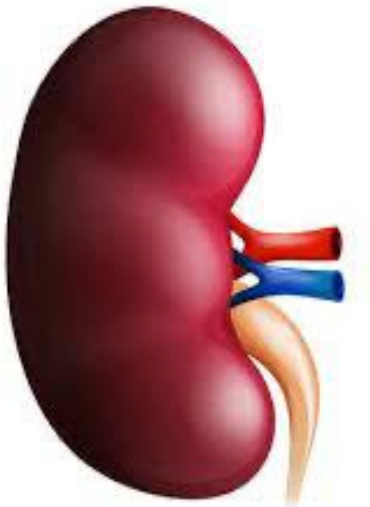


What have we learned in the **last 10 years**

- Renal Cell Carcinoma -

Umberto Capitanio

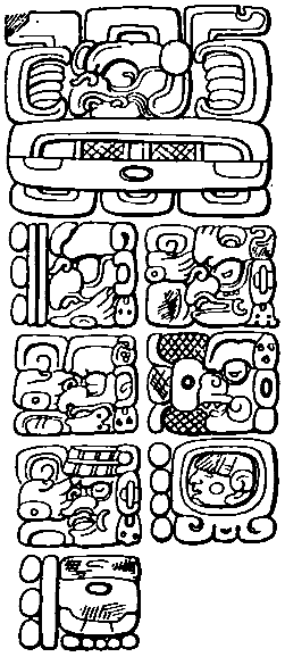


**I.R.C.C.S. Ospedale
San Raffaele**

Gruppo San Donato

What have we learned in the last 10 years (2012-2022) – Renal Cancer

In **2012, world was ending** (according to eschatological beliefs that cataclysmic or transformative events would occur on December 2012)



u_capitanio

What have we learned in the last 10 years (2012-2022) – Renal Cancer

Stage
I

Stage
II

Stage
III

Stage
IV

“Surgical therapy is the only curative therapeutic approach for the treatment of RCC”

Stage	Surgery	
T1	Nephron-sparing surgery	Open
		Laparoscopic
	Radical nephrectomy	Laparoscopic
		Open
T2	Radical nephrectomy	Laparoscopic
		Open
	Nephron-sparing surgery	

20¹2



What have we learned in the last 10 years (2012-2022) – Renal Cancer

Stage
I

Stage
II

Stage
III

Stage
IV

Growth Kinetics of Small Renal Masses on Active Surveillance Results from 318 patients in the DISSRM Registry

SRM grow slowly
Average:
0.09cm/year



Few SRM grow rapidly.

Average Growth Rate:

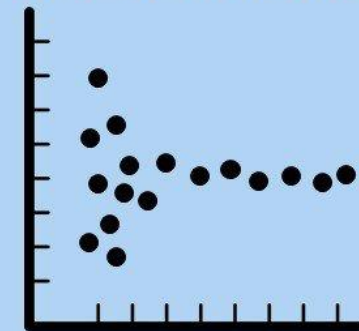
<0 cm/year 35%

0 cm/year 7%

0-0.5cm/year 41%

>0.5 cm/year 17%

Growth Rates vary
within first year,
stabilize thereafter.



of THE JOURNAL
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Official Journal of the
American
Urological
Association

Uzosike, et al. J Urol. March, 2018.

