

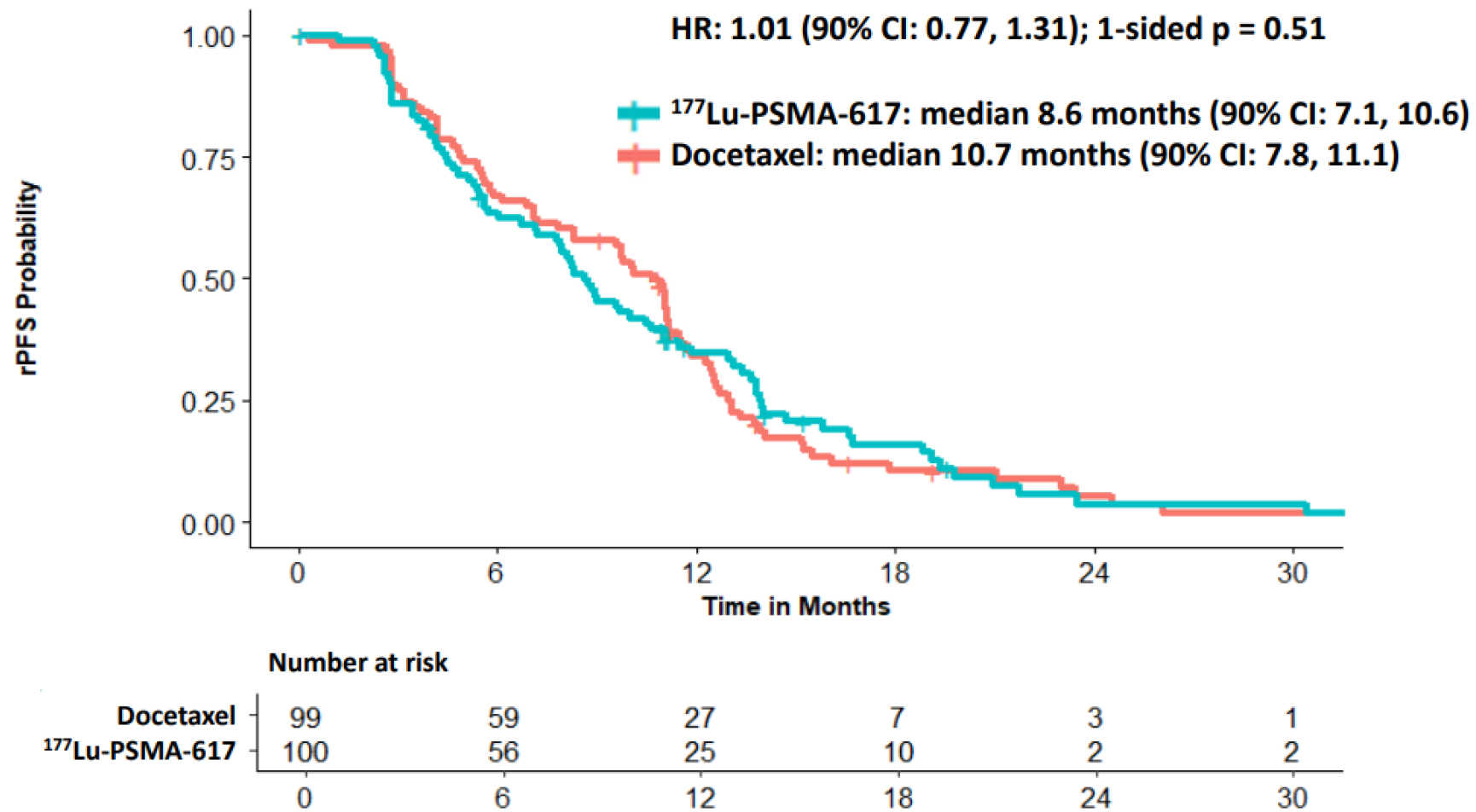
Docetaxel 75mg/m² elke 3 w x 12

^{177}Lu -PSMA-167 7.4GBq (+-10%) elke 6 w x 6

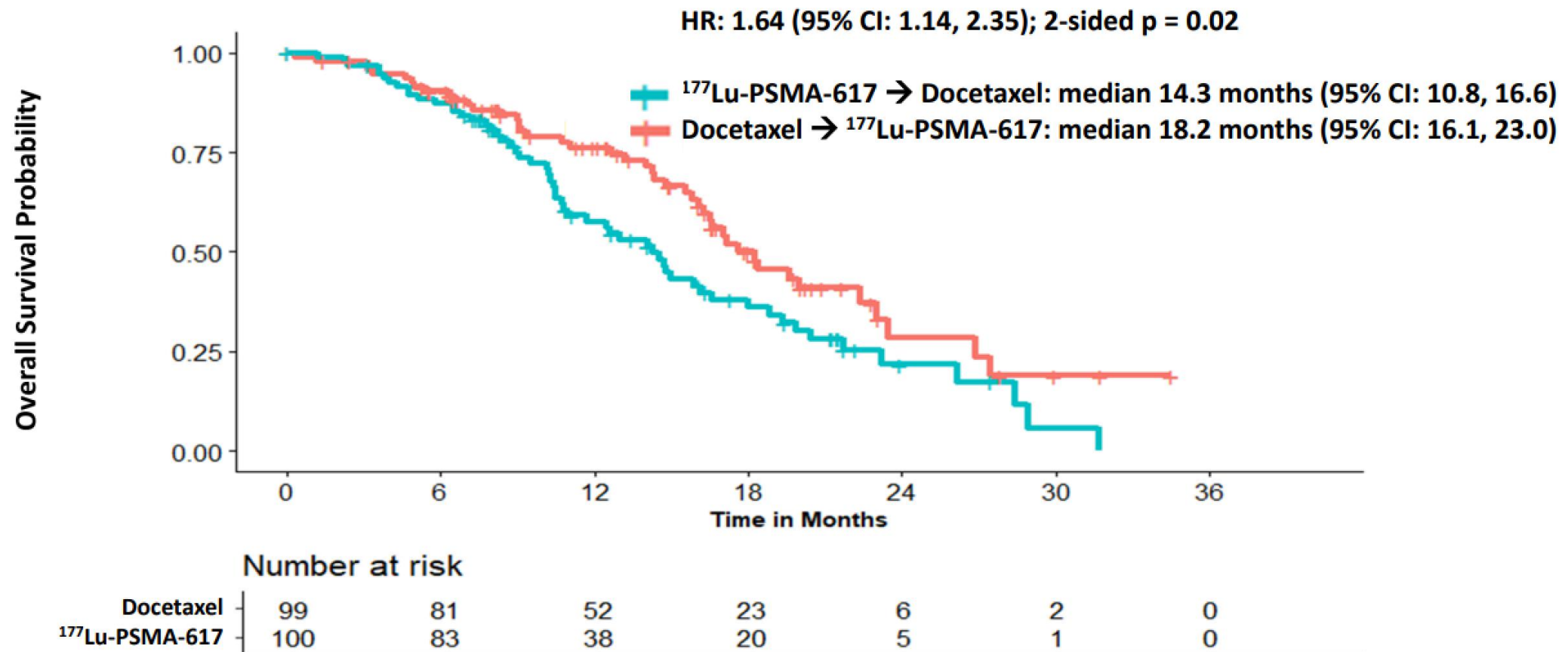
Primaire eindpunt: rPFS1

Sec eindpunt: OS

PR.21: rPFS1



PR.21: OS



Canadian Cancer Trials Group (CCTG) Study PR.21 (Fase II)



Key eligibility criteria

- mCRPC: chemo-naïef, post-ARPI
- PSMA positief (uptake>lever)
- ECOG 0-2

1:1 randomization

^{177}Lu -PSMA-167 7.4GBq (+-10%) elke 6 w x 6

38%

Docetaxel 75mg/m² elke 3 w x 12

progressie

Primaire eindpunt: rPFS1

Sec eindpunt: OS

Docetaxel 75mg/m² elke 3 w x 12

57%

^{177}Lu -PSMA-167 7.4GBq (+-10%) elke 6 w x 6



Prostaat

Blaas



Prostaat

Blaas



**Wat is de optimale peri-operatieve
systeemtherapie bij UCC?**

**Kan ctDNA ons helpen bij adjuvante
behandeling?**



**Wat is de optimale peri-operatieve
systeemtherapie bij UCC?**

Peri-operatieve UCC fase 3 trials



	design	EFS/DFS	OS
NIAGARA	durvalumab, per-operative, open label	✓	✓
AMBASSADOR	pembrolizumab, adjuvant, open label	✓	Immature
CM-274	nivolumab, adjuvant, placebo control	✓	Immature
IMvigor010	atezolizumab, adjuvant, open label	✗	✗

