



BMUC

UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

**Post conference
meeting 2021**

Urology

Dr. Charles Van Praet

Ghent University Hospital

Conflicts of interest



- I have the following potential conflict(s) of interest to report

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports:	-
Receipt of honoraria or consultation fees:	Astellas, IPSEN, Corza Medical
Participation in a company sponsored speaker's bureau:	-
Stock shareholder:	-
Spouse/partner:	-
Other support (please specify):	-

Content



- Prostate cancer
 - Screening EAU update
 - Stockholm3 trial
 - LAPRO trial update
- Bladder cancer
 - NMIBC: nadofaragene firadenovec
 - MIBC: ctDNA testing in peri-operative management
- Renal cell carcinoma
 - Carmena update
 - Neo-adjuvant TKI in localized and locally advanced RCC

A teal-colored header image featuring a microscopic view of cells, likely prostate cancer cells, showing their irregular shapes and dense arrangement.

Prostate Cancer

“Precision makes perfect”

PSMANIA



ASCO 2021: PSMA Radioligand Therapy Improves Survival in Metastatic Prostate Cancer

EAU 2021: PSMA in Diag

ESMO 2021: Patient-Reported Outcomes in Prostate Cancer Patients Receiving PSMA-Targeted Radionuclide Therapy

3,082 results



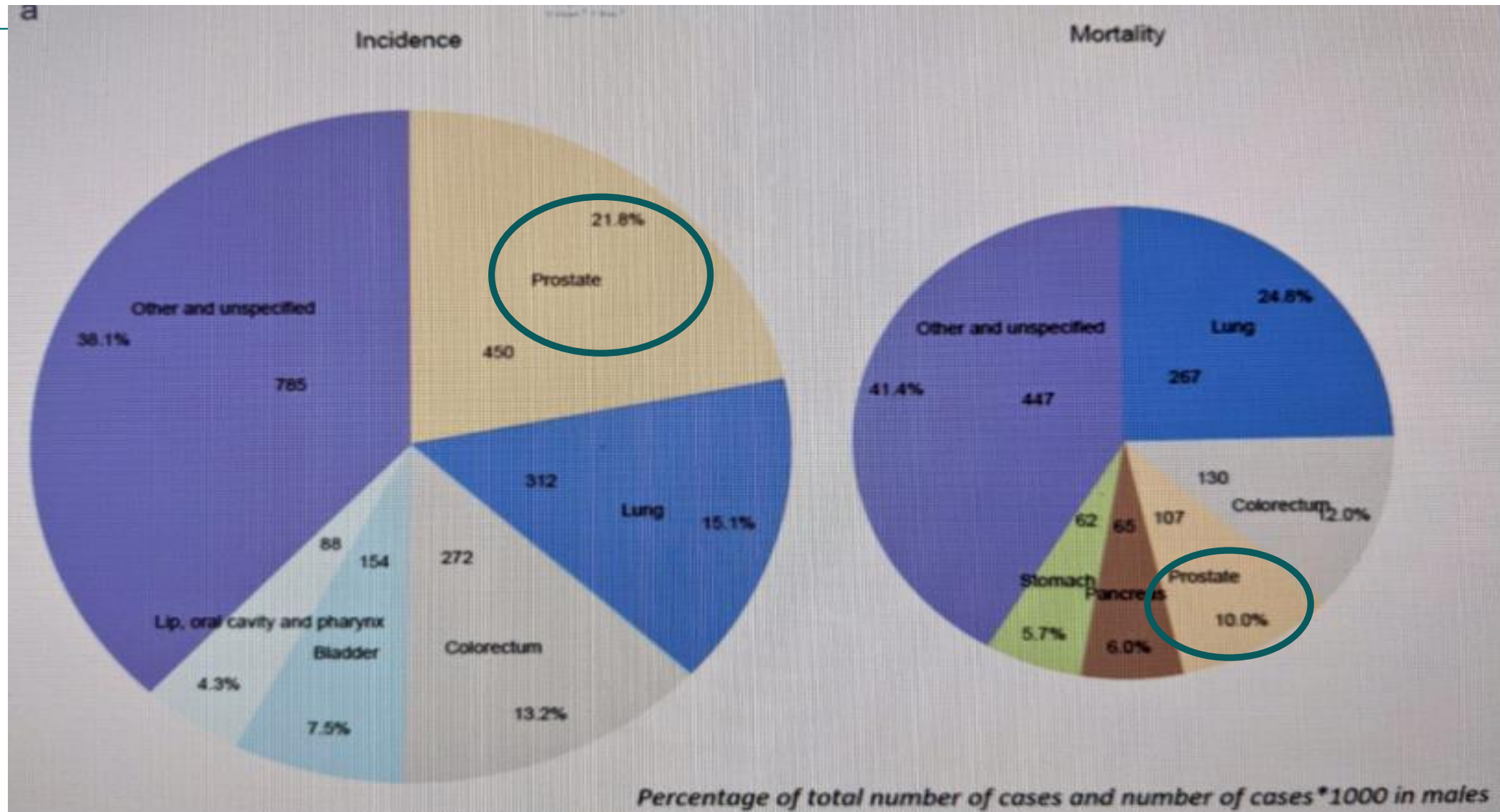
[¹⁷⁷Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 3 trial

Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Irvani, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedy, Nat, Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, Andrew B, Guminiski, Edward Hsiao, Wei Chua, Peter Lin, Alison Y Zhang, Margaret M McJannett, Martin R Stockler, Jo, Andrew J Martin, Ian D Davis, for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Group†

PRIMARY CANCER—PROSTATE, TESTIS, AND BLADDER
Phase 3 study of lutetium-177-PSMA-617 in patients with metastatic castration-resistant prostate cancer (TheraP).



Prostate cancer screening



Prostate cancer screening

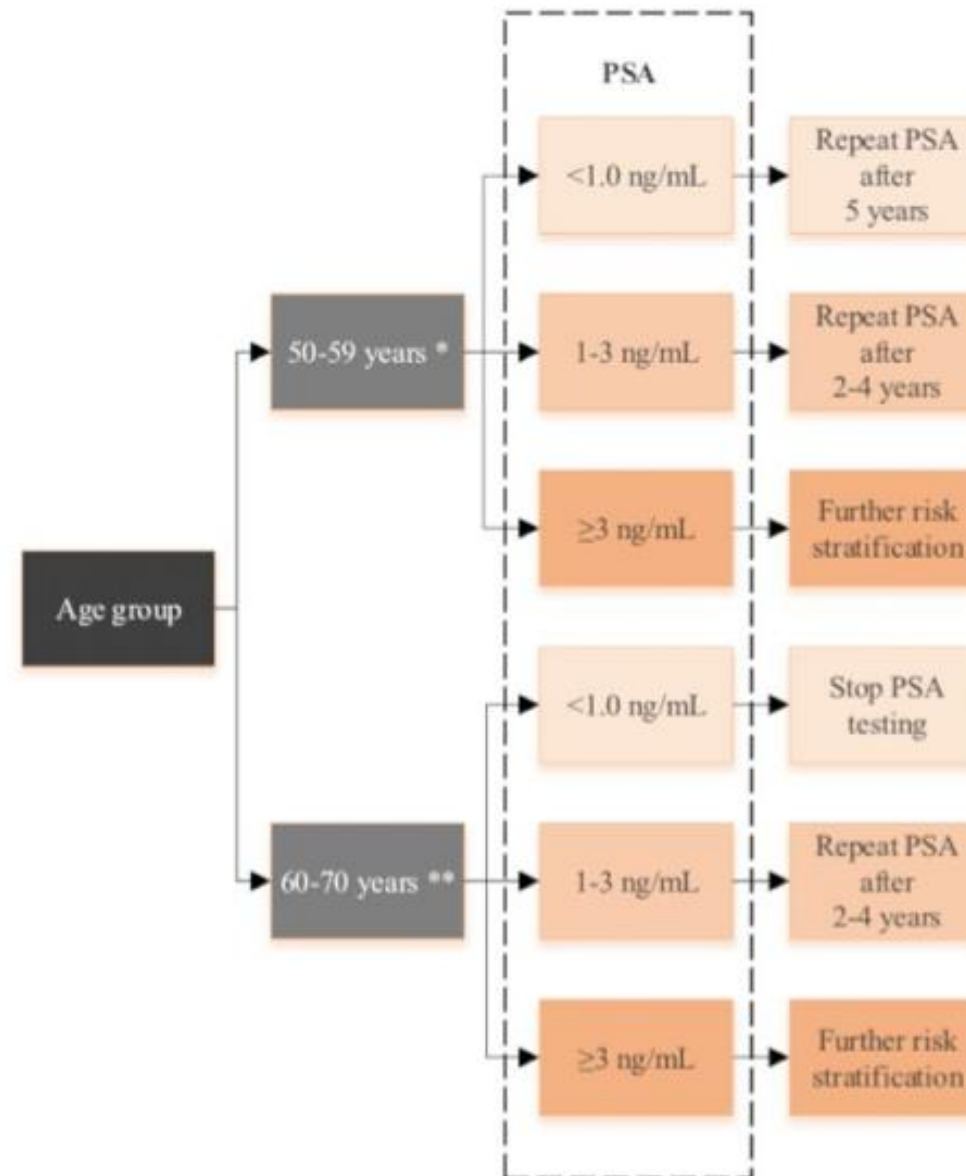


Review – Prostate Cancer

Prostate-specific Antigen Testing as Part of a Risk-Adapted Early Detection Strategy for Prostate Cancer: European Association of Urology Position and Recommendations for 2021

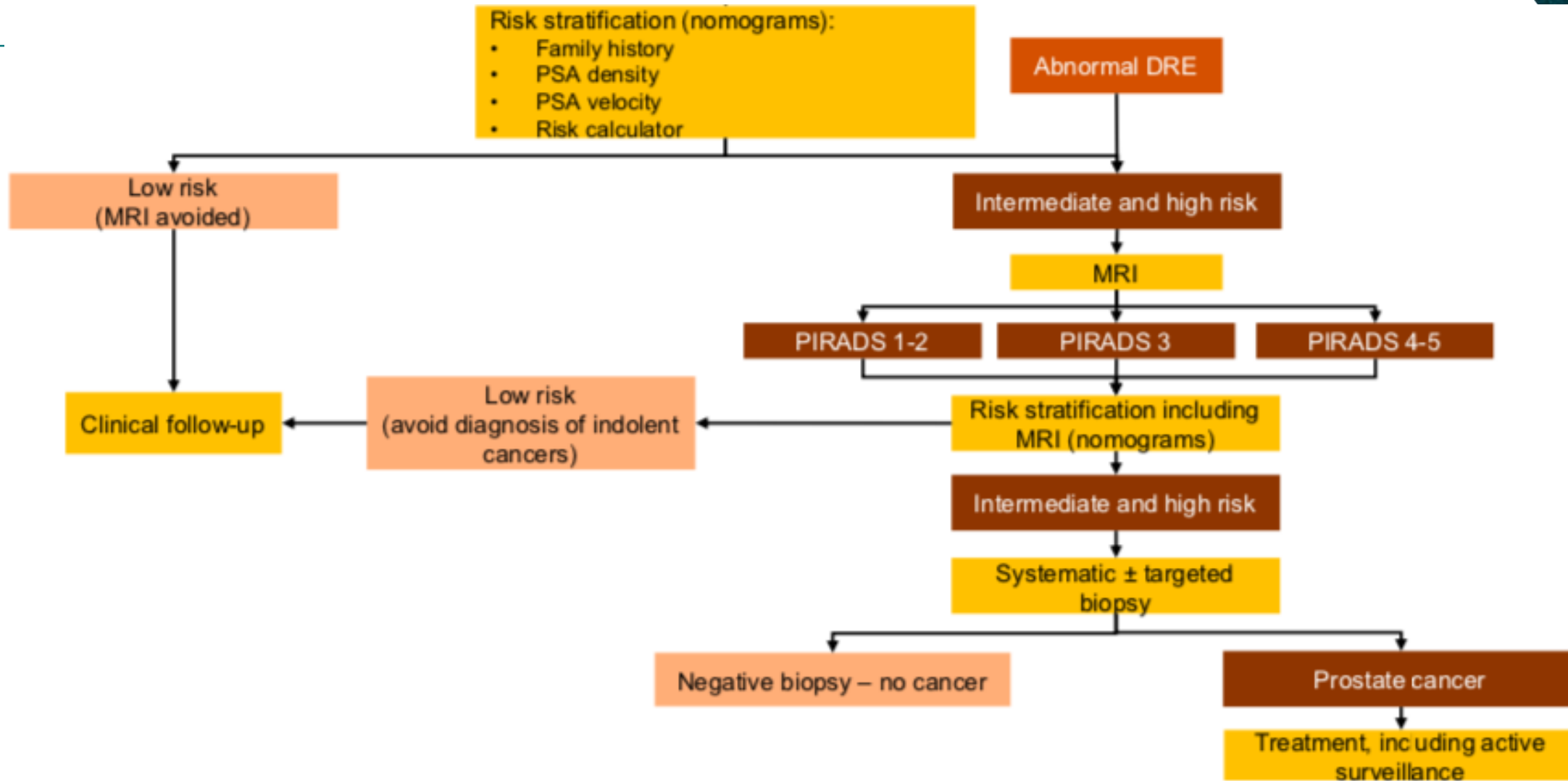
Hendrik Van Poppel^{a,}, Monique J. Roobol^b, Christopher R. Chapple^c, James W.F. Catto^{d,e}, James N'Dow^{f,g}, Jens Sønksen^{h,i}, Arnulf Stenzl^j, Manfred Wirth^k*

