ANTONI VAN LEEUWENHOEK
NEDERLANDS KANKER INSTITUUT

Masterclass urologische oncologie

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Disclosures

- Aandelen of persoonlijke belangen: Geen
- Onderzoeksfinanciering: Bayer B.V.
- Consultancy/advies: Merck/MSD
  AstraZeneca B.V.
  Ipsen B.V.
  Johnson & Johnson
  Novartis

Overzicht

- Casuistiek
- Standaard systeembehandeling
- Innovaties
- Wat is er in aantocht?

- Prostaatcarcinoom, niercelcarcinoom

Take home message

- Intensieve systeemtherapie bij diagnose van mHSPC geeft langere overleving
- Wat is de optimale eerstelijns ‘triple therapie’?
- De opkomst van de ‘drug holiday’

Casus, Dhr G, 63jr

- 2016 Gonartrose rechts
- 2016 AVNRT, ablatie
- 2022-7 Locoregionaal prostaatcarcinoom, pT3b N0 M0, Gleason 5+4=9, iPSA 8.9
- 2022-7 RALP met lymfeklierdissectie
- 2023 blaashalsstenose, open blaashalsplastiek
- 2025 biochemisch recidief prostaatcarcinoom, PSMA-PET/CT: avide afwijking vesikel

Behandeling?

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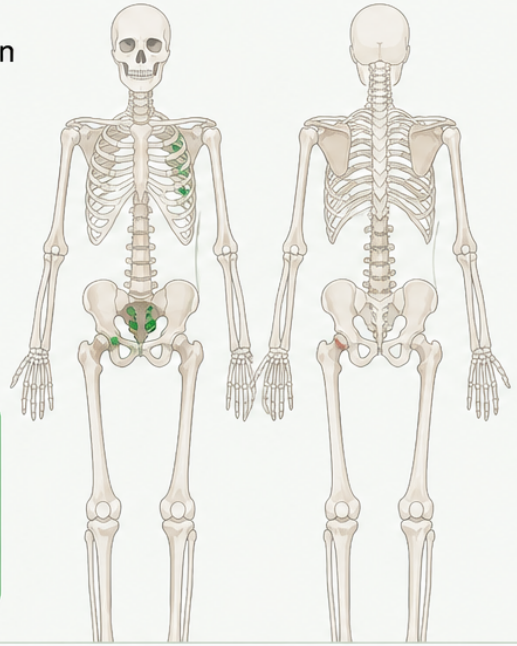
- 2025-11 Gemetastaseerd prostaatcarcinoom, PSMA-PET/CT: metastasen costa links, lymfeklieren

Behandeling?

De klinische kenmerken voor therapie keuze

Laag volume

- ≤ 4 botmetastasen
- geen viscerale metastasen



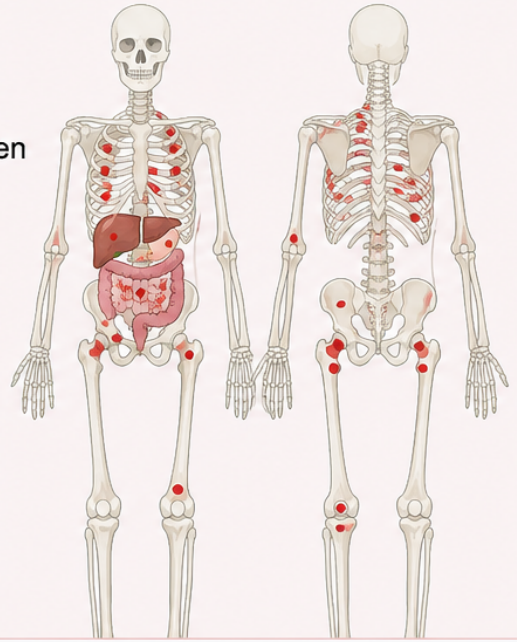
Voorbeelden

- 1–3 botmetastasen
- beperkt tot skelet

Hoog volume

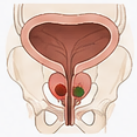
- > 4 botmetastasen

  en/of
- viscerale metastasen



Voorbeelden

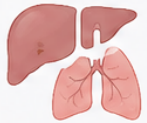
- > 4 botmetastasen
- metastasen in organen (lever, longen, etc.)



Primaire tumor (prostaat)

Botmetastase (laag volume)

Botmetastase (hoog volume)

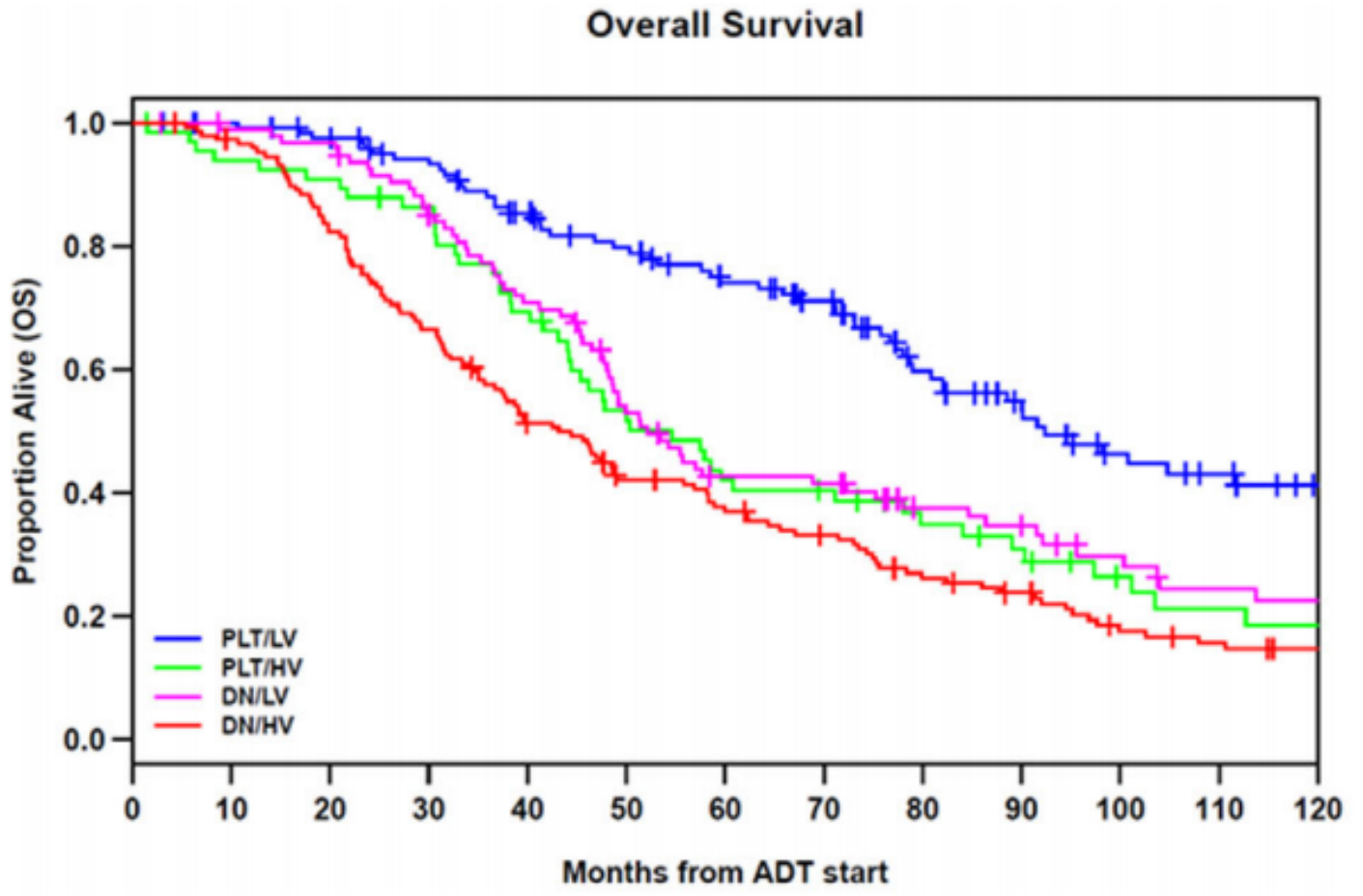


Viscerale metastase

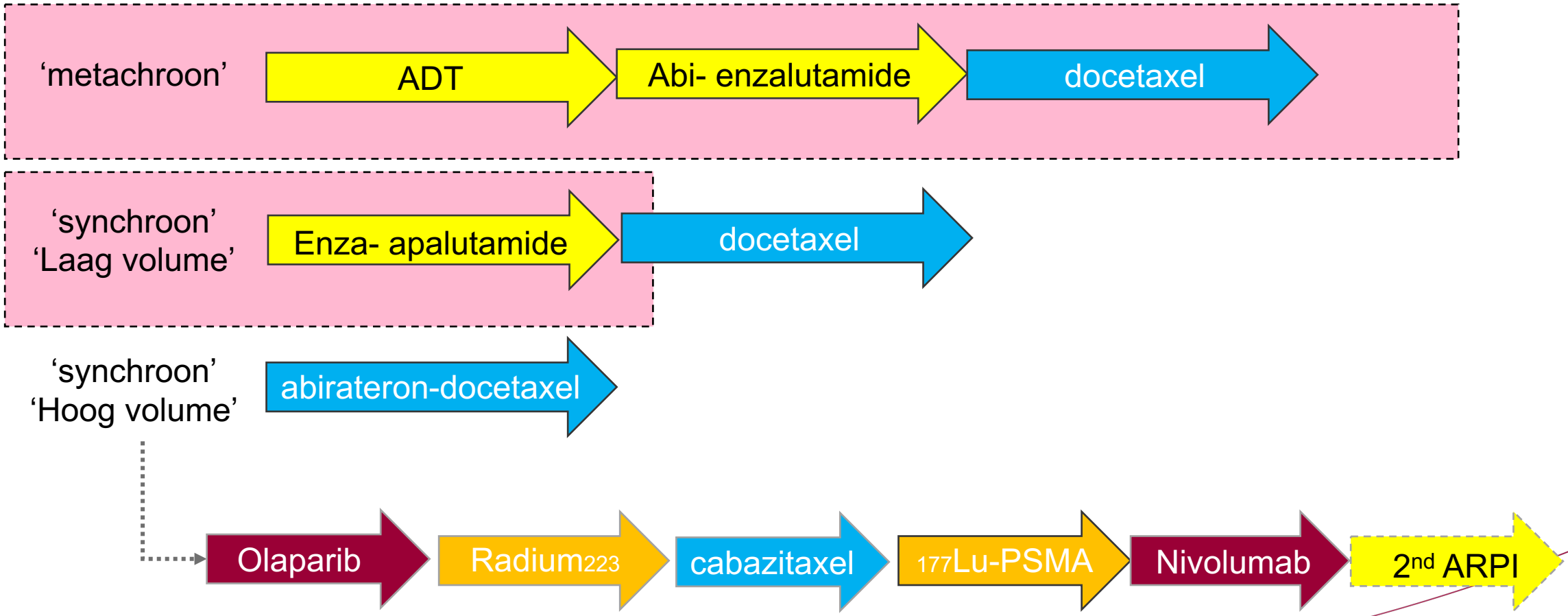
De klinische kenmerken voor therapie keuze

SYNCHROON

METACHROON



‘Patient journey prostaat’



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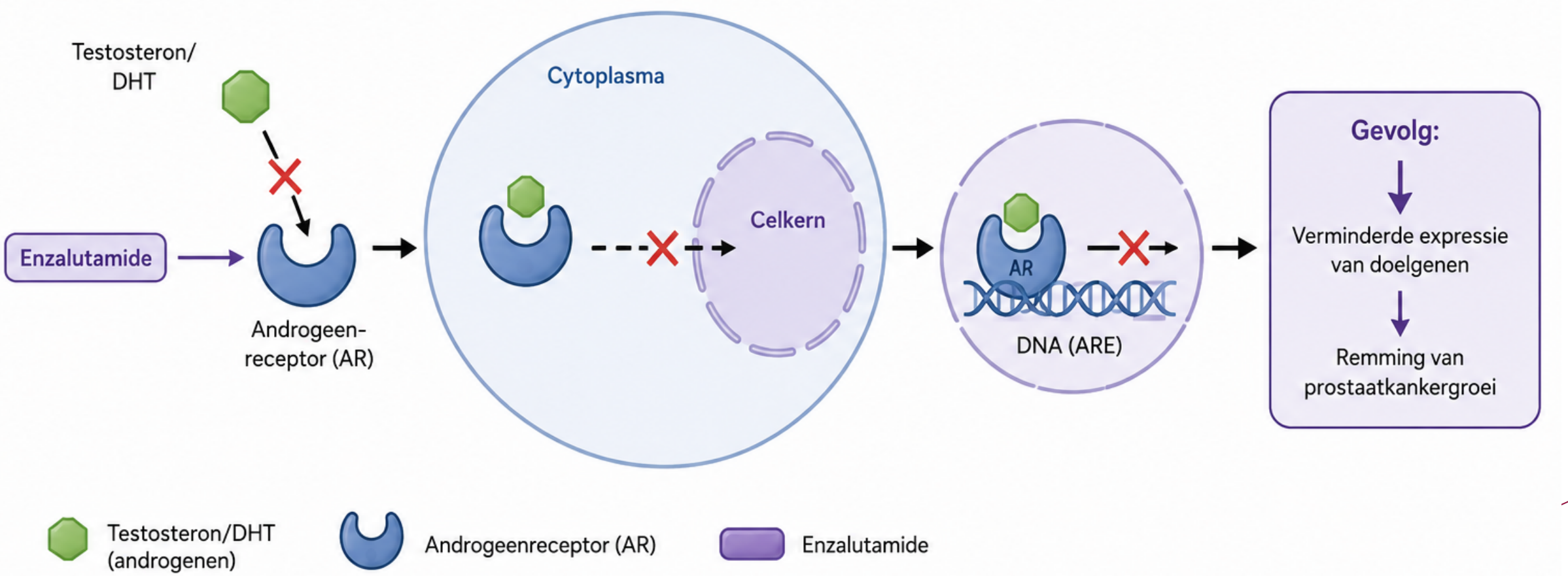
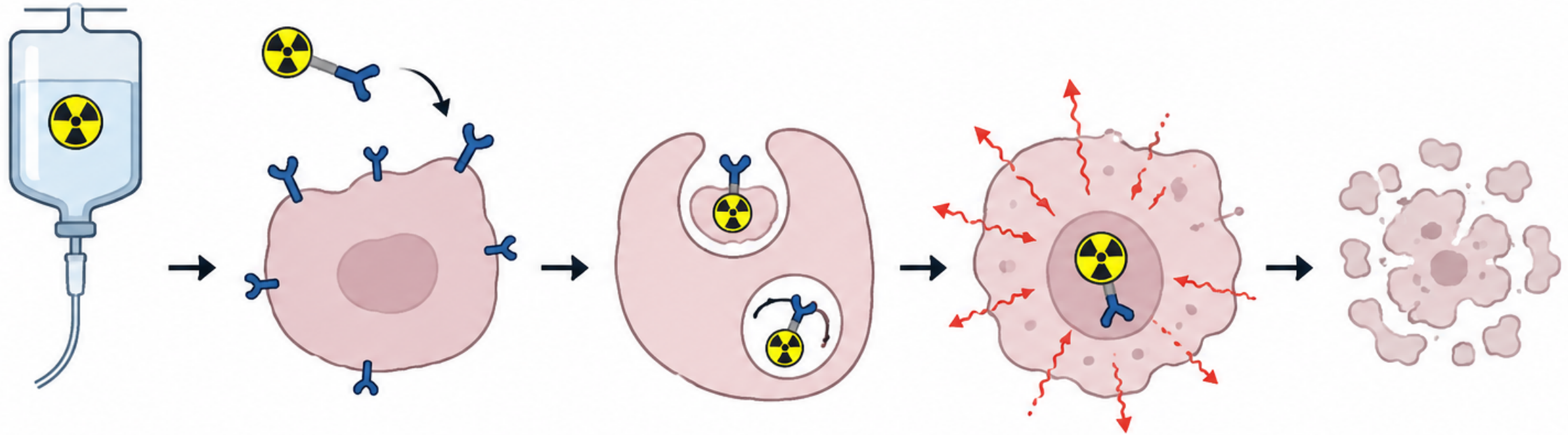
Behandeling ADT monotherapie?