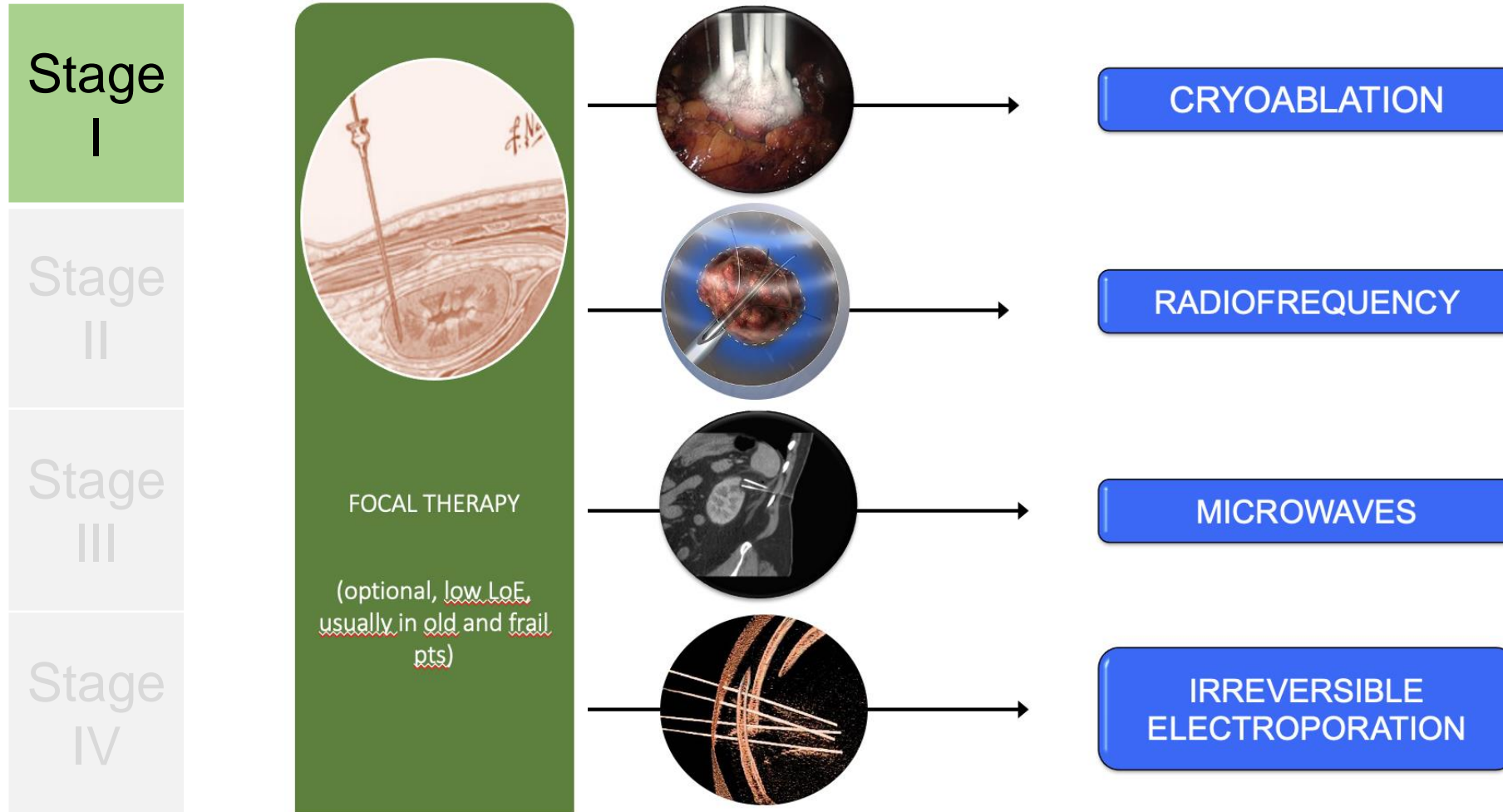
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2022



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What have we learned in the last 10 years (2012-2022) – Renal Cancer



2022



What have we learned in the last 10 years (2012-2022) – Renal Cancer

Stage
I

Stage
II

Stage
III

Stage
IV

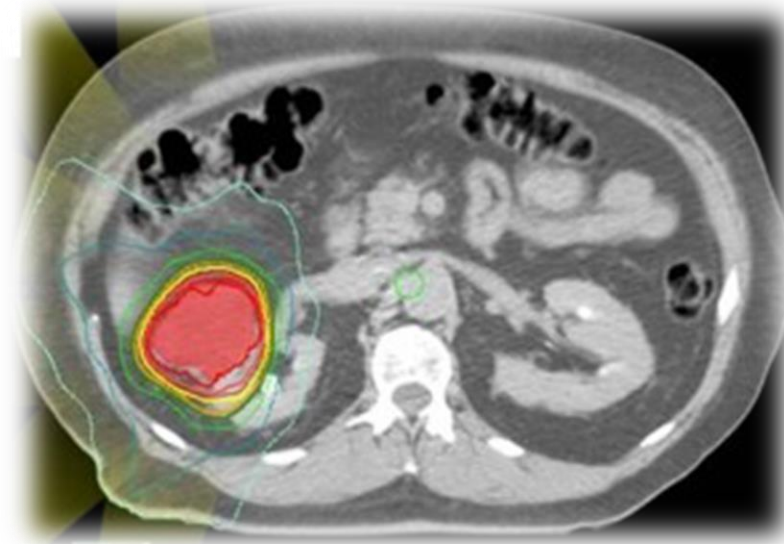
5-year outcomes after stereotactic ablative body radiotherapy for primary renal cell carcinoma: an individual patient data meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney)