+/- 50%: Cisplatinum-gemcitabine-durvalumab = SOC

+/- 50%: Cisplatinum-ineligible: observatie of nivolumab bij PD-L1 $\geq$ 1%



Perioperative Enfortumab Vedotin Plus Pembrolizumab in Participants With Muscle-invasive Bladder Cancer Who Are Cisplatin-ineligible: Phase 3 KEYNOTE-905 Study

Christof Vulsteke¹, Hristos Z. Kaimakliotis², Pongwut Danchaivijitr³, Maksym Sabadash⁴, Alejo Rodriguez-Vida⁵, Zhentao Zhang⁶, Vagif Atduev⁷, Yunus E. Goger⁸, Steffen Rausch⁹, Seok-Ho Kang¹⁰, Yohann Lorient¹¹, Jens Bedke¹², Matthew D. Galsky¹³, Peter H. O'Donnell¹⁴, Michael Mihm¹⁵, Changting Meng¹⁶, Caizhi David Huang¹⁷, Chethan Ramamurthy¹⁷, Blanca Homet Moreno¹⁷, Anders Ullén¹⁸

¹Integrated Cancer Center Ghent, AZ Maria Middelares, Ghent, Belgium, and Center for Oncological Research, Antwerp University, Antwerp, Belgium; ²Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Indianapolis, IN, USA; ³Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand; ⁴Lviv State Regional Oncological Center, Lviv, Ukraine; ⁵Hospital del Mar, Barcelona, Spain; ⁶Parkview Cancer Institute, Fort Wayne, IN, USA; ⁷Volga District Medical Center, Federal Medical-Biological Agency, Nizhny Novgorod, Russia; ⁸Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Hastanesi, Konya, Türkiye; ⁹Eberhard Karls University, Tübingen, Germany; ¹⁰Korea University Anam Hospital; Seoul, South Korea; ¹¹Institut Gustave Roussy, Université Paris-Saclay, Villejuif, France; ¹²Eva Mayr-Stihl Cancer Center, Klinikum Stuttgart, Stuttgart, Germany; ¹³Icahn School of Medicine at Mount Sinai, Tisch Cancer Institute, New York, NY, USA; ¹⁴The University of Chicago, Chicago, IL, USA; ¹⁵Astellas Pharma Inc, Northbrook, IL, USA; ¹⁶Pfizer, Bothell, WA, USA; ¹⁷Merck & Co., Inc., Rahway, NJ, USA; ¹⁸Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden and Department of Pelvic Cancer, Genitourinary Oncology and Urology unit, Karolinska University Hospital, Stockholm, Sweden



Christof Vulsteke

Perioperative (periop) enfortumab vedotin (EV) plus pembrolizumab (pembro) in participants (pts) with muscle-invasive bladder cancer (MIBC) who are cisplatin-ineligible: The phase III KEYNOTE-905 study

BERLIN AUDITORIUM - HUB 27

Keynote-905



Key eligibility criteria

- MIBC (cT2–T4aN0/1M0) by central assessment
- ≥50% Urothelial histology
- Cisplatin-ineligible per Galsky criteria or cisplatin-declining (18%)
- ECOG PS 0-2

3XEV-P

Enfortumab vedotin 1.25 mg/kg d1 and d8 IV Q3W +
Pembrolizumab 200 mg IV Q3W

1:1 randomisation
N: 344

Immediately to...

