Cancer Conference Update: ESMO Congress 2025 — Urothelial Bladder Cancer and Prostate Cancer

A CME/MOC-Accredited Live Webinar

Thursday, November 20, 2025
5:00 PM – 6:00 PM ET

Faculty

Terence Friedlander, MD
Rana R McKay, MD

Moderator

Neil Love, MD

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Faculty

Terence Friedlander, MD
Professor of Medicine and Robert and Virginia O'Reilly Family Endowed Chair
Chief, Division of Hematology/Oncology
Zuckerberg San Francisco General Hospital
Helen Diller Family Comprehensive Cancer Center
University of California, San Francisco
San Francisco, California

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Rana R McKay, MD
Professor of Medicine and Urology
Associate Director, Clinical Research
Co-Lead, Genitourinary Program
Moores Cancer Center
University of California San Diego
San Diego, California

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP and Natera Inc.

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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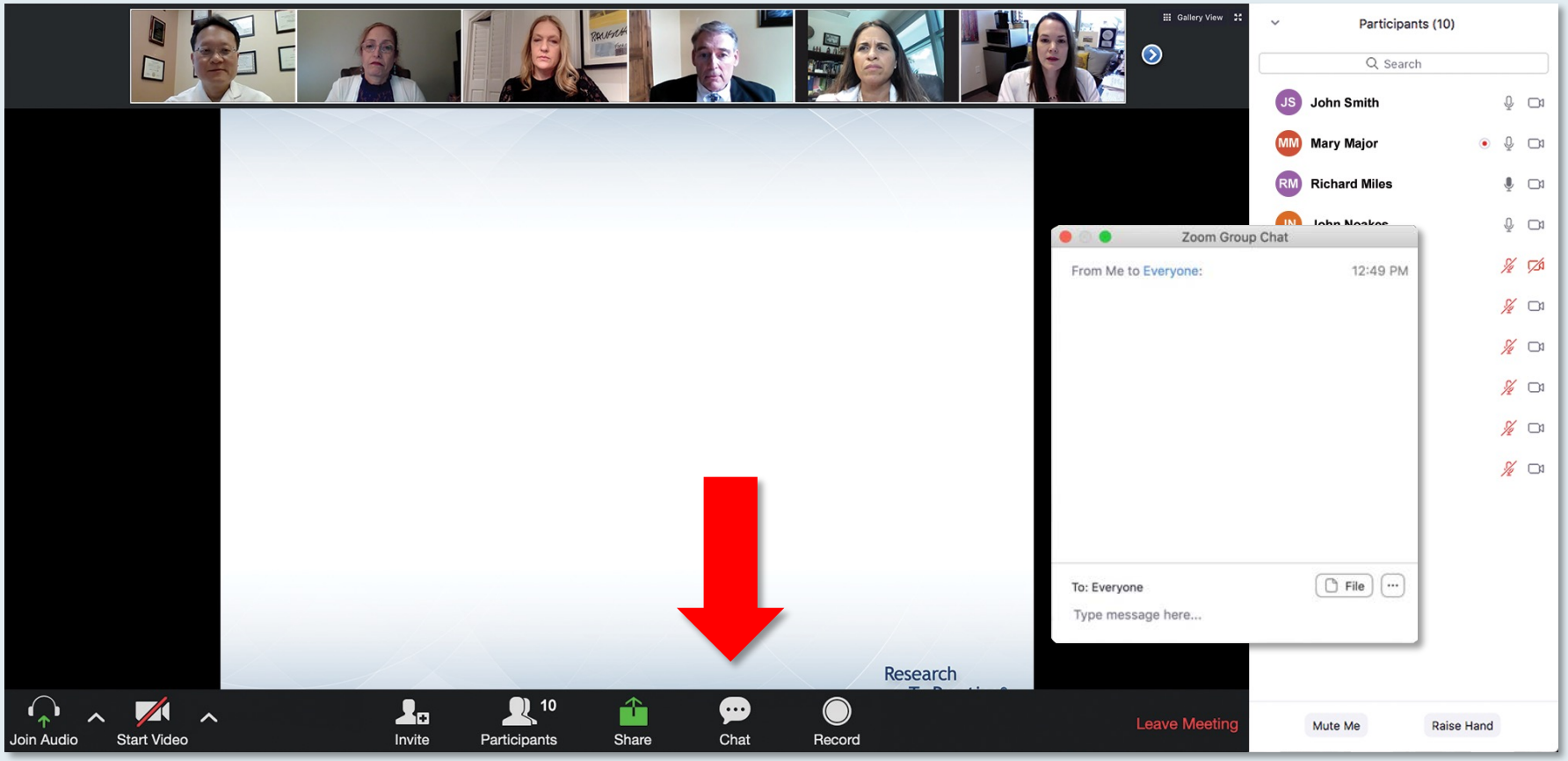
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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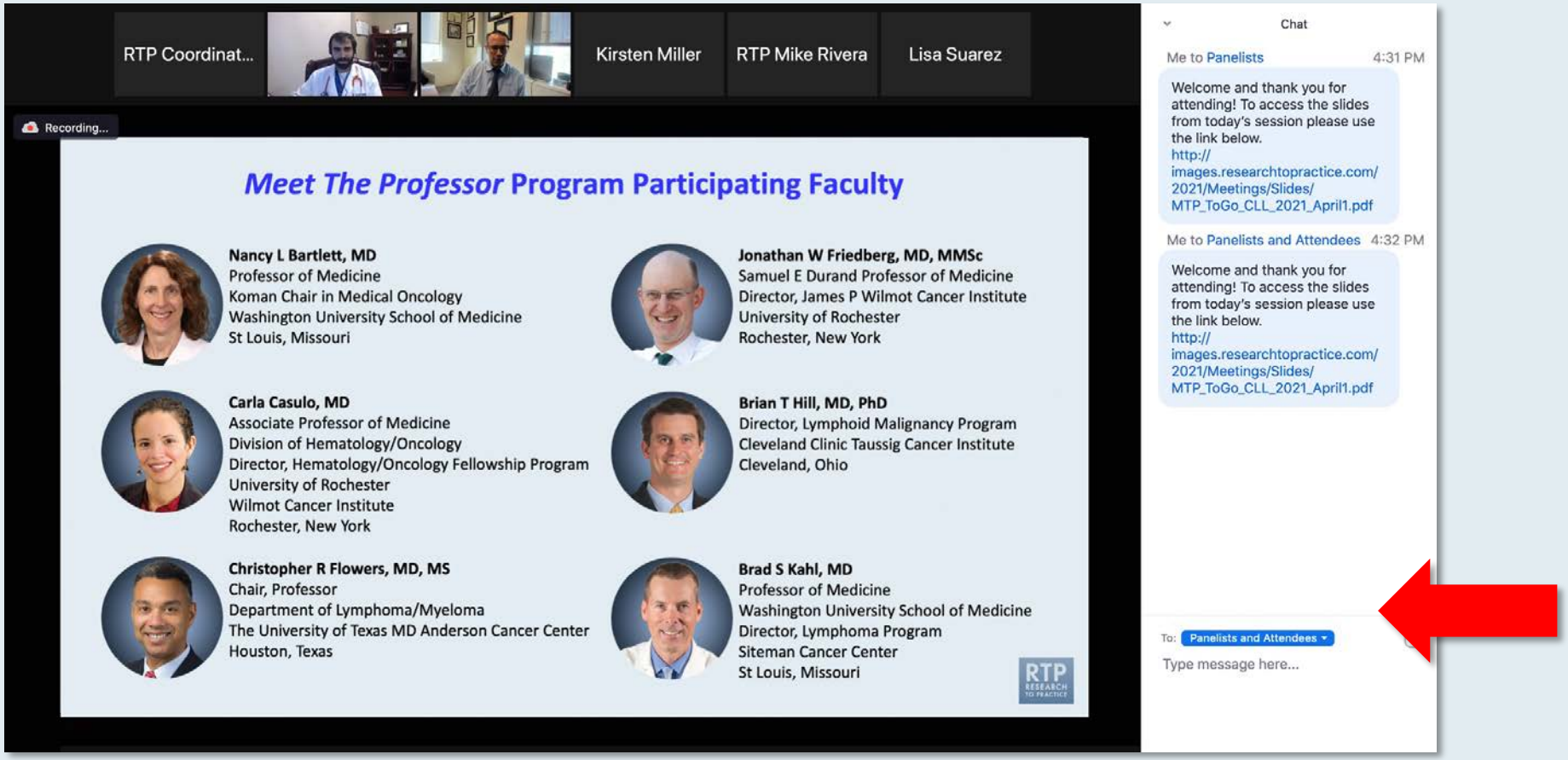
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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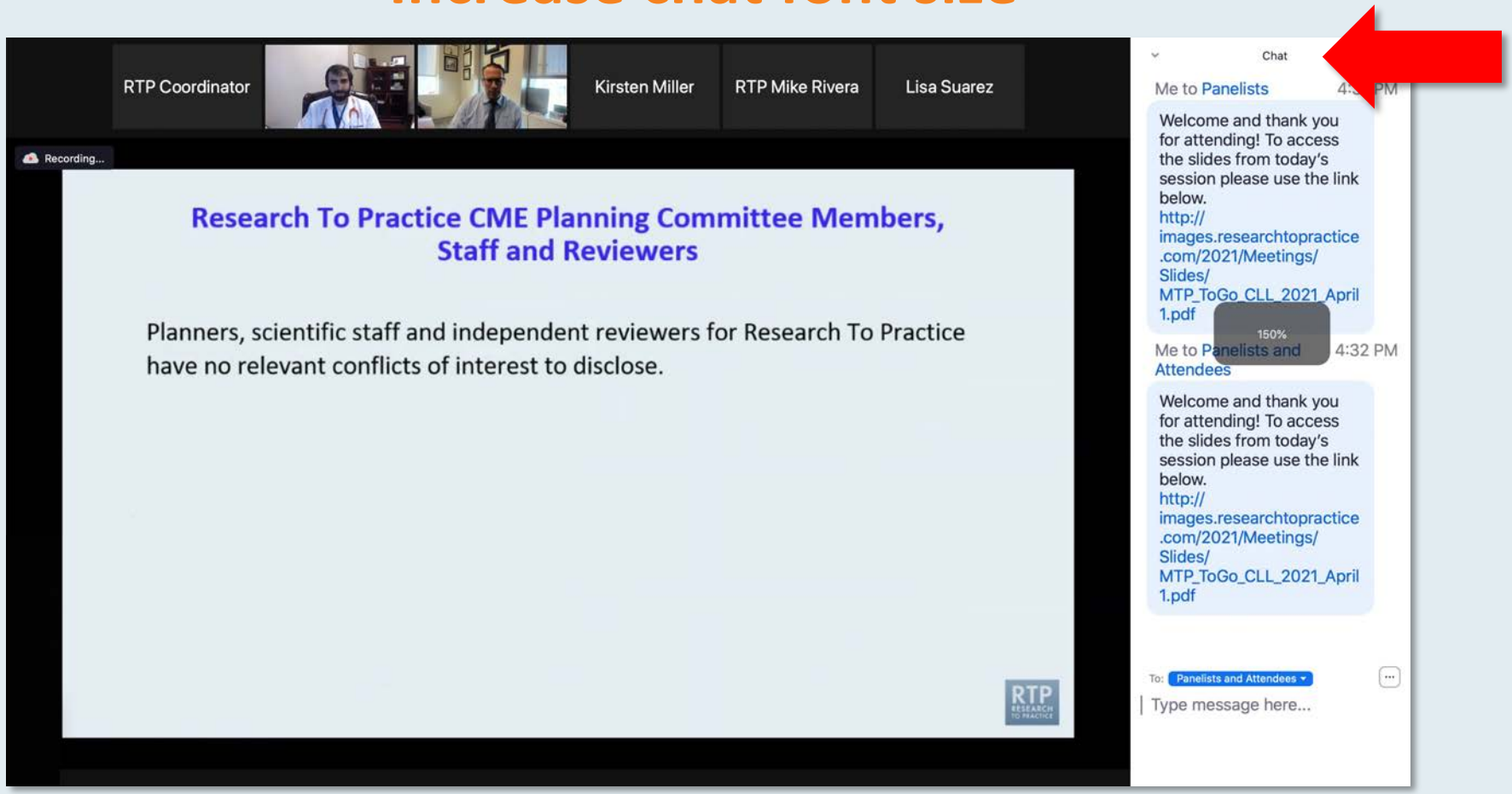
Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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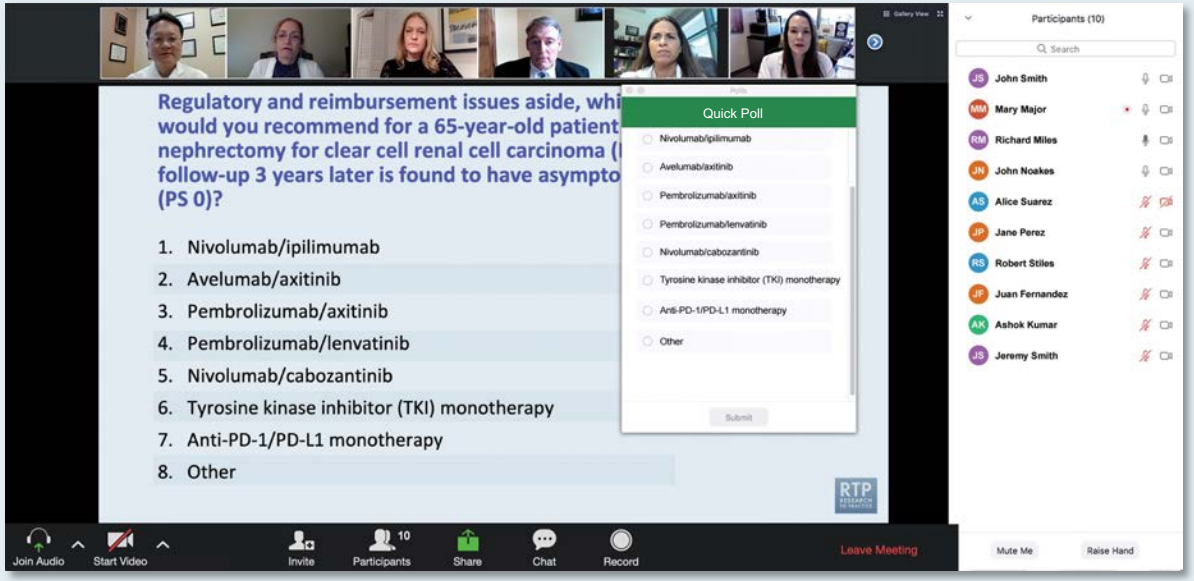

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Prostate Cancer — Proceedings from a Multitumor Symposium in Partnership with Florida Cancer Specialists & Research Institute

DR EMMANUEL S ANTONARAKIS
UNIVERSITY OF MINNESOTA

DR MATTHEW R SMITH
MASSACHUSETTS GENERAL HOSPITAL CANCER CENTER

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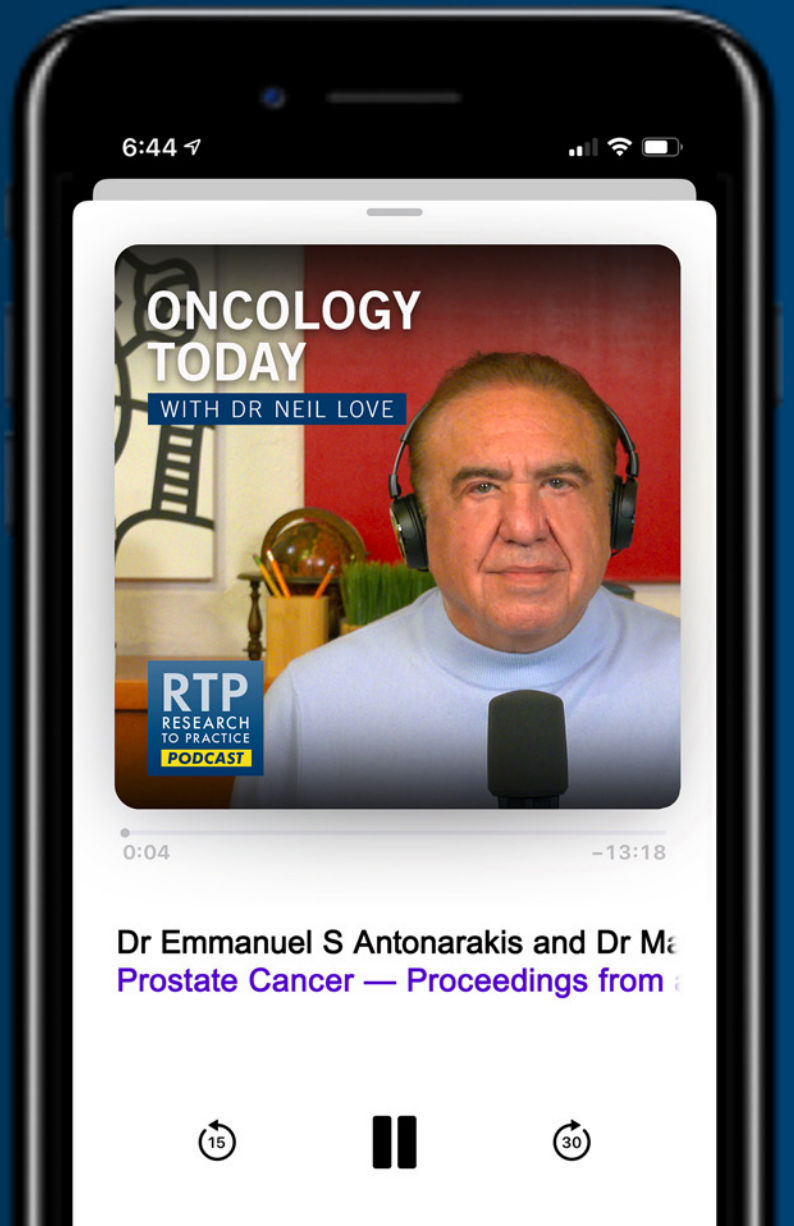

Exciting CME Events You Do Not Want to Miss

A Friday Satellite Symposium Series Preceding the 67th ASH Annual Meeting

Friday, December 5, 2025

Acute Myeloid Leukemia
7:30 AM – 9:30 AM ET

Myelofibrosis and Systemic Mastocytosis
3:15 PM – 5:15 PM ET

Chronic Lymphocytic Leukemia
11:30 AM – 1:30 PM ET

Follicular Lymphoma and Diffuse Large B-Cell Lymphoma
7:00 PM – 9:00 PM ET

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Cases from the Community: Investigators Discuss the Optimal Management of Breast Cancer

A 3-Part CME Satellite Symposium Series

Antibody-Drug Conjugates for Metastatic Breast Cancer

Tuesday, December 9, 2025

7:00 PM – 8:30 PM CT

HER2-Positive Breast Cancer

Wednesday, December 10, 2025

7:00 PM – 9:00 PM CT

Endocrine-Based Therapy

Thursday, December 11, 2025

7:00 PM – 9:00 PM CT

Moderator

Neil Love, MD

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Hematologic Cancers: A 3-Part ASH 2025 Review

A CME/MOC-Accredited Webinar Series

Relapsed/Refractory Multiple Myeloma

Monday, December 15, 2025

5:00 PM – 6:00 PM ET

Immune Thrombocytopenia

Tuesday, December 16, 2025

5:00 PM – 6:30 PM ET

Bispecific Antibodies in Lymphoma

Wednesday, December 17, 2025

5:00 PM – 6:00 PM ET

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Grand Rounds

CME/MOC-Accredited Interactive Series

November 2025 to April 2026

Three Series

Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

Host a 1-hour session at your institution:
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Save The Date

Fifth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us.

Information on how to obtain CME, ABIM MOC and ABS credit will be provided at the conclusion of the activity in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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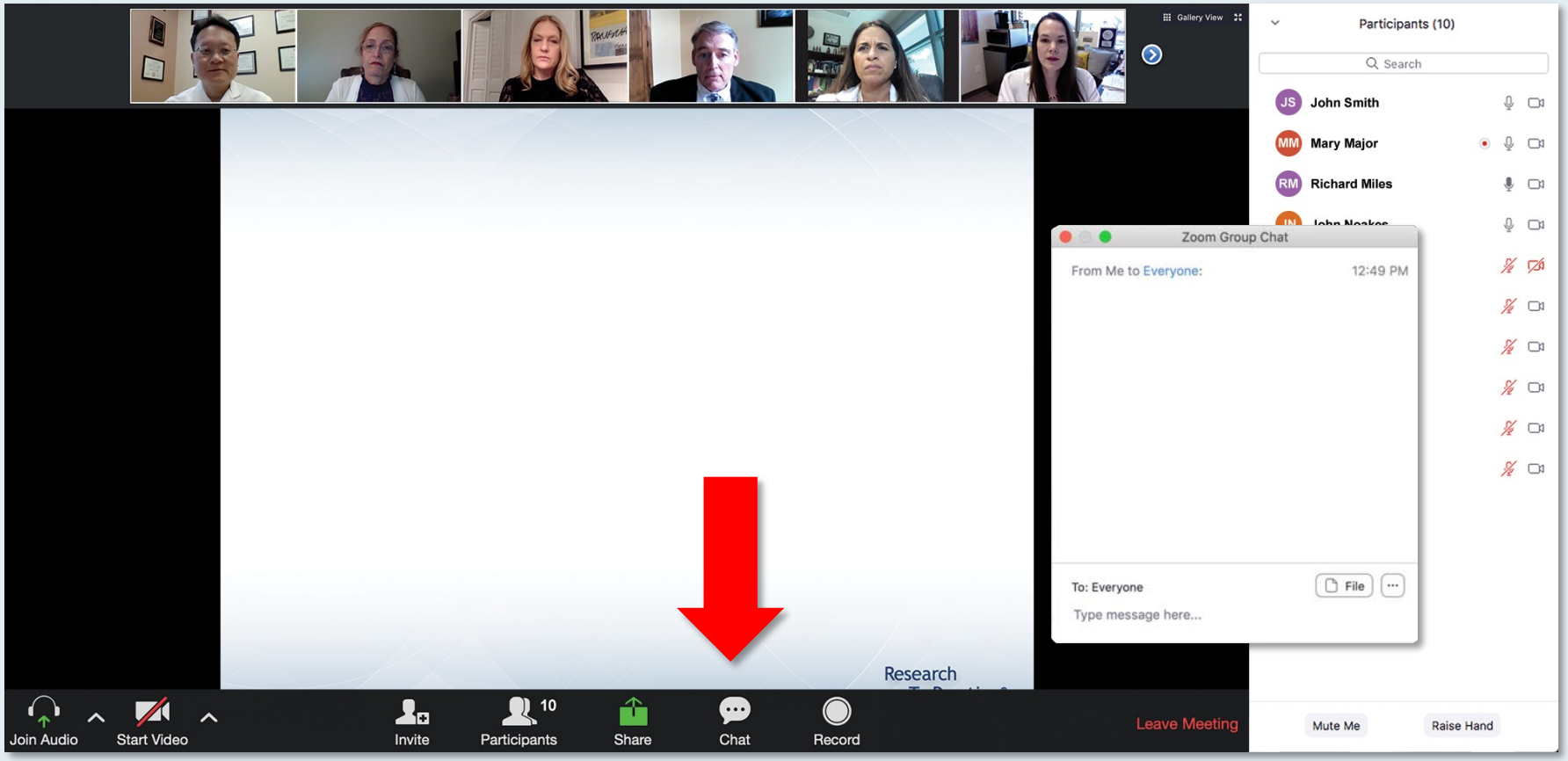

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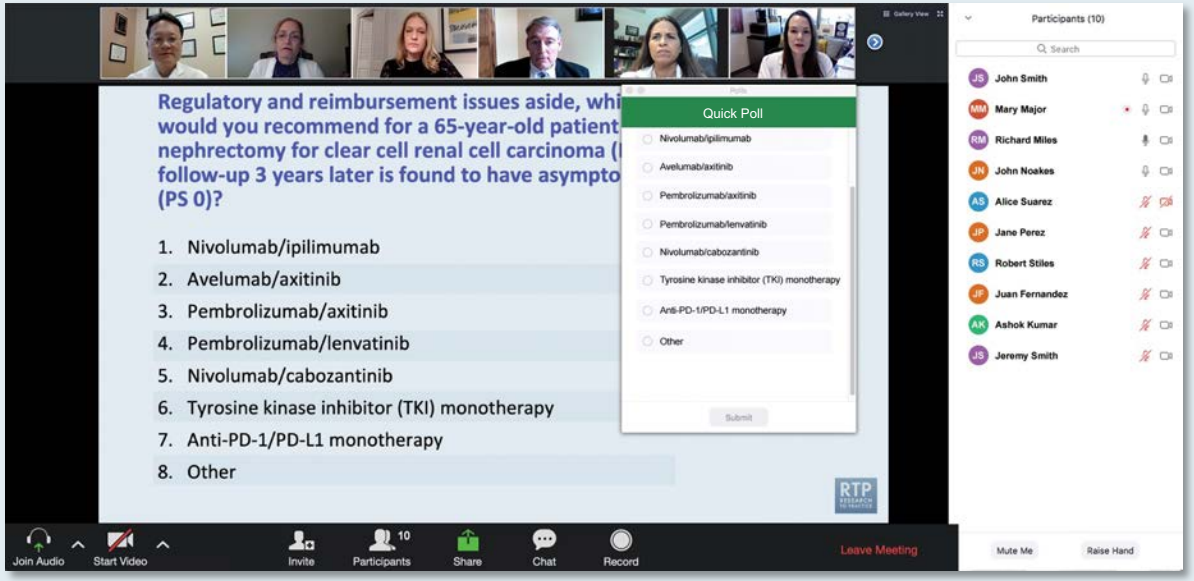

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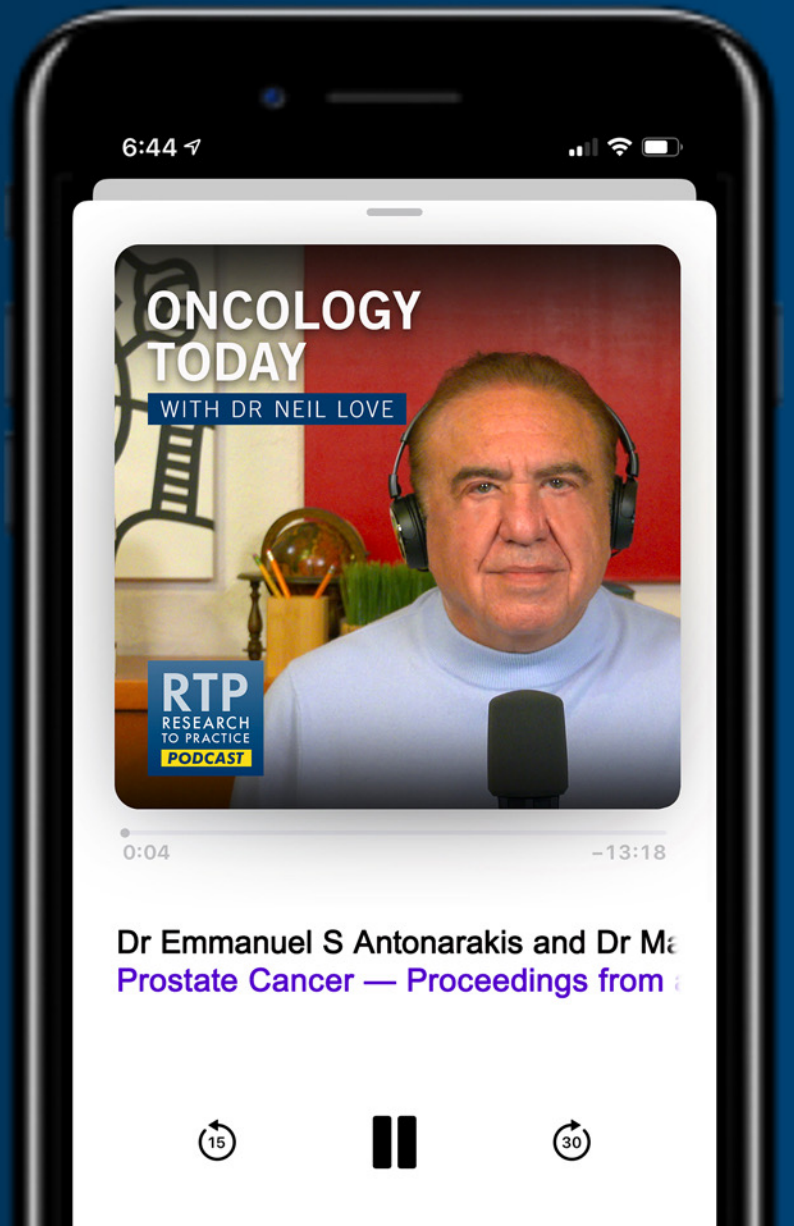

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Agenda

Module 1: Prostate Cancer

- Capivasertib for Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)
- PARP Inhibitors and Androgen Receptor Pathway Inhibitors (ARPIs) for Metastatic Prostate Cancer
- Biochemically Recurrent Prostate Cancer
- Lutetium Lu 177 Vipivotide Tetraxetan for mHSPC
- Radiation Therapy and Androgen Deprivation Therapy with or without an ARPI

Module 2: Urothelial Bladder Cancer

- Neoadjuvant and Perioperative Treatment Approaches for Muscle Invasive Bladder Cancer (MIBC)
- Circulating Tumor DNA and Adjuvant Immunotherapy for MIBC
- HER2-Targeted Antibody-Drug Conjugates for Metastatic Urothelial Bladder Cancer (mUBC)
- Targeting TROP2 in mUBC
- Immunotherapy and BCG for Non-Muscle-Invasive Bladder Cancer

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Key Datasets in Prostate Cancer

- Fizazi K et al. A phase III study of capivasertib (capi) + abiraterone (abi) vs placebo (pbo) + abi in patients (pts) with PTEN deficient de novo metastatic hormone-sensitive prostate cancer (mHSPC): CAPItello-281. ESMO 2025;Abstract 2383O.
- Azad A et al. First interim efficacy analysis of the phase I/II PETRANHA trial of saruparib + androgen receptor pathway inhibitors (ARPI) in patients (pts) with metastatic prostate cancer (mPC). ESMO 2025;Abstract 2384MO.
- Galceran JC et al. Time to response with talazoparib (TALA) + enzalutamide (ENZA) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) in TALAPRO-2. ESMO 2025;Abstract 2428P.
- Freedland S et al. EMBARK: Overall survival with enzalutamide in biochemically recurrent prostate cancer. ESMO 2025;Abstract LBA87.
- Aggarwal R et al. Final results from PRESTO: A phase III open-label study of combined androgen blockade in patients (pts) with high-risk biochemically relapsed prostate cancer (BRPC) (AFT-19). ESMO 2025;Abstract LBA88.

Key Datasets in Prostate Cancer (Continued)

- Tagawa S et al. Phase III trial of [177Lu]Lu-PSMA-617 combined with ADT + ARPI in patients with PSMA-positive metastatic hormone-sensitive prostate cancer (PSMAddition). ESMO 2025;Abstract LBA6.
- Nguyen P et al. Randomised phase III trial of androgen deprivation therapy (ADT) with radiation therapy with or without enzalutamide for high risk, clinically localised prostate cancer: ENZARAD (ANZUP 1303). ESMO 2025;Abstract LBA86.

Capivasertib for mHSPC

- Fizazi K et al. A **phase III** study of **capivasertib (capi)** + abiraterone (abi) vs placebo (pbo) + abi in patients (pts) with **PTEN deficient de novo metastatic hormone-sensitive prostate cancer (mHSPC): CAPItello-281**. ESMO 2025;Abstract 2383O.