- 190 patients
- cT1a – cT1b
- Single or multiple fractions

- 12 institutions (Australia, Canada, Germany, Japan, and the USA)



Lancet Oncol 2022



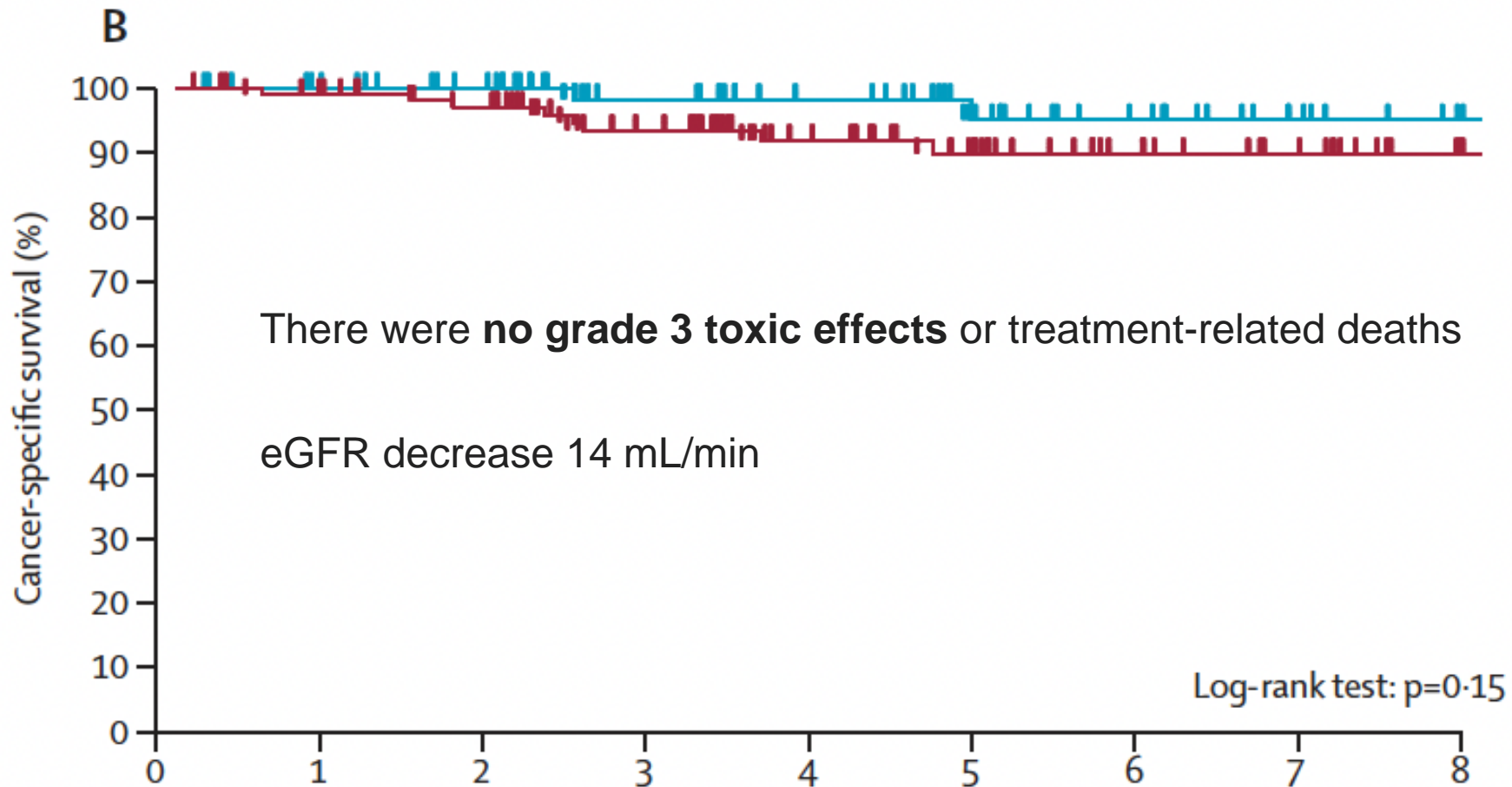
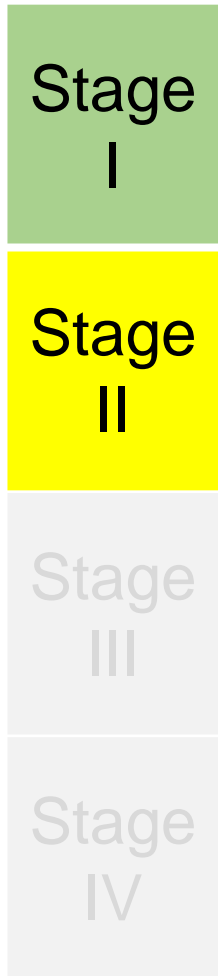
2022