6XEV-P, 8xP

Enfortumab vedotin 1.25 mg/kg d1 and d8 IV Q3W +
Pembrolizumab 200 mg IV Q3W

Primary endpoint

- EFS

Key secondary endpoint

- OS
- pCR

**Radical
cystectomy**

88%

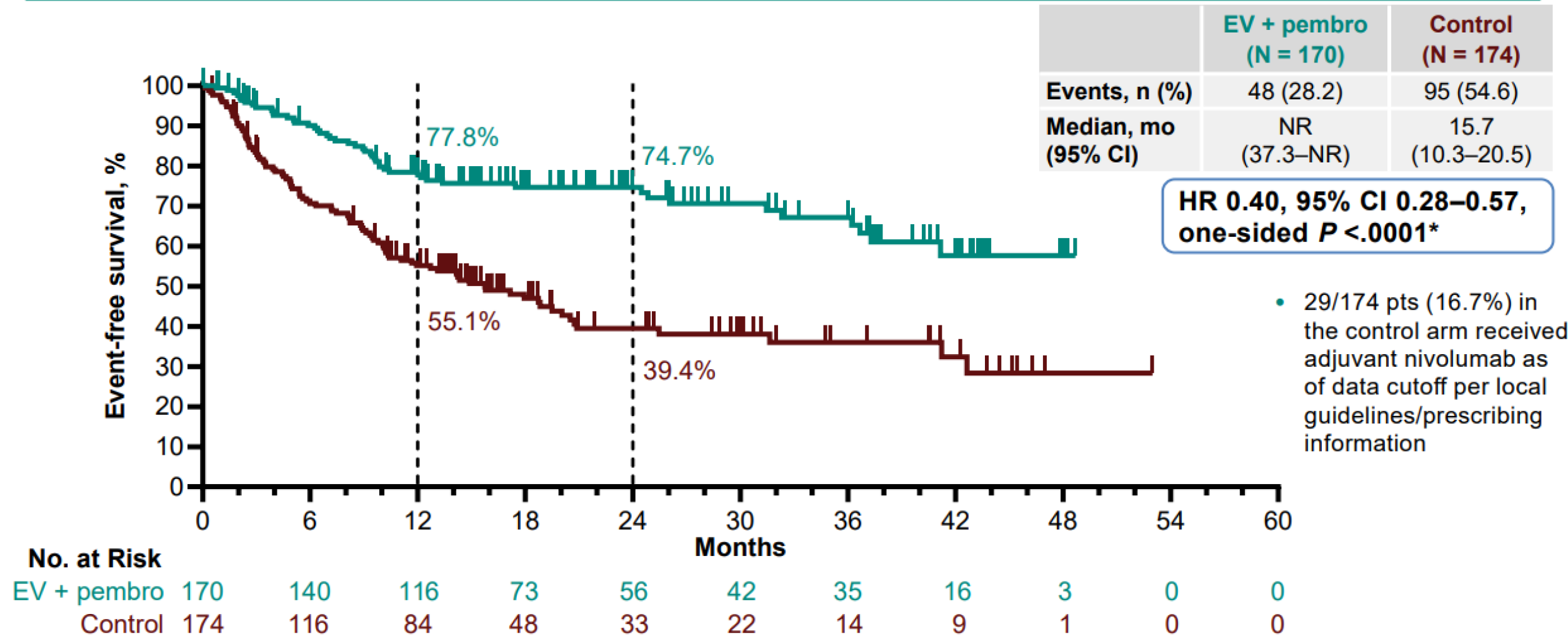
66%

89%

No treatment
(16% nivolumab)