Abstract 2383O

BERLIN 2025 ESMO congress

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

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY

ORIGINAL ARTICLE

Capivasertib plus abiraterone in PTEN-deficient metastatic hormone-sensitive prostate cancer: CAPItello-281 phase III study☆

K. Fizazi[1*], N. W. Clarke[2], M. De Santis[3,4], H. Uemura[5], A. P. Fay[6], N. Karadurmus[7], M. Kwiatkowski[8], C. Alvarez-Fernandez[9,10], S. Jiang[11], M. Sotelo[12], D. Parslow[13], N. Oliveira[14,15], T. G. Kwon[16], D. Ye[17], S. Boudewijns[18], P. Danchaivijitr[19], C. Rooney[20], C. Gresty[20], M. Yeste-Velasco[21], J. Logan[22] & D. J. George[23], for the CAPItello-281 Study Group†

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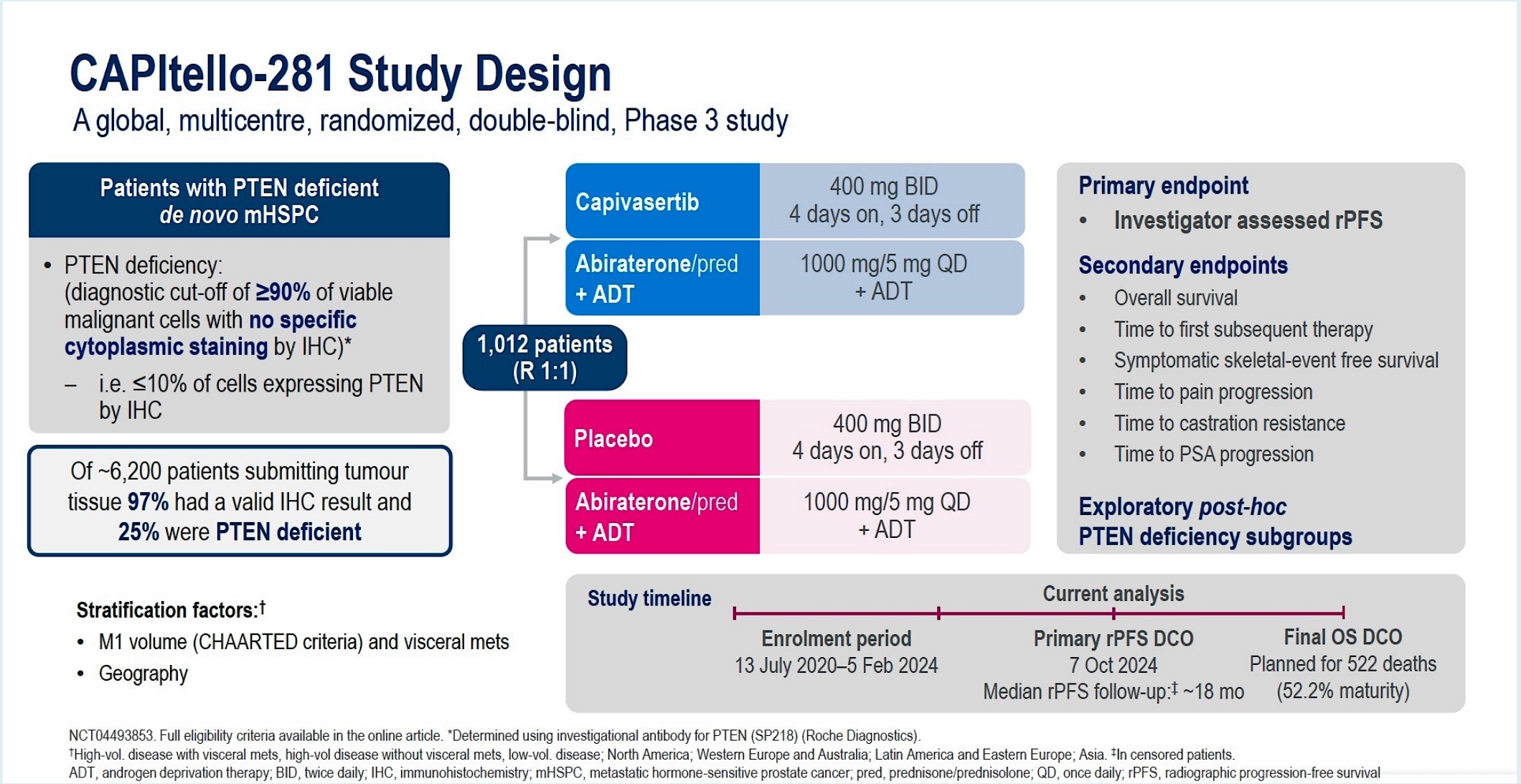
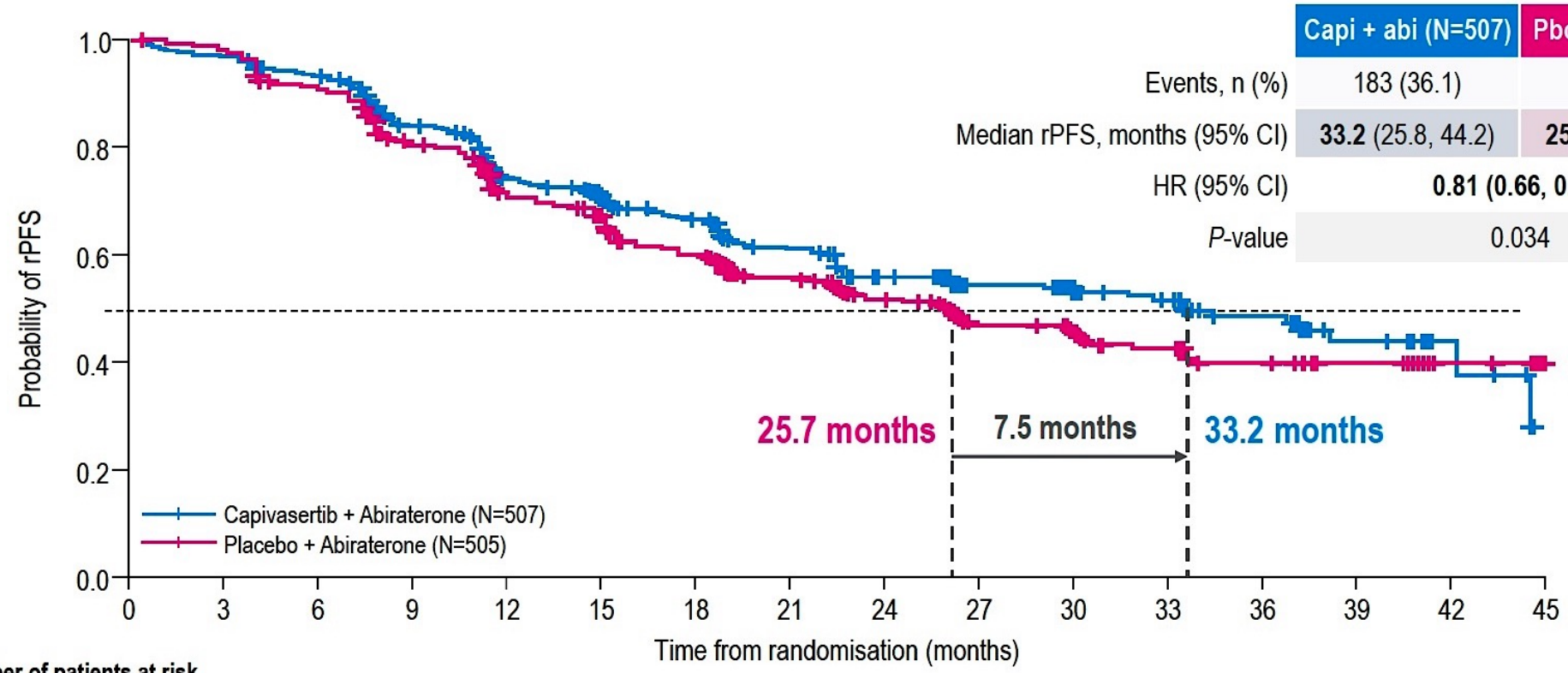
Phase III CAPItello-281 Study Design



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

Fizazi K et al. ESMO 2025;Abstract 2383O.

Phase III CAPItello-281: Investigator-Assessed rPFS



	Capi + abi (N=507)	Pbo + abi (N=505)
Events, n (%)	183 (36.1)	215 (42.6)
Median rPFS, months (95% CI)	**33.2** (25.8, 44.2)	**25.7** (22.0, 29.9)
HR (95% CI)	**0.81 (0.66, 0.98)**	
P-value	0.034	

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

A stratified log-rank test was used to calculate two-sided P values. HRs and 95% CIs were calculated using a stratified Cox proportional-hazards model. Median follow-up: 18.4 months (capi + abi), 18.5 months (pbo + abi)
abi, abiraterone; capi, capivasertib; CI, confidence interval; HR, hazard ratio; pbo, placebo; rPFS, radiographic progression-free survival

Fizazi K et al. ESMO 2025;Abstract 2383O.
Fizazi K et al. Ann Oncol. 2025 Oct 19:S0923-7534(25)04936-1.

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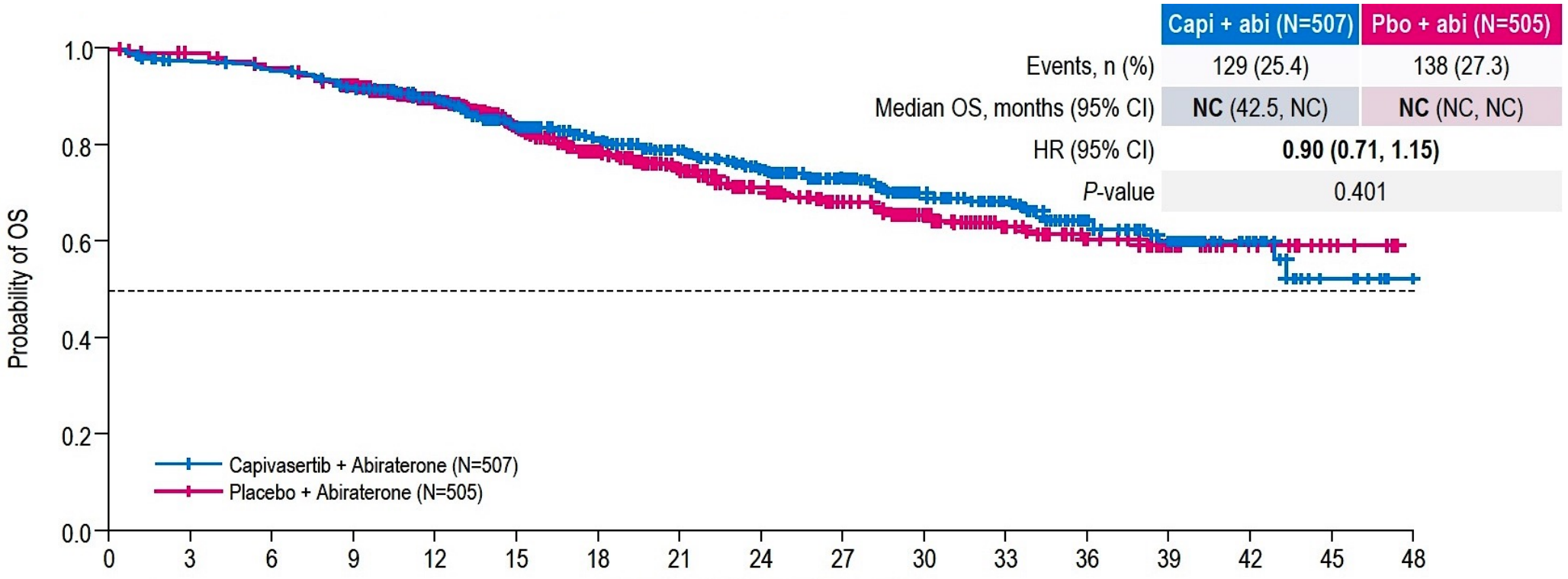
Phase III CAPItello-281: Interim OS



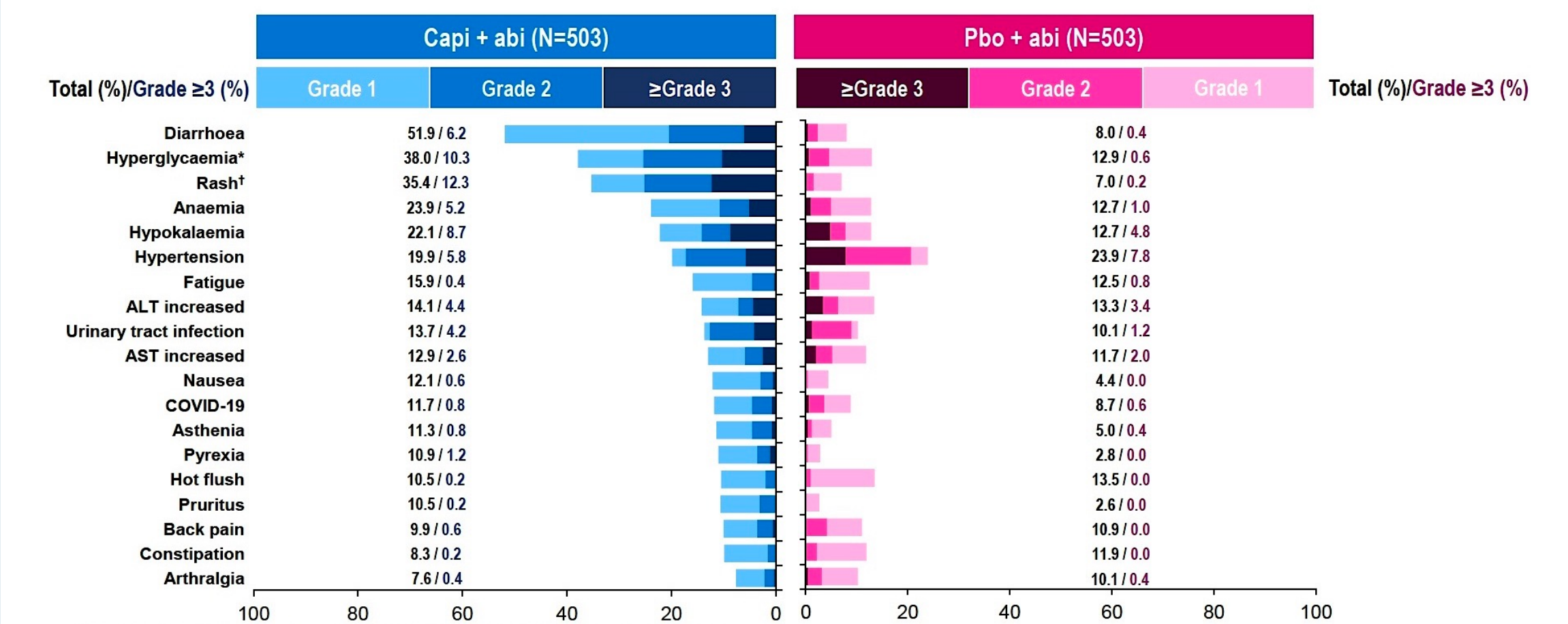
Number of patients at risk

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

A stratified log-rank test was used to calculate two-sided P values. HRs and 95% CIs were calculated using a stratified Cox proportional-hazards model.
CI, confidence interval; HR, hazard ratio; NC, not calculable; OS, overall survival; pbo, placebo

Fizazi K et al. ESMO 2025;Abstract 2383O.
Fizazi K et al. Ann Oncol. 2025 Oct 19:S0923-7534(25)04936-1.

Phase III CAPItello-281: Common Adverse Events



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

*Grouped term (includes the preferred terms of blood glucose increased, hyperglycaemia). †Grouped term (includes the preferred terms of erythema, rash, rash erythematous, rash macular, rash maculo-papular, rash popular, rash pruritic).

abi, abiraterone; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; capi, capivasertib; pbo, placebo

Fizazi K et al. ESMO 2025;Abstract 2383O.

Fizazi K et al. Ann Oncol. 2025 Oct 19:S0923-7534(25)04936-1.

RTP RESEARCH TO PRACTICE

Phase III CAPItello-281: Authors' Conclusions

- Patients with **PTEN deficient mHSPC** have **poor prognosis** and reduced benefit from current SoC
- CAPItello-281 met its primary objective showing a **statistically significant rPFS benefit with capi + abi** vs pbo + abi
  - Median rPFS: capi + abi arm **33.2** months vs pbo + abi **25.7** months (HR 0.81, 95% CI 0.66, 0.98; *P* = 0.034)
- Consistent benefits were also observed in **secondary endpoints** and **clinically relevant pre-defined subgroups**
  - OS was immature and further follow-up is planned
- Post-hoc analyses at **increased PTEN cutoffs** showed **greater treatment effect** with **capi + abi**
- The most common Grade ≥3 AEs of rash and hyperglycaemia are **expected with AKT inhibition**

Capivasertib in combination with abiraterone represents a potential first-in-class targeted treatment for patients with PTEN deficient mHSPC

Fizazi K et al. ESMO 2025;Abstract 2383O.
Fizazi K et al. Ann Oncol. 2025 Oct 19:S0923-7534(25)04936-1.

Dr McKay: Case Presentation

Patient: 66-year-old male

Clinical Course:

- De novo metastatic high-volume disease diagnosed February 2025
- Prostate biopsy: Gleason 5+4=9, PSA 287 ng/mL
- Widespread bone metastases throughout axial and appendicular skeleton
- Multiple bilateral lung metastases (largest 1.4 cm)
- Genomic sequencing of prostate biopsy tissue revealed PTEN loss
- IHC confirmed PTEN loss in 95% of tumor cells
- Started ADT + abiraterone 1000 mg daily with prednisone in March 2025
- Added capivasertib 200 mg BID (4 days on/3 days off schedule) based on PTEN loss
- Given instructions to start loperamide at first episode of diarrhea
- Initiated close lab monitoring including glucose monitoring

PARP Inhibitors and Androgen Receptor Pathway Inhibitors for Metastatic Prostate Cancer

- Azad A et al. **First interim efficacy analysis** of the **phase I/II PETRANHA trial** of **saruparib** + androgen receptor pathway inhibitors (ARPI) in patients (pts) with **metastatic prostate cancer (mPC)**. ESMO 2025;Abstract 2384MO.
- Galceran JC et al. **Time to response** with **talazoparib (TALA) + enzalutamide (ENZA)** in patients (pts) with **metastatic castration-resistant prostate cancer (mCRPC)** in **TALAPRO-2**. ESMO 2025;Abstract 2428P.

Abstract 2384MO

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2384MO

First interim efficacy analysis of the Phase 1/2 PETRANHA trial of saruparib + androgen receptor pathway inhibitors in patients with metastatic prostate cancer

Arun Azad,[1] Anthony M. Joshua,[2] Mark Voskoboynik,[3] Peter Sankey,[4] Simon Pacey,[5] Patrick Pilié,[6] Elisabeth Heath,[7] Andrew Weickhardt,[8] Laurence Krieger,[9] Consuelo Buttigliero,[10] Eleni Efstathiou,[11] Lisa Horvath,[12] Robert Jones,[13] Marco Maruzzo,[14] Benjamin Webb,[15] Niedzica Camacho,[16] Younghwa Kim,[17] Bruno De Paula,[17] Tsveta Milenkova,[17] Andrew Hudson[18]

[1]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; [2]Department of Medical Oncology, Kingshorn Cancer Centre, St Vincent's Hospital, Sydney, Australia; [3]Department of Medical Oncology, Alfred Health, Monash University, Melbourne, Australia; [4]Department of Oncology, University Hospitals Plymouth NHS Trust, Derriford Hospital, Plymouth, UK; [5]Department of Oncology, Cambridge University Hospitals NHS Foundation Trust & Department of Oncology, Clinical School, University of Cambridge, Addenbrookes Hospital, Cambridge, UK; [6]Department of Genitourinary Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA; [7]Department of Oncology, Mayo Clinic Comprehensive Cancer Center, Rochester, MN, USA; [8]Department of Medical Oncology, Olivia Newton-John Cancer and Wellness Centre, Austin Health, Heidelberg, Australia; [9]Department of Medical Oncology, Genesis Care, North Shore, Sydney, Australia; [10]Department of Oncology, University of Turin at San Luigi Hospital, Orbassano, Italy; [11]Department of Genitourinary Oncology, Houston Methodist Cancer Center, Houston, TX, USA; [12]Department of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, Australia; [13]University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, Scotland; [14]Oncology Unit 1, Istituto Oncologico Veneto IOV - IRCCS, Padova, Italy; [15]Early Oncology Statistics, AstraZeneca, Cambridge, UK; [16]Oncology Data Science, Oncology R&D, AstraZeneca, Cambridge, UK; [17]Early Oncology R&D, AstraZeneca, Cambridge, UK; [18]Department Clinical Oncology, The Christie NHS Foundation Trust, Manchester, UK

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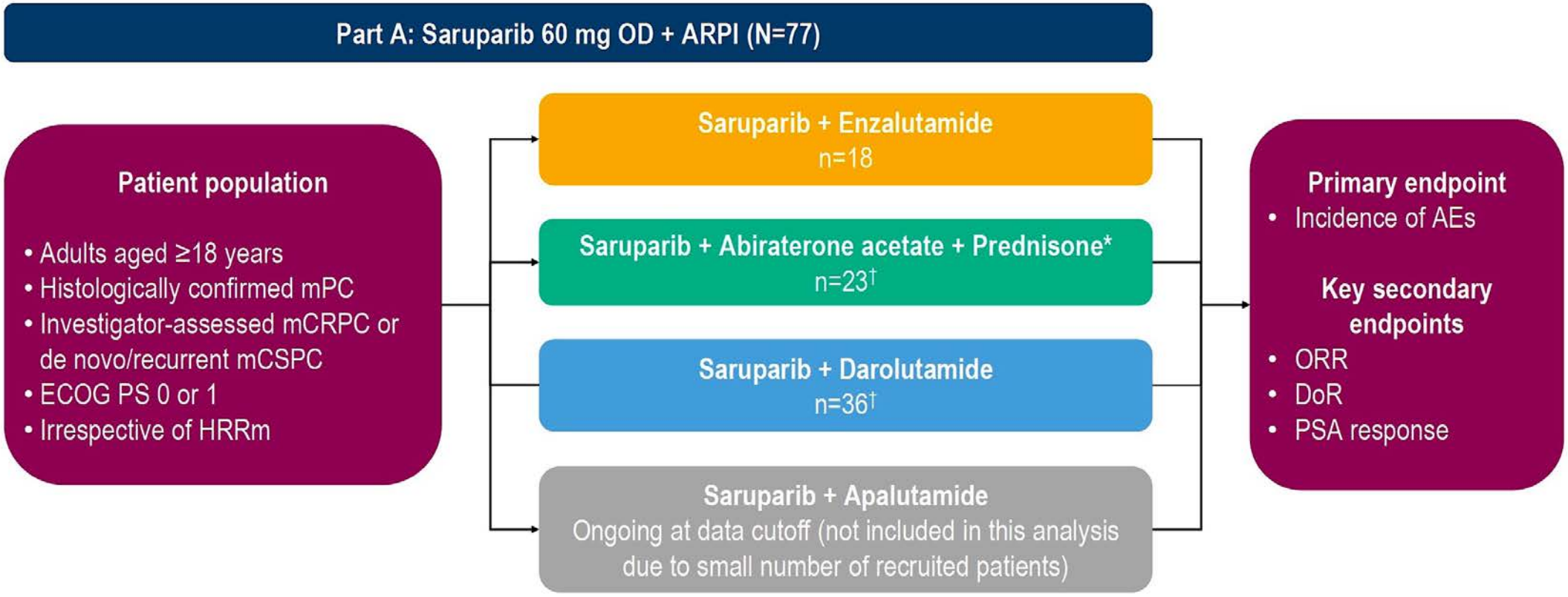
RTP RESEARCH TO PRACTICE

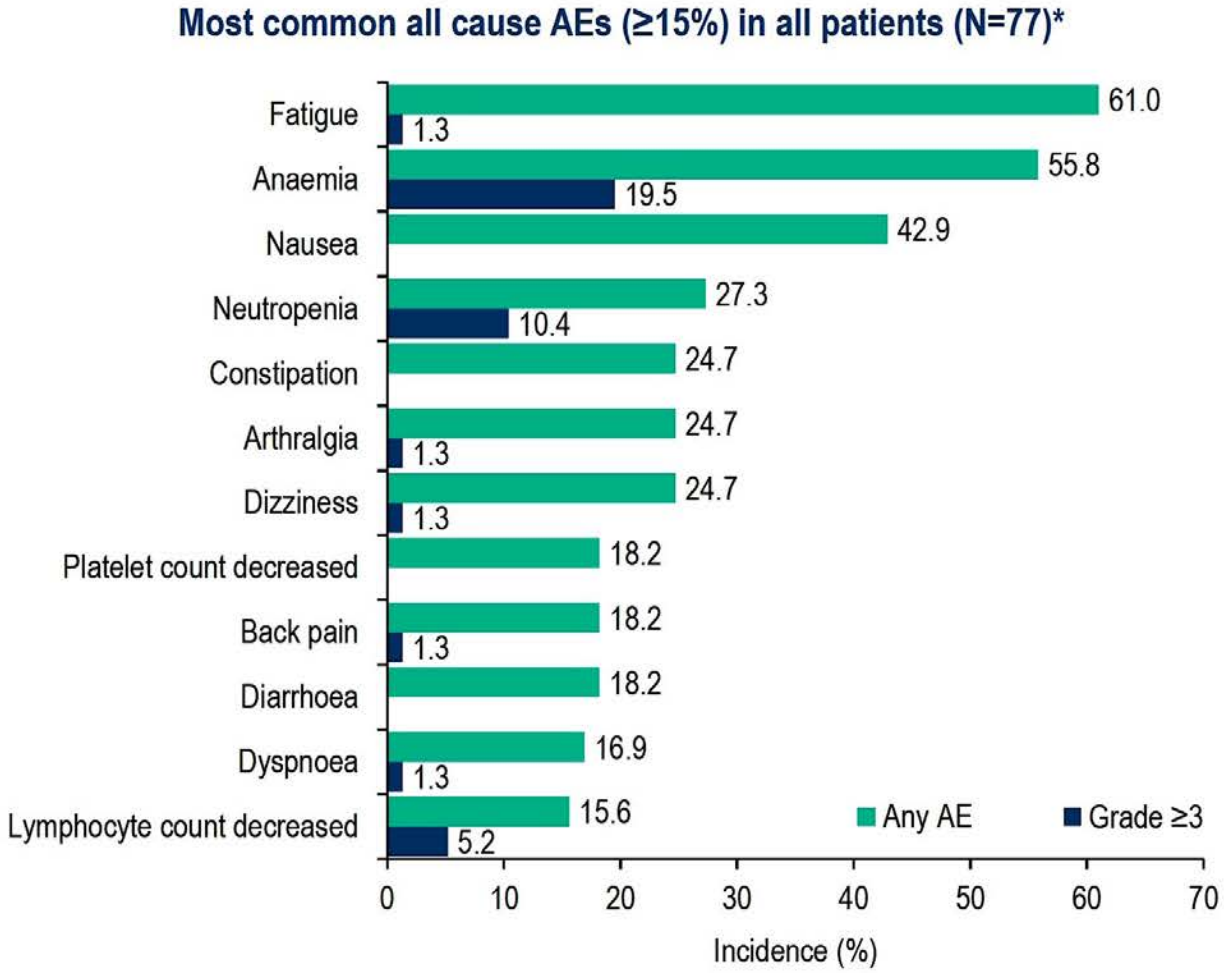
Phase I/II PETRANHA Study Design

- Part A median duration of follow-up: 18.1 months (range, 0.2–28.2).



Azad A et al. ESMO 2025;Abstract 2384MO.

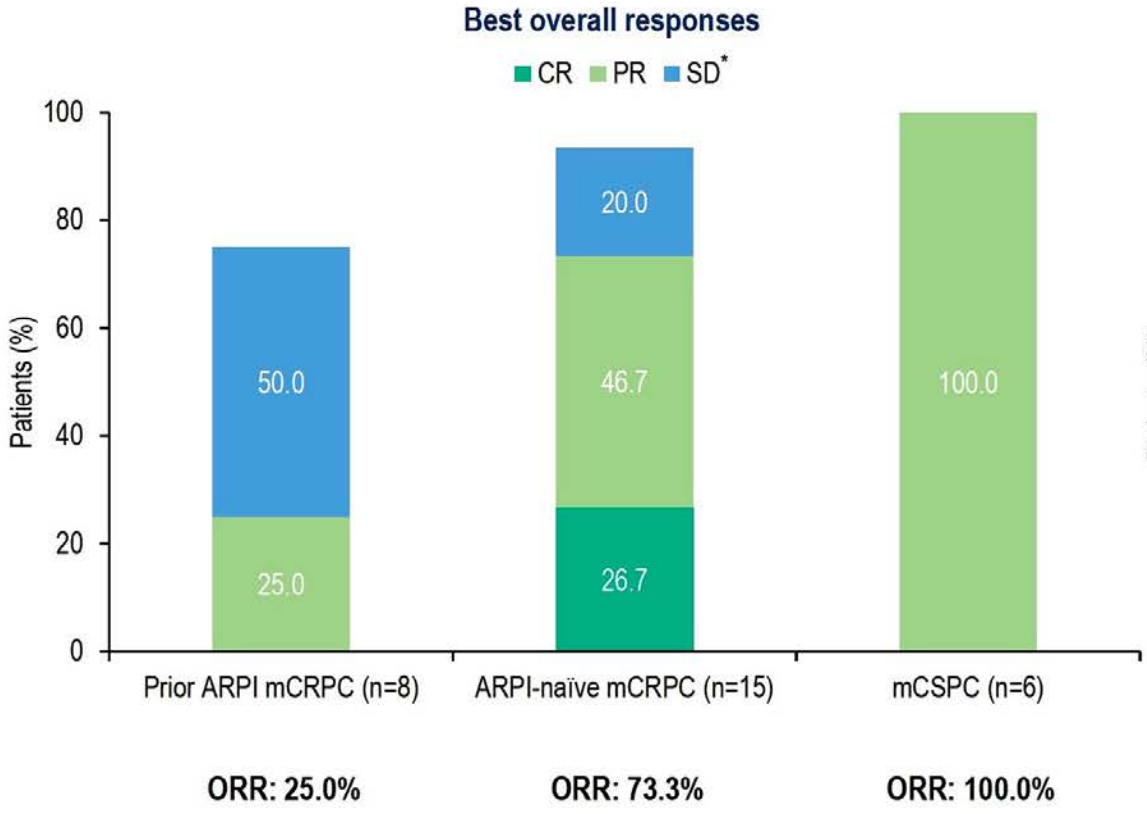
Phase I/II PETRANHA Primary Endpoint: Incidence of Adverse Events (AEs)

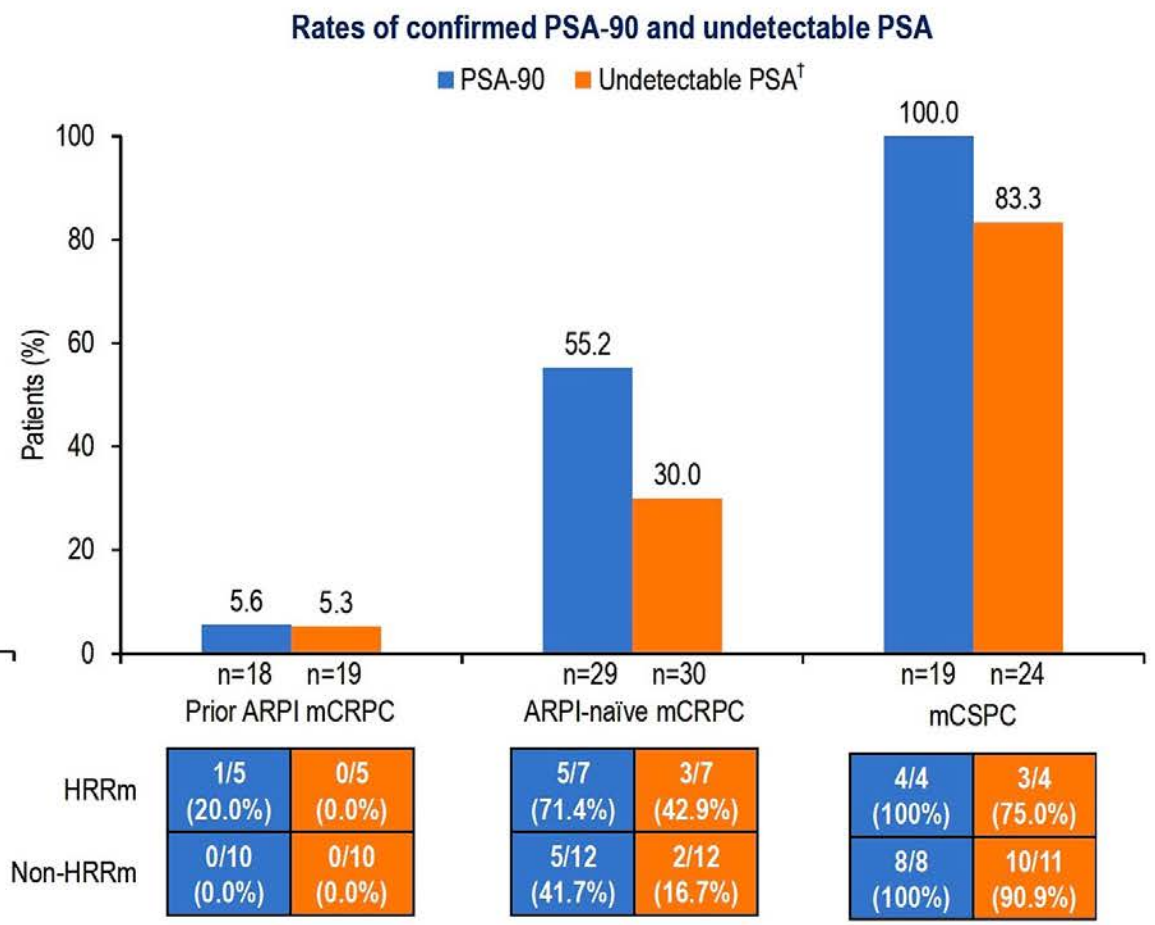


- Grade ≥3 AEs occurred in 46.8% of patients, with a relatively low incidence of anaemia (19.5%) and GI events (2.6%)†.
- Any AE leading to discontinuation of saruparib and ARPI occurred in 10.4% and 3.9% patients, respectively.
- No cases of myelodysplastic syndrome were reported.

Azad A et al. ESMO 2025;Abstract 2384MO.

Phase I/II PETRANHA: Responses





Azad A et al. ESMO 2025;Abstract 2384MO.

Phase I/II PETRANHA: Authors' Conclusions

- Saruparib in combination with different ARPIs had manageable toxicity,[1] with a comparable or lower incidence of Grade ≥3 AEs than similar combinations of nonselective PARP inhibitors.[2-4]

- Interim efficacy results were promising, with high rates of responses irrespective of HRRm status.
  - ORR (73.3%) was high in patients with ARPI-naïve mCRPC.
  - Undetectable PSA levels were reached in 83.3% of patients with mCSPC.

- The Phase 3 EvoPAR-Prostate01 trial (NCT06120491) is currently ongoing and evaluating saruparib in combinations with ARPIs in mCSPC.

Azad A et al. ESMO 2025;Abstract 2384MO.

2428P

Time to Response With Talazoparib Plus Enzalutamide in Patients With Metastatic Castration-Resistant Prostate Cancer in TALAPRO-2

Joan Carles,[1] Neeraj Agarwal,[2] Arun A. Azad,[3] Stefanie Zschäbitz,[4] André P. Fay,[5] Steven M. Yip,[6] Jan Oldenburg,[7] Ugo De Giorgi,[8,*] Neal D. Shore,[9] Peter C. C. Fong,[10] Sarah Hanson,[11] Matko Kalac,[11] Xun Lin,[12] Karim Fizazi[13]

Phase III TALAPRO-2 Study: ORR, Time to Response and Duration of Objective Response

	Talazoparib Plus Enzalutamide			Placebo Plus Enzalutamide		
	ORR; n/N	Median TTR, mo (Range)	Median Duration of Soft Tissue OR, mo (95% CI)	ORR; n/N	Median TTR, mo (Range)	Median Duration of Soft Tissue OR, mo (95% CI)
Unselected cohort[3]	61%; 72/119	2.0 (1.6–11.3)	20.4 (16.1–31.3)	44%; 57/130	1.9 (1.6–24.8)	19.8 (12.0–24.0)
HRR-non-deficient subgroup*	54%; 27/50	1.9 (1.6–11.0)	22.2 (9.3–36.9)	36%; 20/56	1.9 (1.6–10.9)	21.4 (6.6–NR)
Undetermined HRR subgroup†	54%; 13/24	3.5 (1.7–8.2)	16.3 (7.4–NR)	62%; 21/34	2.1 (1.6–5.3)	19.8 (9.0–34.1)
HRR-deficient subgroup‡	71%; 32/45	2.1 (1.6–11.3)	20.3 (10.3–35.4)	40%; 16/40	2.0 (1.6–24.8)	14.8 (6.3–41.5)
HRR-deficient cohort[4]	69%; 50/72	2.1 (1.6–22.1)	22.1 (14.4–32.2)	38%; 25/65	1.9 (1.6–24.8)	11.4 (7.1–16.6)

CI=confidence interval; ctDNA=circulating tumor DNA; HRR=homologous recombination repair; n=number of patients with complete or partial response; N=number of patients with measurable disease; NR=not reached; OR=objective response; ORR=objective response rate; TTR=time to objective response.

*By both ctDNA and tumor tissue test; †HRR-deficient by ctDNA or tumor tissue test and unknown by the other, or unknown by both; ‡By either ctDNA or tumor tissue test.

Galceran JC et al. ESMO 2025;Abstract 2428P.