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Siva et al. Lancet Oncol. 2022

What have we learned in the last 10 years (2012-2022) – Renal Cancer



2022



What have we learned in the last 10 years (2012-2022) – Renal Cancer

Stage
I

Stage
II

Stage
III

Stage
IV

***”There is no indication for adjuvant
therapy following surgery”***

20¹2



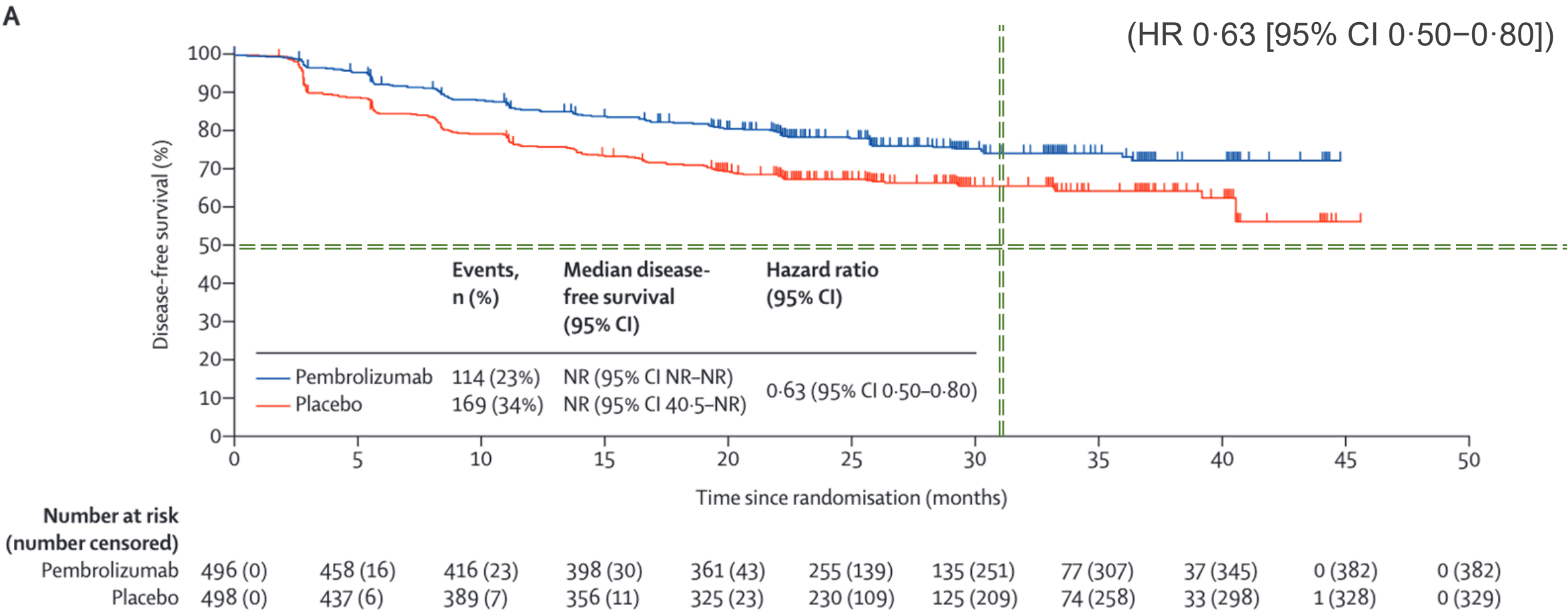
What have we learned in the last 10 years (2012-2022) – Renal Cancer

Stage	TRIAL	n	NCT	Inclusion criteria	Treatment arm		PFS	OS
Stage I	S-TRAC	600	00375674	High risk (UISS)	Sunitinib	TKI	6.8 vs 5.6 HR 0.76	
Stage II	ASSURE	1943	00326898	pT1b G3-4 or pT2-4 or pN1	Sunitinib Sorafenib	TKI		
	PROTECT	1,500	01235962	pT2 G3-4 or pT3-4 or pN1	Pazopanib	TKI		
Stage III	ATLAS	724	01599754	pT2-4 or pN1	Axinitinib	TKI		
	SORCE	1,666	00492258	Intermediate and high risk	Sorafenib	TKI		
	EVEREST	1,218	01120249	Intermediate and high risk	Everolimus	mTORi		
Stage IV	ARISER	864	00087022	T1b-T2G3-4 or T3-4 or pN1	Girentuximab	Tumor antigen Ab		



