Multidisciplinary Approach to Renal Cell Carcinoma

Ochsner Multidisciplinary Cancer Update

October 9, 2025

Ochsner Health

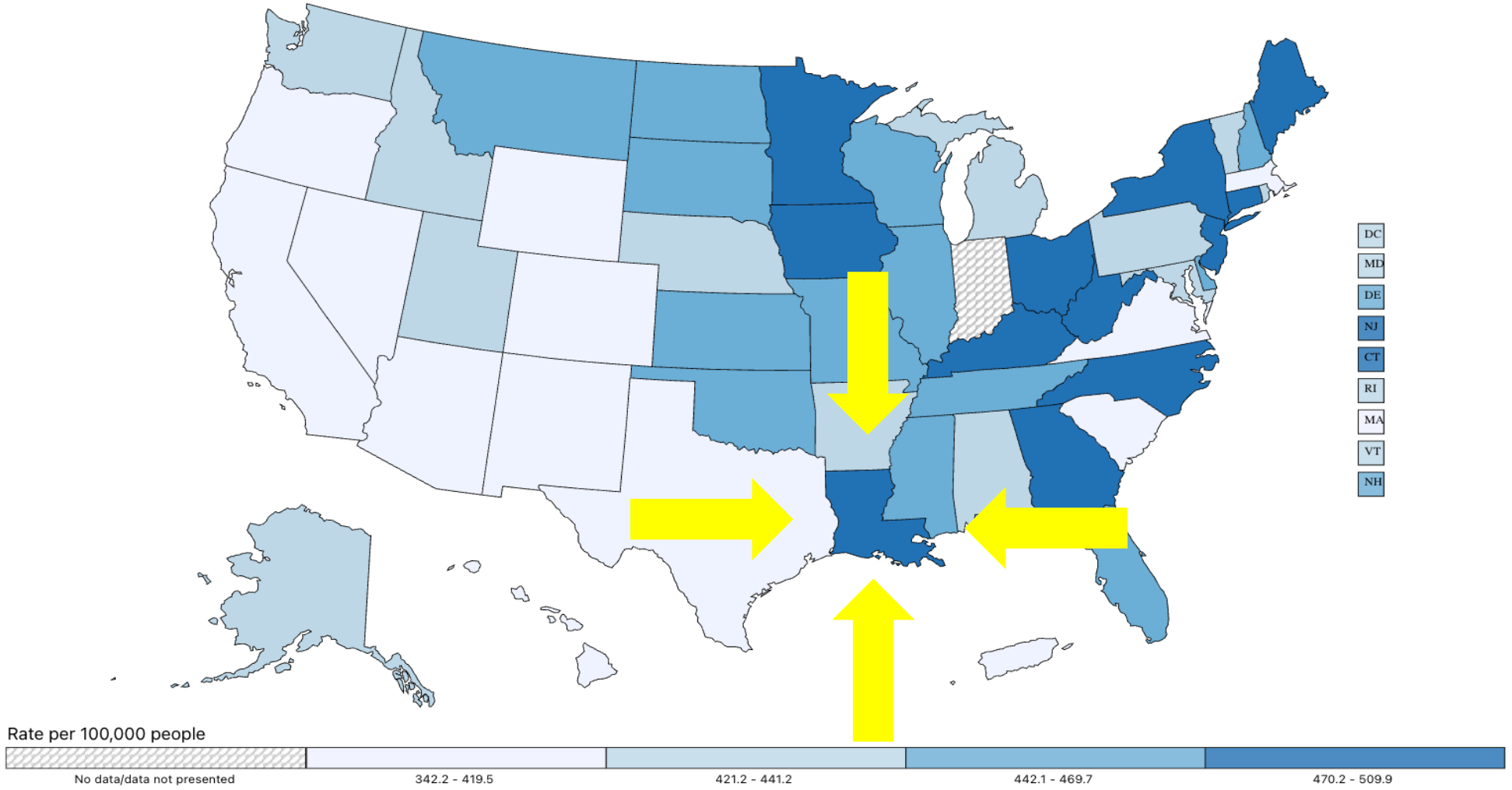
Disclosure

- None

Patient Population

- M>F → relative risk 1.7 men compared to women
- Median age 64
- 8th most common cancer in the US
- ~80000 new cases/annually / ~15,000 deaths
- 20-30% diagnosed with metastatic disease
- 12% 5yr survival in metastatic disease

Rate of New Cancers in the United States, 2021

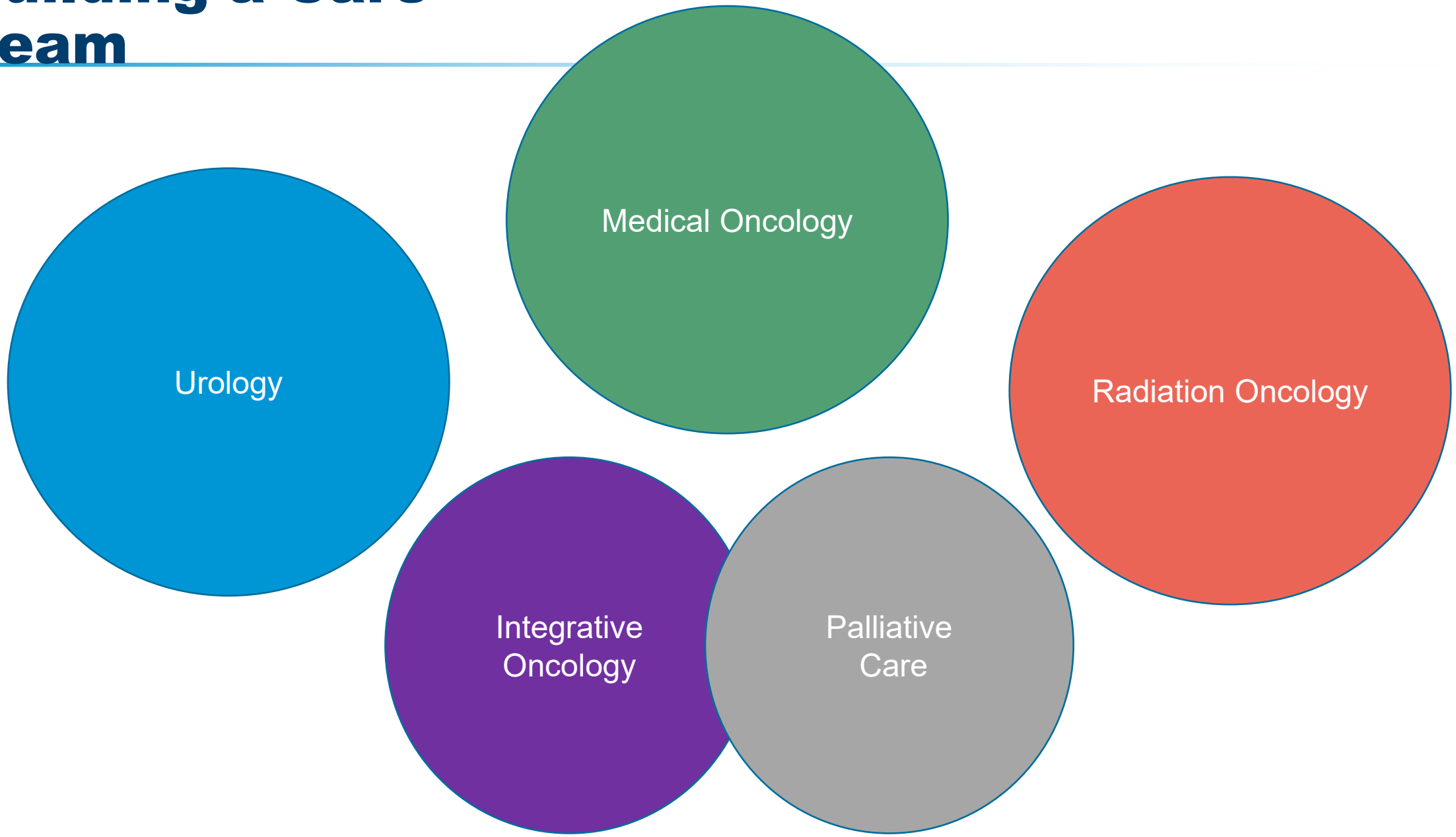


Source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, released in June 2024.

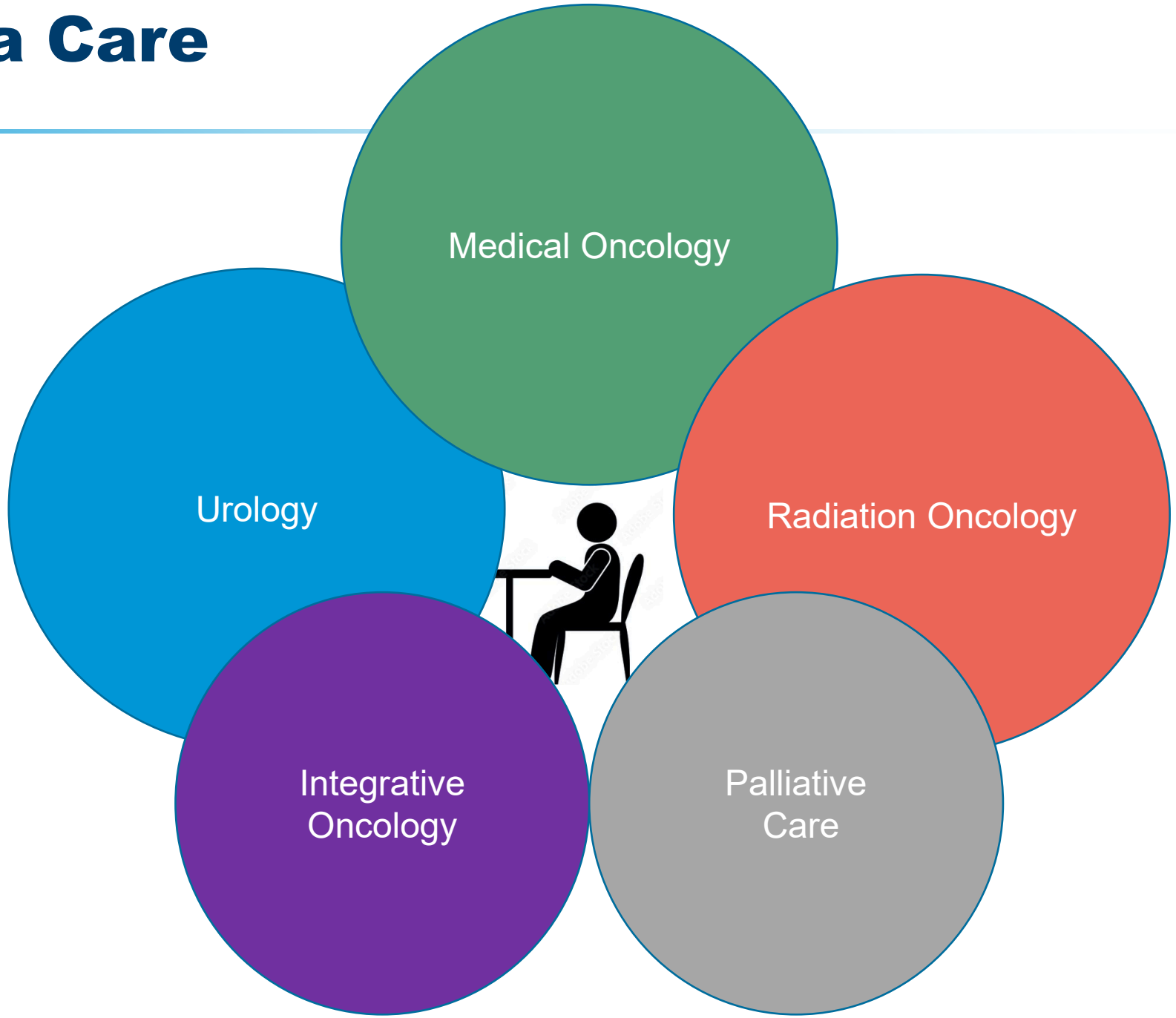
Who the Patient Saw First…

Urologist	Medical Oncologist
Control symptoms of primary tumor	Morbidity of surgery
Phase III trials showing OS benefit	No proven benefit in IO era
Resection of resistant clones	Delay to systemic treatment
Long-term remission noted w/ surgical resection of metastatic RCC	impaired CrCl, increased risk of HTN
Nephrectomy patient compromise 80-90% of trial Participants	Unlikely benefit in those with competing risk comorbidities and impaired performance status

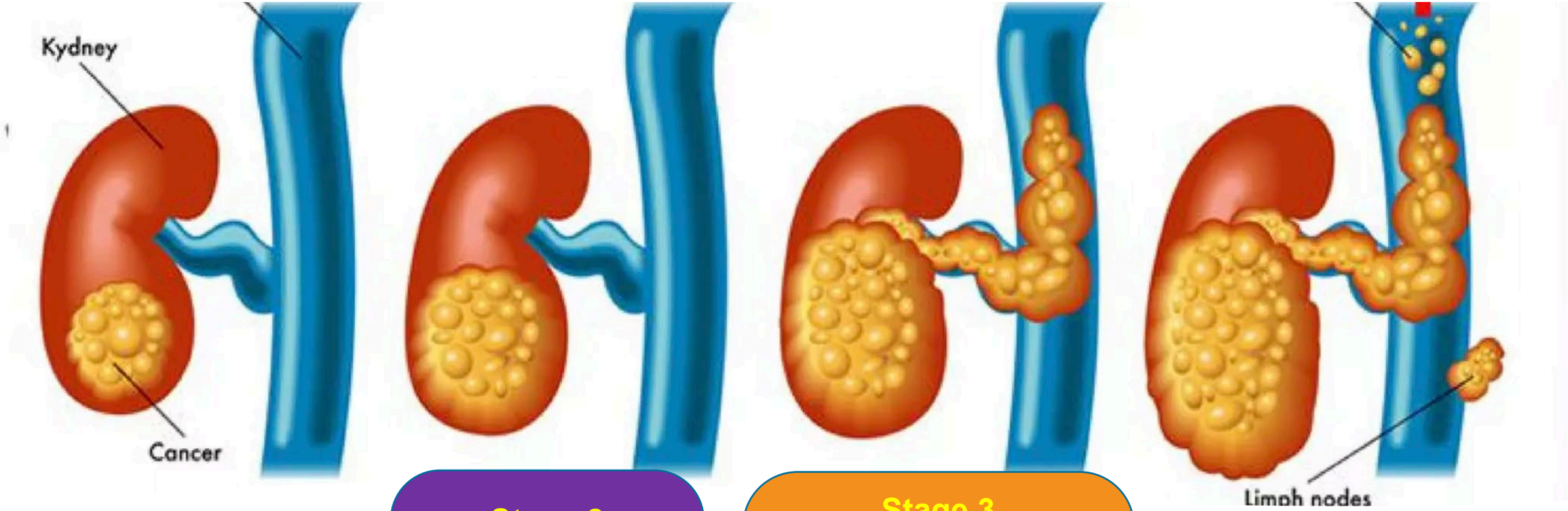
Building a Care Team



Building a Care Team



Cancer Staging



Stage 1

Small

Confined to kidney

Stage 2

Larger

Confined to kidney

Stage 3

Growing into Fat surrounding kidney
Venous structures
Vena cava

Stage 4

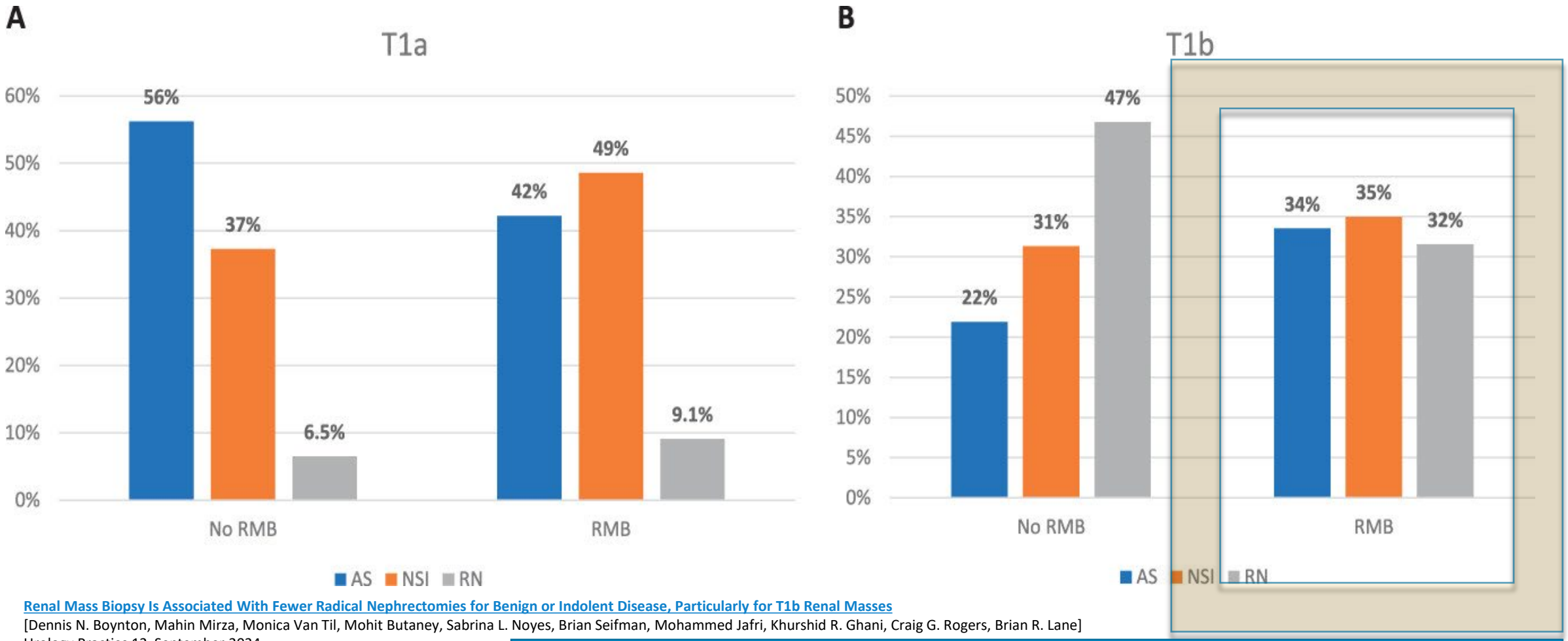
Lymph Nodes
Distant spread

Early Stage Disease

- Robotic surgery has dynamically changed morbidity and complications associated with partial nephrectomy
  - Thrombus cases
  - Disaster abdomens

