Nancy Ann Dawson, MD
Medstar Georgetown University Hospital

Nancy Ann Dawson, MD, is an internationally recognized genito-urinary cancer expert. She joined the Lombardi Comprehensive Cancer Center in 2007 as Professor of Medicine and Oncology. She is the Director of the Genito-urinary Medical Oncology Program at Medstar Georgetown University Hospital and is the Leader of the Genitourinary Program for the Medstar Lombardi Cancer Center Network.

Dr. Dawson graduated cum laude from Georgetown University School of Medicine in 1979. She completed her residency and fellowship at Walter Reed Army Medical Center where she spent her entire 20 year military career. At the peak of her military career she was Chief of Hematology and Oncology at Walter Reed Army Medical Center and the Consultant to the Surgeon General of the Army for Hematology and Oncology. She retired as a Colonel in 1999. Dr. Dawson next served as Director of Clinical Research and Director of Genito-urinary oncology at the Greenebaum Comprehensive Cancer Center in Baltimore, Maryland from 1999 to 2007.

Dr. Dawson was the first woman to specialize in prostate cancer in the United States. Over her many year career, Dr. Dawson has spearheaded phase I, II and III trials in bladder, kidney and prostate cancer. Her work has contributed significantly to the standard of care for urologic cancers over the years, earning her many awards and recognitions. Chief among them is the Legion of Merit, the highest non-battlefield recognition awarded by the United States Armed Forces, for her exceptional performance and outstanding service in the field of prostate cancer.

Practice Changing Approaches to GU Malignancies. ASCO 2023

Nancy A. Dawson, M.D.

Director, GU Medical Oncology Program

Lombardi Comprehensive Cancer Center

Medstar Georgetown University Hospital

Washington, DC

Primary RPLND in Seminoma stage IIA-IIB ≤3cm

Combined preliminary results SWENOTECA X and COTRIMS

Tandstad T, Kjellman A, Almås B, Bergdahl AG, Cohn-Cedermark GE, Gerdtsson A, Glimelius I, Halvorsen DL, Haugnes HS, Hedlund A, Hellstrøm M, Karlsdottir A, Larsen SM, Negaard HFS, Paffenholz P, Pfister D, Seelemeyer F, Stahl O, Thor A, Wahlquist R, Heidenreich A

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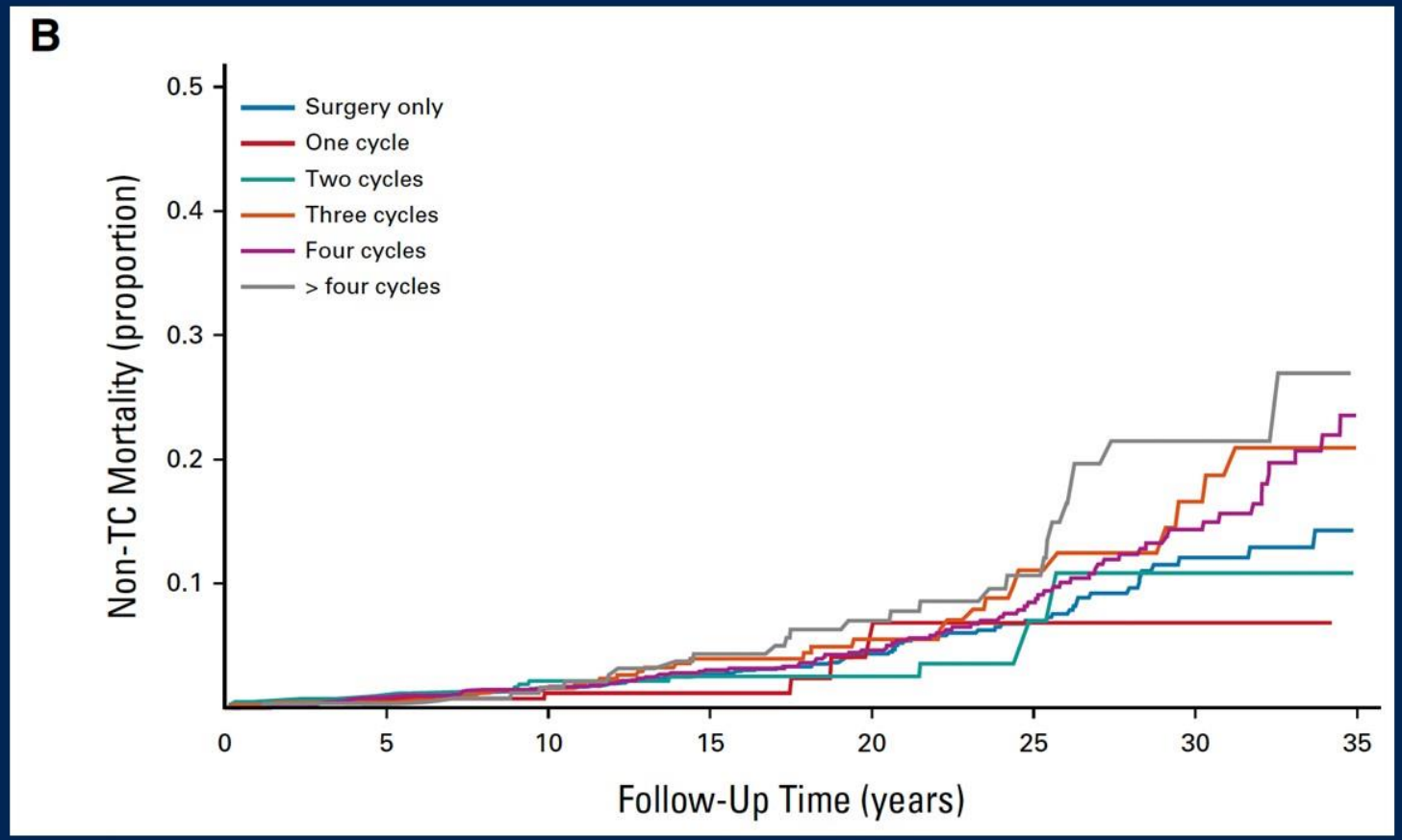
Current treatment

TABLE 5. HRs for Total Non-TC Mortality and Non-TC SC Mortality According to Follow-Up

Variable	All Non-TC Mortality	
	Age-Adjusted HR (95% CI)	Multivariable HR (95% CI)
Treatment groups		
Surgery	1 (ref)	1 (ref)
PBCT	**1.42 (1.05 to 1.91)**	**1.42 (1.05 to 1.91)**
RT	**1.61 (1.23 to 2.12)**	**1.94 (1.39 to 2.73)**
PBCT plus RT	**2.79 (1.89 to 4.13)**	**3.27 (2.14 to 5.00)**
Cisplatin-based chemotherapy cycles[a]		
Surgery	1 (ref)	1 (ref)
1	0.79 (0.25 to 2.53)	0.78 (0.25 to 2.49)
2	0.43 (0.16 to 1.19)	0.43 (0.15 to 1.17)
3	1.47 (0.91 to 2.39)	1.43 (0.88 to 2.33)
4	**1.41 (1.01 to 1.99)**	**1.43 (1.02 to 2.01)**
> 4	**2.04 (1.25 to 3.35)**	**1.98 (1.21 to 3.25)**
Carboplatin, adjuvant	1.21 (0.38 to 3.86)	1.39 (0.43 to 4.52)
RT field		
Surgery	1 (ref)	1 (ref)
L-field	**1.60 (1.21 to 2.12)**	**1.94 (1.38 to 2.73)**
Paraaortic	1.48 (0.89 to 2.44)	1.77 (1.03 to 3.03)
Supra- and infradiaphragmatic	**5.07 (2.04 to 12.63)**	**6.17 (2.42 to 15.70)**
RT dose for first abdominal RT field, Gy		
Surgery	1 (ref)	1 (ref)
1-20	1.75 (0.24 to 12.69)	2.05 (0.28 to 14.97)
20-29	1.31 (0.87 to 1.98)	1.55 (0.98 to 2.44)
30-39	**1.68 (1.26 to 2.23)**	**2.00 (1.41 to 2.85)**
≥ 40	**1.54 (1.04 to 2.28)**	**1.85 (1.18 to 2.88)**
Histology		
Nonseminoma	1 (ref)	1 (ref)
Seminoma	**1.23 (1.02 to 1.50)**	0.93 (0.71 to 1.23)



Hellesnes et al. JCO 2021

PRESENTED BY: Torgrim Tandstad

Why primary RPLND

- No increased risk of late toxicity affecting mortality
- Many smaller series and new trials, e.g., SEMS and PRIMETEST
- COTRIMS started in 2018

Results I: SWENOTECA / COTRIMS

- Five centers
- 94 patients (66 SWENOTECA, 28 Cologne)
  - 58 (62%) Primary CS I
  - 36 (38%) CS IIA/B
- Median age at RPLND 41.8 years (21-79)
- Median follow-up since RPLND 21 months (range 4-61)

Results II: SWENOTECA / COTRIMS

- 26 robotic (28%)
- 10 patients with Clavian-Dindo > 2
- 23 patients received adjuvant chemotherapy

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Abstract 5006: Long term follow-up analysis of plasma miR371 expression to detect early relapse in patients with clinical stage I testicular germ cell tumors on surveillance.

Dr. Lucia Nappi MD, PhD

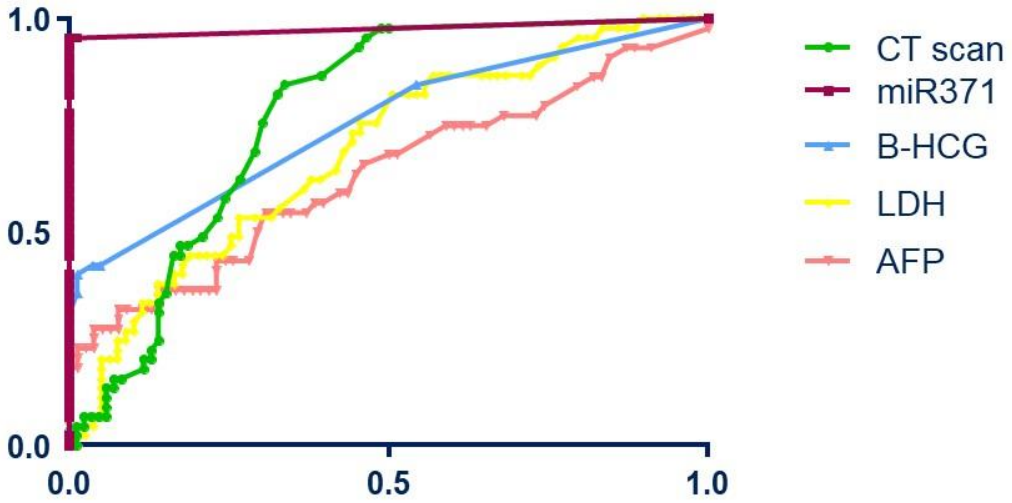
Assistant Professor - University of British Columbia, Department of Urologic Sciences

Medical Oncologist - British Columbia Cancer – Vancouver Centre

Senior Research Scientist - Vancouver Prostate Centre, Vancouver, BC, Canada

@LuciaNappi4

Background: miR371 detects viable GCM across the spectrum of GCT stages



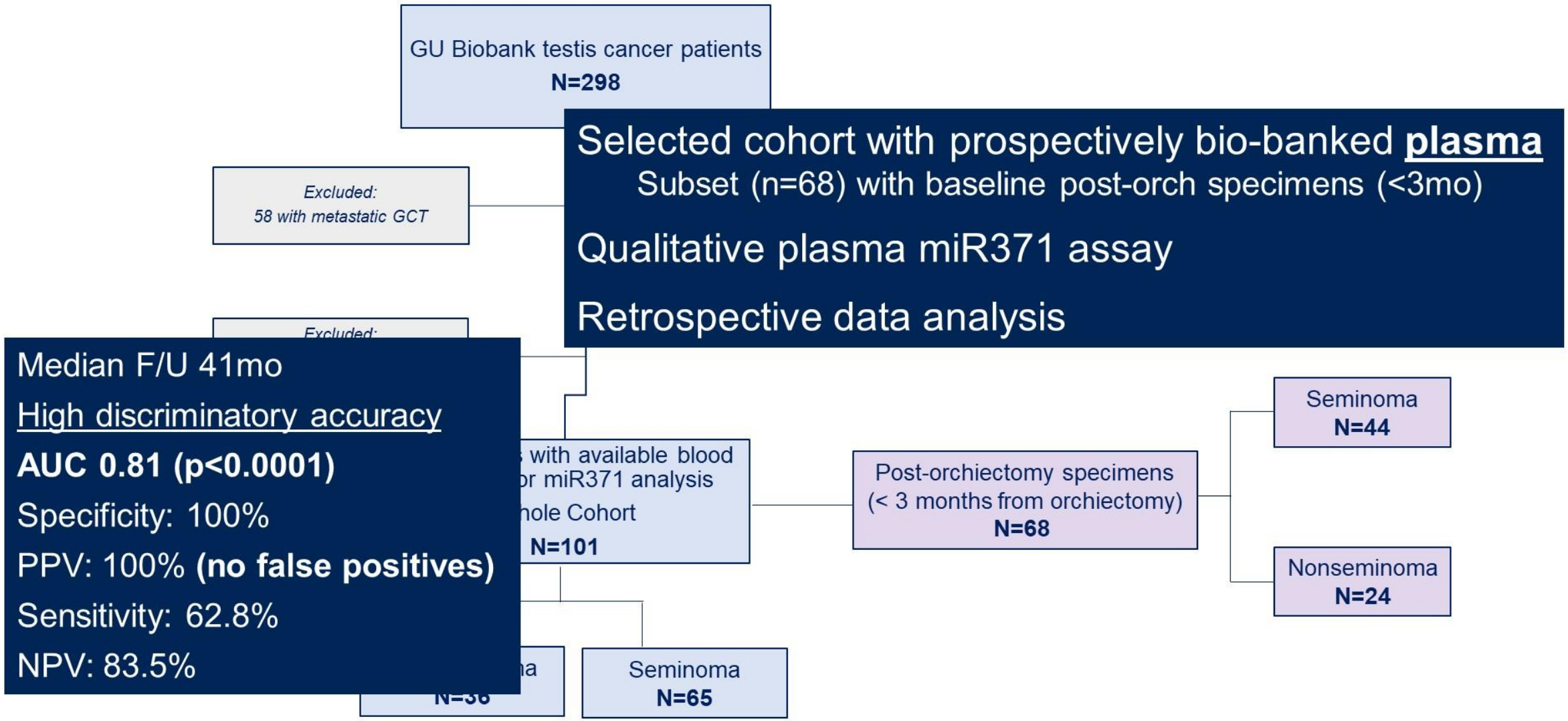
AUC = 0.96
Sensitivity = 96%
Specificity = 100%
Positive predictive value = 100%
Negative predictive value = 98%

What about in early stage disease and particularly in CSI?

miR371 positive	44 True Positives	0 False Positives	44 Positive Tests
miR371 negative	2 False Negatives	86 True Negatives	88 Negative Tests
Total samples	46 confirmed viable GCTs	86 with no confirmed viable GCTs	132

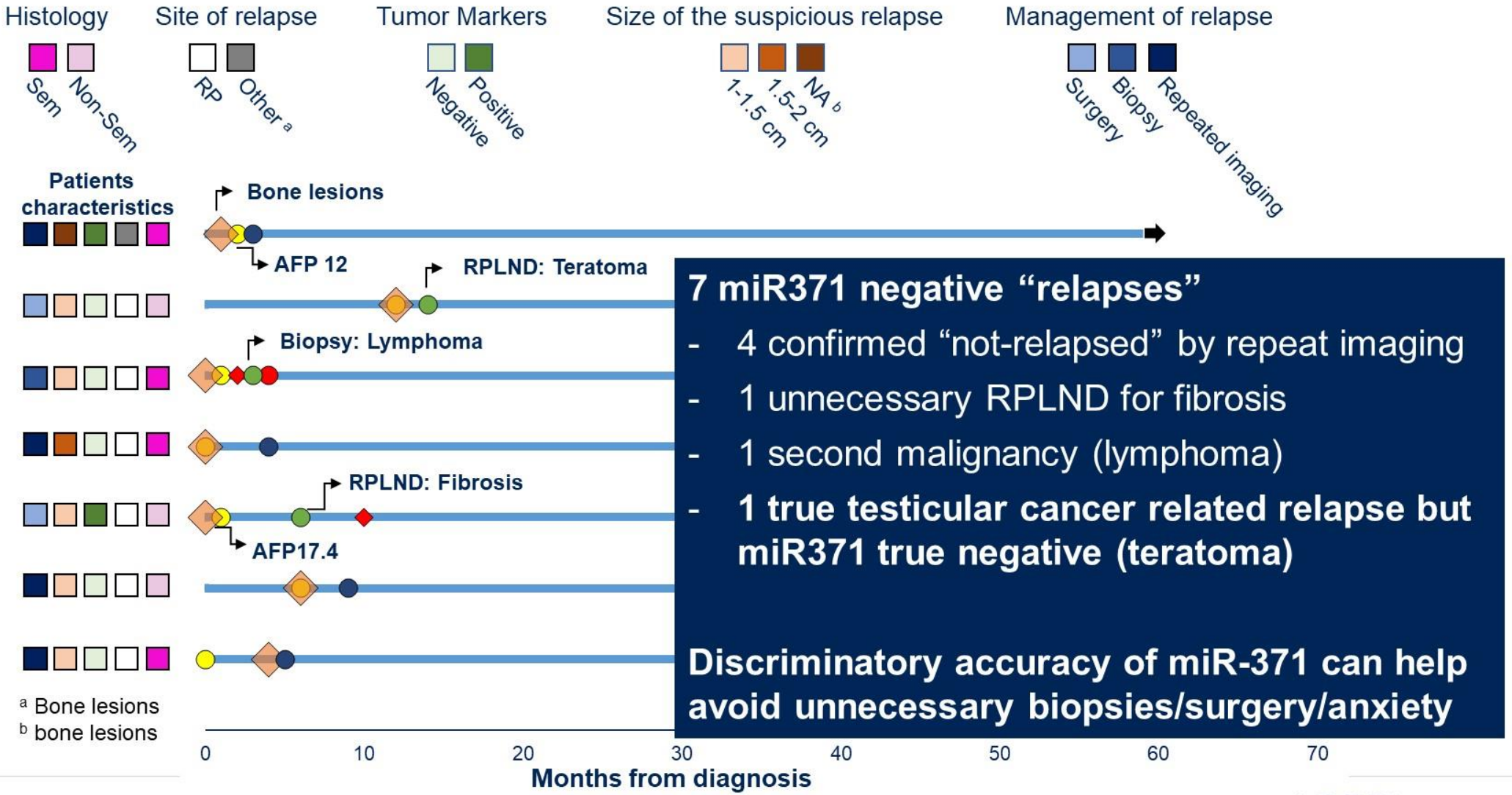
Nappi et al, JCO 2019

Results – Study Population



PRESENTED BY: Lucia Nappi, MD, PhD

Results – miR371 true negative unrelapsed patients

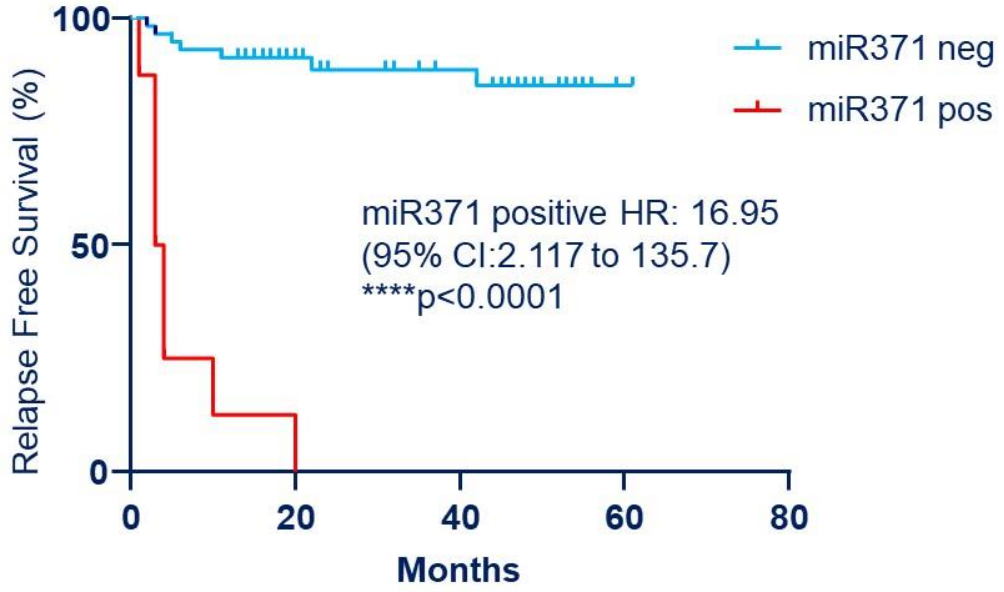


7 miR371 negative "relapses"

- 4 confirmed "not-relapsed" by repeat imaging
- 1 unnecessary RPLND for fibrosis
- 1 second malignancy (lymphoma)
- **1 true testicular cancer related relapse but miR371 true negative (teratoma)**

Discriminatory accuracy of miR-371 can help avoid unnecessary biopsies/surgery/anxiety

Results – RFS in the post-orchiectomy cohort



miR371 negative	60	38	25	1	0
miR371 positive	8	1	0	0	0

Status	N	Median RFS (months)
miR371 negative	60	Not Reached
miR371 positive	8	3.5

Post-orch (n=68)
- Median F/U 32mo

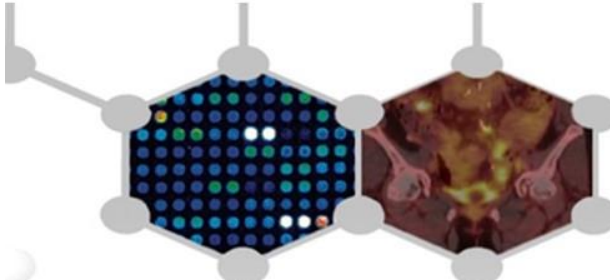
miR371 positive (n=8)
- 8/8 relapses
- All within 2y
- No false positives

miR371 negative (n=60)
- 7/60 relapses (12%)
- mostly early

Predict ~50% of relapses
- AUC 0.76* (p=0.0017)

Practice Changers in GCTs

- Primary RPLND preformed by experienced centers is a new SOC option for Seminoma stage IIA-IIB
- miRNA 371 has high specificity, PPV and NPV in germ cell malignancies. Currently being validated in a prospective observational cohort study, SWOG 1823



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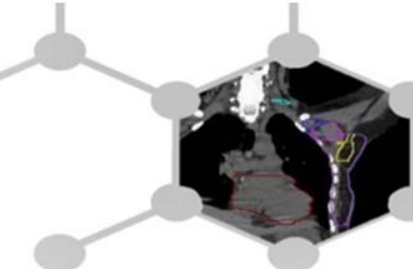
Advancing Research. Improving Lives.™



Development and validation of an AI-derived digital pathology-based biomarker to predict benefit of long-term androgen deprivation therapy with radiotherapy in men with localized high-risk prostate cancer across multiple phase III NRG/RTOG trials

Andrew J. Armstrong, Vinnie Y.T. Liu, Ramprasaath R. Selvaraju, Emmalyn Chen, Jeffry P. Simko, Sandy Devries, A. Oliver Sartor, Howard M. Sandler, Osama Mohamad, Andre Esteva, Phuoc T. Tran, Daniel E. Spratt, John H. Carson, Christopher Peters, Elizabeth Gore, Steve P. Lee, Jedidiah M. Monsoon, Joseph P. Rodgers, Felix Y. Feng, Paul L. Nguyen

2023 ASCO – June 4th, 2023

Duke Cancer Institute

@AarmstrongDuke
@DukeCancer
@DrPaulNguyen
@NRGOnc

ArteraAI

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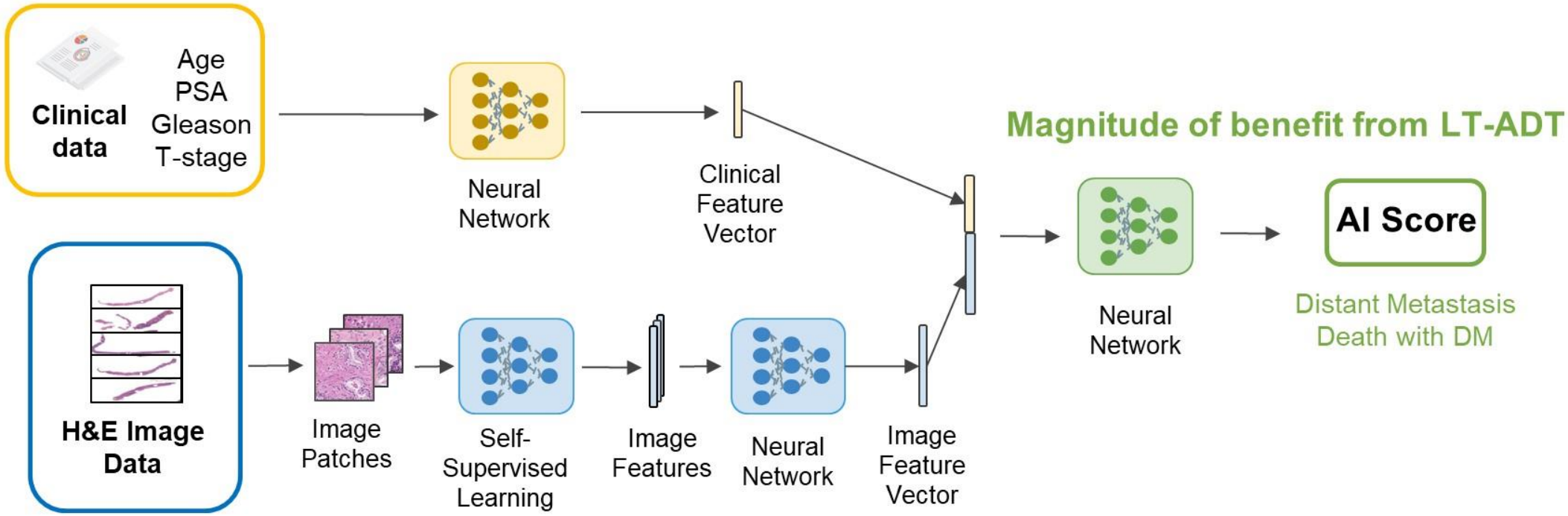
NCI National Clinical Trials Network
a National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