Phase III TALAPRO-2: Authors' Conclusions

The median TTR was short in patients with mCRPC receiving talazoparib plus enzalutamide (unselected cohort, 2.0 months; HRR-deficient cohort, 2.1 months) and those receiving placebo plus enzalutamide (unselected cohort, 1.9 months; HRR-deficient cohort, 1.9 months)

The median time to PSA response was 1.9 months for patients in both cohorts and consistent regardless of HRR gene alteration status

TTR = time to response; mCRPC = metastatic castration-resistant prostate cancer; HRR = homologous recombination repair; PSA = prostate-specific antigen

Galceran JC et al. ESMO 2025;Abstract 2428P.

Dr McKay: Case Presentation

Patient: 63-year-old male

Clinical Course:

- Initial diagnosis 2019: Gleason 4+4=8, PSA 18.7 ng/mL, T3a disease on MRI
- Treated with definitive radiation therapy + ADT for 2 years
- PSA nadir 0.34 ng/mL after completion of therapy
- 2022: Rising PSA with rapid doubling time of 3 months
- CT CAP and bone scan revealed retroperitoneal lymph nodes and 4 bone metastases in spine and pelvis
- Restarted ADT in late 2022
- PSA responded well, dropping to 0.56 ng/mL
- Maintained response for 1.5 years

Dr McKay: Case Presentation (Continued)

Clinical Course:

- Mid-2024: PSA rising to 5.6 ng/mL with imaging showing disease progression
- CT CAP and bone scan demonstrated retroperitoneal lymph nodes and 4 bone metastases in the pelvis and spine.
- Germline testing revealed BRCA2 mutation
- Somatic tumor profiling from original RP specimen also showed BRCA2 mutation
- Started olaparib 300 mg BID + abiraterone 1000 mg daily with prednisone in April 2025
- PSA decreased from 12.8 to 0.9 ng/mL after 7 months
- Tolerating therapy with fatigue, anemia requiring initial dose hold, then resuming with same dose with stability of anemia

Biochemically Recurrent Prostate Cancer

- Freedland S et al. **EMBARK: Overall survival** with **enzalutamide** in **biochemically recurrent prostate cancer**. ESMO 2025;Abstract LBA87.
- Aggarwal R et al. **Final results from PRESTO:** A **phase III** open-label study of **combined androgen blockade** in patients (pts) with **high-risk biochemically relapsed prostate cancer (BRPC)** (AFT-19). ESMO 2025;Abstract LBA88.

Abstract LBA87

Plain Language Summary

Video

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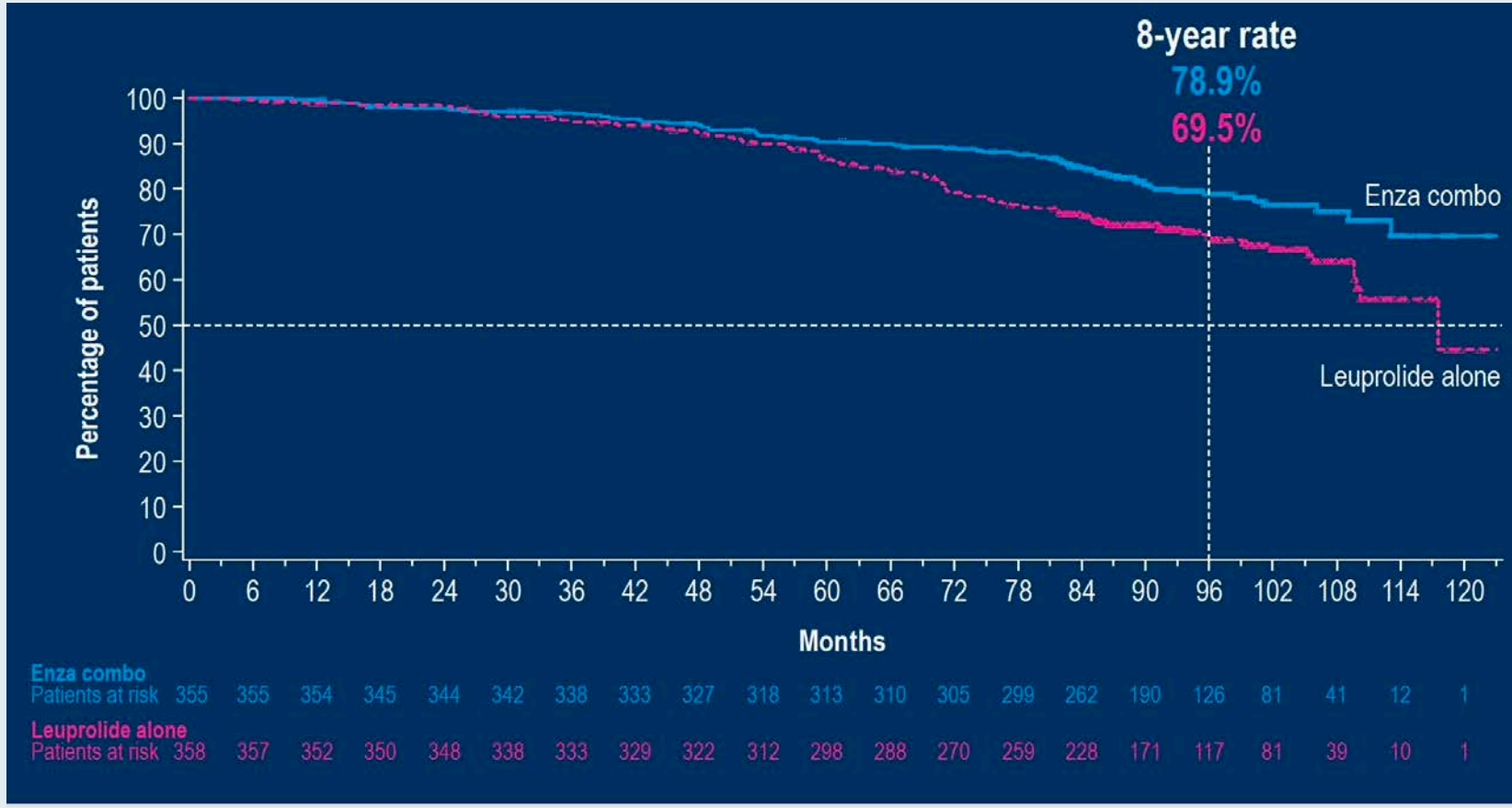
Overall survival with enzalutamide in biochemically recurrent prostate cancer

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 Urologia, Fundación Instituto Valenciano de Oncologia, 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

Phase III EMBARK: Overall Survival with Enzalutamide Combination



	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)

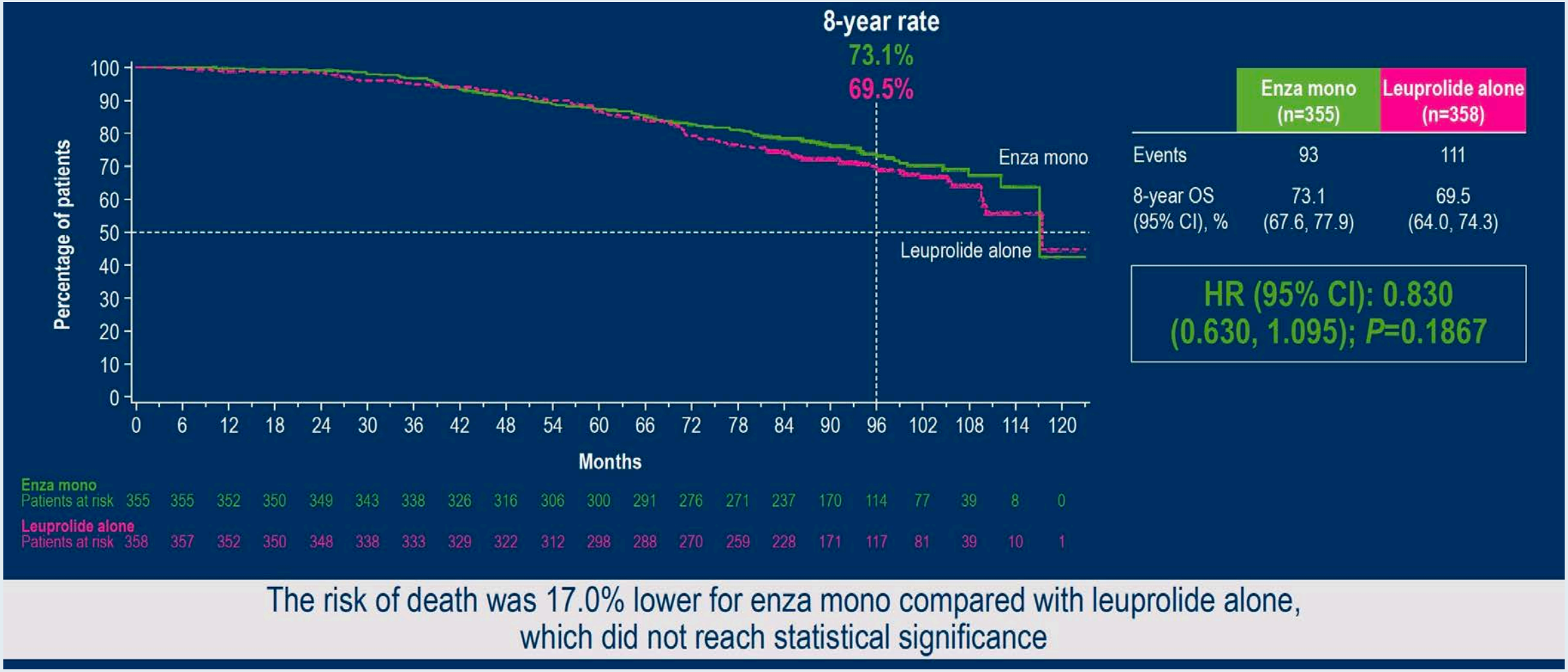
HR (95% CI): 0.597 (0.444, 0.804); *P*=0.0006

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

Freedland S et al. ESMO 2025;Abstract LBA87.

RTP RESEARCH TO PRACTICE

Phase III EMBARK: Overall Survival with Enzalutamide Monotherapy



	Enza mono (n=355)	Leuprolide alone (n=358)
Events	93	111
8-year OS (95% CI), %	73.1 (67.6, 77.9)	69.5 (64.0, 74.3)

HR (95% CI): 0.830 (0.630, 1.095); *P*=0.1867

The risk of death was 17.0% lower for enza mono compared with leuprolide alone, which did not reach statistical significance

Freedland S et al. ESMO 2025;Abstract LBA87.

RTP RESEARCH TO PRACTICE

Phase III EMBARK: Authors' Conclusions

- Enza combo reduced the risk of death by more than 40% vs leuprolide alone in patients with hrBCR prostate cancer
- Enza mono led to a numerically lower risk of death vs leuprolide alone, although the difference did not reach statistical significance
- Significant improvements in time to first use of new antineoplastic therapy, time to symptomatic skeletal events, and PFS2 further highlight the benefit of both enza combo and enza mono
- No new safety signals were observed in the long-term safety analysis

Freedland S et al. ESMO 2025;Abstract LBA87.

Abstract LBA88

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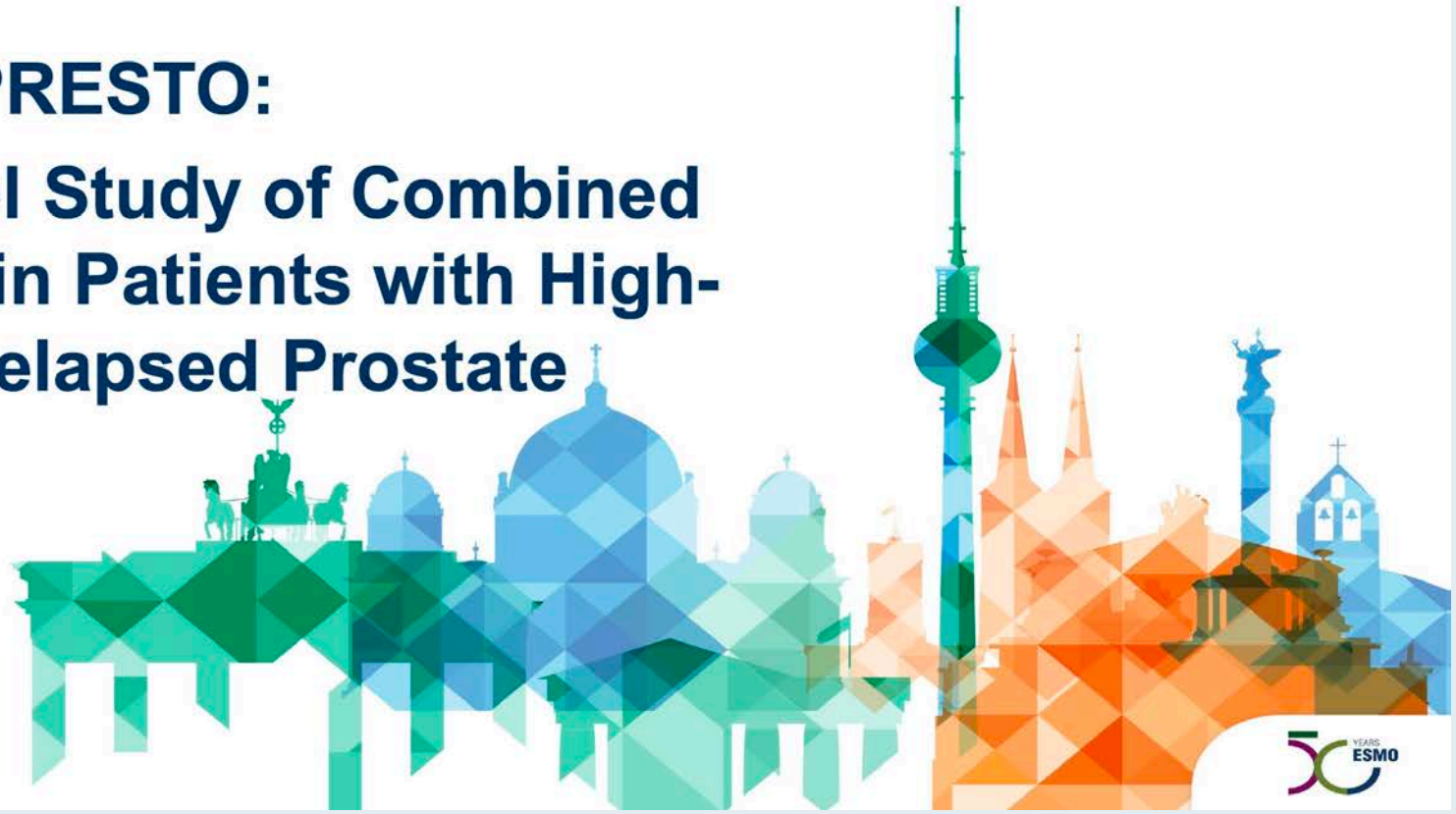
Final Results From PRESTO:

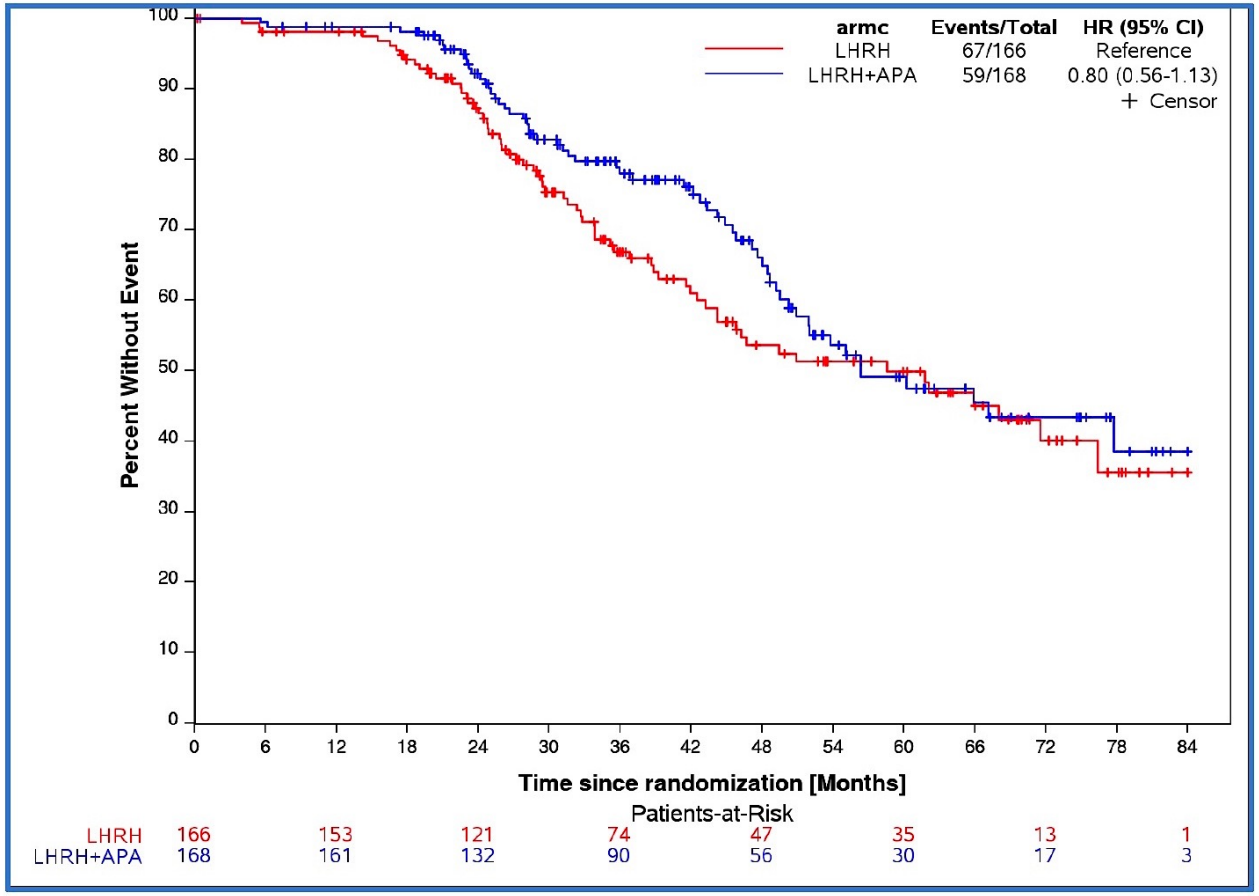
A Phase 3 Open-label Study of Combined Androgen Blockade in Patients with High-risk Biochemically Relapsed Prostate Cancer (AFT-19)

Rahul Aggarwal, on behalf of the Alliance AFT-19 Study Investigators

19 October 2025



Phase III PRESTO: Metastases-Free Survival (MFS) with Androgen Deprivation Therapy (ADT) and Apalutamide versus ADT

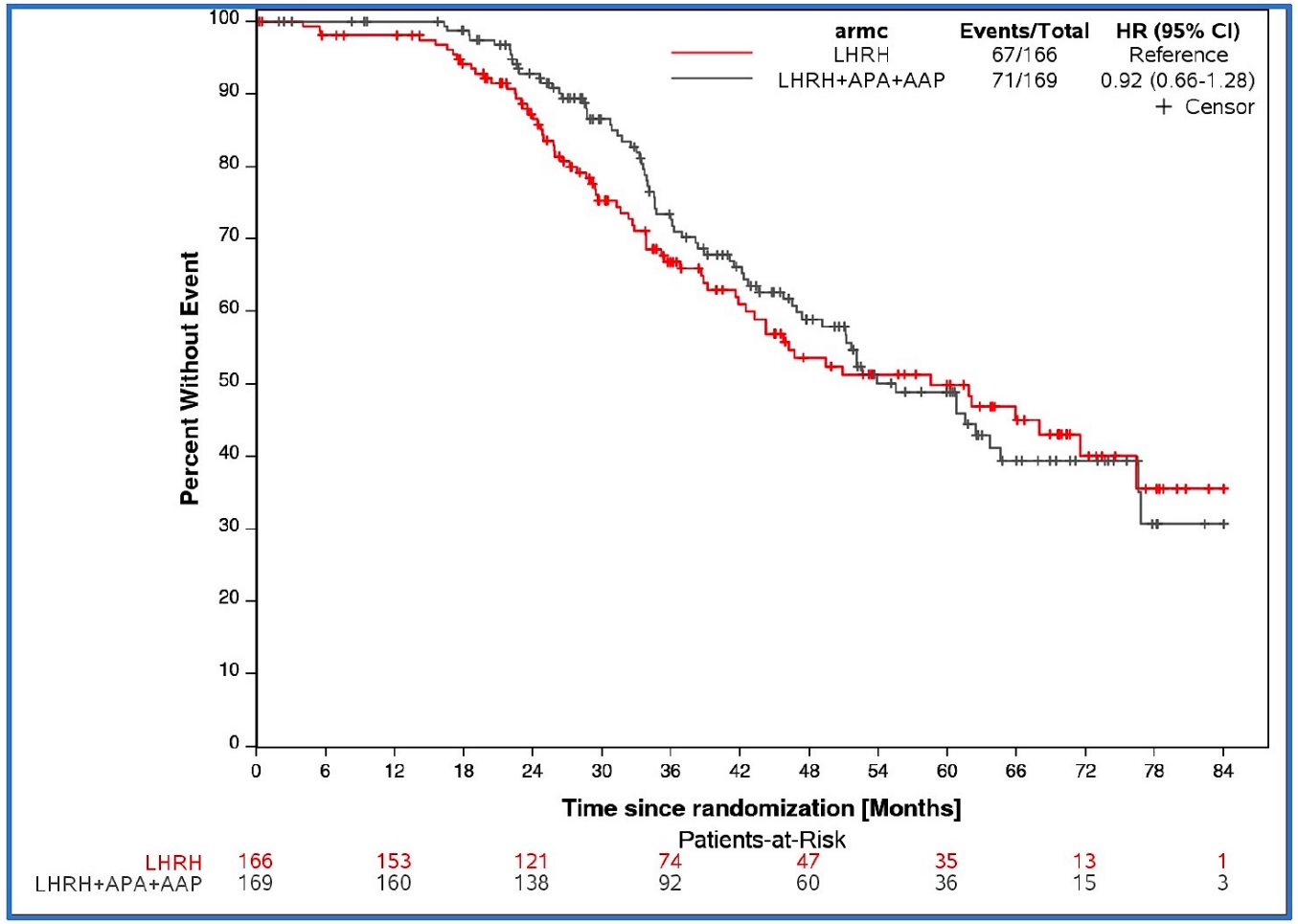


- 126 MFS events (38% of patients randomized)
- Cox proportional hazard ratio = **0.80 (95% CI: 0.56 – 1.13)**
- Proportional hazards assumption violated
- Difference in restricted mean survival over the first 48 months between ADT + apalutamide vs. ADT was **2.92 months (95%CI: 0.45 – 5.39)**

Aggarwal R et al. ESMO 2025;Abstract LBA88.

RTP RESEARCH TO PRACTICE

Phase III PRESTO: Metastases-Free Survival with ADT Combined with Apalutamide + Abiraterone Acetate with Prednisone (AAP) versus ADT



- 138 MFS events (41% of patients randomized)
- Cox proportional hazard ratio = **0.92 (95% CI: 0.56 – 1.13)**
- Difference in restricted mean survival over the first 48 months between ADT + apalutamide + AAP vs. ADT was **2.41 months (95% CI: -0.20 – 4.62)**

Aggarwal R et al. ESMO 2025;Abstract LBA88.

Phase III PRESTO: Authors' Conclusions

- Combined androgen signaling blockade with ADT plus apalutamide, given for a finite treatment period of 12 months, appears to improve clinically relevant long term endpoints in patients with high-risk biochemically recurrent prostate cancer.
- There did not appear to be additional benefit with the further inclusion of abiraterone acetate + prednisone, along with added toxicity.
- The combination of ADT + apalutamide is included as a treatment option for high-risk biochemically recurrent prostate cancer in consensus guidelines.[1]

Aggarwal R et al. ESMO 2025;Abstract LBA88.

RTP RESEARCH TO PRACTICE

Dr McKay: Case Presentation

Patient: 68-year-old male

Clinical Course:

- Initial diagnosis: Gleason 4+4=8 prostate adenocarcinoma, PSA 12.3 ng/mL
- Underwent radical prostatectomy in 2021
- Post-operative PSA nadir: 0.02 ng/mL
- PSA rose to 0.25 ng/mL by early 2023
- Received salvage radiation therapy (70 Gy) without ADT
- PSA nadir post-radiation: 0.02 ng/mL
- PSA began rising again in 2024, reaching 1.2 ng/mL by January 2025
- PSA doubling time: 6 months

Dr McKay: Case Presentation (Continued)

Clinical Course:

- Conventional imaging negative (CT/bone scan)
- PSMA PET/CT showed no definitive metastatic disease
- Started on enzalutamide 160 mg daily without ADT in February 2025
- PSA decreased to <0.01. Testosterone also decreased to castrate levels.
- Completed 1 year of therapy and then discontinued treatment.

Lutetium Lu 177 Vipivotide Tetraxetan for mHSPC

- Tagawa S et al. **Phase III trial of [177Lu]Lu-PSMA-617** combined with ADT + ARPI in patients with **PSMA-positive metastatic hormone-sensitive prostate cancer (PSMAddition)**. ESMO 2025;Abstract LBA6.

Abstract LBA6

BERLIN 2025 ESMO congress

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**

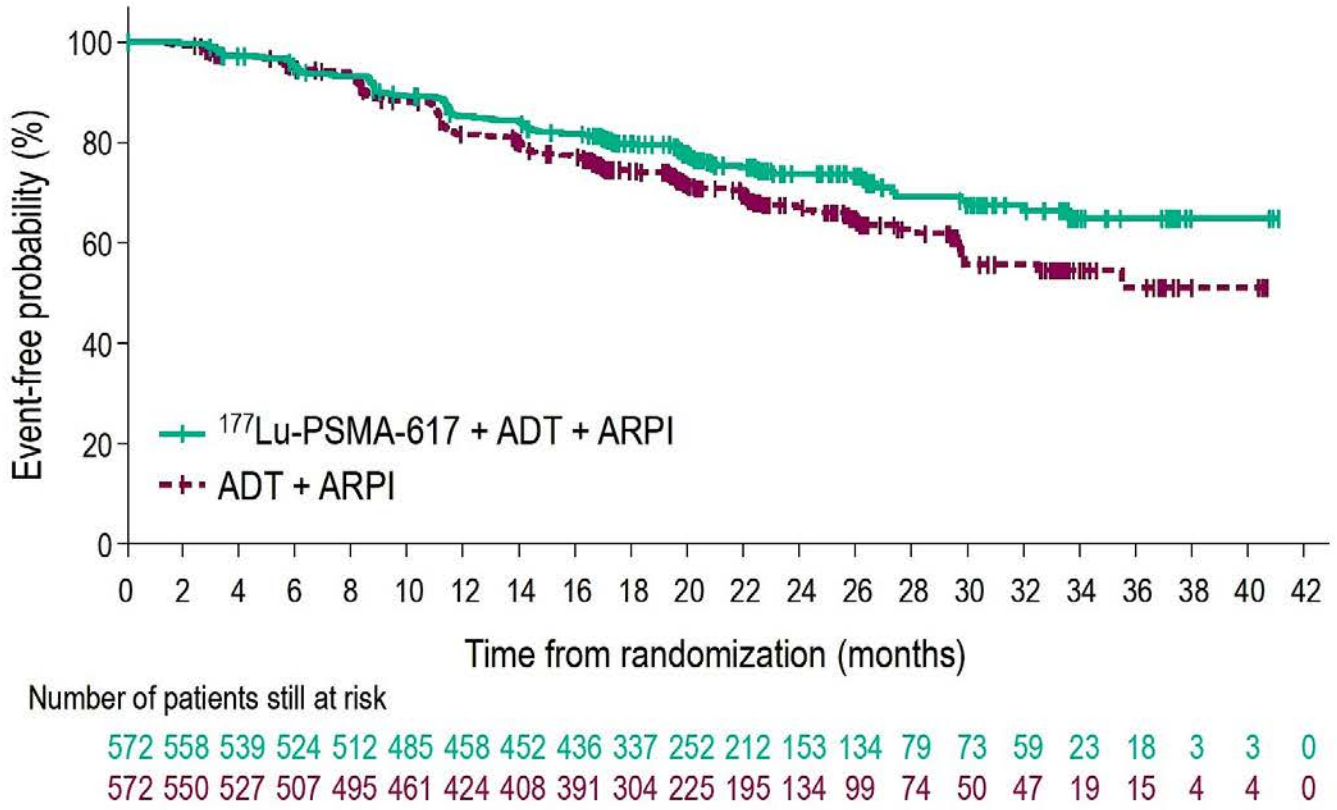
19 October 2025

*Equal contributors

50 YEARS ESMO

RTP RESEARCH TO PRACTICE

Phase III PSMAddition: Radiographic Progression-Free Survival by BIRC

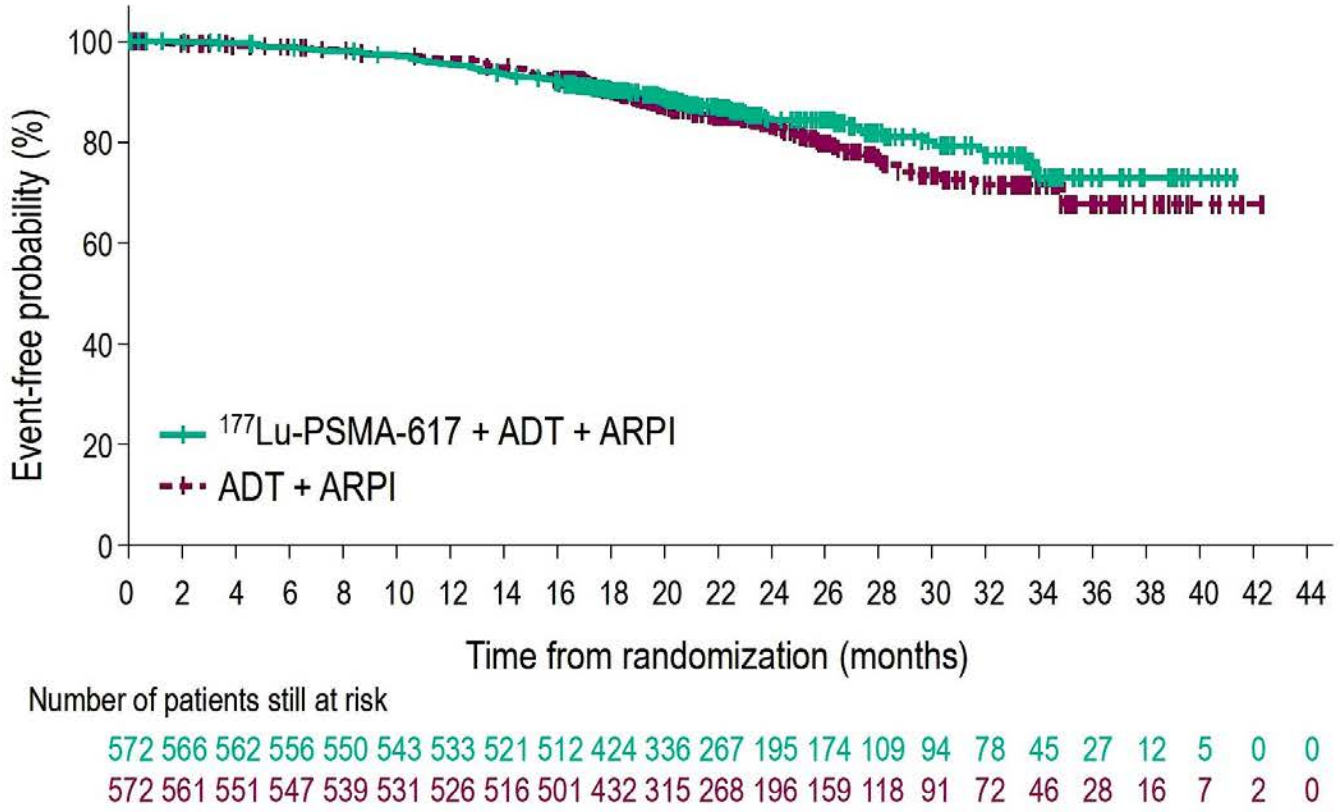


	^{177}Lu-PSMA-617 + ADT + ARPI (N = 572)	ADT + ARPI (N = 572)
Events – n (%) rPD Death without rPD	139 (24.3) 112 (19.6) 27 (4.7)	172 (30.1) 152 (26.6) 20 (3.5)
HR (95% CI)	0.72 (0.58, 0.90)	
p value	0.002[a]	
Median rPFS (95% CI) – months	NR (NE, NE)	NR (29.7, NE)

Tagawa ST et al. ESMO 2025;Abstract LBA6.

RTP RESEARCH TO PRACTICE

Phase III PSMAddition: Interim Overall Survival (OS)



	^{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)

Tagawa ST et al. ESMO 2025;Abstract LBA6.

RTP RESEARCH TO PRACTICE

Phase III PSMAddition: Adverse Events (AEs) of Special Interest

Patients with AE in grouping – n (%)	^{177}Lu-PSMA-617 + ADT + ARPI (N = 564)		ADT + ARPI (N = 565)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Dry mouth[a]	262 (46.5)	0	22 (3.9)	0
Cytopenias	248 (44.0)	81 (14.4)	115 (20.4)	28 (5.0)
Anaemia[b]	158 (28.0)	28 (5.0)	79 (14.0)	16 (2.8)
Neutropenia[c]	83 (14.7)	21 (3.7)	24 (4.2)	5 (0.9)
Thrombocytopenia[d]	63 (11.2)	10 (1.8)	19 (3.4)	3 (0.5)
Fractures	52 (9.2)	16 (2.8)	43 (7.6)	15 (2.7)
Renal events[e]	40 (7.1)	9 (1.6)	26 (4.6)	5 (0.9)
Second primary malignancies	37 (6.6)	24 (4.3)	31 (5.5)	14 (2.5)
Dry eye	33 (5.9)	0	3 (0.5)	0
Intracranial haemorrhage	6 (1.1)	4 (0.7)	4 (0.7)	2 (0.4)

Tagawa ST et al. ESMO 2025;Abstract LBA6.

Phase III PSMAddition: Authors' Conclusions

- **Combining ^{177}Lu-PSMA-617 with ADT + ARPI led to statistically significant improvement in rPFS in patients with PSMA-positive mHSPC, versus ADT + ARPI**
  - rPFS benefit was consistent across subgroups
  - There was a positive trend in OS; follow-up for mature data is ongoing
  - PSA, PFS, mCRPC and SSE results favoured the ^{177}Lu-PSMA-617 combination arm
- **Safety findings were consistent with the known profile of ^{177}Lu-PSMA-617, with no unexpected concerns about combination with ADT+ARPI**
  - AEs were more frequent in the ^{177}Lu-PSMA-617 combination arm, most commonly dry mouth, fatigue and nausea
- **There were no clinically significant differences in time to worsening in HRQoL and pain**

These findings indicate that combining ^{177}Lu-PSMA-617 with ADT + ARPI provides clinically meaningful benefit in patients with PSMA-positive mHSPC

Tagawa ST et al. ESMO 2025;Abstract LBA6.