Primary Endpoint: EFS^a by BICR

ITT Population

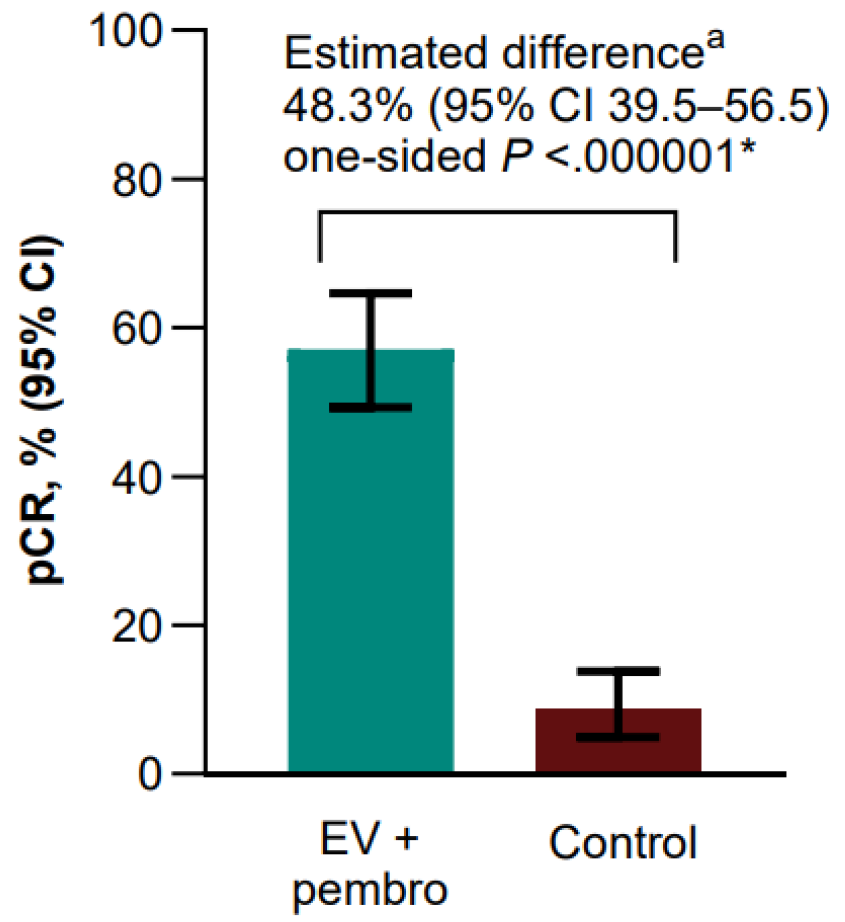


NR, not reached. * denotes statistical significance (one-sided boundary 0.0097). ^aTime from randomization to first occurrence of: radiographic PD precluding surgery; biopsy-proven residual MIBC (pts who did not undergo surgery); gross residual disease post-surgery or newly detected metastatic disease at surgery; local/distant recurrence post-surgery (imaging or biopsy); or death (any cause). Any new high-risk NMIUC was also considered an event. Pts who did not undergo surgery were considered as having an EFS event if they met criteria for EFS events at any point in time or were censored within ≤16 wks from last dose of neoadjuvant therapy or surgery.

Data cutoff date: 6 June 2025

Key Secondary Endpoint: pCR by Central Pathology Review

ITT Population



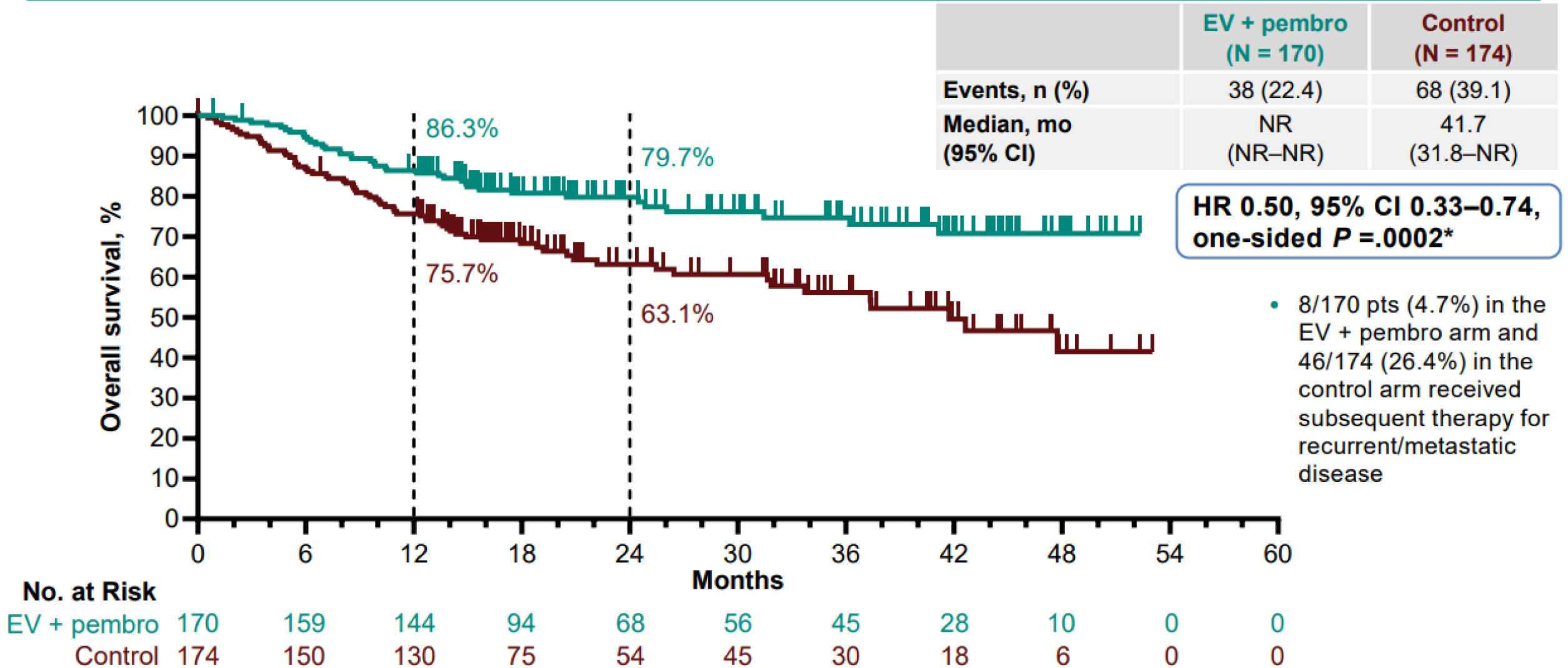
	EV + pembro (N = 170)	Control (N = 174)
pCR, n	97	15
pCR rate, % (95% CI)	57.1 (49.3–64.6)	8.6 (4.9–13.8)

- **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

* denotes statistical significance (one-sided boundary 0.00025).
^aBased on stratified Miettinen and Nurminen method.