Overzicht onderzoek



Overzicht onderzoek

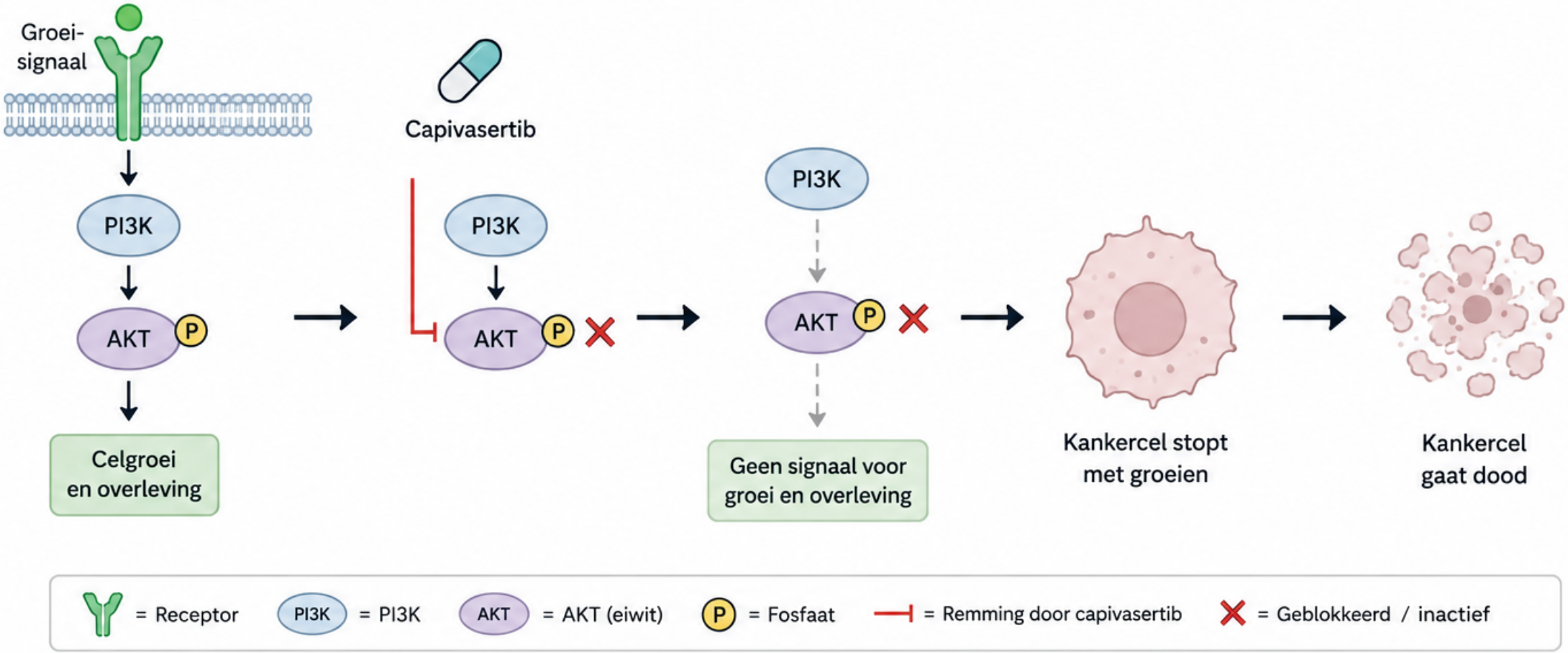


Lutetium-177 (Lu-177)

PSMA (Prostaat Specifiek Membraan Antigeen)

Lu-PSMA

Overzicht onderzoek



LBA87

Plain Language Summary

Video

BERLIN 2025 ESMO congress

Overall survival with enzalutamide in biochemically recurrent prostate cancer

Neal D. Shore,[1] Murilo de Almeida Luz,[2] Ugo De Giorgi,[3] Martin Gleave,[4] Geoffrey T. Gotto,[5] Christopher M. Pieczonka,[6] Gabriel P. Haas,[7] Choung-Soo Kim,[8] Miguel Ramirez-Backhaus,[9] Antti Rannikko,[10] Matko Kalac,[11] Swetha Sridharan,[12] Matt Rosales,[7] Yiyun Tang,[13] Ronald F. Tutrone Jr,[14] Balaji Venugopal,[15] Arnauld Villers,[16] Henry H. Woo,[17] Fong Wang,[13] and Stephen J. Freedland[18]

[1]START Carolinas/Carolina Urologic Research Center, Myrtle Beach, SC, USA; [2]Division of Urologic Oncology, Erasto Gaertner Hospital, Curitiba, Brazil; [3]Department of Medical Oncology, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Meldola, Italy; [4]Vancouver Prostate Centre, University of British Columbia, Vancouver, BC, Canada; [5]Southern Alberta Institute of Urology, University of Calgary, Calgary, AB, Canada; [6]Clinical Research, U.S. Urology Partners and Associated Medical Professionals of New York, Syracuse, NY, USA; [7]Oncology Global Development, Astellas Pharma Inc., Northbrook, IL, USA; [8]Department of Urology, Ewha Womans University Mokdong Hospital, Seoul, South Korea; [9]Servicio de Urología, Fundación Instituto Valenciano de Oncología, Valencia, Spain; [10]Department of Urology and Research Program in Systems Oncology, University of Helsinki, Helsinki, Finland; [11]Global Product Development, Pfizer Inc., New York, NY, USA; [12]Department of Radiation Oncology, Calvary Mater Newcastle, Waratah, NSW, Australia; [13]Pfizer Oncology Division, Pfizer Inc., South San Francisco, CA, USA; [14]Chesapeake Urology Research Associates, Towson, MD, USA; [15]Beatson West of Scotland Cancer Centre, University of Glasgow, Glasgow, UK; [16]Department of Urology, University of Lille, Claude Huriez Hospital, Centre Hospitalier Universitaire Lille, Lille, France; [17]Department of Urology, Blacktown and Mount Druitt Hospitals, Blacktown, NSW, Australia; Department of Uro-Oncology, Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [18]Department of Urology, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA; Section of Urology, Durham VA Medical Center, Durham, NC, USA

Stephen J. Freedland, MD

Study design

Patient population:

- Screening PSA ≥1 ng/mL after RP or ≥2 ng/mL above the nadir after primary EBRT
- PSADT ≤9 mo
- No metastases on bone scan and CT/MRI per central read – conventional imaging-negative
- T ≥150 ng/dL
- Prior hormonal therapy ≥9 mo prior to R (neoadjuvant/adjuvant for ≤36 mo or ≤6 mo for rising PSA) allowed

Stratification factors:

- Screening PSA (≤10 ng/mL vs >10 ng/mL)
- PSADT (≤3 mo vs >3 to ≤9 mo)
- Prior hormonal therapy (yes vs no)

R 1:1:1

N=1068

- **Enzalutamide (160 mg oral QD) + leuprolide acetate (22.5 mg IM Q12w) n=355 Blinded**
- **Placebo + leuprolide acetate (22.5 mg IM Q12w) n=358 Blinded**
- **Enzalutamide monotherapy (160 mg oral QD) n=355 Unblinded**

PSA <0.2 ng/mL at week 36?

- Yes → **Week 37**: Suspend treatment at week 37; Monitor PSA (reinitiate if PSA rises)†
- No → Remain on treatment

Primary analysis

Open-label period: Continuing assigned treatment

- Safety follow-up (30 days after last dose)
- Long-term follow-up (every 12 weeks until the final OS analysis)‡:
  - Survival status
  - New antineoplastic therapies for prostate cancer
  - Symptomatic skeletal events
  - PFS2

Primary endpoint: MFS by BICR for enzalutamide + leuprolide vs leuprolide alone

Key secondary endpoints: MFS by BICR for enzalutamide monotherapy vs leuprolide alone, time to PSA progression, time to first use of new antineoplastic therapy, OS

Other secondary endpoints included: Time to first symptomatic skeletal event, safety

Exploratory endpoint: PFS2

†Study treatment was suspended once at week 37 if PSA was <0.2 ng/mL and restarted when PSA was ≥5.0 ng/mL without prior RP or ≥2 ng/mL with prior RP.
‡OS was a key alpha-protected secondary endpoint. Updated results from the following endpoints were not alpha-protected and are thus considered nominal: time to first use of new antineoplastic therapy, time to first symptomatic skeletal event, and PFS2.
BICR, blinded independent central review; CT, computed tomography; D, day; EBRT, external beam radiation therapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnetic resonance imaging; OS, overall survival; PFS2, progression-free survival on first subsequent therapy; PSA, prostate-specific antigen; PSADT, PSA doubling time; Q, every; R, randomization; RP, radical prostatectomy; T, testosterone; w, weeks.
Freedland SJ, et al. *New Engl J Med.* 2023;389(16):1453–1465.

Table 1. Baseline Demographic and Disease Characteristics (Intention-to-Treat Population).*

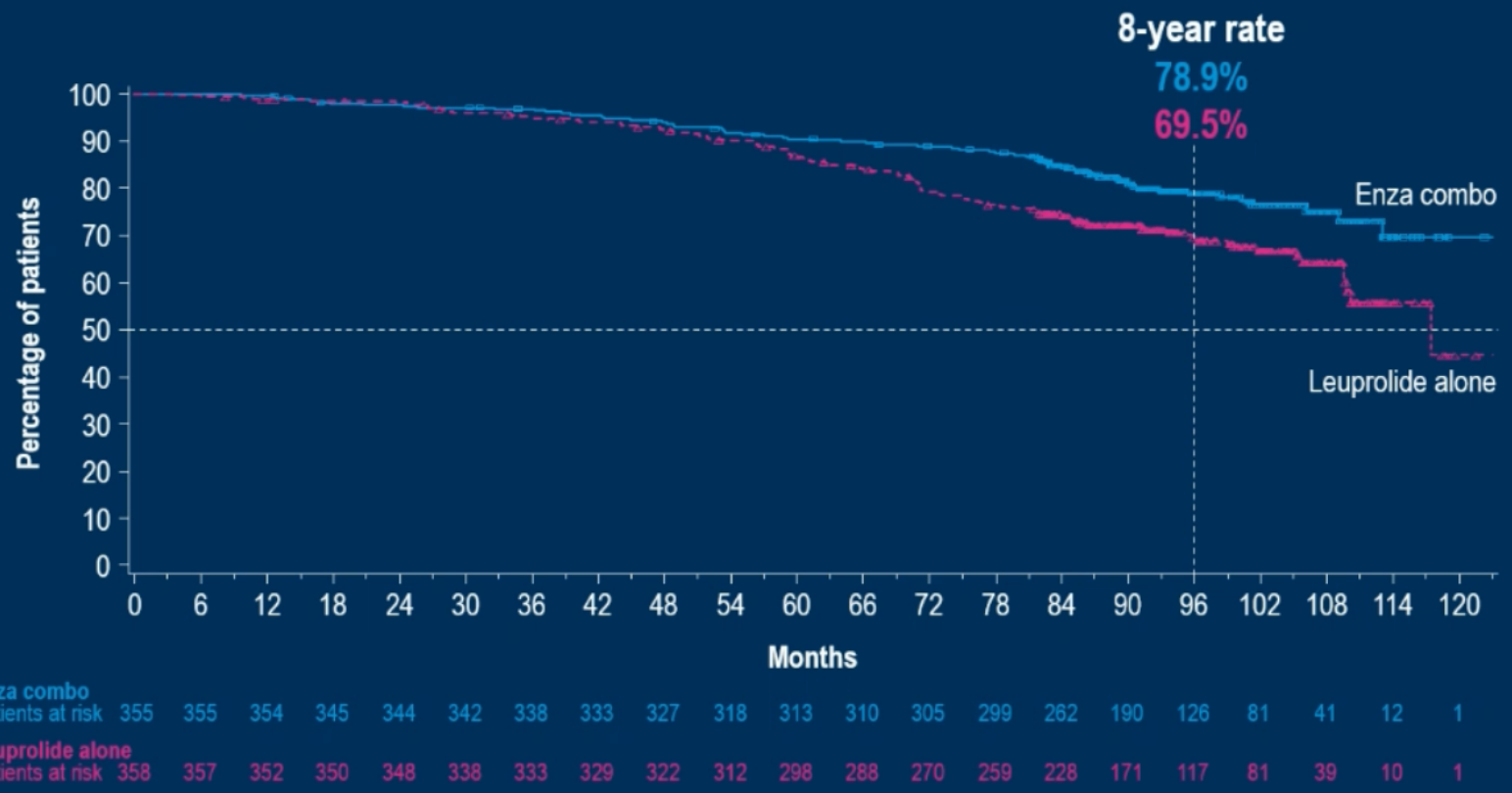
Characteristic	Enzalutamide + Leuprolide (N = 355)	Leuprolide Alone (N = 358)	Enzalutamide Monotherapy (N = 355)
Median age (range) — yr	69 (51–87)	70 (50–92)	69 (49–93)
Age group — no. (%)			
<65 yr	81 (22.8)	91 (25.4)	91 (25.6)
65 to <75 yr	201 (56.6)	180 (50.3)	174 (49.0)
≥75 yr	73 (20.6)	87 (24.3)	90 (25.4)
Race or ethnic group — no. (%)†			
White	293 (82.5)	301 (84.1)	295 (83.1)
Asian	26 (7.3)	26 (7.3)	26 (7.3)
Black	16 (4.5)	16 (4.5)	15 (4.2)
American Indian or Alaska Native	4 (1.1)	1 (0.3)	0
Native Hawaiian or other Pacific Islander	1 (0.3)	0	0
Other	5 (1.4)	9 (2.5)	5 (1.4)
PSA doubling time — no. (%)			
≤3 mo	69 (19.4)	80 (22.3)	76 (21.4)
>3 to 6 mo	187 (52.7)	142 (39.7)	164 (46.2)
>6 to 9 mo	98 (27.6)	135 (37.7)	114 (32.1)
Missing data	1 (0.3)	1 (0.3)	1 (0.3)
Median PSA doubling time (range) — mo§	4.6 (0.9–9.6)	5.0 (1.1–10.8)	5.0 (1.0–18.9)
Median serum PSA level (range) — ng/ml	5.0 (1.0–308.3)	5.5 (1.1–163.3)	5.3 (1.1–37.0)
Previous hormonal therapy — no. (%)			
Yes	107 (30.1)	113 (31.6)	112 (31.5)
No	248 (69.9)	245 (68.4)	243 (68.5)
Primary definitive therapy — no. (%)			
Prostatectomy alone	90 (25.4)	75 (20.9)	99 (27.9)
Radiation therapy alone	86 (24.2)	104 (29.1)	90 (25.4)
Prostatectomy and radiation therapy	179 (50.4)	179 (50.0)	166 (46.8)

* Percentages may not total 100 because of rounding. PSA denotes prostate-specific antigen.
† Race or ethnic group was reported by the patients. The "Other" category includes patients who identified as multiple races or ethnic groups.
‡ Eastern Cooperative Oncology Group (ECOG) performance-status scores range from 0 to 5, with higher scores indicating greater disability.
§ PSA doubling time at baseline was calculated on the basis of a sequence of PSA values tested over time during the enrollment period. Some baseline PSA doubling time values exceeded the enrollment threshold of less than 9 months owing to discrepancies in the PSA values captured in the case-report forms as compared with the values used for the enrollment calculation.