Pembrolizumab versus placebo as post-nephrectomy adjuvant therapy for clear cell renal cell carcinoma (KEYNOTE-564): 30-month follow-up analysis of a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

Powles T et al. *Lancet Oncol* 2022



What have we learned in the last 10 years (2012-2022) – Renal Cancer

Stage
I

Stage
II

Stage
III

Stage
IV

"Cytoreductive nephrectomy is recommended for metastatic RCC"

Table 3: Recommendations for first and second line systemic therapy in mRCC

Treatment	Risk or prior treatment	Recommended agent
First-line	Low- or intermediate-risk mRCC	Sunitinib Bevacizumab + IFN- α Pazopanib
	High-risk mRCC	Temsirolimus

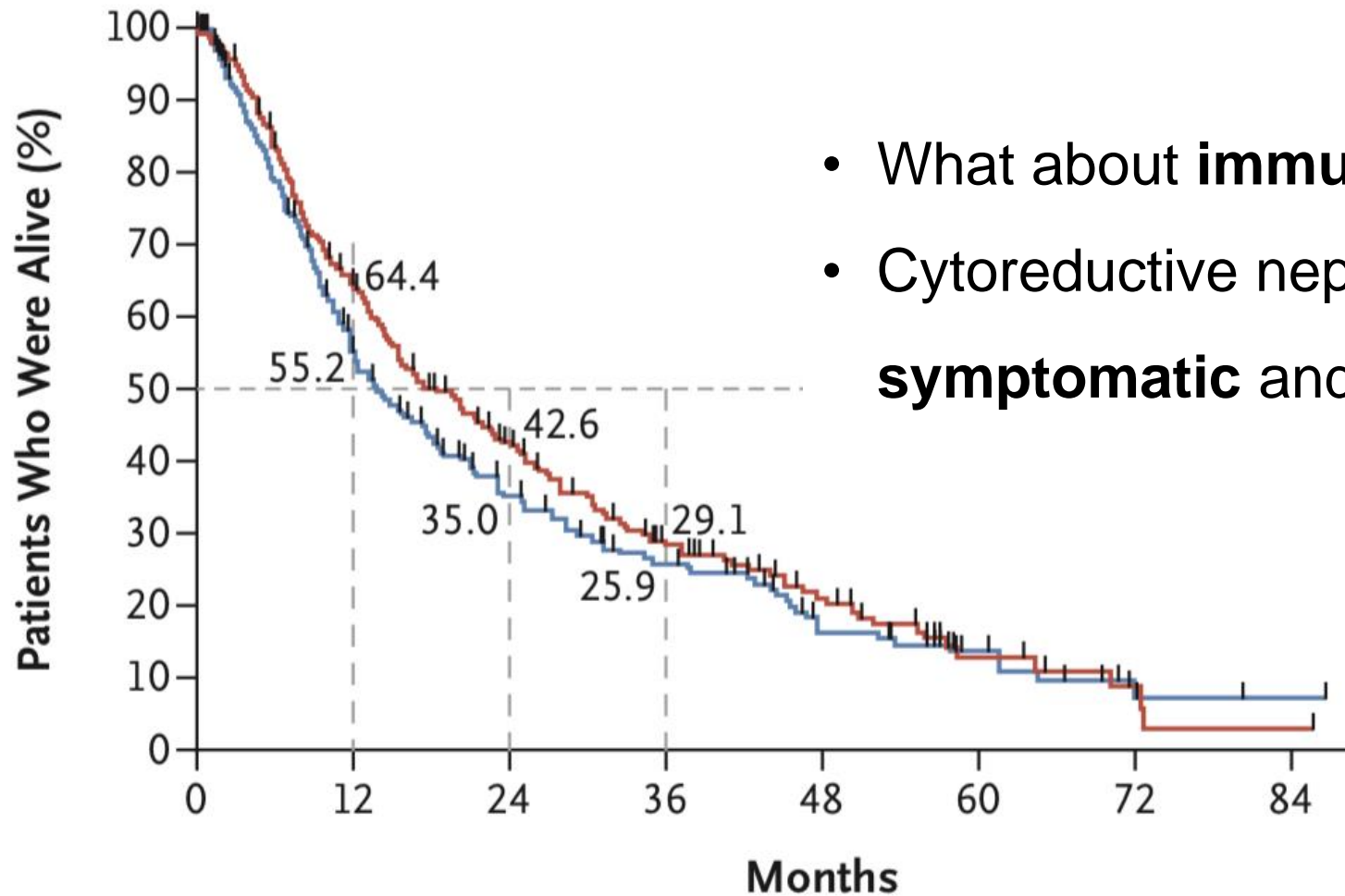
20¹2



ORIGINAL ARTICLE

Sunitinib Alone or after Nephrectomy
in Metastatic Renal-Cell Carcinoma

A Overall Survival



- What about **immunotherapy**?
- Cytoreductive nephrectomy **still an option** in **symptomatic** and/or **oligomets**