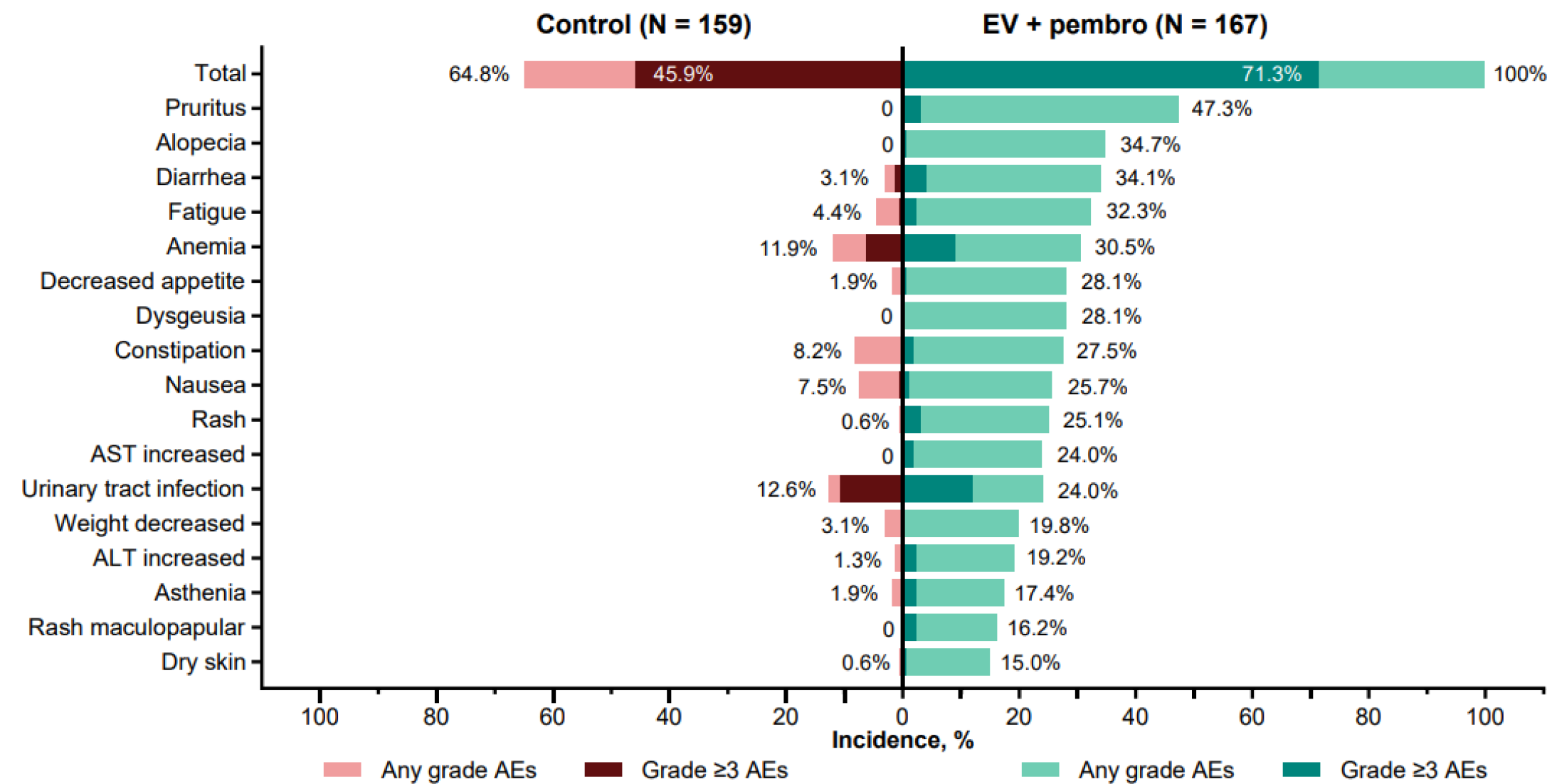
Key Secondary Endpoint: OS

ITT Population



Common TEAEs^a (Incidence $\geq 15\%$), All Phases of Treatment

Safety Analysis Population



^aCollected up to 30 days after cessation of study treatment.