RTP RESEARCH TO PRACTICE

Dr McKay: Case Presentation

Patient: 72-year-old male

Clinical Course:

- De novo metastatic disease diagnosed March 2025: Gleason 5+4=9, PSA 156 ng/mL
- Bone metastases in spine and pelvis, no visceral disease
- Some minimal bony pain in lower back
- PSMA PET/CT showed high PSMA expression in all metastatic lesions
- Started ADT + abiraterone 1000 mg daily with prednisone in April 2025
- Based on PSMAddition trial approach, also initiated [177Lu]Lu-PSMA-617 in May 2025
- PSA dropped to <0.2 by 6 months. Received all 6 doses of treatment.
- Developed fatigue and dry mouth but well managed

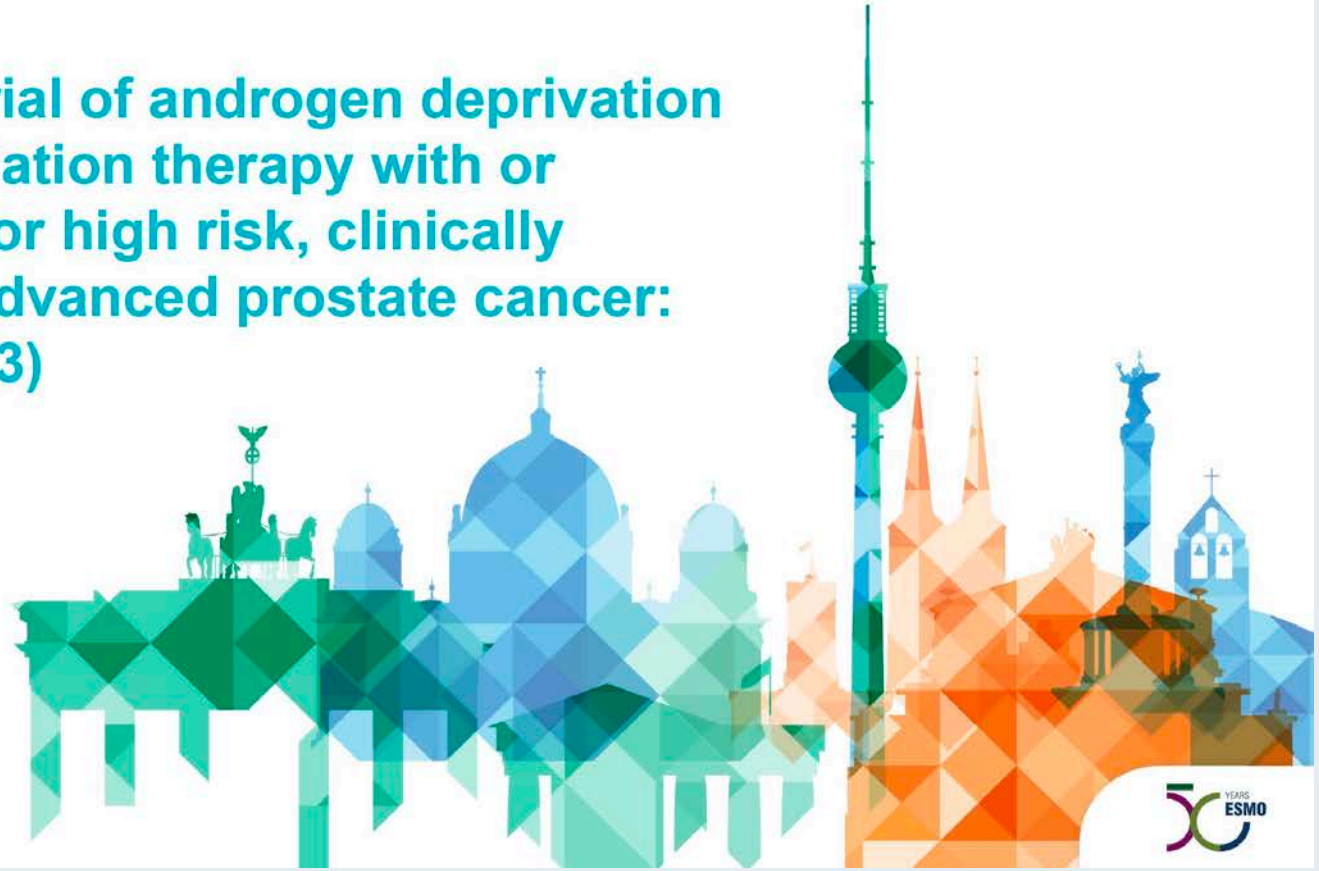
Radiation Therapy and ADT with or without an ARPI

- Nguyen P et al. Randomised **phase III** trial of androgen deprivation therapy (ADT) with radiation therapy **with or without enzalutamide** for high risk, **clinically localised prostate cancer: ENZARAD (ANZUP 1303)**. ESMO 2025;Abstract LBA86.

Abstract LBA86

Randomised phase 3 trial of androgen deprivation therapy (ADT) with radiation therapy with or without enzalutamide for high risk, clinically localised, and locally advanced prostate cancer: ENZARAD (ANZUP 1303)

Paul L. Nguyen, C.J. Sweeney, M.R. Stockler, H. Thomas, B. Mak, A. Zhang, T.S. Lim, C. Jose, J. Martin, N. Patanjali, D. Pryor, P. Tran, S. Mangar, A. Mihai, M. Beresford, F. Sedlmayer, P.J. Kelly, S. Hughes, I.D. Davis, S. Williams



19 October, 2025

Phase III ENZARAD Study Design

Eligibility

Localised prostate cancer
High risk of recurrence
Suitable for EBRT

Stratification

Gleason score 8-10
T3-4 disease
N1 disease
PSA ≥20 ng/mL
Brachytherapy boost
Pelvic nodal RT
Study Site

N=800

R

1:1

Enzalutamide 160mg daily for 24 months
+ LHRHA for 24 months
+ RT starting after 16 weeks ± brachy ± nodal

Conventional NSAA for 6 months
+ LHRHA for 24 months
+ RT starting after 16 weeks ± brachy ± nodal

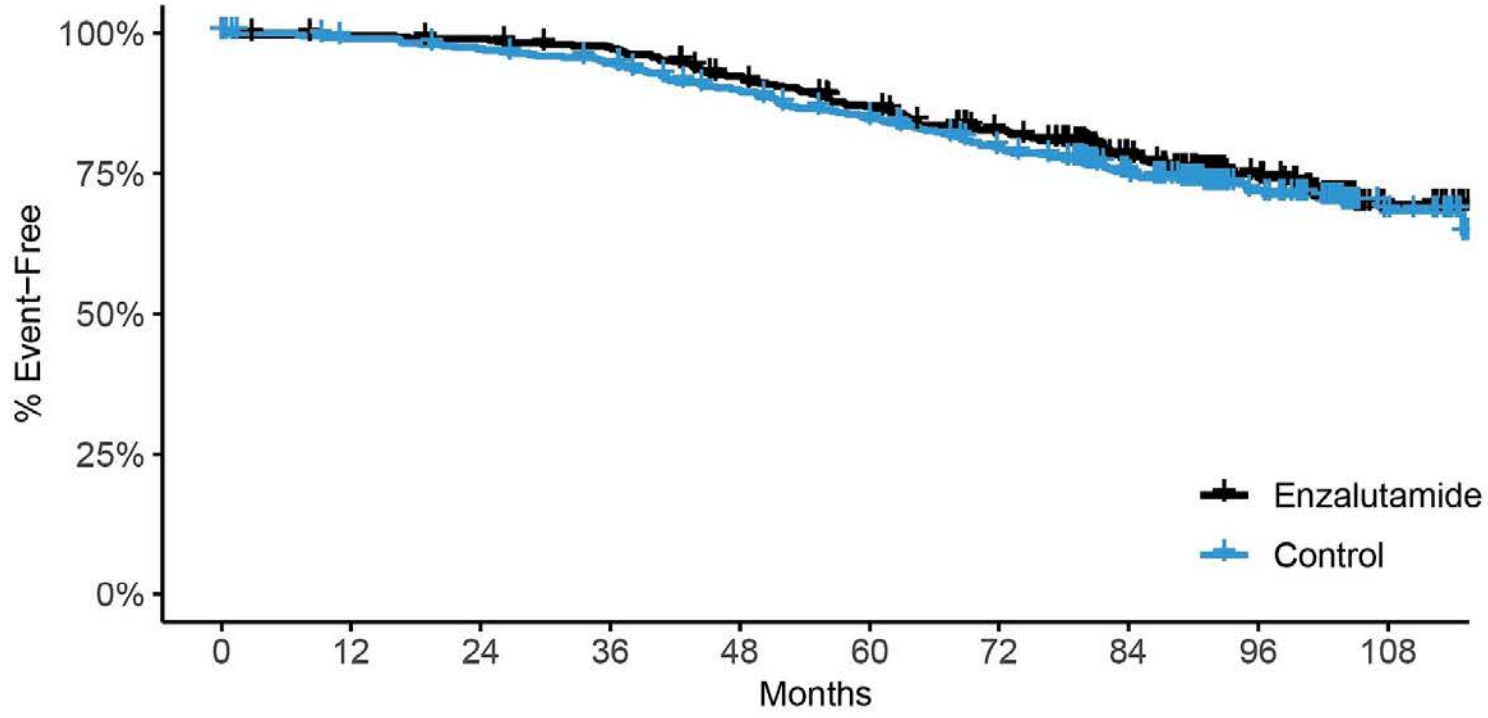
Endpoints

Metastasis-free survival (primary)
Overall survival
Cause specific survival
PSA progression free survival
Clinical progression free survival
Castration-resistance
Health related quality of life
Adverse events
Incremental cost-effectiveness

Primary Endpoint:
MFS based on conventional imaging (CT or MRI or bone scan, per ICECAP)
Lesions on PSMA-PET alone insufficient
Event = metastasis or death from any cause before metastasis

Nguyen PL et al. ESMO 2025;Abstract LBA86.

Phase III ENZARAD Primary Endpoint: MFS by Conventional Imaging



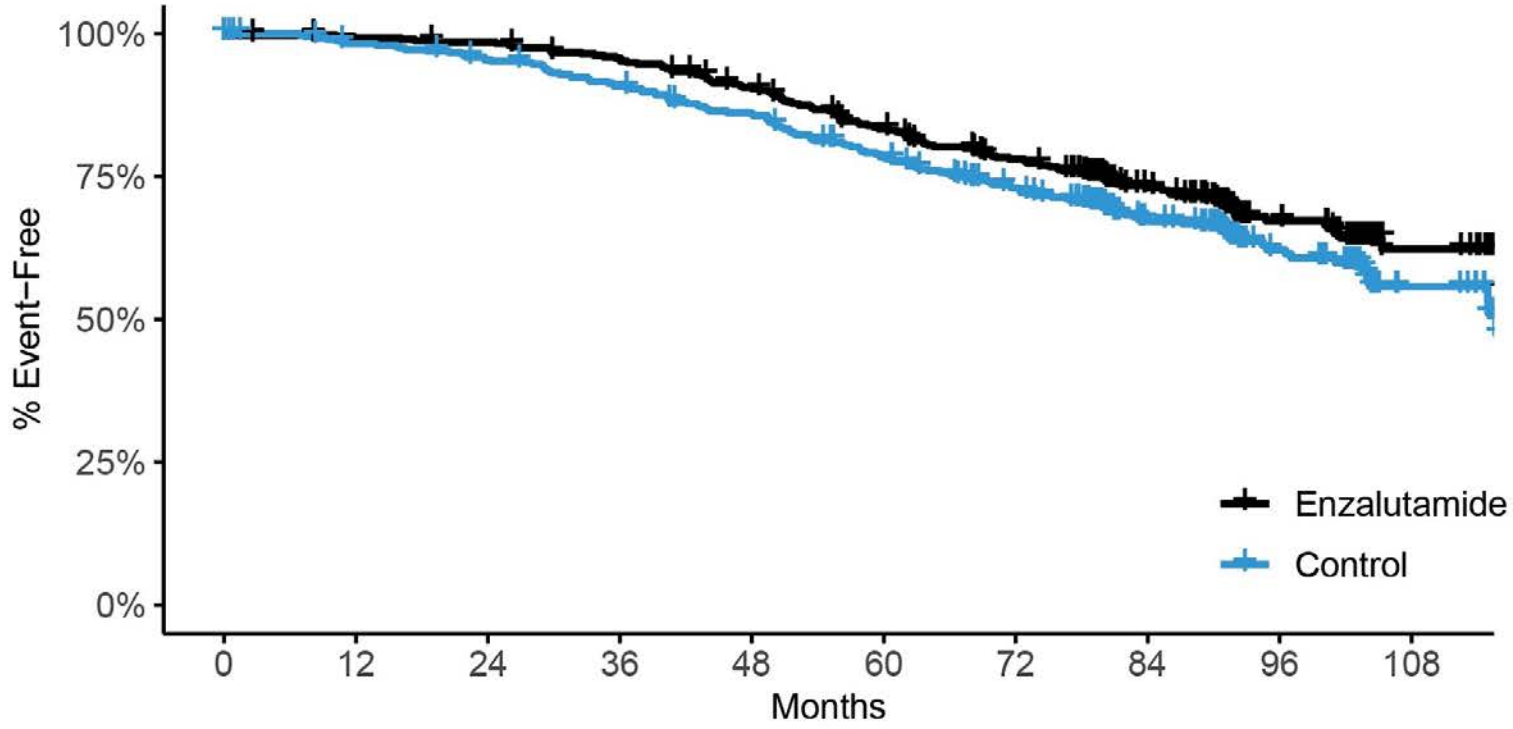
	events/N	MFS 8y
ENZA	98/401	74%
NSAA	109/401	72%

HR = 0.88 (95% CI 0.67, 1.15)
2p = 0.34 (log-rank test)

Median FU = 8 years

Nguyen PL et al. ESMO 2025;Abstract LBA86.

Phase III ENZARAD: PSA Progression-Free Survival



	events/N	PFS 8y
ENZA	121/401	67%
NSAA	145/401	62%

HR = 0.78 (0.61, 0.99)
2p = 0.044 (log-rank test)

Number at risk (number censored)

	401 (0)	394 (4)	390 (5)	377 (7)	353 (11)	320 (16)	290 (26)	204 (96)	95 (191)	30 (251)
	401 (0)	387 (7)	374 (9)	355 (10)	332 (14)	299 (18)	267 (30)	184 (95)	84 (184)	31 (230)

Nguyen PL et al. ESMO 2025;Abstract LBA86.

RTP RESEARCH TO PRACTICE

Phase III ENZARAD: Authors' Conclusions

ENZARAD did not find a meaningful MFS benefit to enzalutamide vs active NSAA control in unselected high-risk localised prostate cancer treated with high-dose radiation and 2 years of ADT

For patients with positive pelvic nodes on CT or MRI or other indications for pelvic field irradiation, ENZARAD supports consideration of adding enzalutamide.

Nguyen PL et al. ESMO 2025;Abstract LBA86.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Prostate Cancer

- Capivasertib for Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)
- PARP Inhibitors and Androgen Receptor Pathway Inhibitors (ARPIs) for Metastatic Prostate Cancer
- Biochemically Recurrent Prostate Cancer
- Lutetium Lu 177 Vipivotide Tetraxetan for mHSPC
- Radiation Therapy and Androgen Deprivation Therapy with or without an ARPI

Module 2: Urothelial Bladder Cancer

- Neoadjuvant and Perioperative Treatment Approaches for Muscle Invasive Bladder Cancer (MIBC)
- Circulating Tumor DNA and Adjuvant Immunotherapy for MIBC
- HER2-Targeted Antibody-Drug Conjugates for Metastatic Urothelial Bladder Cancer (mUBC)
- Targeting TROP2 in mUBC
- Immunotherapy and BCG for Non-Muscle-Invasive Bladder Cancer

Key Datasets in Bladder Cancer

- De Santis M et al. Durvalumab (D) in combination with bacillus Calmette-Guérin (BCG) for BCG-naïve, high-risk non-muscle-invasive bladder cancer (NMIBC): Final analysis of the phase III, open-label, randomised POTOMAC trial. ESMO 2025;Abstract LBA108.
- Vulsteke C et al. 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. ESMO 2025;Abstract LBA2.
- van der Heijden M et al. Health-related quality of life (HRQoL) outcomes from the NIAGARA trial of perioperative durvalumab (D) plus neoadjuvant chemotherapy (NAC) in muscle-invasive bladder cancer (MIBC). ESMO 2025;Abstract 3069MO.
- Necchi A et al. Neoadjuvant gemcitabine intravesical system (TAR-200) + cetrelimab (CET) or CET alone in patients (pts) with muscle-invasive bladder cancer (MIBC): SunRISe-4 (SR-4) primary analysis and biomarker results. ESMO 2025;Abstract LBA112.
- Powles T et al. IMvigor011: A phase III trial of circulating tumour (ct)DNA-guided adjuvant atezolizumab vs placebo in muscle-invasive bladder cancer. ESMO 2025;Abstract LBA8.

Key Datasets in Bladder Cancer (Continued)

- Galsky MD et al. Adjuvant nivolumab vs placebo for high-risk muscle-invasive urothelial carcinoma: 5-year efficacy and ctDNA results from CheckMate 274. ESMO 2025;Abstract 3068O.
- Guo J et al. Disitamab vedotin (DV) plus toripalimab (T) versus chemotherapy (C) in first-line (1L) locally advanced or metastatic urothelial carcinoma (la/mUC) with HER2-expression. ESMO 2025;Abstract LBA7.
- Makker V et al. Trastuzumab deruxtecan (T-DXd) for pretreated patients (pts) with HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) part 1 final analysis. ESMO 2025;Abstract 957P.
- Rha SY et al. Datopotamab deruxtecan (Dato-DXd) + rilvegostomig (rilve) in patients (pts) with locally advanced or metastatic urothelial cancer (a/mUC): Results from the phase II TROPION-PanTumor03 study. ESMO 2025;Abstract 3072MO.

Neoadjuvant and Perioperative Treatment Approaches for MIBC

- Vulsteke C et al. **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**. ESMO 2025;Abstract LBA2.
- van der Heijden M et al. **Health-related quality of life (HRQoL)** outcomes from the **NIAGARA** trial of **perioperative durvalumab (D)** plus neoadjuvant chemotherapy (NAC) in **muscle-invasive bladder cancer (MIBC)**. ESMO 2025;Abstract 3069MO.
- Necchi A et al. **Neoadjuvant gemcitabine intravesical system (TAR-200)** + cetrelimab (CET) or CET alone in patients (pts) with **muscle-invasive bladder cancer (MIBC): SunRISe-4 (SR-4) primary analysis** and biomarker results. ESMO 2025;Abstract LBA112.

Abstract LBA2

BERLIN 2025 ESMO congress

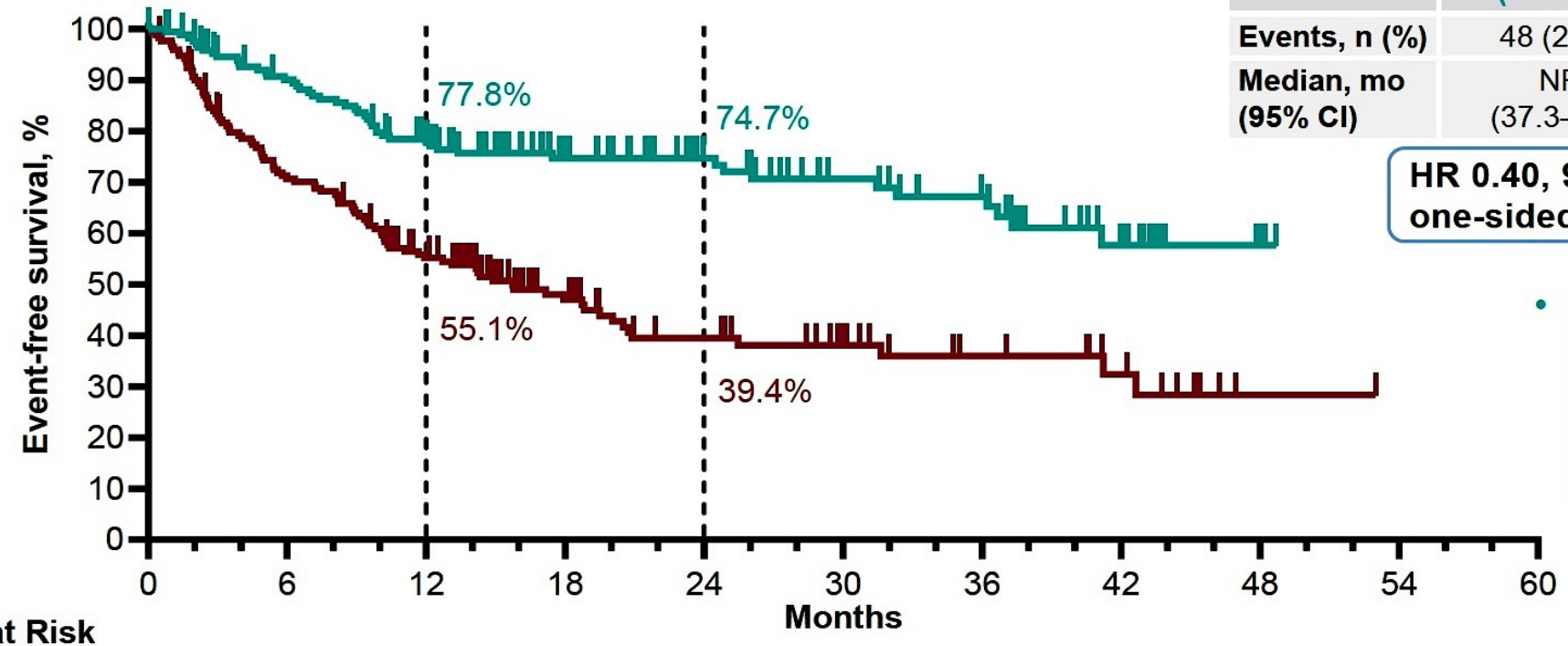
Perioperative Enfortumab Vedotin Plus Pembrolizumab in Participants With Muscle-invasive Bladder Cancer Who Are Cisplatin-ineligible: Phase 3 KEYNOTE-905 Study

Christof Vulsteke[1], Hristos Z. Kaimakliotis[2], Pongwut Danchaivijitr[3], Maksym Sabadash[4], Alejo Rodriguez-Vida[5], Zhentao Zhang[6], Vagif Atduev[7], Yunus E. Goger[8], Steffen Rausch[9], Seok-Ho Kang[10], Yohann Loriot[11], Jens Bedke[12], Matthew D. Galsky[13], Peter H. O'Donnell[14], Michael Mihm[15], Changting Meng[16], Caizhi David Huang[17], Chethan Ramamurthy[17], Blanca Homet Moreno[17], Anders Ullén[18]

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

RTP RESEARCH TO PRACTICE

Phase III KEYNOTE-905: Event-Free Survival in the Intent-to-Treat Population by Blinded Independent Central Review



	EV + pembro (N = 170)	Control (N = 174)
Events, n (%)	48 (28.2)	95 (54.6)
Median, mo (95% CI)	NR (37.3–NR)	15.7 (10.3–20.5)

HR 0.40, 95% CI 0.28–0.57, one-sided *P* <.0001*

- 29/174 pts (16.7%) in the control arm received adjuvant nivolumab as of data cutoff per local guidelines/prescribing information

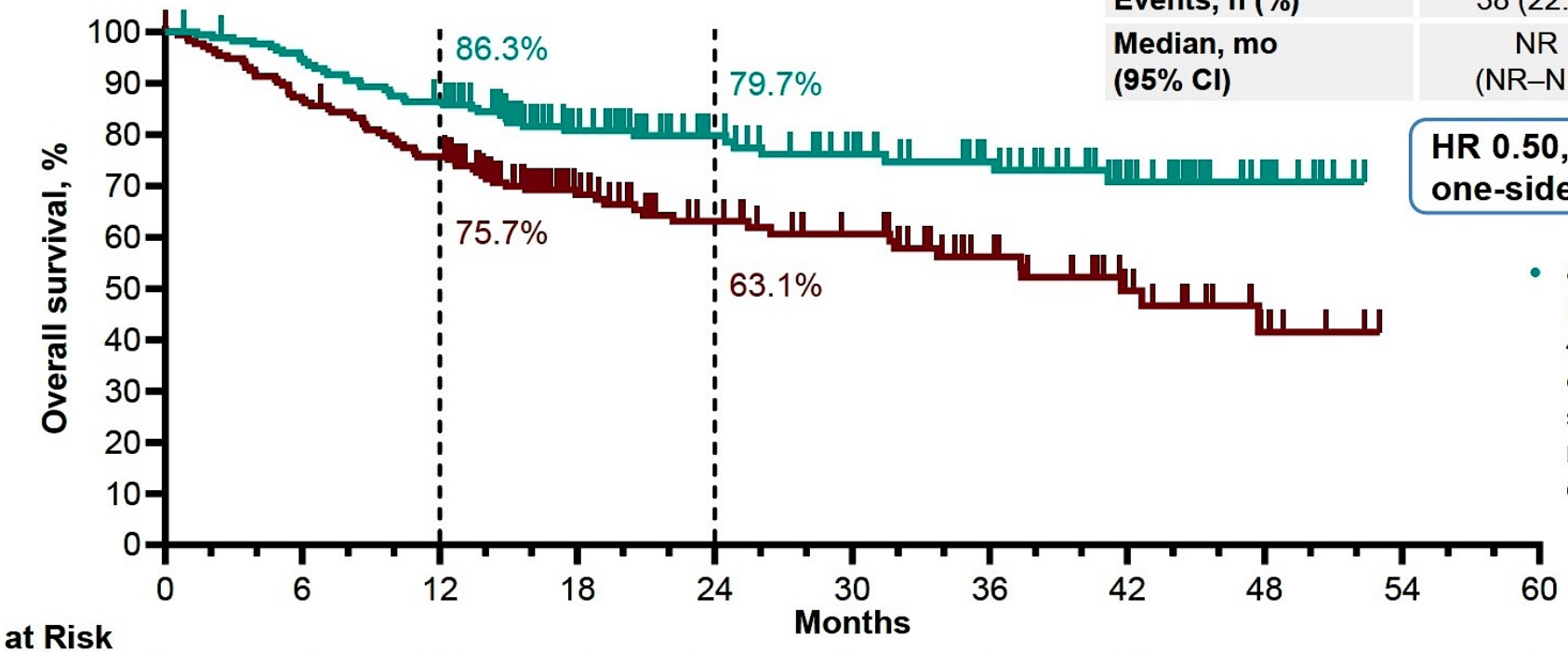
NR, not reached. * denotes statistical significance (one-sided boundary 0.0097). [a]Time from randomization to first occurrence of: radiographic PD precluding surgery; biopsy-proven residual MIBC (pts who did not undergo surgery); gross residual disease post-surgery or newly detected metastatic disease 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

Vulsteke C et al. ESMO 2025;Abstract LBA2.

Phase III KEYNOTE-905: Overall Survival

	EV + pembro (N = 170)	Control (N = 174)
Events, n (%)	38 (22.4)	68 (39.1)
Median, mo (95% CI)	NR (NR–NR)	41.7 (31.8–NR)



HR 0.50, 95% CI 0.33–0.74, one-sided *P* =.0002*

- 8/170 pts (4.7%) in the EV + pembro arm and 46/174 (26.4%) in the control arm received subsequent therapy for recurrent/metastatic disease

NR, not reached. * denotes statistical significance (one-sided boundary 0.00488).

Data cutoff date: 6 June 2025

Vulsteke C et al. ESMO 2025;Abstract LBA2.

RTP RESEARCH TO PRACTICE

Phase III KEYNOTE-905: Authors' Conclusions

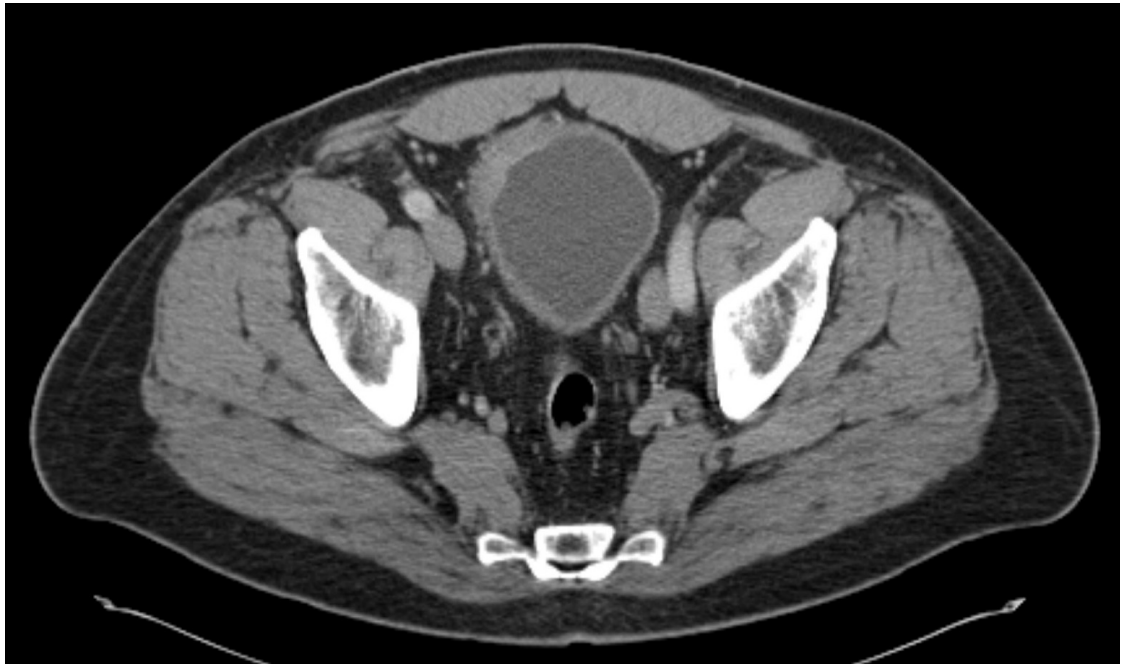
- Neoadjuvant EV + pembro, RC + PLND, and adjuvant EV + pembro significantly and meaningfully improved EFS, OS, and pCR rate in participants with MIBC who are ineligible for or declined cisplatin-based chemotherapy
  - EFS and OS benefit was generally consistent across key subgroups
- Perioperative EV + pembro did not impact the ability of participants to undergo curative intent surgery
- The safety profile of perioperative EV + pembro was manageable and consistent with prior reports of this regimen in the locally advanced/metastatic urothelial carcinoma setting; no new safety signals were observed
- KEYNOTE-905 is the first phase 3 study to show improved efficacy outcomes with perioperative therapy relative to surgery for patients with MIBC who are ineligible for cisplatin-based chemotherapy
  - Perioperative EV + pembro added to RC + PLND may represent a new standard of care in this population with high unmet clinical need

RC = radical cystectomy; PLND = pelvic lymph node dissection

Vulsteke C et al. ESMO 2025;Abstract LBA2.

Dr Friedlander: Case Presentation

- 66 y.o. M with HTN and hyperlipidemia with new onset hematuria
- CT Urogram: lobulated mass along the right anterolateral bladder wall measuring 2.6 x 2.9 x 2.7 cm, irregular wall thickening. R
  - R pelvis 1.3cm suspicious for metastasis.
  - CT chest negative
  - TURBT: 5cm tumor at R dome of the bladder.
    - Path: Muscle-invasive papillary urothelial carcinoma, high-grade with sarcomatoid (5%) and micropapillary (5%) subtype morphology and glandular differentiation (<5%)
  - Cr 1.45



Dr Friedlander: Case Presentation (Continued)

- Met with medical oncology. Discussed low likelihood of cure with cisplatin-based chemotherapy and surgery.
  - "Isn't there anything better?"
- Mid 2024: **Starts 4 cycles of EV + Pembrolizumab**
  - Course c/b pruritus, grade 2 rash responsive to topical steroids, fatigue, and slowly increasing peripheral neuropathy.
- Undergoes radical cystectomy with ileal conduit.
  - Pathology: ypT0N0, 0/25 LNs **complete response!**

Dr Friedlander: Case Presentation (Continued)

- Post-op
  - What is the role of more therapy?
    - Discussion of the ongoing KN-B15/EV-304 and KN-905/EV-303 trials
    - ctDNA negative
  - Starts adjuvant EV + P for 5 more cycles
    - Course c/b by fatigue, cough, pruritic, dry eye, blisters at ostomy site
  - Remains in remission (?cured?), however intermittent fevers due to either recurrent infection or autoimmune phenomenon, still not clear.

