

Late breaking session on uro-oncology

Medical Oncology

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bmuc.be/bmuc2025



**12th Belgian Multidisciplinary
Meeting on Urological Cancers**

COI

- Advisory board Janssen



OVERALL SURVIVAL



Prostate

Kidney

Bladder

Prostate

TALAPRO-2
OS results

Enzalutamide - Talazoparib in 1L mCRPC

Talapro-2

Key eligibility criteria

- 1L mCRPC
- ECOG 0-1
- Ongoing castration

Stratification factors

- Prior abiraterone (5%)/docetaxel (21%)

Enzalutamide + Talazoparib

1:1 randomization

Enzalutamide + Placebo

Primary endpoint:

- rPFS by BICR

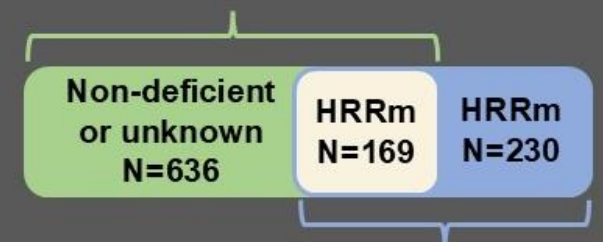
Already met (ASCO 2023)

Key secondary endpoint:

- OS (alpha controlled)

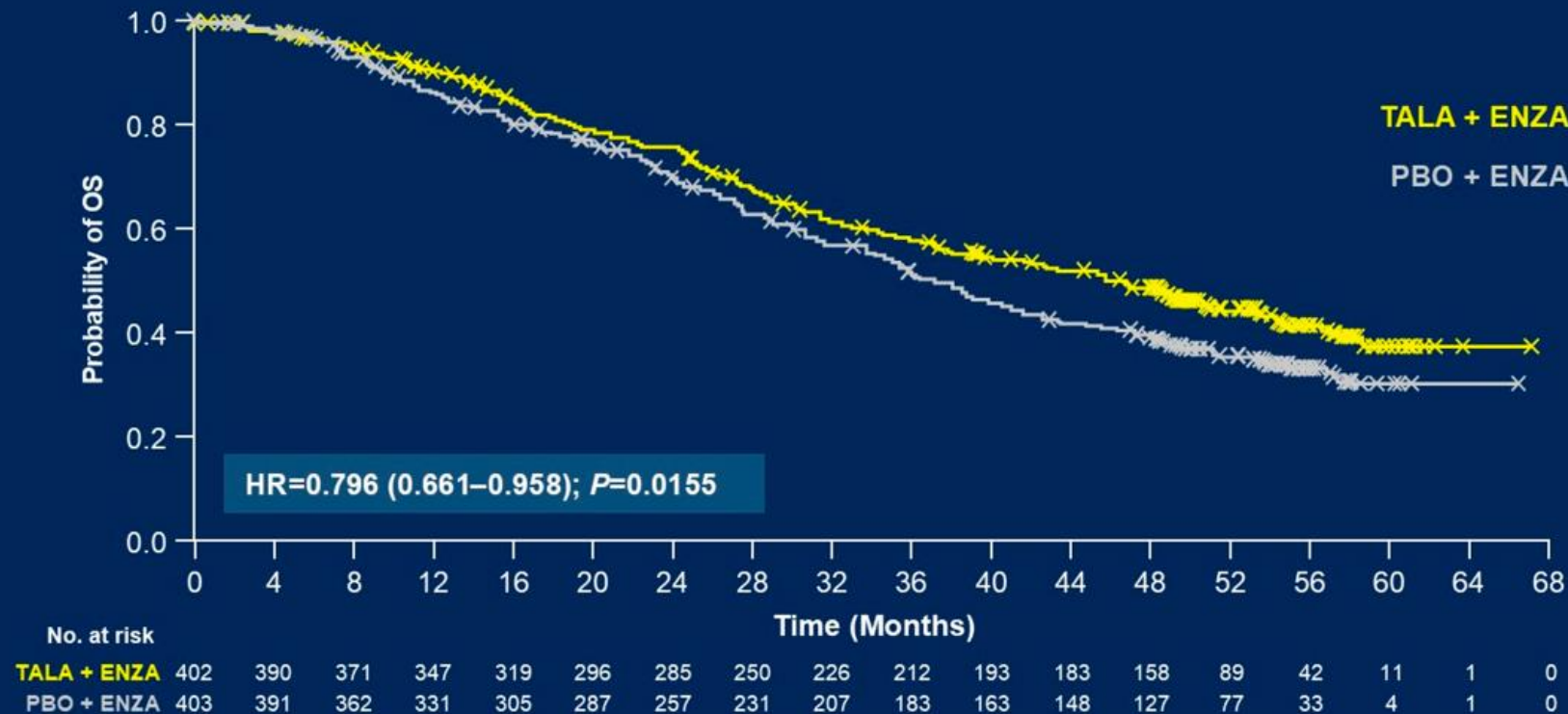
Sequential enrollment in two cohorts:

Unselected (Cohort 1), N=805



Overall Survival (Final Analysis)

20.4% reduction in risk of death, >8 months improvement in median OS



Events/patients

211/402

243/403

Median OS
(95% CI), mo

45.8 (39.4–50.8)

37.0 (34.1–40.4)

8.8 months improvement

Median follow-up for OS was
52.5 months

For statistical significance at the final overall survival analysis, the stratified log-rank 2-sided *P* value needed to be ≤ 0.022 based on a group spending function.

Data cutoff: September 3, 2024.

Sequential enrollment in two cohorts:

Unselected (Cohort 1), N=805

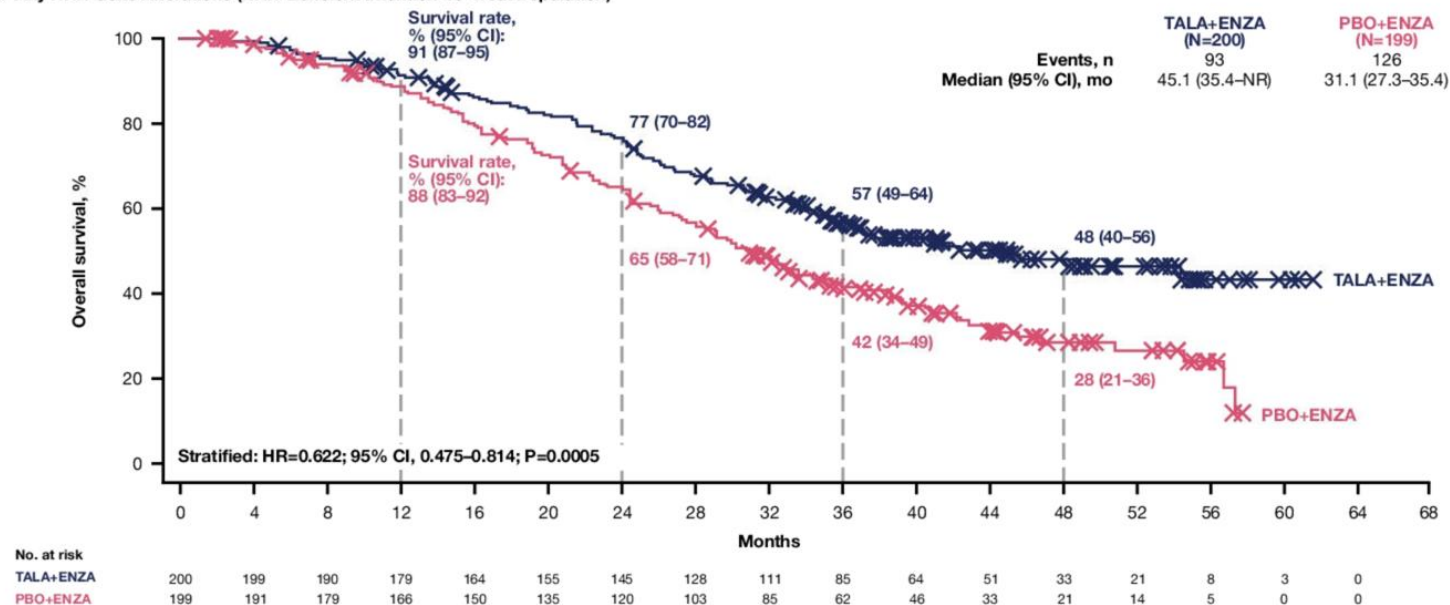
Non-deficient
or unknown
N=636

HRRm
N=169

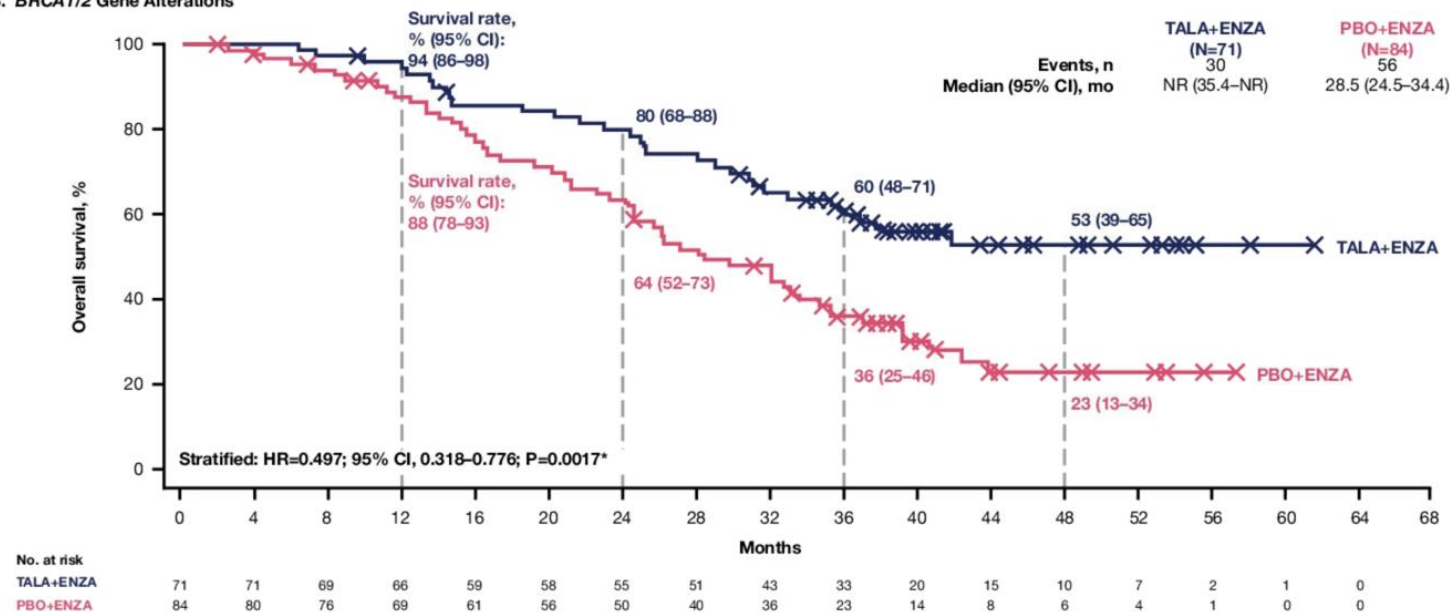
HRRm
N=230

HRRm only (Cohort 2), N=399

A. Any HRR Gene Alterations (HRR-Deficient Intention-To-Treat Population)



B. BRCA1/2 Gene Alterations



Sequential enrollment in two cohorts:

Unselected (Cohort 1), N=805

**Non-deficient
or unknown
N=636**

**HRRm
N=169**

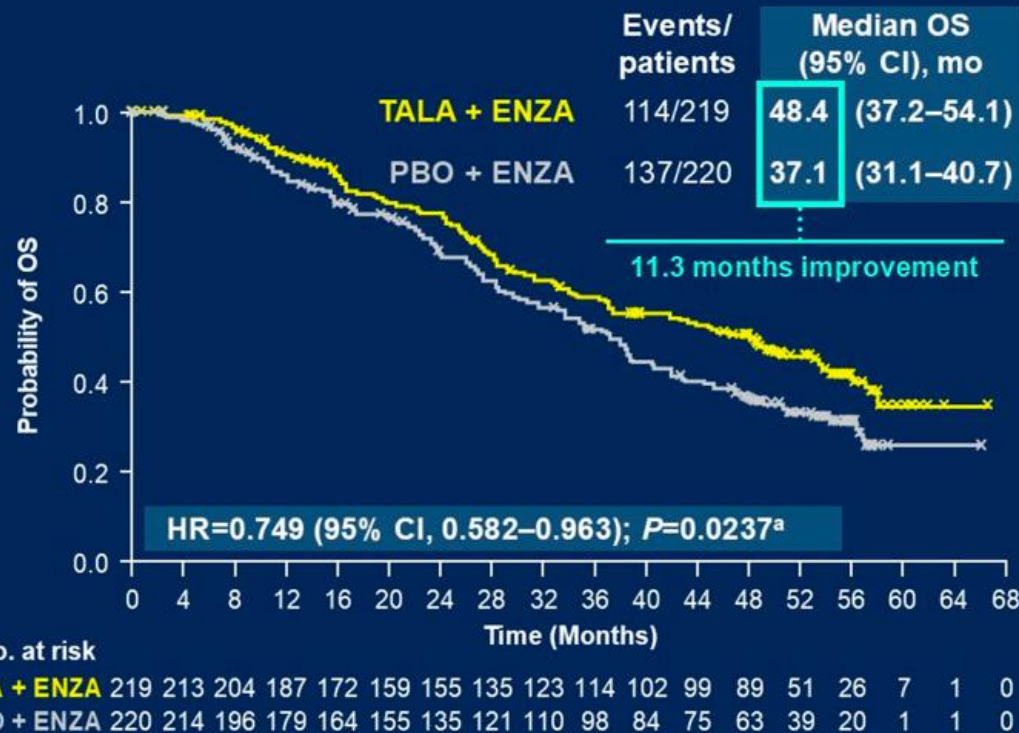
**HRRm
N=230**

HRRm only (Cohort 2), N=399

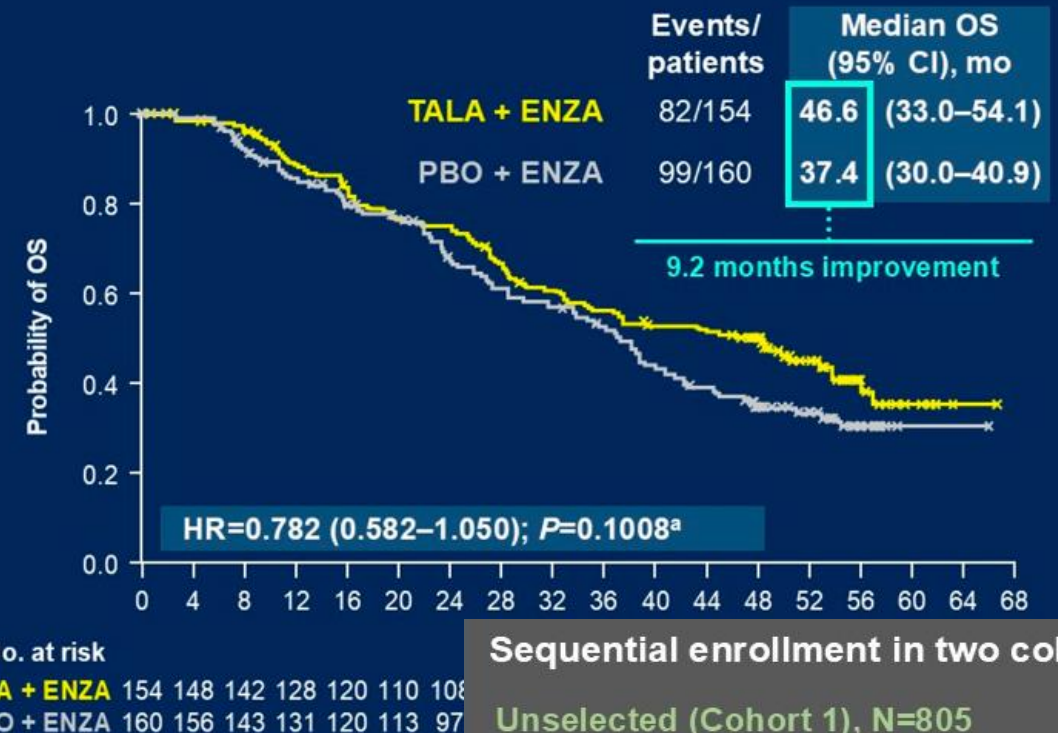
Overall Survival in Subgroups With No Alterations Detected by Both ctDNA and Tumor Tissue

Clinically meaningful reduction in risk of death in patients without *BRCA* or HRR alterations

No *BRCA* alteration detected



No HRR alteration detected



Post hoc analysis employing all available test results of prescreening/screening samples including both prospective and retrospective analysis. Data cutoff: September 3, 2024. ^aReported 2-sided *P* values are nominal and descriptive.

Sequential enrollment in two cohorts:

Unselected (Cohort 1), N=805



HRRm only (Cohort 2), N=399

Most Common All-Cause TEAEs



Data cutoff: September 3, 2024. Figure includes TEAEs reported in ≥20% of patients in either arm.