- Surgeons must be the gateway for shared decision making as many options are available:
  - Ablation
  - Surgery
  - Active surveillance
  - Radiotherapy

Early Stage Disease



Renal Mass Biopsy Is Associated With Fewer Radical Nephrectomies for Benign or Indolent Disease, Particularly for T1b Renal Masses
[Dennis N. Boynton, Mahin Mirza, Monica Van Til, Mohit Butaney, Sabrina L. Noyes, Brian Seifman, Mohammed Jafri, Khurshid R. Ghani, Craig G. Rogers, Brian R. Lane]
Urology Practice 12, September 2024
DOI: (10.1097/UPJ.0000000000000710)

Non-malignant pathology decreased 7% in those w/ PNx and 10% in RNx

HISTOTRIPSY (HISTOSONICS)

HOPE4LIVER

90% local control @ 12 months

5-year outcomes after stereotactic ablative body radiotherapy for primary renal cell carcinoma: an individual patient data meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney)

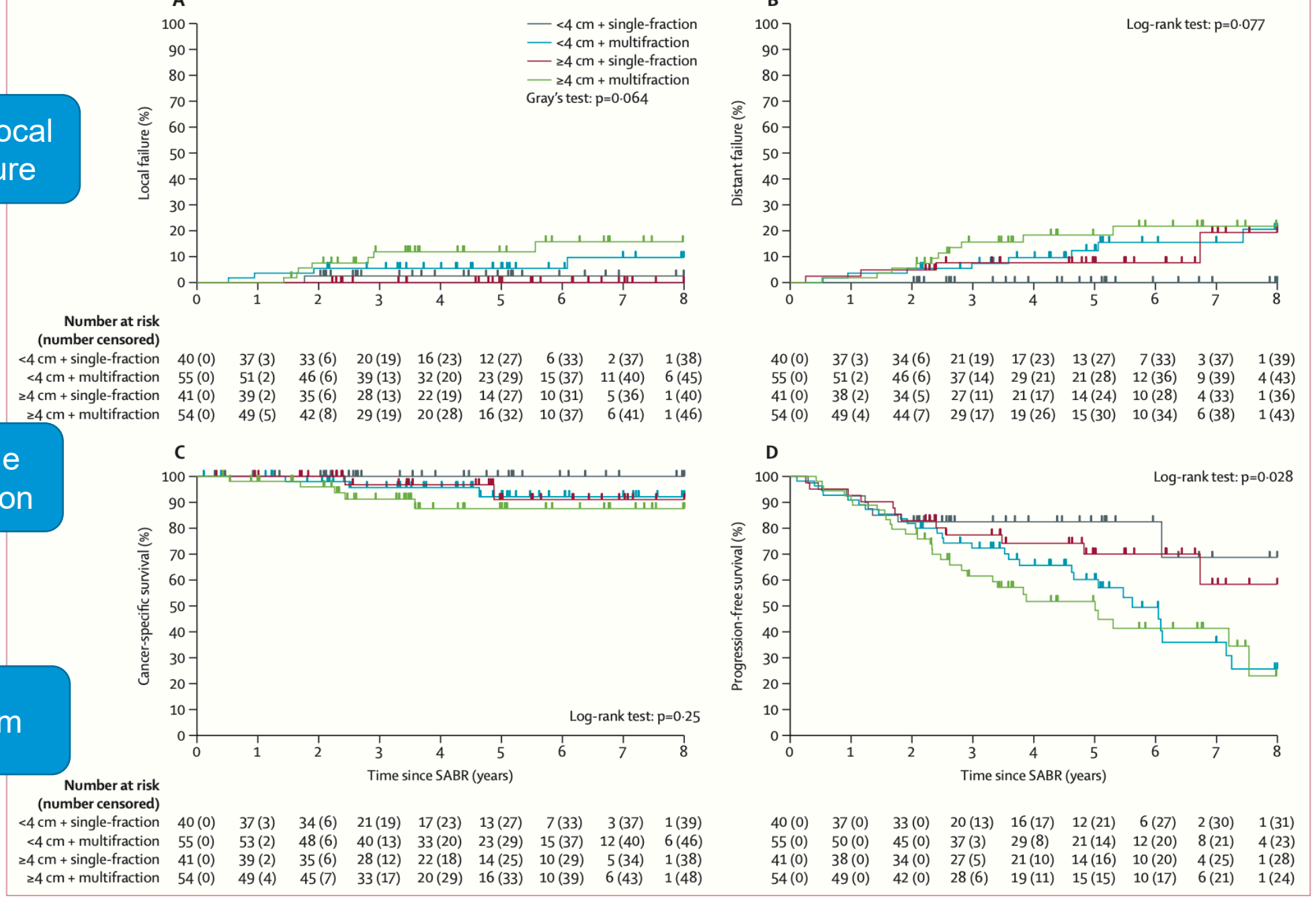
Shankar Siva, Muhammad Ali, Rohann J M Correa, Alexander Muacevic, Lee Ponsky, Rodney J Ellis, Simon S Lo, Hiroshi Onishi, Anand Swaminath,

- 12 centers
- 2007 – 2018 , median f/u 5 years
- Median tumor size 4cm
- 75% deemed non-operable
- Median decrease in GFR 14.2ml
- 4% required dialysis (caveat 29% solitary kidney)
- No grade 3 toxicities, only 1 grade 4 toxicity

5% local failure

Single Fraction

<4cm



Number at risk (number censored)

<4 cm + single-fraction	40 (0)	37 (3)	33 (6)	20 (19)	16 (23)	12 (27)	6 (33)	2 (37)	1 (38)
<4 cm + multifraction	55 (0)	51 (2)	46 (6)	39 (13)	32 (20)	23 (29)	15 (37)	11 (40)	6 (45)
≥4 cm + single-fraction	41 (0)	39 (2)	35 (6)	28 (13)	22 (19)	14 (27)	10 (31)	5 (36)	1 (40)
≥4 cm + multifraction	54 (0)	49 (5)	42 (8)	29 (19)	20 (28)	16 (32)	10 (37)	6 (41)	1 (46)

<4 cm + single-fraction	40 (0)	37 (3)	34 (6)	21 (19)	17 (23)	13 (27)	7 (33)	3 (37)	1 (39)
<4 cm + multifraction	55 (0)	51 (2)	46 (6)	37 (14)	29 (21)	21 (28)	12 (36)	9 (39)	4 (43)
≥4 cm + single-fraction	41 (0)	38 (2)	34 (5)	27 (11)	21 (17)	14 (24)	10 (28)	4 (33)	1 (36)
≥4 cm + multifraction	54 (0)	49 (4)	44 (7)	29 (17)	19 (26)	15 (30)	10 (34)	6 (38)	1 (43)

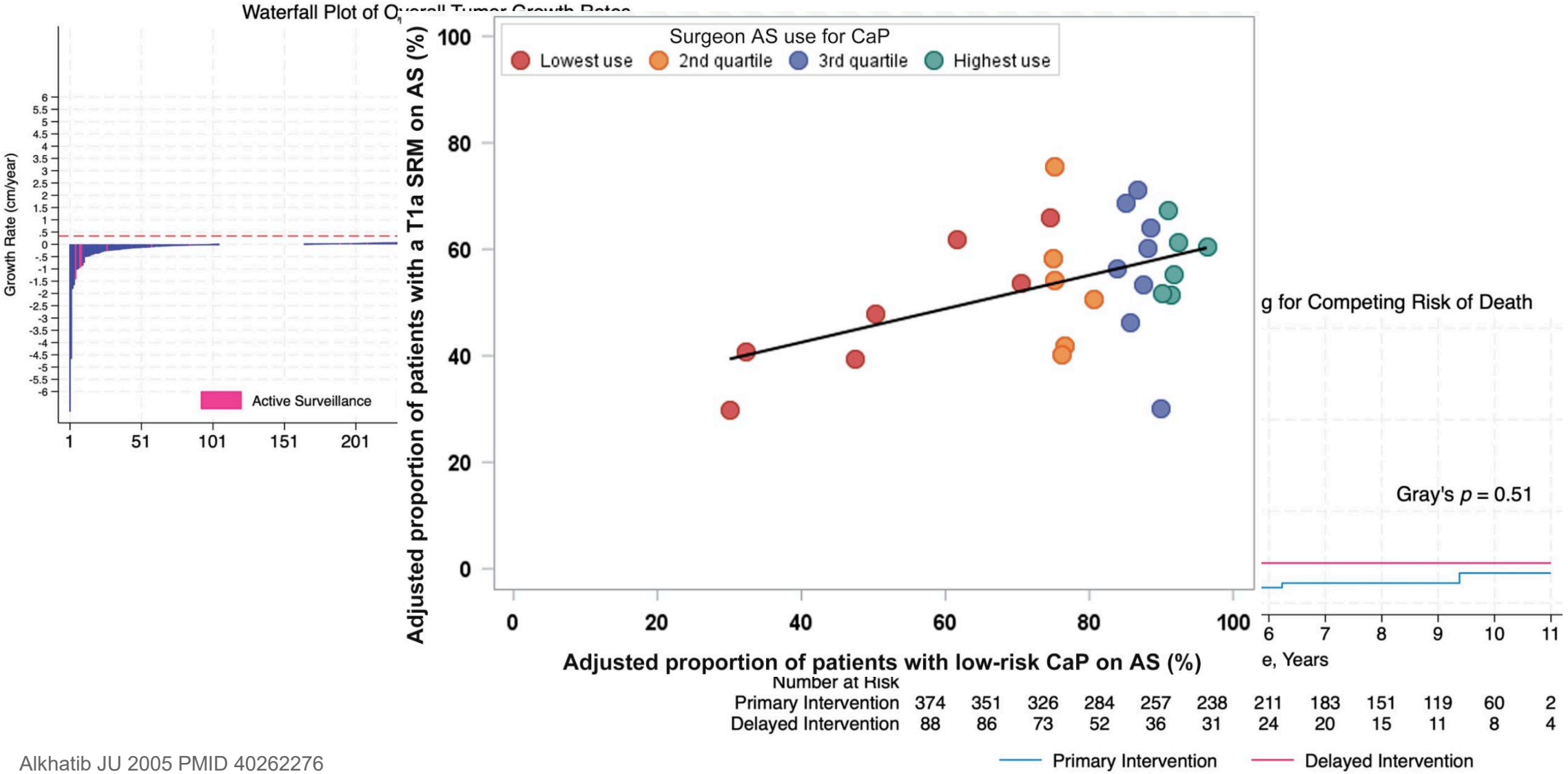
Number at risk (number censored)

<4 cm + single-fraction	40 (0)	37 (3)	34 (6)	21 (19)	17 (23)	13 (27)	7 (33)	3 (37)	1 (39)
<4 cm + multifraction	55 (0)	53 (2)	48 (6)	40 (13)	33 (20)	23 (29)	15 (37)	12 (40)	6 (46)
≥4 cm + single-fraction	41 (0)	39 (2)	35 (6)	28 (12)	22 (18)	14 (25)	10 (29)	5 (34)	1 (38)
≥4 cm + multifraction	54 (0)	49 (4)	45 (7)	33 (17)	20 (29)	16 (33)	10 (39)	6 (43)	1 (48)

<4 cm + single-fraction	40 (0)	37 (0)	33 (0)	20 (13)	16 (17)	12 (21)	6 (27)	2 (30)	1 (31)
<4 cm + multifraction	55 (0)	50 (0)	45 (0)	37 (3)	29 (8)	21 (14)	12 (20)	8 (21)	4 (23)
≥4 cm + single-fraction	41 (0)	38 (0)	34 (0)	27 (5)	21 (10)	14 (16)	10 (20)	4 (25)	1 (28)
≥4 cm + multifraction	54 (0)	49 (0)	42 (0)	28 (6)	19 (11)	15 (15)	10 (17)	6 (21)	1 (24)

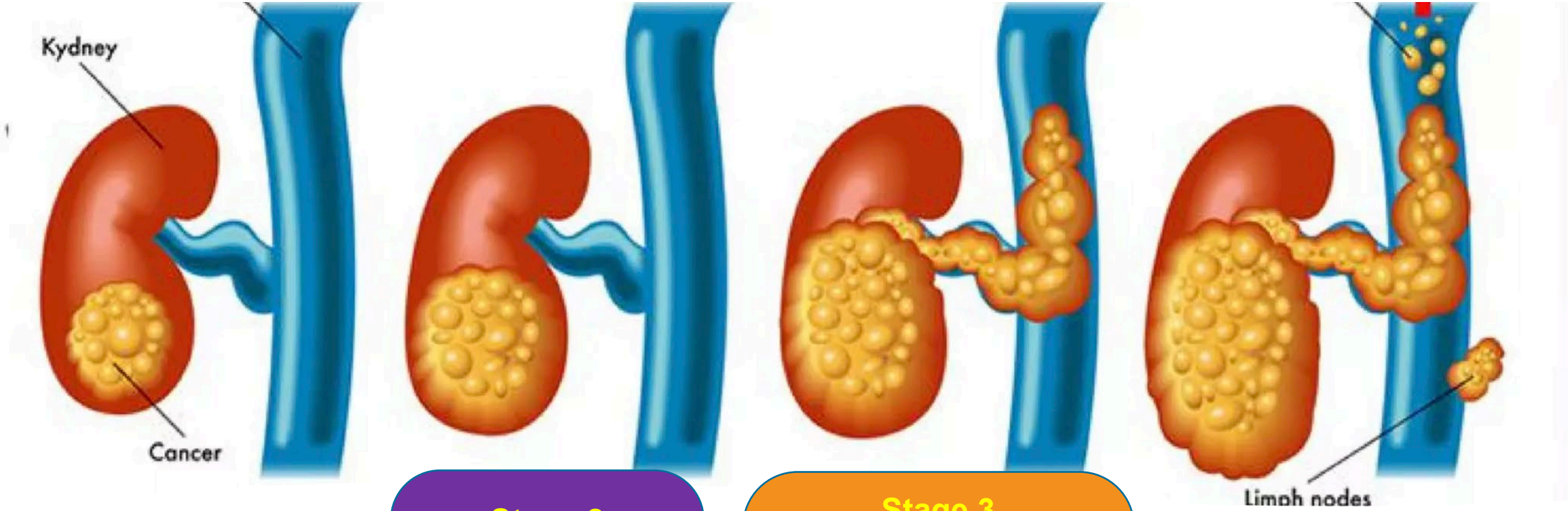
Figure 2: **Kaplan-Meier plots stratified by maximum tumour dimension (<4 cm *vs* ≥4 cm) and single-fraction versus multifraction SABR**
Plots are shown for local failure (A), distant failure (B), cancer-specific survival (C), and progression-free survival (D). Local and distant failure based on cumulative incidence function and competing risk model with death as competing event. Vertical dashes denote censored patients. SABR=stereotactic ablative body radiotherapy.