ArteraAI Multimodal Artificial Intelligence (MMAI) Architecture



AI score = magnitude of benefit (predictive biomarker)
(risk of DM with RT + ST-ADT vs RT + LT-ADT)

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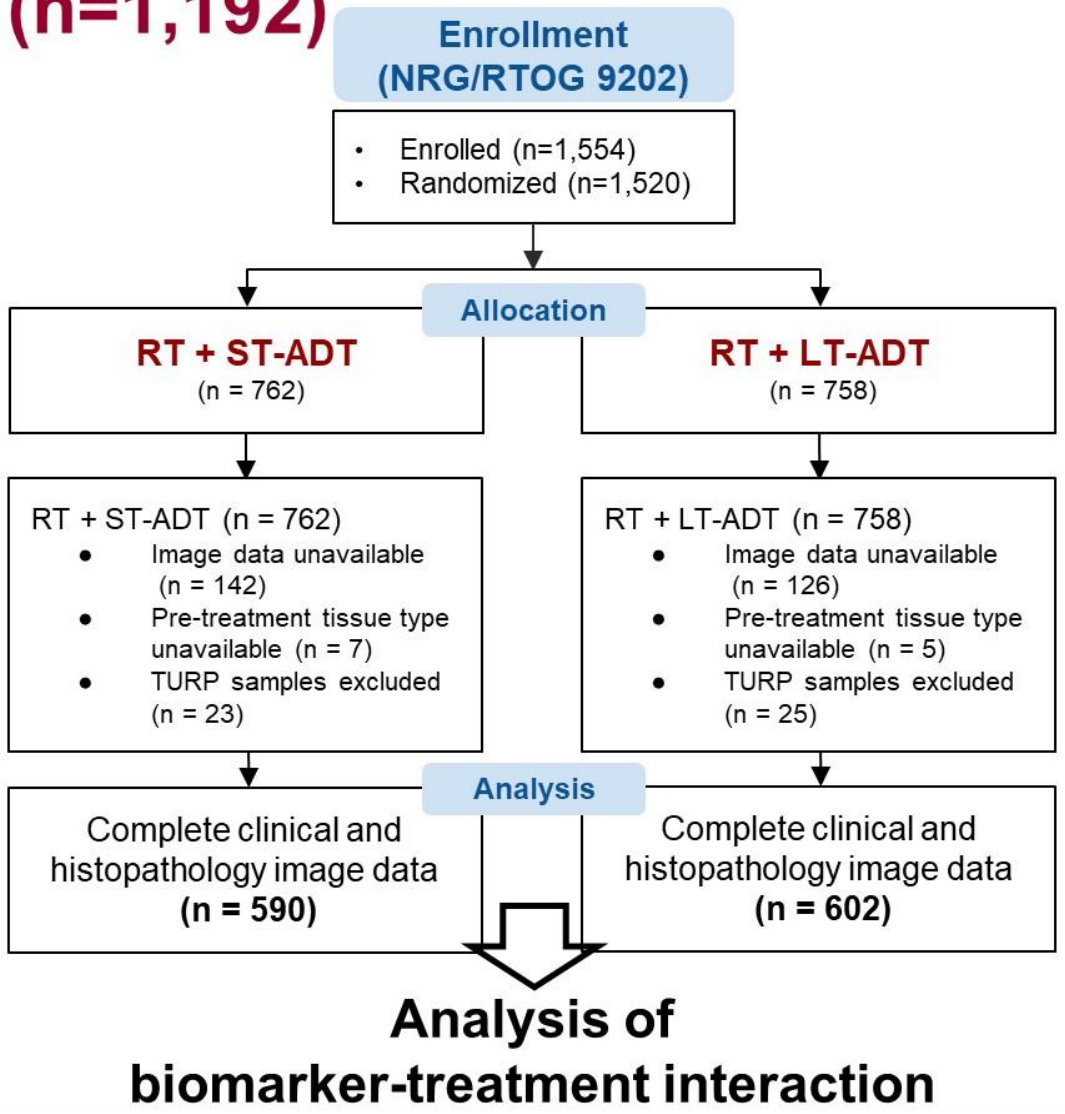
Validation of LT-ADT Predictive Biomarker in Phase III NRG/RTOG 9202 (n=1,192)

- **Patient population:** High-risk (80%)
- **Treatment arms:** ST-ADT (4 months) and LT-ADT (28 months) with RT (prostate/pelvis)
- **Positive trial**: demonstrated benefits of LT-ADT in reducing DFS, DM, PCSM, and improving OS vs. ST-ADT

- **Endpoints:** DM (Primary) and Death with DM (Secondary) to avoid confounding by non-PC related mortality events (>50%)



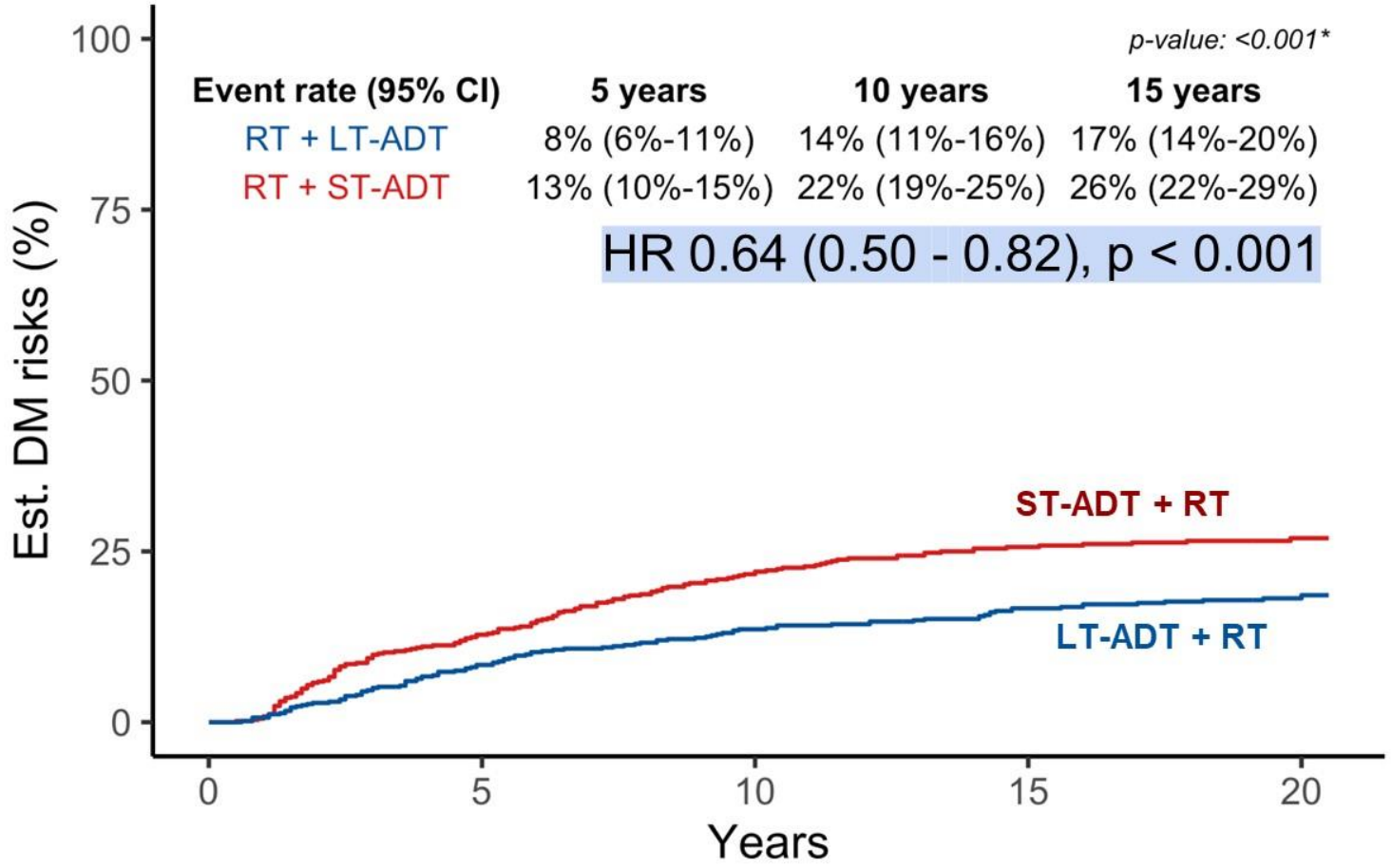
NRG ONCOLOGY™

Lawton CAF et al IJROBP 2017; Horwitz EM et al JCO 2008

Courtesy of Spratt et al. ASCO GU 2022 (modified)

Results in Overall Cohort NRG/RTOG 9202

Treatment benefit from addition of LT-ADT observed



Similar results to 20-year 9202 follow-up overall
Lawton CAF et al IJROBP 2017

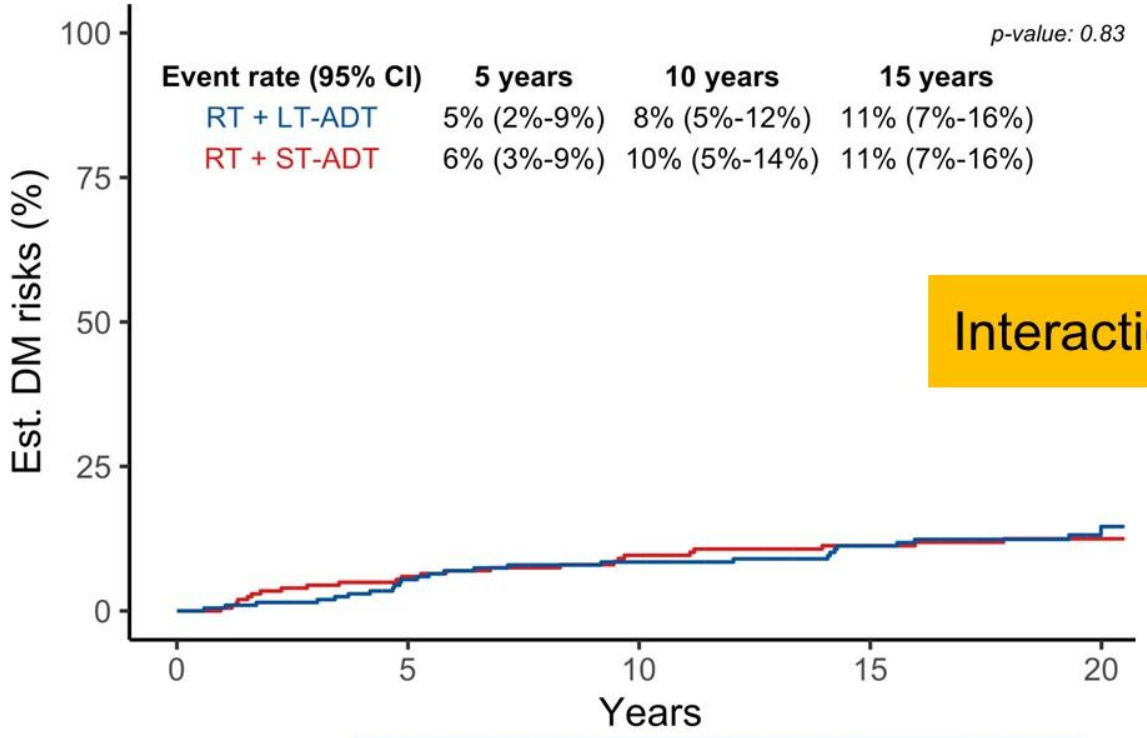
NRG ONCOLOGY™ Similar results observed for Death with DM endpoint: HR 0.64 (0.50 - 0.83), p < 0.001

Primary Endpoint Results (DM)

~⅓ of men with high-risk prostate cancer could safely avoid LT-ADT

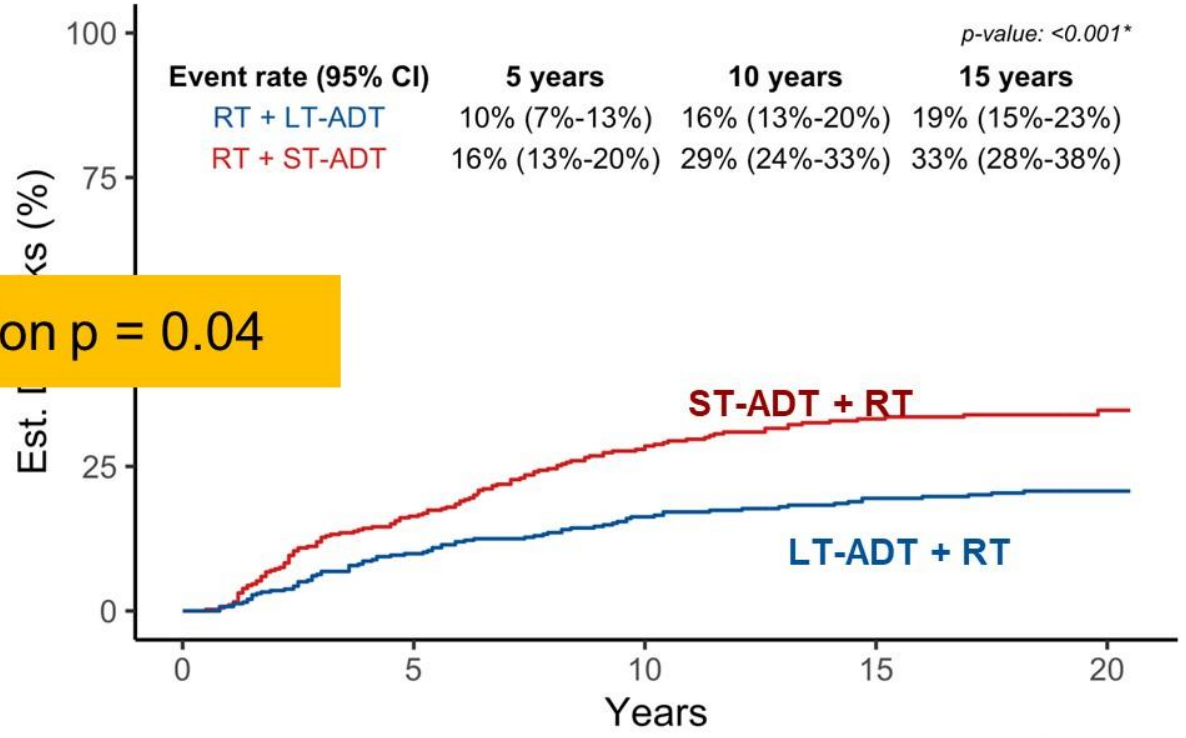
254 men (21%) developed DM, and risk differed by AI Biomarker groups AND treatment

Biomarker Negative Group (n = 407)



HR 1.06 (0.61 - 1.84), p = 0.84

Biomarker Positive Group (n = 785)



HR 0.55 (0.41 - 0.73), p < 0.001

Interaction p = 0.04

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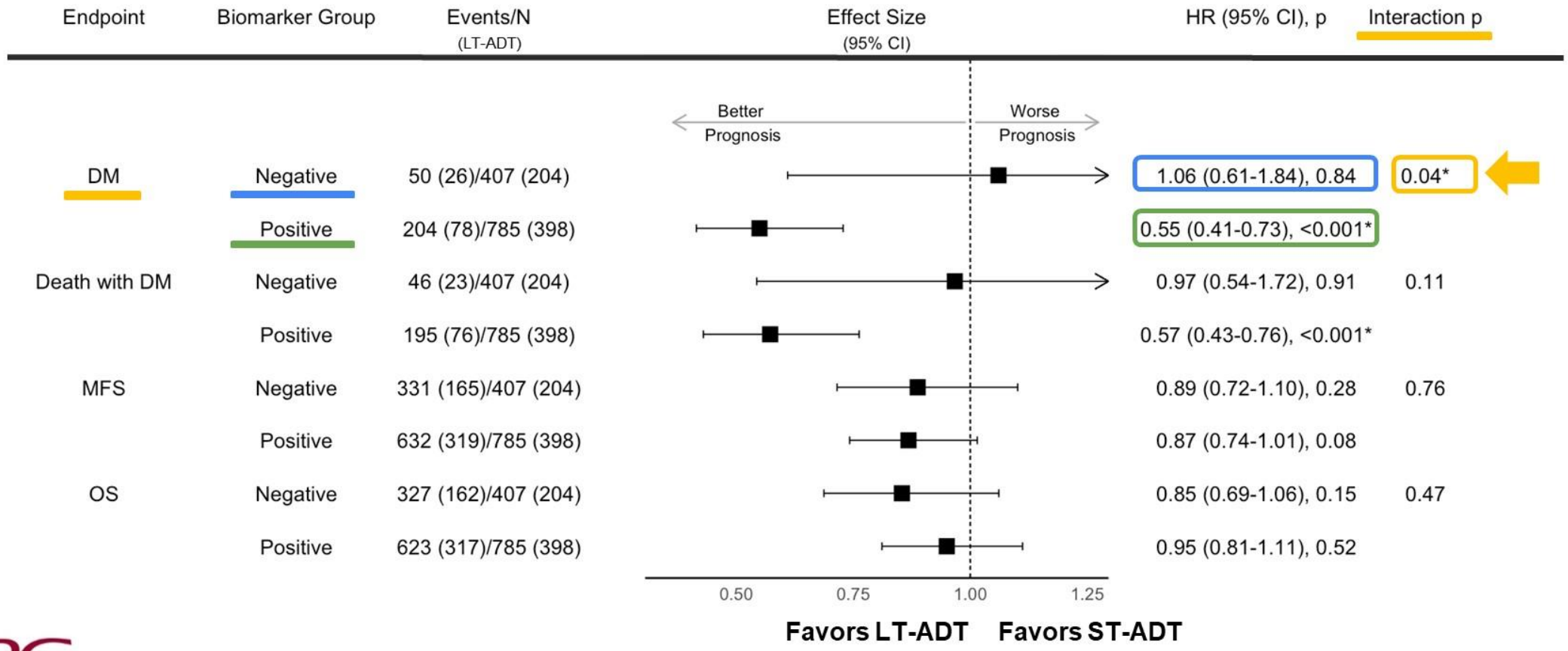
Results

MMAI predictive model successfully identified differential benefit from the addition of LT-ADT to RT



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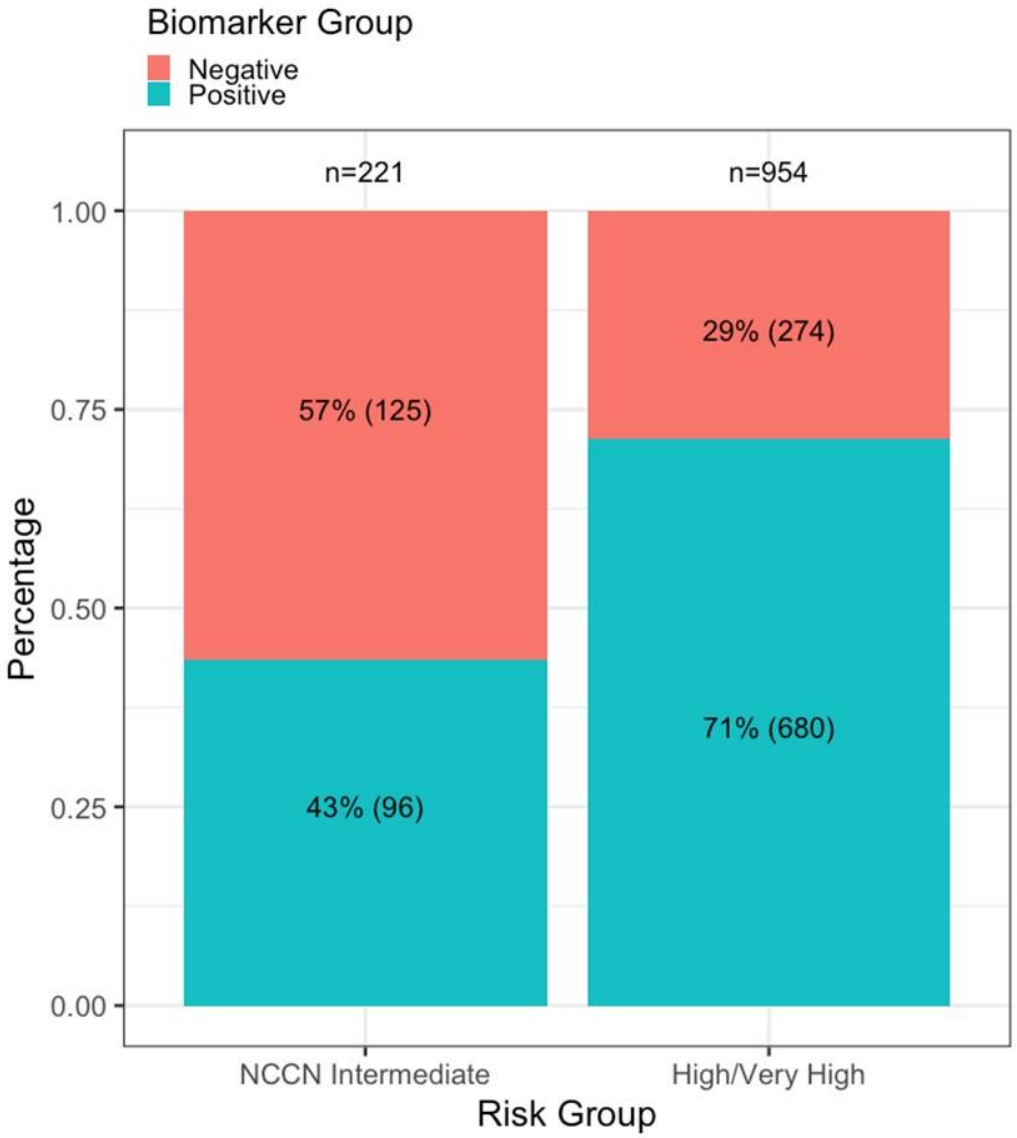
Clinical Impact



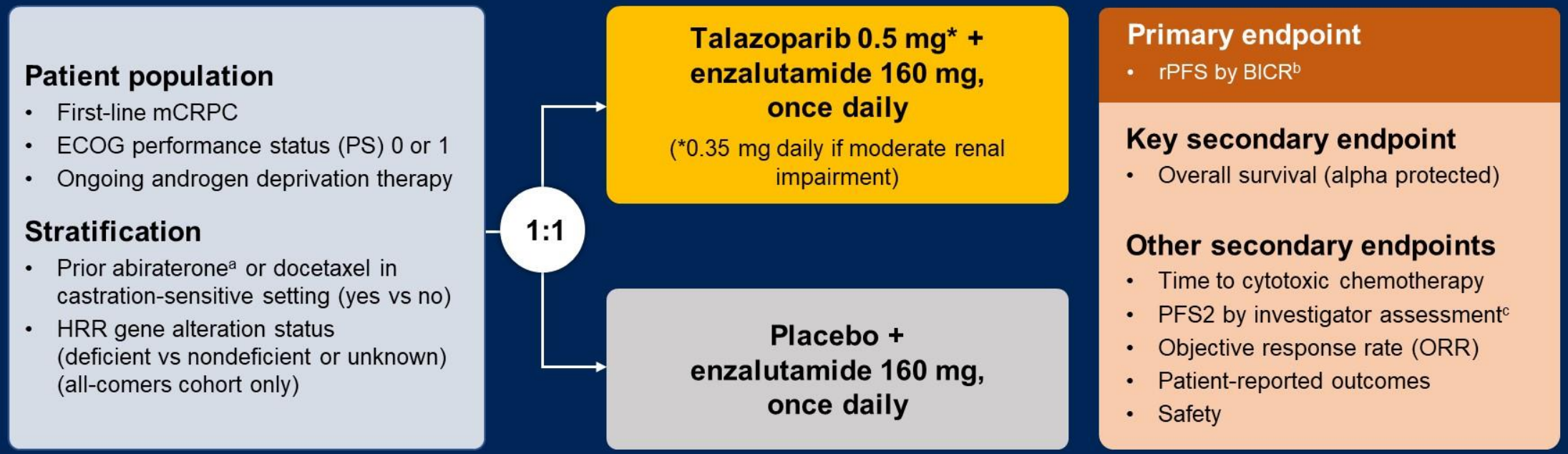
29% of patients with at least one NCCN High/Very High risk feature would benefit from treatment shortening (ST-ADT), given lack of benefits with LT-ADT on DM and Death with DM

But also…

43% of NCCN Intermediate Risk patients may benefit from treatment intensification (LT-ADT) to reduce DM and Death with DM. Consistent with MARCAP meta-analysis

Kishan AU et al Lancet Onc 2022

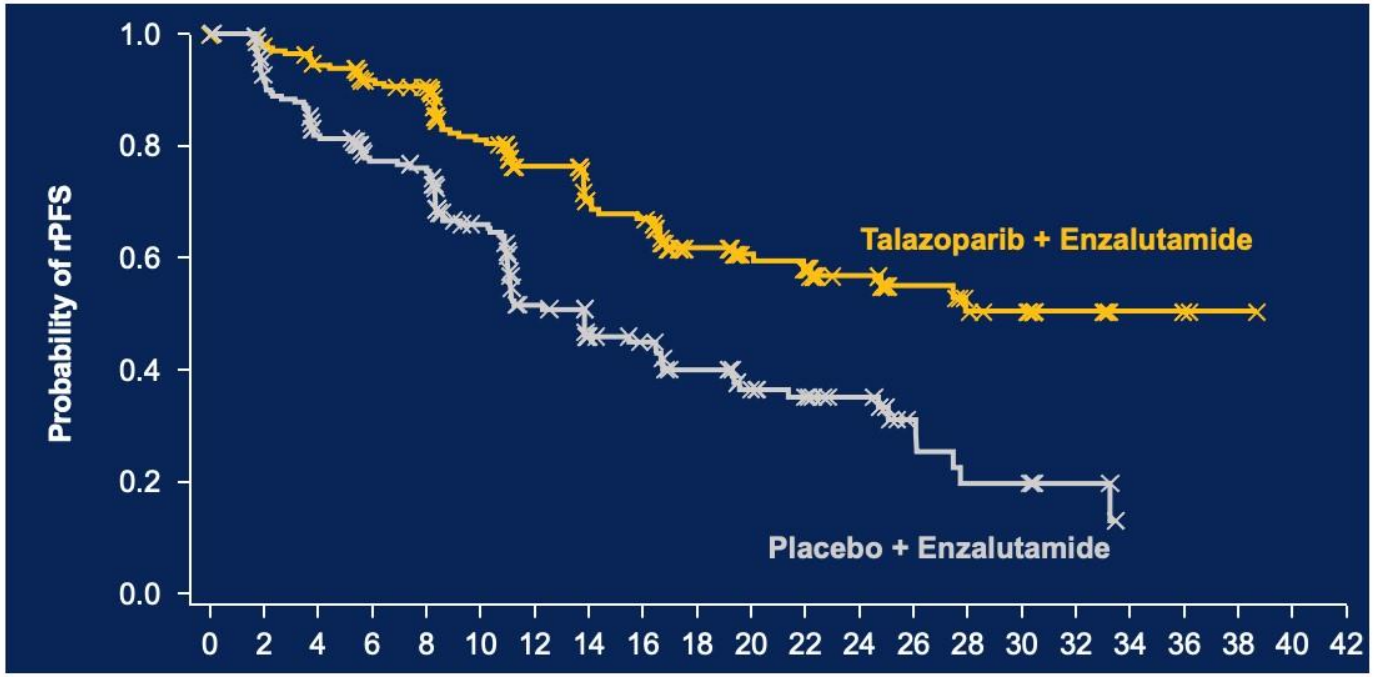
TALAPRO-2: A Randomized, Double-blind, Placebo-Controlled Study



Samples prospectively assessed for HRR gene alterations *(BRCA1, BRCA2, PALB2, ATM, ATR, CHEK2, FANCA, RAD51C, NBN, MLH1, MRE11A, CDK12)* using FoundationOne®CDx and/or FoundationOne®Liquid CDx

BICR=blinded independent central review; rPFS=radiographic progression-free survival.
[a]One patient in each treatment arm received prior orteronel. [b]Per RECIST version 1.1 (soft tissue disease) and Prostate Cancer Clinical Trials Working Group 3 (bone disease). [c]Time from randomization to the date of documented progression on the first subsequent antineoplastic therapy or death from any cause, whichever occurred first.