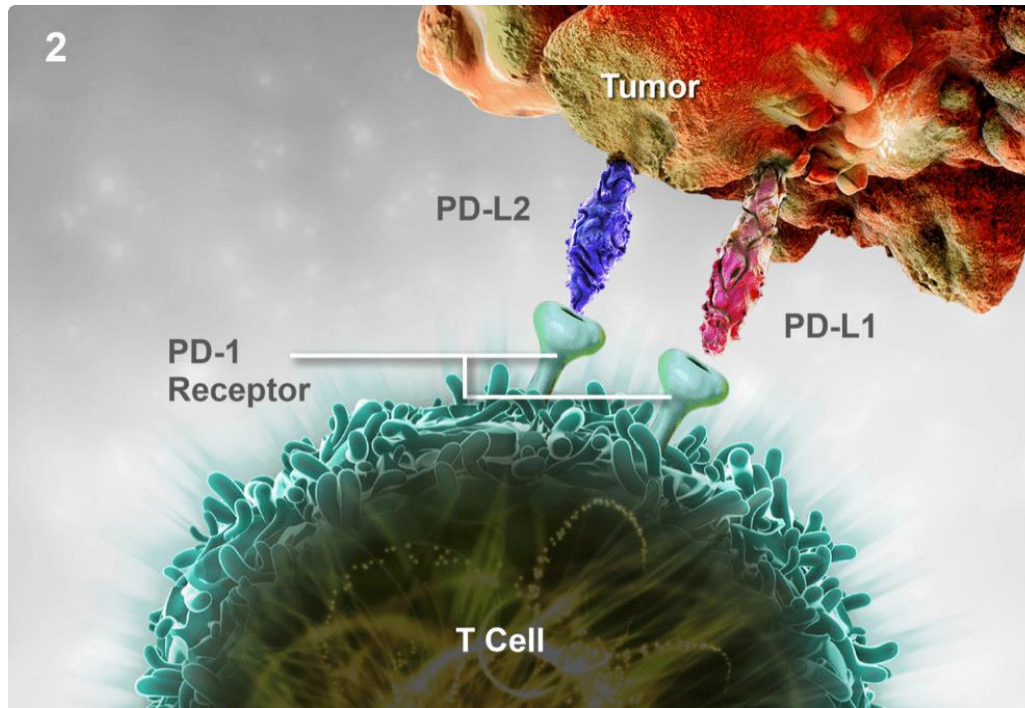
What have we learned in the last 10 years (2012-2022) – Renal Cancer

Stage
I

Stage
II

Stage
III

Stage
IV



nivolumab/cabozantinib [1b]
pembrolizumab/axitinib [1b]
pembrolizumab/lenvatinib [1b]
nivolumab/ipilimumab [1b]

What have we learned in the last 10 years (2012-2022) – Renal Cancer

Functional
outcomes

Frailty

Hospital
Quality

Genomics

Research focused on

urological outcomes, only



- Number of cases
- Bleeding
- Complications
- Ischemia time
- Surgical margins
- Cancer control

THE PAST

Research focused on

(holistic) patients' outcomes



- Overall survival
- Renal function
- Cardiovascular events
- Comorbidities
- Frailty
- QoL

THE PRESENT and THE FUTURE

What have we learned in the last 10 years (2012-2022) – Renal Cancer

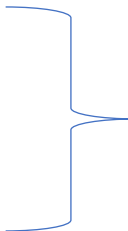
Association of renal function with oncological outcomes

Functional
outcomes

Frailty

Hospital
Quality

Genomics

- **not intuitive**
- CKD determines:
 1. a vicious loop in which the **immune system** is:
 - both activated in a proinflammatory direction
 - and suppressed
 - finally leading to uremia-related immune deficiency
 2. Preferential loss of number and function of **lymphoid cells** through:
 - loss of thymic function
 - attrition of telomeres
 - expanded memory T-cell population «premature immunological aging»
 3. Decreased physical and mental health status (contributes to decrease the host's defenses)