DISSRM Registry



Alkhatib JU 2005 PMID 40262276

Cancer Staging



Stage 1

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Confined to kidney

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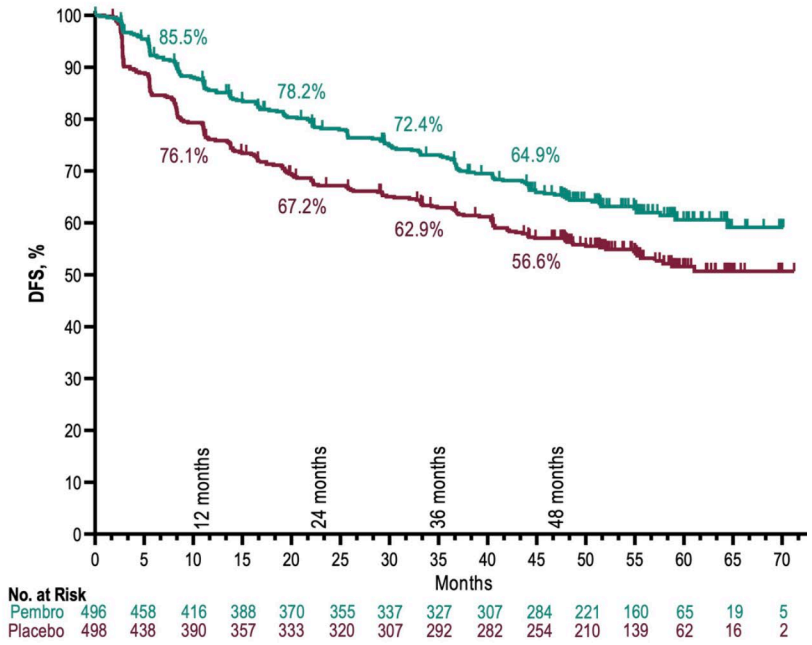
Growing into Fat surrounding kidney
Venous structures
Vena cava

Stage 4

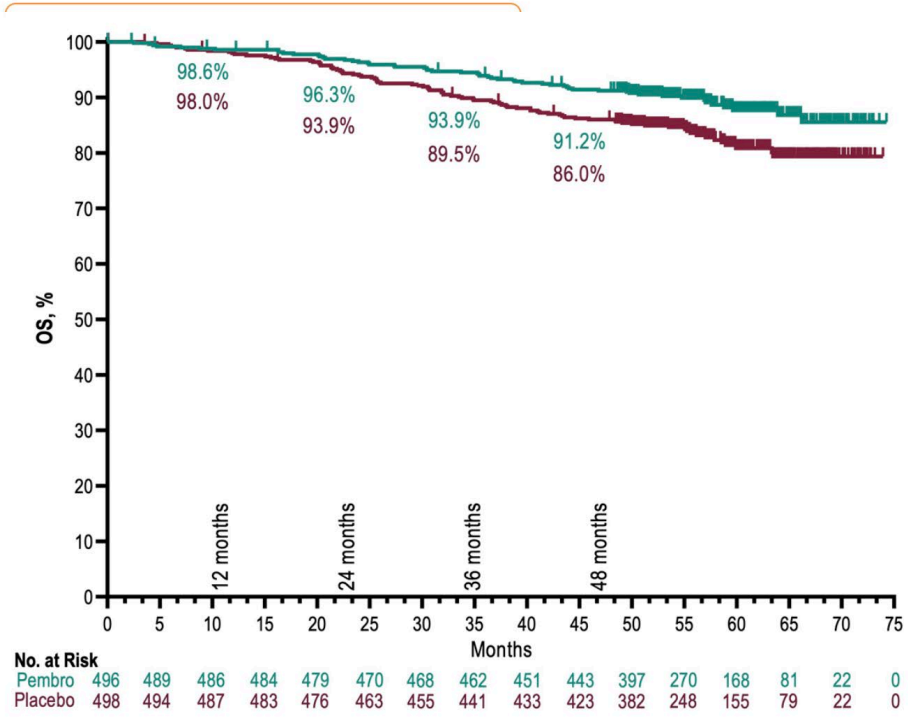
Lymph Nodes
Distant spread

Keynote 564



	Pembro (N = 496)	Placebo (N = 498)
Events, n	174	224
Median, mo (95% CI)	NR (NR–NR)	NR (54.9–NR)

Median follow-up was 57.2 months (range, 47.9–74.5)



	Pembro (N = 496)	Placebo (N = 498)
Events, n	55	86
Median, mo (95% CI)	NR (NR–NR)	NR (NR–NR)

Median follow-up was 57.2 months (range, 47.9–74.5)

HR 0.62 (95% CI 0.44–0.87); *P* =.002*

Grade 3 and 4 Toxicity = 20%

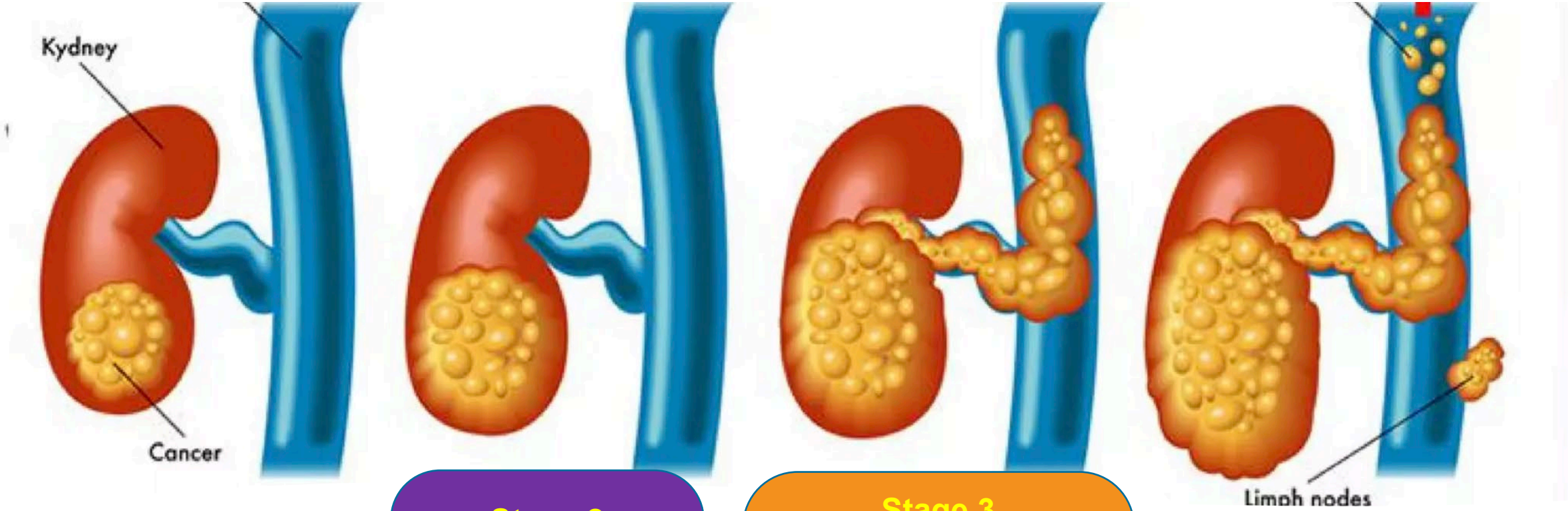
Biomarkers for patient selection

Many patients went on to subsequent therapy

*** denotes statistical significance**. P-value boundary for OS at IA3 was 0.0072 (1-sided) per Lan-DeMets O'Brien-Fleming spending approximation α-spending function. As this key secondary endpoint was formally met, any future OS analyses will be descriptive only.

Data cutoff date: September 15, 2023.

Cancer Staging



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Lymph Nodes
Distant spread

Prior to 2006

TABLE 2. Summary of Study

First Author, Reference	Type of St	
Flanigan and Yonover[2] SWOG 8949 (2001) EORTC 30587 (2001)	Phase III	8.1 months; PFS 0; p = .05; N: 11.7 months; PFS 1; p = .08; : 4.8 months
Mickisch et al[3]	Phase III	months (HR 0.54; 95% CI, 0.31–0.94)
Flanigan et al[4] (2004)	Meta-analy	7.8 months (HR 0.69; p = .002)
Pantuck et al[5] (2001)	Retrospect	ar OS, 19.6%
Choueiri et al[17] (2011)	Retrospect targeted	nths (no CN); HR 0.44; p < .01; 08; poor risk: no benefit; p = .06
Heng et al[18] (2014)	Retrospect targeted	nths (no CN); p < .0001

Abbreviation: CN, cytoreductive nephrectomy le.

CYTOREDUCTIVE NEPHRECTOMY AND METASTATIC RENAL CANCER

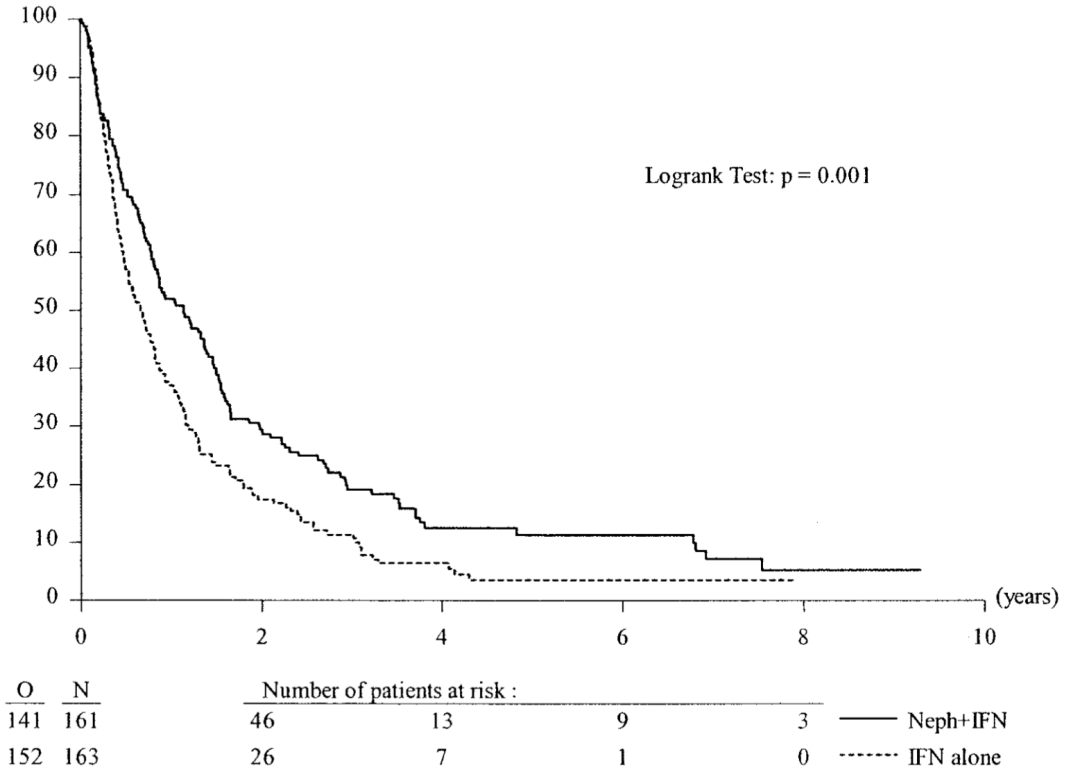
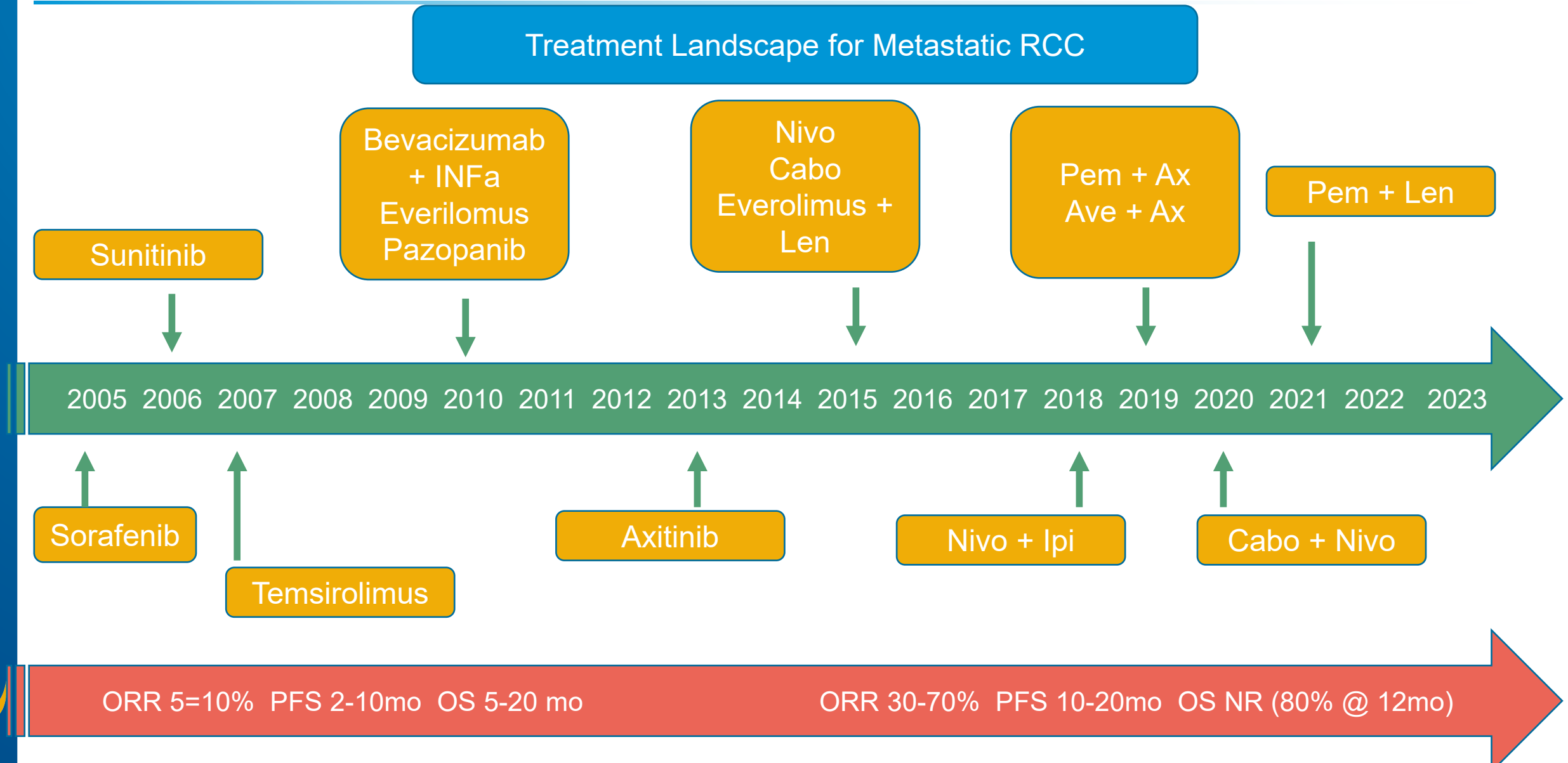


FIG. 1. Duration of survival in combined SWOG and EORTC trials. *O*, observation. *N*, nephrectomy

Vaishampayan ASCO Book 2006
Flanigan JU 2004 PMID 14767273

Immune Checkpoint Inhibitors



Key Trials Primary mRCC w/ ICI

Trial	Drug Combination	# Pts w/ Primary Tumor	PFS	OS	CR	ADE
Checkmate 214 Mot	Ipi + Nivo vs.	22%	11.6 vs. 8.4mo (p=0.03, NS)	NR vs 26 mo	9%	G3-4 : 46%
Ch 9E Ch 202			16.6 vs 8.3 mo (p=<0.001)	85.7% @ 12 mo vs 75.6 % (p=0.001)	8%	≥G3 75.3%
Ja Mo			13.8 vs 8.4mo (p=<0.001)	11.6 vs 10.7mo	4.4%	≥G3 71%
Keynote 426 Rini JCO 2023	Pemb + Axi vs Sunitinib	16.6%	15.1 vs 11.1mo (p=<0.001)	Median survival not reached (10% improvement @ 12mo)	5.8%	≥G3 75.8%
CLEAR Motzer NEJM 2020	Pemb + Len vs Eve + Len vs Sunitinib	25.1%	23.9 vs 9.2mo (p=<0.001)	79.2% @ 24mo vs. 66 mo	16%	≥G3 82%

Patients are living longer but complete response is still remains low

*PFS OS in PD-L1 + tumors

The Selection for Cytoreductive Nephrectomy (SCREEN) Score: Improving Surgical Risk Stratification by Integrating Common Radiographic Features

2006-2007
Multi-institutional database
Upfront CN: 914 pts

SCREEN SCORE:

Systemic symptoms
>3 more metastatic sites
Total metastatic burden ≥ 5cm
Bone metastatic
Low serum Hb
Low serum albumin
NO/Lymph ration ≥ 4

IMDC risk model

Factors	Patients,*n* (%)	mOS, mo (IQR)
0	34	120 (33–NR)
1	150	37 (12–83)
2	183	20 (7–47)
3	115	28 (11–50)
4		
5		
6		
Favorable ris		
Intermediate		
Poor risk (≥3		