TALAPRO-2: Phase 3 study of talazoparib (TALA) + enzalutamide (ENZA) versus placebo (PBO) + ENZA as first-line (1L) treatment for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) harboring homologous recombination repair (HRR) gene alterations



	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	66	104
Median (95% CI), months	Not reached (NR) (21.9–NR)	13.8 (11.0–16.7)
HR (95% CI)	0.45 (0.33–0.61); *P* < 0.0001	

Median follow-up for rPFS was 17.5 and 16.8 months, respectively

[1]Clarke et al, NEJM Evidence, 2022
[2]Chi et al, JCO, 2023

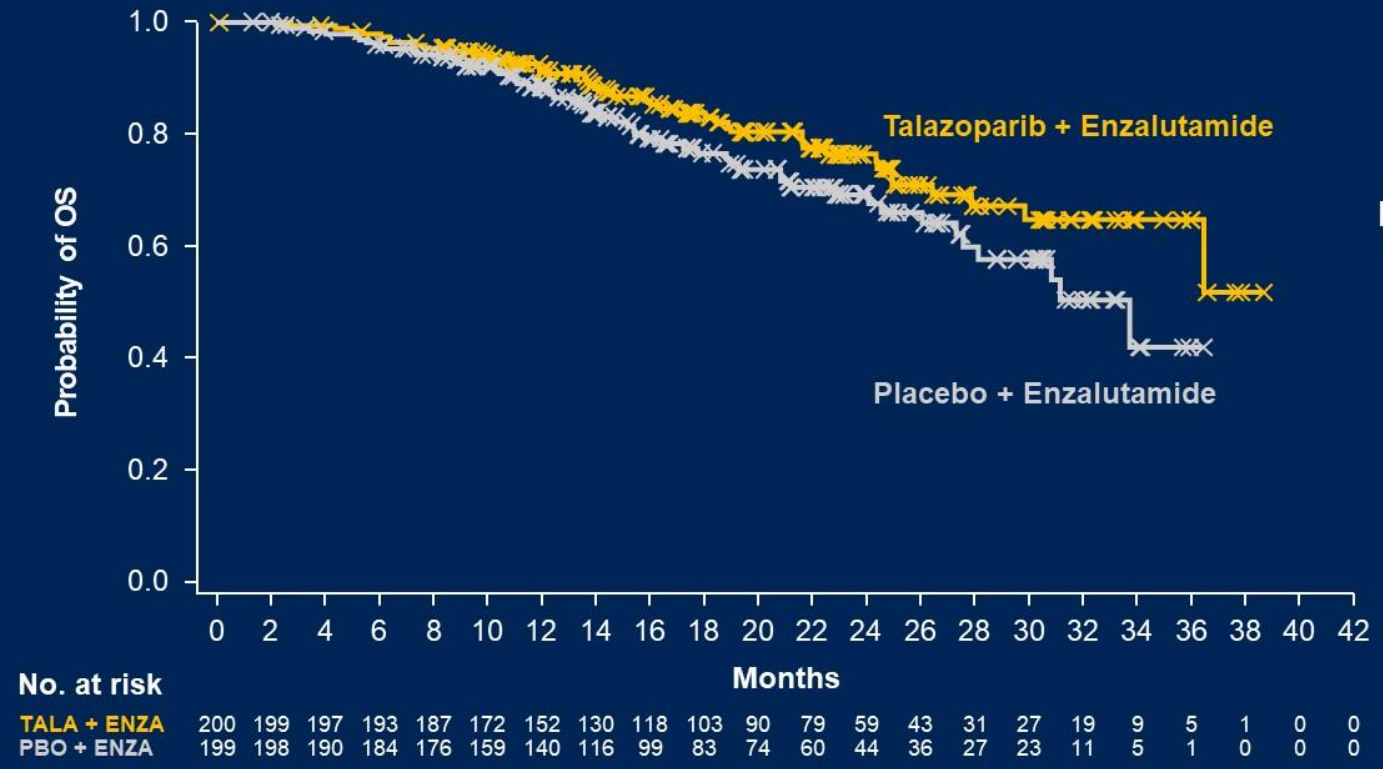
- **BRCA1/2 are great predictive biomarkers for PARP inhibitors**
- **Efficacy of Enzalutamide + Talazoparib is as good as other ARi + PARPi combinations**

Trial	Therapies	rPFS HRRm (CI)	rPFS BRCA1/2 (CI)
TALAPRO-2[1]	**Enzalutamide + Talazoparib**	**0.45 (0.33-0.61)**	**0.20 (0.11-0.36)**
PROpel[2]	Abiraterone + Olaparib	0.50 (0.34-0.73)	0.23 (0.12-0.43)
MAGNITUDE[3]	Abiraterone + Niraparib	0.73 (0.56-0.96)	0.53 (0.36-0.79)

[1]Fizazi et al, ASCO GU, 2023
[2]Clarke et al, NEJM Evidence, 2022
[3]Chi et al, JCO, 2023

TALAPRO-2 HRR-Deficient: Overall Survival (Interim Analysis)

Overall survival data are immature (24% maturity overall)

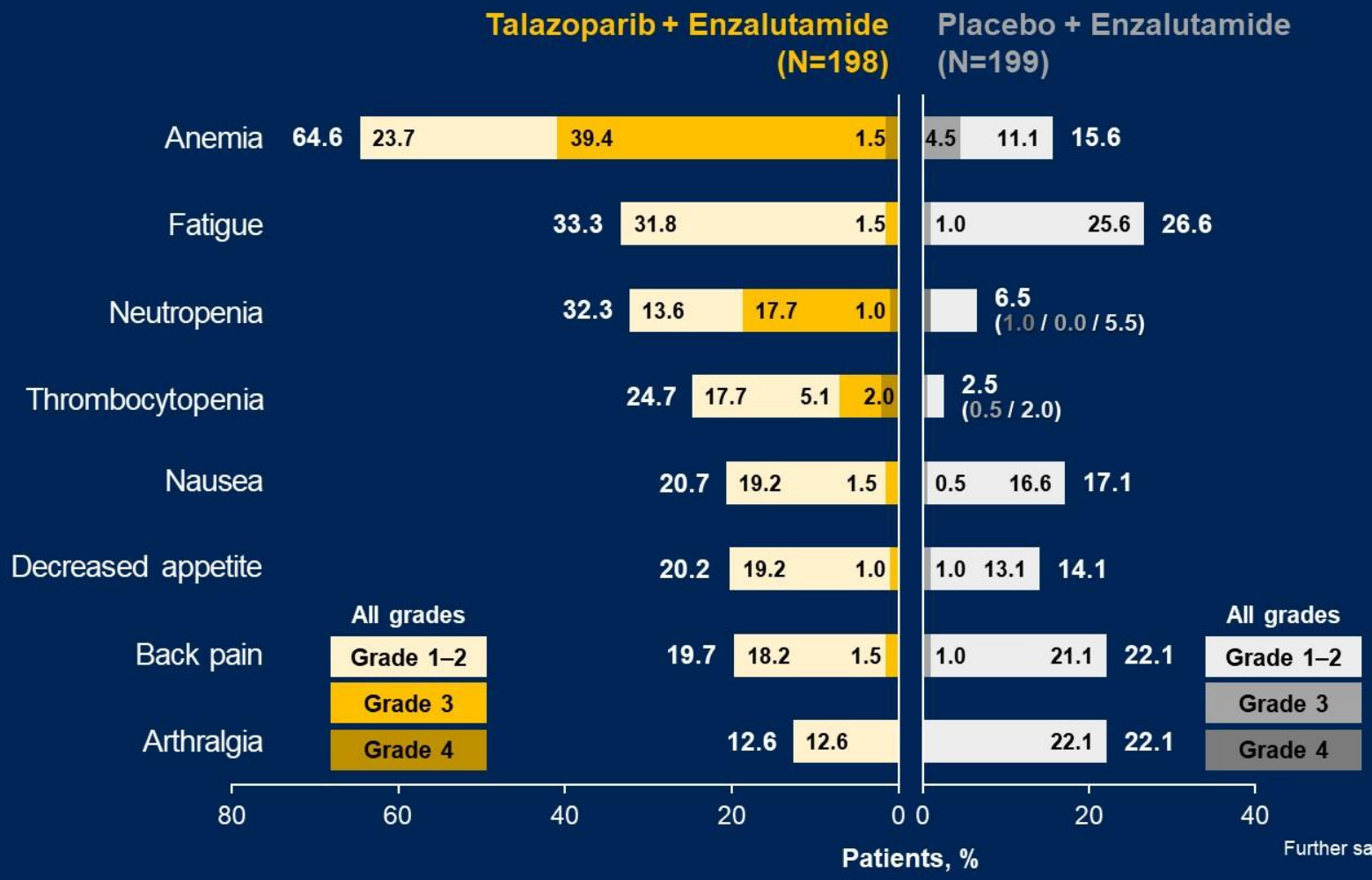


	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	43	53
Median (95% CI), months	NR (36.4–NR)	33.7 (27.6–NR)
HR (95% CI)	HR 0.69 (95% CI, 0.46–1.03) *P* = 0.068	

***BRCA*m HR 0.61 (95% CI, 0.31–1.23; *P* = 0.16)**
non-*BRCA*m HR 0.71 (95% CI, 0.43–1.18; *P* = 0.18)

18 patients in the control arm and 3 patients in the talazoparib arm subsequently received olaparib

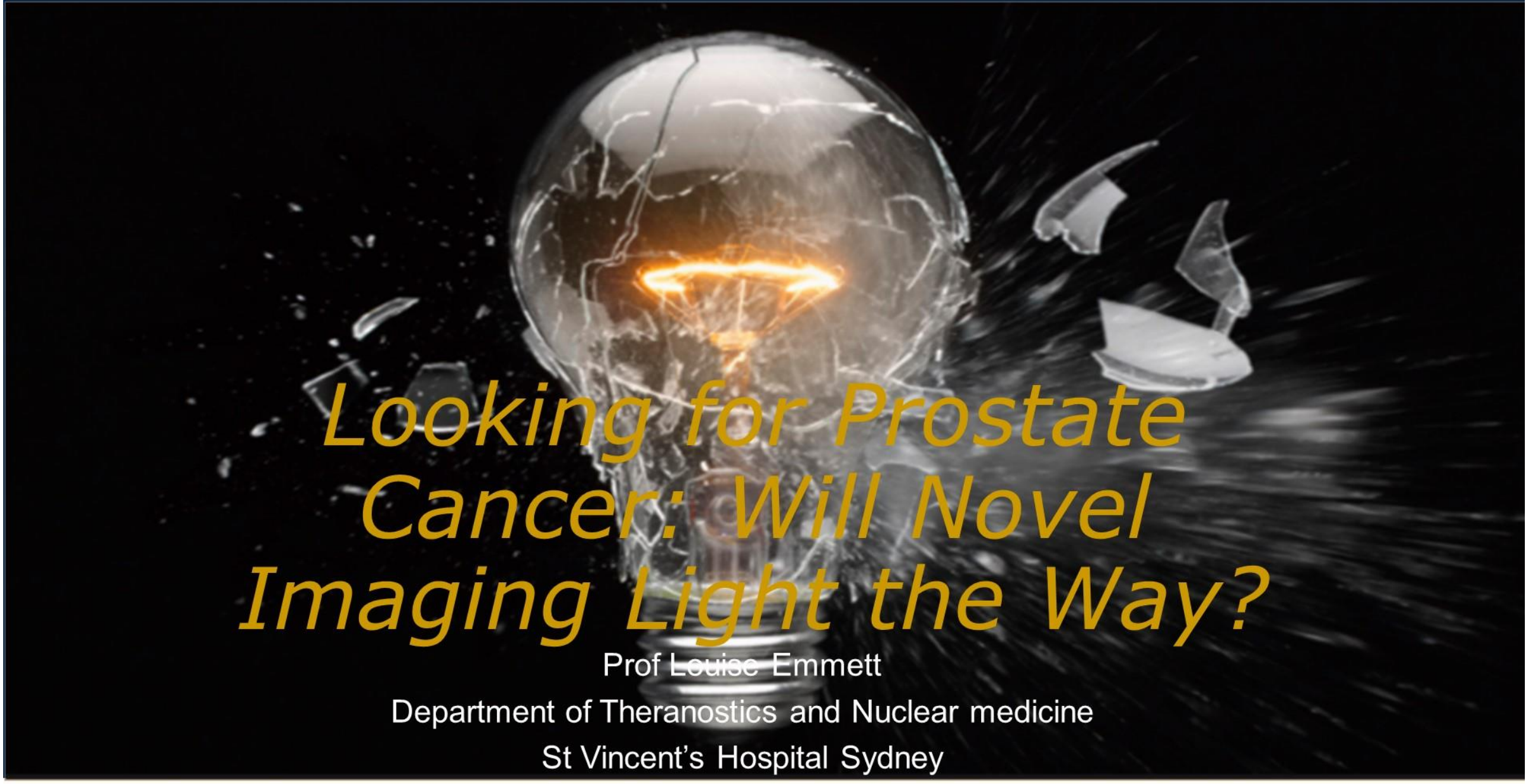
TALAPRO-2 HRR-Deficient: Most Common All-Cause TEAEs



In the talazoparib arm:

- Most common TEAEs leading to a dose reduction of talazoparib were:
  - Anemia (42.9%)
  - Neutropenia (15.2%)
  - Thrombocytopenia (5.6%)
- 55.6% had grade 1–2 anemia at baseline
- Grade 3–4 anemia
  - Median time to onset was 3.2 months
  - Reported in 40.9% of patients
- 4.0% discontinued talazoparib due to anemia
- The median relative dose intensity of talazoparib remained >80%

Further safety details can be found by accessing abstract No. 5053 (poster No. 147)



Looking for Prostate Cancer: Will Novel Imaging Light the Way?

Prof Louise Emmett

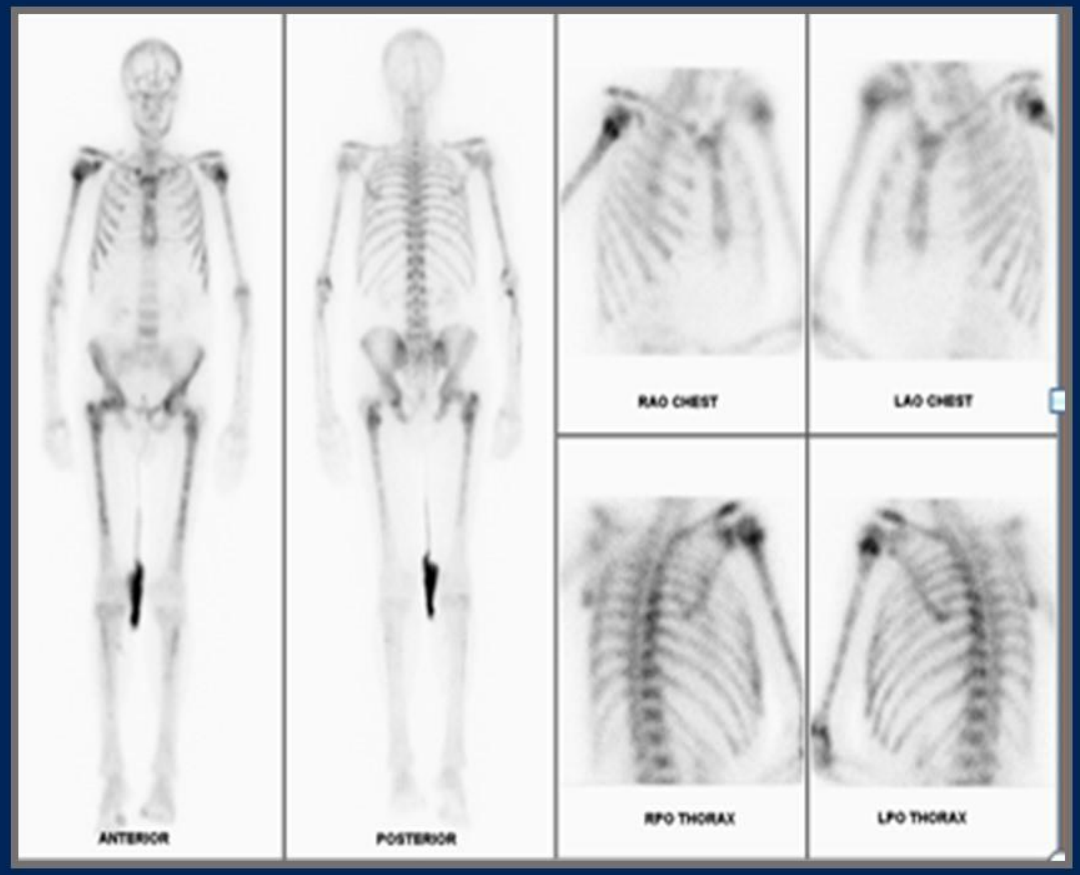
Department of Theranostics and Nuclear medicine

St Vincent's Hospital Sydney

2023 ASCO ANNUAL MEETING

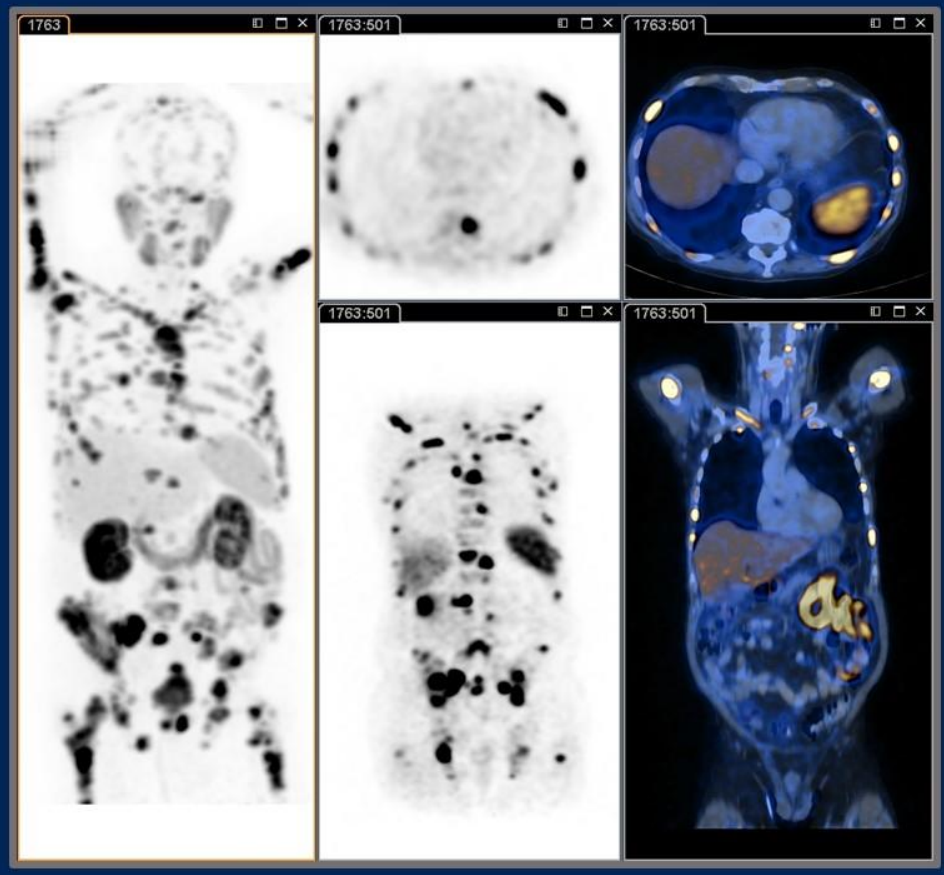
#ASCO23

OLD TECHNOLOGY



BONE scan

NEW TECHNOLOGY



PSMA PET CT

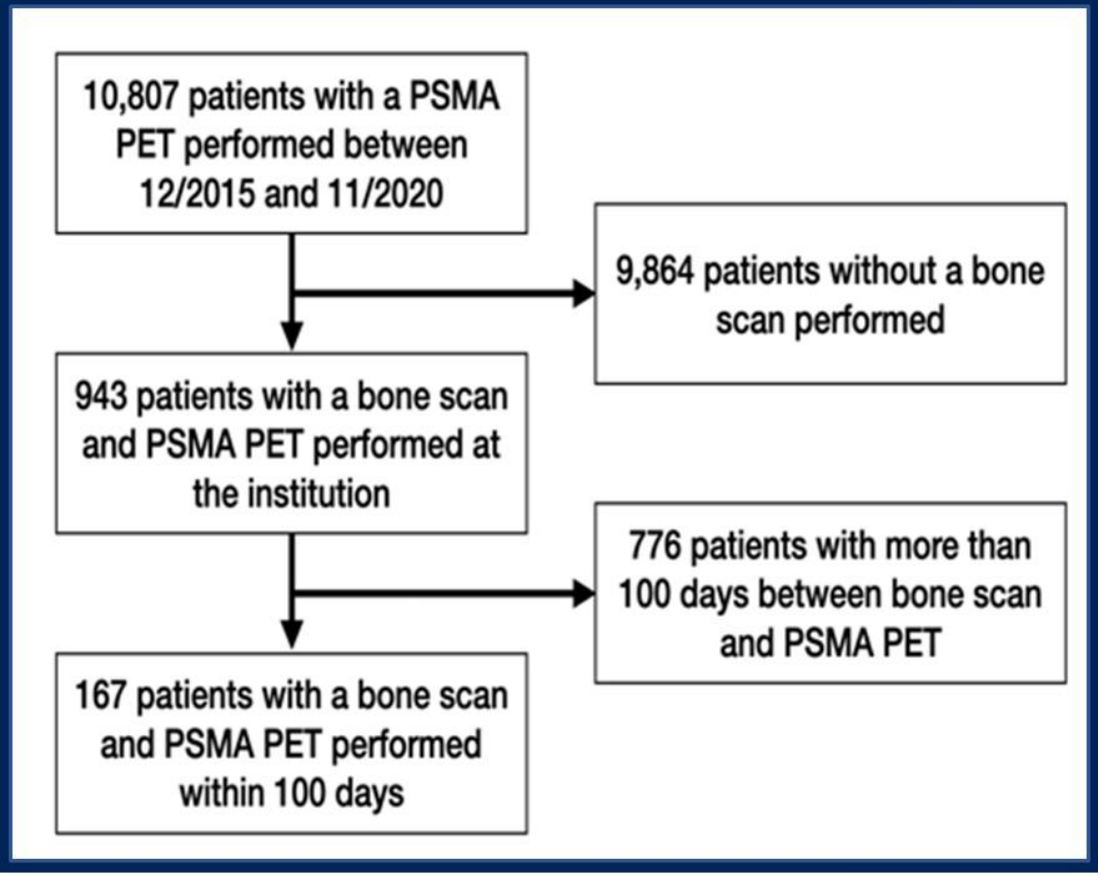
Do Bone Scans Over Stage Disease Compared to PSMA PET? An international multicenter retrospective study with blinded independent readers

Wolfgang P. Fendler[5], Thomas A. Hope,[1,2] Fei Jiang ,[4] Daniel Thompson,[1] Francesco Barbato,[5] Roxanna Juarez,[1] Miguel Hernandez Pampaloni ,[1] Martin Allen-Auerbach ,[3] Pawan Gupta,[3] Matthias Benz,[3] Jeremie Calais[3]

STUDY AIM: Evaluate the ability of bone scans to detect osseous metastatic burden using PSMA PET as a reference standard.