Freedland *et al*, NEJM 2023

Stephen J. Freedland, MD

Overall survival: Enza combo



	Enza combo (n=355)	Leuprolide alone (n=358)
Events	73	111
8-year OS (95% CI), %	78.9 (73.9, 83.1)	69.5 (64.0, 74.3)

HR (95% CI): 0.597 (0.444, 0.804); *P*=0.0006

The risk of death was 40.3% lower for enza combo compared with leuprolide alone

Intent-to-treat population. The median follow-up was 94.2 months in the enza combo group and 94.0 months in the leuprolide-alone group. OS was defined as the time between randomization and death due to any cause. HRs were calculated using a Cox regression model with treatment as the only covariate, with stratification according to PSA level at screening, PSADT, and previous hormonal therapy, as reported in the interactive Web-response system. The two-sided *P*-values were determined on the basis of a log-rank test, stratified according to PSA level at screening, PSADT, and previous hormonal therapy, as reported in the interactive Web-response system. The data cutoff date was May 27, 2025. The squares and triangles indicate censored data.
CI, confidence interval; enza combo, enzalutamide plus leuprolide; HR, hazard ratio; OS, overall survival; PSA, prostate-specific antigen; PSADT, PSA doubling time.

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Please scan this QR code with your smartphone camera or app to view the associated ***Supplementary material***, ***Plain-Language summary***, *and* ***Animated Video***

A Phase 3 study of capivasertib plus abiraterone versus placebo plus abiraterone in patients with PTEN deficient *de novo* metastatic hormone-sensitive prostate cancer: CAPItello-281

Karim Fizazi, Noel W. Clarke, Maria De Santis, Hirotsugu Uemura, Andre Poisl Fay, Nuri Karadurmus, Mariusz Kwiatkowski, Carlos Alvarez-Fernandez, Shusuan Jiang, Miguel Sotelo, Dominique Parslow, Niara Oliveira, Tae Gyun Kwon, Dingwei Ye, Steve Boudewijns, Pongwut Danchaivijitr, Mahmuda Khatun, Marc Yeste-Velasco, Jill Logan, Daniel J. George

Karim Fizazi MD, PhD

Department of Cancer Medicine, Institut Gustave Roussy, Centre Oscar Lambret, University of Paris Saclay, Villejuif, France

Berlin, Germany

17–21 October

50 YEARS ESMO

CAPItello-281 Study Design

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

Patients with PTEN deficient *de novo* mHSPC

- PTEN deficiency: (diagnostic cut-off of **≥90%** of viable malignant cells with **no specific cytoplasmic staining** by IHC)*
  - i.e. ≤10% of cells expressing PTEN by IHC

Of ~6,200 patients submitting tumour tissue **97%** had a valid IHC result and **25%** were **PTEN deficient**

1,012 patients (R 1:1)

Capivasertib	400 mg BID 4 days on, 3 days off
Abiraterone/pred + ADT	1000 mg/5 mg QD + ADT
Placebo	400 mg BID 4 days on, 3 days off
Abiraterone/pred + ADT	1000 mg/5 mg QD + ADT

Primary endpoint

- **Investigator assessed rPFS**

Secondary endpoints

- Overall survival
- Time to first subsequent therapy
- Symptomatic skeletal-event free survival
- Time to pain progression
- Time to castration resistance
- Time to PSA progression

Exploratory *post-hoc* PTEN deficiency subgroups

Stratification factors:†

- M1 volume (CHAARTED criteria) and visceral mets
- Geography

Study timeline

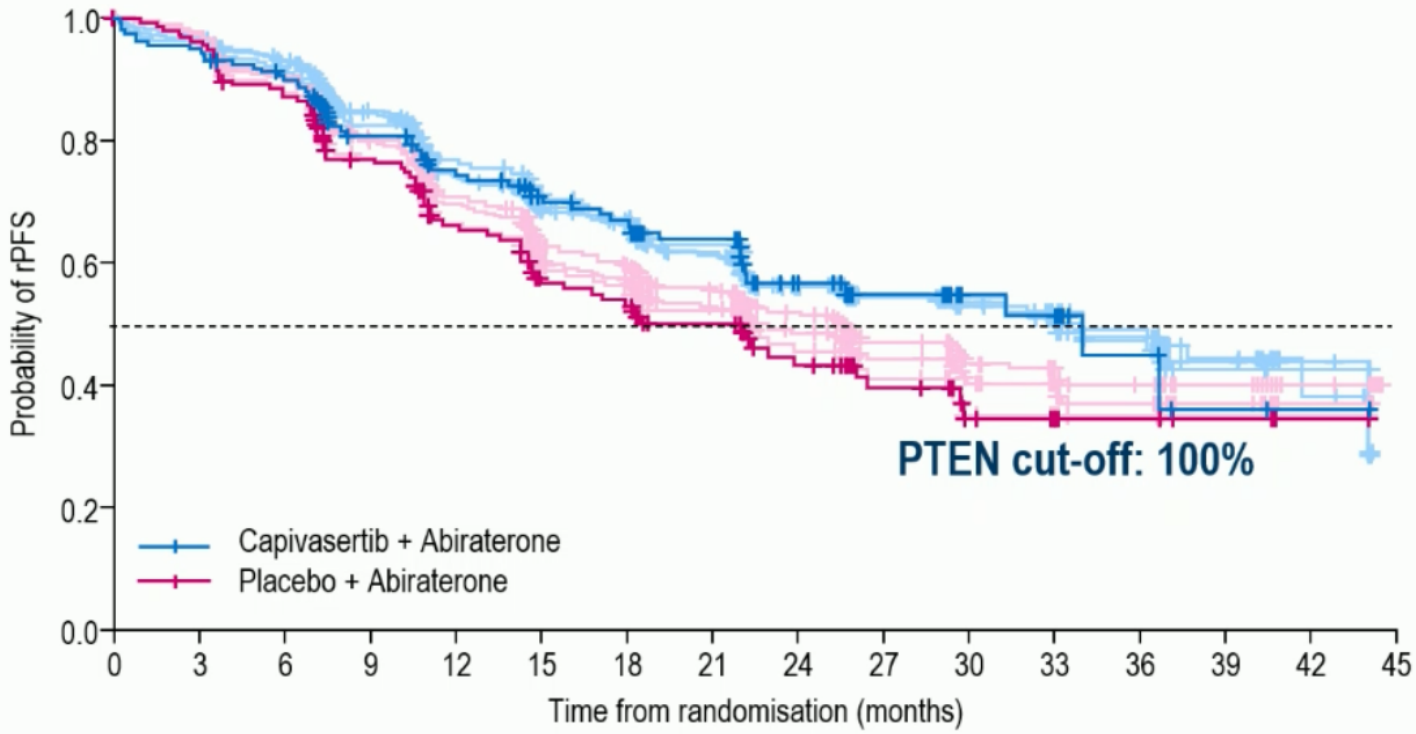
Current analysis

Enrolment period	Primary rPFS DCO	Final OS DCO
13 July 2020–5 Feb 2024	7 Oct 2024 Median rPFS follow-up:‡ ~18 mo	Planned for 522 deaths (52.2% maturity)

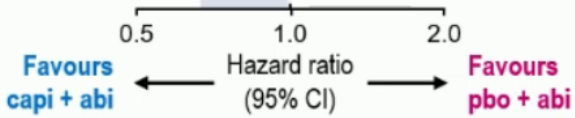
NCT04493853. Full eligibility criteria available in the online article. *Determined using investigational antibody for PTEN (SP218) (Roche Diagnostics).
†High-vol. disease with visceral mets, high-vol disease without visceral mets, low-vol. disease; North America; Western Europe and Australia; Latin America and Eastern Europe; Asia. ‡In censored patients.
ADT, androgen deprivation therapy; BID, twice daily; IHC, immunohistochemistry; mHSPC, metastatic hormone-sensitive prostate cancer; pred, prednisone/prednisolone; QD, once daily; rPFS, radiographic progression-free survival

Karim Fizazi MD, PhD

CAPItello-281 PTEN subgroups: investigator-assessed rPFS



PTEN cutoff	Patients, n Capi + abi	Patients, n Pbo + abi	Median rPFS, months Capi + abi	Median rPFS, months Pbo + abi	HR (95% CI)
All randomised patients (≥90%)	507	505	33.2	25.7	0.81 (0.66, 0.98)
≥95%	404	410	33.2	22.7	0.75 (0.60, 0.94)
≥99%	205	196	34.1	22.4	0.71 (0.52, 0.97)
100%	169	162	34.1	22.1	0.68 (0.48, 0.96)



rPFS maturity in PTEN subgroups was consistent with the overall population

abi, abiraterone; capi, capivasertib; CI, confidence interval; HR, hazard ratio; pbo, placebo; rPFS, radiographic progression-free survival

Karim Fizazi MD, PhD

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Phase 3 trial of [^{177}Lu]Lu-PSMA-617 combined with ADT + ARPI in patients with PSMA-positive metastatic hormone-sensitive prostate cancer (PSMAddition)

Presenter: Scott T Tagawa,* Weill Cornell Medicine, New York, NY, USA

Co-authors: Oliver Sartor,* Josep M Piulats, Fred Saad, Karim Fizazi, Alison Reid, Himisha Beltran, Gero Kramer, Hakim Mahammedi, Matthias Eiber, Shilpa Gupta, Daniel Castellano, Ralph Hauke, Hyun Kim, Cheol Kwak, See Tong Pang, Emmanuel Bouillaud, Angela Zhang, Olga Sakharova, Michael J Morris*, **on behalf of the PSMAddition investigators**

19 October 2025

*Equal contributors

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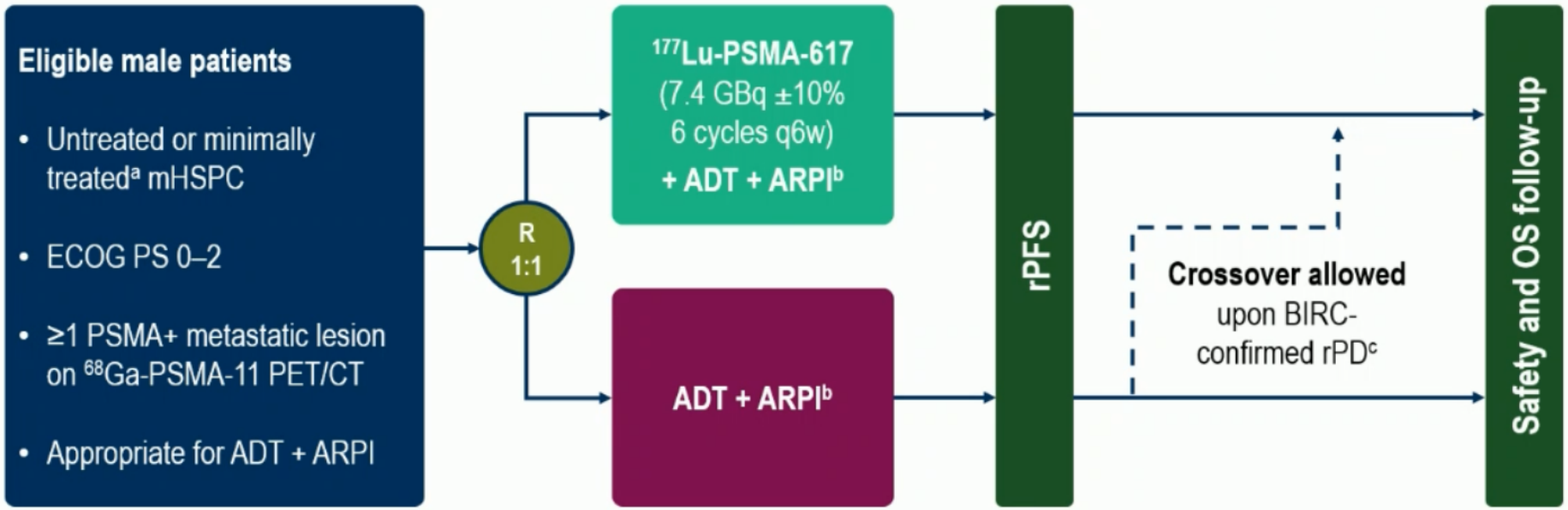
PSMAddition: randomized phase 3 trial of ^{177}Lu-PSMA-617 in mHSPC



Stratification factors
- Disease volume (high/low) – per CHAARTED criteria[1]
- Age ≥ 70 years (yes/no)
- Previous or planned treatment of primary tumour by radiation or prostatectomy (yes/no)