What have we learned in the last 10 years (2012-2022) – Renal Cancer

Functional
outcomes

Frailty

Hospital
Quality

Genomics

Frail vs. no frail patients:

- Overall complications: **43** vs. 29% ($p < 0.001$)
- Major complications: **17** vs. 10% ($p < 0.001$)
- Blood transfusions: **11** vs. 7.7% ($p < 0.001$)
- Non-home-based discharge: **13** vs. 8% ($p < 0.001$)
- Length of stay: **4** vs. 3 days ($p < 0.001$)
- Total hospital charges: **\$33,550** vs. \$31,032 ($p < 0.001$)



Interestingly, roughly **half of frail patients (n=1,198; 44%)** **did not exhibit** other well-known risk factor for adverse outcomes, namely **obesity or Charlson Comorbidity index ≥ 2**

What have we learned in the last 10 years (2012-2022) – Renal Cancer

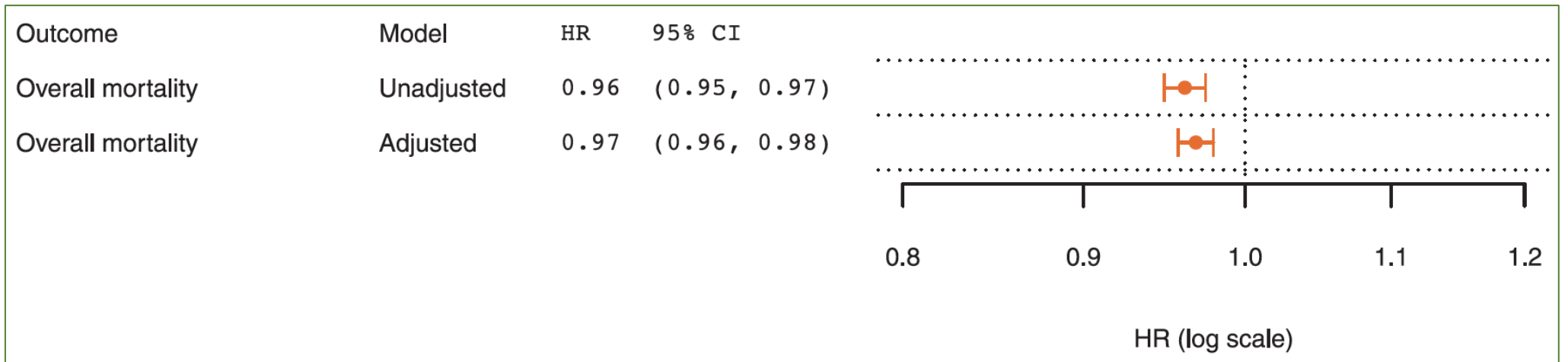
Functional
outcomes

Frailty