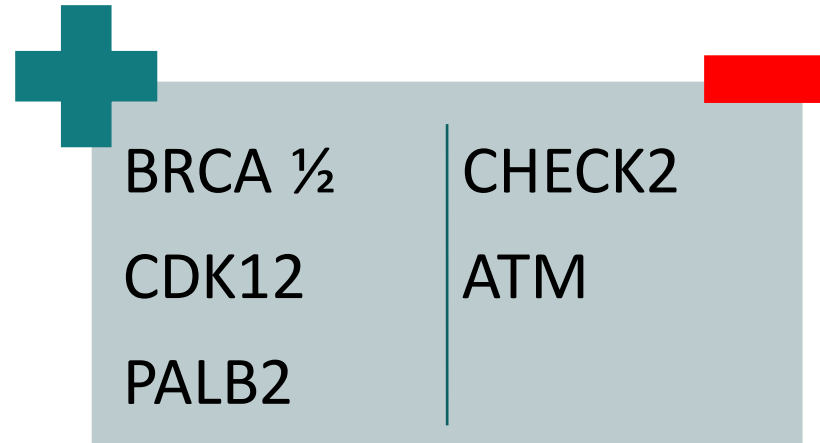
In the talazoparib arm:

- 49.0% had grade 1–2 anemia at baseline
- Most common TEAEs leading to a dose reduction of talazoparib were:
 - Anemia (46.2%)
 - Neutropenia (16.3%)
 - Thrombocytopenia (6.2%)
- Grade 3–4 anemia
 - Reported in 49.0% of patients
 - Median time to onset was 3.3 months
 - 42.2% received an RBC transfusion (median of two transfusions)
- 8.5% discontinued talazoparib due to anemia
- Median duration of treatment with talazoparib was 19.7 months

When to use enzalutamide - talazoparib ?

- Fit patient (ECOG 0-1)
 - No prior ARPI (vanishing population)
 - BRCAm
- Small population in clinical practice

- In HRR mutated:



Fallah et al, JCO 2024

- In non HRR mutated: benefit/risk?

Prostate

Kidney

Bladder

Kidney

COSMIC - 313
OS results

Ipilimumab-nivolumab-cabozantinib in 1L mRCC

COSMIC-313

Key eligibility criteria

- 1L mRCC
- IMDC intermed or poor risk
- KPS>60%
- Clear cell component

Ipilimumab - Nivolumab - Cabozantinib

-> Nivolumab - Cabozantinib

1:1 randomization

Ipilimumab - Nivolumab - Placebo

-> Nivolumab - Placebo

Primary endpoint:

- PFS

Already met (ESMO 2022)

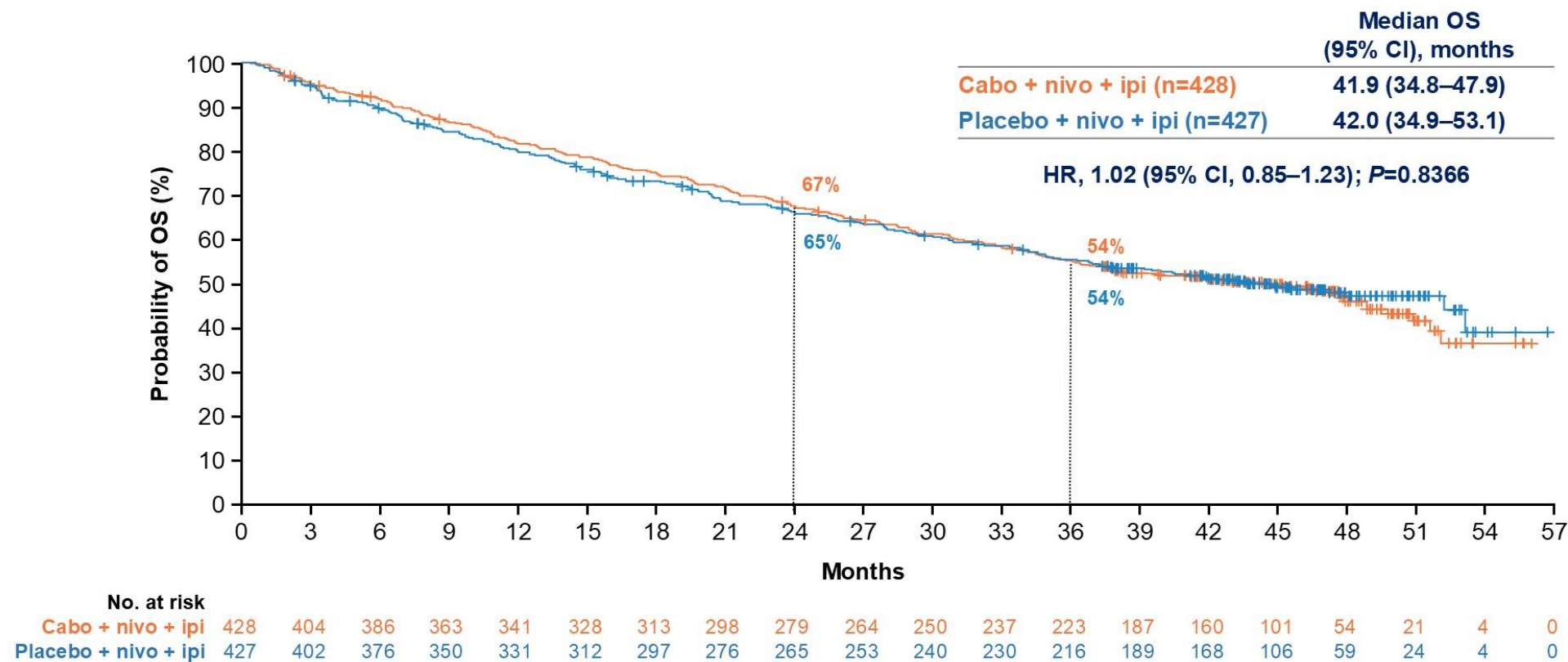
Key secondary endpoint:

- OS



OS in the ITT Population

OS was comparable between arms



Median follow-up of 45.0 months.

COSMIC-313

8

Albiges L et al. ASCO GU 2025

Treatment Exposure and Summary of AEs (Safety Population)

Treatment exposure and dose modifications

	Cabo + nivo + ipi (n=426)	Placebo + nivo + ipi (n=423)
Median duration of exposure of study treatment, months (range)	13.7 (0.2–53.4)	10.3 (0.1–55.3)
Median average daily dose of cabo/placebo, mg (range)	22.4 (3.6–40.0)	35.2 (0.8–40.0)
Median nivo infusions per patient, n (range)	11.0 (1–52)	9.0 (1–48)
1 / 2 / 3 / 4 cycles of ipi administered, %	7 / 22 / 13 / 58	6 / 7 / 13 / 74
Dose modification (any treatment component) due to AE, %	92	76
Treatment-related AE leading to discontinuation of ≥1 component, %	49	26

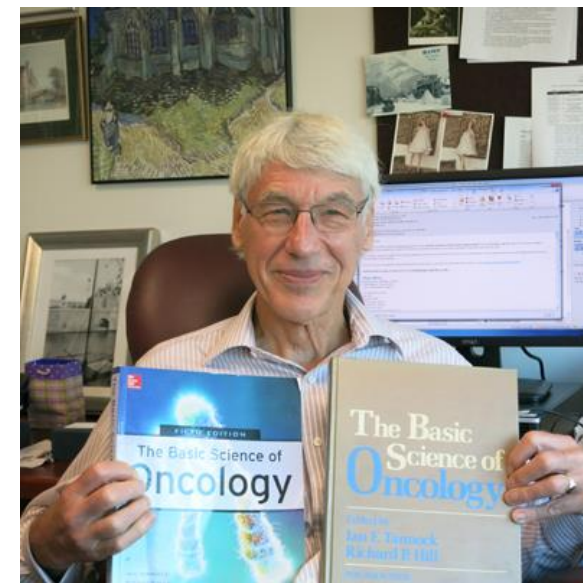
Most common treatment-related AEs (any grade in ≥25% of patients)

	Cabo + nivo + ipi (n=426)		Placebo + nivo + ipi (n=423)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Treatment-related AE, %	99	75	91	43
Alanine aminotransferase increased	46	26	19	6
Aspartate aminotransferase increased	44	19	17	5
Diarrhea	43	5	21	3
Palmar-plantar erythrodysesthesia syndrome	29	4	5	0
Hypothyroidism	26	<1	17	0
Hypertension	25	9	7	2
Pruritus	21	0	26	<1

- Use of systemic immune-modulating medications* for AE was 73.0% in the cabo + nivo + ipi arm and 56.7% in the control arm

*Includes glucocorticoids and other immunosuppressants. AE, adverse event.

Wise words by Ian Tannock



What should we call a therapy that increases
PFS, has no effect on survival, and adds toxicity?