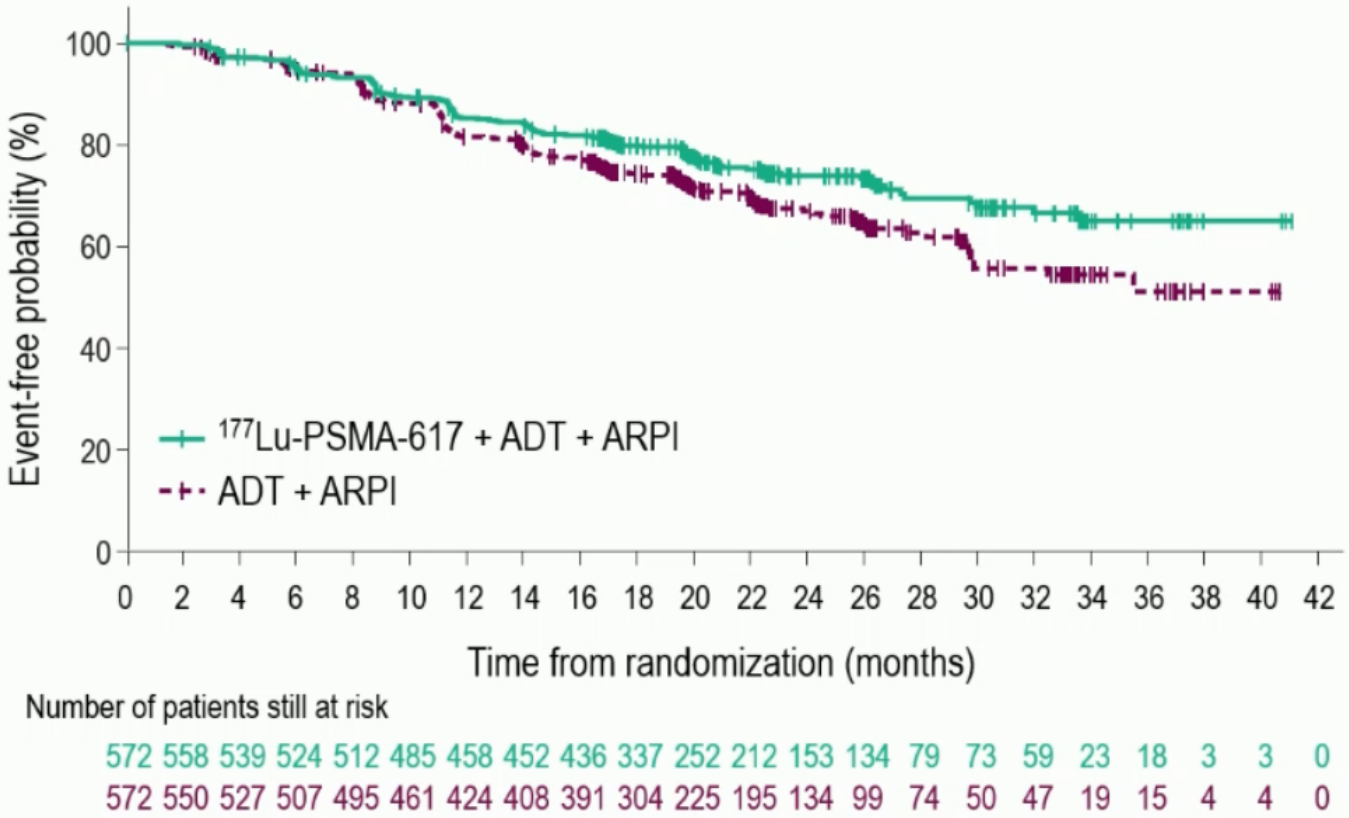
Follow-up periods
- rPFS: until event in all patients
- Safety: 30 days then 24 and 48 weeks after treatment discontinuation
- OS: every 90 days after last contact

[a] ADT in the neo-/adjuvant setting and/or up to 45 days of ADT/ARPI for metastatic disease was allowed before study entry | [b] Any ARPI with one switch allowed | [c] ADT/ARPI not mandatory after crossover
ADT, androgen deprivation therapy; BIRC, blinded independent review committee; ECOG PS, Eastern Cooperative Oncology Group performance status; OS, overall survival; PET/CT, positron-emission tomography/computed tomography; q6w, every 6 weeks; rPD, radiographic disease progression; rPFS, radiographic progression-free survival

1. Sweeney CT *et al. N Engl J Med* 2015;373:737–46

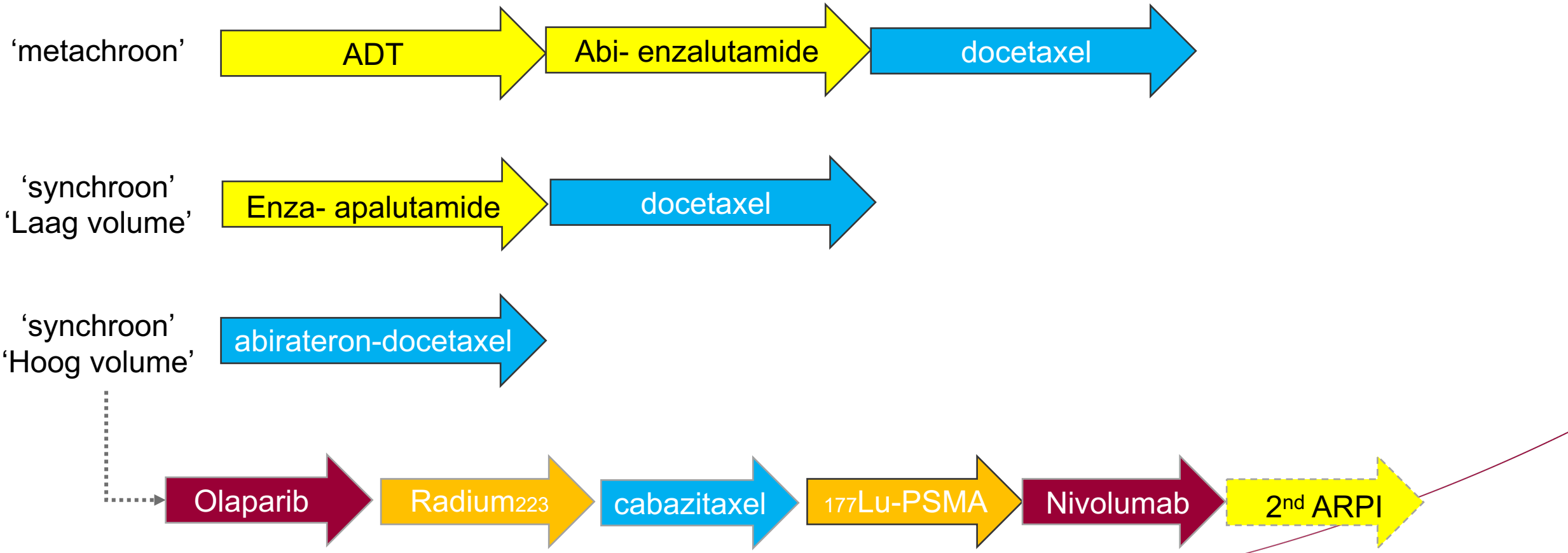
Data cut-off: 13 January 2025

rPFS by BIRC – the primary endpoint was met

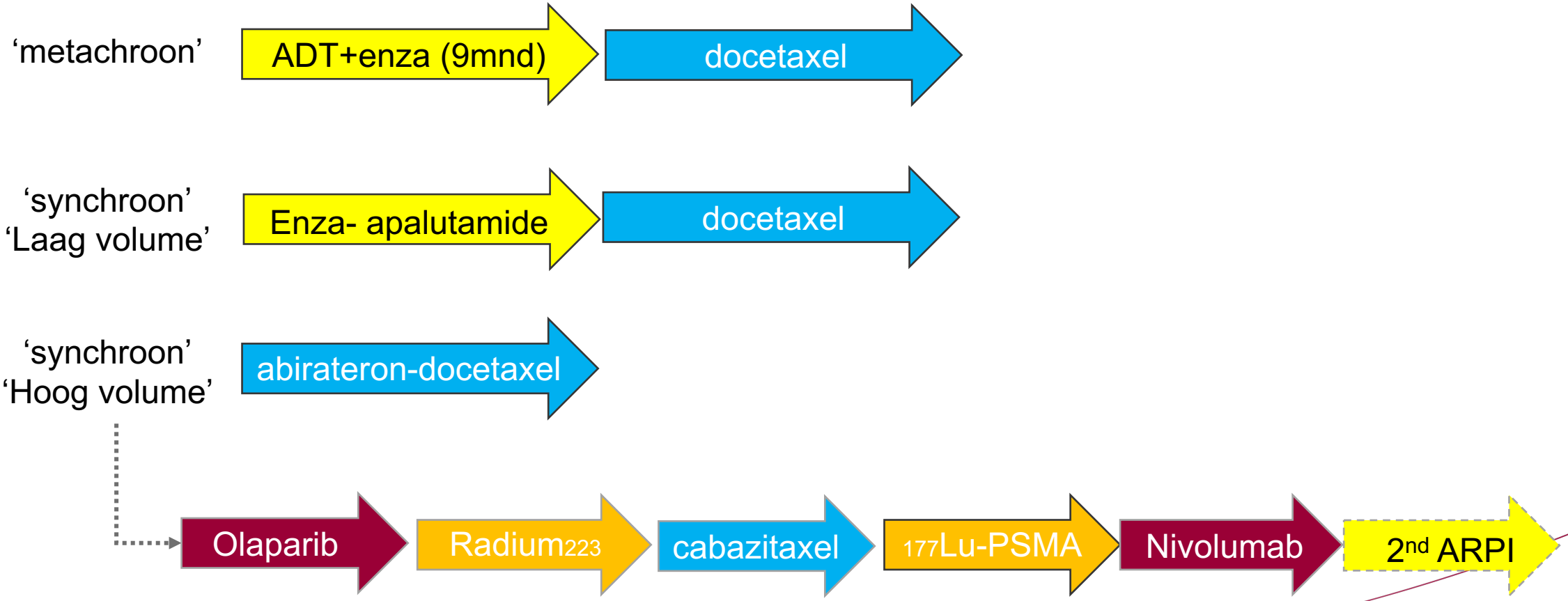


	^{177}Lu-PSMA-617 + ADT + ARPI (N = 572)	ADT + ARPI (N = 572)
Events – n (%) rPD Death without rPD	139 (24.3) 112 (19.6) 27 (4.7)	172 (30.1) 152 (26.6) 20 (3.5)
HR (95% CI)	0.72 (0.58, 0.90)	
p value	0.002[a]	
Median rPFS (95% CI) – months	NR (NE, NE)	NR (29.7, NE)

‘Patient journey prostaat’



‘Patient journey prostaat’



Onderzoeksvragen

- Multimorbiditeit en cardiovasculaire toxiciteit
- Immuuntherapie: tumor-reactieve T-cellen tegen prostaatcarcinoom
- De strijd tegen AR amplificatie: de AR PROTACs
- Nieuwe radionucliden: actinium en terbium
- De rol van radiotherapie in de mHSPC behandeling?

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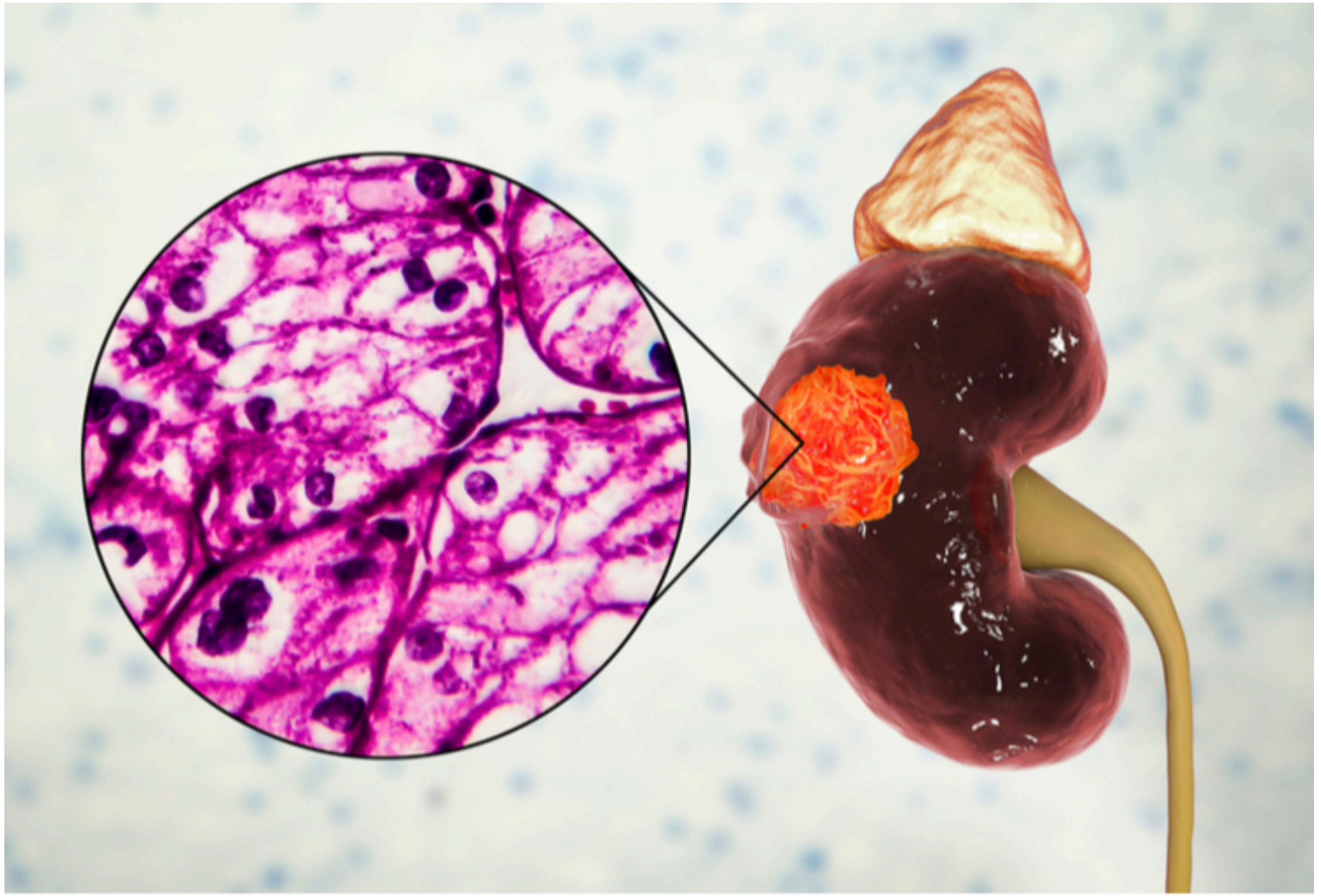
Behandeling ADT monotherapie? **> EMBARK: ADT+enzalutamide**

Take home message

- Intensieve systeemtherapie bij diagnose van mHSPC geeft langere overleving
- Wat is de optimale eerstelijns ‘triple therapie’?
- De opkomst van de ‘drug holiday’



Take home message

- Neo-adjuvante immuuntherapie: hoog actief voor kleine groep
- Leibovich risico score: biomarker voor adjuvante therapie
- HIF2-remmers: een nieuwe klasse medicatie in opkomst

Overzicht

- Standaard systeembehandeling
- Casuistiek
- Innovaties
- Wat is er in aantocht?

- Prostaatcarcinoom, niercelcarcinoom

Casus 2 Dhr H, 71jr

- 2014 hernia inguinalis
- 2024 Hematurie
- 2025-1 locoregionaal heldercellig niercelcarcinoom links; cT3a N1 M0
- 2025-1 radicale nefrectomie links, pT3a N1 (1/15 lnn); R0
- 2025-1 postoperatief abces in nefrectomie holte, drain cotrim metronidazol
- 2025-1 MRSA positief

Adjuvante therapie?

Casus 2 Dhr H, 71jr

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- 2025-1 MRSA positief

Adjuvante therapie?