Retrospective study: PSMA and bone scans undertaken within 100 days re-read (3 blinded readers)

Evaluated patients with prostate cancer from staging to mCRPC.



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- 17% patients M1b on PSMA 30% M1b on Bone scan.
- 57% of positive bone scan findings at staging bone scan false positive.
- Insufficient numbers to evaluate findings in mCSPC.

Imaging Results in 167 Patients

	Initial staging	BCR/CSPC	CRPC	Overall
Bone scan vs PSMA PET comparison				
Both + (TP)	10 (13)	17 (28)	21 (70)	48 (29)
Both – (TN)	51 (66)	28 (47)	5 (17)	84 (50)
BS+/PSMA- (FP)	13 (17)	5 (8)	0 (0)	18 (11)
PSMA+/BS- (FN)	3 (4)	10 (17)	4 (13)	17 (10)

Bone Scan	All Patients (167)	Initial Staging (77)
PPV	73%	43%
NPV	82%	94%
Specificity	82%	80%

Practice Changers in Prostate Cancer

- AI-derived digital pathology based biomarker can predict that 1/3 of men with high risk localized prostate cancer will not benefit for LT-ADT and should instead get ST-ADT. In start up at certain centers.
- Adding talazoparib to enzalutamide in mCRPC with HRR gene alterations improves rPFS, QOL. DO MOLECULAR TESTING !
- PSMA PET is an imaging biomarker and is the new gold standard for prostate cancer. No role for bone scans for most patients.

2023 ASCO ANNUAL MEETING

MULTICENTER RANDOMIZED PHASE III OF DOSE DENSE MVAC OR GC AS PERIOPERATIVE CHEMOTHERAPY FOR MUSCLE INVASIVE BLADDER CANCER

Overall Survival at 5 years in the GETUG/AFU V05 VESPER trial

Ch Pfister, G Gravis, A Flechon, C Chevreau, H Mahammedi, B Laguerre, A Guillot,

F Joly, Y Allory, V Harter and S Culine for the Vesper trial investigators

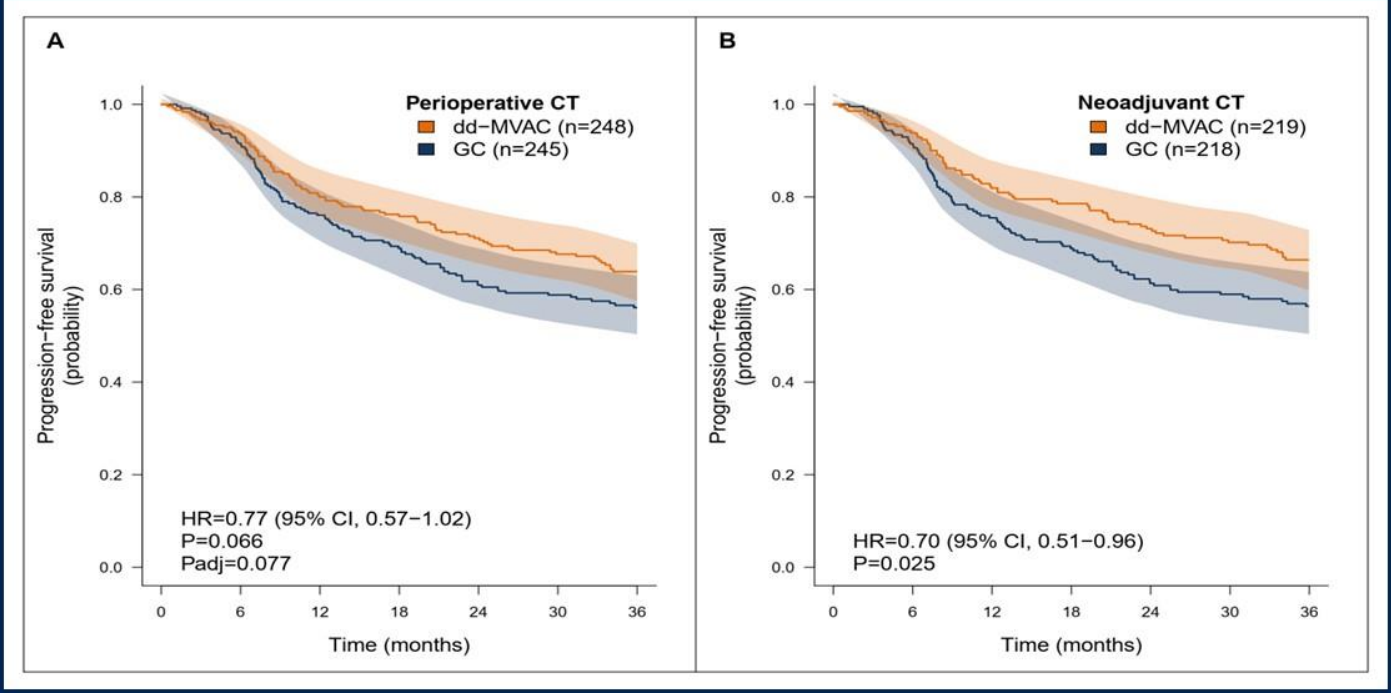
Trial design (1)

Chemotherapy

- **4 cycles of GC** — Gemcitabine 1250 mg/m² d1 and d8; Cisplatin 70 mg/m² d1 — **every 3 weeks**
- **6 cycles of ddMVAC** — Methotrexate 30 mg/m² d1; Vinblastine 3 mg/m² d2; Doxorubicin 30 mg/m² d2; Cisplatin 70 mg/m² d2; ***+ G-CSF support from d3 to d9*** — **every 2 weeks**

PFS at 3 years

2021 ESMO congress
16-21 September 2021

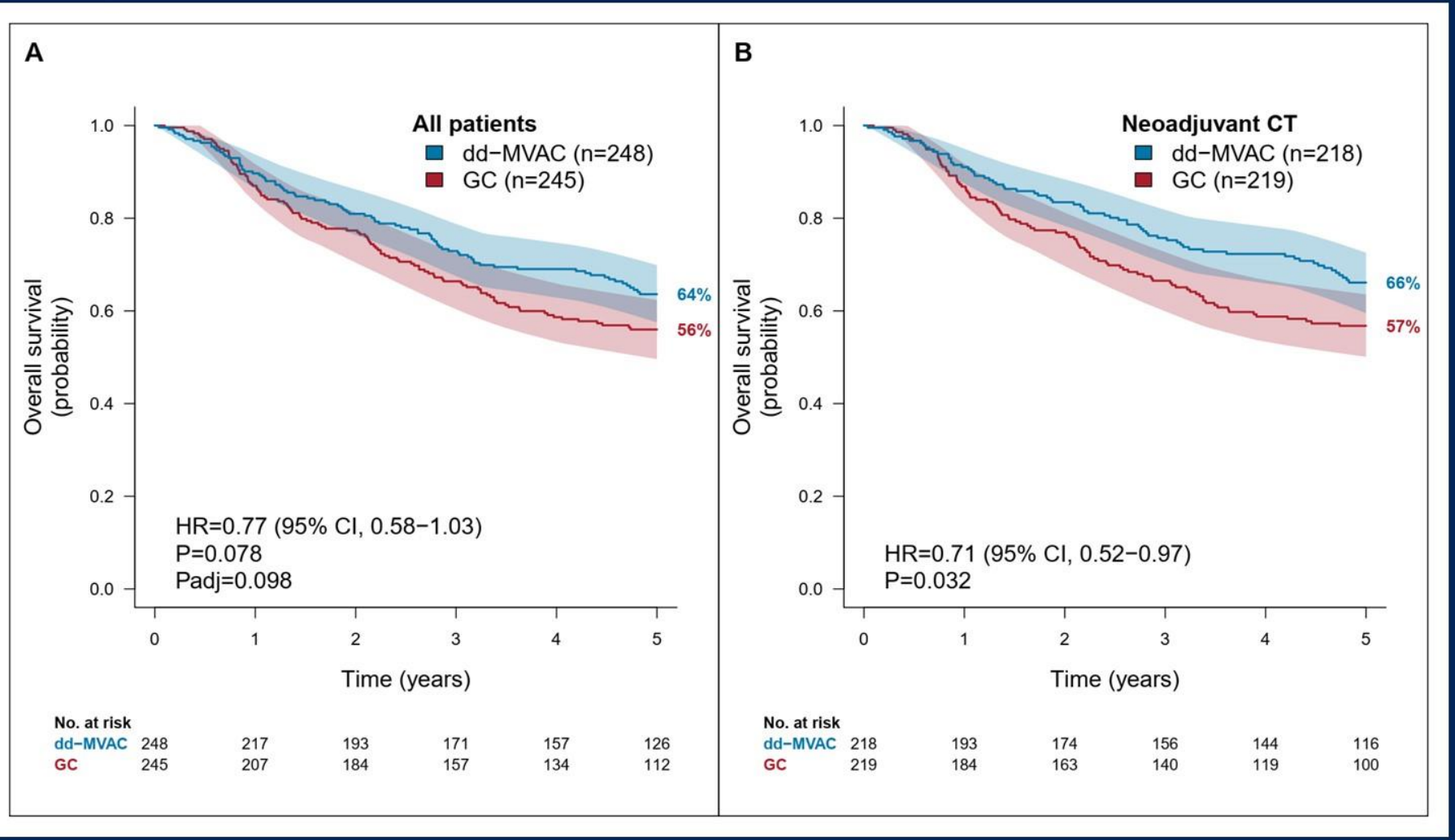


Perioperative dd-MVAC improve 3-y PFS over GC

In the neoadjuvant group, better bladder tumor local control with a significant improvement on 3-y PFS in the dd-MVAC arm

Pfister et al. J Clin Oncol 2022

Results (1) Overall Survival at 5 years



Results (3)

Causes of Death

	GC	dd-MVAC
Bladder cancer progression	94	63
Toxic death	1	3
Cardiovascular event	3	5
Second cancer	2	2
Intercurrent disease	2	7
Unknown cause of death without relapse	1	5
Other undocumented death	1	1

Results (5)

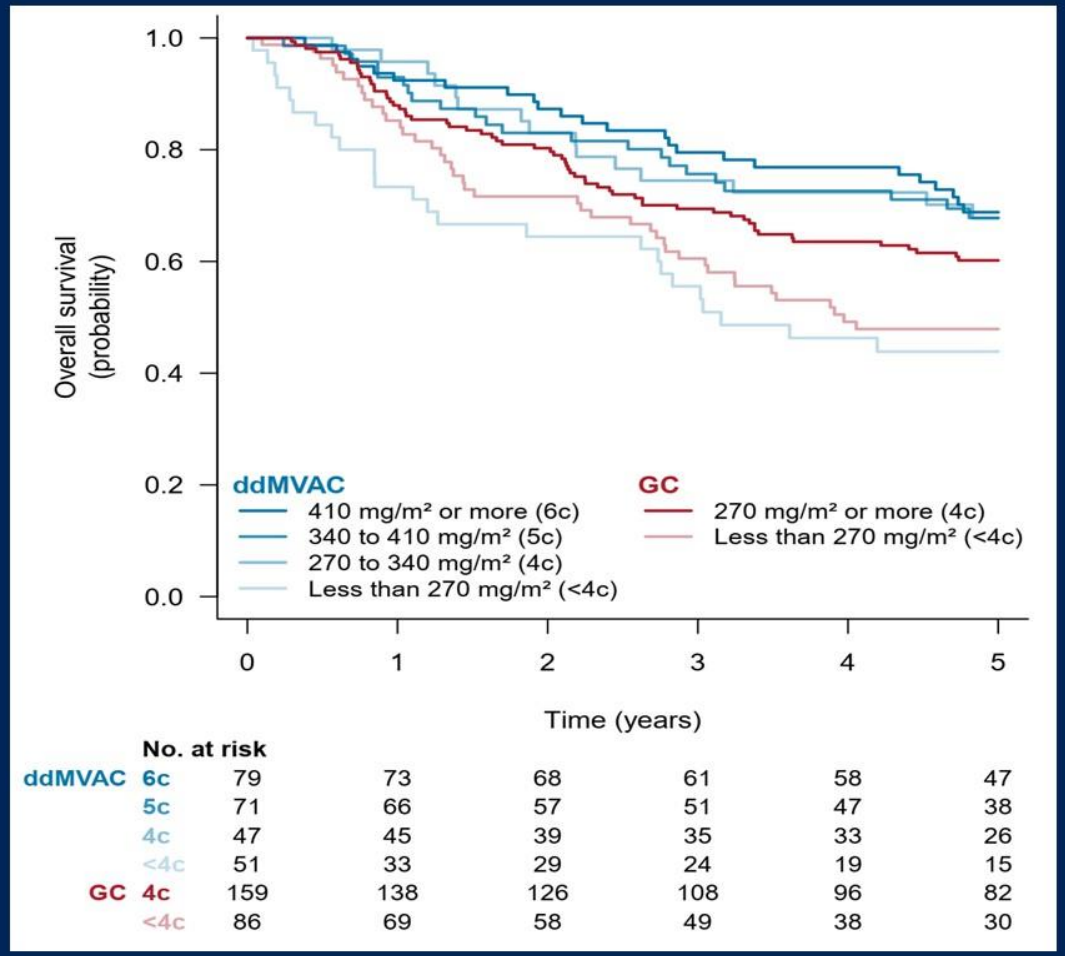
OS stratified by CT arm and number of cycles delivered

Importance of cumulative cisplatin dose

Poor OS *< 4 full doses cisplatin*

Median OS *GC arm 4 full doses cisplatin*

High OS *dd-MVAC arm > 4 full doses cisplatin*



		No. at risk					
ddMVAC	6c	79	73	68	61	58	47
	5c	71	66	57	51	47	38
	4c	47	45	39	35	33	26
	<4c	51	33	29	24	19	15
GC	4c	159	138	126	108	96	82
	<4c	86	69	58	49	38	30

2023 ASCO ANNUAL MEETING

Study EV-103 Dose Escalation/Cohort A: Long-term Outcome of Enfortumab Vedotin + Pembrolizumab in First-line (1L) Cisplatin-ineligible Locally Advanced or Metastatic Urothelial Carcinoma (la/mUC) with Nearly 4 Years of Follow-up

Shilpa Gupta, MD[1]; Jonathan E. Rosenberg, MD[2]; Rana R. McKay, MD[3]; Thomas W. Flaig, MD[4]; Daniel Peter Petrylak, MD[5]; Christopher J. Hoimes, DO[6]; Terence W. Friedlander, MD[7]; Mehmet Asim Bilen, MD[8]; Sandy Srinivas, MD[9]; Earle Burgess, MD[10]; Jaime R. Merchan, MD[11]; Scott Tagawa, MD[12]; Jason Brown, MD[13]; Yao Yu, PhD[14]; Anne-Sophie Carret, MD[14]; Heidi S. Wirtz, PharmD, PhD[14]; Maria Guseva, MD, PharmD[15]; Blanca Homet Moreno, MD, PhD[16]; Matthew I. Milowsky, MD[17]

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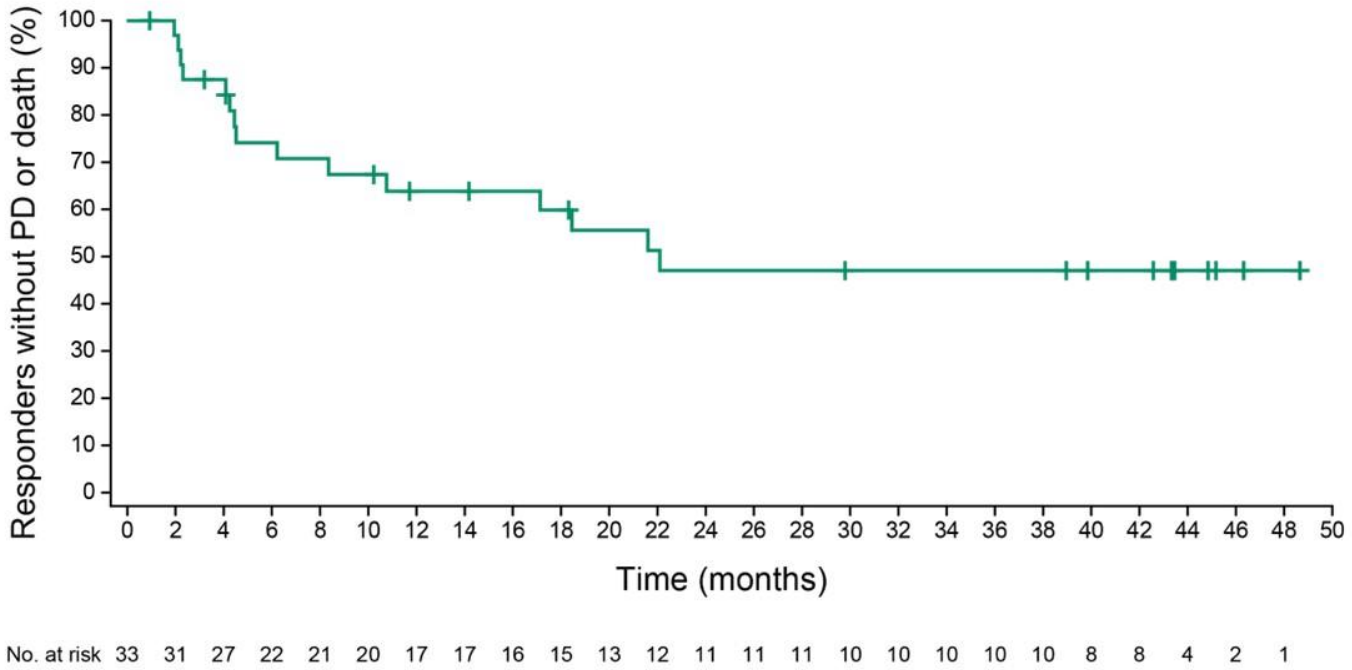
Duration of Response by BICR

1L EV+P is associated with durable responses

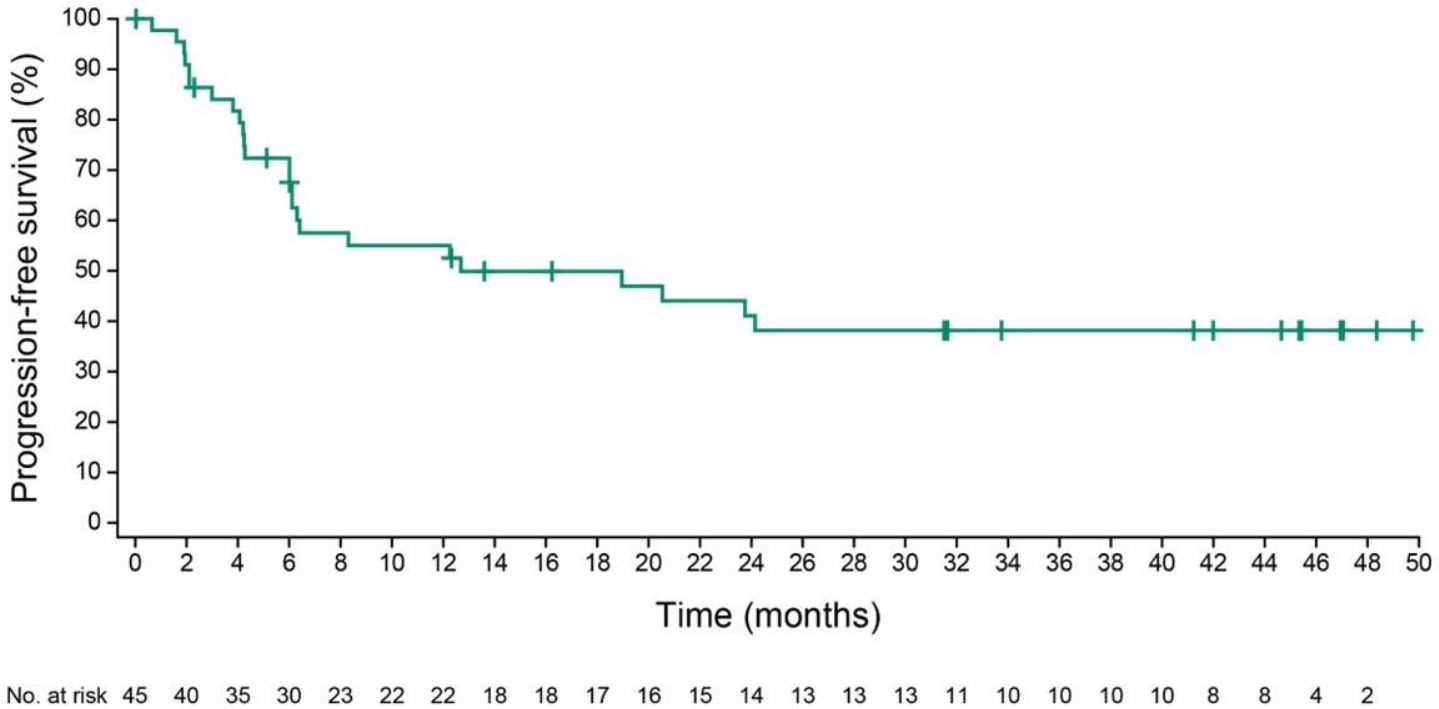


	Dose Escalation + Cohort A (N = 45)
DOR events, n	15
Median DOR (95% CI[a])	22.1 months (8.38-NE)
Patients without PD or death at:	
6 months, % (95% CI[a])	74.1 (54.82-86.17)
12 months, % (95% CI[a])	63.9 (44.19-78.17)
24 months, % (95% CI[a])	47.0 (27.57-64.31)

BICR = blinded independent central review; CI = confidence interval; DOR = duration of response; EV = enfortumab vedotin; NE = not estimable; P = pembrolizumab, PD = progressive disease; 1L = first-line
[a]CI was calculated using the complementary log-log transformation method (Collett, 1994)

Progression-Free Survival by BICR

41.1% of patients were progression-free at 24 months

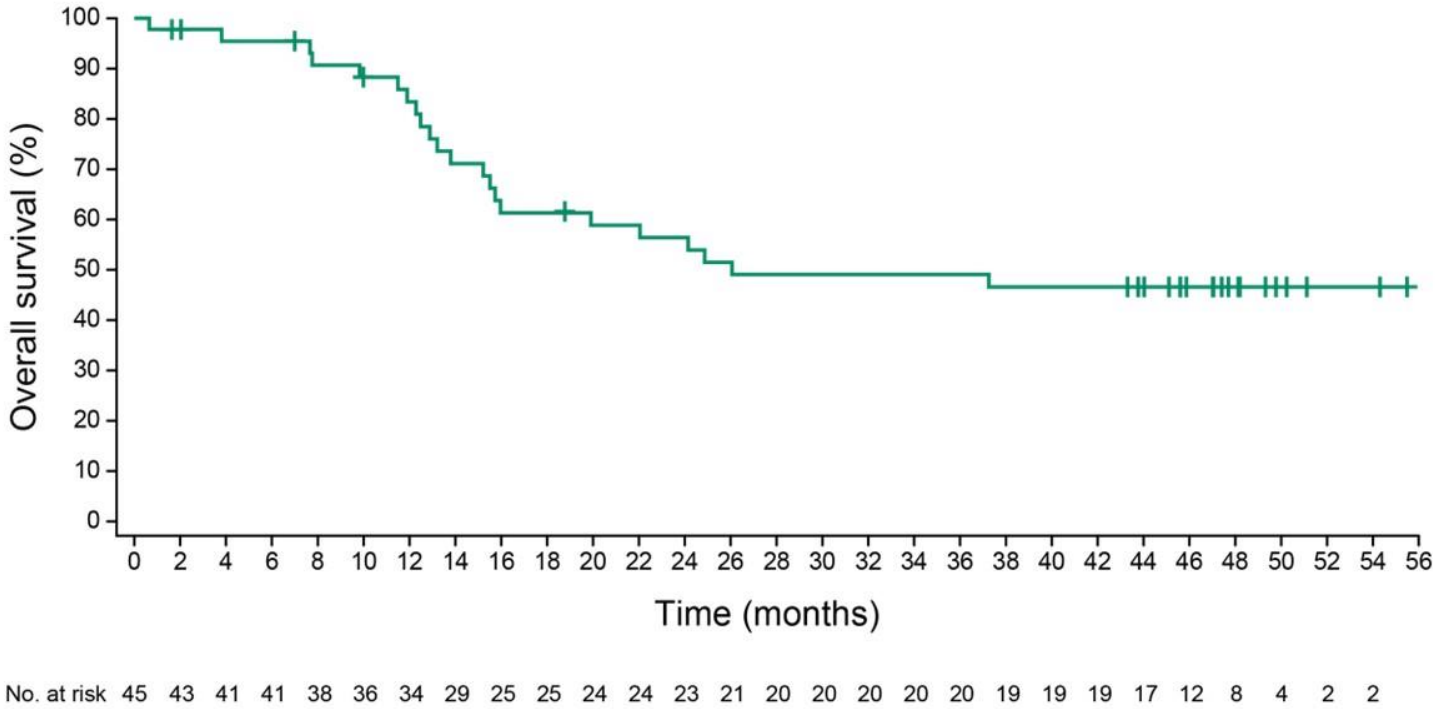


	Dose Escalation + Cohort A (N = 45)
PFS events, n	25
Median PFS (95% CI[a])	12.7 months (6.11-NE)
PFS rate[b] at:	
6 months, % (95% CI[a])	72.4 (56.47-83.26)
12 months, % (95% CI[a])	55.0 (38.84-68.58)
24 months, % (95% CI[a])	41.1 (25.69-55.88)