IMDC = Inter

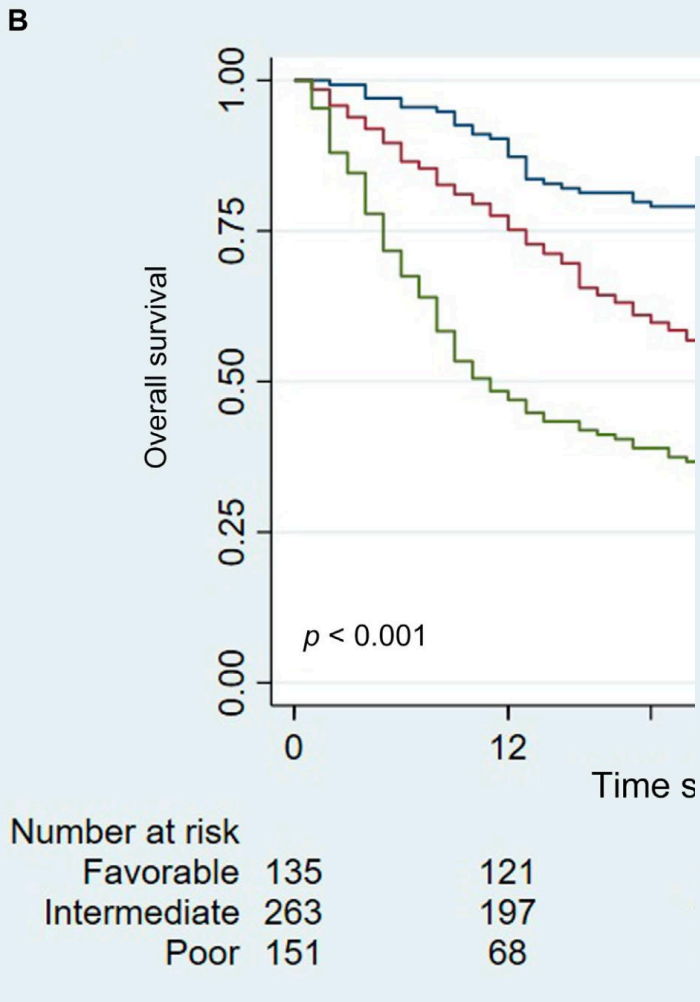
SCREEN model

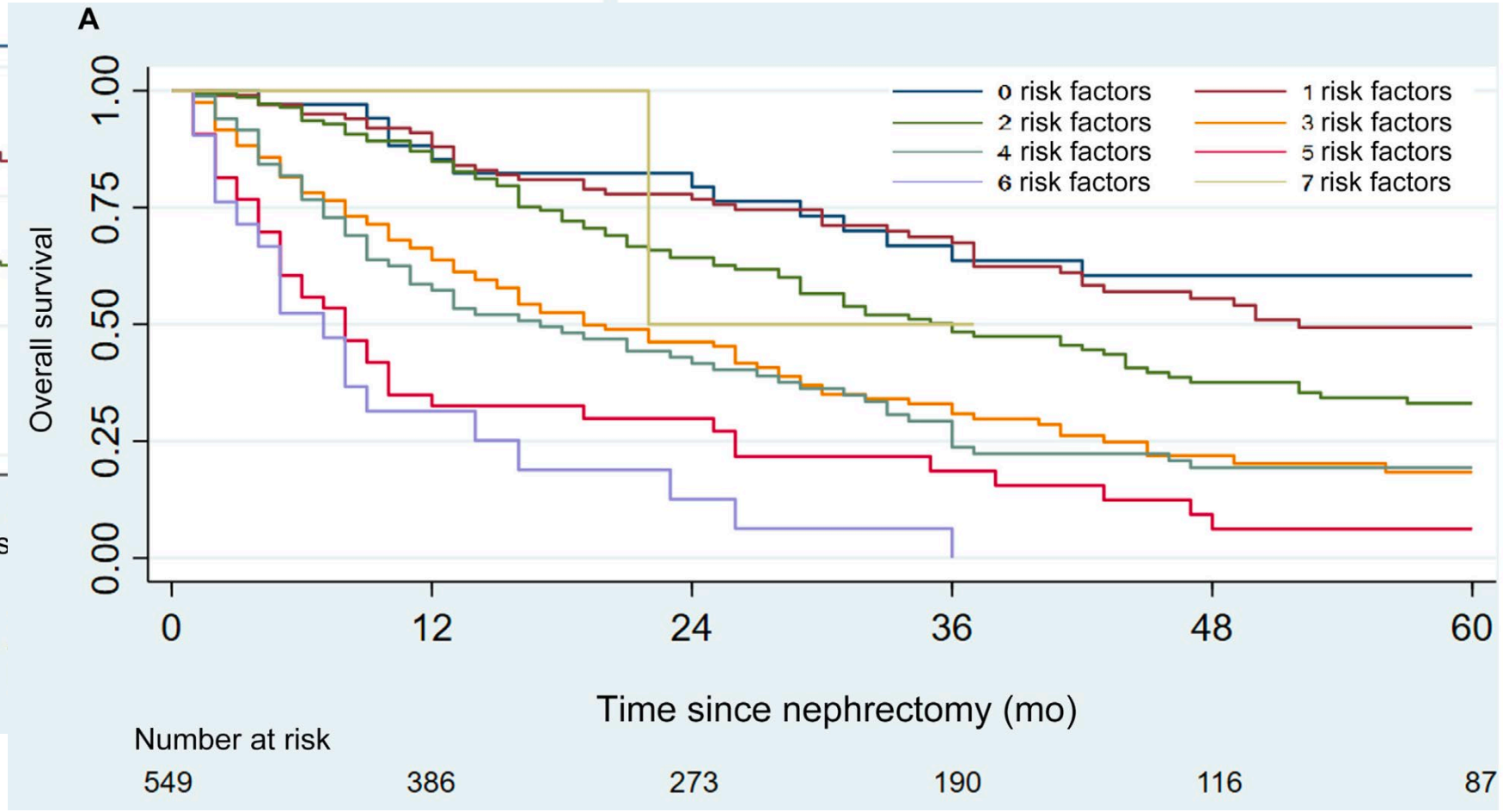
Factors	Patients,*n* (%)	mOS, mo (IQR)
0	34	NR (29–NR)
1	98	52 (26–120)
2	136	35 (16–113)
3	120	19 (8–43)
4	82	16 (7–36)
5	44	8 (4–26)
6	20	5 (2–14)
7	0	
Favorable risk (0–1)	132 (25)	64 (26–NR)
Intermediate risk (2–3)	256 (48)	28 (12–62)
Poor risk (≥4)	148 (27)	10 (5–33)

= interquartile range; mOS = median overall survival; NR = not reached.

Abel EAU 2023 PMID 37442673

The Selection for Cytoreductive Nephrectomy (SCREEN) Score: Improving Surgical Risk Stratification by Integrating Common Radiographic Features



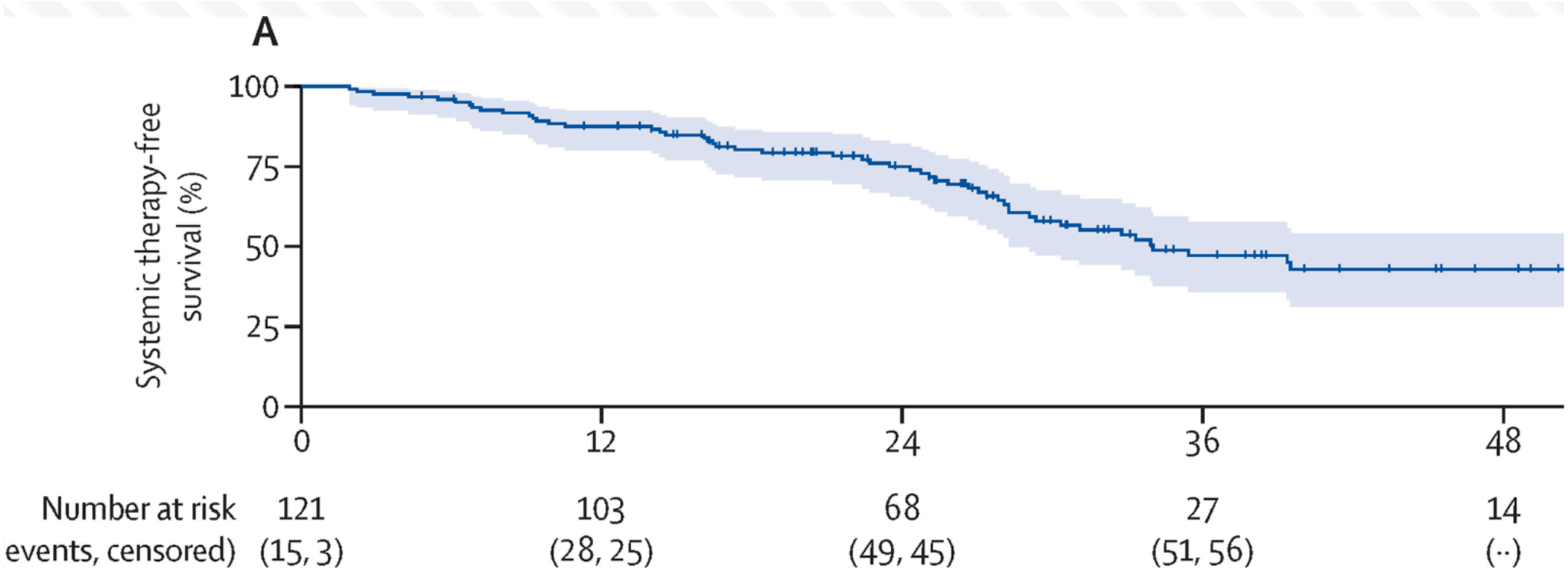


Metastasis-directed radiotherapy without systemic therapy for oligometastatic clear-cell renal-cell carcinoma: primary efficacy analysis of a single-arm, single-centre, phase 2 trial

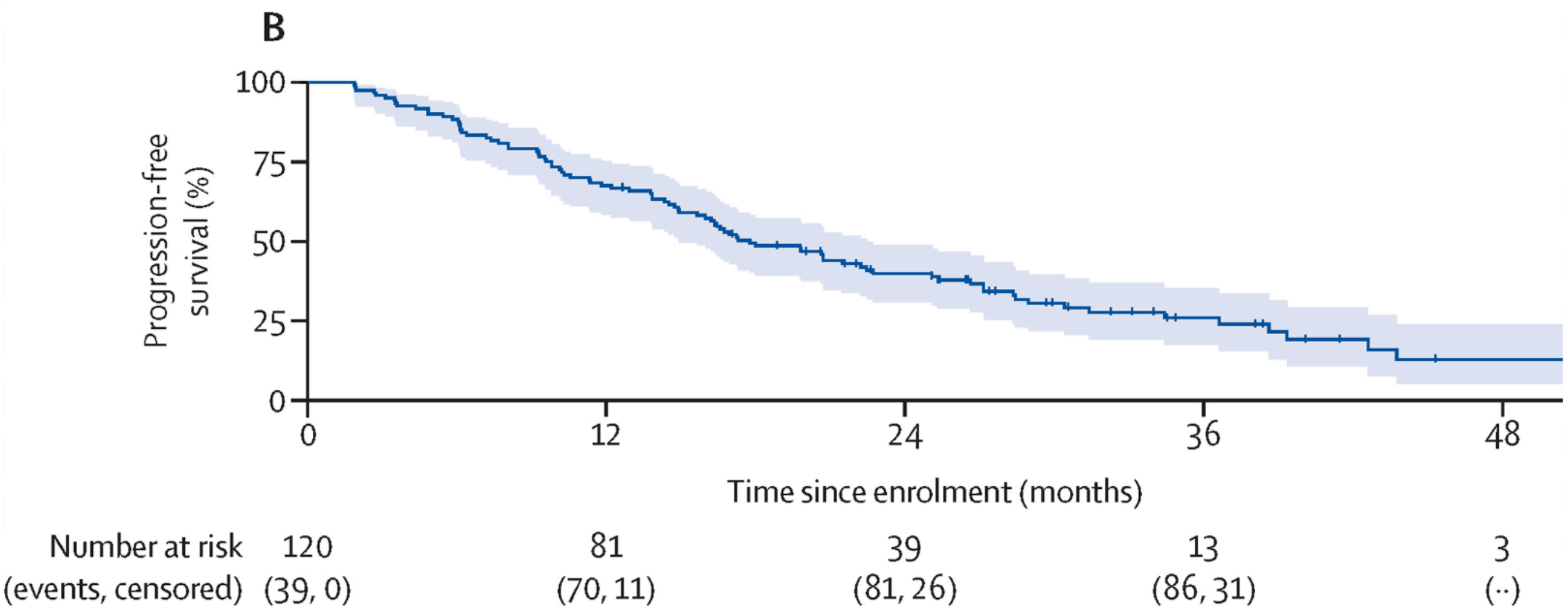
Chad Tang, Alexander D Sherry, Aaron Seo, Kieko Hara, Haesun Choi, Suyu Liu, Xiaowen Sun, Anya Montoya, Ethan B Ludmir, Amishi Y Shah,

- Clear Cell Carcinoma
- 1-5 metastasis
- 2018-2023 – met directed therapy off systemic therapy w/ limited XRT for progression
- 98% had pervious nephrectomy
- Patients were allowed to have previous systemic therapy, surgery, metastectomy, or radiotherapy
- Most common sites radiated included lung and lymph nodes

Met Directed Radiotherapy



Met Directed Radiotherapy

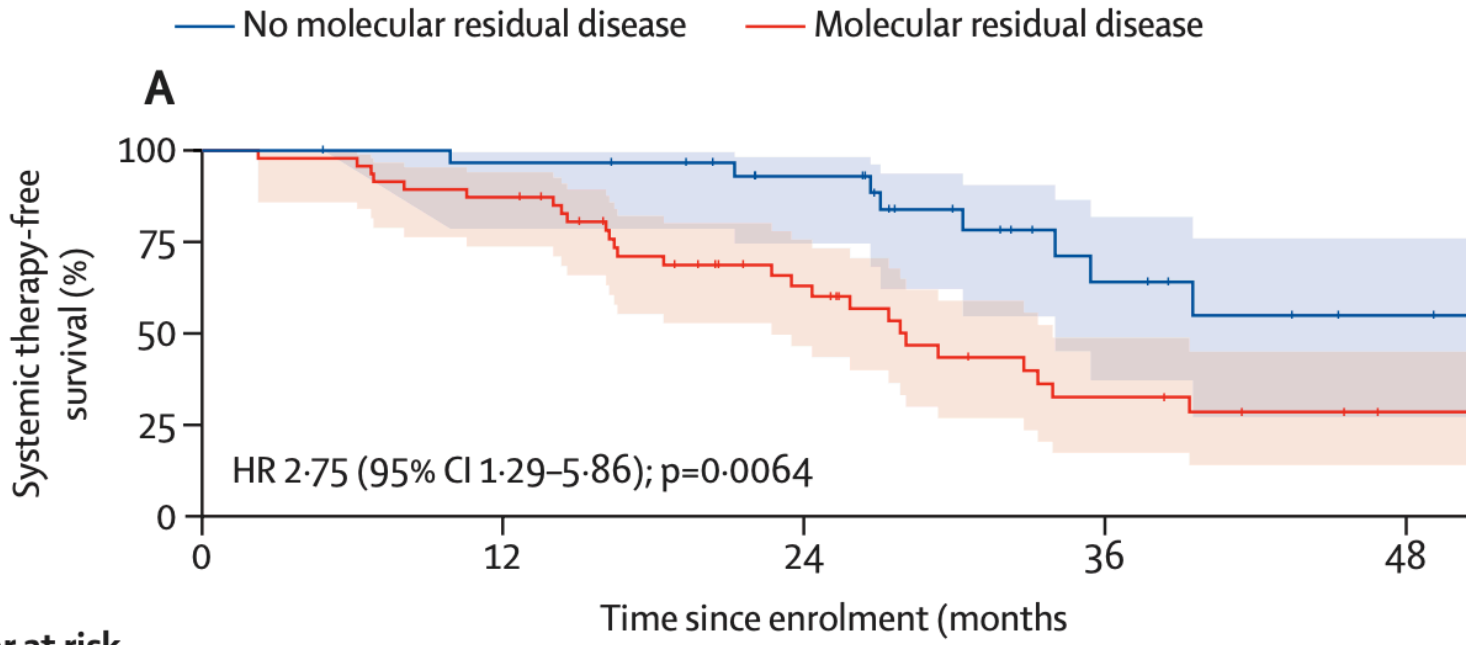


Primary outcomes of systemic therapy-free survival in the intention-to-treat population (n=121; A) and progression-free

Met Directed Radiotherapy

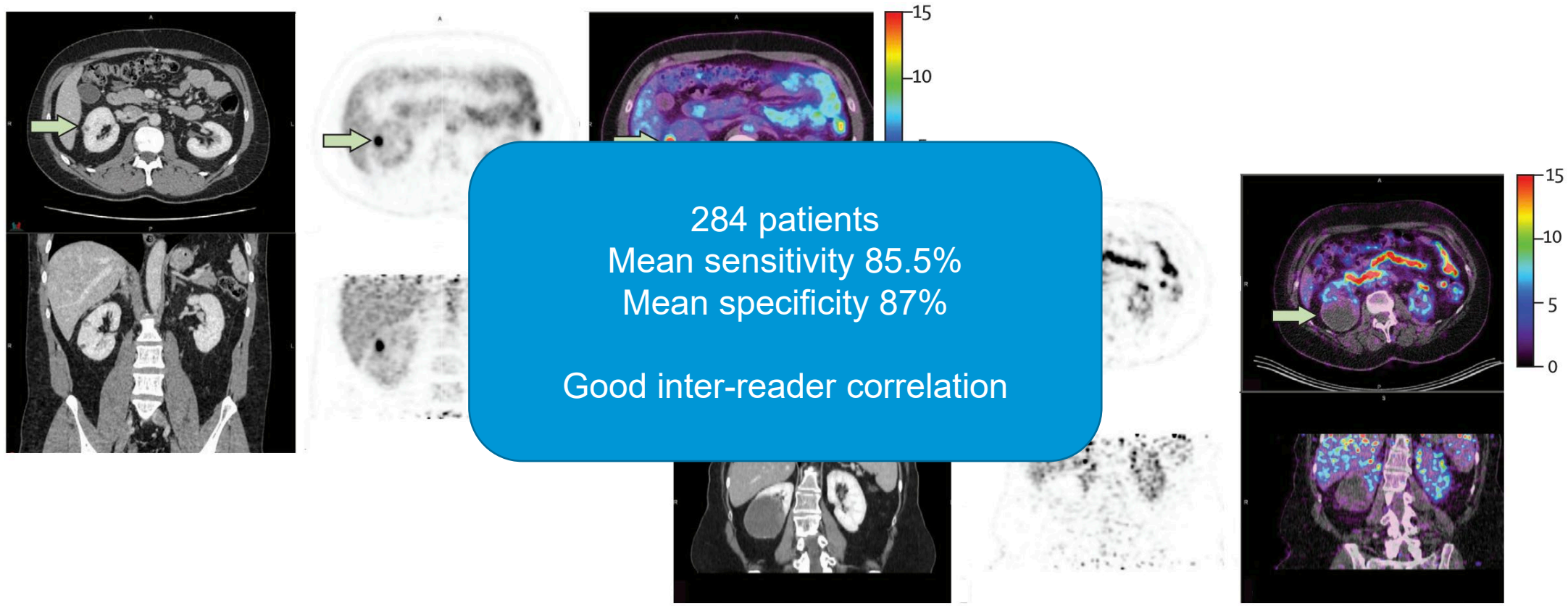
Natera ctDNA MRD test

Prognostic in this small subset



Number at risk (events, censored)					
Molecular residual disease	47 (6, 0)	41 (16, 9)	22 (25, 13)	9 (26, 17)	4 (··)
No molecular residual disease	31 (1, 1)	29 (2, 6)	23 (7, 15)	9 (8, 19)	4 (··)