BARCELONA 2024 ESMO congress

A Randomised Phase 3 Trial of Neoadjuvant Durvalumab Plus Chemotherapy Followed by Radical Cystectomy and Adjuvant Durvalumab in Muscle-invasive Bladder Cancer (NIAGARA)

Thomas Powles,[1] Michiel S. van der Heijden,[2] Matthew D. Galsky,[3] Hikmat Al-Ahmadie,[4] Joshua J. Meeks,[5] Hiroyuki Nishiyama,[6] Toan Quang Vu,[7] Lorenzo Antonuzzo,[8] Paweł Wiechno,[9] Vagif Atduev,[10] Ariel G. Kann,[11] Tae-Hwan Kim,[12] Cristina Suarez,[13] Chao-Hsiang Chang,[14] Florian Roghmann,[15] Mustafa Özgüroğlu,[16] Jon Armstrong,[17] Svetlana Ho,[18] Stephan Hois,[18] James W. F. Catto[19]

[1]Barts Cancer Institute ECMC/BRC, Queen Mary University of London, Barts Health NHS Trust, London, UK; [2]Department of Medical Oncology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; [3]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]Memorial Sloan Kettering Cancer Center, Department of Pathology, New York, NY, USA; [5]Departments of Urology, Biochemistry and Molecular Genetics, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA; [6]Department of Urology, University of Tsukuba, Tsukuba, Japan; [7]Department of Internal Medicine 3, Vietnam National Cancer Hospital, Hanoi, Vietnam; [8]Sodc Ematologia - Azienda Ospedaliera - Universitaria Careggi, Florence, Italy; [9]Department of Uro-oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [10]Volga District Medical Center, Federal Medical-Biological Agency, Nizhny Novgorod, Russia; [11]Clinical Oncology, Hospital Alemão Oswaldo Cruz, São Paulo, Brazil; [12]Department of Urology, Kyungpook National University Chilgok Hospital, Daegu, Korea; [13]Vall d'Hebron Institute of Oncology, Universitat Autònoma de Barcelona, Barcelona, Spain; [14]Department of Urology and School of Medicine, China Medical University and Hospital, Taichung, Taiwan; [15]Department of Urology, University Hospital of Ruhr-University Bochum, Marien Hospital, Herne, Germany; [16]Cerrahpaşa School of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Türkiye; [17]AstraZeneca, Cambridge, UK; [18]AstraZeneca, Gaithersburg, MD, USA; [19]University of Sheffield, Sheffield, UK

LBA5

Presenter: Thomas Powles, MBBS, MRCP, MD, London, UK

The NEW ENGLAND JOURNAL of MEDICINE

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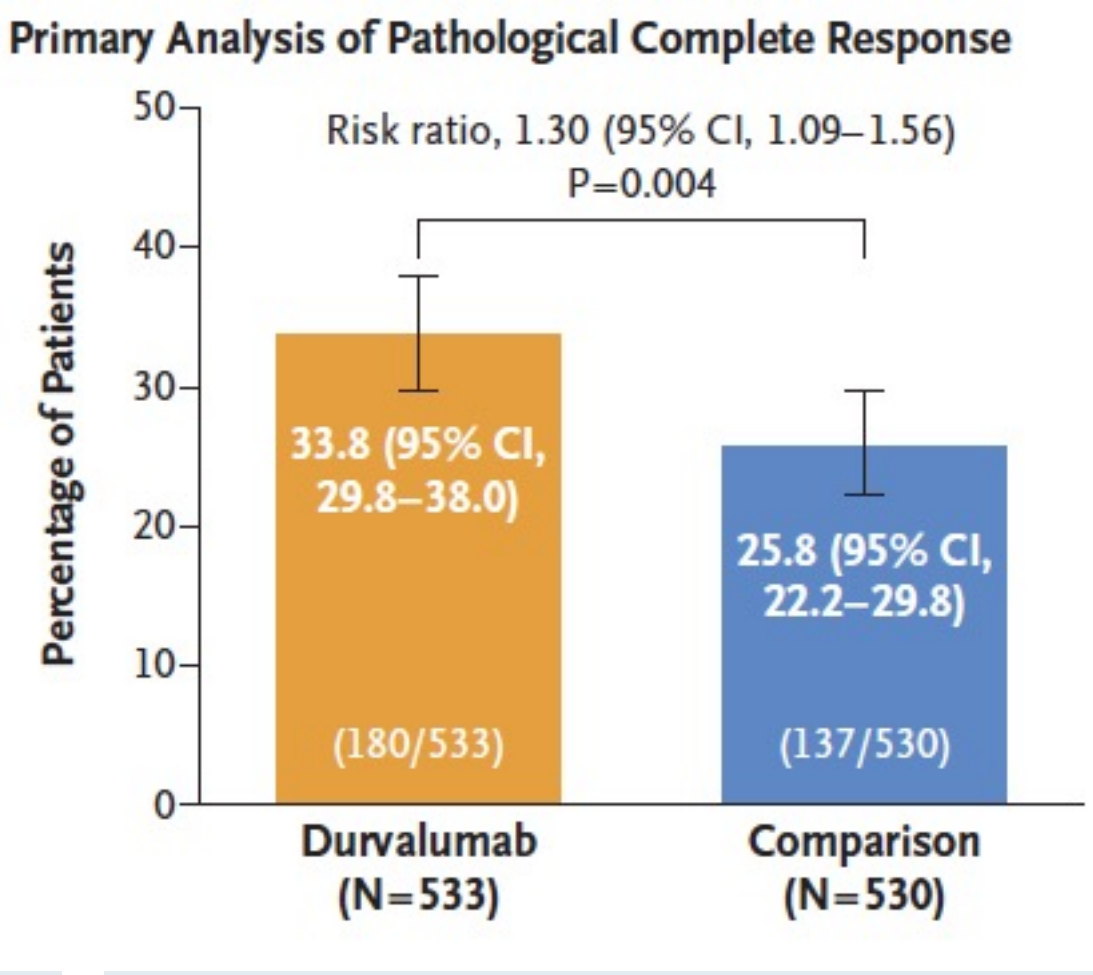
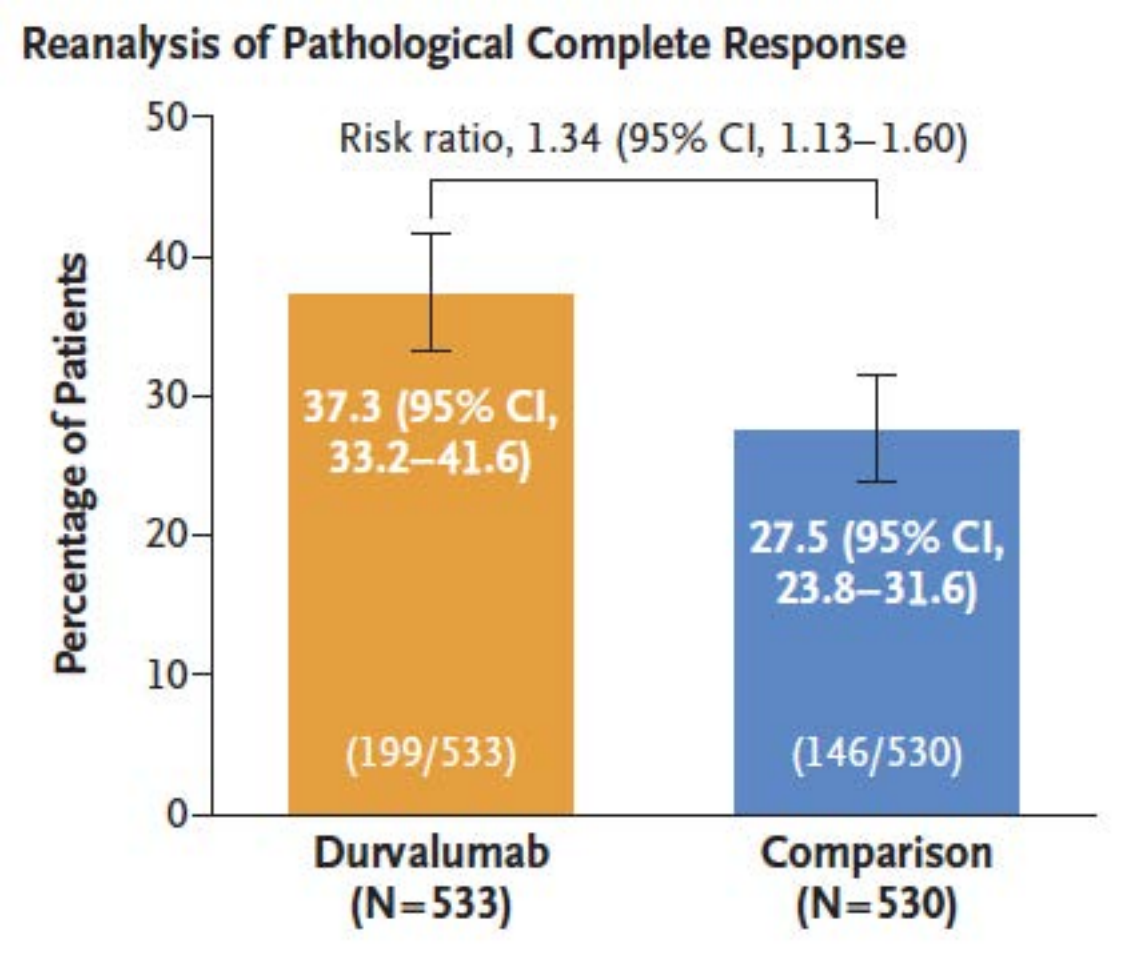
Perioperative Durvalumab with Neoadjuvant Chemotherapy in Operable Bladder Cancer

T. Powles, J.W.F. Catto, M.D. Galsky, H. Al-Ahmadie, J.J. Meeks, H. Nishiyama, T.Q. Vu, L. Antonuzzo, P. Wiechno, V. Atduev, A.G. Kann, T.-H. Kim, C. Suárez, C.-H. Chang, F. Roghmann, M. Özgüroğlu, B.J. Eigl, N. Oliveira, T. Buchler, M. Gadot, Y. Zakharia, J. Armstrong, A. Gupta, S. Hois, and M.S. van der Heijden, for the NIAGARA Investigators*

RTP RESEARCH TO PRACTICE

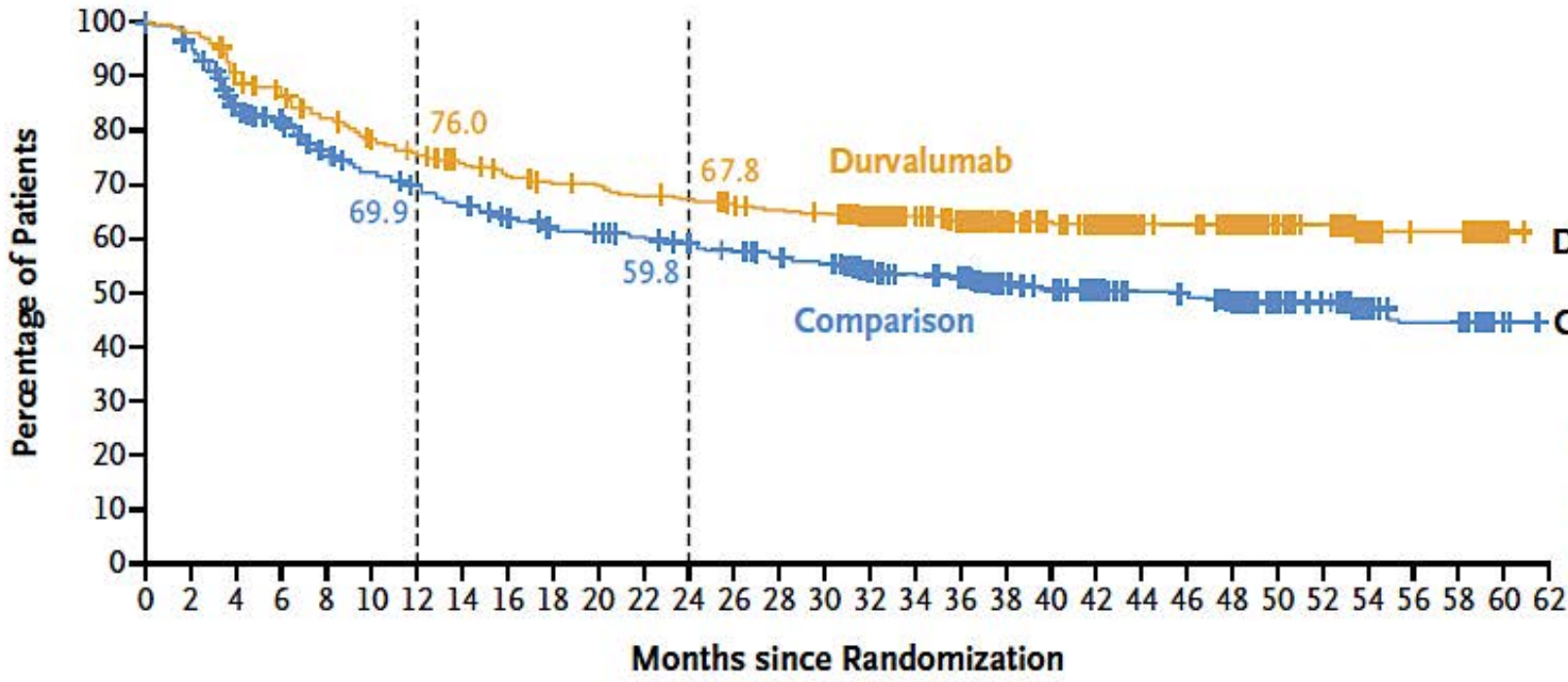
NIAGARA: Pathologic Complete Response with Perioperative Durvalumab and Neoadjuvant Chemotherapy





Powles T et al. ESMO 2024;Abstract LBA5; Powles T et al. *N Engl J Med* 2024;391(19):1773-86.

NIAGARA: Event-Free Survival with Perioperative Durvalumab and Neoadjuvant Chemotherapy



	No. of Patients with Event/Total No. (%)	Median Event-free Survival (95% CI)
		mo
Durvalumab	187/533 (35.1)	NR (NR–NR)
Comparison	246/530 (46.4)	46.1 (32.2–NR)

Hazard ratio for event, 0.68 (95% CI, 0.56–0.82)

Stratified P<0.001 by log-rank test

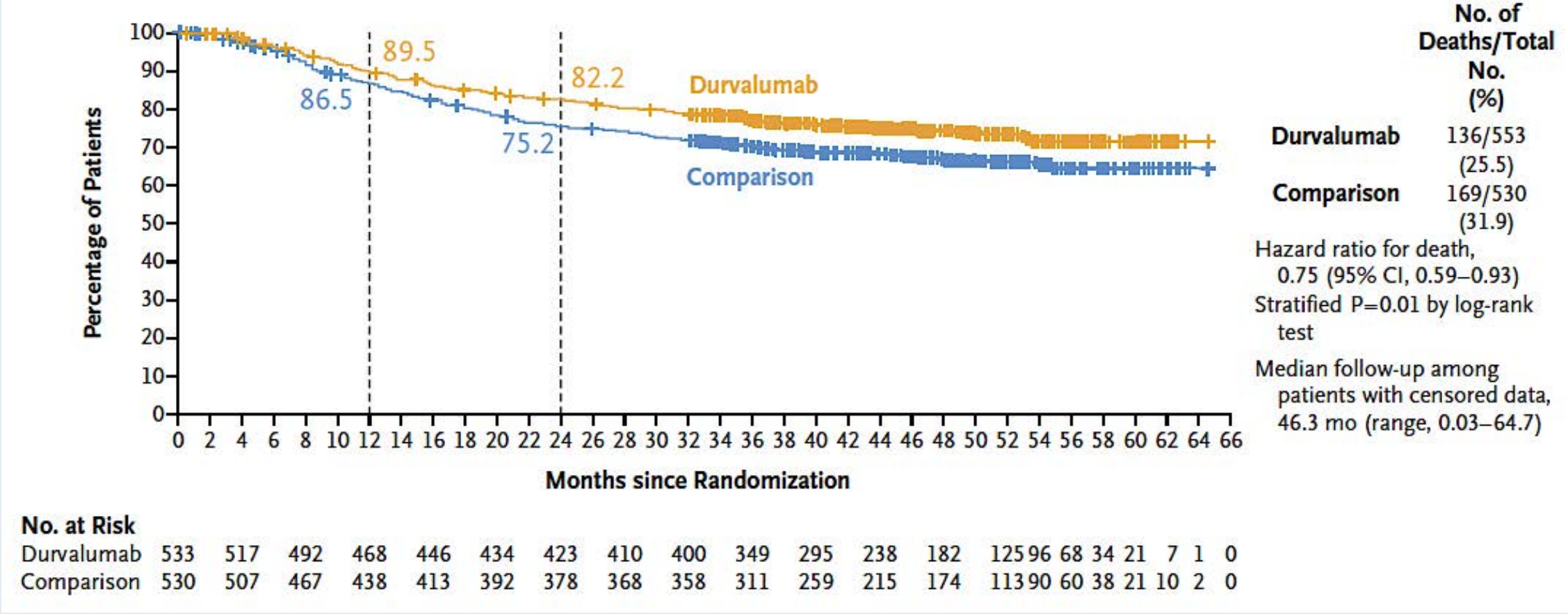
Median follow-up among patients with censored data, 42.3 mo (range, 0.03–61.3)

No. at Risk

Durvalumab	533	475	424	386	356	344	330	315	282	255	202	141	115	86	81	32	20	20	1	0
Comparison	530	437	381	343	313	296	281	264	228	214	172	132	94	69	62	24	18	16	2	0

Powles T et al. ESMO 2024;Abstract LBA5; Powles T et al. *N Engl J Med* 2024;391(19):1773-86.

NIAGARA: Overall Survival with Perioperative Durvalumab and Neoadjuvant Chemotherapy



Powles T et al. ESMO 2024;Abstract LBA5; Powles T et al. *N Engl J Med* 2024;391(19):1773-86.

Phase III NIAGARA: Authors' Conclusions

- NIAGARA is the first Phase 3 perioperative immunotherapy study in MIBC and has demonstrated a statistically significant and clinically meaningful improvement in EFS and OS
  - EFS HR, 0.68 (95% CI, 0.56–0.82), *P*<0.0001
  - OS HR, 0.75 (95% CI, 0.59–0.93), *P*=0.0106
- EFS and OS benefits with durvalumab were consistent across subgroups
- The pCR results and the significant OS benefit support the perioperative approach
- Addition of perioperative durvalumab to NAC was tolerable and manageable, with no new safety signals
- Neoadjuvant durvalumab did not delay surgery and did not impact the ability of patients to undergo/complete surgery

NIAGARA supports perioperative durvalumab with NAC as a potential new standard treatment for patients with cisplatin-eligible MIBC

Data cutoff 29 Apr 2024. CI, confidence interval; EFS, event-free survival; HR, hazard ratio; MIBC, muscle-invasive bladder cancer; NAC, neoadjuvant chemotherapy; OS, overall survival; pCR, pathologic complete response; RC, radical cystectomy.

Powles T et al. ESMO 2024;Abstract LBA5.

Abstract 3069MO

BERLIN 2025 ESMO congress

#3069MO

Health-Related Quality of Life (HRQoL) Outcomes From the NIAGARA Trial of Perioperative Durvalumab (D) Plus Neoadjuvant Chemotherapy (NAC) in Muscle-Invasive Bladder Cancer (MIBC)

Michiel S. van der Heijden,[1] Thomas Powles,[2] Matthew D. Galsky,[3] James W.F. Catto,[4] Joshua J. Meeks,[5] Ruslan Zukov,[6] Kouji Izumi,[7] Kuan-Hua Huang,[8] Muhammet Bekir Hacioglu,[9] Syed A. Hussain,[10] Andrea Necchi,[11] Herlinde Dumez,[12] Marco Julius Schnabel,[13] Pierre Bigot,[14] Angela Estay,[15] Arthur Gregory Lui,[16] Carolina Cernadas,[17] Kamila Bigos,[18] Stephan Hois,[19] Hiroyuki Nishiyama[20]

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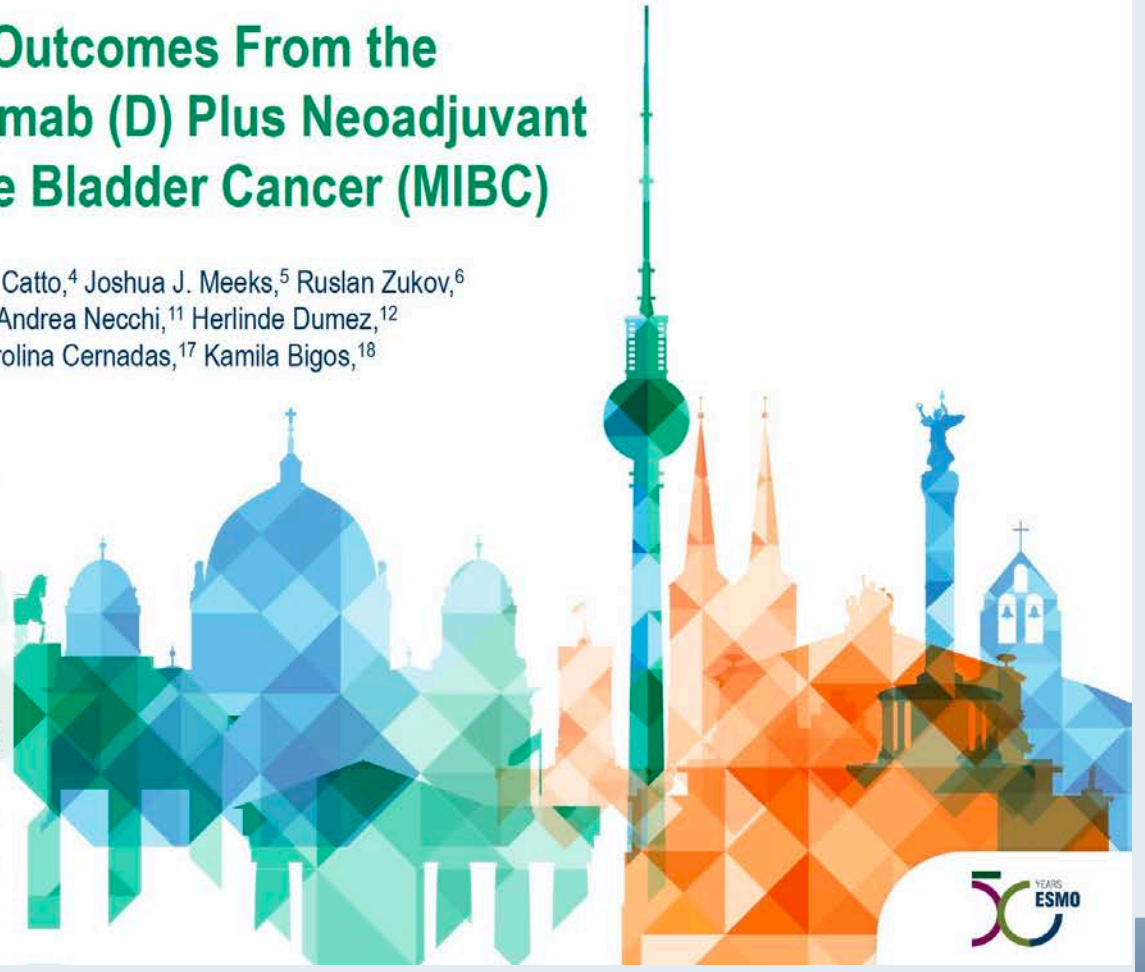
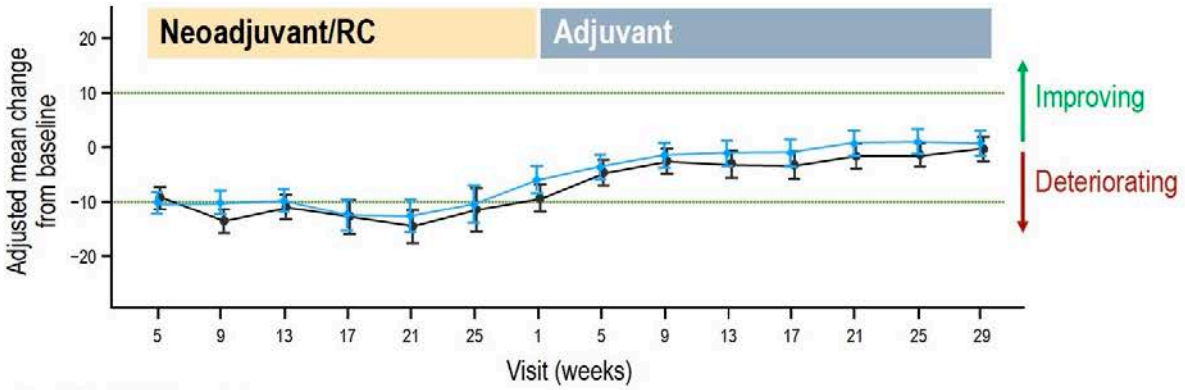


Phase III NIAGARA: EORTC QLQ-C30 Change from Baseline

Addition of perioperative durvalumab to NAC did not adversely impact GHS/QoL, or physical functioning subscale scores

GHS/QoL

Difference between arms for overall mean CFB: 1.6 (95% CI, –0.44 to 3.69)

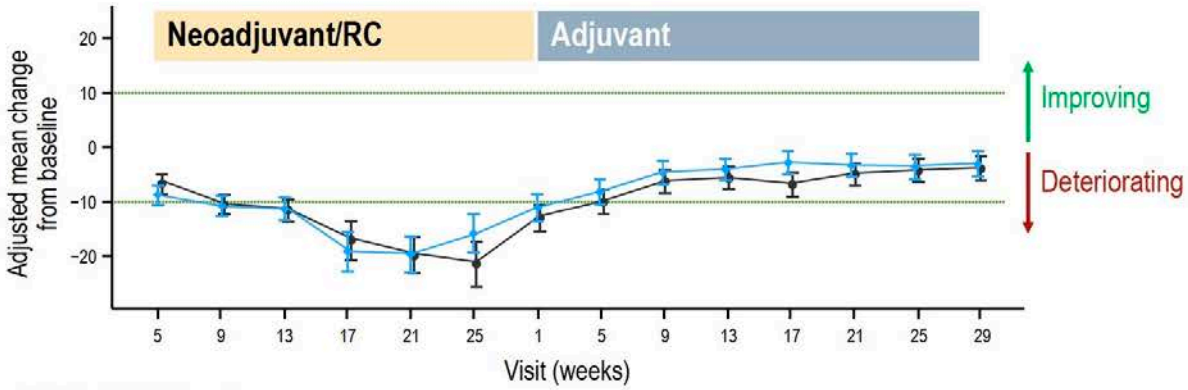


patients included in the analysis

Durvalumab arm	357	332	283	207	173	107	180	204	203	201	203	197	181	181
Comparator arm	364	310	262	193	165	75	183	203	182	179	193	180	188	175

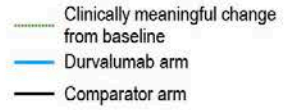
Physical Functioning

Difference between arms for overall mean CFB: 1.2 (95% CI, –0.80 to 3.17)



patients included in the analysis

Durvalumab arm	357	332	283	207	173	107	180	204	203	201	203	197	181	181
Comparator arm	364	310	262	193	165	75	183	203	182	179	193	180	188	175



EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Core Quality of Life questionnaire

van der Heijden M et al. ESMO 2025;Abstract 3069MO.

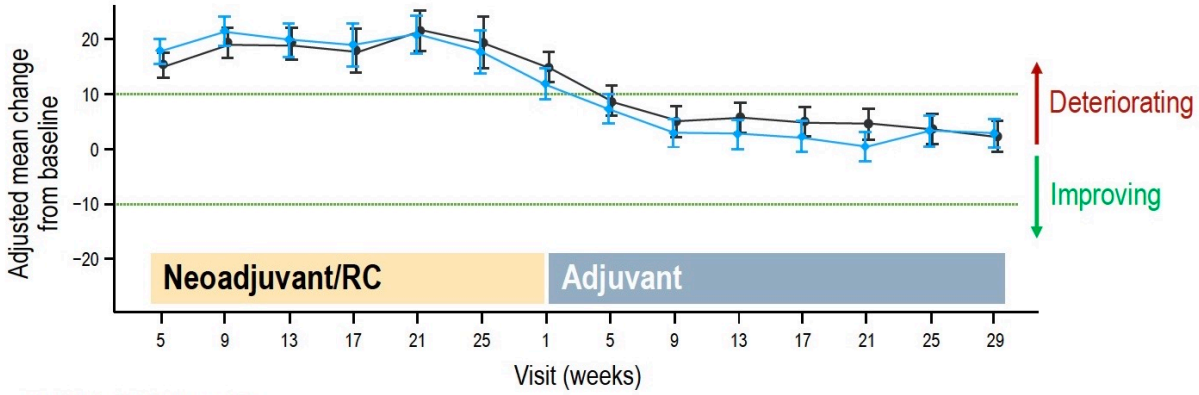
RTP RESEARCH TO PRACTICE

Phase III NIAGARA: EORTC QLQ-C30 Change from Baseline (Continued)

Addition of perioperative durvalumab to NAC did not adversely impact fatigue, or pain subscale scores

Fatigue

Difference between arms for overall mean CFB: –0.9 (95% CI, –3.25 to 1.52)

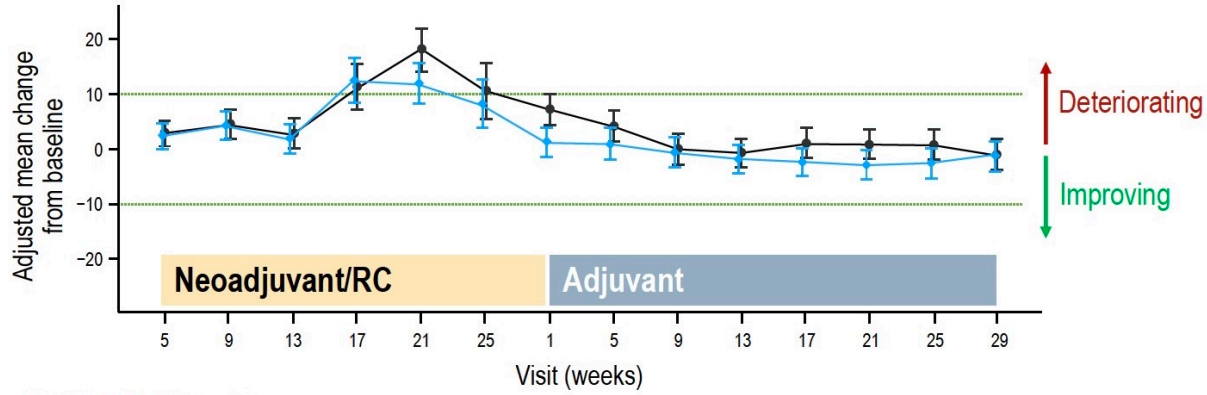


patients included in the analysis

Durvalumab arm	357	332	283	207	173	107	180	204	203	201	203	197	181	181
Comparator arm	364	310	262	193	165	75	183	203	182	179	193	180	188	175

Pain

Difference between arms for overall mean CFB: –2.1 (95% CI, – 4.44 to 0.16)



patients included in the analysis

Durvalumab arm	357	332	283	207	173	107	180	204	203	201	203	197	181	181
Comparator arm	364	310	262	193	165	75	183	203	182	179	193	180	188	175

Clinically meaningful change from baseline
Durvalumab arm
Comparator arm

van der Heijden M et al. ESMO 2025;Abstract 3069MO.

RTP RESEARCH TO PRACTICE

Phase III NIAGARA: Authors' Conclusions

- We report the largest prospective analysis of HRQoL in patients with MIBC receiving perioperative treatment
- In the neoadjuvant and radical cystectomy period, both treatment arms had worsening HRQoL scores, which improved in the adjuvant treatment period
- No clinically meaningful differences were observed between treatment arms for EORTC QLQ-C30 across the study period
- Comparable time to definitive deterioration was reported across all reported EORTC QLQ-C30 subscales
- There was no adverse impact on the EQ-5D-5L visual analogue scale score, with no differences between treatment arms across the study period

Scan the QR code to access:

- Slide presentation including plain language summary

Addition of perioperative durvalumab to NAC significantly improved EFS and OS without adversely impacting patient-reported outcomes

EFS, event-free survival; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; EQ-5D-5L, EuroQol 5-dimension, 5-level version; HRQoL, health-related quality of life; MIBC, muscle-invasive bladder cancer; NAC, neoadjuvant chemotherapy; OS, overall survival.

van der Heijden M et al. ESMO 2025;Abstract 3069MO.

Dr Friedlander: Case Presentation

- 61 y.o. woman with chronic eczema on dupilumab (anti-IL-4/IL-13) presented with renal colic, found to have R-sided hydroureteronephrosis.
- 1/2025: ureteroscopy: tumor around the right ureteral orifice. No upper tract disease.
  - Pathology: high grade urothelial carcinoma, with extensive muscularis mucosae invasion, LVI+.
- CT urogram: Irregular wall thickening at the R uretero-vesicular junction. No metastatic disease in the abdomen/pelvis.

Dr Friedlander: Case Presentation (Continued)

- Not a good candidate for chemoRT due to hydronephrosis.
- Pt elects for neoadjuvant therapy followed by cystectomy.
- Long discussion with dermatology about risks of eczema exacerbation
- Feb 2025: **Starts 4 cycles of cisplatin 70mg/m2 + gemcitabine 1000mg/m2 + durvalumab 1500mg** (NIAGARA regimen)
- Course c/b the following
  - Cis/gem: fatigue, mild renal dysfunction, nausea
  - Durvalumab: grade 2 psoriatic plaque over chest and arm improved with topical steroids. No eczema exacerbation.