BICR = blinded independent central review; CI = confidence interval; NE = not estimable; PFS = progression-free survival
[a]CI was calculated using the complementary log-log transformation method (Collett, 1994)
[b]As estimated using Kaplan-Meier method

Overall Survival

Median survival exceeds 2 years



	Dose Escalation + Cohort A (N = 45)
OS events, n	22
Median OS (95% CI[a])	26.1 months (15.51-NE)
OS rate[b] at:	
6 months, % (95% CI[a])	95.4 (83.00-98.84)
12 months, % (95% CI[a])	83.4 (68.25-91.72)
24 months, % (95% CI[a])	56.4 (40.03-69.91)
Median follow-up time	47.0 months

CI = confidence interval; NE = not estimable; OS = overall survival
[a]CI was calculated using the complementary log-log transformation method (Collett, 1994)
[b]As estimated using Kaplan-Meier method

Treatment-Related Adverse Events of Special Interest for Enfortumab Vedotin

Skin reactions and PN were the most common treatment-related AESI for EV

	Dose Escalation + Cohort A (N = 45)	
	Any Grade n (%)	**Grade ≥3 n (%)**
Skin reactions	30 (66.7)	9 (20.0)
Rash maculo-papular	16 (35.6)	5 (11.1)
Rash macular	7 (15.6)	0
Peripheral neuropathy[a]	28 (62.2)	2 (4.4)
Ocular disorders	18 (40.0)	0
Dry eye	16 (35.6)	0
Blurred vision	5 (11.1)	0
Corneal disorders	1 (2.2)	0
Hyperglycemia	5 (11.1)	4 (8.9)
Infusion related reactions	3 (6.7)	1 (2.2)

AESI = adverse events of special interest; EV = enfortumab vedotin; PN = peripheral neuropathy; TRAE = treatment-related adverse events

[a] Peripheral neuropathy Standardised MedDRA Queries (broad scope). n=8 patients had pre-existing peripheral neuropathy and n=37 did not have pre-existing peripheral neuropathy. Pre-existing condition includes medical history and conditions ongoing at baseline

- Most of the events were of low grade (1 or 2)
- The TRAEs for EV were consistent with previously observed results

PRESENTED BY: Dr. Shilpa Gupta, MD

Onset, Improvement, and Resolution for TRAEs of Special Interest for Enfortumab Vedotin

The majority of the EV AESI events improved or resolved

	Total Number of Events[a] N	Events[a] with Improvement n (%)	Events[a] with Resolution n (%)	Median Time To: Onset of First Event, Months (range)	Improvement,[b] Months (range)	Resolution,[c] Months (range)
Skin reaction	65	2 (3.1)	58 (89.2)	0.7 (0.1-15.7)	0.7 (0.2-1.2)	1.2 (0.1-27.1)
Peripheral neuropathy	43	20 (46.5)	10 (23.3)	2.4 (0.7-12.5)	6.6 (0.3-27.4)	7.2 (3.5-19.1)
Hyperglycemia	7	1 (14.3)	6 (85.7)	0.5 (0.3-3.5)	0.5 (0.5-0.5)	1.6 (0.5-19.7)

AESI = adverse event of special interest; EV = enfortumab vedotin; TRAE = treatment-related adverse event

[a]**Patients could have had more than one event**

[b]Improvement defined as at least one grade improvement from the worst grade at the last assessment

[c]Resolution defined as a return to baseline grade or better at the last assessment or recovered outcome

Most Common Treatment-Emergent Adverse Events of Special Interest for Pembrolizumab

Severe skin reactions were the most common treatment-emergent adverse event of special interest for P

	Dose Escalation + Cohort A (N = 45)	
	Any Grade[a] n (%)	**Grade ≥3 n (%)**
Severe skin reactions	11 (24.4)	10 (22.2)
Rash maculo-popular	5 (11.1)	5 (11.1)
Dermatitis bullous	4 (8.9)	2 (4.4)
Pneumonitis	4 (8.9)	1 (2.2)
Colitis	3 (6.7)	1 (2.2)
Hypothyroidism	3 (6.7)	0

P = pembrolizumab
[a]Occurred in >5% of patients

- The safety for P was consistent with previously observed results, except for severe skin reactions, which were reported with a higher incidence in this study

Phase 3 THOR Study: Results of Erdafitinib Versus Chemotherapy in Patients With Advanced or Metastatic Urothelial Cancer With Select Fibroblast Growth Factor Receptor Alterations

Yohann Loriot[1], Nobuaki Matsubara[2], Se Hoon Park[3] , Robert A. Huddart[4], Earle F. Burgess[5], Nadine Houede[6], Severine Banek[7], Brigitte Laguerre[8], Valentina Guadalupi[9], Ja Hyeon Ku[10], Spyros Triantos[11], Sydney Akapame[11], Kris Deprince[12], Sutapa Mukhopadhyay[13], Arlene O Siefker-Radtke[14]

[1]Department of Cancer Medicine, INSERM U981, Gustave Roussy, Université Paris-Saclay, Villejuif, France; [2]Department of Medical Oncology, National Cancer Center Hospital East, Chiba, Japan; [3]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Section of Radiotherapy and Imaging, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton, UK; [5]Medical Oncology Department, Levine Cancer Institute, Charlotte, NC; [6]Medical Oncology Department, Institut de Cancérologie du Gard - CHU Caremeau, Nîmes, France and Montpellier University, Montpellier, France; [7]Department of Urology, University Hospital Frankfurt, Goethe Universtity Frankfurt, Frankfurt am Main, Germany; [8]Department of Medical Oncology, Centre Eugene Marquis, Rennes, France; [9]Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy; [10]Seoul National University Hospital, Seoul, South Korea; [11]Janssen Research & Development, Spring House, PA; [12]Janssen Research & Development, Beerse, Belgium; [13]Janssen Research & Development, Lexington, MA; [14]Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Presented at the 2023 ASCO Annual Meeting; June 2-6, 2023; Chicago, IL, USA.

Erdafitinib is a Pan-FGFR Inhibitor With Activity in Metastatic Urothelial Carcinoma

- ***FGFRalt*** are observed in **~20% of advanced or mUC** and may function as oncogenic drivers[1,2]

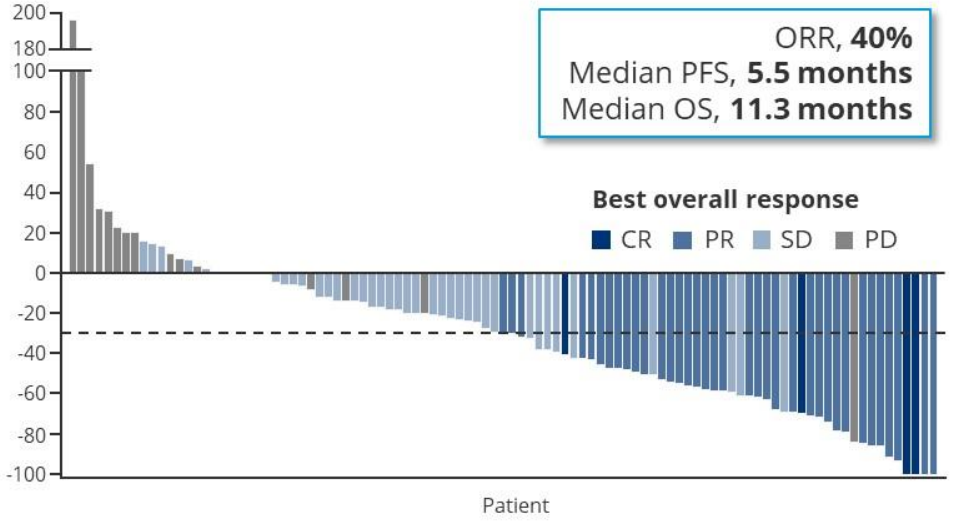
Erdafitinib is an oral selective pan-FGFR tyrosine kinase inhibitor[3]

  - Erdafitinib was granted accelerated approval in the United States and is approved in 17 other countries to treat locally advanced or mUC in adults with susceptible *FGFR3/2alt* who have progressed after platinum-containing chemotherapy[4-6]

- **THOR** is a confirmatory, randomized phase 3 study:

  - Cohort 1 assessed whether erdafitinib improved survival over chemotherapy in patients with *FGFRalt* mUC who progressed on or after ≥1 prior treatment that included anti–PD-(L)1

In the single-arm phase 2 BLC2001 trial, erdafitinib showed a benefit in patients with *FGFR-altered* advanced urothelial cancer[4]



Patients received erdafitinib 8 mg/d with pharmacodynamically guided uptitration to 9 mg/d.

FGFR, fibroblast growth factor receptor; *FGFRalt*, *FGFR* alterations; mUC, metastatic urothelial carcinoma; ORR, overall response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival.
[a]Patients received erdafitinib 8 mg/d with pharmacodynamically guided uptitration to 9 mg/d.

1. Necchi A, et al. *Eur Urol Focus*. 2019;5:853-586; 2. di Martino E, et al. *Future Oncol.* 2016;12:2243-2263; 3. Perera TPS, et al. *Mol Cancer Ther.* 2017;16:1010-1020; 4. Loriot Y, et al. *N Engl J Med.* 2019;381:338-348; 5. BALVERSA® (erdafitinib) [package insert]. Horsham, PA: Janssen Products, LP; 2023; 6. Siefker-Radtke AO, et al. *Lancet Oncol.* 2022;23:248-258.

Phase 3 THOR Study: Erdafitinib Versus Chemotherapy of Choice in Patients With Advanced Urothelial Cancer and Selected FGFR Aberrations

Cohort 1

Key eligibility criteria

- Age ≥18 years
- Metastatic or unresectable UC
- Confirmed disease progression
- Prior tx with anti–PD-(L)1
- 1-2 lines of systemic tx
- Select *FGFR3/2alt* (mutation/fusion)[a]
- ECOG PS 0-2

1:1
N=266[b]

R

Erdafitinib
(n=136)
Once-daily erdafitinib 8 mg with pharmacodynamically guided uptitration to 9 mg

Chemotherapy of Choice
(n=130)
docetaxel or vinflunine once every 3 weeks

Stratification factors: region (North America vs European Union vs rest of world), ECOG PS (0 or 1 vs 2), and disease distribution (presence vs absence of visceral [lung, liver, or bone] metastases)

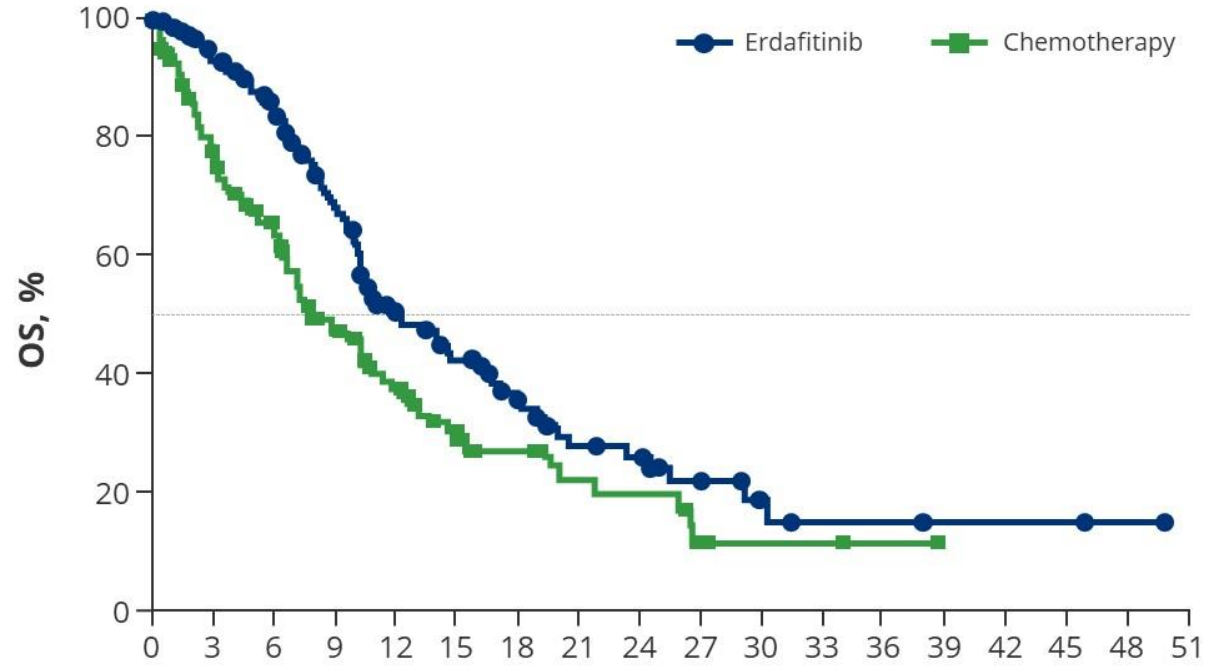
Primary end point:
- OS

Key secondary end points:
- PFS
- ORR
- Safety

NCT03390504

[a]Molecular eligibility can be confirmed using either central or local historical *FGFR* test results (Qiagen assay). If a patient was enrolled based on local historical testing, a tissue sample must still be submitted at the time of enrollment for retrospective confirmation (by central lab) of *FGFR* status. Tumors must have ≥1 of the following translocations: *FGFR2-BICC1*, *FGFR2-CASP7*, *FGFR3-TACC3_V1*, *FGFR3-TACC3_V3*, *FGFR3-BAIAP2L1*; or 1 of the following *FGFR3* gene mutations: R248C, S249C, G370C, Y373C.
[b]Number of patients randomized at the time of the interim analysis (data cutoff January 15, 2023).
ECOG PS, Eastern Cooperative Oncology Group performance status; FGFR, fibroblast growth factor receptor; *FGFR3/2alt*, *FGFR3/2* alterations; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q3W, every 3 weeks; tx, treatment; UC, urothelial cancer.

Overall Survival for Erdafitinib Was Superior to Investigator's Choice of Chemotherapy

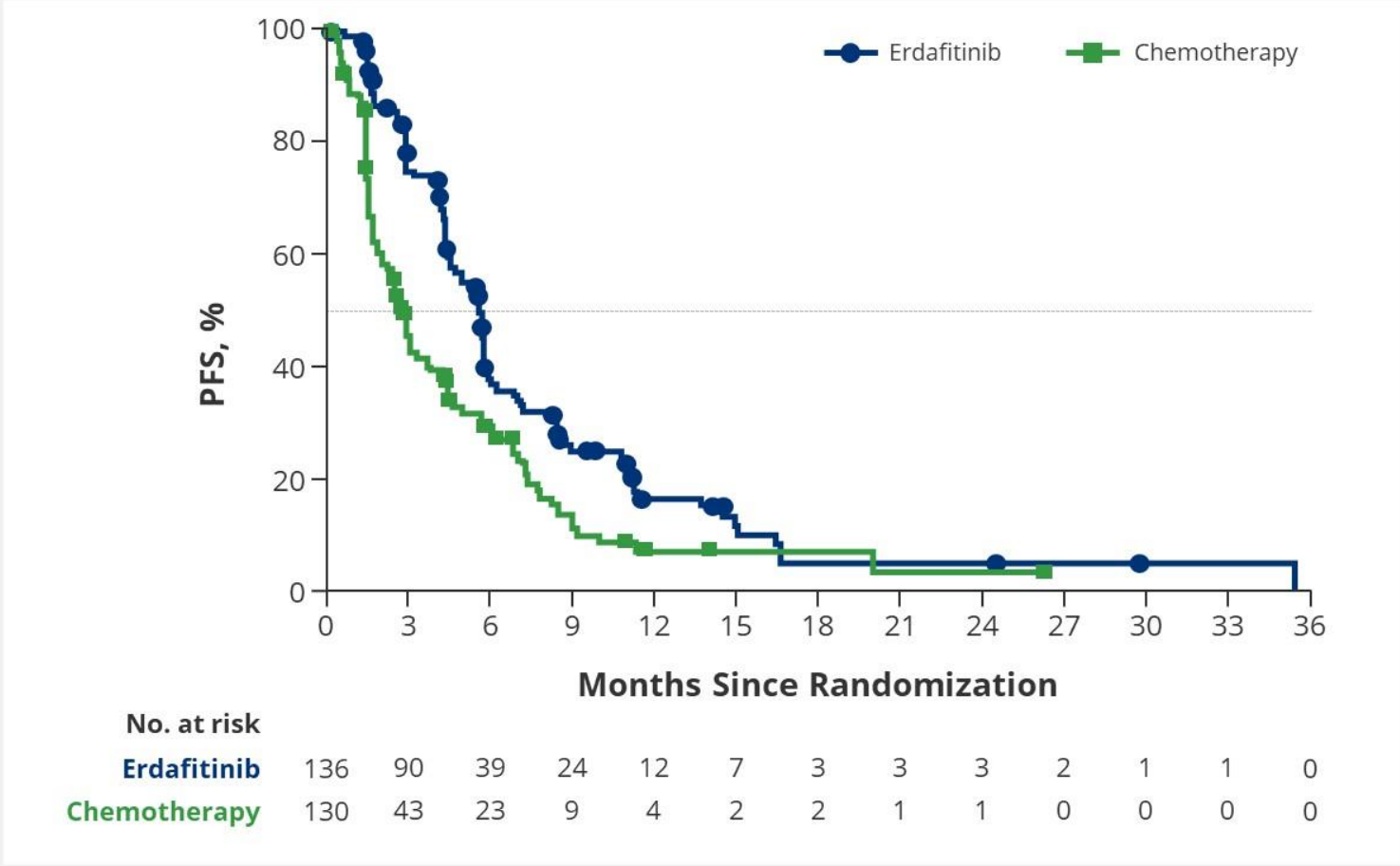


No. at risk																		
Erdafitinib	136	117	97	74	46	35	25	17	15	9	5	3	3	2	2	2	1	0
Chemotherapy	130	87	66	43	30	18	13	9	8	3	2	2	1	0	0	0	0	0

- Median follow-up was 15.9 months
- Median OS was 12.1 months for erdafitinib versus 7.8 months for chemotherapy
- Erdafitinib reduced the risk of death by 36% versus chemotherapy
  - HR, 0.64 (95% CI, 0.47-0.88; *P* = 0.005)[a]
- Based on these interim analysis results, the IDMC recommended to stop the study, unblind data, and cross over patients from chemotherapy to erdafitinib

CI, confidence interval; HR, hazard ratio; IDMC, independent data monitoring committee; OS, overall survival.
[a]The significance level for stopping for efficacy was p=0.019, corresponding to a HR of 0.69.

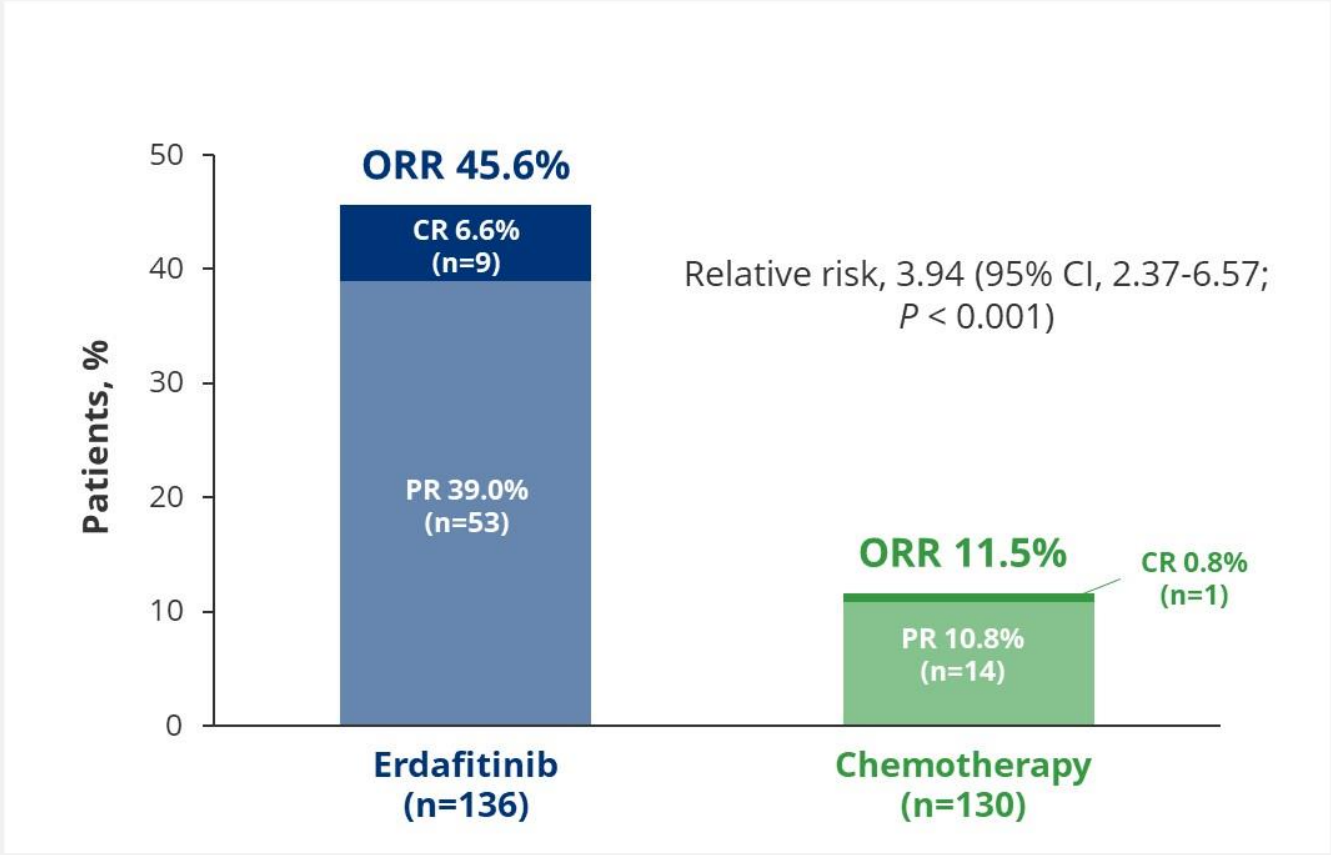
Erdafitinib Significantly Improved Progression-Free Survival Versus Chemotherapy



- Median PFS was 5.6 versus 2.7 months for erdafitinib versus chemotherapy
- Erdafitinib reduced the risk of progression or death by 42% versus chemotherapy
  - HR, 0.58 (95% CI, 0.44-0.78; *P* = 0.0002)

CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

Objective Response Rate Was Significantly Higher for Erdafitinib Versus Chemotherapy[a]



CI, confidence interval; CR, complete response; ORR, objective response rate; PR, partial response.
[a]Responses were best overall response per investigator assessment.

The Safety Profiles Were Consistent With the Known Profiles of Erdafitinib and Chemotherapy (2/2)

Patients with AEs of interest, n (%)	Erdafitinib (n=135)		Chemotherapy (n=112)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Nail disorders[a]	90 (66.7)	15 (11.1)	6 (5.4)	0
Skin disorders[b]	74 (54.8)	16 (11.9)	14 (12.5)	0
Eye disorders (excluding central serous retinopathy)[c]	57 (42.2)	3 (2.2)	6 (5.4)	0
Central serous retinopathy[d]	23 (17.0)	3 (2.2)	0	0

[a]Nail disorders: nail bed bleeding, nail discoloration, nail disorder, nail dystrophy, nail ridging, nail toxicity, onychalgia, onychoclasis, onycholysis, paronychia, onychomadesis.
[b]Skin disorders: blister, dry skin, erythema, hyperkeratosis, palmar erythema, palmar-plantar erythrodysesthesia syndrome, plantar erythema, rash, rash erythematous, rash generalized, rash macular, rash maculo-papular, skin atrophy, skin exfoliation, skin fissures, skin lesion, skin ulcer, toxic skin eruption, xeroderma.
[c]Eye disorders (excluding central serous retinopathy): blepharitis, cataract, cataract subcapsular, conjunctival hemorrhage, conjunctival hyperemia, conjunctival irritation, corneal erosion, corneal infiltrates, dry eye, eye inflammation, eye irritation, eye pain, foreign body sensation in eyes, keratitis, lacrimation increased, night blindness, ocular hyperemia, photophobia, vision blurred, visual acuity reduced, visual impairment, xanthopsia, xerophthalmia, chorioretinitis, conjunctivitis, ulcerative keratitis.
[d]Central serous retinopathy: retinal detachment, vitreous detachment, retinal edema, retinopathy, chorioretinopathy, detachment of retinal pigment epithelium, detachment of macular retinal pigment epithelium, macular detachment, serous retinal detachment, subretinal fluid, retinal thickening, chorioretinitis, serous retinopathy, maculopathy, choroidal effusion.
AE, adverse event.