[^{89}Zr]Zr-girentuximab for PET–CT imaging of clear-cell renal cell carcinoma: a prospective, open-label, multicentre, phase 3 trial



284 patients
Mean sensitivity 85.5%
Mean specificity 87%

Good inter-reader correlation

Shuch Lancet Onc 2024 32623821

STARLITE 2

Key Inclusion Criteria

- Age ≥ 18 years
- Locally advanced unresectable or metastatic RCC with clear cell component or positive CAIX expression
- PD after prior systemic therapy including ≥1 anti PD-1 or PD-L1 antibody
- No limit to prior number of lines of treatment
- ≥1 evaluable lesion by RECIST 1.1 on ^{89}Zr- girentuximab PET/CT
- Adequate organ function

Key Exclusion Criteria

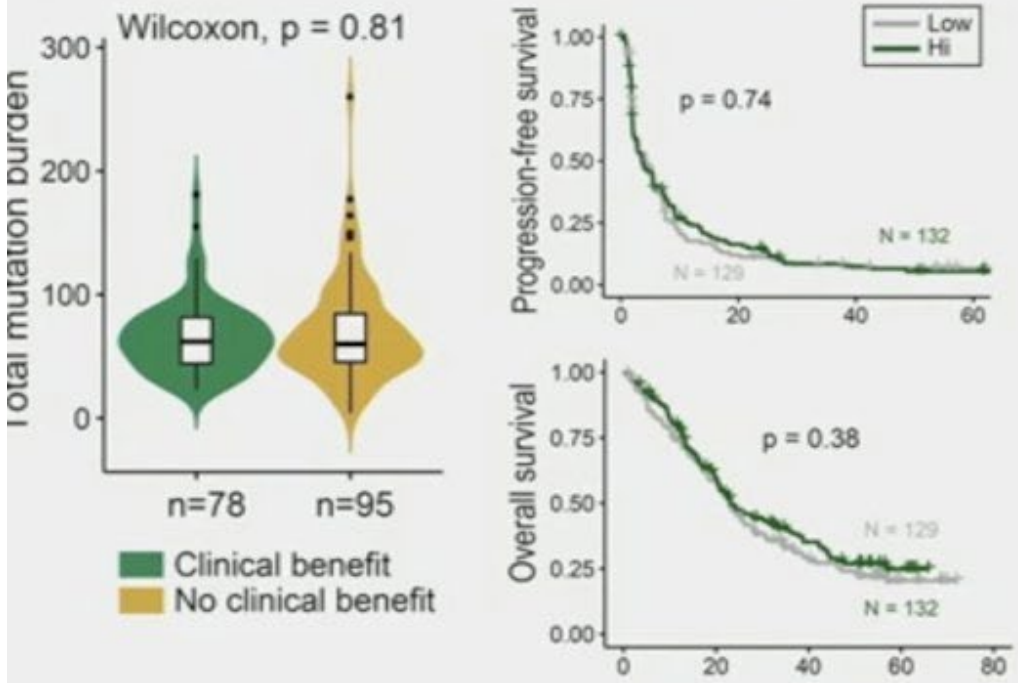
- Radiation within 14 days prior to treatment start
- Symptomatic or active untreated brain mets >1cm or active untreated spinal cord or leptomeningeal mets
- > 10mg prednisone or equivalent in last 2 years for autoimmune disease
- IO therapy discontinued for immune-related AE
- Anti-cancer therapy within 2 weeks or major surgery within 4 weeks of enrollment
- Uncontrolled hypercalcemia
- Other malignancies
- Current pregnancy
- Bleeding diathesis or untreated coagulopathy

Darren Feldman MSKCC
TELIX pharma

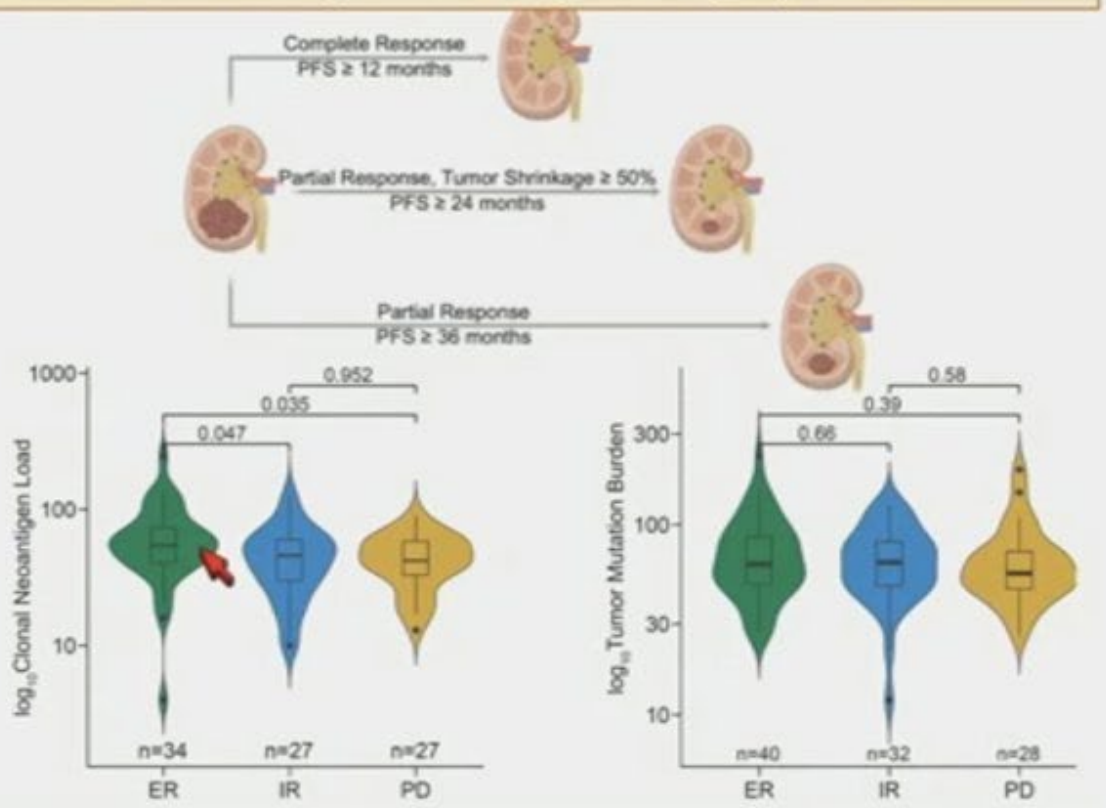
Biomarkers

TMB does not impact ICI response, but *clonal* neoantigens may drive "exceptional" outcomes

Total mutation burden (TMB) does <u>not</u> impact ICI response in RCC



Clonal (aka "truncal") neoantigens are association with exceptional response (ER) to ICI

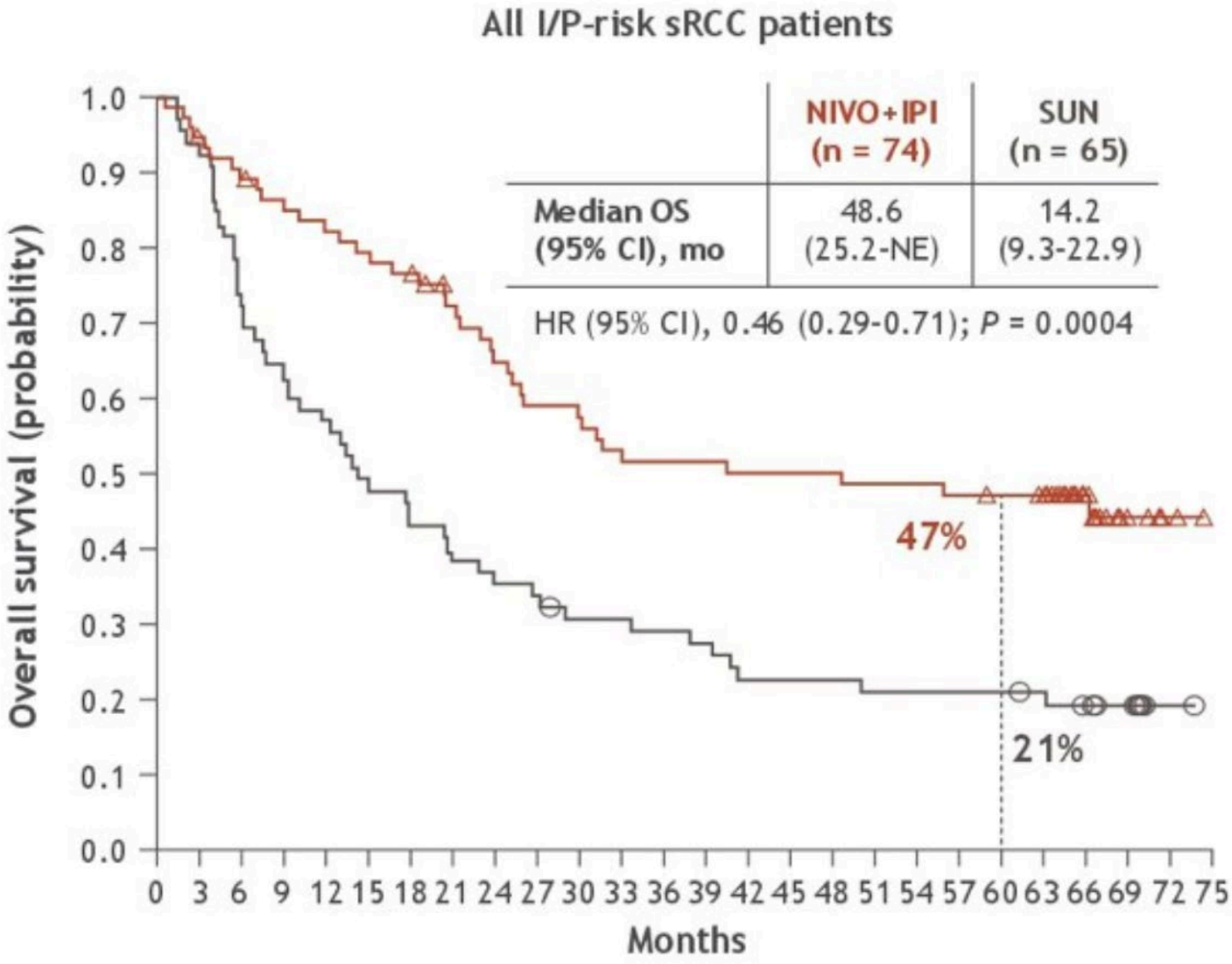


1. Braun., *Nat Med*, 2020. PMID: 32472114; 2. Jammihal, Saliby, *manuscript in revision*

Histology

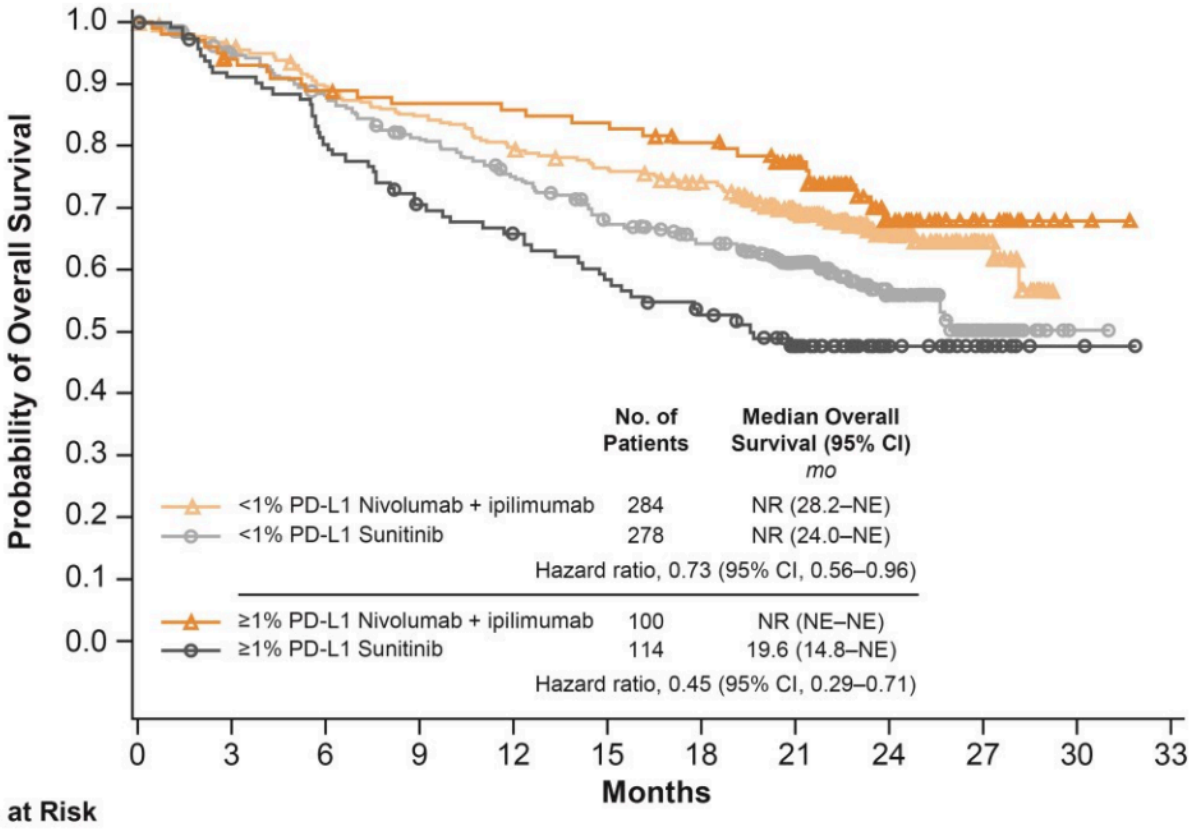
Checkmate-214

Clear improvement in response to ICI vs TKI



Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma

Figure S4. Kaplan–Meier Curves for Overall Survival According to PD-L1 Expression Level in IMDC Intermediate- and Poor-risk Patients

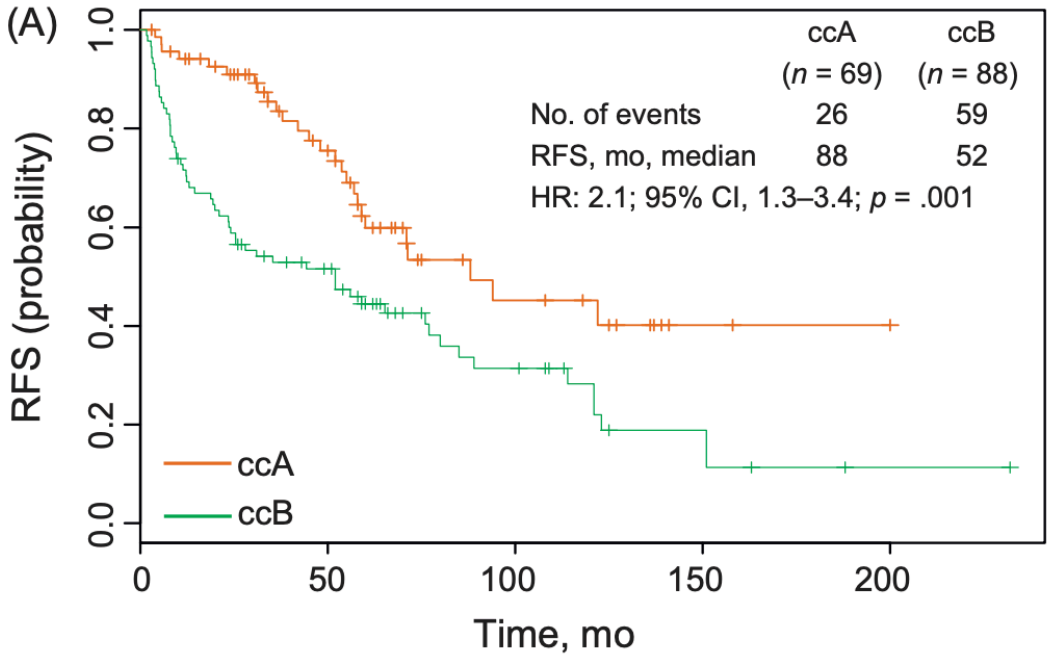


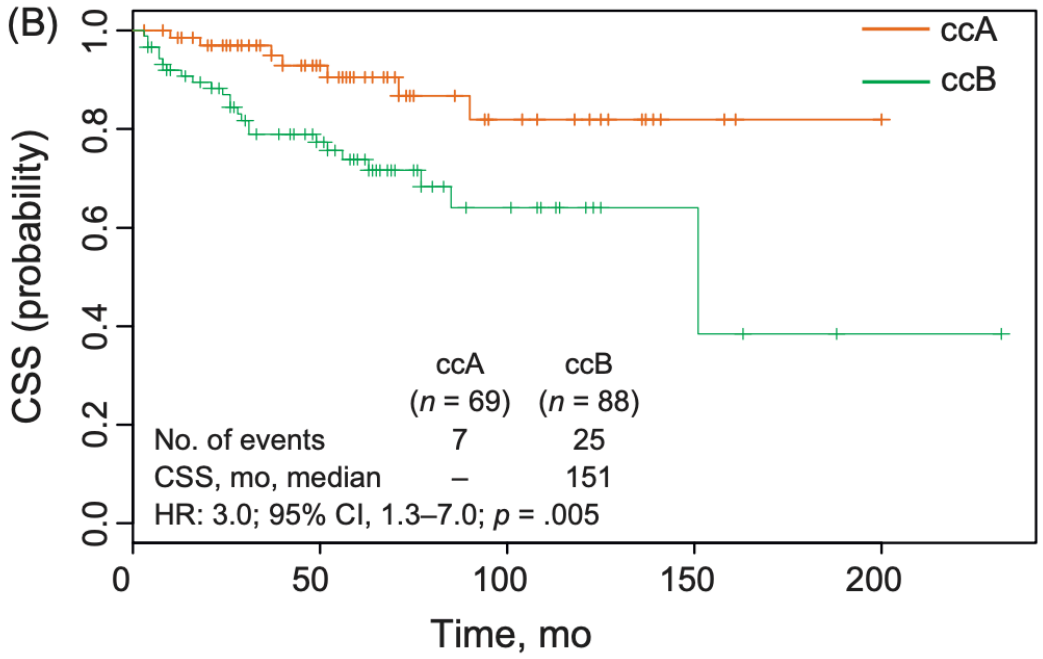
PD-L1 expression did not change response to Nivo + IPI