Dr Friedlander: Case Presentation (Continued)

- Tolerates 4 cycles of therapy then radical cystectomy with neobladder
- Pathology: High grade UC invasive into the muscularis mucosae and perivesical adipose tissue, 0/16 LN, pT3N0. Post-op ctDNA undetetcable
- June 2025: What to do?
  - Continue Durvalumab?
  - Switch to EV + P?
  - Surveillance?
- Pt elects to continue durvalumab, ctDNA remains negative as of now
  - Psoriasis controlled with topical steroids
  - Working with dermatology to consider steroid sparing alternatives

Abstract LBA112

Neoadjuvant gemcitabine intravesical system (TAR-200) + cetrelimab or cetrelimab alone in patients with muscle-invasive bladder cancer: SunRISe-4 primary analysis and biomarker results

Andrea Necchi,[1] Felix Guerrero-Ramos,[2] Paul L Crispen,[3] Bernardo Herrera-Imbroda,[4] Rohan Garje,[5] Bernadett Szabados,[6,7] Charles C Peyton,[8] Benjamin Pradere,[9] Ja Hyeon Ku,[10] Neal Shore,[11] Martin Bögemann,[12] Mark A Preston,[13] Evanguelos Xylinas,[14] Cinty Gong,[15] Mohamad Hasan,[16] Karen Urtishak,[16] Hind Stitou,[17] Sumeet Bhanvadia,[16] Hussein Sweiti,[16] Sarah P Psutka[17]

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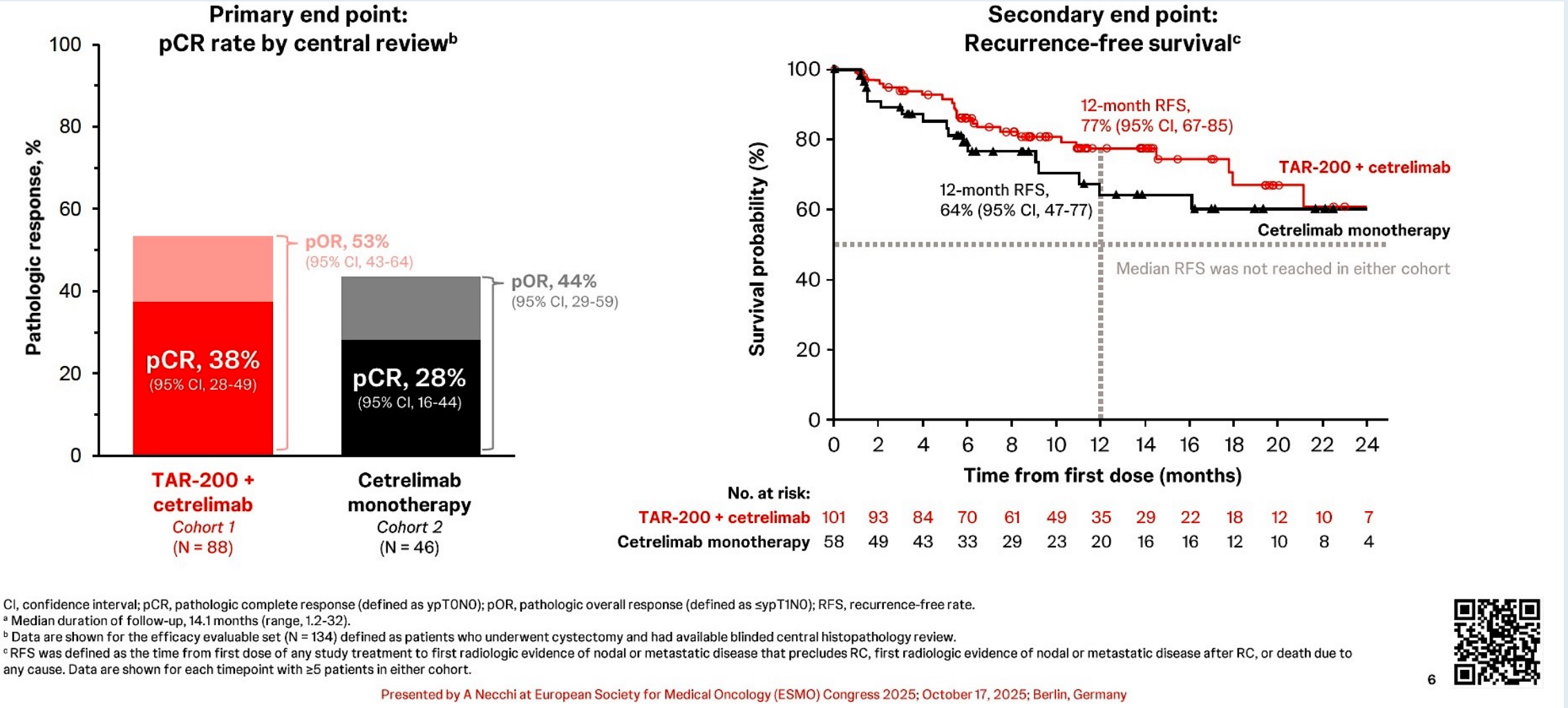
Presented by A Necchi at European Society for Medical Oncology (ESMO) Congress 2025; October 17, 2025; Berlin, Germany

Phase II SunRISe-4: Pathologic Complete Response Rates and Recurrence-Free Survival



CI, confidence interval; pCR, pathologic complete response (defined as ypT0N0); pOR, pathologic overall response (defined as ≤ypT1N0); RFS, recurrence-free rate.
[a] Median duration of follow-up, 14.1 months (range, 1.2-32).
[b] Data are shown for the efficacy evaluable set (N = 134) defined as patients who underwent cystectomy and had available blinded central histopathology review.
[c] RFS was defined as the time from first dose of any study treatment to first radiologic evidence of nodal or metastatic disease that precludes RC, first radiologic evidence of nodal or metastatic disease after RC, or death due to any cause. Data are shown for each timepoint with ≥5 patients in either cohort.

6

Presented by A Necchi at European Society for Medical Oncology (ESMO) Congress 2025; October 17, 2025; Berlin, Germany

Necchi A et al. ESMO 2025;Abstract LBA112.

Phase II SunRISe-4: Authors' Conclusions

- At the primary analysis of SunRISe-4, neoadjuvant **gemcitabine intravesical system + cetrelimab** showed a high pCR rate (**38%**) and 12-month RFS rate (**77%**), supporting further investigation of the combination in MIBC
- **Cetrelimab monotherapy** showed a pCR rate (**28%**) and 12-month RFS rate (**64%**) consistent with previous studies of neoadjuvant checkpoint inhibitor monotherapy[1-3]
- No new safety signals were observed in either treatment cohort
- Exploratory utDNA/ctDNA MRD results support further investigation as predictive biomarkers for residual disease after neoadjuvant therapy in MIBC
  - At baseline, 82% of patients with visibly complete TURBT were utDNA positive
  - **utDNA negative status** at week 12, as a potential marker of local disease, was strongly associated with **pCR**
  - **ctDNA negative status**, as a potential marker of non-local disease, was strongly associated with **longer RFS**, but not associated with pCR

1. Powles T, et al. Nat Med. 2019;25:1706-1714. 2. Necchi A, et al. Eur Urol. 2020;77:439-446. 3. Basile G, et al. Clin Cancer Res. 2022;28:5107-5114.

Presented by A Necchi at European Society for Medical Oncology (ESMO) Congress 2025; October 17, 2025; Berlin, Germany

Necchi A et al. ESMO 2025;Abstract LBA112.

Circulating Tumor DNA and Adjuvant Immunotherapy for MIBC

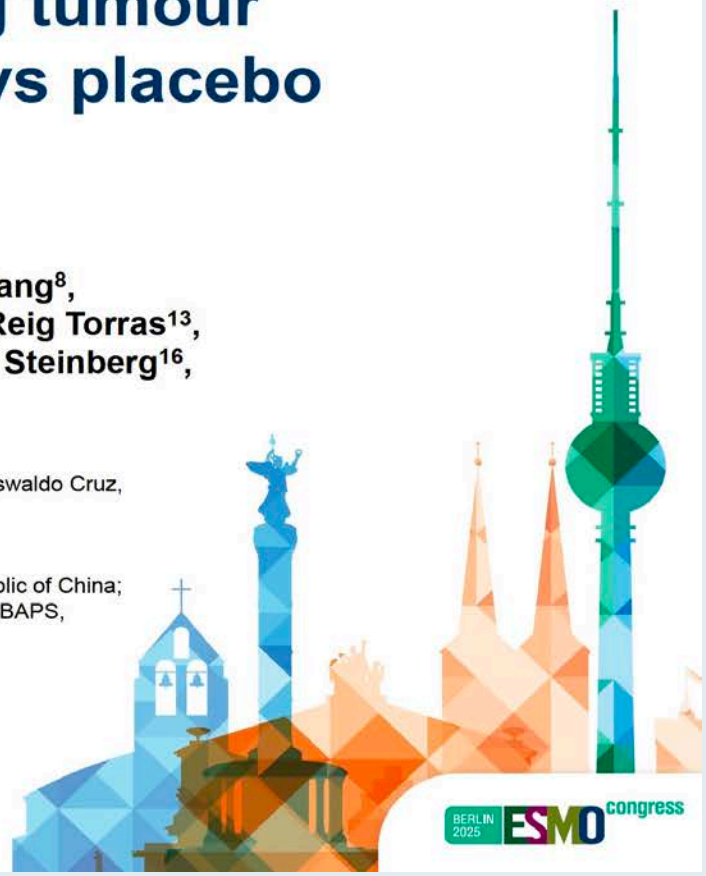
- Powles T et al. IMvigor011: A **phase III** trial of **circulating tumour (ct)DNA-guided adjuvant atezolizumab** vs placebo in **muscle-invasive bladder cancer**. ESMO 2025;Abstract LBA8.
- Galsky MD et al. Adjuvant **nivolumab** vs placebo for **high-risk muscle-invasive urothelial carcinoma**: **5-year efficacy and ctDNA results** from **CheckMate 274**. ESMO 2025;Abstract 3068O.

Abstract LBA8

IMvigor011: a Phase 3 trial of circulating tumour (ct)DNA-guided adjuvant atezolizumab vs placebo in muscle-invasive bladder cancer

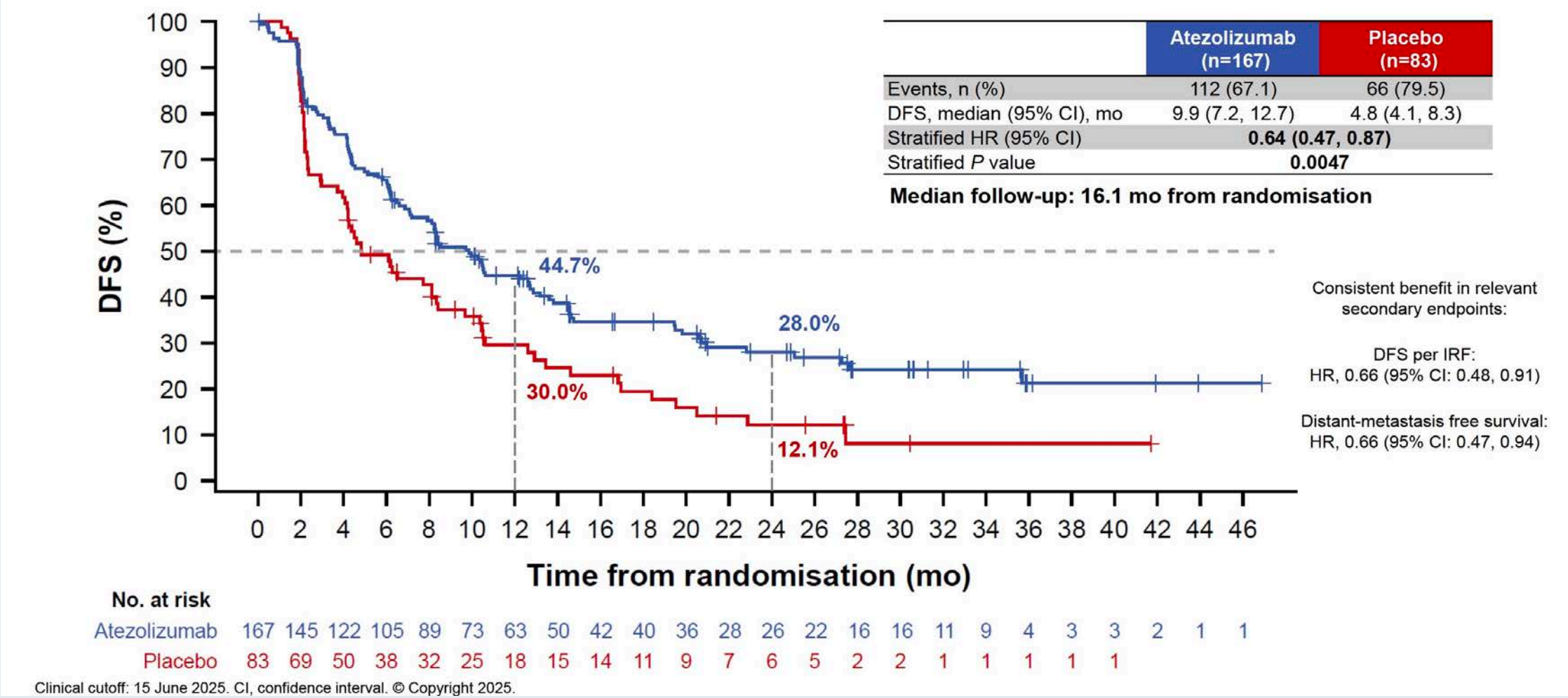
Thomas Powles[1], Ariel G. Kann[2], Daniel Castellano[3], Marine Gross-Goupil[4], Hiroyuki Nishiyama[5], Sergio Bracarda[6], Jørgen Bjerggaard Jensen[7], Shusuan Jiang[8], Ja Hyeon Ku[9], Marco Maruzzo[10], Dingwei Ye[11], Rafael Morales-Barrera[12], Oscar Reig Torras[13], Andrea Necchi[14,15], Wei Zou[16], Zoe June Assaf[16], Jacqueline Vuky[16], Elizabeth E. Steinberg[16], Joaquim Bellmunt[17], Jürgen E. Gschwend[18]

[1]Barts Cancer Institute, NIHR Biomedical Research Centre, Queen Mary University of London, London, UK; [2]Hospital Alemão Oswaldo Cruz, São Paulo, Brazil; [3]Hospital Universitario 12 de Octubre, Madrid, Spain; [4]University Hospital of Bordeaux, Bordeaux, France; [5]University of Tsukuba, Tsukuba, Japan; [6]Azienda Ospedaliera Santa Maria, Terni, Italy; [7]Aarhus University, Aarhus, Denmark; [8]Hunan Cancer Hospital, Changsha, People's Republic of China; [9]Seoul National University Hospital, Seoul, Republic of Korea; [10]Istituto Oncologico Veneto IOV - IRCCS, Padova, Italy; [11]Fudan University Shanghai Cancer Center, Shanghai, People's Republic of China; [12]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [13]Department of Medical Oncology, IDIBAPS, Hospital Clinic, Barcelona, Spain; [14]Department of Medical Oncology, IRCCS San Raffaele Hospital, Milan, Italy; [15]Vita-Salute San Raffaele University, Milan, Italy; [16]Genentech, Inc., South San Francisco, CA, USA; [17]Dana-Farber Cancer Institute and Harvard University, Boston, MA, USA; [18]Technical University Munich, Munich, Germany



Presented by: Thomas Powles, MBBS, MRCP, MD

Phase III IMvigor011: Investigator-Assessed Disease-Free Survival for Patients Whose Disease Tested ctDNA Positive



	Atezolizumab (n=167)	Placebo (n=83)
Events, n (%)	112 (67.1)	66 (79.5)
DFS, median (95% CI), mo	9.9 (7.2, 12.7)	4.8 (4.1, 8.3)
Stratified HR (95% CI)	**0.64 (0.47, 0.87)**	
Stratified *P* value	**0.0047**	

Median follow-up: 16.1 mo from randomisation

Consistent benefit in relevant secondary endpoints:

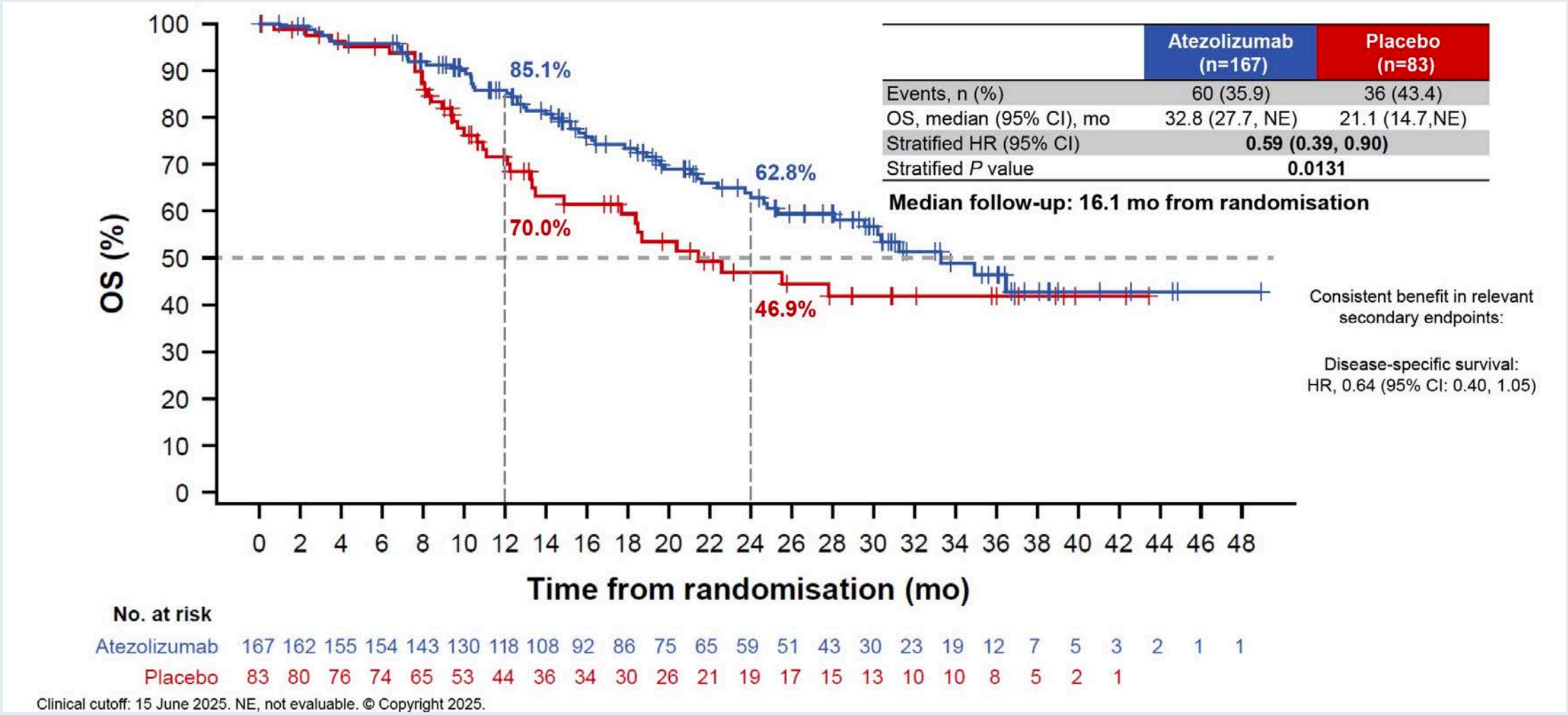
DFS per IRF:
HR, 0.66 (95% CI: 0.48, 0.91)

Distant-metastasis free survival:
HR, 0.66 (95% CI: 0.47, 0.94)

Clinical cutoff: 15 June 2025. CI, confidence interval.

Powles T et al. ESMO 2025;Abstract LBA8.

Phase III IMvigor011: OS for Patients Whose Disease Tested ctDNA Positive



	Atezolizumab (n=167)	Placebo (n=83)
Events, n (%)	60 (35.9)	36 (43.4)
OS, median (95% CI), mo	32.8 (27.7, NE)	21.1 (14.7,NE)
Stratified HR (95% CI)	**0.59 (0.39, 0.90)**	
Stratified *P* value	**0.0131**	

Median follow-up: 16.1 mo from randomisation

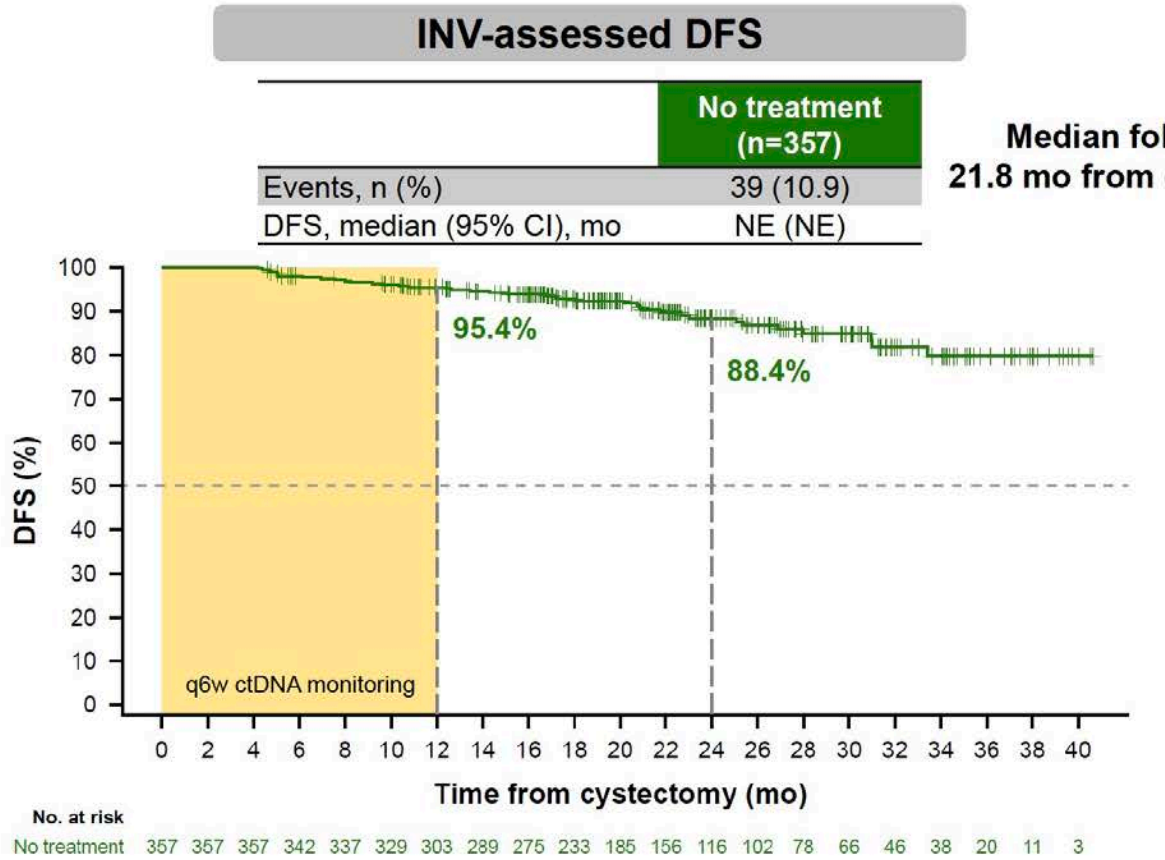
Consistent benefit in relevant secondary endpoints:

Disease-specific survival:
HR, 0.64 (95% CI: 0.40, 1.05)

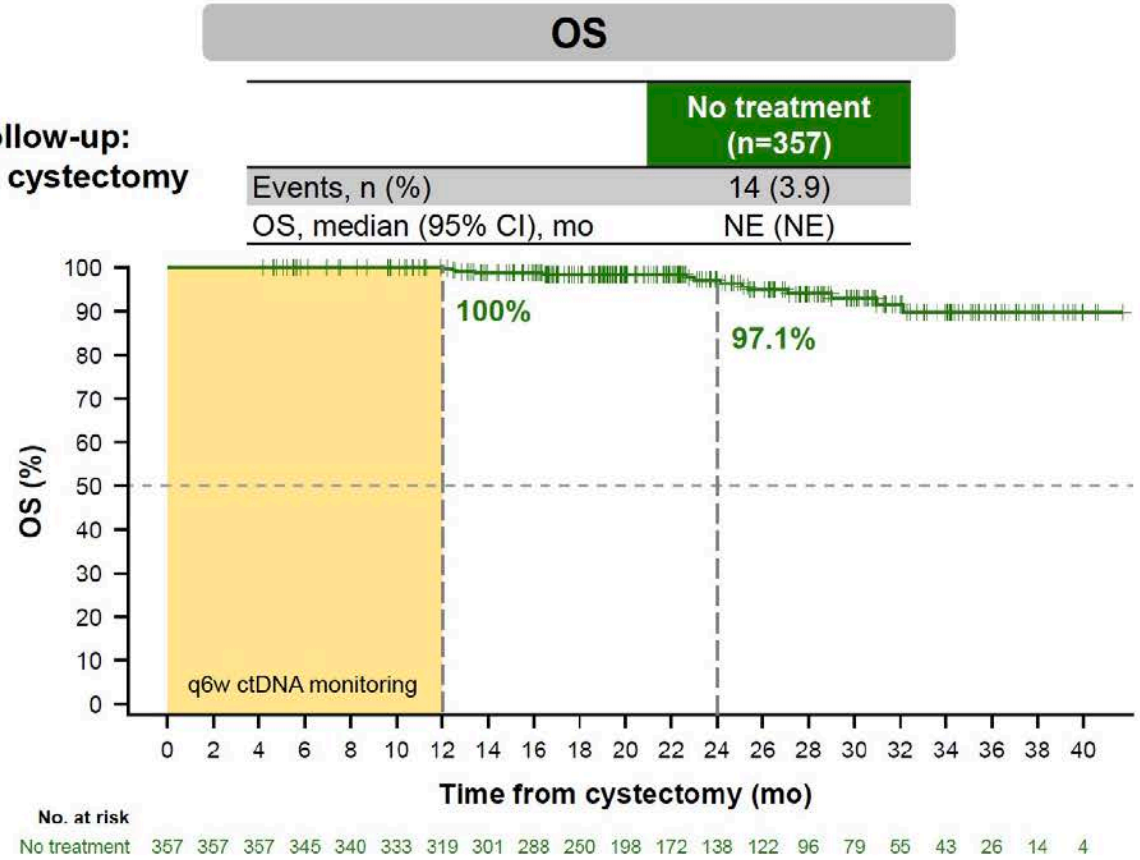
Clinical cutoff: 15 June 2025. NE, not evaluable.

Powles T et al. ESMO 2025;Abstract LBA8.

Phase III IMvigor011: Disease-Free Survival (DFS) and OS for Patients Whose Disease Tested ctDNA Positive



Median follow-up: 21.8 mo from cystectomy



8 DFS events were deaths not clearly attributed to disease recurrence

15 patients (4.2%) who experienced disease recurrence during the ctDNA monitoring period were discontinued from the study and censored for OS

Clinical cutoff: 15 June 2025. To be included in the ctDNA− efficacy-evaluable population, patients must have ≥1 negative test result and no positive test result, had ≥1 post-baseline clinical outcome assessment and completed 1 y of surveillance or discontinued from surveillance without a ctDNA+ result. q6w, every 6 weeks

Powles T et al. ESMO 2025;Abstract LBA8.

Phase III IMvigor011: Authors' Conclusions

- Adjuvant atezolizumab demonstrated statistically significant DFS and OS improvements vs placebo in patients with MIBC identified as ctDNA+ through serial MRD testing
  - Clinical benefit with atezolizumab was generally consistent across key subgroups, including patients excluded from prior adjuvant trials (e.g. those with pT2N0 disease), which suggests that ctDNA status enhances risk determination beyond classical surgical pathological staging
  - Similar efficacy was observed in patients with ctDNA+ status at baseline and those who converted to ctDNA+ status with repeated testing
- Patients who persistently tested ctDNA− had low risk of recurrence and death
- The atezolizumab safety profile was tolerable, with no new findings
- **These findings indicate that serial ctDNA monitoring can identify patients with MIBC who benefit from adjuvant atezolizumab while sparing patients who persistently test ctDNA− from unnecessary treatment**

MRD = molecular residual disease

Powles T et al. ESMO 2025;Abstract LBA8.

Abstract 3068O

BERLIN 2025 ESMO congress

BERLIN GERMANY
17-21 OCTOBER 2025

Adjuvant nivolumab vs placebo for high-risk muscle-invasive urothelial carcinoma: 5-year efficacy and ctDNA results from CheckMate 274

Matthew D. Galsky,[1] Jürgen E. Gschwend,[2] Matthew I. Milowsky,[3] Michael Schenker,[4] Begoña P. Valderrama,[5] Yoshihiko Tomita,[6] Aristotelis Bamias,[7] Thierry Lebret,[8] Shahrokh F. Shariat,[9] Se Hoon Park,[10] Mads Agerbaek,[11] Gautam Jha,[12] Frank Stenner,[13] Dingwei Ye,[14] Fabio Giudici,[15] Jessica Connors,[16] Saurabh Gupta,[16] Joshua Zhang,[16] Dean F. Bajorin,[17] Johannes Alfred Witjes[18]

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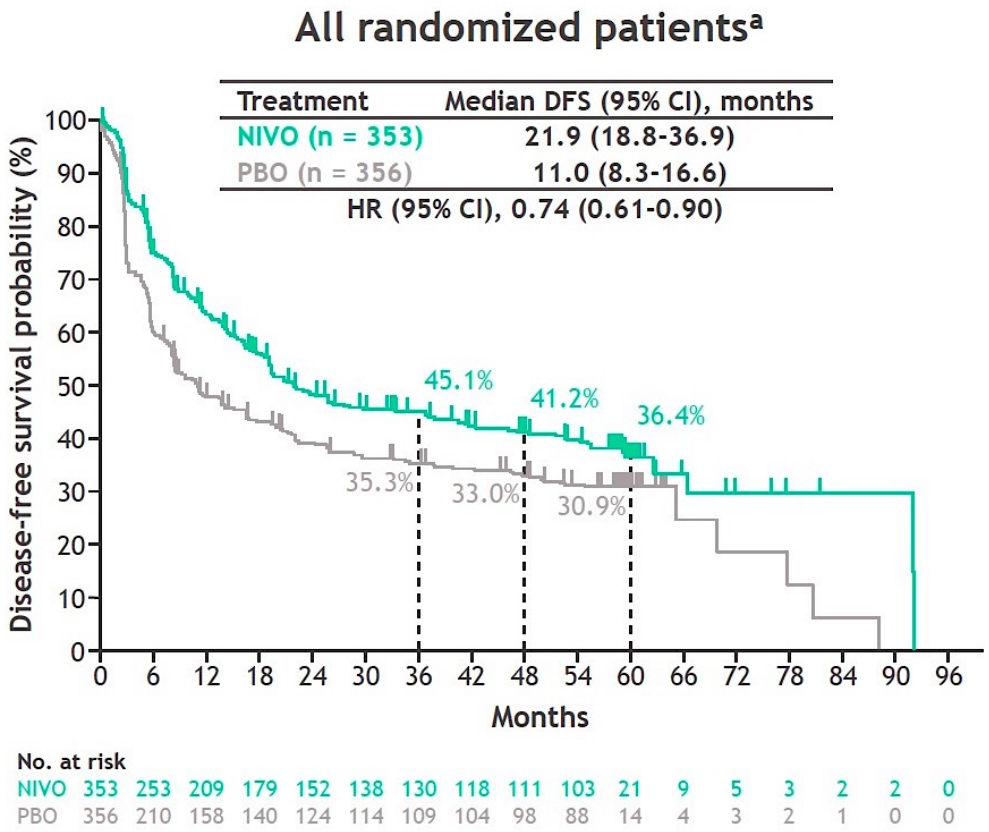
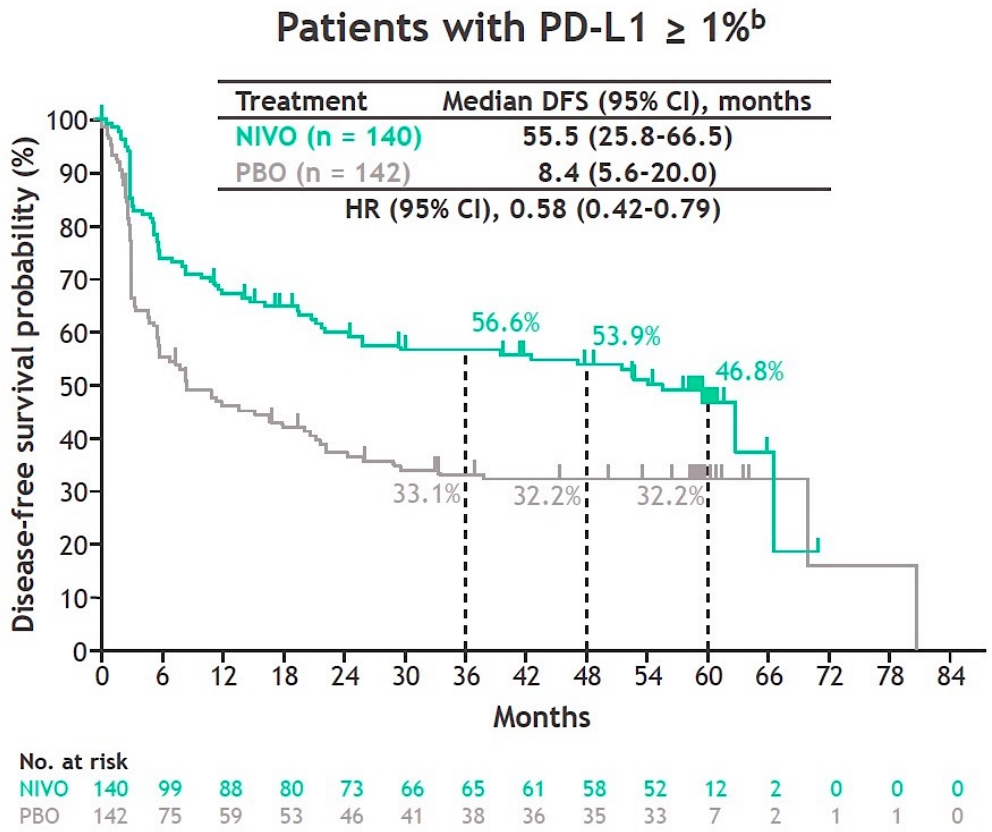
Presentation number 3068O

Phase III CheckMate 274: Disease-Free Survival for All Randomly Assigned Patients and Patients with PD-L1 ≥1%



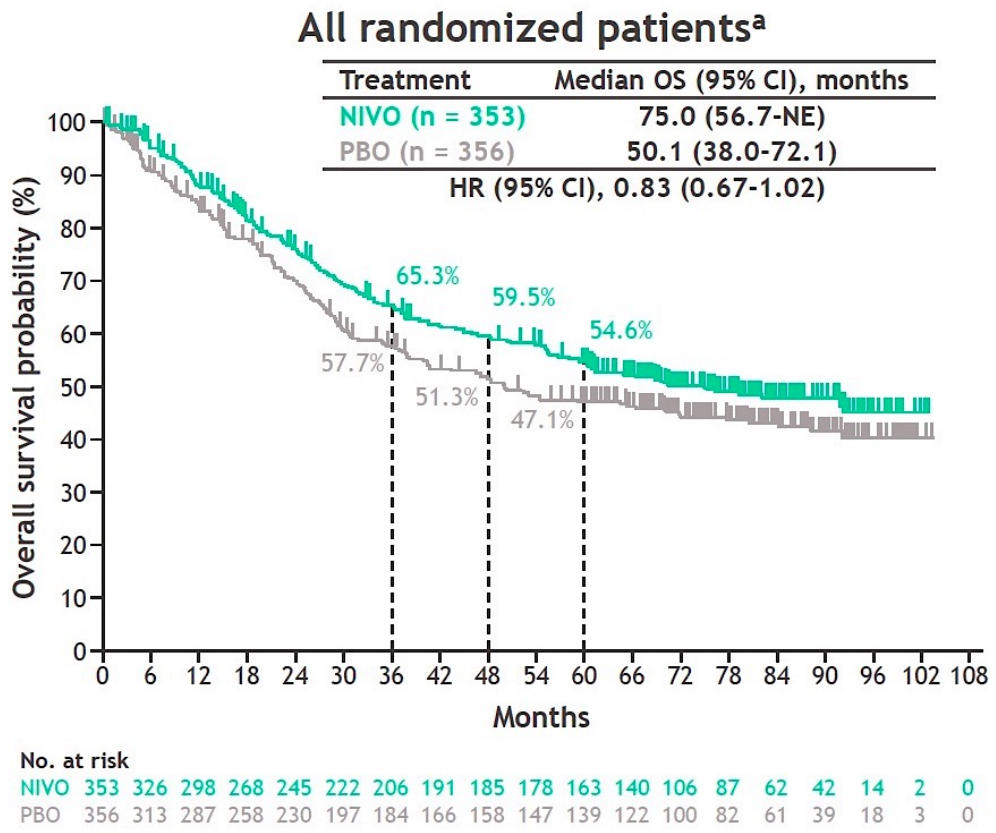


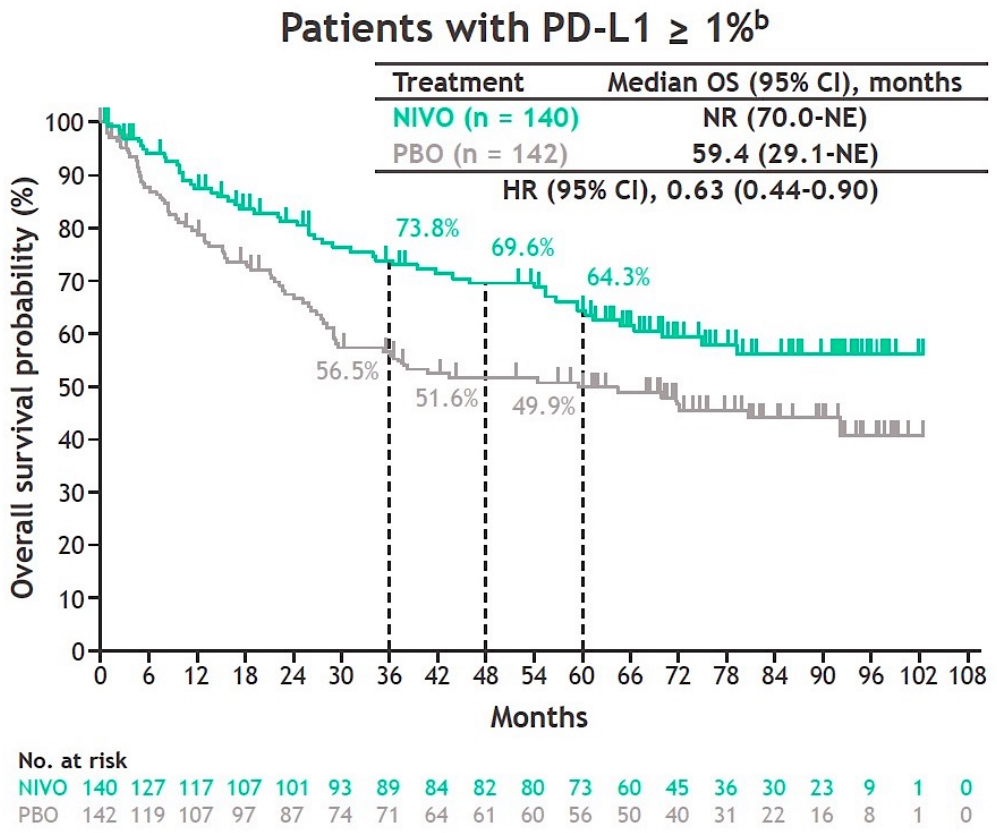
- At 5 years of follow up, long-term benefits were sustained with NIVO vs PBO in all randomized patients and patients with tumor PD-L1 expression ≥ 1%

[a]Minimum follow-up, 59.6 months; median follow-up, 43.4 months. [b]Minimum follow-up, 60.0 months; median follow-up, 52.9 months. Minimum follow-up is defined as the time from last patient randomized to clinical cutoff date. Median follow-up is defined as the time from randomization to death or last known alive date (for patients who are alive).