Efficacy: THOR, EV-301 and TROPHY-U-1

	Median Survival (Months)	Progression Free Survival (Months)	Complete Response (%)	Partial Response (%)
THOR	12.1	5.6	6.6	39.0
EV-301	12.9	5.5	4.9	35.7
TROPHY-U-01	10.9	5.4	5.3	22.1

Loriot Y LBA 4619 Proc ASCO 2023; Powles T et al NEJM 2021;Tagawa S et al JCO 2021

Toxicity: THOR, EV-103 and TROPHY-U-1

	All Grades (%)	Grade 3 or 4 (%)
Erdafitinib	78.5	5.2
Hyperphosphatemia	54.8	3.0
Diarrhea	17.2	2.2
Central Serous Retinopathy		
Enfortumab Vedotin		
Peripheral Sensory Neuropathy	33.8	3.0
Rash	16.2	7.4
Neutropenia	6.8	4.7
Sacituzumab Govitecan		
Neutropenia	46.0	34
Diarrhea	65.0	4

Practice Changers in Urothelial Cancer

- Neoadjuvant Dose Dense MVAC X 6 cycles compared with GC X 4 cycles improved OS at 5 years. Better survival was shown with higher cumulative dose of cisplatin. More cisplatin improves outcome.
- Enfortumab Vedtin + Pembrolizumab is now FDA approved in cisplatin ineligible mUC based on high ORR, DOR and OS.
- Erdafintinib post anti PD(L)-1 treatment in FGFR 3/2 altered mUC improved ORR, PFS and OS compared to chemotherapy.
- ALL patients with mUC need to be tested for FGFR3/2 alterations

2023 ASCO® ANNUAL MEETING

Adjuvant nivolumab plus ipilimumab vs placebo for patients with localized renal cell carcinoma at high risk of relapse after nephrectomy: subgroup analyses from the phase 3 CheckMate 914 (Part A) trial

Robert J. Motzer,[1] Paul Russo,[1] Viktor Grünwald,[2] Yoshihiko Tomita,[3] Philippe Barthélémy,[4] Jeffrey C. Goh,[5] Hernan Javier Cutuli,[6] Steven Blum,[7] Sai Vikram Vemula,[7] Burcin Simsek,[7] Julia Spiridigliozzi,[7] Aleksander Chudnovsky,[7] Axel Bex[8,9]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]Clinic for Internal Medicine (Tumor Research) and Clinic for Urology, West-German Cancer Center Essen, University Hospital Essen, Essen, Germany; [3]Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [4]Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [5]ICON Research, South Brisbane, QLD, Australia; [6]Hospital Sirio Libanes, Buenos Aires, Argentina; [7]Bristol Myers Squibb, Princeton, NJ; [8]Netherlands Cancer Institute, Amsterdam, the Netherlands; [9]University College London, London, UK

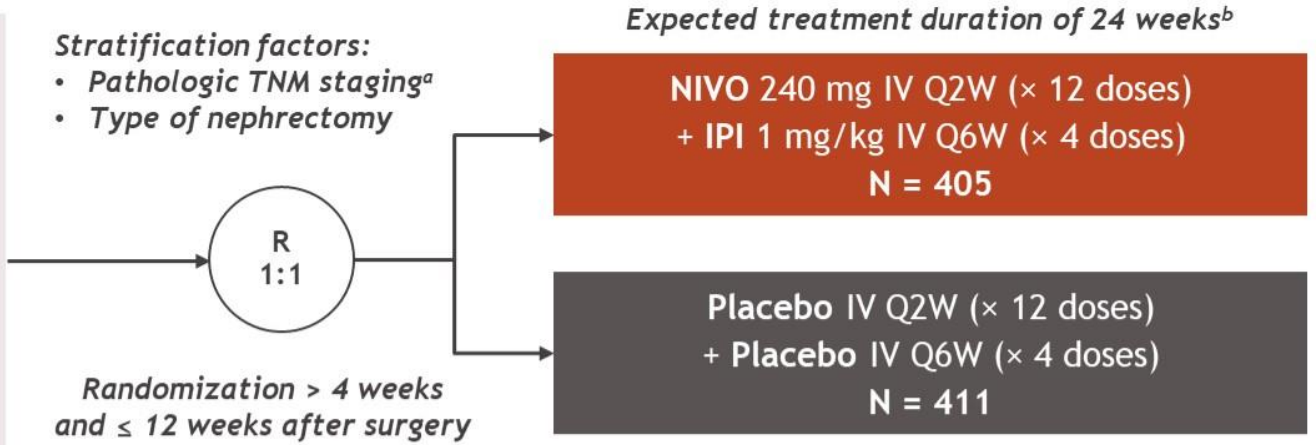
Abstract number 4506

Study design and treatment schedule (Part A)

N = 816

Key inclusion criteria[1,2]

- Radical or partial nephrectomy
- Predominant clear cell histology
- Pathologic TNM staging:
  - pT2a, G3 or G4, N0 M0/pT2b, G any, N0 M0
  - pT3, G any, N0 M0
  - pT4, G any, N0 M0/pT any, G any, N1 M0
- No evidence of residual disease or metastases after nephrectomy, confirmed by BICR

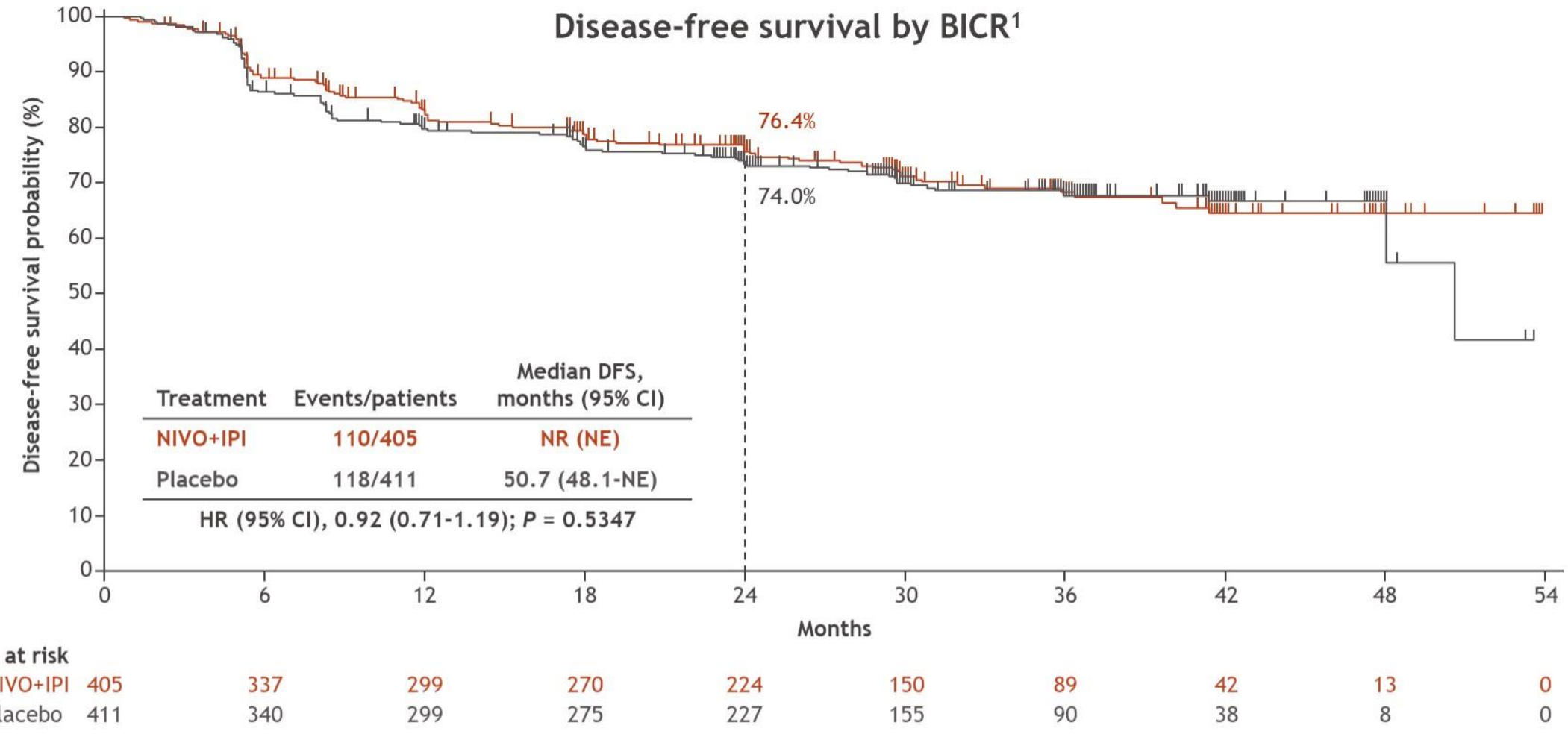


Primary endpoint: DFS by BICR for NIVO+IPI vs placebo
Secondary endpoints: OS for NIVO+IPI vs placebo, safety of NIVO+IPI

Schedule	Cycle 1		Cycle 2		Cycle 3		Cycle 4		Cycle 5		Cycle 6		Cycle 7		Cycle 8		Cycle 9		Cycle 10		Cycle 11		Cycle 12	
Study week	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Dosing[c]	NIVO+IPI		NIVO		NIVO		NIVO+IPI		NIVO		NIVO		NIVO+IPI		NIVO		NIVO		NIVO+IPI		NIVO		NIVO	
	PBO+PBO		PBO		PBO		PBO+PBO		PBO		PBO		PBO+PBO		PBO		PBO		PBO+PBO		PBO		PBO	

Median follow-up, 37.0 months (minimum follow-up, 15.4 months).
[a]Stratification by TNM staging (pT2a, G3 or G4, N0 M0 or pT2b, G any, N0 M0 vs pT3, G any, N0 M0 vs pT4, G any, N0 M0 or pT any, G any, N1 M0). [b]Treatment could be extended up to 36 weeks to accommodate dose delays. [c]Dose given on day 1 of each cycle.
G, grade; IV, intravenously; PBO, placebo; Q×W, every × weeks.
1. ClinicalTrials.gov. Accessed April 28, 2023. https://clinicaltrials.gov/ct2/show/NCT03138512. 2. Motzer RJ, et al. *Lancet* 2023;401:821-832.

Adjuvant NIVO+IPI in CheckMate 914 (primary endpoint)



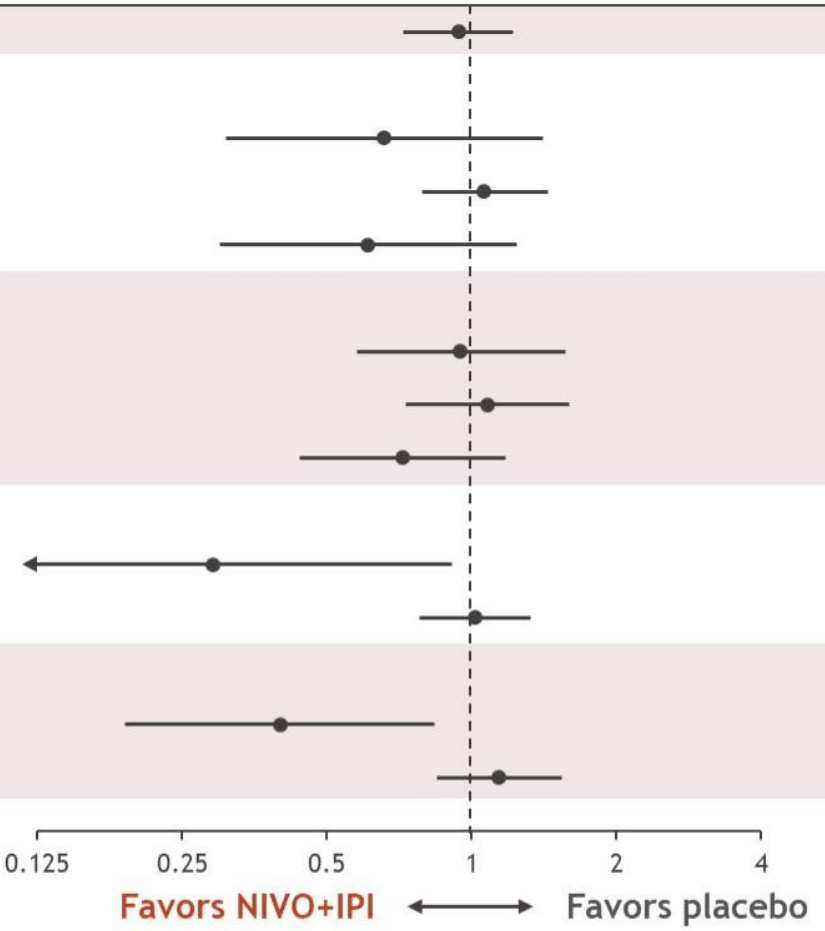
As the DFS endpoint was not met, no formal OS analysis was performed (in total, there were 33 deaths in the NIVO+IPI arm and 28 deaths in the placebo arm).

1. Motzer RJ, et al. *Lancet* 2023;401:821-832.

CI, confidence interval; HR, hazard ratio. NE, not estimable; NR, not reached.

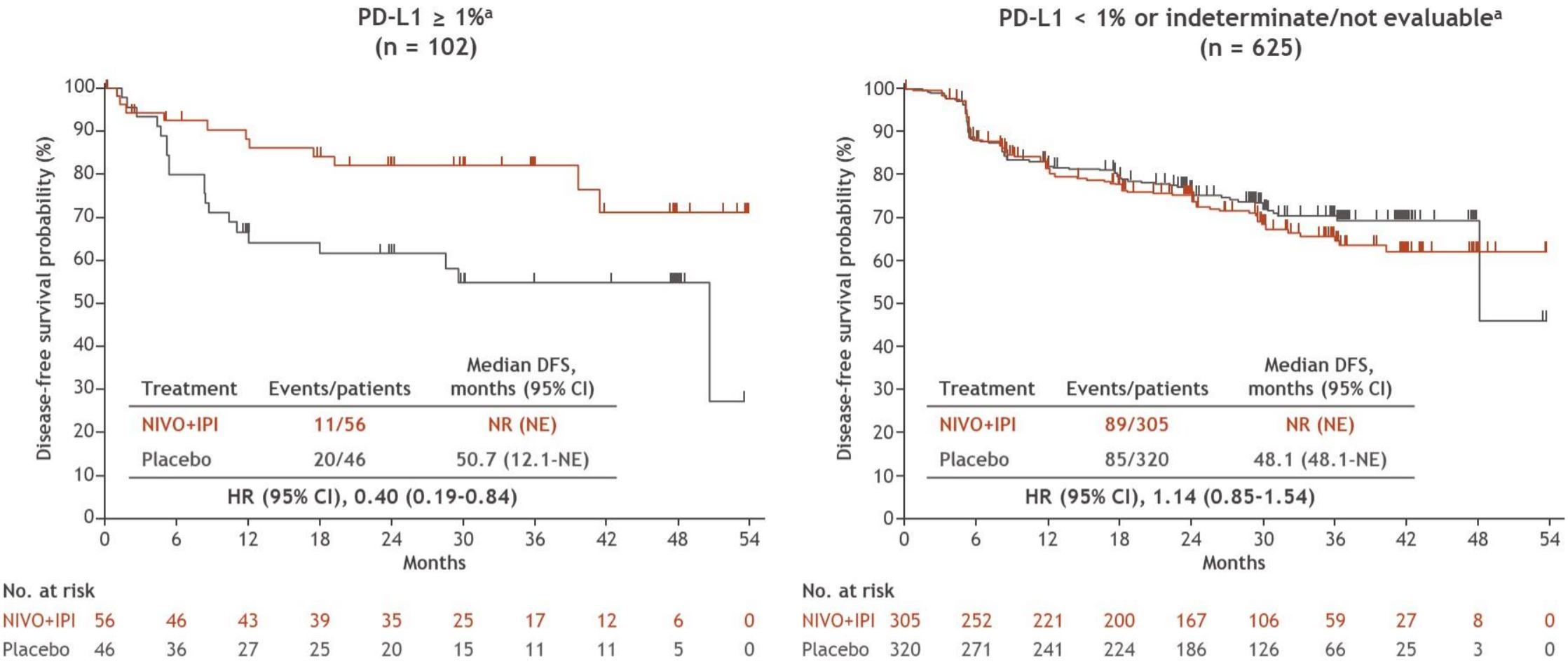
Disease-free survival per BICR *in select subgroups*

Subgroup	NIVO+IPI Events/no. of patients	Placebo Events/no. of patients	Unstratified HR for DFS (95% CI)
Overall	110/405	118/411	0.94 (0.72-1.22)
TNM staging per CRF			
pT2a, G3 or G4, N0 M0/pT2b, G any, N0 M0	11/59	17/58	0.66 (0.31-1.41)
pT3, G any, N0 M0	85/313	83/317	1.06 (0.79-1.44)
pT4, G any, N0 M0/pT any, G any, N1 M0	14/32	18/35	0.61 (0.30-1.24)
RCC pathology grade[a] per CRF			
G1-2	29/136	33/147	0.95 (0.58-1.57)
G3	54/189	47/173	1.08 (0.73-1.60)
G4	27/80	38/91	0.72 (0.44-1.18)
Sarcomatoid features			
Yes	4/19	12/21	0.29 (0.09-0.91)
No	106/386	106/390	1.02 (0.78-1.33)
Baseline tumor PD-L1 status[b]			
≥ 1%	11/56	20/46	0.40 (0.19-0.84)
< 1% or indeterminate/not evaluable	89/305	85/320	1.14 (0.85-1.54)



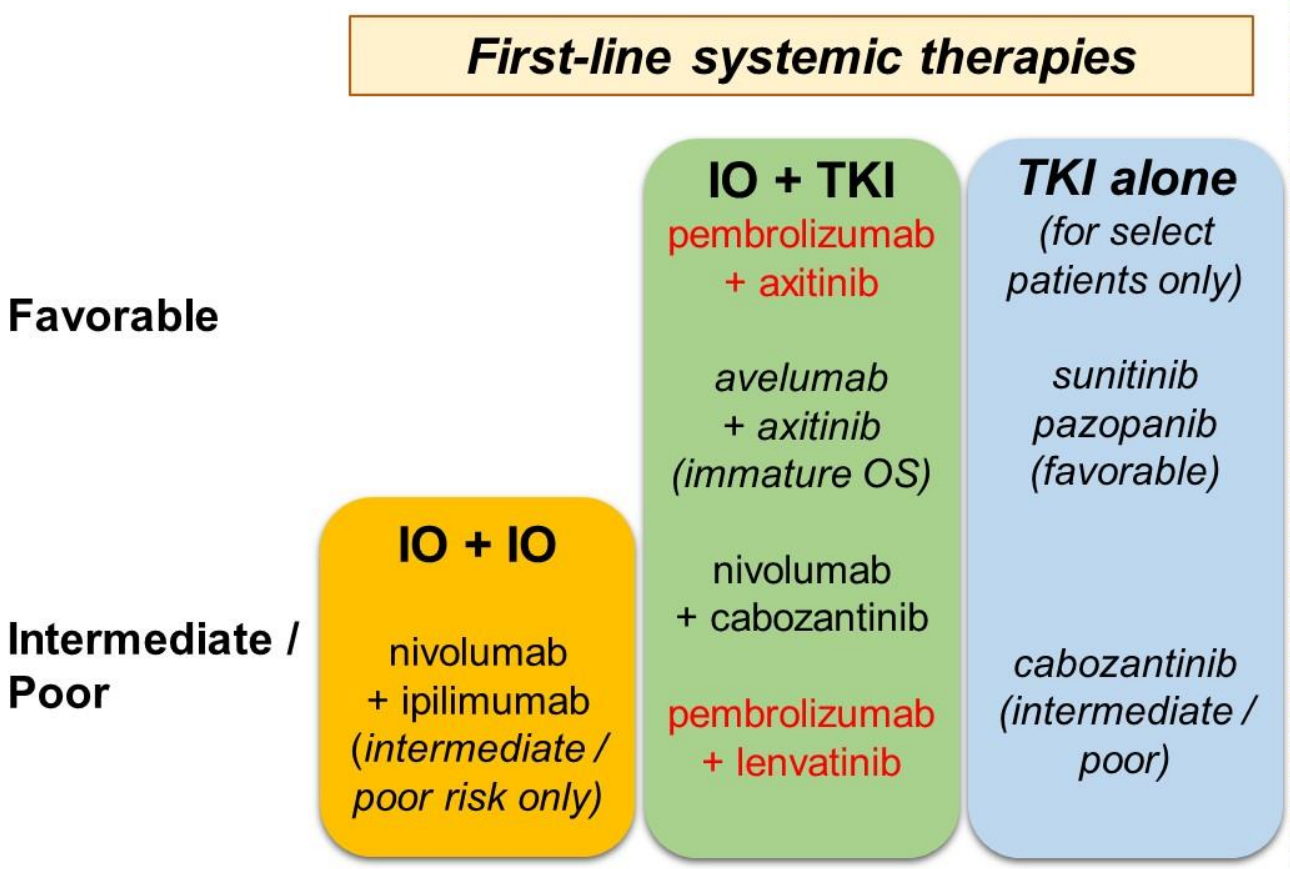
[a]Data were reported using the Fuhrman grading system for the duration of enrollment. If assessment of RCC pathology grade was performed using the WHO/ISUP system, grade was correlated back to the Fuhrman system in order to assess eligibility. [b]Data by tumor PD-L1 expression were analyzed from a March 2023 database lock as these data were not available from the July database lock used for all other data reported in this presentation.

Disease-free survival per BICR *in patients by PD-L1 expression*



[a]Data by tumor PD-L1 expression were analyzed from a March 2023 database lock as these data were not available from the July database lock used for all other data reported in this presentation.

Discussion for oral abstract session: genitourinary cancer – kidney and bladder



Abstract LBA4501 (Rini):
Pembrolizumab plus axitinib versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma: 5-year analysis of KEYNOTE-426.

Abstract 4502 (Hutson):
Final prespecified overall survival (OS) analysis of CLEAR: 4-year follow-up of lenvatinib plus pembrolizumab (L+P) vs sunitinib (S) in patients (pts) with advanced renal cell carcinoma (aRCC).