**Wat is de optimale peri-operatieve
systeemtherapie bij UCC?**

**Kan ctDNA ons helpen bij adjuvante
behandeling?**



**Kan ctDNA ons helpen bij adjuvante
behandeling?**

Bij de oncoloog na cystectomie...

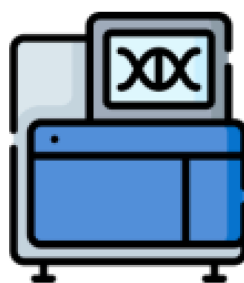


Tumour-informed ctDNA tests

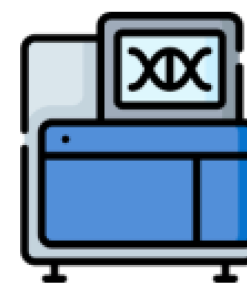
Retrieve tumour
tissue



Sequence tissue to
find truncal mutations



Sequence cfDNA for
these mutations



IMvigor011

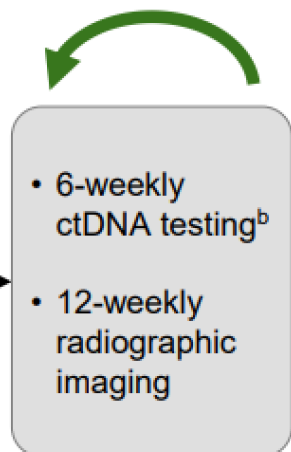


Screening

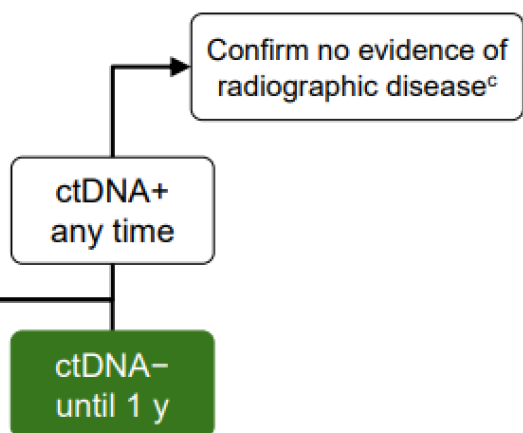
- MIBC within 6–24 weeks of radical cystectomy
- Histologically confirmed (y)pT2–T4aN0M0 or (y)pT0–T4aN+M0 urothelial cancer
- No evidence of radiographic disease
- Prior neoadjuvant chemotherapy permitted
- ECOG PS 0–2