Indicatie

- Keynote 564, ccRCC

T2a WHO graad 4 of sarcomatoide dedifferentiatie

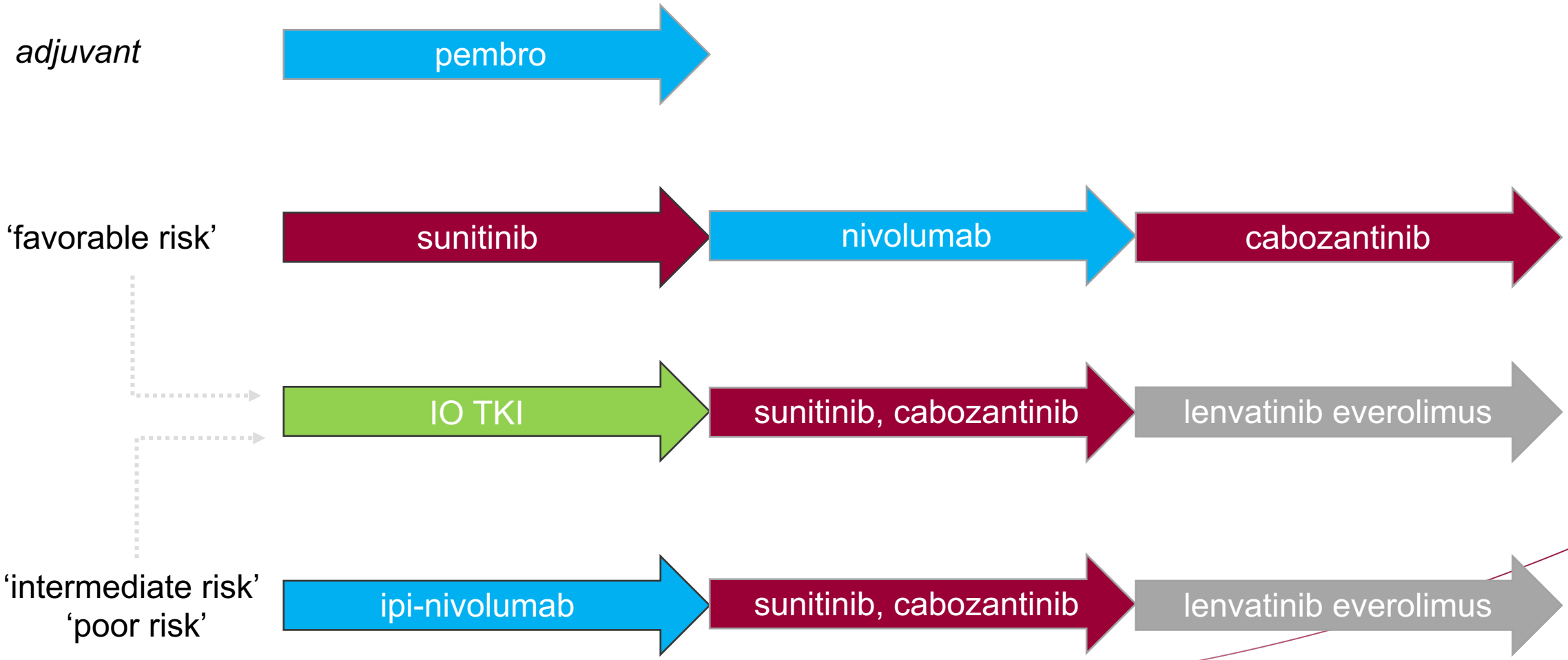
T3

Elk T stadium N+

M1 NED (<1jr)

- 12wk na nefrectomie

‘Patient journey RCC’

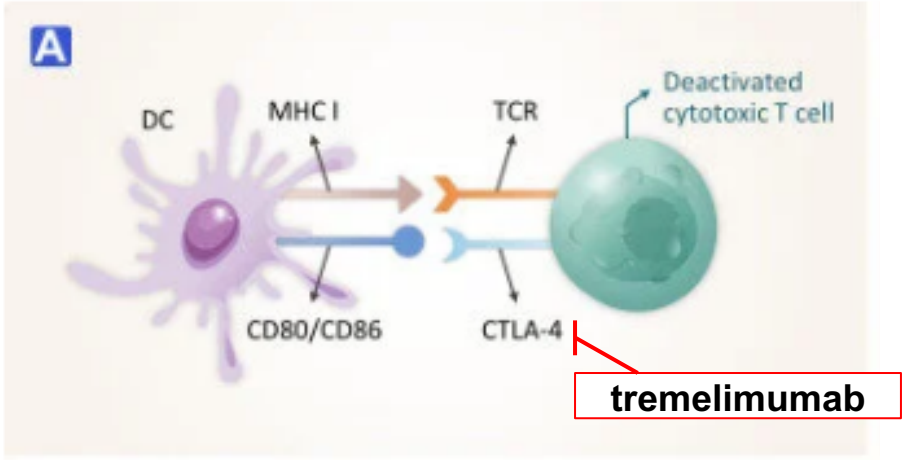


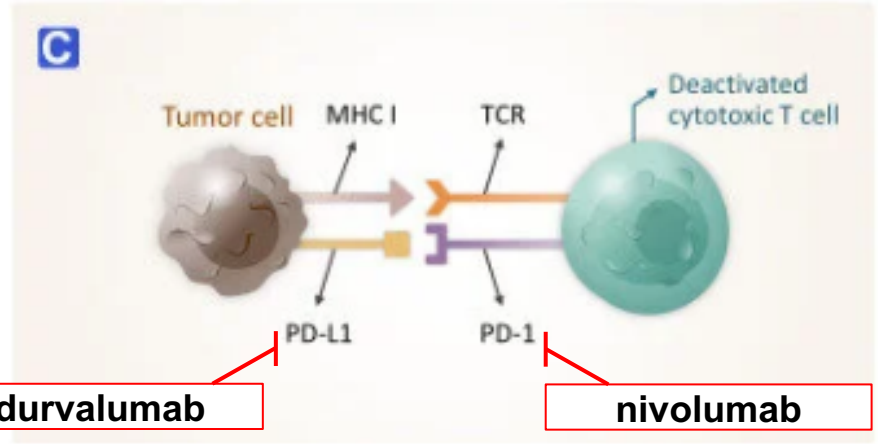
Overzicht onderzoek

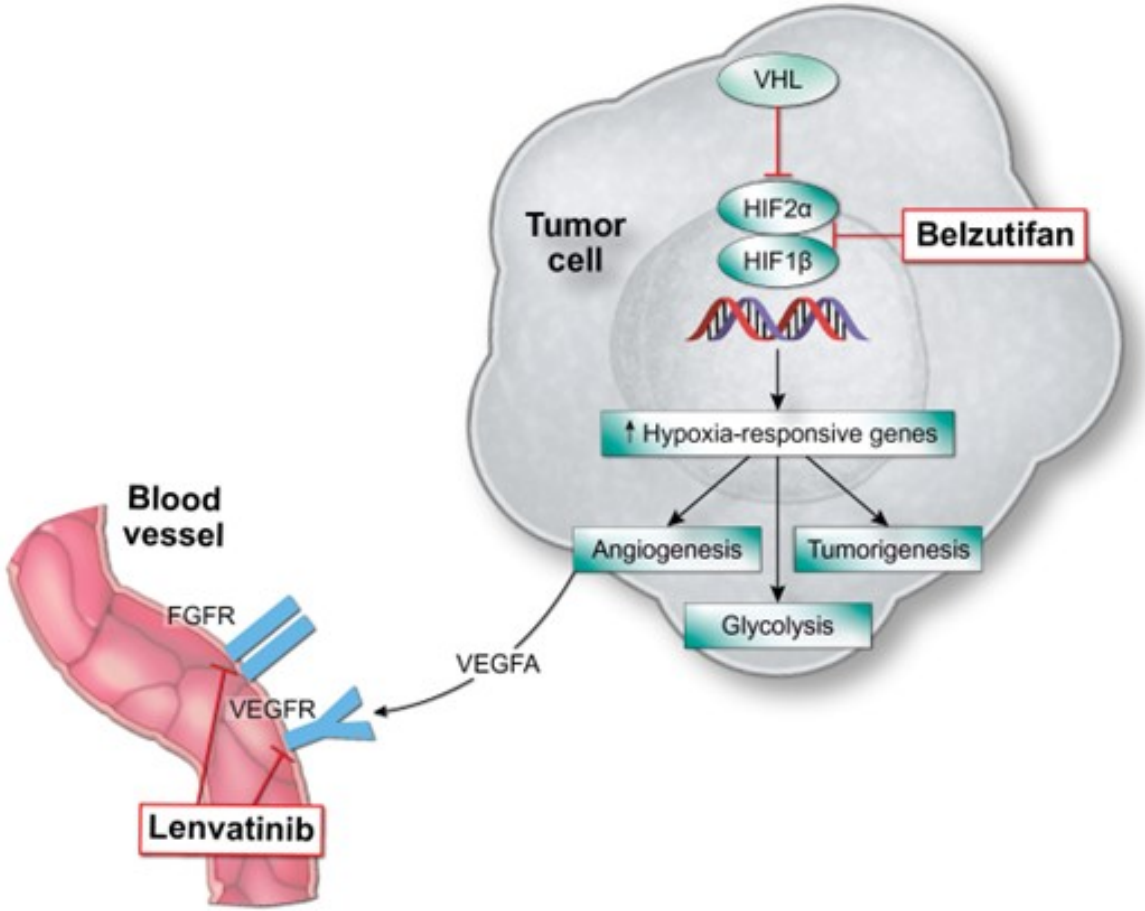
Niercelcarcinoom

- RAMPART	durvalumab tremelimumab	ongepubliceerd
- Litespark-011	belzutifan	ongepubliceerd
- NESCIO	nivolumab ipilimumab relatlimab	ongepubliceerd

Werking immuuntherapie en belzutifan

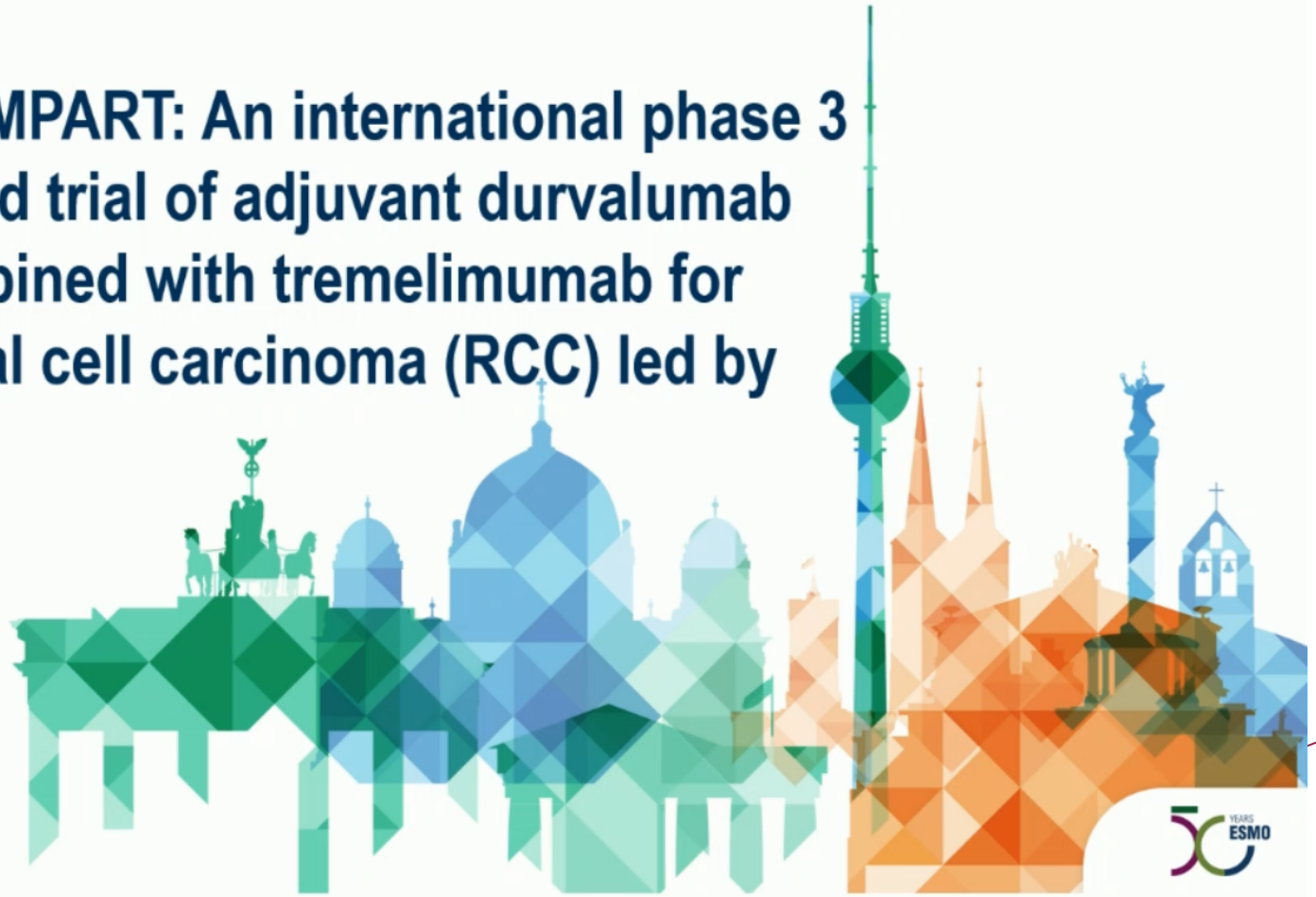






BERLIN 2025 ESMO congress

First results from RAMPART: An international phase 3 randomised-controlled trial of adjuvant durvalumab monotherapy or combined with tremelimumab for resected primary renal cell carcinoma (RCC) led by MRC CTU at UCL

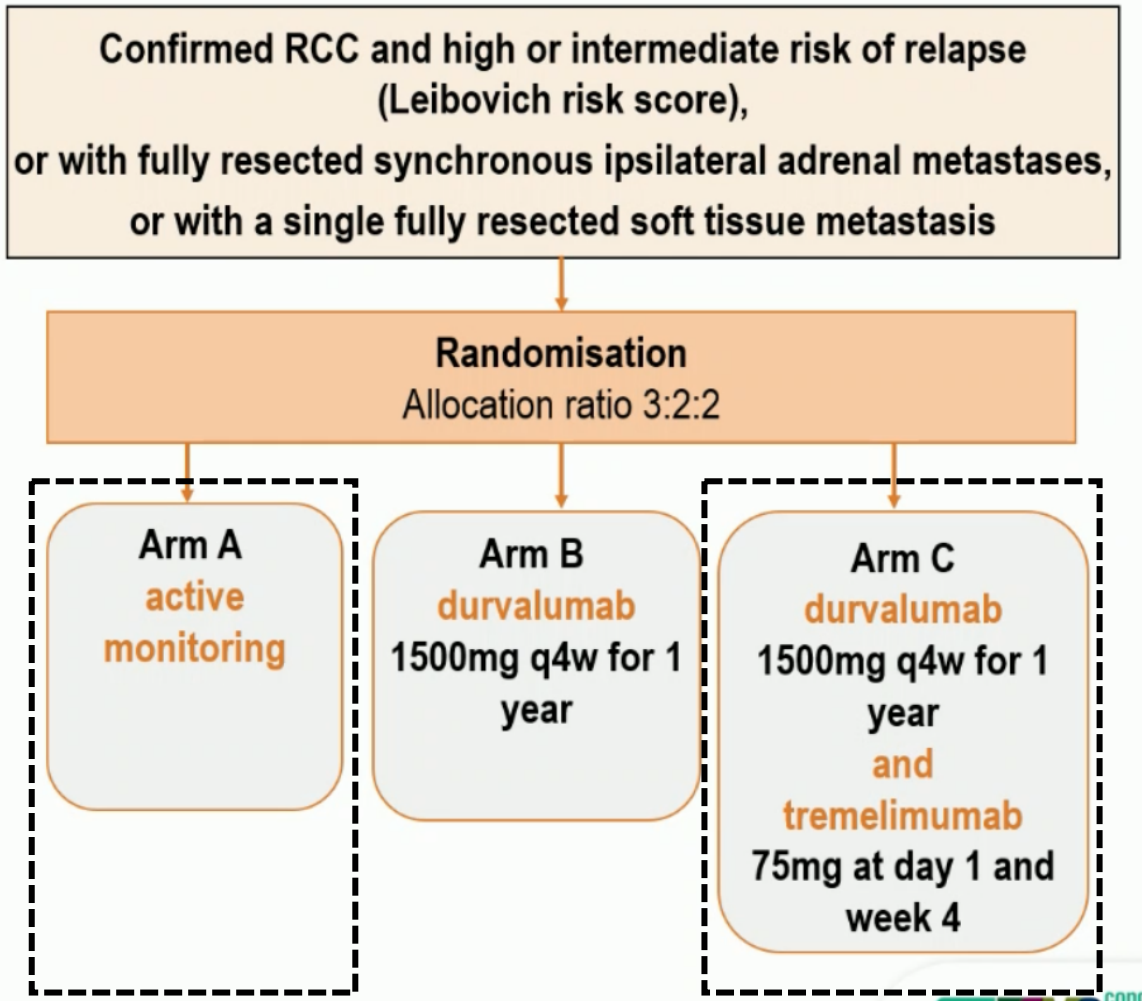


James Larkin

18 October 2025

RAMPART Trial Design

- Multi-arm multi-stage (MAMS) platform design
- Original sample size: 1750
- Impacted by COVID-19 and KEYNOTE-564 results
- Modified design blinded to accumulating outcome data
- New target sample size: 750
- Primary outcome: Disease Free Survival (DFS)
- Pre-specified and pre-powered analysis: DFS by risk of relapse at baseline
- Durvalumab and tremelimumab (Arm C) versus active monitoring (Arm A)