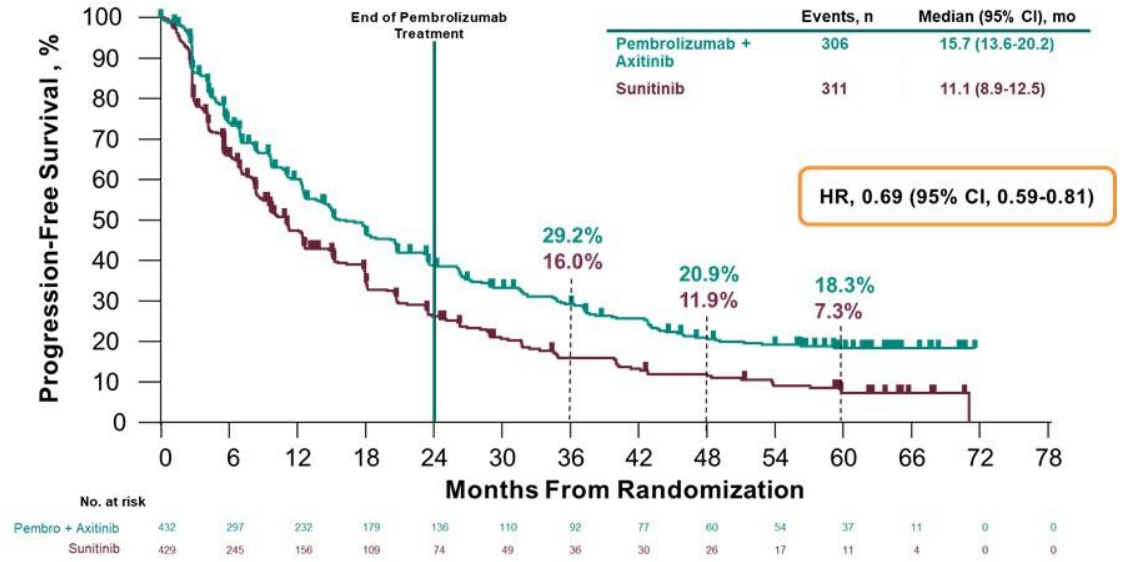
PRESENTED BY: David A. Braun, MD, PhD @BraunMDPhD

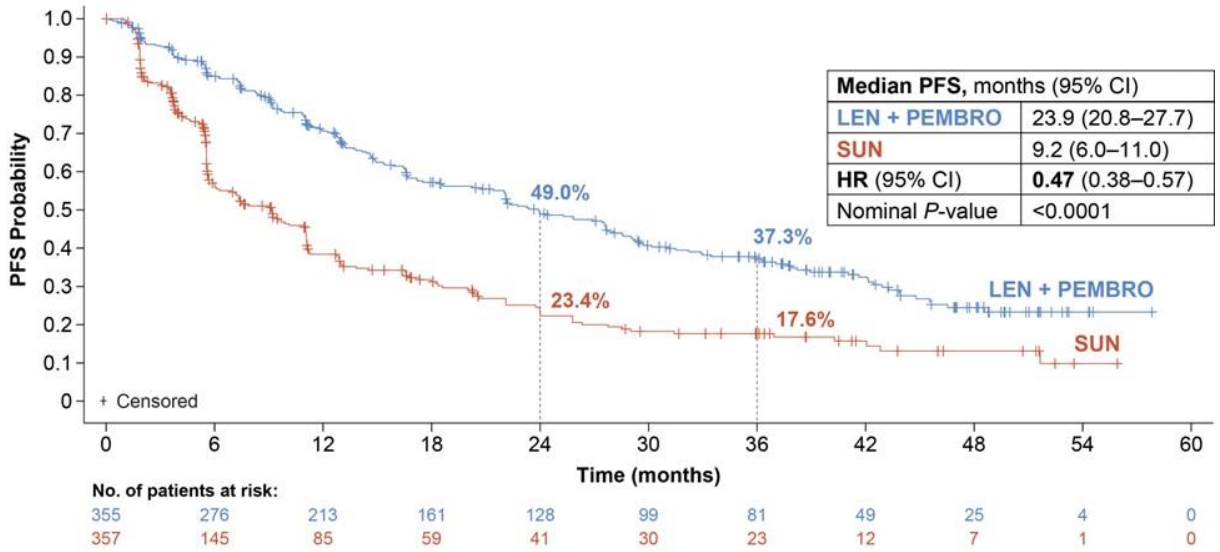
Is IO+TKI superior to TKI alone for front-line ccRCC treatment? Yes (↑PFS)

KN-426
(pembrolizumab+axitinib)

Strongly positive for PFS

CLEAR
(pembrolizumab+lenvatinib)

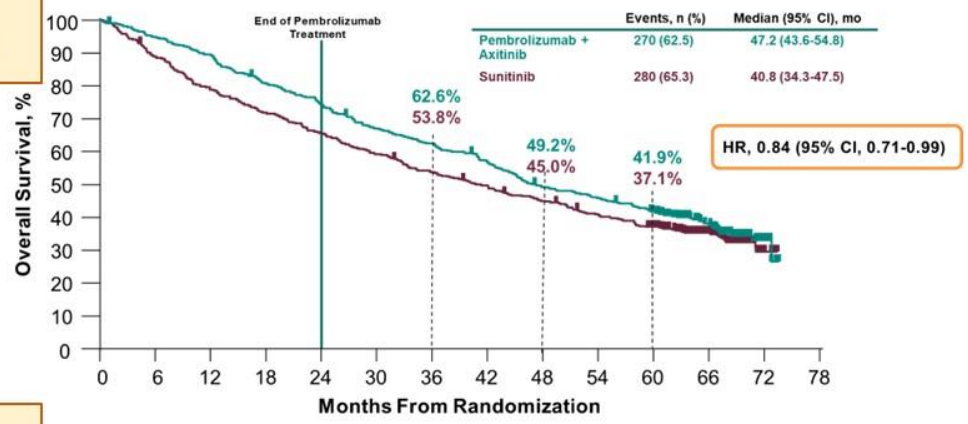




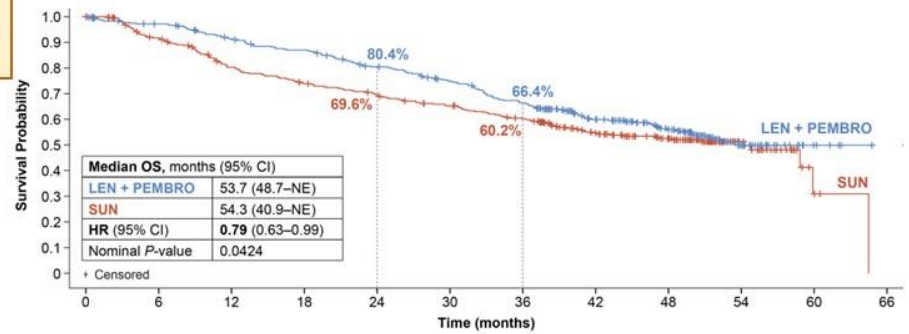
Rini, ASCO 2023, LBA4501; Motzer & Hutson, ASCO 2023, 4501.

Is IO+TKI superior to TKI alone for front-line ccRCC treatment? Yes (↑OS)

KN-426
(pembrolizumab+axitinib)



CLEAR
(pembrolizumab+lenvatinib)



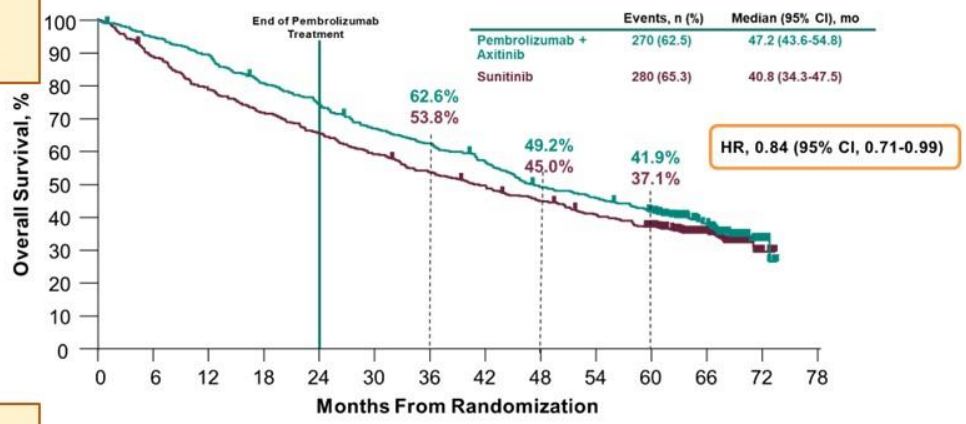
*Positive for OS, but questions around **durability****

Rini, ASCO 2023, LBA4501; Motzer & Hutson, ASCO 2023, 4501.

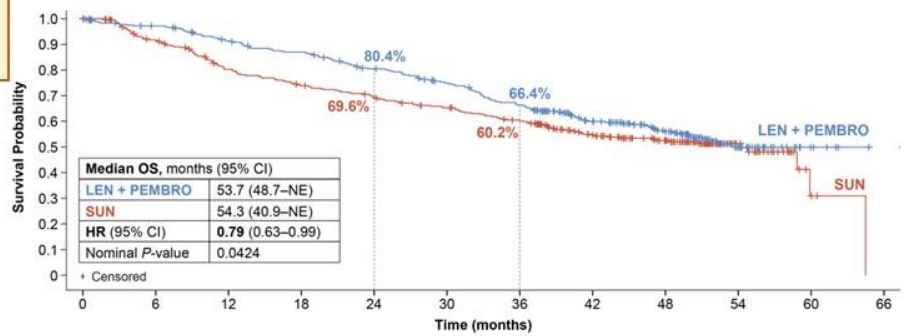
*Imbalance in subsequent therapies

Is IO+TKI superior to TKI alone for front-line ccRCC treatment? Yes (↑OS)

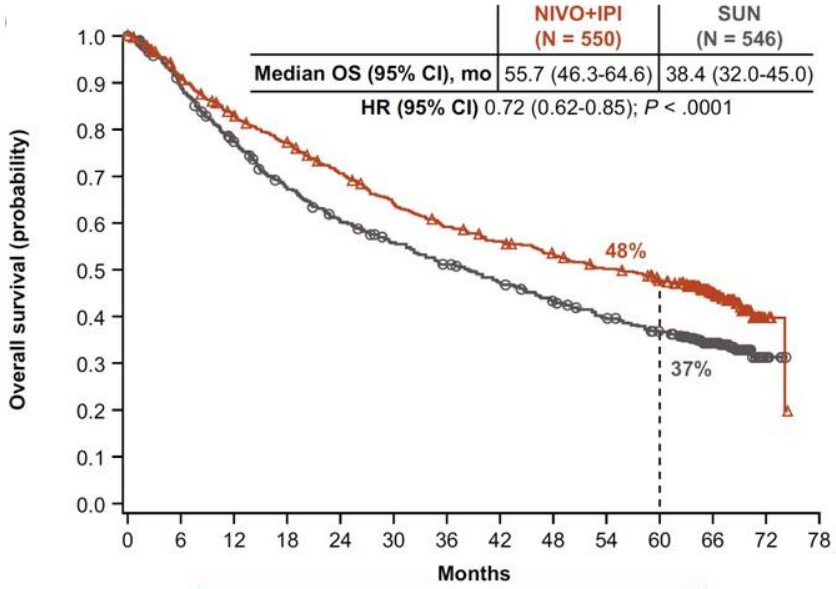
KN-426
(pembrolizumab+axitinib)



CLEAR
(pembrolizumab+lenvatinib)



CM-214
(nivolumab+ipilimumab)

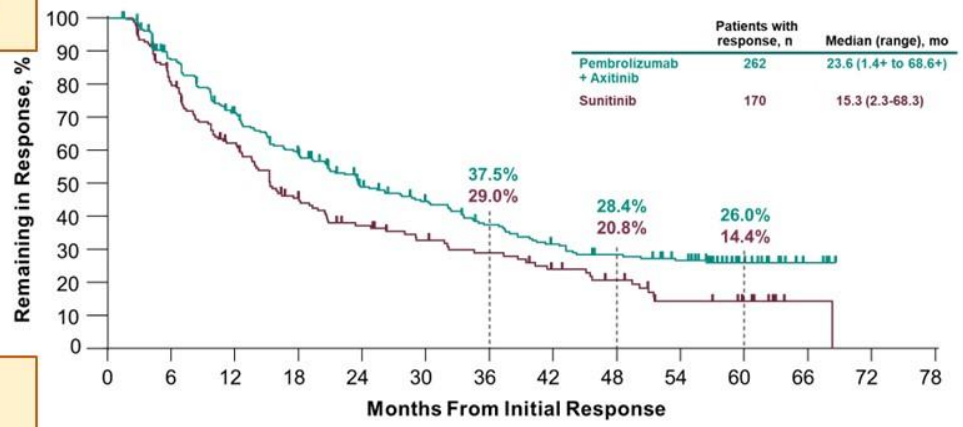


IO+IO maintains OS benefit over time

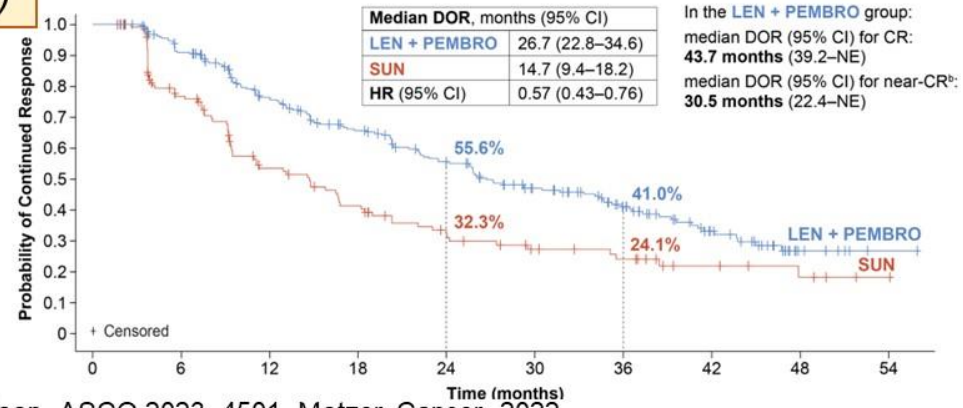
Rini, ASCO 2023, LBA4501; Motzer & Hutson, ASCO 2023, 4501, Motzer, Cancer, 2022.

Are IO+TKI responses durable? Maybe

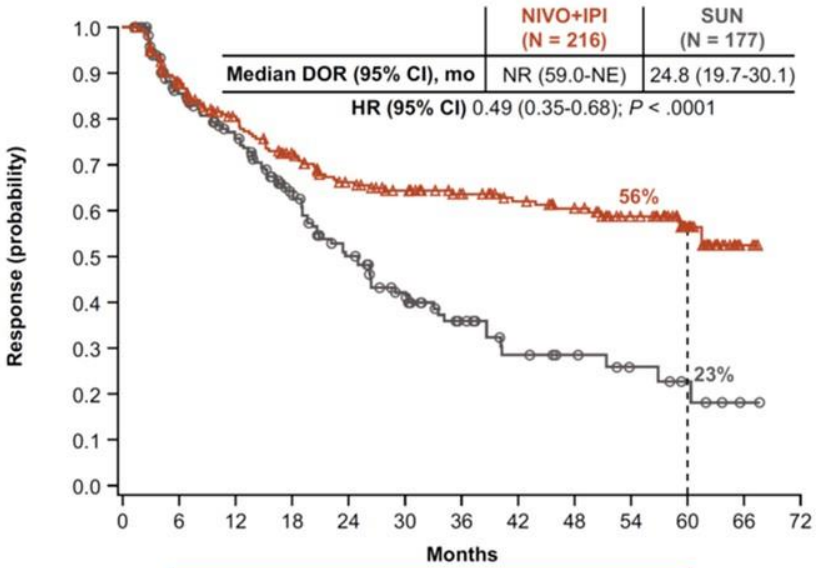
KN-426
(pembrolizumab+axitinib)



CLEAR
(pembrolizumab+lenvatinib)



CM-214
(nivolumab+ipilimumab)

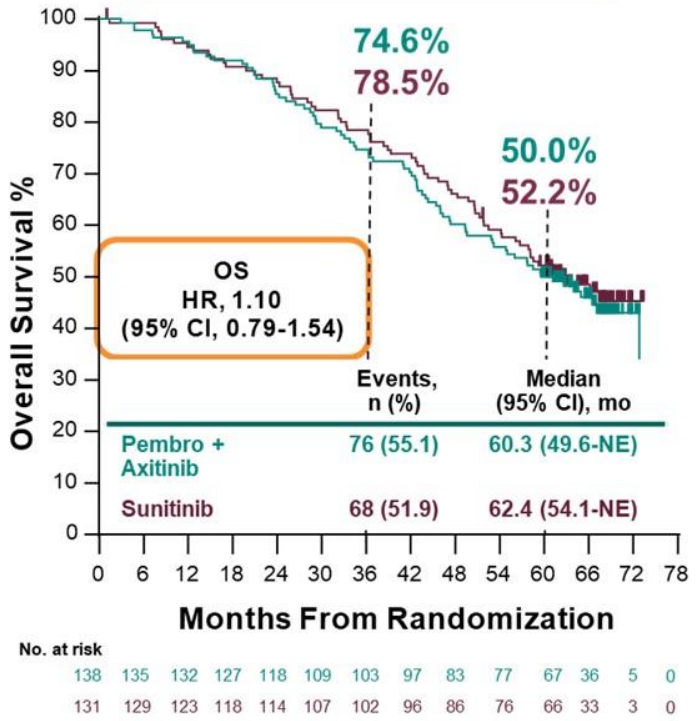


>50% of IO+IO response are durable

Rini, ASCO 2023, LBA4501; Motzer & Hutson, ASCO 2023, 4501, Motzer, Cancer, 2022.

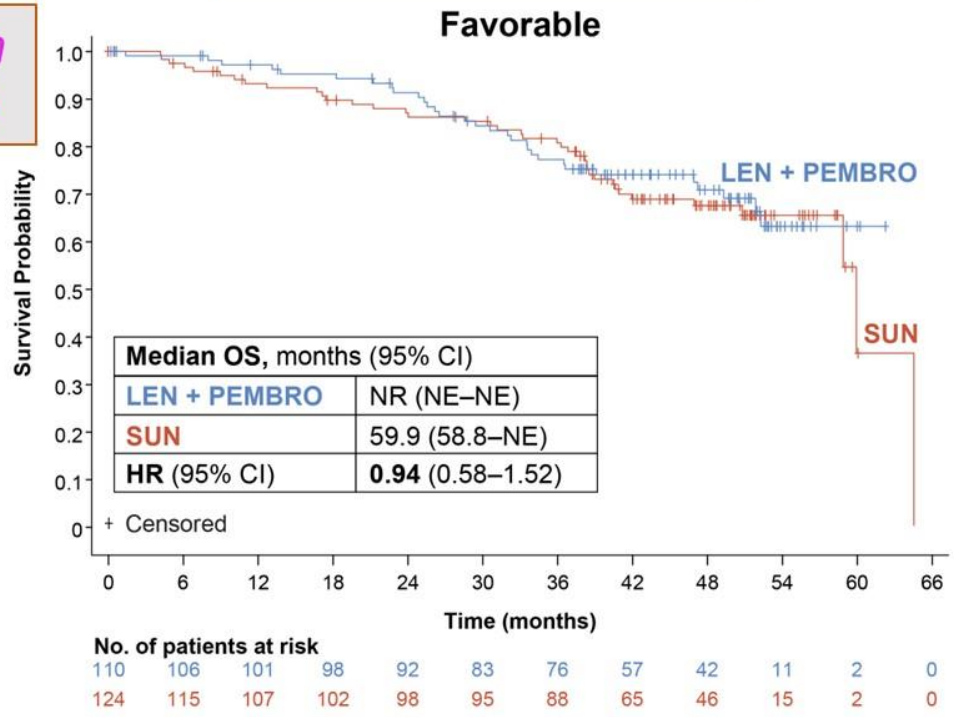
Does IO+TKI improve OS for patients with IMDC favorable risk RCC? Probably not

KN-426
(pembrolizumab+axitinib)



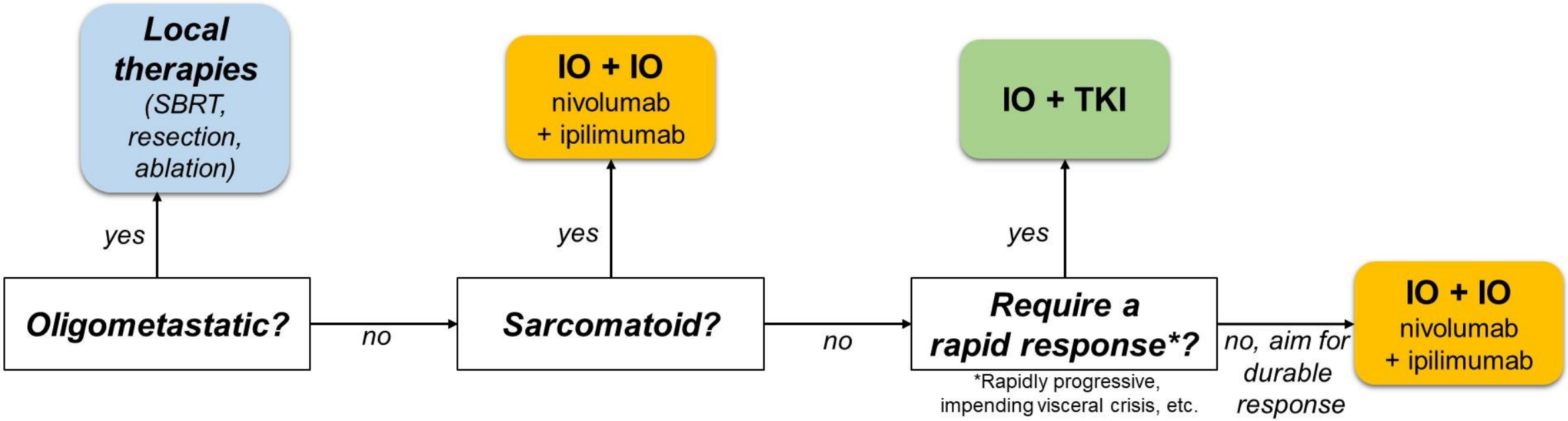
No OS benefit in IMDC favorable

CLEAR
(pembrolizumab+lenvatinib)



Rini, ASCO 2023, LBA4501; Motzer & Hutson, ASCO 2023, 4501.

My front-line ccRCC treatment paradigm*



***DISCLAIMER: views are my own**. Assumes clear cell RCC, patient who requires treatment (not active surveillance), no contraindication to IO, and IMDC intermediate/poor risk disease. Actual treatment decisions made collaboratively with the patient.*

Abstract LBA4500 (Choueiri): CONTACT-03

Clinical Question:	Does “re-challenge” with ICI+TKI improve outcomes vs TKI alone in patients previously treated with ICI-based therapy?

PRESENTED BY: David A. Braun, MD, PhD @BraunMDPhD

CONTACT-03: atezolizumab + cabozantinib vs cabozantinib alone in ICI-refractory RCC

- **Eligibility**
  - Advanced clear cell or non-clear cell
  - Progression on or after ICI (adjuvant, 1st or 2nd line)
- **Number of patients**
  - 522 randomized
- **Treatment**
  - Cabozantinib 60mg daily vs
    Cabozantinib **60**mg daily + atezolizumab 1200mg q3w
- **Key endpoints:**
  - Primary: PFS (central), OS
  - Secondary: PFS (investigator), ORR, DOR, safety

Characteristic	Atezo +Cabo N = 263	Cabo N = 259
Histology		
Clear cell (no sarcomatoid)	78.7%	77.2%
Non-clear cell (no sarc)	11.4%	12.0%
Any sarcomatoid	9.5%	10.8%
Most recent ICI		
Adjuvant	0.4%	0.4%
1st line	54.8%	51.0%
2nd line	44.9%	47.9%

Very few post-adjuvant patients

Choueiri, ASCO 2023, LBA4500.

Does re-challenge with ICI improve response? No

No difference in:
- *Response*
- *Primary PD rate*
- *Disease control*
- *Duration of response*

	RECIST 1.1 per central review[a]		RECIST 1.1 per investigator[a]	
	Atezo + Cabo (n=259)	Cabo (n=254)	Atezo + Cabo (n=263)	Cabo (n=259)
Confirmed objective response, n, (%) [95% CI]	105 (40.5) [34.5, 46.8]	104 (40.9) [34.8, 47.3]	100 (38.0) [32.1, 44.2]	108 (41.7) [35.6, 48.0]
Complete response, n (%)	0	2 (0.8)	4 (1.5)	2 (0.8)
Partial response, n (%)	105 (40.5)	102 (40.2)	96 (36.5)	106 (40.9)
Stable disease, n (%)	131 (50.6)	121 (47.6)	127 (48.3)	120 (46.3)
Progressive disease, n (%)	11 (4.2)	13 (5.1)	24 (9.1)	17 (6.6)
Not evaluable or missing, n (%)	12 (4.6)	16 (6.3)	12 (4.6)	14 (5.4)
Ongoing response at data cutoff, n/N (%)[b]	53/105 (50.5)	55/104 (52.9)	58/100 (58.0)	48/108 (44.4)
Median duration of response (range), mo	12.7 (2.1+ to 22.9+)	14.8 (2.3+ to 25.6+)	NE (2.1+ to 23.2+)	12.2 (2.1+ to 25.6+)

Choueiri, ASCO 2023, LBA4500.

Is cabozantinib effective after prior ICI? Yes

METEOR: ORR 21%

CaboPoint: ORR 29.5%

	RECIST 1.1 per central review[a]		RECIST 1.1 per investigator[a]	
	Atezo + Cabo (n=259)	Cabo (n=254)	Atezo + Cabo (n=263)	Cabo (n=259)
Confirmed objective response, n, (%) [95% CI]	105 (40.5) [34.5, 46.8]	104 (40.9) [34.8, 47.3]	100 (38.0) [32.1, 44.2]	108 (41.7) [35.6, 48.0]
Complete response, n (%)	0	2 (0.8)	4 (1.5)	2 (0.8)
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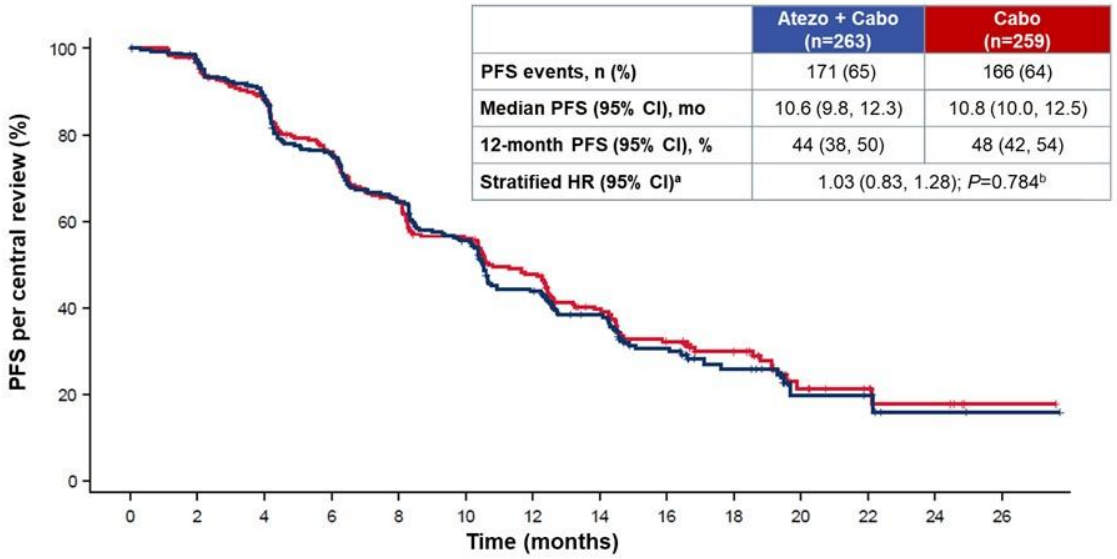
Not evaluable or missing, n (%)	12 (4.6)	16 (6.3)	12 (4.6)	14 (5.4)
Ongoing response at data cutoff, n/N (%)[b]	53/105 (50.5)	55/104 (52.9)	58/100 (58.0)	48/108 (44.4)
Median duration of response (range), mo	12.7 (2.1+ to 22.9+)	14.8 (2.3+ to 25.6+)	NE (2.1+ to 23.2+)	12.2 (2.1+ to 25.6+)

Choueiri, ASCO 2023, LBA4500; Choueiri, N Engl J Med, 2015; Albiges, ASCO GU 2023.