Motzer NEJM 2018 29562145

ClearCode34: A Prognostic Risk Predictor for Localized Clear Cell Renal Cell Carcinoma

ClearCode34



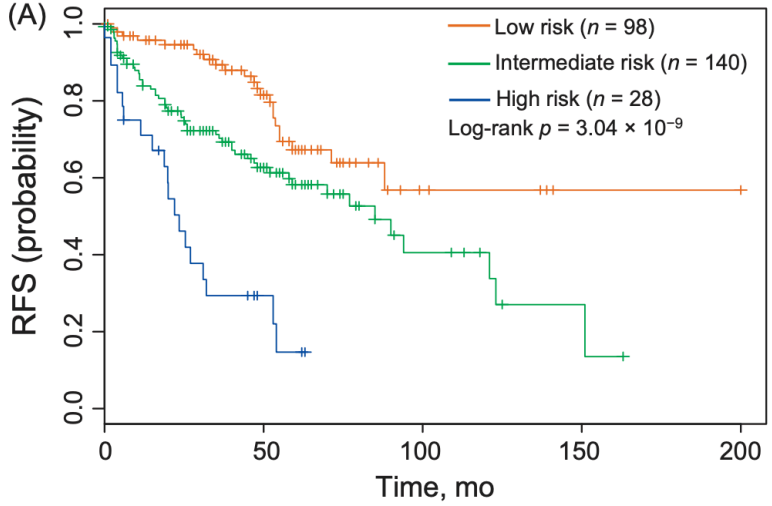


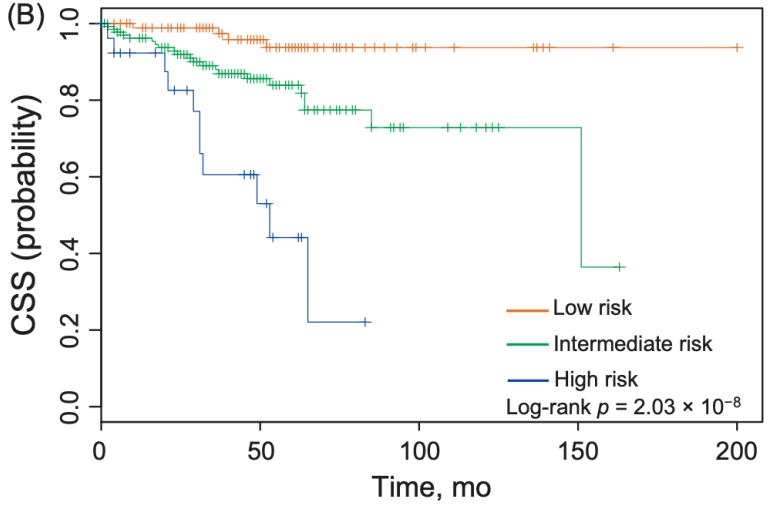
test set

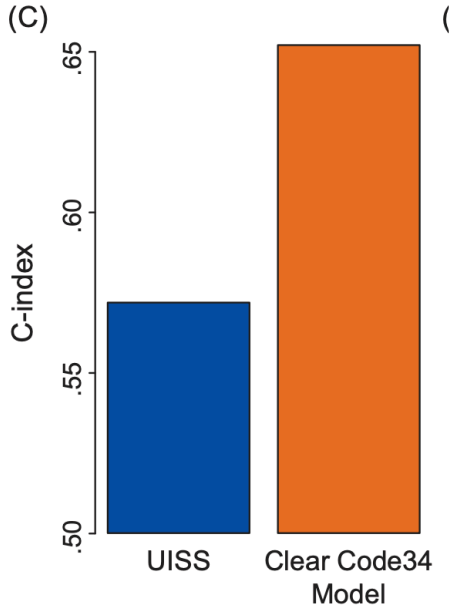
Compare model to established algorithms

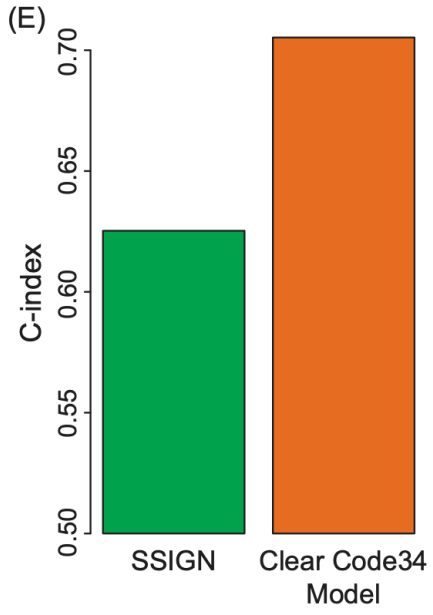
Brooks EAU 2014 24613583

ClearCode34: A Prognostic Risk Predictor for Localized Clear Cell Renal Cell Carcinoma









ClearCode + Grade + Stage

Outperformed known prognostic models

Brooks EAU 2014 24613583

Clear Cell Type A and B Molecular Subtypes in Metastatic Clear Cell Renal Cell Carcinoma: Tumor Heterogeneity and Aggressiveness

91 patients
Surgically resected ccRCC
46 M0 and 45 M1
ClearCode 34 – gene expression microarray

43% discordance between Primary and Met
23% discordance between Mets
22% discordance within primary

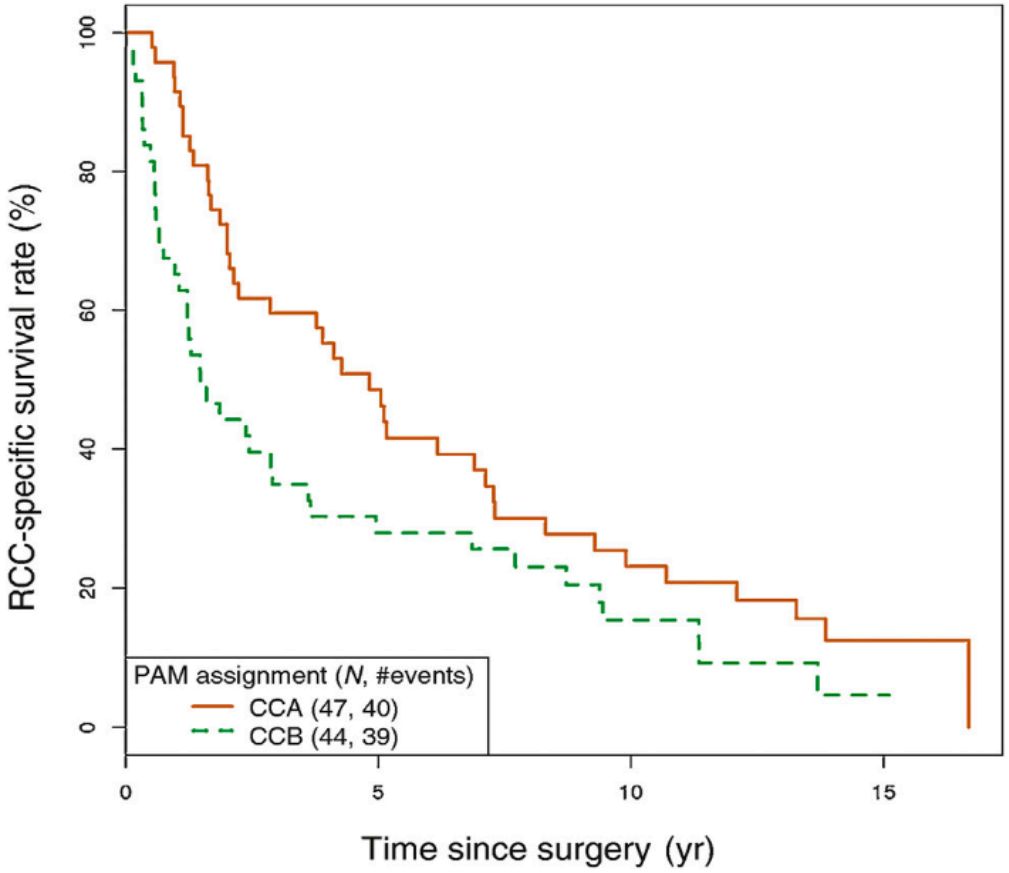
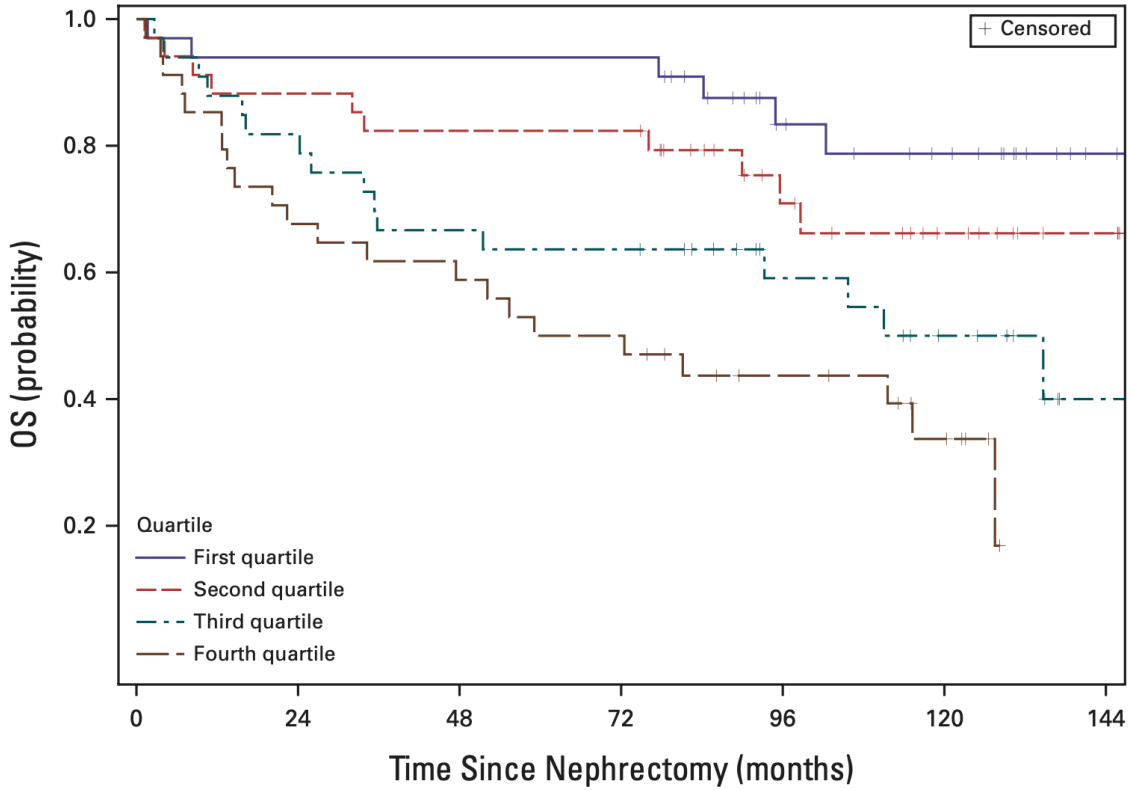


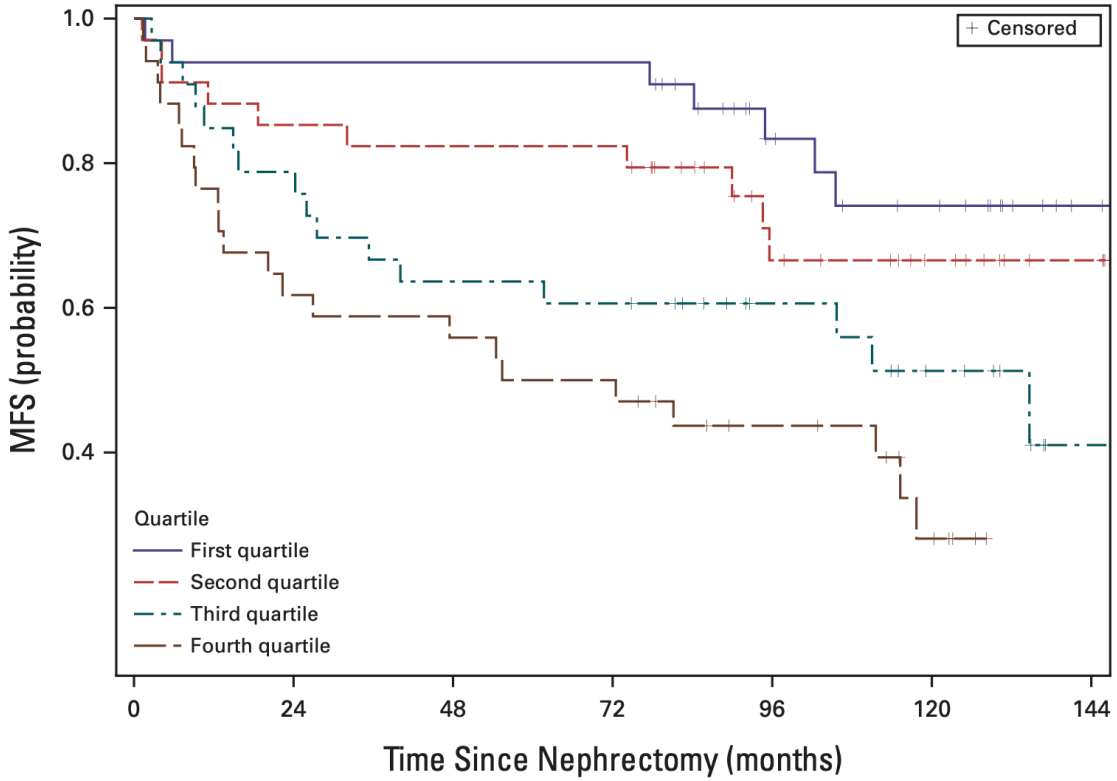
Fig. 2 – Renal cell carcinoma (RCC)–specific survival from the time of primary nephrectomy for patients assigned to ccA subtype compared to patients assigned to ccB subtype. Subtype assignment was based on gene expression profiles obtained from primary clear cell RCC (ccRCC) tumors.

Serie EAU 2017 27899233

Protein Biomakers

Plasma Kidney Injury Molecule-1 for Preoperative Prediction of Renal Cell Carcinoma Versus Benign Renal Masses, and Association With Clinical Outcomes





Variable	HR	95% CI	*P*
Log pKIM-1	1.31	1.10 to 1.54	.0019

Variable	HR	95% CI	*P*
Log pKIM-1	1.29	1.10 to 1.53	.0025

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IMmotion010 +

Circulating kidney injury molecule-1 (KIM-1) biomarker analysis in IMmotion010: A randomized phase 3 study of adjuvant (adj) atezolizumab (atezo) vs placebo (pbo) in patients (pts) with renal cell carcinoma (RCC) at increased risk of recurrence after resection.

	KIM-1 High		KIM-1 Low	
Median DFS, mo	35.9		57.2	
HR (95% CI)	1.75 (1.40, 2.17)			
	Atezo (n=151)	**Pbo (n=149)**	**Atezo (n=229)**	**Pbo (n=223)**
Median DFS, mo	NE	21.2	57.2	NE
HR (95% CI)	0.72 (0.53, 0.99)		1.12 (0.88, 1.63)	

NE, not evaluable.