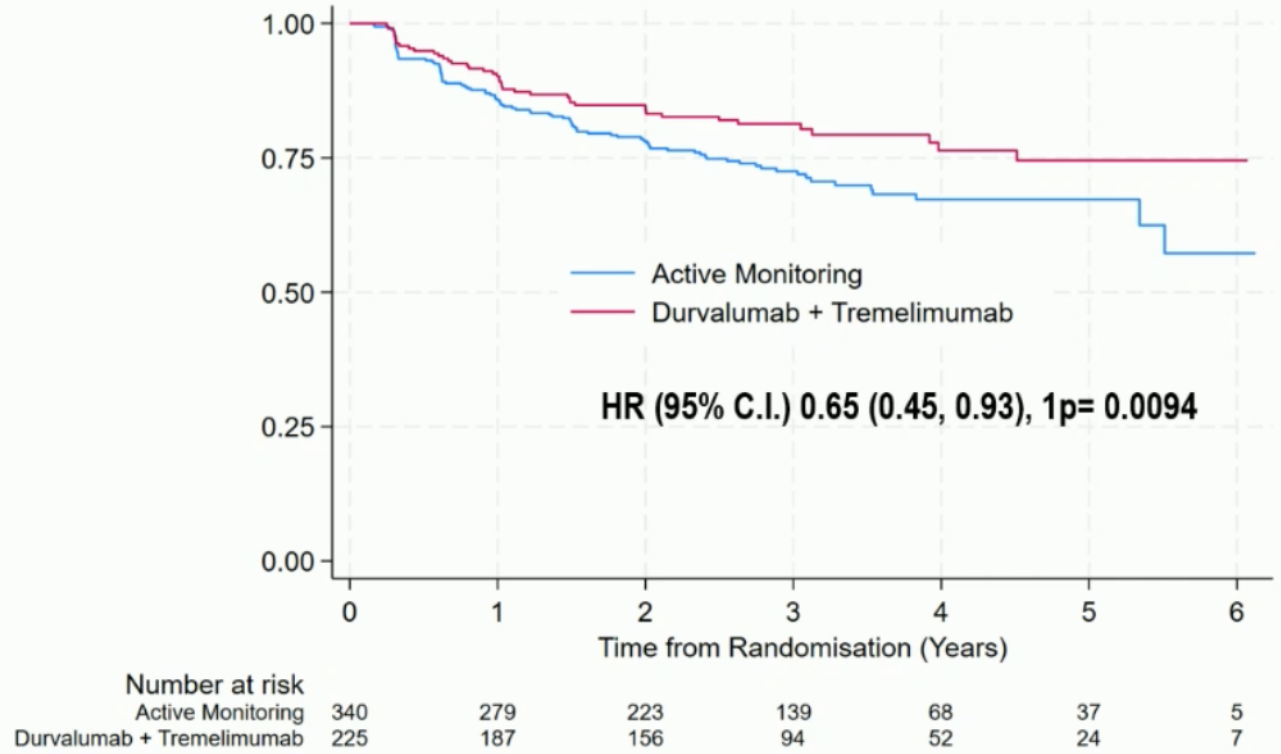


RAMPART Baseline Characteristics

	Active Monitoring (n= 340)	Durvalumab + Tremelimumab (n= 225)
Age at Randomisation (Years), Mean (SD)	59.6 (10.1)	58.9 (10.0)
Female	96 (28.2%)	63 (28.0%)
WHO PS 1	65 (19.1%)	43 (19.1%)
Radical Nephrectomy	287 (84.4%)	191 (84.9%)
Histology		
Clear Cell	285 (83.8%)	191 (84.9%)
Non-Clear Cell	55 (16.2%)	34 (15.1%)
Risk of Relapse		
Intermediate Leib.	151 (44.4%)	103 (45.8%)
High Leib.	172 (50.6%)	111 (49.3%)
M1NED	17 (5.0%)	11 (4.9%)
T Stage		
pT1	38 (11.5%)	23 (10.5%)
pT2	39 (11.8%)	33 (15.0%)
pT3	252 (76.1%)	161 (73.2%)
pT4	2 (0.6%)	3 (1.4%)
Lymph Node Status		
pNx/pN0	307 (93.3%)	209 (95.9%)
pN1	22 (6.7%)	9 (4.1%)

James Larkin

RAMPART Disease Free Survival (DFS) – ITT Population



3-year DFS	
Durvalumab + Tremelimumab (N= 225)	**Active Monitoring (N= 340)**
81%	73%
Median Follow Up: 3 years	

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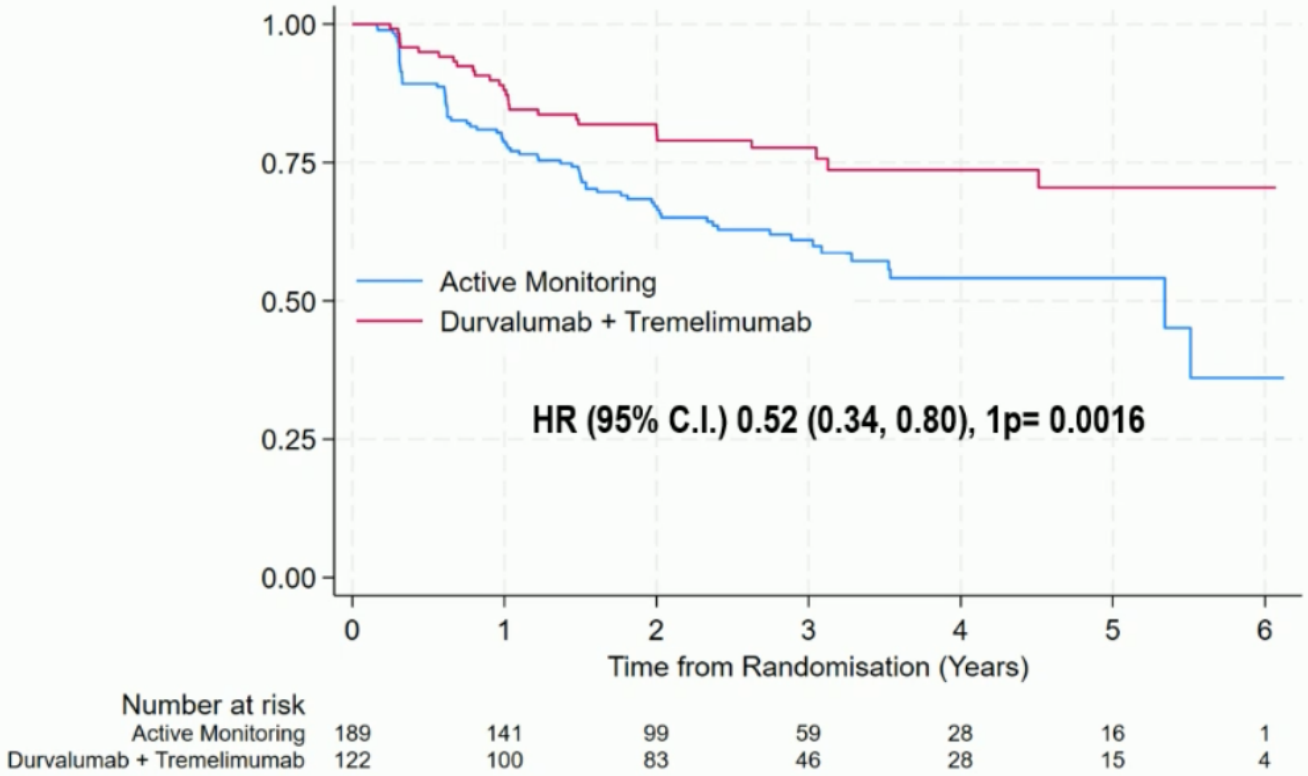
RAMPART DFS in the Higher Risk Population – ITT



Pre-specified, pre-powered subgroup analysis

3-year DFS	
Durvalumab + Tremelimumab (N= 122)	**Active Monitoring (N= 189)**
78%	61%
Median Follow Up: 3 years	

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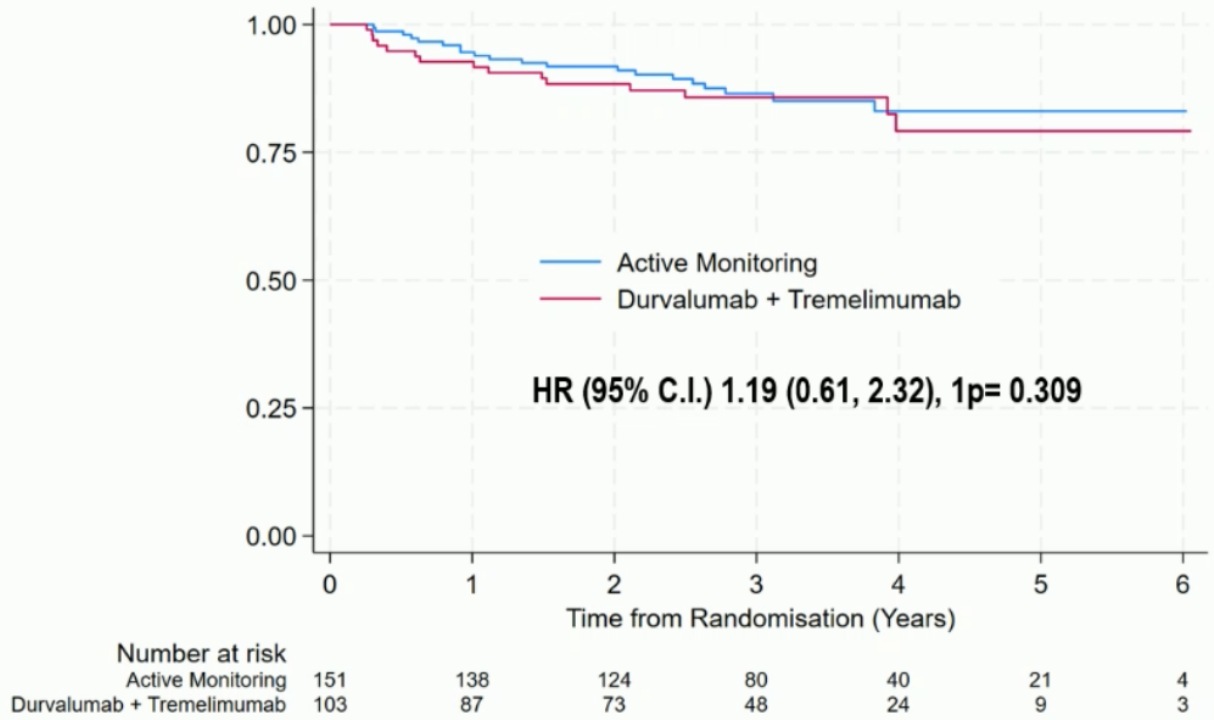
RAMPART DFS in the Intermediate Risk Population - ITT



Pre-specified, pre-powered subgroup analysis

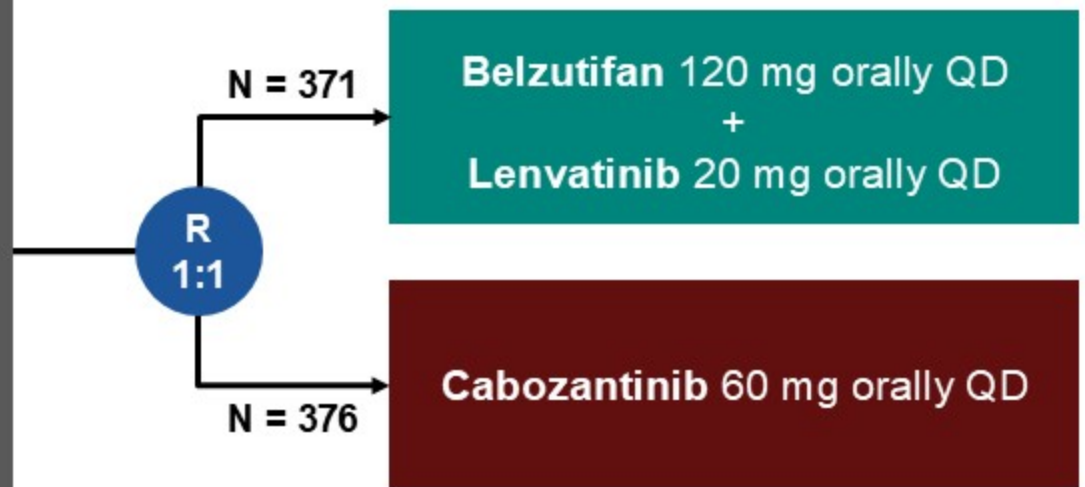
3-year DFS	
Durvalumab + Tremelimumab (N= 103)	**Active Monitoring (N= 151)**
86%	87%
Median Follow Up: 3.1 years	

James Larkin

LITESPARK-011 Study (NCT04586231)

Key Eligibility Criteria

- Unresectable, locally advanced or metastatic clear cell RCC
- Karnofsky Performance Status score ≥70%
- ≤2 prior systemic regimens
- Progression on/after anti−PD-(L)1 mAb as 1L or 2L therapy or progression ≤6 months of the last dose of adjuvant anti−PD-(L)1 mAb
- Prior VEGFR-TKI was permitted



Stratification Factors

- IMDC prognostic score:[a] 0 vs. 1-2 vs. 3-6
- Line of treatment for prior anti−PD-(L)1: 1L, adjuvant, neoadjuvant-adjuvant vs. 2L
- Geographic region: North America vs. western Europe vs. rest of world

Dual Primary Endpoints:

- PFS per RECIST 1.1 by BICR
- OS

Key Secondary Endpoint:

- ORR per RECIST 1.1 by BICR

Other Secondary Endpoints Include:

- DOR per RECIST 1.1 by BICR
- Safety

Exploratory Endpoints Include:

- Time to deterioration in patient-reported outcomes

BICR, blinded independent central review; QD, daily.