Hospital
Quality

Genomics

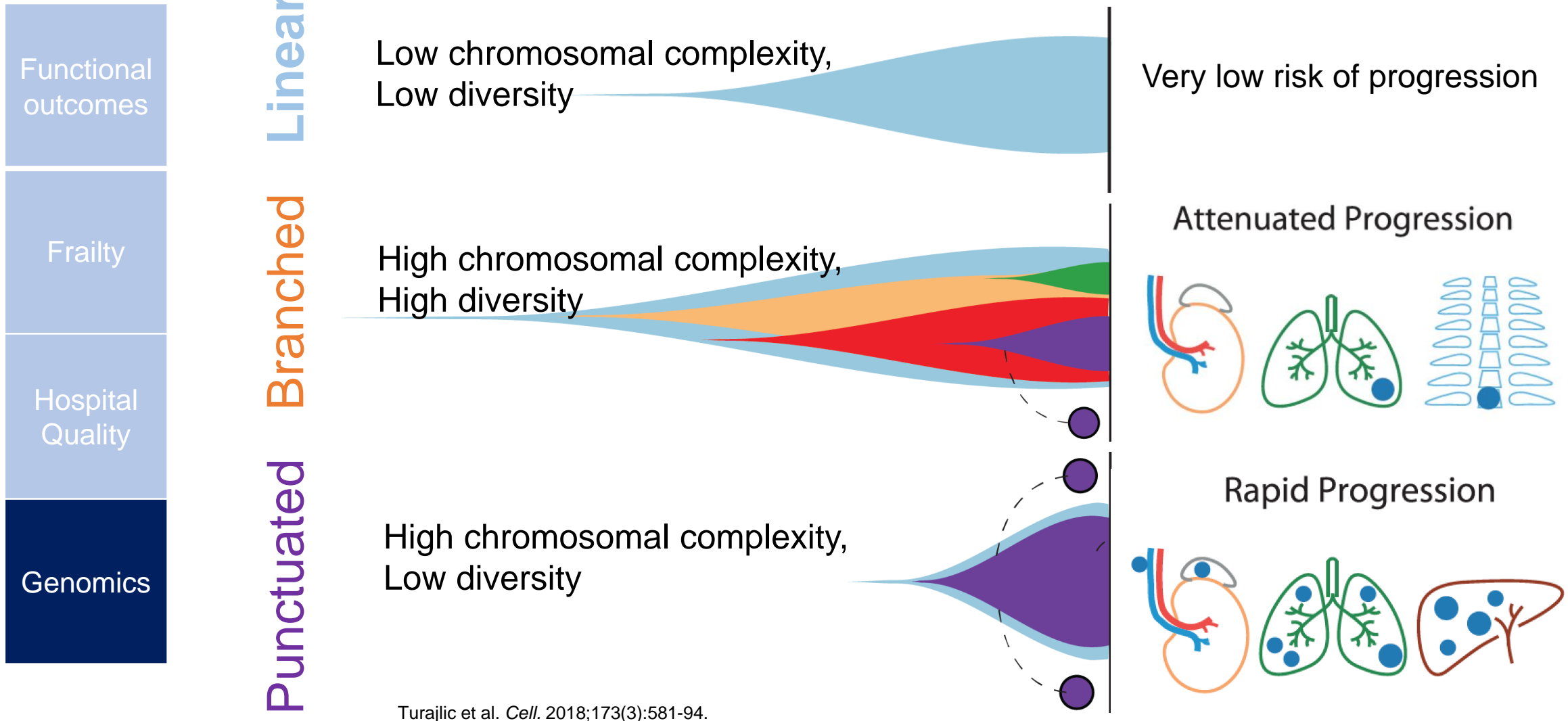
National Cancer Database (1,100 hospitals)



#5 Quality Indicators (QI) defined as % of:

1. T1a tumors undergoing PN
2. T1-2 tumors receiving lap or rob surgery
3. PSM following PN for T1
4. Length of hospital stay (LOS)
5. 30-d unplanned readmission

What have we learned in the last 10 years (2012-2022) – Renal Cancer



What will be the future in the next 10 years (2022-2032) – Renal Cancer

Stage
I

- Biomarkers
 - Screening
 - Detection
 - Prognosis
 - Prediction
 - Follow-up

Stage
II

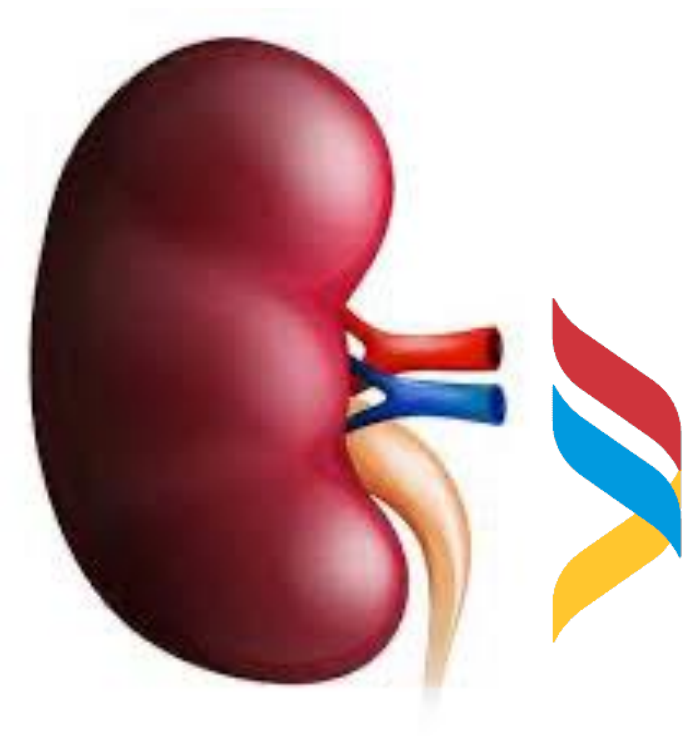
Stage
III

Stage
IV

- Radiomics
- Tailored clinical decision
- Novel drugs
- SBRT+IO



What will be the future in the **next 10 years (2022-2032)** – Renal Cancer



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