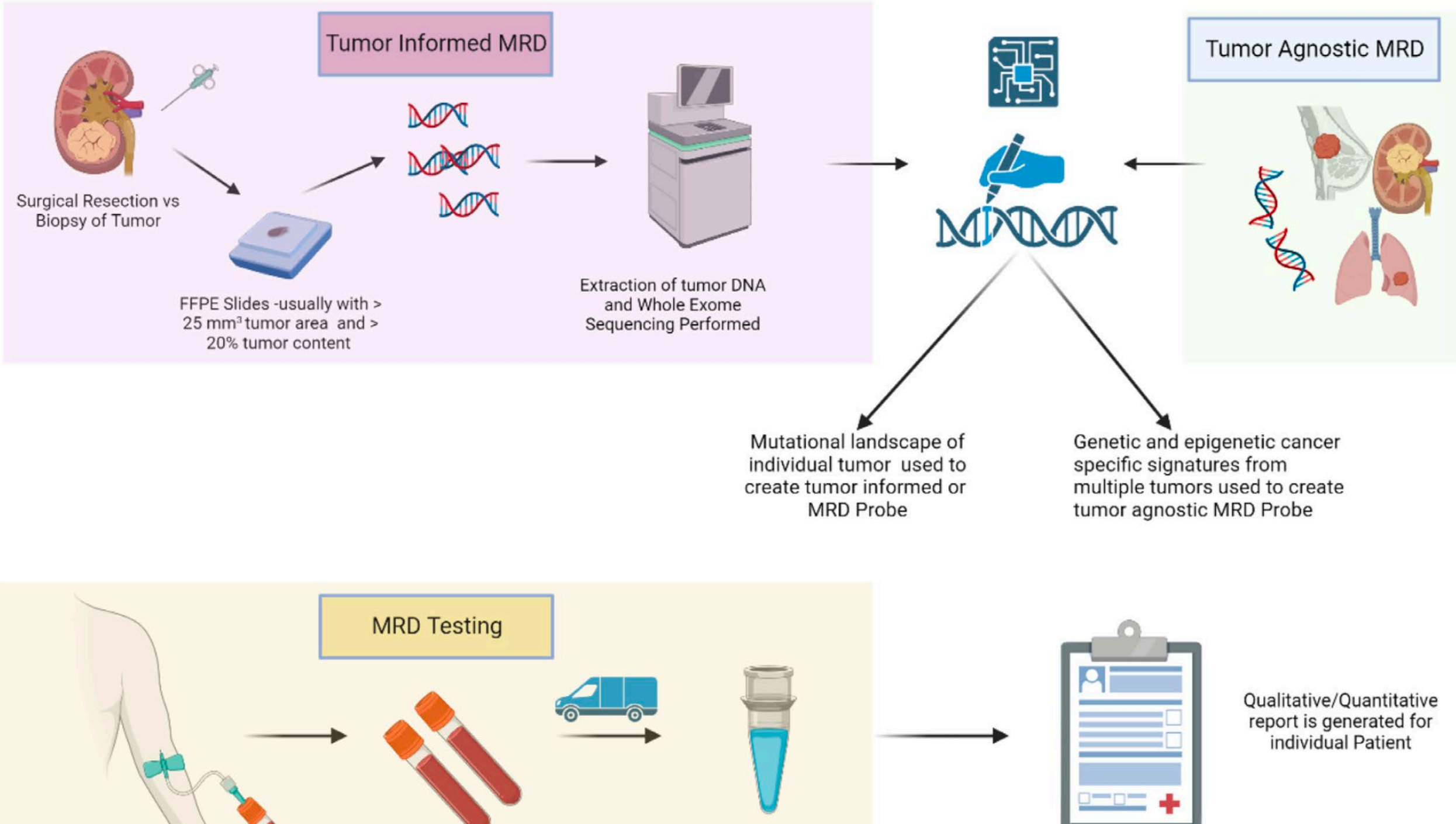
KIM 1 >30% conferred overall worse DFS (on treatment or not)

Rise in KIM 1 on treatment lead to worse DFS

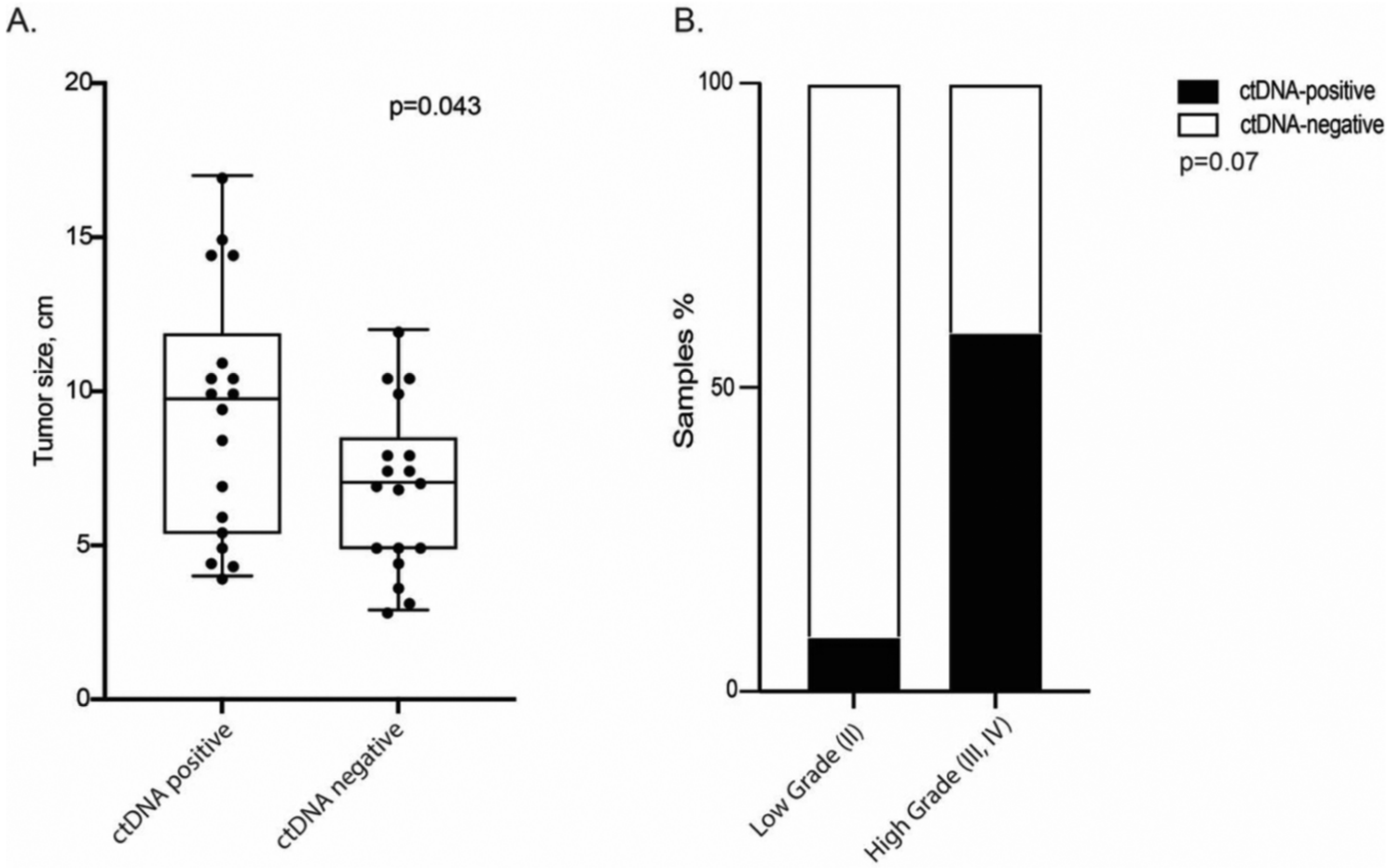
Atezo improved DFS in KIM 1 high compared to Pbo but not in KIM 1 low

Median KIM 1 levels were higher at recurrence

Circulating Tumor DNA


Tumor Informed MRD
Surgical Resection vs Biopsy of Tumor
FFPE Slides -usually with > 25 mm³ tumor area and > 20% tumor content
Extraction of tumor DNA and Whole Exome Sequencing Performed
Tumor Agnostic MRD
Mutational landscape of individual tumor used to create tumor informed or MRD Probe
Genetic and epigenetic cancer specific signatures from multiple tumors used to create tumor agnostic MRD Probe
MRD Testing
Qualitative/Quantitative report is generated for individual Patient

Association of circulating tumor DNA with patient prognosis in surgically resected renal cell carcinoma



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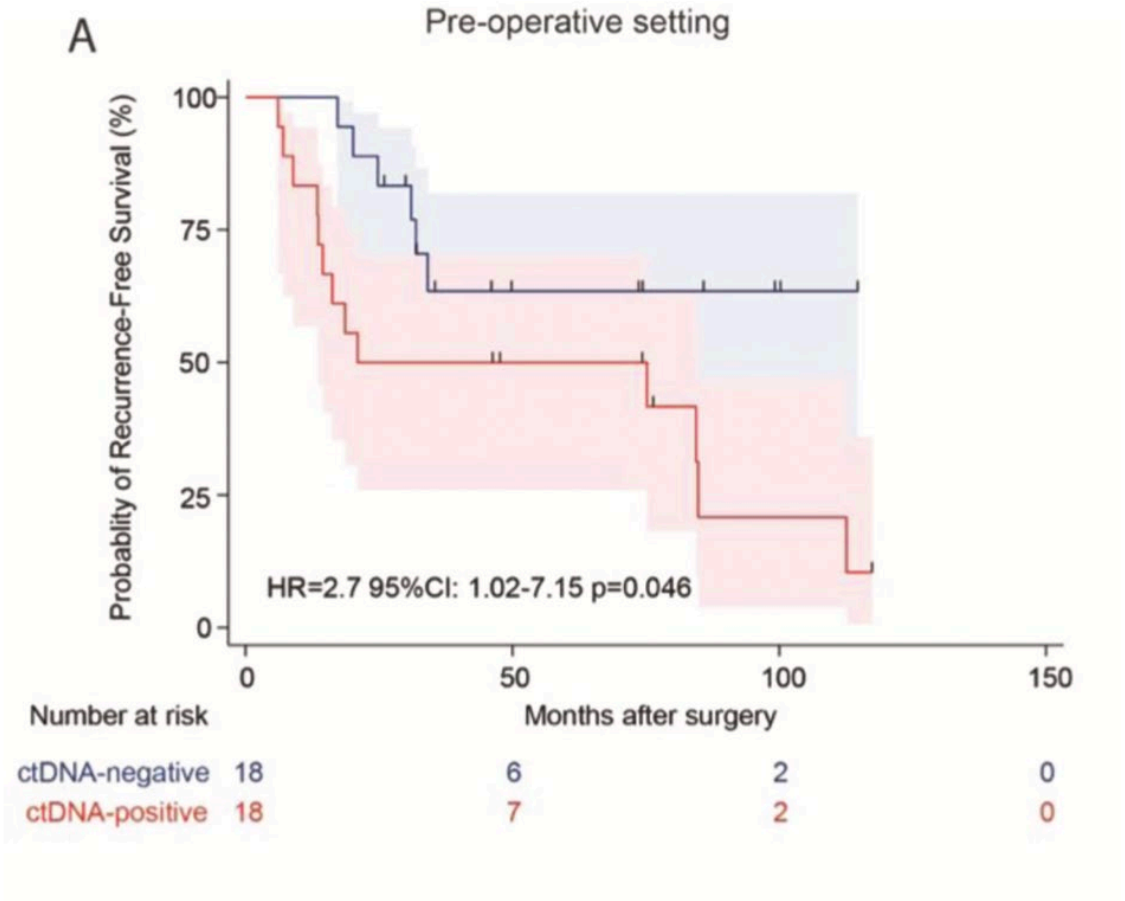
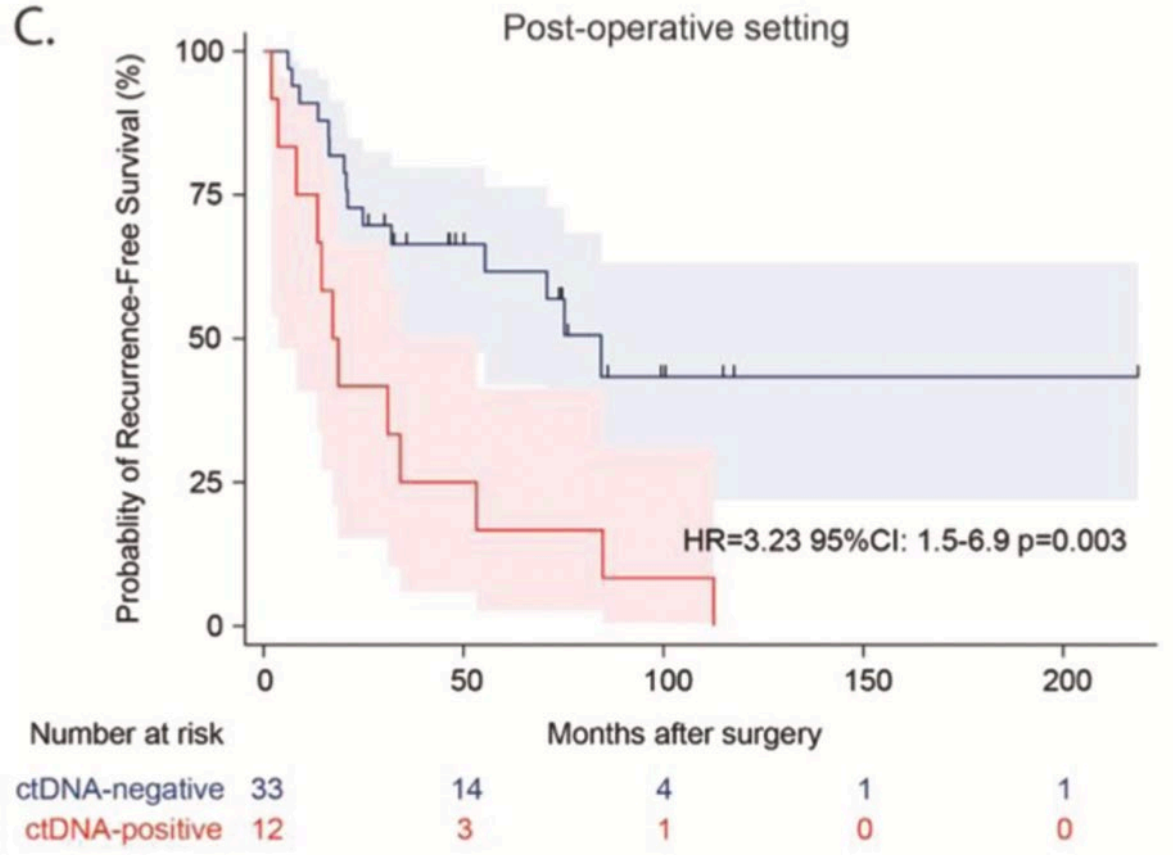
Association of circulating tumor DNA with patient prognosis in surgically resected renal cell carcinoma





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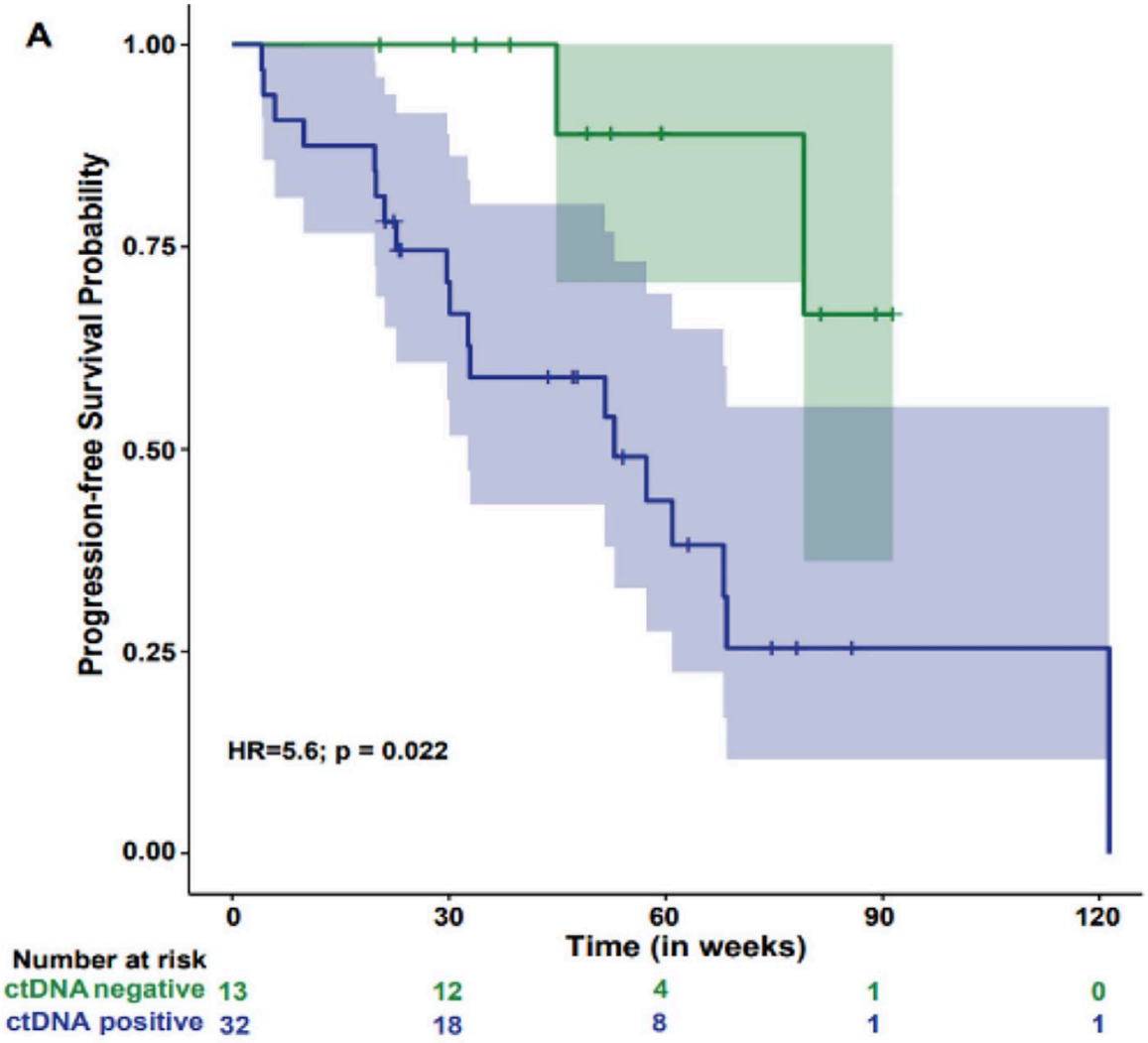
High Sensitivity Circulating Tumor-DNA Assays in Renal Cell Carcinoma–Are we there yet?