Surveillance ctDNA monitoring

until 1 y post-cystectomy^a



Repeat testing
if ctDNA–



Treatment

Atezolizumab (1680 mg)
IV q4w for up to 1 y

Placebo
IV q4w for up to 1 y

Follow-up

Treatment
follow-up

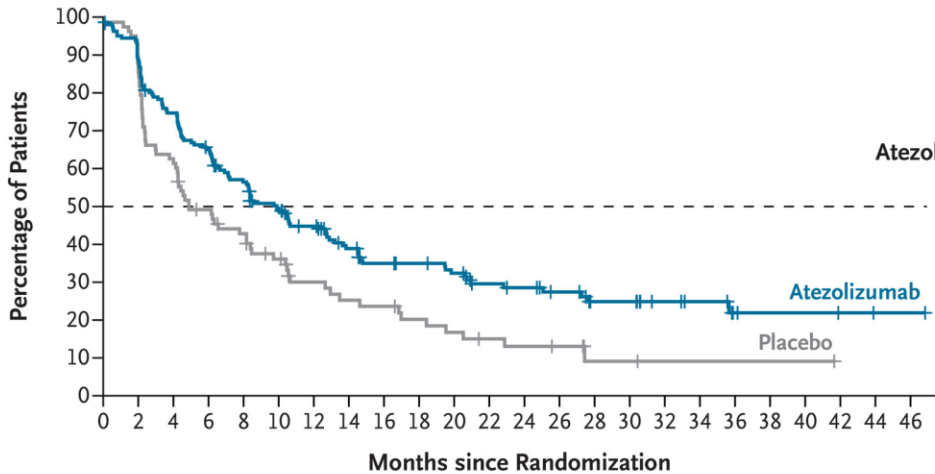
No treatment

Surveillance
follow-up

Primary endpoint: INV-assessed DFS
Key secondary endpoint: OS



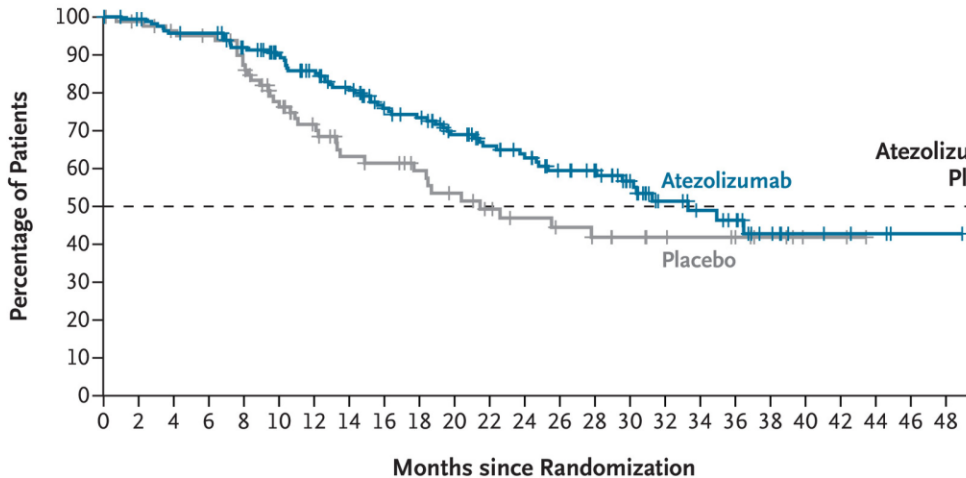
A Disease-free Survival among All Patients with ctDNA-Positive Status



No. at Risk

Atezolizumab	167	145	122	105	89	73	63	50	42	40	36	28	26	22	16	16	11	9	4	3	3	2	1	1
Placebo	83	69	50	38	32	25	18	15	14	11	9	7	6	5	2	2	1	1	1	1	1	1	1	1

B Overall Survival among All Patients with ctDNA-Positive Status

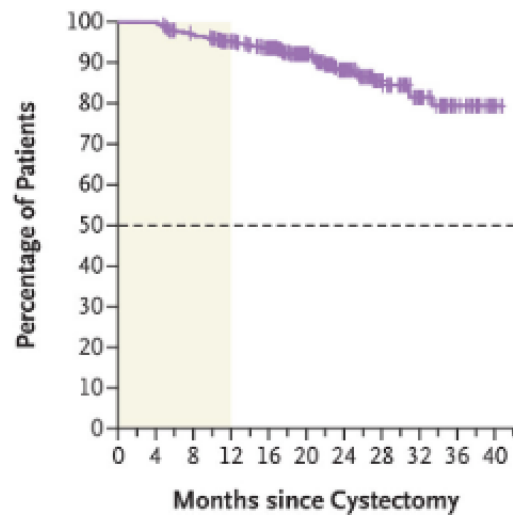


No. at Risk

Atezolizumab	167	162	155	154	143	130	118	108	92	86	75	65	59	51	43	30	23	19	12	7	5	3	2	1	1
Placebo	83	80	76	74	65	53	44	36	34	30	26	21	19	17	15	13	10	10	8	5	2	1			

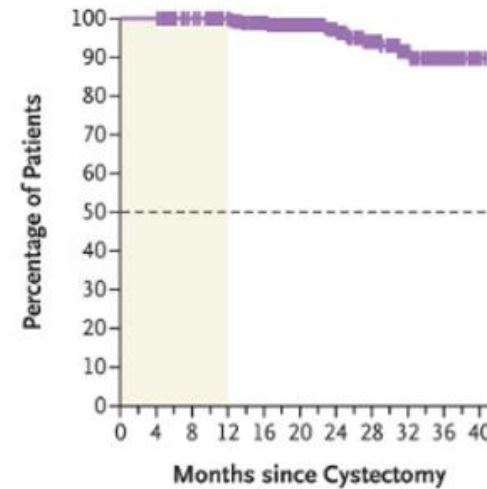


C Disease-free Survival among Patients with Persistent ctDNA-Negative Status



No. at Risk
 No atezolizumab 357 357 337 303 275 185 116 78 46 20 3
 or placebo

F Overall Survival among Patients with Persistent ctDNA-Negative Status



No. at Risk
 No atezolizumab 357 357 340 319 288 198 138 96 55 26 4
 or placebo

CAVE: Hervalrisico met 1 ctDNA negatief staal post-op: 30%

Toekomst?



Thomas?



Q&A