Galsky MD et al. ESMO 2025;Abstract 3068O.

Phase III CheckMate 274: Interim Overall Survival for All Randomly Assigned Patients and Patients with PD-L1 ≥1%



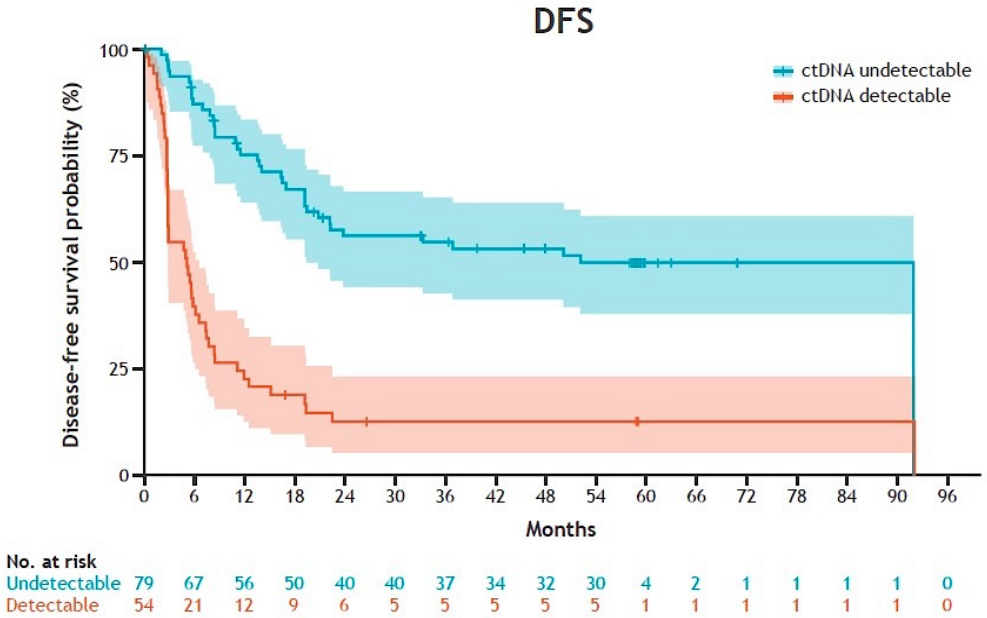


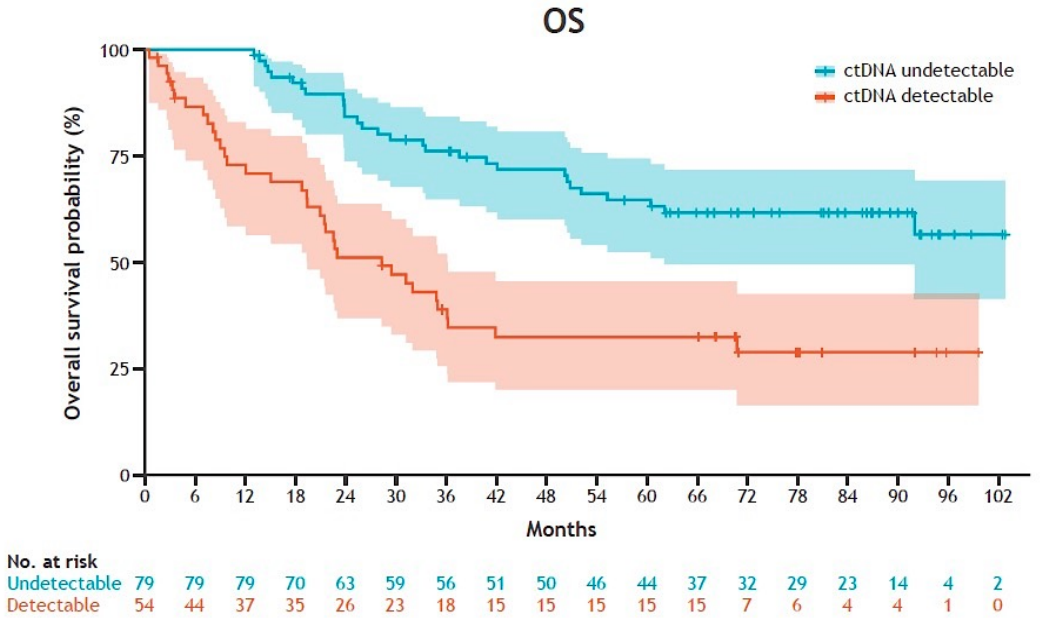
- At 5 years of follow-up, median OS (from interim analyses) was longer for adjuvant NIVO vs PBO in all randomized patients and in patients with tumor PD-L1 expression ≥ 1%

[a]Minimum follow-up, 59.6 months; median follow-up, 43.4 months. [b]Minimum follow-up, 60.0 months; median follow-up, 52.9 months. Minimum follow-up is defined as the time from last patient randomized to clinical cutoff date. Median follow-up is defined as the time from randomization to death or last known alive date (for patients who are alive).

Galsky MD et al. ESMO 2025;Abstract 3068O.

Correlation of ctDNA Status with DFS and OS





	ctDNA undetectable (n = 79)	ctDNA detectable (n = 54)
Median DFS (95% CI), months	52.1 (19.4-NE)	5.0 (2.8-6.5)
DFS HR (95% CI)	0.30 (0.18-0.48)	

	ctDNA undetectable (n = 79)	ctDNA detectable (n = 54)
Median OS (95% CI), months	NR (62.0-NE)	28.2 (19.4-36.1)
OS HR (95% CI)	0.44 (0.25-0.76)	

- ctDNA analysis was performed on 133 of 709 randomized patients (18.8%); 54 of 133 patients (40.6%) had detectable ctDNA
- The size of the dataset was limited by sample collection; results should be interpreted with caution
- Patients with undetectable ctDNA showed > 10-fold longer median DFS vs patients with detectable ctDNA

Minimum follow-up, 61.3 months; median follow-up, 41.8 months in ctDNA-evaluable patients. Post hoc exploratory analyses. Baseline ctDNA was measured using the Signatera assay.

Galsky MD et al. ESMO 2025;Abstract 3068O.

Phase III CheckMate 274: Authors' Conclusions

- With extended 5 years minimum follow-up in CheckMate 274, adjuvant NIVO continued to show DFS benefits vs PBO, and median OS and median DSS were longer with NIVO vs PBO in both the all randomized and PD-L1 ≥ 1% MIUC populations
- In patients with MIBC, NIVO was associated with DFS benefits and showed a trend toward OS benefit regardless of prior cisplatin exposure
- In exploratory post hoc ctDNA analyses, NIVO improved DFS and OS by more than 2-fold and 1.5-fold, respectively, vs PBO within the ctDNA-detectable subgroup
  - However, conclusions are limited due to small sample size
- No new safety signals were observed since the previous database lock as patients have been off treatment for at least 4 years[1,2]
- Subcutaneous NIVO has been shown to provide clinical equipoise to standard IV dosing[3] and may provide an alternative for patients across various tumors[4-7]
- These results provide additional support for adjuvant NIVO as a standard of care for high-risk MIUC after radical resection, potentially providing an opportunity for curative outcome

1. Bajorin DF, et al. *N Engl J Med* 2021;384:2102-2114. 2. Galsky MD, et al. *J Clin Oncol* 2025;43:15-21. 3. Albiges L, et al. *Ann Oncol* 2024;15:S0923-7534(24)03996-6. 4. Nivolumab/hyaluronidase [package insert]. Princeton, NJ, USA: Bristol Myers Squibb; 2025. 5. Lonardi S, et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 4-8, 2021. Poster 2575. 6. Zhao Y, et al. Presented at the Society for Immunotherapy of Cancer (SITC) Annual Meeting; November 6-10, 2024; San Diego, CA, USA. Poster 524. 7. Nivolumab [summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb; June 2025.

Galsky MD et al. ESMO 2025;Abstract 3068O.

Dr Friedlander: Case Presentation

- 62 yo M with long tobacco history, HTN, presents with hematuria. Workup shows high grade pT1 NMIBC
  - June-Nov 2024: Receives BCG induction and maintenance
- 12/2024: Cysto with new posterior wall nodule
- Feb 2025: TURBT: HG T1 UC, +lymphovascular invasion (+LVI), no muscle invasion
- cfDNA (Signatera™) negative

Lymphovascular Invasion in Transurethral Resection Specimens as Predictor of Progression and Metastasis in Patients With Newly Diagnosed T1 Bladder Urothelial Cancer

Kang Su Cho, Ho Kyung Seo, Jae Young Joung, Weon Seo Park, Jae Y. Ro, Kyung Seok Han, Jinsoo Chung and Kang Hyun Lee*

From the Urologic Oncology Clinic (KSC, HKS, JYJ, KSH, JC, KHL) and Department of Pathology (WSP), Center for Specific Organs Cancer, National Cancer Center, Goyang, Korea, and Department of Pathology, Methodist Hospital and Research Institute, Weill Medical College of Cornell University (JYR), Houston, Texas

Purpose: We evaluated the clinical significance of lymphovascular invasion in transurethral resection of bladder tumor specimens in patients with newly diagnosed T1 urothelial carcinoma of the bladder.

Materials and Methods: Enrolled in the study were 118 patients with newly diagnosed T1 urothelial carcinoma of the bladder who underwent transurethral resection of bladder tumor between 2001 and 2007. Patient records were retrieved from a prospectively maintained bladder cancer database. We evaluated the correlation between lymphovascular invasion and other clinicopathological features, and the impact of lymphovascular invasion on disease recurrence, disease progression and metastasis.

Results: Lymphovascular invasion was histologically confirmed in 33 patients (28.0%). While lymphovascular invasion correlated with tumor grade ($p = 0.002$), it was not associated with gender, age, bladder tumor history, tumor size, multiplicity or concomitant carcinoma in situ. Recurrence, progression and metastasis developed in 45 (38.1%), 19 (16.1%) and 10 patients (8.5%), respectively. Univariate analysis showed that lymphovascular invasion was marginally associated with recurrence and significantly associated with progression ($p = 0.011$) and metastasis ($p = 0.019$). Multivariate Cox proportional hazards analysis revealed that recurrence was significantly associated with lymphovascular invasion ($p = 0.029$), and with bladder tumor history ($p < 0.001$), tumor size ($p = 0.031$) and multiplicity ($p = 0.043$). Lymphovascular invasion was the only independent prognostic factor associated with progression ($p = 0.016$).

Conclusions: In patients with newly diagnosed T1 urothelial carcinoma of the bladder lymphovascular invasion in transurethral resection of bladder tumor specimens predicts disease progression and metastasis.

Abbreviations and Acronyms

LVI = lymphovascular invasion

TUR = transurethral resection

TURBT = TUR of bladder tumor

Submitted for publication April 6, 2009.

Study received National Cancer Center institutional review board approval.

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For another article on a related topic see page 2932.

Dr Friedlander: Case Presentation (Continued)

- Tumor board: Pt at high risk for progression to MIBC/metastases given
  - No response to BCG
  - +LVI

- April 2025: Discussed role of neoadjuvant systemic therapy vs RC vs RT
  - “I am really active, love to travel, hoping to avoid side effects”
  - cfDNA now positive: 0.05 mean tumor molecules (MTM)/ml

- Pt elects for RC alone, hoping no systemic therapy will be needed

Dr Friedlander: Case Presentation (Continued)

- RC with neobladder
  - Path: pT3bN2, 3/12 LNs+, HER2 3+. Left ureteral soft tissue margin+.
  - Also Gl 3+4, pT2N0 prostate cancer
  - Post op course c/b pelvic fluid collection requiring drain

- 1st post op visit: cfDNA negative!
  - Pt encouraged, but high concern for relapse. Still recovering from surgery.

- 2nd post op visit: cfDNA now positive 2.2 MTM/ml
  - “Sounds like I should get some chemo or immunotherapy?”

- Summer 2025: **Starts cisplatin + gemcitabine + durvalumab**

Dr Friedlander: Case Presentation (Continued)

FINAL RESULTS SUMMARY

Signatera Negative

MTM/mL: Not Detected

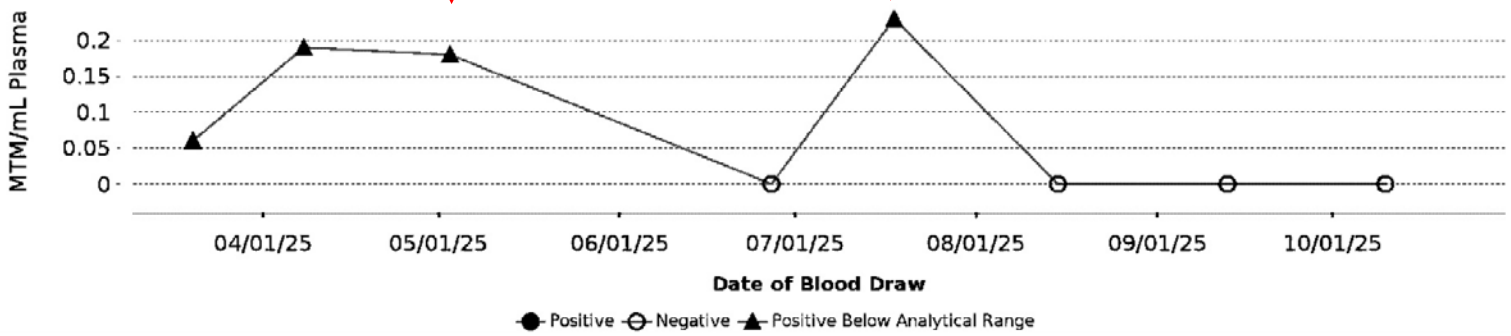
Mean tumor molecules per mL is calculated based on the mean of ctDNA molecules detected per mL of the patient's plasma. *See Limitations section below.*

Surgery

Adjuvant Cis/Gem/Durva

Higher than expected cell-free DNA (cfDNA) levels were found in this plasma specimen. Excessive cfDNA may decrease clinical sensitivity.

Historical Results



Date	Reported MTM/mL
Oct 10, 2025	0.00
Sep 13, 2025	0.00
Aug 15, 2025	0.00
Jul 18, 2025	0.23
Jun 27, 2025	0.00
May 03, 2025	0.18
Apr 08, 2025	0.19
Mar 20, 2025	0.06

HER2-Targeted Antibody-Drug Conjugates for Metastatic Urothelial Carcinoma

- Guo J et al. **Disitamab vedotin (DV) plus toripalimab (T)** versus chemotherapy (C) in first-line (1L) **locally advanced or metastatic urothelial carcinoma (la/mUC) with HER2-expression**. ESMO 2025;Abstract LBA7.
- Makker V et al. **Trastuzumab deruxtecan (T-DXd)** for pretreated patients (pts) with **HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) part 1 final analysis**. ESMO 2025;Abstract 957P.

Abstract LBA7

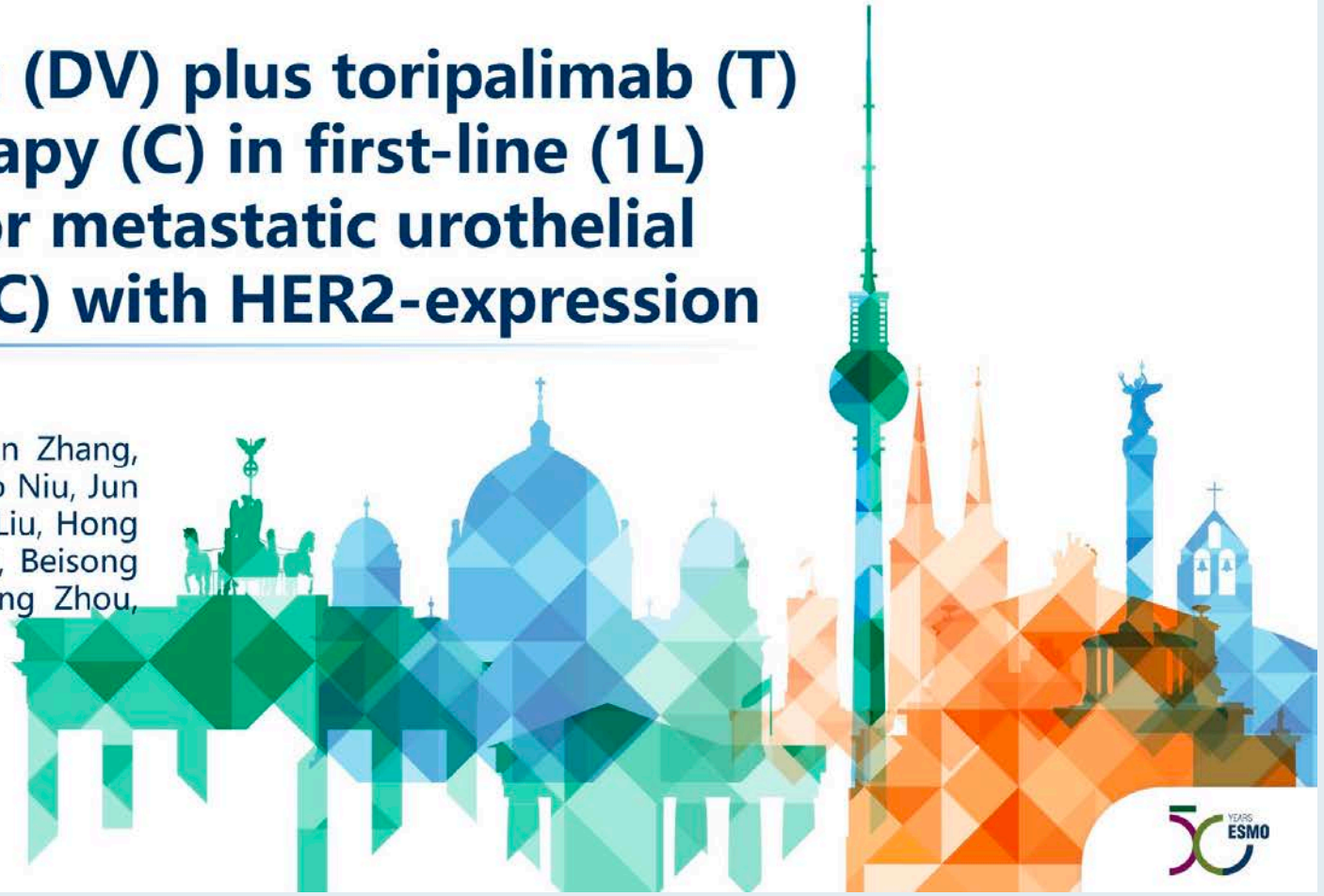
Number: LBA7

BERLIN 2025 ESMO congress

Disitamab vedotin (DV) plus toripalimab (T) versus chemotherapy (C) in first-line (1L) locally advanced or metastatic urothelial carcinoma (la/mUC) with HER2-expression

Phase III RC48-C016 study

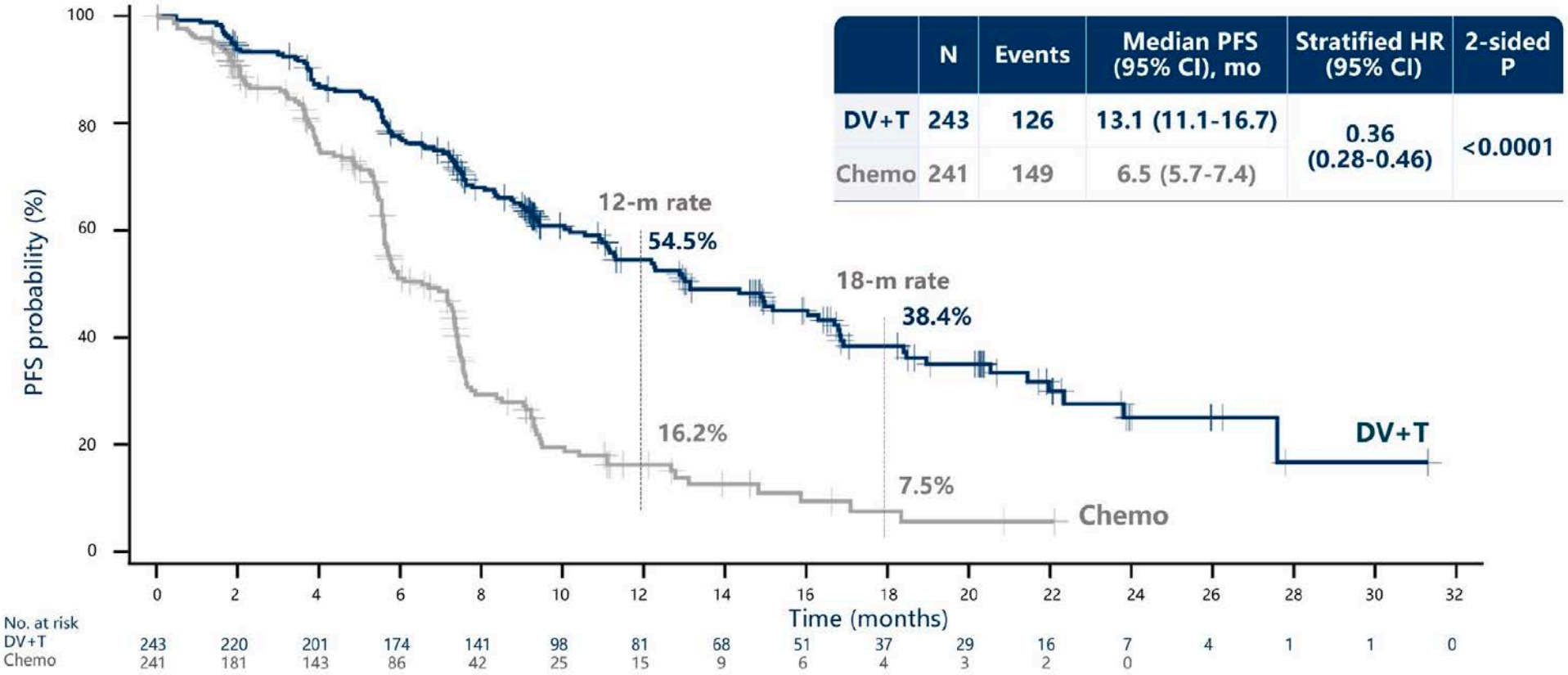
Xinan Sheng, Gongqian Zeng, Cuijian Zhang, Qingyun Zhang, Jiasheng Bian, Haitao Niu, Jun Li, Yanxia Shi, Kai Yao, Bin Hu, Ziling Liu, Hong Liao, Zhixian Yu, Baiye Jin, Lu Zhang, Beisong Liu, Jianmin Fang, Zhisong He, Aiping Zhou, Jun Guo



Presenter: Jun Guo, MD
October 19, 2025

Phase III RC48-C016: PFS by BIRC

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

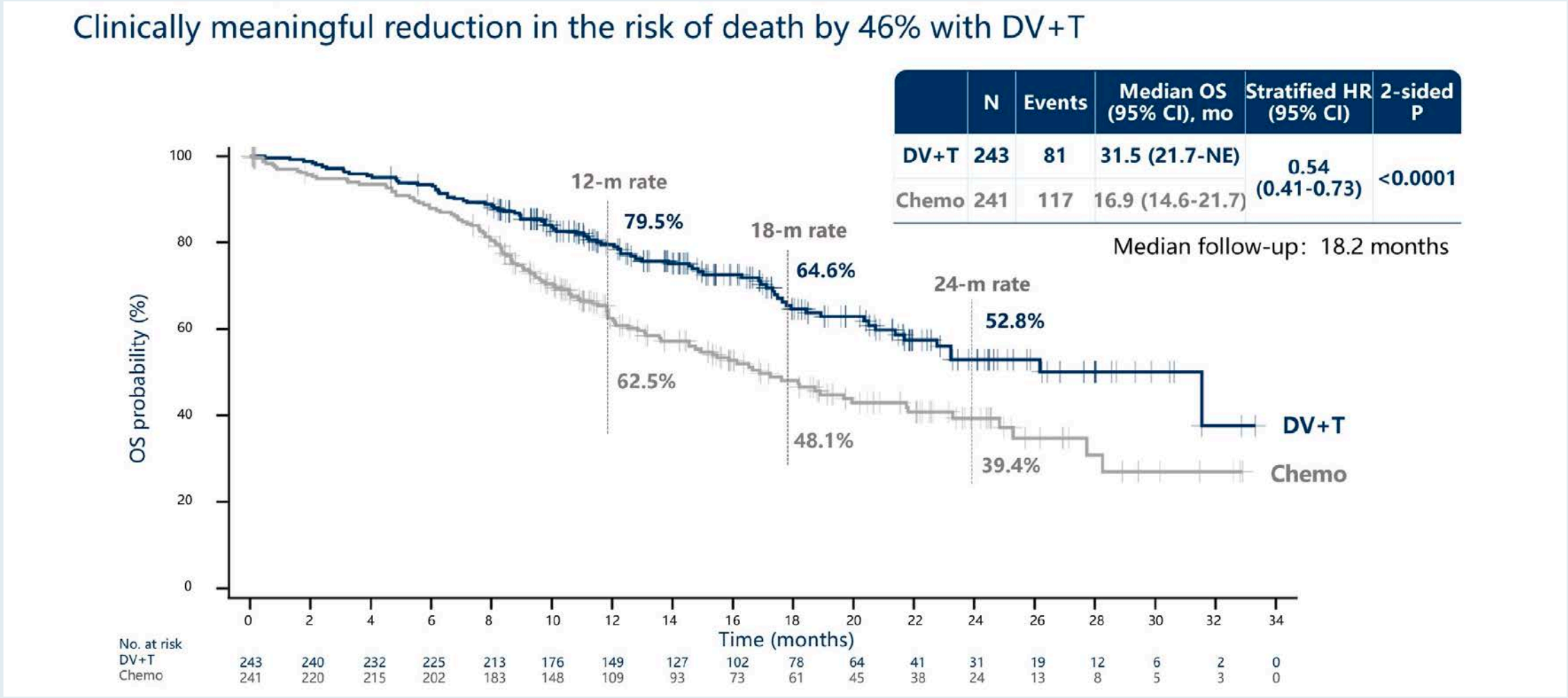


	N	Events	Median PFS (95% CI), mo	Stratified HR (95% CI)	2-sided P
DV+T	243	126	13.1 (11.1-16.7)	0.36 (0.28-0.46)	<0.0001
Chemo	241	149	6.5 (5.7-7.4)		

- The investigator assessment (median: 12.3 vs 6.2 months; stratified HR: 0.36 [95% CI: 0.28-0.46]) was consistent with BIRC.

Guo J et al. ESMO 2025;Abstract LBA7.

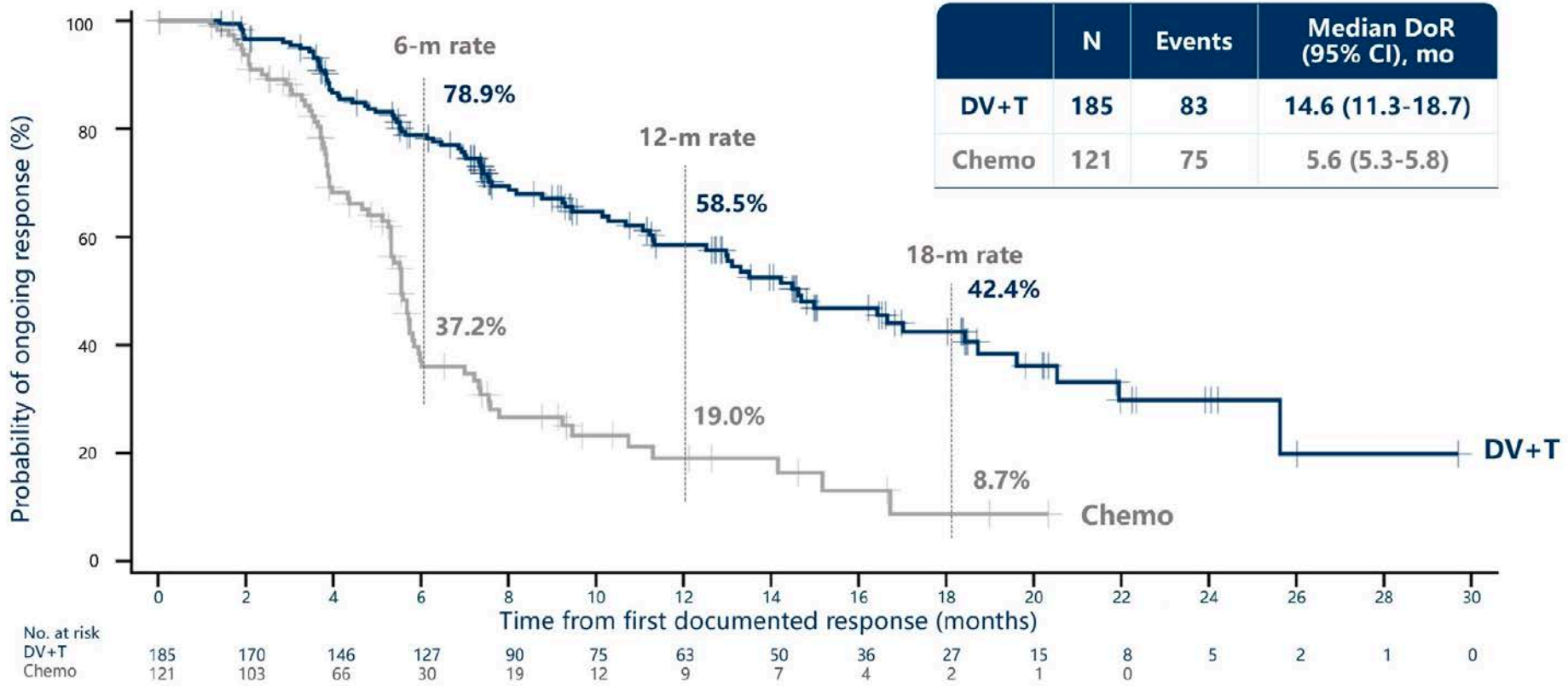
Phase III RC48-C016: Overall Survival



Guo J et al. ESMO 2025;Abstract LBA7.

Phase III RC48-C016: Duration of Response

Significant improvement in DoR in patients with DV+T by BICR and investigators



	N	Events	Median DoR (95% CI), mo
DV+T	185	83	14.6 (11.3-18.7)
Chemo	121	75	5.6 (5.3-5.8)

- The investigator assessment (median: 13.1 vs 5.5 months) was consistent with BIRC.

Guo J et al. ESMO 2025;Abstract LBA7.

RTP RESEARCH TO PRACTICE

Phase III RC48-C016: Authors' Conclusions

- The Phase III RC48-C016 study demonstrated for the first time superiority of an anti-HER2 antibody drug conjugate plus an anti-PD1 inhibitor in a biomarker-selected patient population with la/mUC.
- DV+T led to a clinically meaningful and statistically significant prolongation of PFS and OS versus chemo in patients with previously untreated HER2-expressing la/mUC.
  - **PFS (per BIRC): median, 13.1 versus 6.5 months; HR, 0.36 (95% CI: 0.28-0.46); P<0.0001.**
  - **OS: median, 31.5 versus 16.9 months; HR, 0.54 (95% CI: 0.41-0.73); P<0.0001.**
  - **PFS and OS benefits are consistent across HER2 expression levels and other prespecified subgroups**
- The safety profile of DV+T was consistent with each agent, and it was more favorable than chemo.
  - **Incidence of grade ≥3 TRAEs: 55.1% with DV+T vs 86.9% with chemo.**
- DV+T offers a valuable new treatment option and represents a potential new standard of care for the 1L treatment of patients with HER2-expressing la/mUC.

Guo J et al. ESMO 2025;Abstract LBA7.