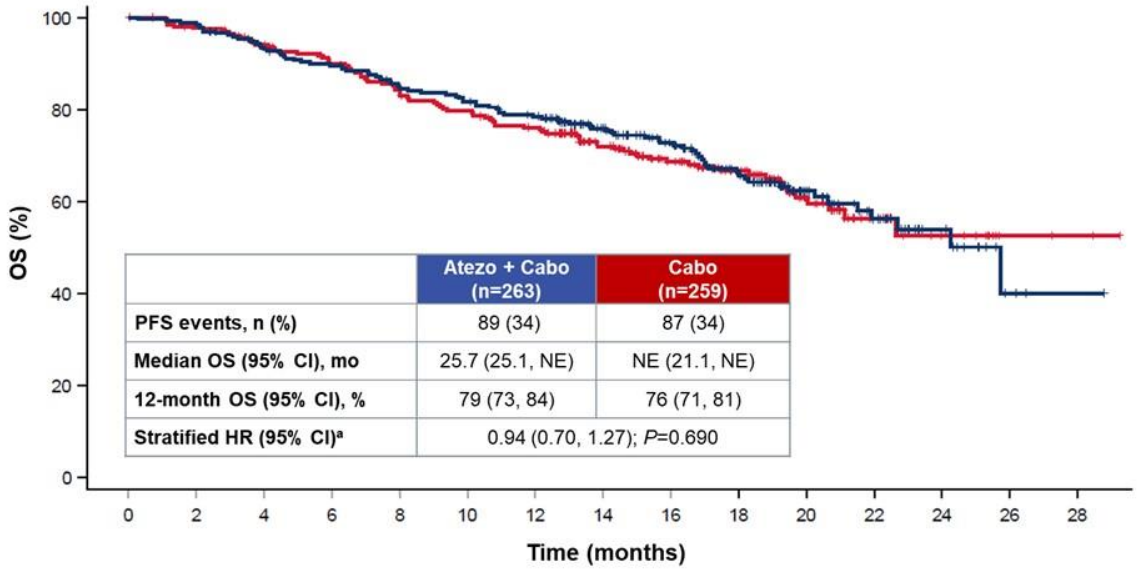
Does re-challenge with ICI improve survival? No

PFS



	Atezo + Cabo (n=263)	Cabo (n=259)
PFS events, n (%)	171 (65)	166 (64)
Median PFS (95% CI), mo	10.6 (9.8, 12.3)	10.8 (10.0, 12.5)
12-month PFS (95% CI), %	44 (38, 50)	48 (42, 54)
Stratified HR (95% CI)[a]	1.03 (0.83, 1.28); *P*=0.784[b]	

OS



	Atezo + Cabo (n=263)	Cabo (n=259)
PFS events, n (%)	89 (34)	87 (34)
Median OS (95% CI), mo	25.7 (25.1, NE)	NE (21.1, NE)
12-month OS (95% CI), %	79 (73, 84)	76 (71, 81)
Stratified HR (95% CI)[a]	0.94 (0.70, 1.27); *P*=0.690	

Choueiri, ASCO 2023, LBA4500.

Is re-challenge with ICI+TKI more toxic than TKI alone? Yes

Adverse event, n (%)	Atezo + Cabo (n=262)	Cabo (n=256)
Any-cause AE	262 (100)	254 (99.2)
Any-cause treatment-related AE	252 (96.2)	249 (97.3)
Grade 3 or 4 AE	177 (67.6)	158 (61.7)
Grade 3 or 4 treatment-related AE	145 (55.3)	121 (47.3)
Death due to AE	17 (6.5)	9 (3.5)
Death due to treatment-related AE	3 (1.1)[a]	0
Serious AE	126 (48.1)	84 (32.8)
Serious treatment-related AE	63 (24.0)	30 (11.7)
AE leading to withdrawal from a trial drug	41 (15.6)	10 (3.9)
AE leading to withdrawal from atezo	29 (11.1)	–
AE leading to withdrawal from cabo	25 (9.5)	10 (3.9)
AE leading to interruption or reduction of a trial drug	240 (91.6)	223 (87.1)
AE leading to interruption of atezo[b]	159 (60.7)	–
AE leading to interruption or reduction of cabo	234 (89.3)	223 (87.1)

Choueiri, ASCO 2023, LBA4500.

First-Line Lenvatinib Plus Pembrolizumab Treatment Across Non–Clear Cell Renal Cell Carcinomas: Results of the Phase 2 KEYNOTE-B61 Study

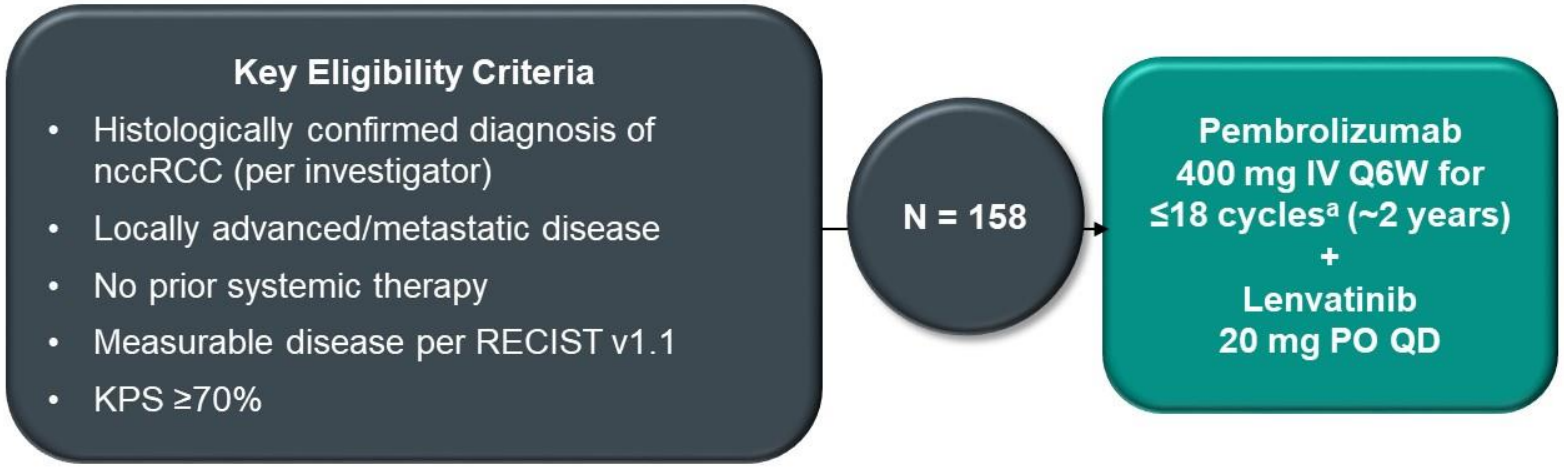
Chung-Han Lee[1]; Howard Gurney[2]; Vagif Atduev[3]; Cristina Suarez[4]; Miguel A. Climent[5]; David Pook[6]; Piotr Tomczak[7]; Philippe Barthelemy[8]; Jae Lyun Lee[9]; Taron Nalbandian[10]; Viktor Stus[11]; Thomas Ferguson[12]; Pawel Wiechno[13]; Erhan Gokmen[14]; Louis Lacombe[15]; Craig Gedye[16]; Joseph E. Burgents[17]; Manish Sharma[17]; Xiang Peng[17]; Laurence Albiges[18]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Macquarie University, Sydney, NSW, Australia; [3]Volga District Medical Center, Federal Medical-Biological Agency, Nizhny Novgorod, Russia; [4]Medical Oncology, Vall d´Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d´Hebron, Vall d´Hebron Barcelona Hospital Campus, Barcelona, Spain; [5]Instituto Valenciano de Oncología, València, Spain; [6]Monash Health, Melbourne, VIC, Australia; [7]Poznan University of Medical Sciences, Poznan, Poland; [8]Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [10]Regional Cancer Center, Kharkiv, Ukraine; [11]Dnipro State Medical University, Dnipro, Ukraine; [12]Fiona Stanley Hospital, Perth, WA, Australia; [13]Oncology Center-Institute Marii Sklodowskiej-Curie, Warszawa, Poland; [14]Ege University Medical Faculty, Izmir, Turkey; [15]Centre de Recherche du CHU de Québec, Québec City, QC, Canada; [16]University of Newcastle, Callaghan, NSW, Australia; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Gustave Roussy, Villejuif, France

Background/Study Design of KEYNOTE-B61

- Immunotherapy-based combinations including pembrolizumab plus lenvatinib are standard of care for first-line clear cell RCC,[1] however these combinations are not well characterized in non–clear cell RCC
- Non–clear cell RCC is a heterogenous group of aggressive tumors with limited treatment options[2,3]
- Pembrolizumab plus lenvatinib showed antitumor activity in patients with advanced non–clear cell RCC who had opportunity for at least 24 weeks of follow-up (n = 82) in the initial analysis of the single-arm, phase 2 KEYNOTE-B61 (NCT04704219) study[4]

Tumor Assessments
- 12 weeks from allocation, then Q6W for 54 weeks, then Q12W thereafter

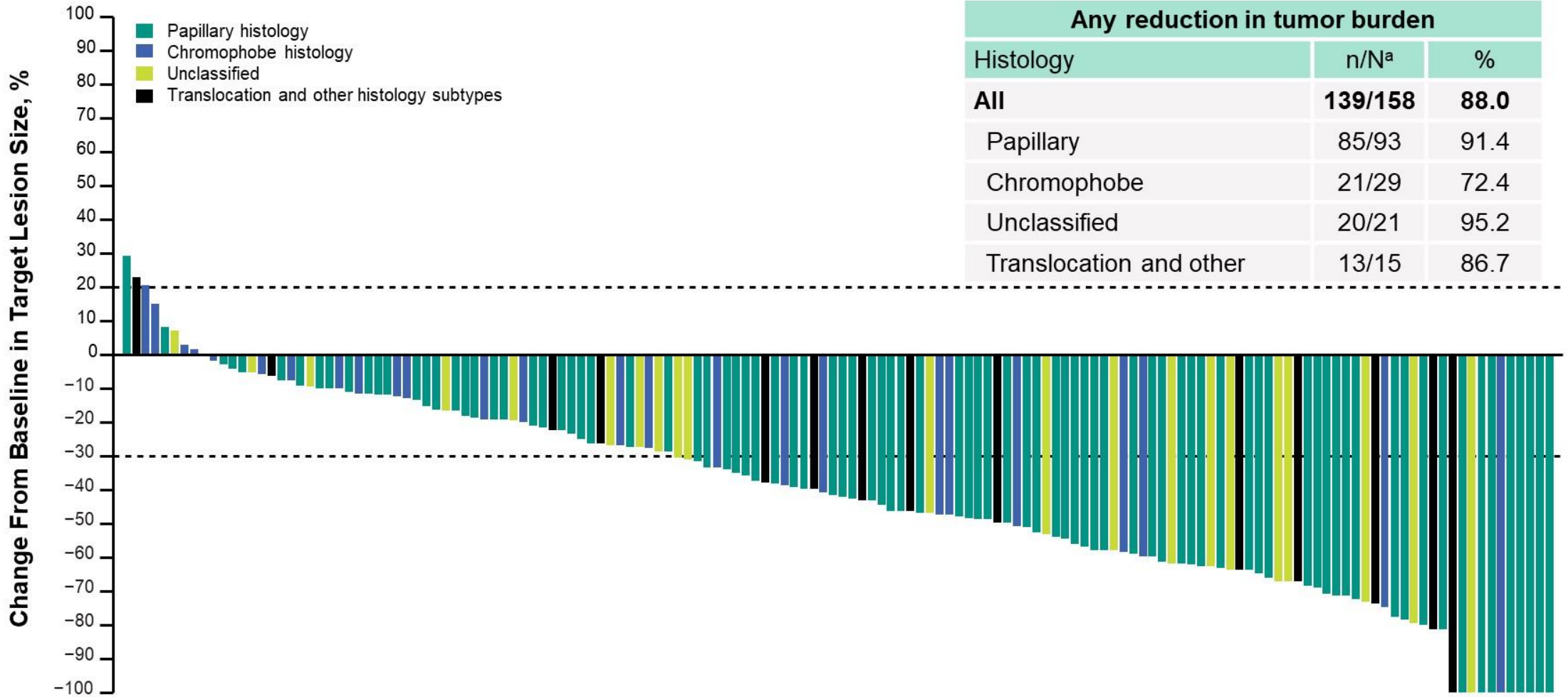


End Points
- Primary: ORR per RECIST v1.1 by BICR
- Secondary: CBR, DCR, DOR, and PFS per RECIST v1.1 by BICR; OS; safety and tolerability

BICR, blinded independent central review; CBR, clinical benefit rate; DCR, disease control rate; DOR, duration of response; IV, intravenously; KPS, Karnofsky Performance Status score; nccRCC, non–clear cell renal cell carcinoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; Q6W, every 6 weeks; Q12W, every 12 weeks; QD, every day; RCC, renal cell carcinoma.

1. Motzer R et al. *N Engl J Med*. 2021;384:1289-1300. 2. Escudier B et al. *Ann Oncol*. 2019;30:706-720. 3. Hsieh JJ et al. Nat Rev Dis Primers. 2017;3:17009. 4. Albiges L et al. *Ann Oncol*. 2022;suppl 7:S660-680.

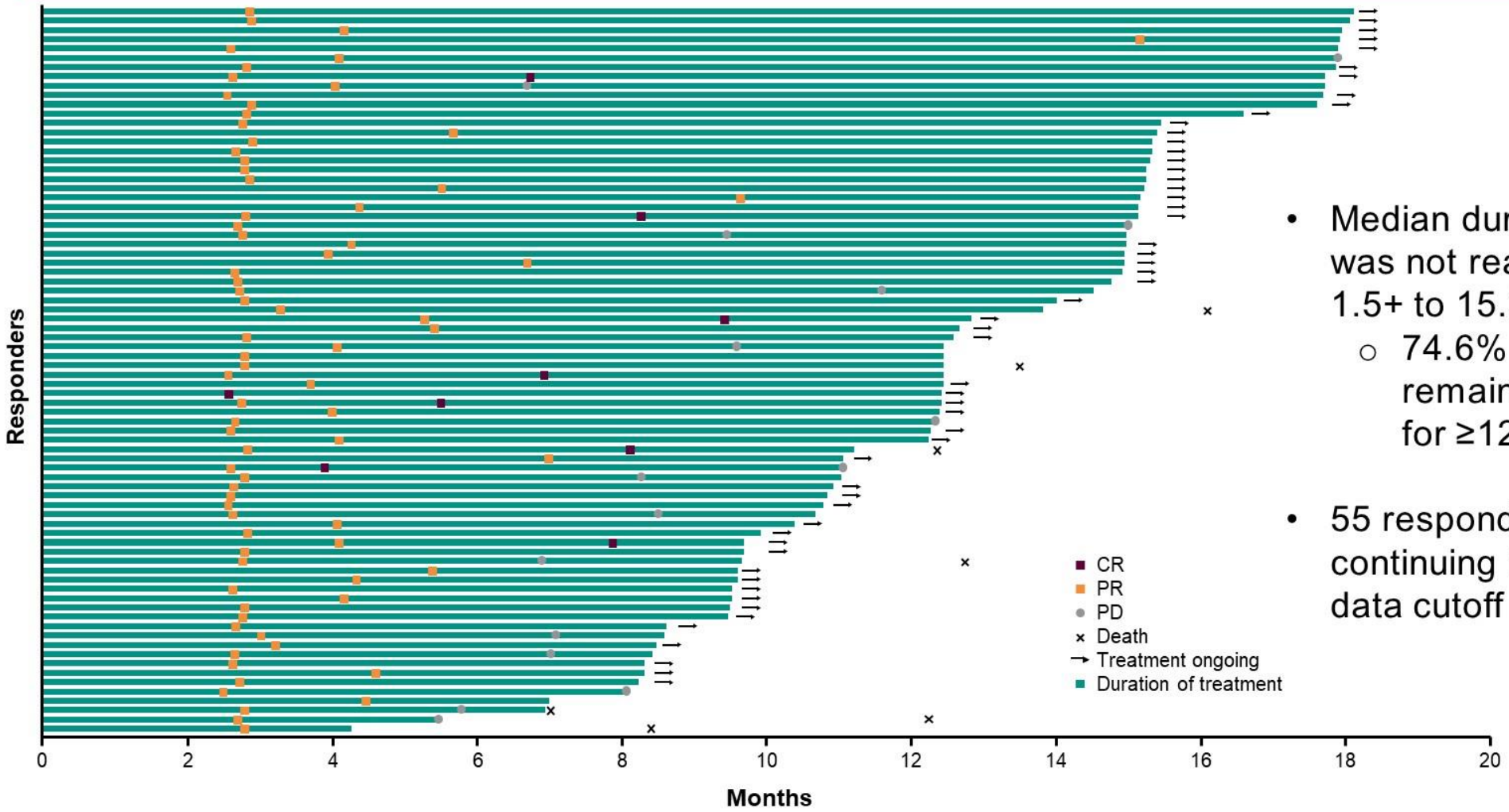
Best Percentage Change From Baseline in Target Lesion Size by Histology



Any reduction in tumor burden		
Histology	n/N[a]	%
All	**139/158**	**88.0**
Papillary	85/93	91.4
Chromophobe	21/29	72.4
Unclassified	20/21	95.2
Translocation and other	13/15	86.7

[a]148 patients had a baseline and ≥1 postbaseline assessment. Data cutoff date: November 7, 2022.

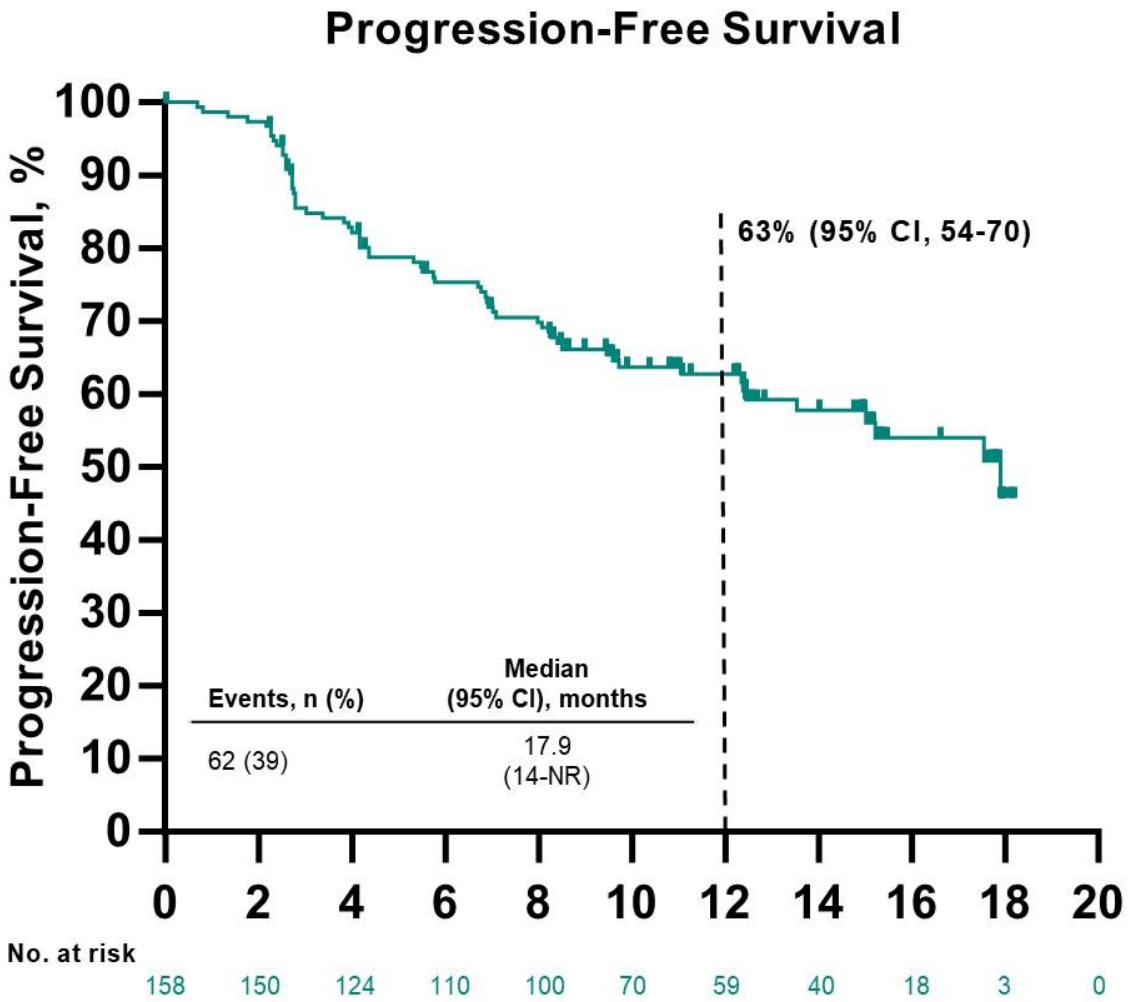
Time to Response and Duration of Response in Patients With a Confirmed Objective Response

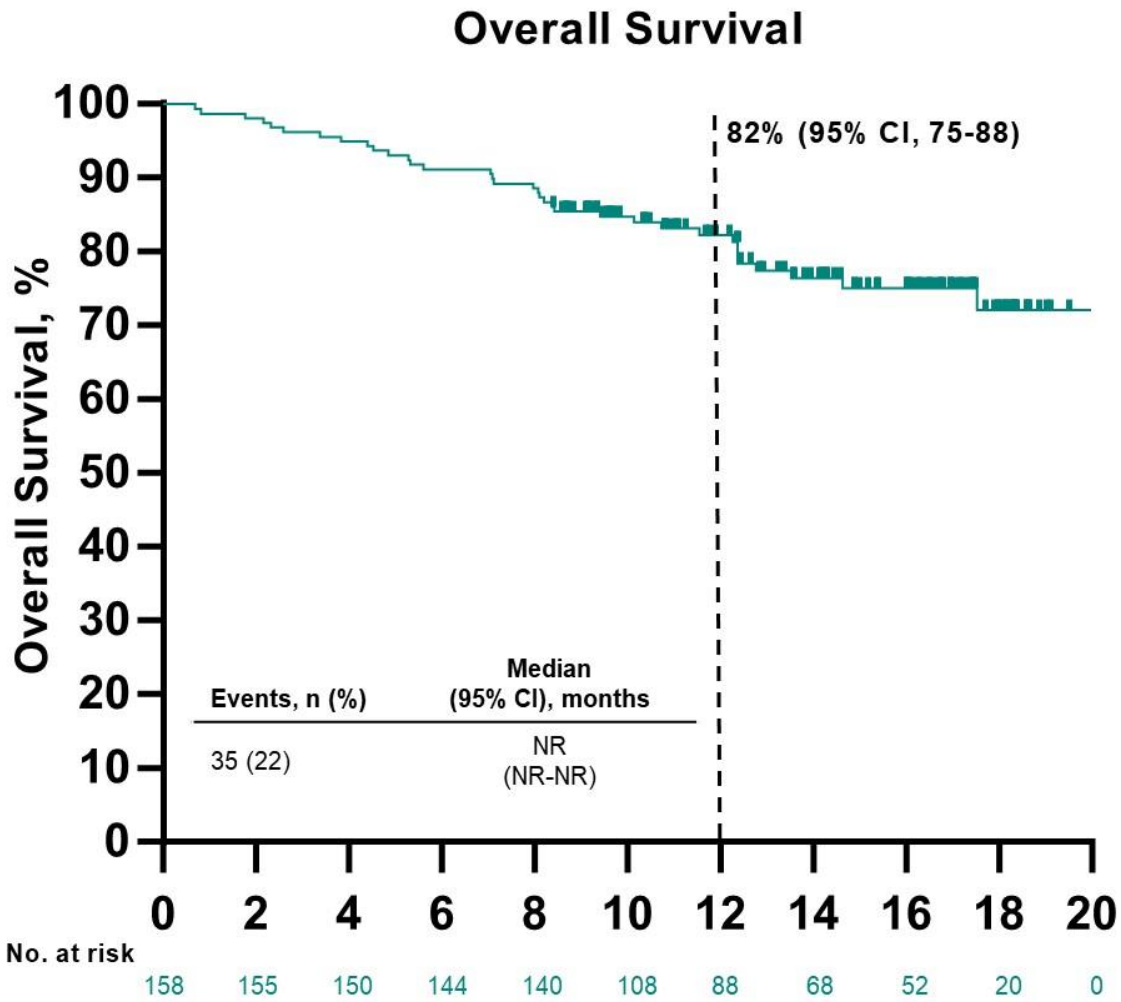


- Median duration of response was not reached (range, 1.5+ to 15.3+)
  - 74.6% of responders remained in response for ≥12 months[a]
- 55 responders were continuing treatment as of data cutoff

+ indicates ongoing response. [a]Per Kaplan-Meier estimates. NR, not reached. Data cutoff date: November 7, 2022.

Progression-Free Survival per RECIST v1.1 and Overall Survival





Data cutoff date: November 7, 2022.

Practice Changers in Renal Cell Carcinoma

- Adjuvant nivolumab and ipilimumab did not improve DFS in high risk RCC post nephrectomy. However analysis suggests that patients with sarcomatoid features or PD-L1+ status may benefit. Think about it.
- Frontline treatment for mccRCC needs to be customized to the patient based on disease extent, histology (sarcomatoid) and goals of therapy (fast response or durable response).
- Anti-PD(L)1 agents should not be used after progression on a prior PD-(L)1 agent. More toxic and may compromise the dosing of TKI agent.
- Pembrolizuamb plus levatanib is active in metastatic non-ccRCC with 12 month PFS of 63% and OS of 82%.

Questions?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