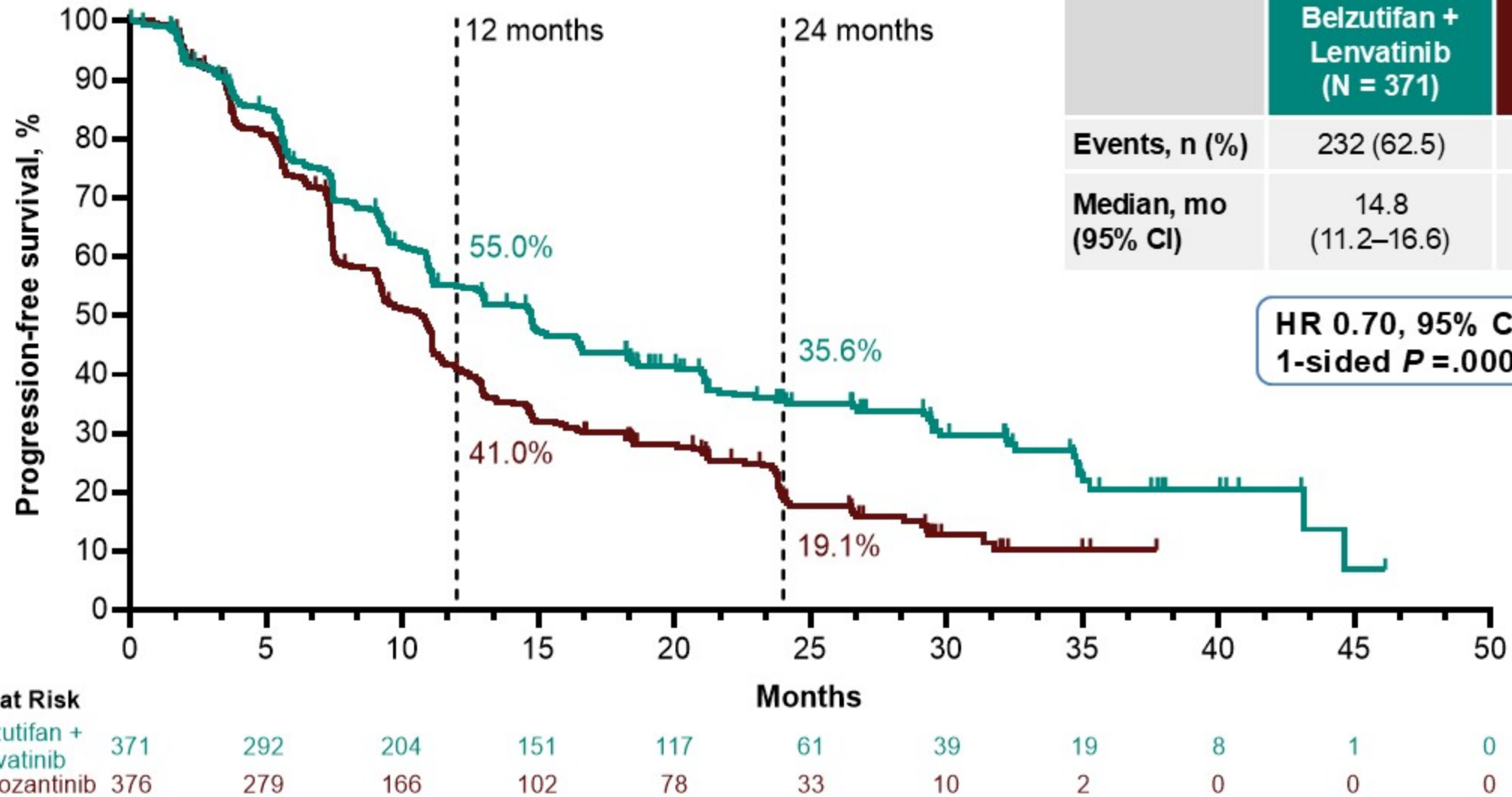
[a]Based on the number of present risk factors (KPS score <80%; time from diagnosis to 1L treatment <1 year; low hemoglobin; high corrected serum calcium; high neutrophils; high levels of platelets) according to the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC).

Baseline Characteristics

Characteristic, n (%)	Belzutifan + Lenvatinib (N = 371)	Cabozantinib (N = 376)
Median age (range), years	63.0 (30–85)	62.5 (30–86)
Sex		
Male	273 (73.6)	292 (77.7)
Female	98 (26.4)	84 (22.3)
KPS score		
90 or 100	276 (74.4)	277 (73.7)
70 or 80	95 (25.6)	99 (26.3)
Geographic region		
North America	64 (17.3)	63 (16.8)
Western Europe	221 (59.6)	216 (57.4)
Rest of world	86 (23.2)	97 (25.8)
IMDC prognostic risk categories		
Favorable (score 0)	84 (22.6)	95 (25.3)
Intermediate (score 1-2)	226 (60.9)	215 (57.2)
Poor (score 3-6)	61 (16.4)	66 (17.6)
Prior lines of therapy		
Adjuvant only	15 (4.0)	18 (4.8)
1	252 (67.9)	251 (66.8)
2	100 (27.0)	107 (28.5)
3	4 (1.1)	0
Number of prior VEGFR-TKIs		
0	158 (42.6)	165 (43.9)
1	203 (54.7)	205 (54.5)
2	10 (2.7)	6 (1.6)

Data cutoff date, IA2: 9 April 2025

Primary Endpoint: PFS per RECIST 1.1 by BICR



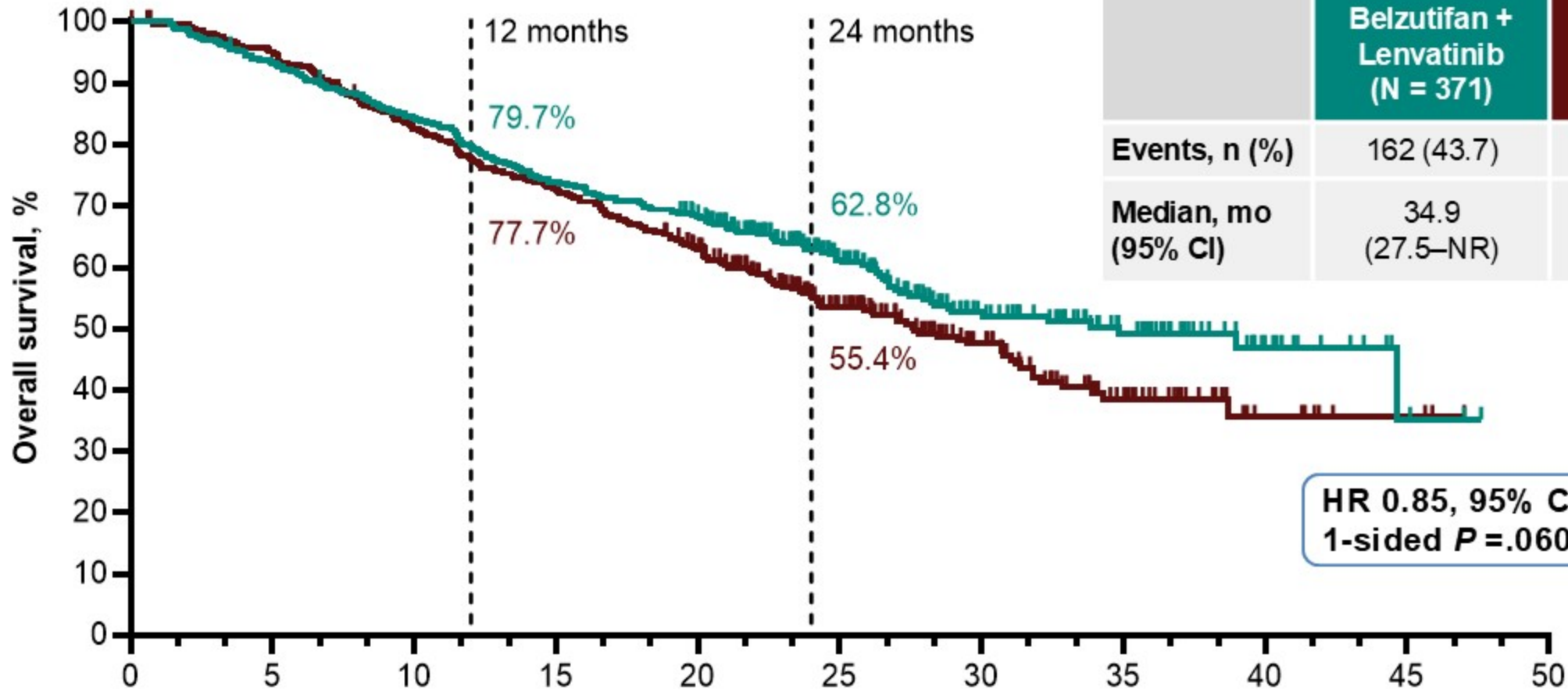
	Belzutifan + Lenvatinib (N = 371)	Cabozantinib (N = 376)
Events, n (%)	232 (62.5)	273 (72.6)
Median, mo (95% CI)	14.8 (11.2–16.6)	10.7 (9.2–11.1)

HR 0.70, 95% CI 0.59–0.84, 1-sided *P* =.00007*

* denotes statistical significance (1-sided boundary 0.0047).

Data cutoff date, IA2: 9 April 2025

Primary Endpoint: OS



	Belzutifan + Lenvatinib (N = 371)	Cabozantinib (N = 376)
Events, n (%)	162 (43.7)	192 (51.1)
Median, mo (95% CI)	34.9 (27.5–NR)	27.6 (24.0–31.4)

HR 0.85, 95% CI 0.68–1.05, 1-sided *P* =.06075

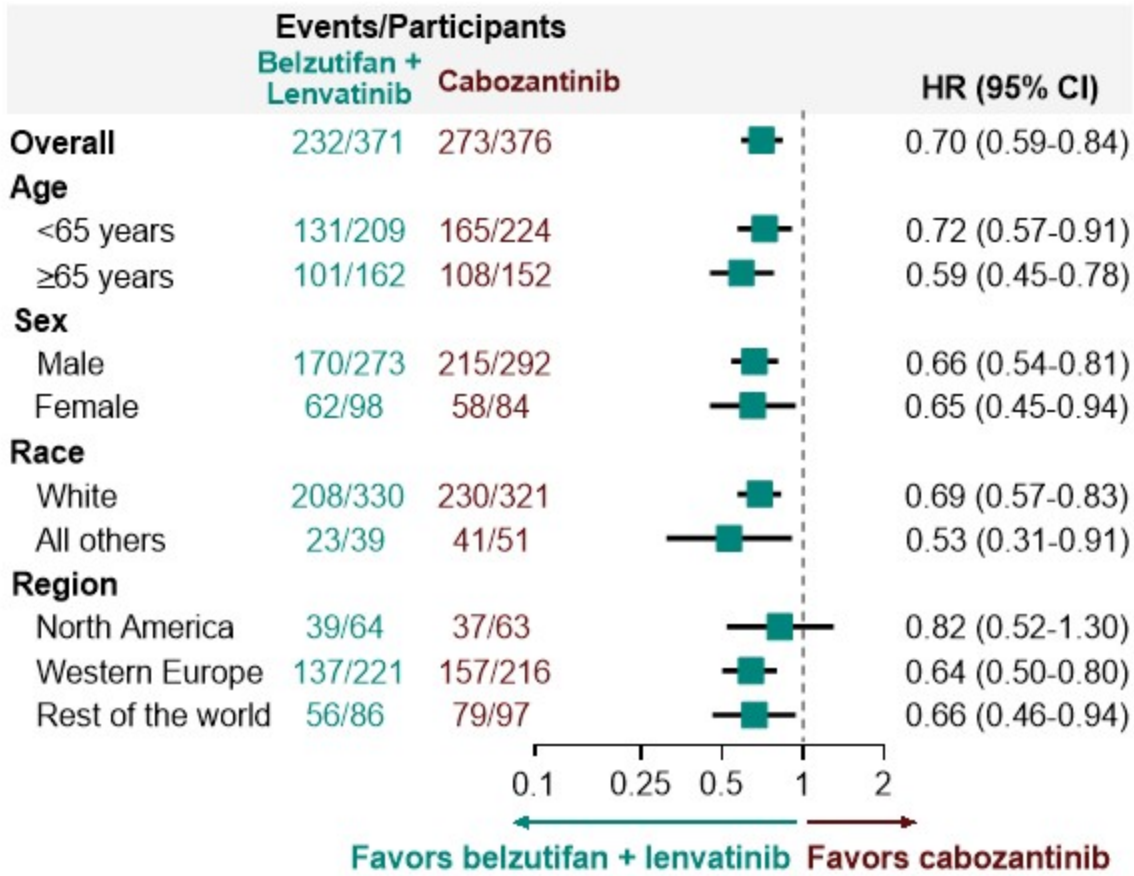
No. at Risk

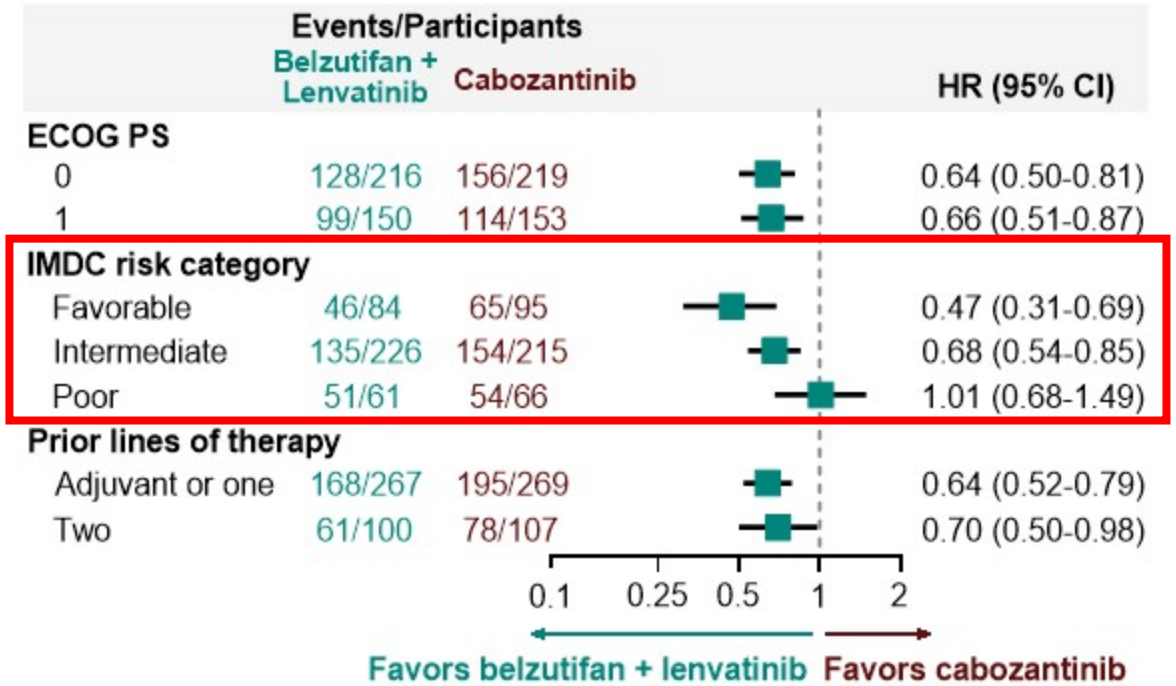
Belzutifan + Lenvatinib	371	345	311	273	246	148	82	47	14	3	0
Cabozantinib	376	355	307	271	225	136	76	36	9	4	0

NR, not reached. OS did not reach statistical significance (1-sided boundary 0.0115).