Abstract 957P

Trastuzumab deruxtecan for pretreated patients with HER2-expressing solid tumors: DESTINY-PanTumor02 Part 1 final analysis

Vicky Makker,[1] Funda Meric-Bernstam,[2] Ana Oaknin,[3] Do-Youn Oh,[4] Anastasiya Mochalova,[5] Arunee Dechaphunkul,[6] Igor Kudryavtsev,[7] Chia-Chi Lin,[8] Antonio Gonzalez-Martin,[9] Mairead G McNamara,[10] Iwona Ługowska,[11] Tarek Meniawy,[12] Vanda Salutari,[13] Thatthan Suksomboon charoen,[14] Teerapat Ungtrakul,[15] Chiedozie Anoka,[16] Ann Smith,[17] Soham Puvvada,[18] Jung-Yun Lee[19]

Phase II DESTINY-PanTumor02 Study Design

Patient population

- Adults with histologically confirmed locally advanced, metastatic, or unresectable solid tumors (excluding breast, colorectal, gastric, and non-small cell lung cancer)
- Disease progression following ≥1 prior systemic treatment or without alternative treatment options; prior HER2-directed therapy was allowed
- HER2-expressing tumors with IHC 3+/2+ scored using current American Society of Clinical Oncology / College of American Pathology (ASCO/CAP) guidelines for scoring HER2 in gastric cancer[8]
- HER2 expression at enrollment was based on local testing; however, if local testing was not available, enrollment was determined by central HER2 testing (HercepTest [DAKO])
  - Retrospective central HER2 testing was performed for patients enrolled based on a local HER2 test result

*Investigator assessed per RECIST 1.1; †included patients with salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1). DCR, disease control rate; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan

Study type

Open label, multicenter, multicohort, Phase 2

Treatment

T-DXd 5.4 mg/kg IV Q3W

Trial registration

NCT04482309

Data cutoff

October 10, 2024

Endpoints

Primary:

- Confirmed ORR*

Secondary:

- DOR*
- DCR*
- PFS*
- OS
- Safety and tolerability

Exploratory:

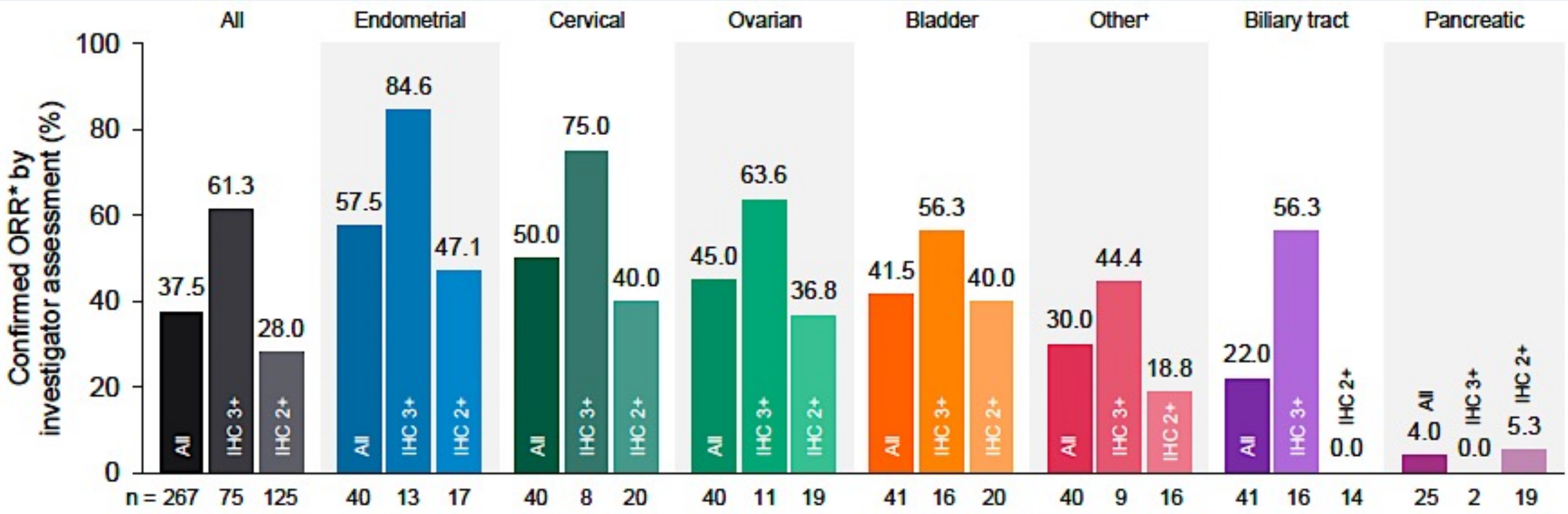
- Subgroup analyses by HER2 status
- Subgroup analyses by biomarker status

Cohorts

- Endometrial
- Cervical
- Ovarian
- Bladder
- Other tumors†
- Biliary tract
- Pancreatic

Makker V et al. ESMO 2025;Abstract 957P.

Phase II DESTINY-PanTumor02 Part 1 Final Analysis: Investigator-Assessed Confirmed ORR by Tumor Cohort and HER2 IHC



Investigator-assessed ORR analyses were performed for patients who received ≥1 dose of T-DXd (n=267). *Confirmed ORR per RECIST 1.1; †included patients with salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1)
HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan

Makker V et al. ESMO 2025;Abstract 957P.

RTP RESEARCH TO PRACTICE

Phase II DESTINY-PanTumor02 Part 1 Final Analysis: Median PFS by Tumor Cohort and HER2 IHC

Median PFS, months (95% CI) [n]*	All patients	HER2 IHC status by central testing		HER2 IHC status at enrollment‡	
		IHC 3+	IHC 2+	IHC 3+	IHC 2+
All	6.9 (5.6, 8.0) [267]	11.9 (8.2, 13.0) [75]	5.4 (4.2, 6.0) [125]	9.7 (7.0, 12.5) [111]	5.1 (4.1, 6.0) [151]
Endometrial	11.1 (7.1, 25.8) [40]	28.1 (7.3, NE) [13]	8.5 (4.6, 15.1) [17]	24.8 (4.5, 35.7) [16]	11.0 (6.0, 19.5) [24]
Cervical	7.0 (4.2, 11.1) [40]	NE (3.9, NE) [8]	4.8 (2.7, 5.7) [20]	NE (3.9, NE) [10]	4.6 (1.4, 8.1) [25]
Ovarian	5.9 (4.0, 8.3) [40]	12.5 (3.1, NE) [11]	4.1 (2.3, 12.6) [19]	12.6 (4.1, NE) [15]	4.4 (2.3, 7.1) [25]
Bladder	7.0 (4.2, 9.7) [41]	7.4 (3.0, 11.9) [16]	7.8 (2.6, 11.6) [20]	7.0 (3.9, 11.5) [27]	7.0 (2.6, 13.0) [14]
Other†	8.8 (5.5, 12.5) [40]	22.3 (5.6, NE) [9]	5.5 (2.8, 8.7) [16]	13.0 (6.3, 23.4) [16]	6.6 (2.9, 8.8) [24]
Biliary tract	4.6 (3.1, 6.0) [41]	7.4 (2.8, 12.5) [16]	4.2 (2.8, 6.0) [14]	6.9 (3.0, 8.0) [22]	3.7 (2.8, 5.1) [19]
Pancreatic	3.2 (1.8, 7.2) [25]	5.4 (2.8, NE) [2]	2.8 (1.4, 9.1) [19]	8.0 (1.2, NE) [5]	3.2 (1.4, 4.9) [20]

Discrepancies in n numbers are owing to patients with central HER2 IHC status of 1+/0/unknown enrolled as IHC 3+/2+ by local testing
*Investigator assessed per RECIST 1.1; †Included patients with salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1); ‡HER2 expression for enrollment was based on local assessment, where available, otherwise enrollment was based on central testing
CI, confidence interval; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NE, not evaluable; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours

Makker V et al. ESMO 2025;Abstract 957P.

Phase II DESTINY-PanTumor02 Part 1 Final Analysis: Median OS by Tumor Cohort and HER2 IHC

Median OS, months (95% CI) [n]	All patients	HER2 IHC status by central testing		HER2 IHC status at enrollment†	
		IHC 3+	IHC 2+	IHC 3+	IHC 2+
All	13.4 (11.9, 15.3) [267]	21.1 (16.0, 26.0) [75]	12.2 (10.7, 13.6) [125]	17.7 (12.8, 23.4) [111]	12.0 (9.6, 13.5) [151]
Endometrial	24.2 (12.8, 33.7) [40]	33.7 (18.9, NE) [13]	16.4 (8.0, 34.7) [17]	29.0 (4.5, NE) [16]	20.3 (8.1, 33.1) [24]
Cervical	13.6 (11.1, 19.7) [40]	35.8 (3.9, NE) [8]	11.6 (5.1, 18.0) [20]	35.8 (3.9, NE) [10]	11.7 (8.0, 13.6) [25]
Ovarian	13.2 (8.0, 17.7) [40]	20.0 (3.8, NE) [11]	13.0 (4.7, 21.9) [19]	20.0 (7.2, NE) [15]	10.7 (5.9, 14.8) [25]
Bladder	12.8 (11.2, 15.1) [41]	13.4 (6.7, 19.8) [16]	13.1 (11.0, 19.9) [20]	12.6 (6.7, 17.2) [27]	13.5 (8.0, 19.9) [14]
Other*	21.0 (12.9, 25.1) [40]	25.1 (11.1, NE) [9]	14.6 (6.8, 22.4) [16]	25.2 (11.1, 40.0) [16]	15.5 (9.6, 22.4) [24]
Biliary tract	7.0 (4.6, 10.2) [41]	12.4 (2.8, 26.3) [16]	6.0 (3.7, 11.7) [14]	7.6 (4.6, 23.7) [22]	5.3 (3.1, 10.2) [19]
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Discrepancies in n numbers are owing to patients with central HER2 IHC status of 1+/0/unknown enrolled as IHC 3+/2+ by local testing
*Included patients with salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1); †HER2 expression for enrollment was based on local assessment, where available, otherwise enrollment was based on central testing
CI, confidence interval; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NE, not evaluable; OS, overall survival

Makker V et al. ESMO 2025;Abstract 957P.

Phase II DESTINY-PanTumor02 Part 1 Final Analysis: Authors' Conclusions

- Consistent with the primary and post-hoc analyses,[1,2] T-DXd continued to show durable and clinically meaningful antitumor activity in patients with HER2-expressing tumors (immunohistochemistry [IHC] 3+/2+), irrespective of whether HER2 IHC status was determined by central or local testing
  - The greatest benefit was observed in patients with HER2 IHC 3+ tumors
  - With extended follow up, safety remained consistent with the known profile of T-DXd, with no new safety signals observed compared with the primary analysis[1]
- These results further reinforce T-DXd as a recommended treatment for pretreated patients with HER2-positive (IHC 3+) tumors[3–5]
  - Part 2 of the study is currently ongoing and is expected to provide further insights into the antitumor activity of T-DXd in pretreated patients with HER2-expressing/amplified solid tumors[6]

Makker V et al. ESMO 2025;Abstract 957P.

Dr Friedlander: Case Presentation

- 72 yo F with HTN, alcohol use disorder, GERD presents with MIBC in 2023
  - S/p 4 cycles of **cisplatin/gemcitabine** then **RC** with ileal conduit
  - Pathology: ypT4aN2Mx, 8/24 LNs +, 2.2cm residual tumor, plasmacytoid histology. HER2 3+

- Receives 6 months of **adjuvant nivolumab**
  - Mid 2024: CT with pelvic nodal and vertebral metastases

- Starts **EV + P** x 3 cycles, complicated by steroid-responsive pneumonitis thought related to EV

Dr Friedlander: Case Presentation (Continued)

- Fall 2024: **SBRT** to all sites of cancer
- Early 2025: New nodal and vertebral disease.
  - **Starts Trastuzumab deruxtecan (T-DXd)**
  - Course c/b mild nausea, alternating constipation and diarrhea 10lb wt loss, loss of taste (progressive), mild malaise 1 week post each infusion, group B strep sepsis despite GCSF
- CT scan after 4 cycles: Stable disease
- CT scan after 6 cycles: Slightly decreased lymphadenopathy, no new lesions
- October 2025: CT scan after 8 cycles with new lung and liver nodules
  - Screening for FX-909 (PPARG inhibitor) clinical trial at UCSF

Targeting TROP2 in mUC

- Rha SY et al. **Datopotamab deruxtecan (Dato-DXd) + rilvegostomig (rilve)** in patients (pts) with **locally advanced or metastatic urothelial cancer (a/mUC): Results** from the **phase II TROPION-PanTumor03** study. ESMO 2025;Abstract 3072MO.

Abstract 3072MO

Datopotamab deruxtecan (Dato-DXd) + rilvegostomig in patients with locally advanced or metastatic urothelial cancer: Results from the phase 2 TROPION-PanTumor03 study

Sun Young Rha,[1] Sung Hee Lim,[2] Fangjian Zhou,[3] Kyung Hae Jung,[4] Piotr Wysocki,[5] Katarzyna Drosik-Rutowicz,[6] Jen-Shi Chen,[7] Hiroya Taniguchi,[8] Yuksel Urun,[9] Kenichi Harano,[10] Salvatore Siena,[11] Chia-Chi Lin,[12] Chi-Feng Chung,[13] Rafael Morales-Barrera,[14] Srikanth Gajavelli,[15] Dakshayini Kulkarni,[16] Shamim Gharagoozloo,[17] Yelena Janjigian,[18] Funda Meric-Bernstam[19]

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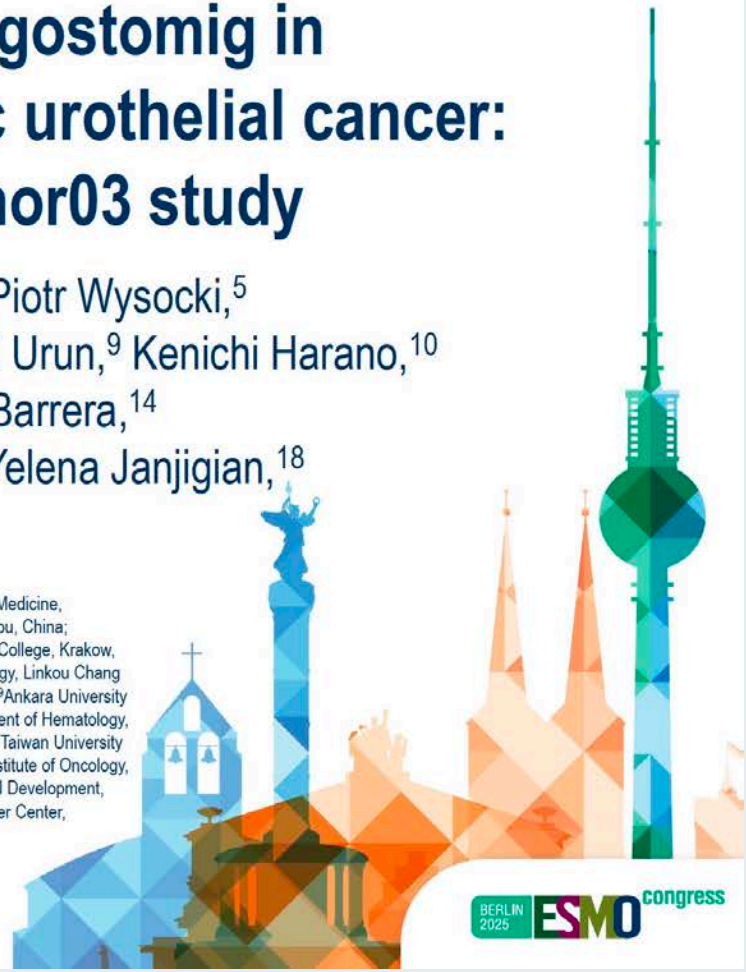
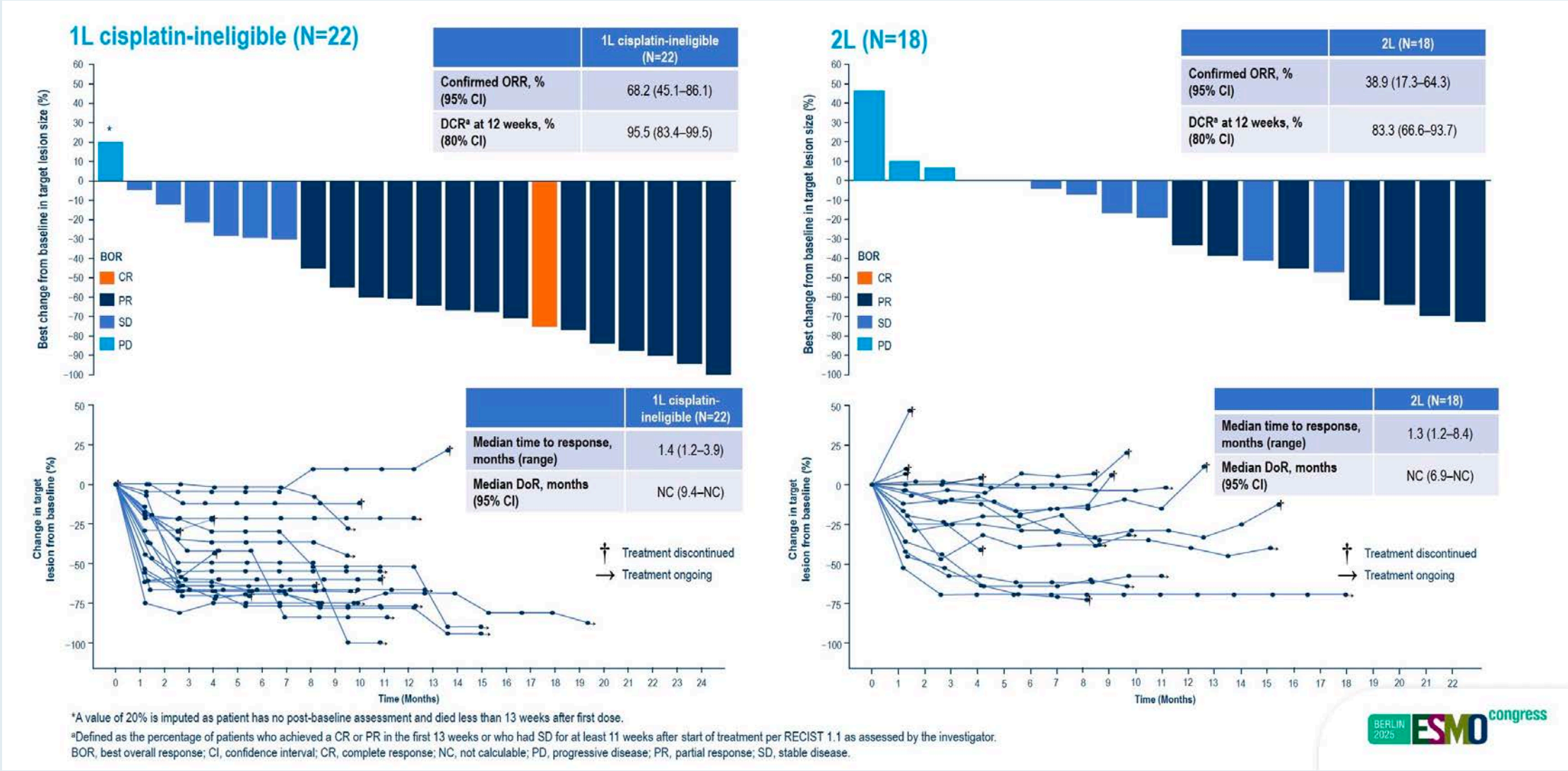


Phase II TROPION-PanTumor03: Investigator-Asssessed Objective Response Rate, Duration of Response



	1L cisplatin-ineligible (N=22)
Confirmed ORR, % (95% CI)	68.2 (45.1–86.1)
DCR[a] at 12 weeks, % (80% CI)	95.5 (83.4–99.5)

	1L cisplatin-ineligible (N=22)
Median time to response, months (range)	1.4 (1.2–3.9)
Median DoR, months (95% CI)	NC (9.4–NC)

	2L (N=18)
Confirmed ORR, % (95% CI)	38.9 (17.3–64.3)
DCR[a] at 12 weeks, % (80% CI)	83.3 (66.6–93.7)

	2L (N=18)
Median time to response, months (range)	1.3 (1.2–8.4)
Median DoR, months (95% CI)	NC (6.9–NC)

*A value of 20% is imputed as patient has no post-baseline assessment and died less than 13 weeks after first dose.

[a]Defined as the percentage of patients who achieved a CR or PR in the first 13 weeks or who had SD for at least 11 weeks after start of treatment per RECIST 1.1 as assessed by the investigator.

BOR, best overall response; CI, confidence interval; CR, complete response; NC, not calculable; PD, progressive disease; PR, partial response; SD, stable disease.

Rha SY et al. ESMO 2025;Abstract 3072MO.

Phase II TROPION-PanTumor03: Overall Safety Summary

	1L cisplatin-ineligible (N=22)	2L (N=18)
TRAEs[a] leading to:		
Dose reduction of any treatment	14 (63.6)	4 (22.2)
Dose interruption of any treatment	10 (45.5)	6 (33.3)
Discontinuation of any treatment	2 (9.1)	3 (16.7)
Death	0	0

	1L cisplatin-ineligible (N=22)		2L (N=18)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
TRAEs[a]	21 (95.5)	4 (18.2)	17 (94.4)	7 (38.9)
Serious TRAEs[a]	0	0	3 (16.7)	3 (16.7)
AESIs for Dato-DXd				
Oral mucositis/stomatitis[b]	9 (40.9)	0	11 (61.1)	1 (5.6)
Ocular surface events[b]	4 (18.2)	0	4 (22.2)	0
Adjudicated drug-related ILD/pneumonitis[b,c]	1 (4.5)	0	2 (11.1)	0
AESIs for rilvegostomig				
Hepatic events[b]	3 (13.6)	0	1 (5.6)	1 (5.6)
Diarrhoea/colitis[b]	1 (4.5)	0	1 (5.6)	0
Dermatitis/rash[b]	11 (50.0)	0	8 (44.4)	0
IRR/hypersensitivity reaction[b]	2 (9.1)	0	0	0

Rha SY et al. ESMO 2025;Abstract 3072MO.

Phase II TROPION-PanTumor03: Authors' Conclusions

- The combination of Dato-DXd + rilvegostomig demonstrated promising efficacy in patients with la/m UC who were cisplatin-ineligible and patients who had progressed on prior platinum-based chemotherapy
- The safety profile of Dato-DXd + rilvegostomig was consistent with previous reports of this combination. No new safety signals were identified
- These results warrant further exploration of Dato-DXd + rilvegostomig in the 1L la/m UC setting

Rha SY et al. ESMO 2025;Abstract 3072MO.

Immunotherapy and BCG for NMIBC

- De Santis M et al. **Durvalumab (D)** in combination with bacillus Calmette-Guérin (BCG) for **BCG-naïve, high-risk non-muscle-invasive bladder cancer (NMIBC): Final analysis** of the **phase III**, open-label, randomised **POTOMAC** trial. ESMO 2025;Abstract LBA108.

Abstract LBA108

BERLIN 2025 ESMO congress

LBA108

Durvalumab (D) in Combination With Bacillus Calmette-Guérin (BCG) for BCG-Naïve, High-Risk Non-Muscle-Invasive Bladder Cancer (NMIBC): Final Analysis of the Phase 3, Open-Label, Randomised POTOMAC Trial

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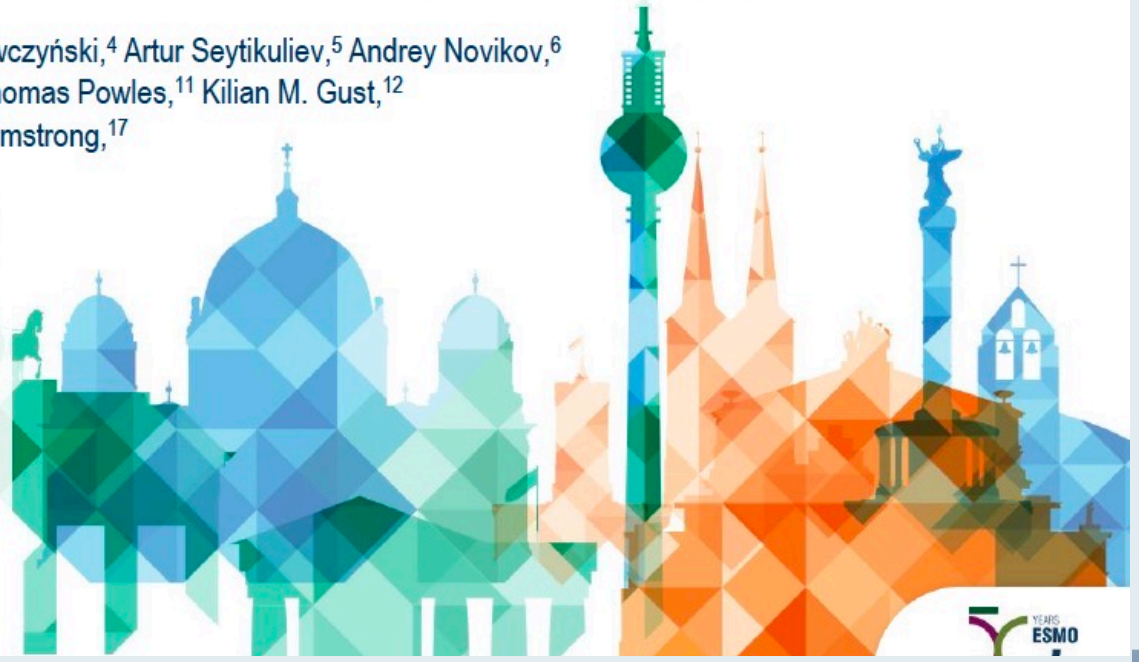
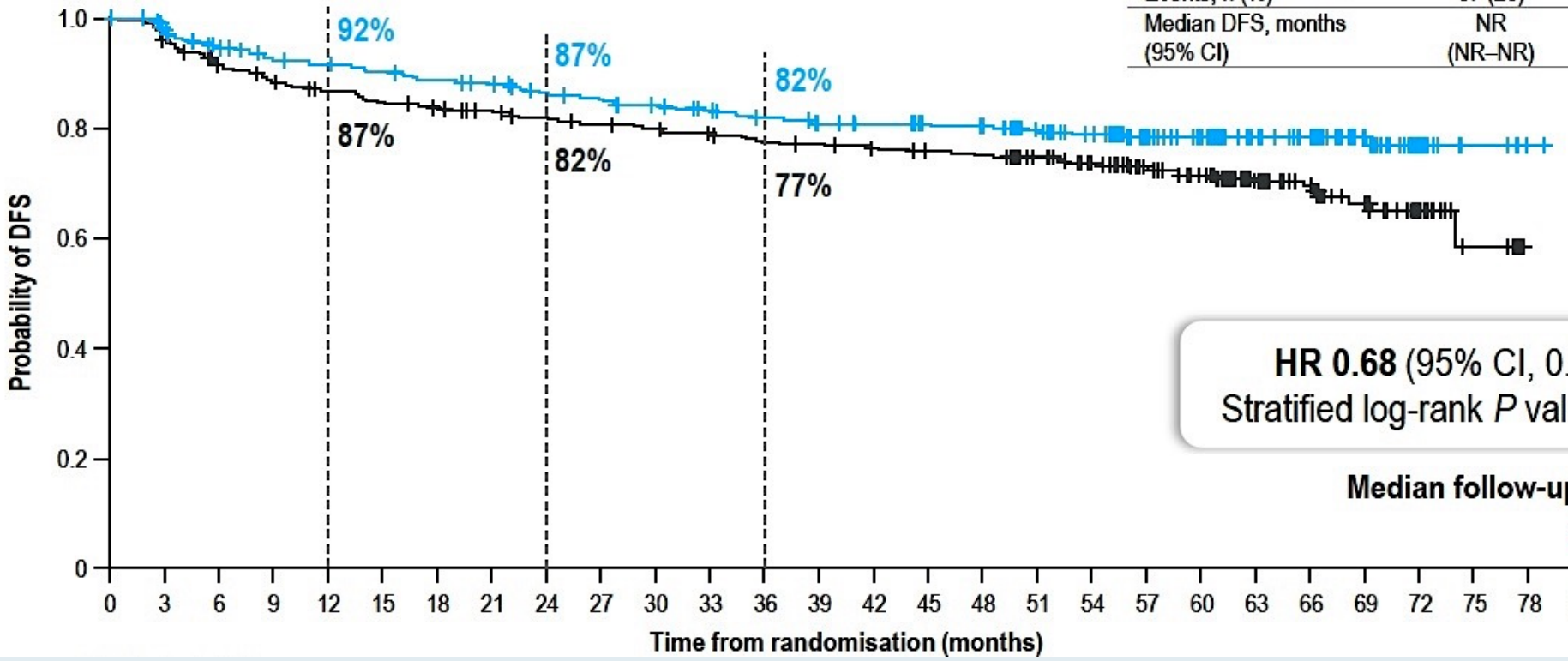


RTP RESEARCH TO PRACTICE

Phase III POTOMAC: Disease-Free Survival (DFS) with Durvalumab/BCG versus BCG

POTOMAC met its primary endpoint with early and sustained DFS benefit

	D+BCG (I+M) N=339	BCG (I+M) N=340
Events, n (%)	67 (20)	98 (29)
Median DFS, months (95% CI)	NR (NR–NR)	NR (74.0–NR)



HR 0.68 (95% CI, 0.50–0.93)
Stratified log-rank *P* value[a] = 0.0154

Median follow-up[b]: 60.7 months

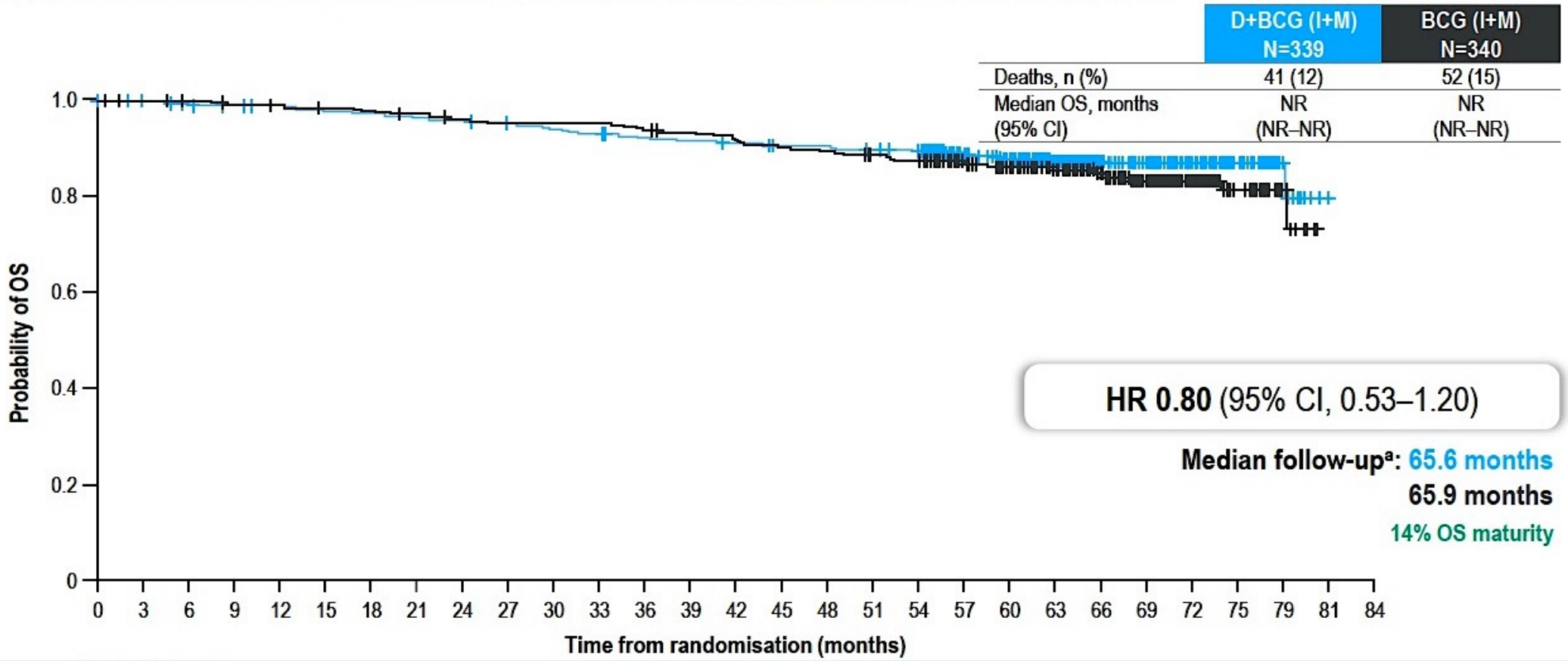
24% DFS maturity

De Santis M et al. ESMO 2025;Abstract LBA108.

RTP RESEARCH TO PRACTICE

Phase III POTOMAC: Overall Survival with Durvalumab/BCG versus BCG

Descriptive analysis showed no detriment to OS with the addition of durvalumab to BCG (I+M) therapy



De Santis M et al. ESMO 2025;Abstract LBA108.

RTP RESEARCH TO PRACTICE

Phase III POTOMAC: Authors' Conclusions

- Durvalumab in combination with BCG (I+M) resulted in a statistically significant and clinically meaningful improvement in DFS vs BCG (I+M) alone in patients with BCG-naïve, high-risk NMIBC at a median of 5 years of follow-up
  - 32% reduction in risk of a DFS event (HR 0.68; 95% CI, 0.50–0.93; *P*=0.0154)
  - Early and sustained DFS benefit with durvalumab (starting at <4 months)
- After a median follow-up of >5 years (14% maturity), a descriptive analysis showed an OS HR of 0.80 (95% CI, 0.53–1.20), demonstrating no detriment to OS with the addition of durvalumab
- Durvalumab plus BCG (I+M) had a tolerable and manageable safety profile that was consistent with the known safety profiles of the individual agents, with no deaths due to treatment-related AEs

Scan the QR code to access:

- Slide presentation
- Plain language summary

POTOMAC supports 1 year of durvalumab in combination with BCG induction and maintenance as a potential new treatment for patients with BCG-naïve, high-risk NMIBC

AE, adverse event; BCG, bacillus Calmette-Guérin; CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; I, induction; M, maintenance; NMIBC, non-muscle-invasive bladder cancer; OS, overall survival.

De Santis M et al. ESMO 2025;Abstract LBA108.

Exciting CME Events You Do Not Want to Miss

A Friday Satellite Symposium Series Preceding the 67th ASH Annual Meeting

Friday, December 5, 2025

Acute Myeloid Leukemia
7:30 AM – 9:30 AM ET

Myelofibrosis and Systemic Mastocytosis
3:15 PM – 5:15 PM ET

Chronic Lymphocytic Leukemia
11:30 AM – 1:30 PM ET

Follicular Lymphoma and Diffuse Large B-Cell Lymphoma
7:00 PM – 9:00 PM ET

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Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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