45 patients
Followed for 48 months
Localized and Metastatic

ctDNA changes over time had 90% correlation with recurrence

83% concordance w/ negative ctDNA and no recurrence

13.6 wk lead time to radiographic progression



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Integrative Oncology Ochsner

- Yoga and mobility
- Mental and emotional wellness
- Acupuncture
- Rehabilitative wellness services
- Diet and Nutrition

Gut Bacte
Immunotl

FMT - fecal microbial transplant

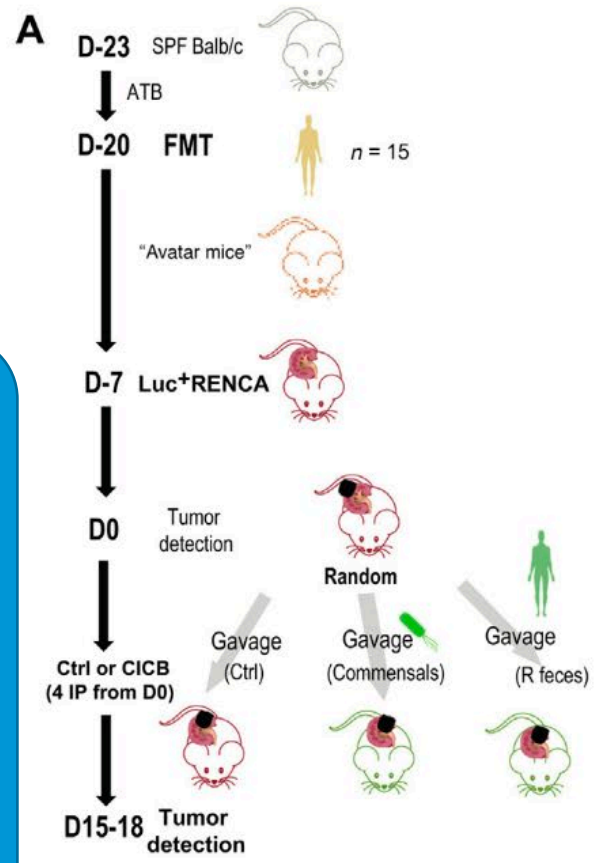
CICB - Anti-PD-1 and CTLA4

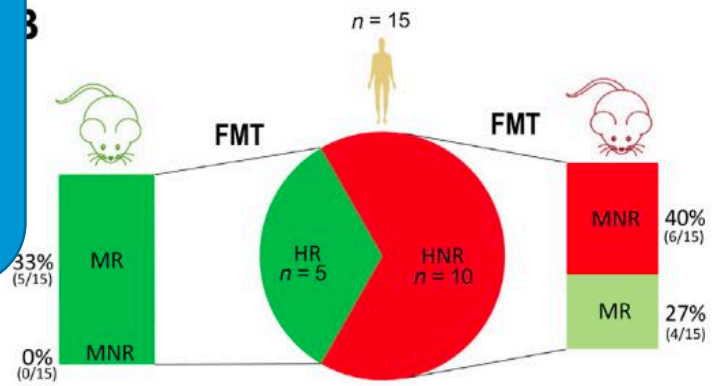
HR – human responders

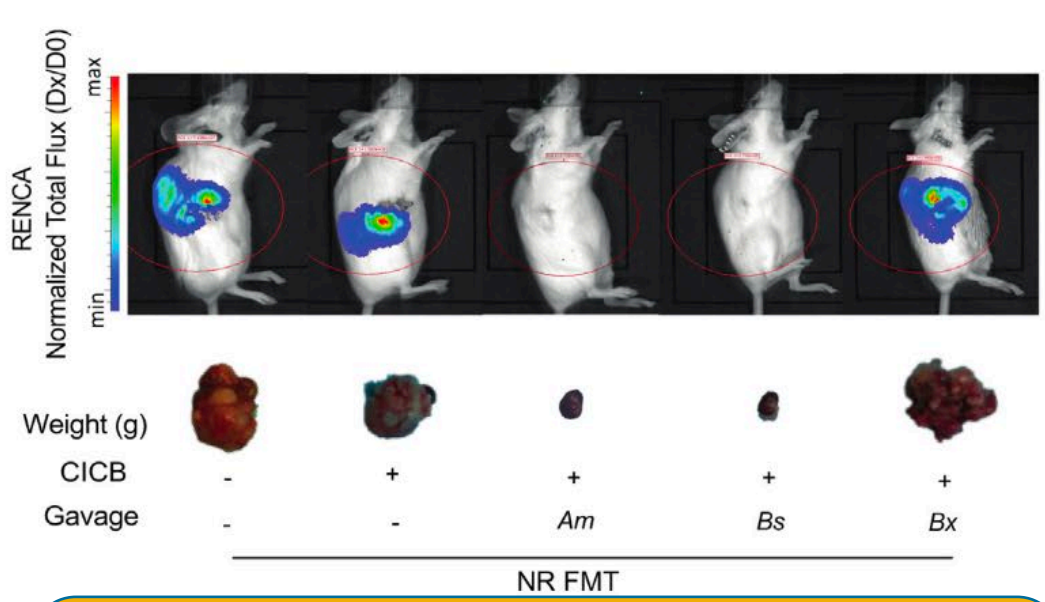
HNR – human non-responders

MR – mouse responders

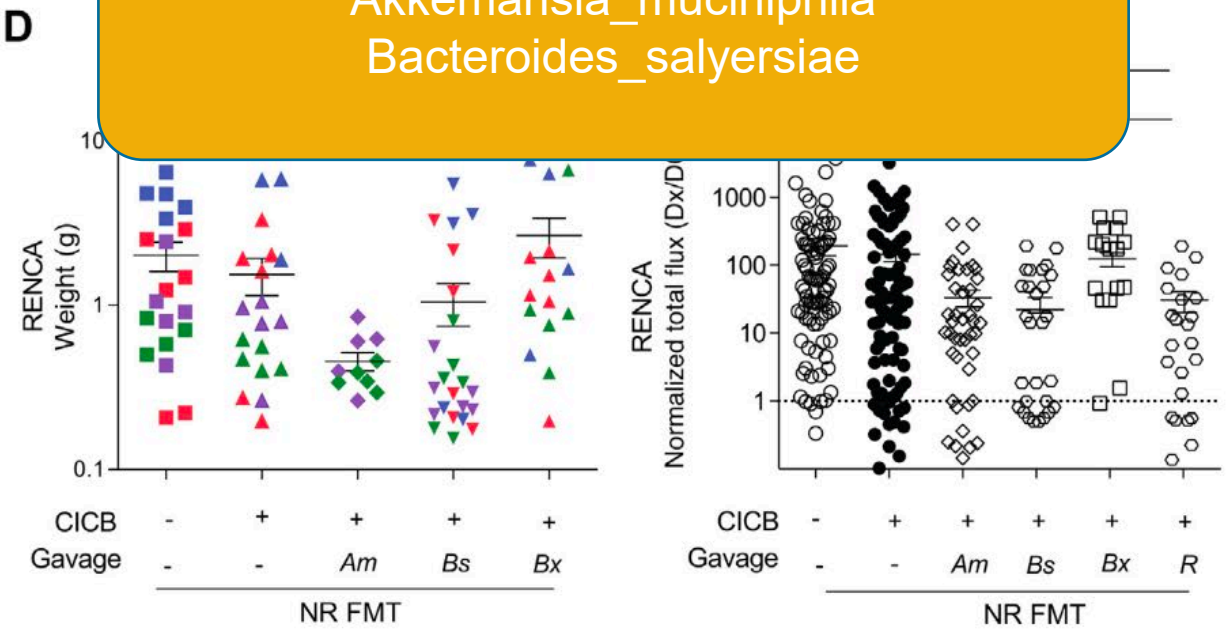
MNR – mouse non-responders





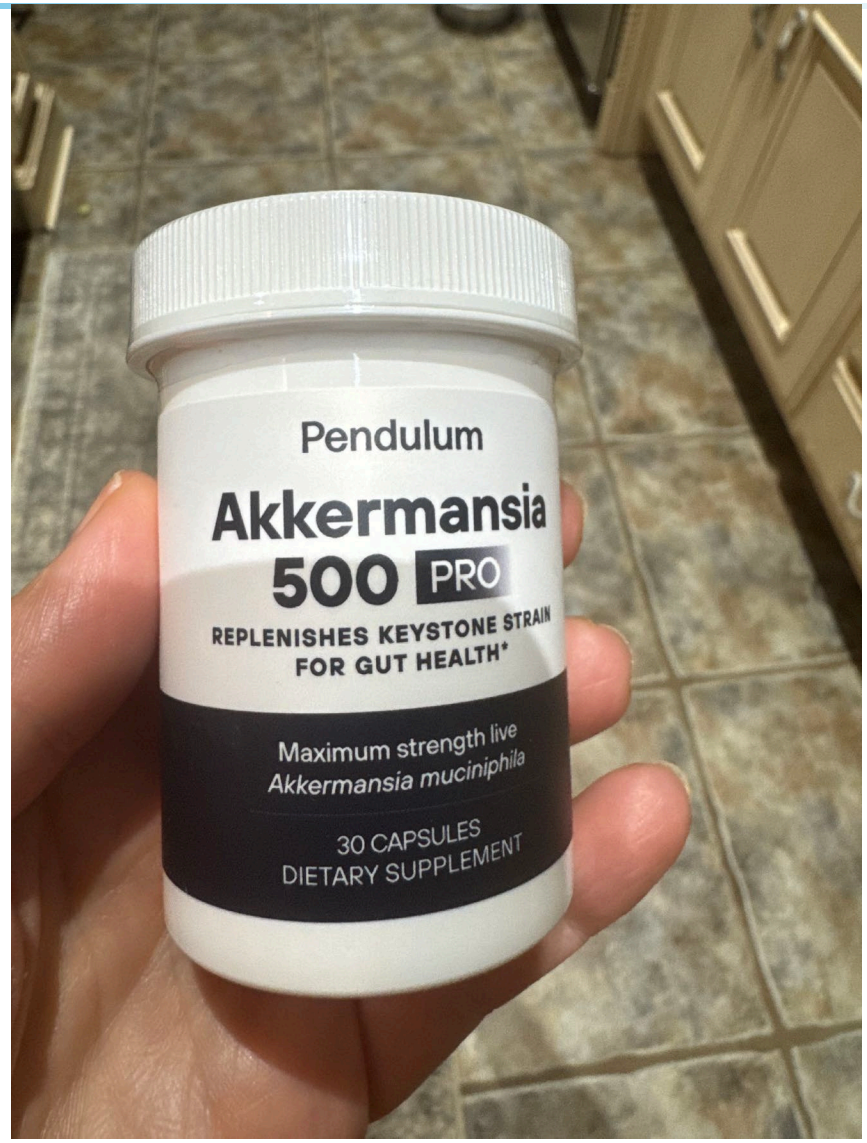


Akkemansia_muciniphila
Bacteroides_salyersiae



Derosa EAU 2020

Akkermansia



Palliative Care

Figure 1: Trends in use of palliative interventions among patients with Stage IV RCC.

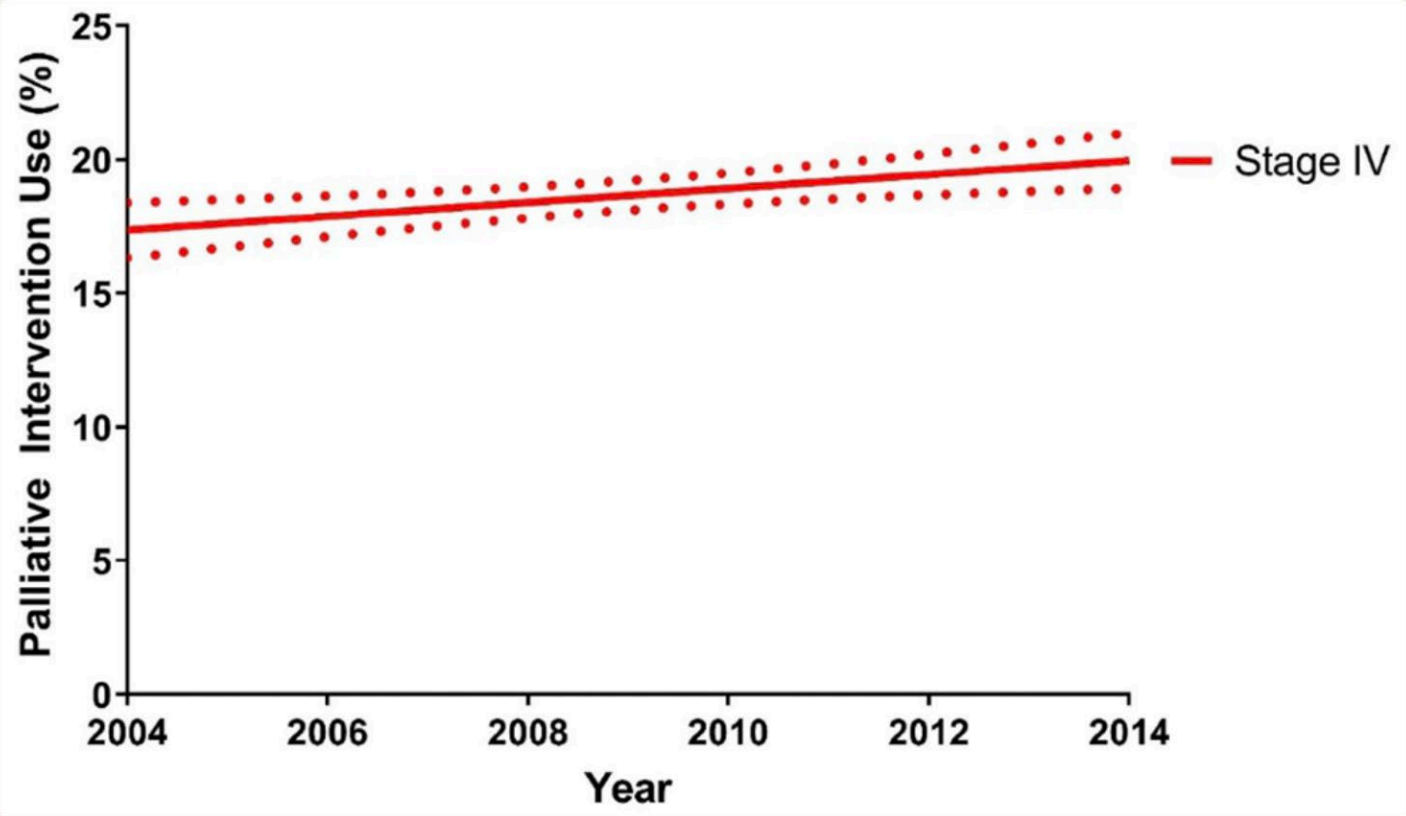
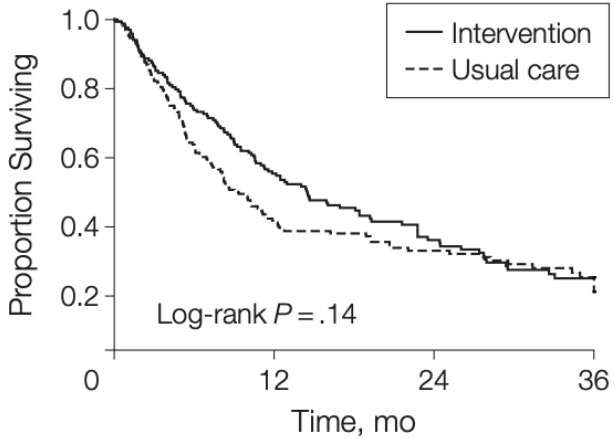


Figure 4. Kaplan-Meier Estimates of Survival According to Treatment Group



No. at risk

Intervention	161	83	35	16
Usual care	161	62	33	16

Survival was calculated as the time of enrollment (within 8 weeks of diagnosis with new or recurrent advanced stage disease) to the time of death or study completion (May 1, 2008). Median survival for the intervention group was 14 months (95% CI, 10.6-18.4 months) and 8.5 months (95% CI, 7.0-11.1 months) for the usual care group (P=.14).

Patel Cin Gen Cancer 2022 PMID 35105510 ; Bakitas JAMA 2009 PMID19690306

Conclusions

- Early stage disease –> consider renal mass biopsy or novel therapies
- Precision medicine is here – Biomarkers are needed
- Medical oncology – escalate, descalate, and choose wisely
- Radiotherapy is critical to both early and advanced disease states
- Theronostics has made its way to Kidney Cancer – hooray!
- Integrative oncology can support and strength therapeutic programs
- Medicine is not always about a cure, but also about compassion → call palliative care

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