HARMFUL



Prostate

Kidney

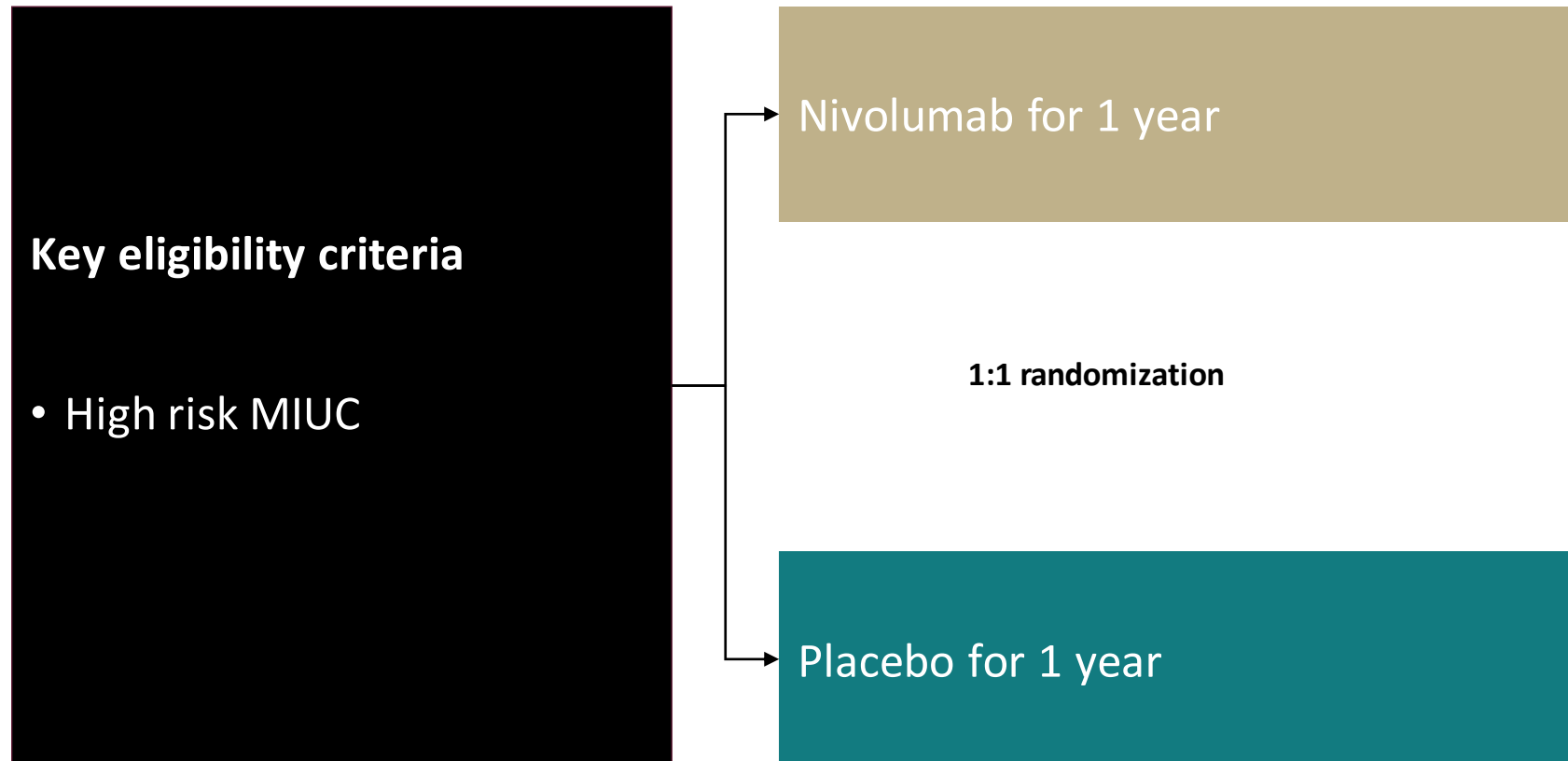
Bladder

Bladder

CHECKMATE - 274
OS results

Adjuvant nivolumab in MIUC

CHECKMATE 274



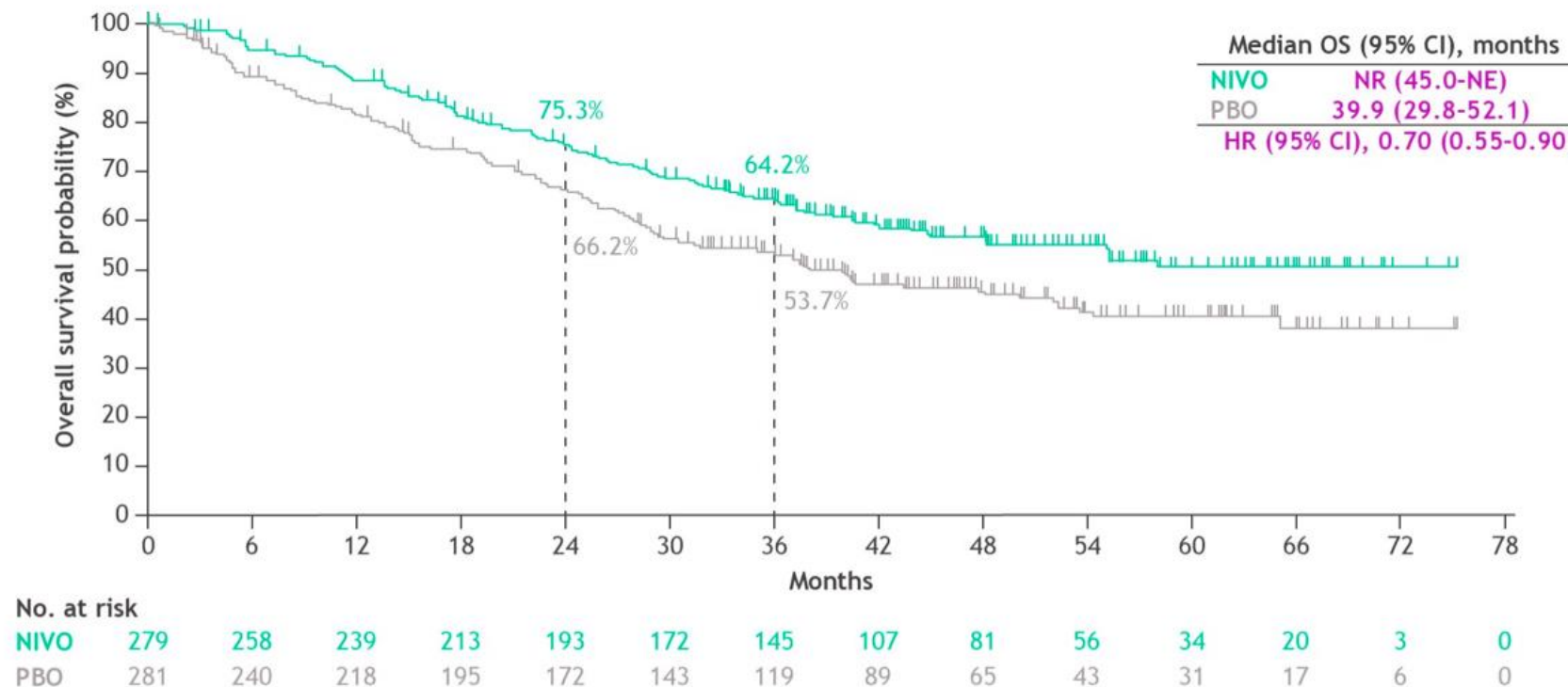
Primary endpoint:

- DFS in ITT and PDL-1 ≥ 1
Already met (ASCO GU 2021)

Key secondary endpoint:

- OS

OS^a: all randomized patients with MIBC



^aInterim OS analysis.
Median follow-up of 36.1 months in the ITT population and 34.5 months in the MIBC population.
Galsky MD, et al. *J Clin Oncol* 2025;43:15-21.

“Follow up for OS is ongoing as the prespecified boundary for significance was not met at the time of these analyses.”

Phase 3 peri-operative IO trials in UCC

	design	OS
NIAGARA	durvalumab, per-operative, open label	✓
AMBASSADOR	pembrolizumab, adjuvant, open label	No trend
CM-274	nivolumab, adjuvant, placebo control	Trend of benefit but NS
IMvigor010	atezolizumab, adjuvant, open label	✗

BUT...

- Open label trials with possibility of informative censoring, e.g. AMBASSADOR pts censored for leaving study in control arm to get approved adjuvant nivolumab
- NIAGARA % post-recurrence IO in control arm unknown
- ...



OVERALL SURVIVAL



In summary

Talazoparib - Enzalutamide gives a OS benefit in unselected and HRRm mCRCP patients. Though most impressive in BRCAm vs HRRm (hodgepodge of different mutations) vs non-HRRm (risk/benefit?).

Triple therapy (nivolumab-ipilimumab-cabozantinib) does not prolong OS and might harm metastatic RCC patients; stick to doublets.

Adjuvant nivolumab is an option in high risk MIUC though with a non-significant OS benefit for now.