Data cutoff date, IA2: 9 April 2025

PFS by BICR in Key Subgroups





Data cutoff date, IA2: 9 April 2025

BERLIN 2025 ESMO congress

Neoadjuvant immunotherapy in locally advanced renal cell carcinoma at risk for recurrence or distant metastases: the randomized phase II NESCIO trial

F. Burgers[1], A. de Ruijter, N. Graafland, M. van Montfoort, M. Lopez-Yurda, P. Hagen, P. Zondervan, S. Rynja, M. Yska, A. de Ruiter, A. Minnee-van Leeuwen, R. de Vries, B. Lagerveld, D. Vis, S. Wilgenhof, J. van Thienen, C. Blank, K. van der Mijn, A. Bex, J. Haanen[1]

[1]Dept. of Medical Oncology, Netherlands Cancer Institute, Amsterdam, the Netherlands

Berlin, 18 Oct 2025

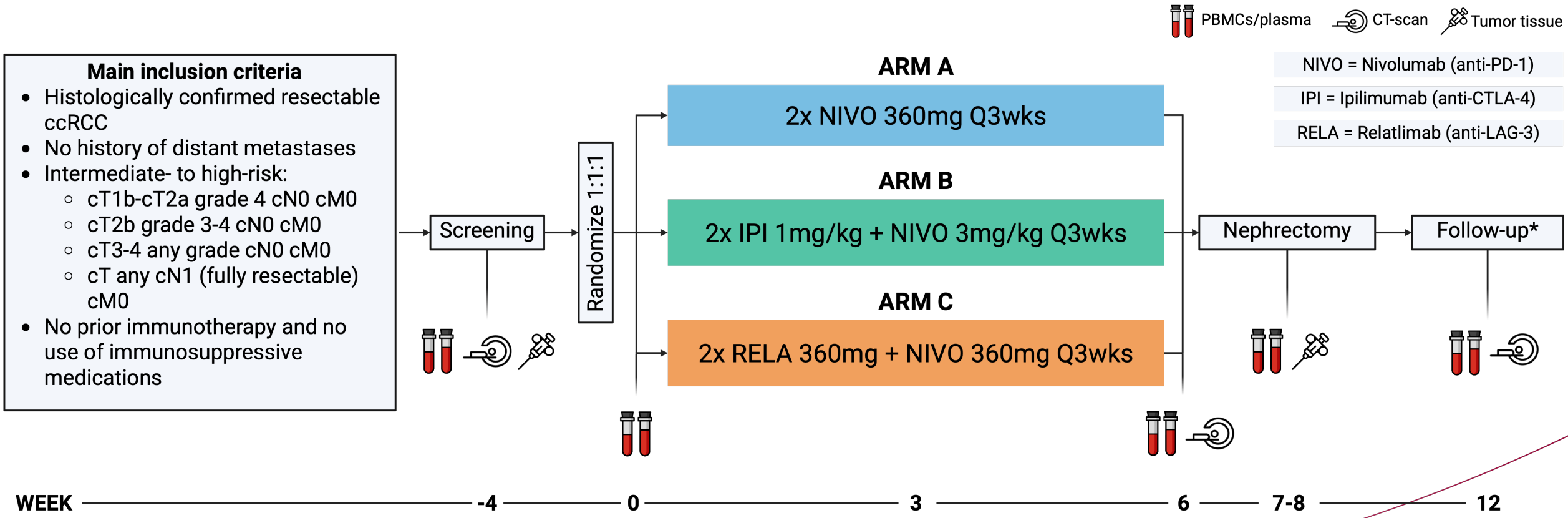
50 YEARS ESMO

Study design

- Investigator initiated, randomized, non-comparative, open-label, two-stage, phase 2 trial

Main inclusion criteria

- Histologically confirmed resectable ccRCC
- No history of distant metastases
- Intermediate- to high-risk:
  - cT1b-cT2a grade 4 cN0 cM0
  - cT2b grade 3-4 cN0 cM0
  - cT3-4 any grade cN0 cM0
  - cT any cN1 (fully resectable) cM0
- No prior immunotherapy and no use of immunosuppressive medications



*Every 3 months for 2 years, then according to institutional standards up to 5 years (in case of no recurrence/ metastases)

Femke Burgers, MD

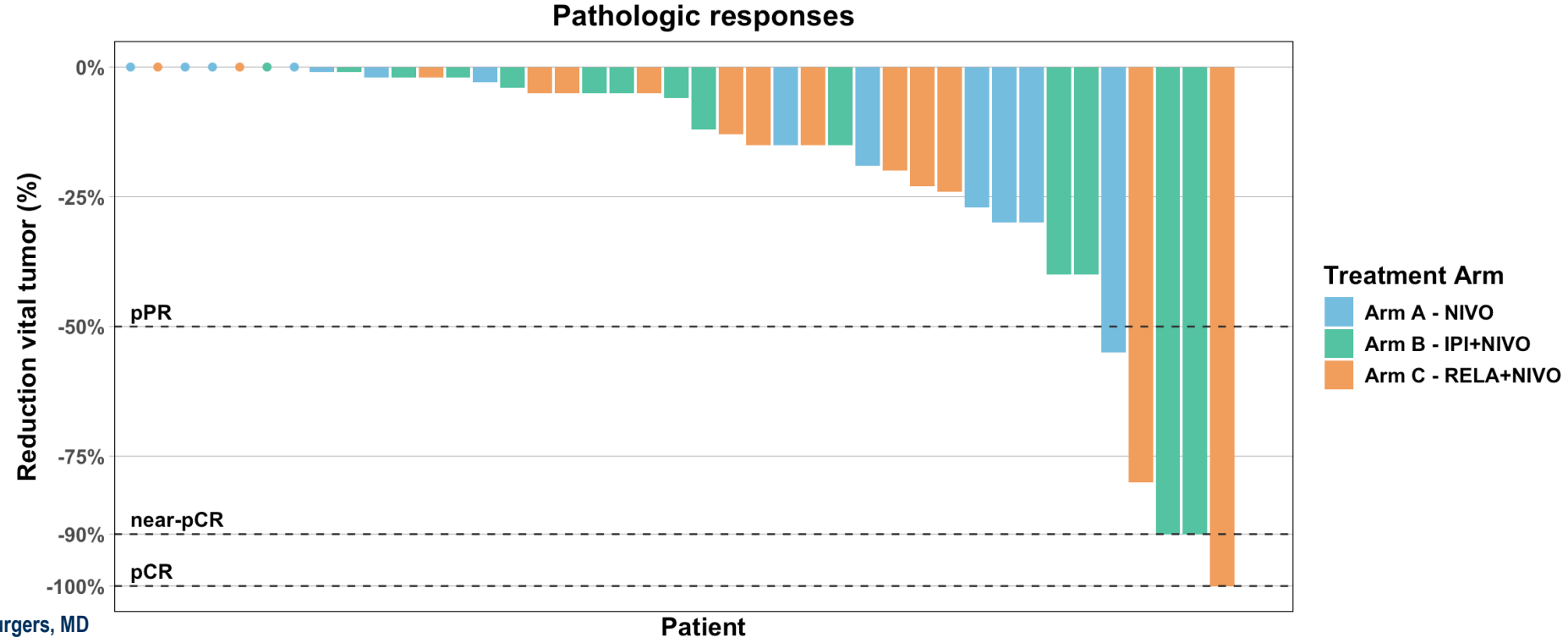
Pathologic responses

pCR = pathologic complete response
near-pCR = near-complete pathologic response
pPR = partial pathologic response

The primary endpoint of at least 2 pathologic responses (first stage) was met for:

- **Arm B - IPI+NIVO**: 2 near-pCR (14.3%)
- **Arm C - RELA+NIVO**: 1 pPR and 1 pCR (14.3%)

Primary endpoint not met for arm A – NIVO: 1 pPR (7.1%)

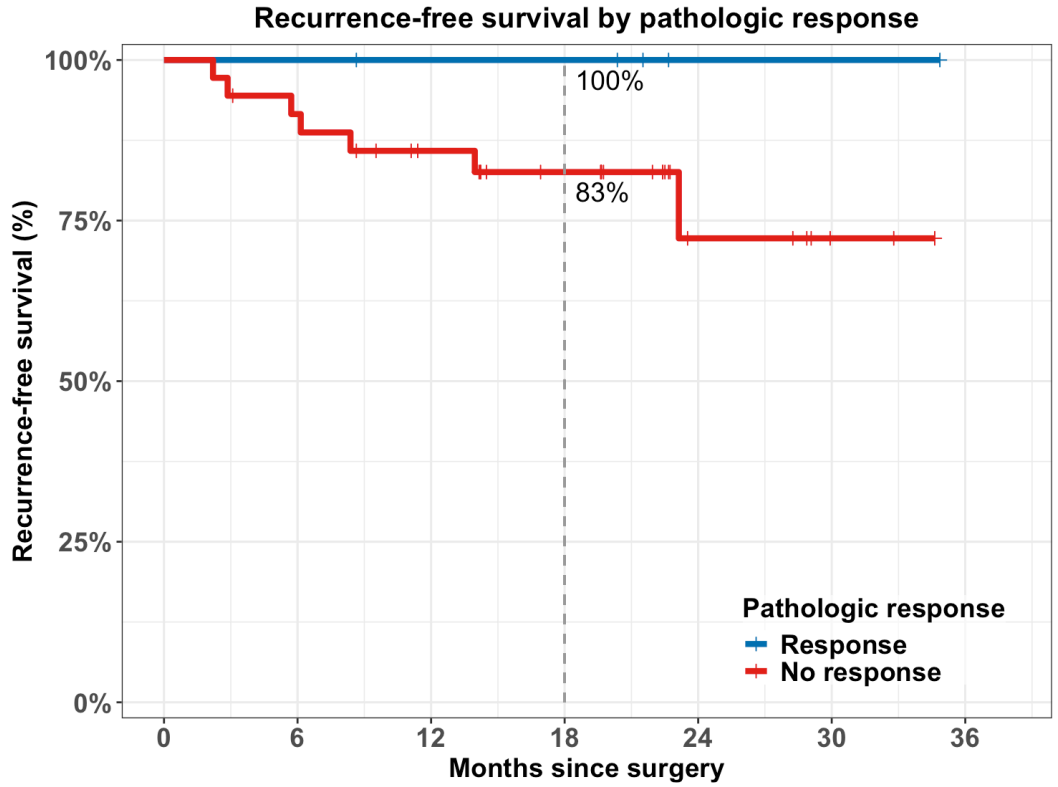


Femke Burgers, MD

RFS based on pathologic response

Exploratory analysis
Preliminary data

At the time of this analysis, all patients with a pathologic response were alive and disease-free

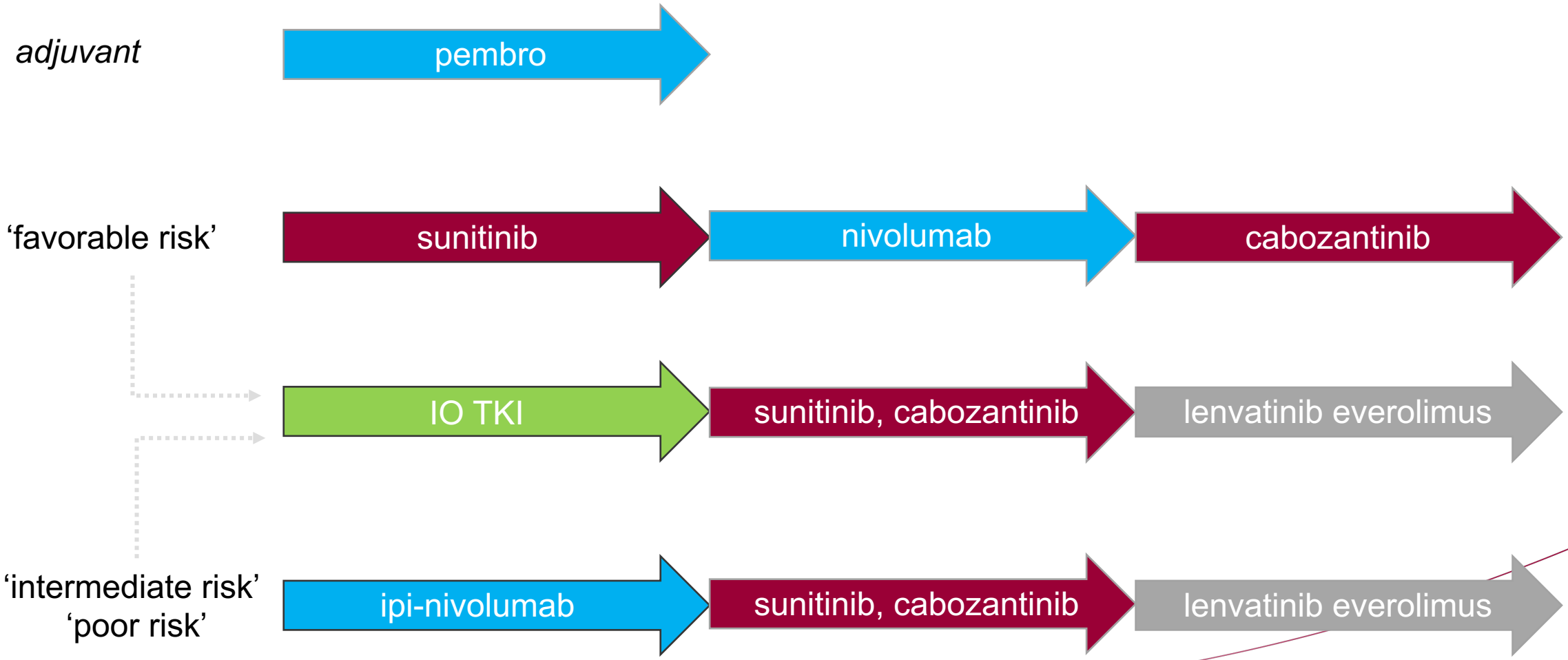


Number at Risk (Events)

Resp	5 (0)	5 (0)	4 (0)	4 (0)	1 (0)	1 (0)	0 (0)
No resp	36 (0)	32 (3)	26 (5)	19 (6)	6 (7)	2 (7)	0 (7)

Femke Burgers, MD

‘Patient journey RCC’



Onderzoeksvragen

- Wat is de beste eerstelijns systeemtherapie?
- HIF2 remmers: de zoektocht naar een optimale combinatie partner
- Is het mogelijk neoadjuvante therapie effectiever te maken?
- Leibovich, KIM1 en ctDNA als biomarkers voor adjuvante therapie

Take home message

- Neo-adjuvante immuuntherapie: hoog actief voor kleine groep
- Leibovich risico score: biomarker voor adjuvante therapie
- HIF2-remmers: een nieuwe klasse medicatie in opkomst

k.vd.mijn@nki.nl