Prostate cancer screening



Healthy men >70yr without important comorbidities and a life expectancy >10-15 years may continue PSA testing

Prostate cancer screening



Stockholm3 – MRI trial



PSA

Systematic
biopsy

ERSPC



PSA

MRI

Targeted
biopsy

PROMIS
PRECISION

...



PSA and/or
genomic testing

MRI

Targeted
biopsy

Stockholm3 – MRI trial

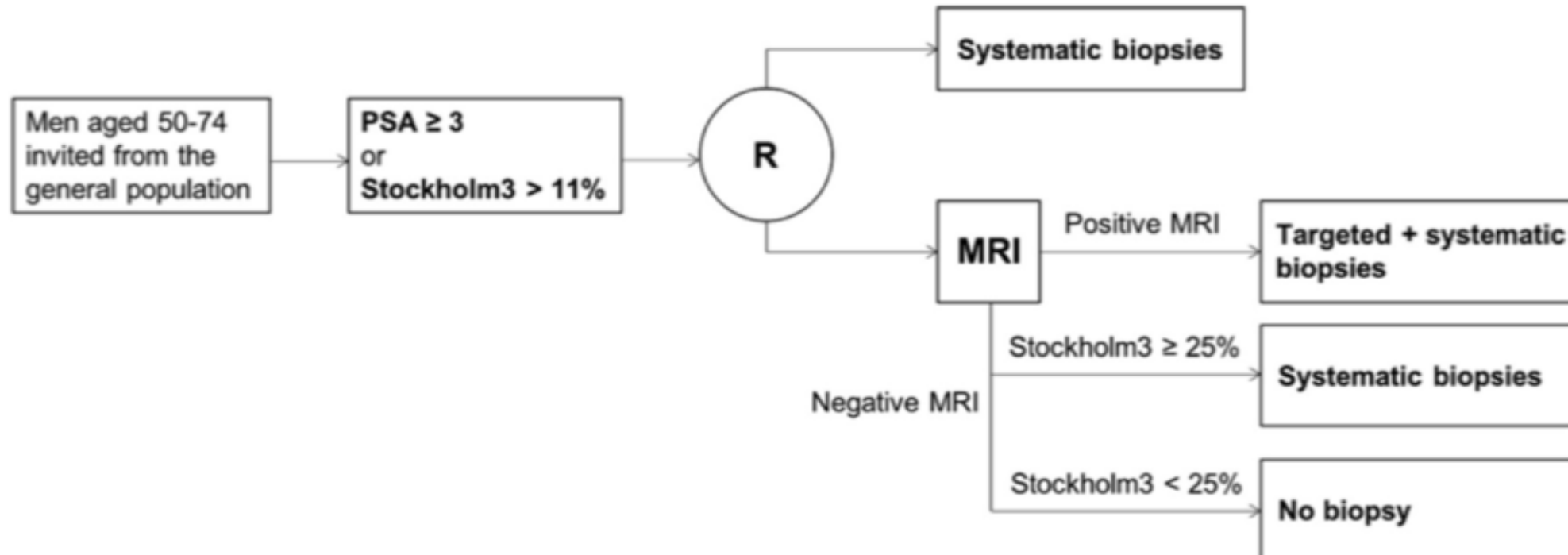


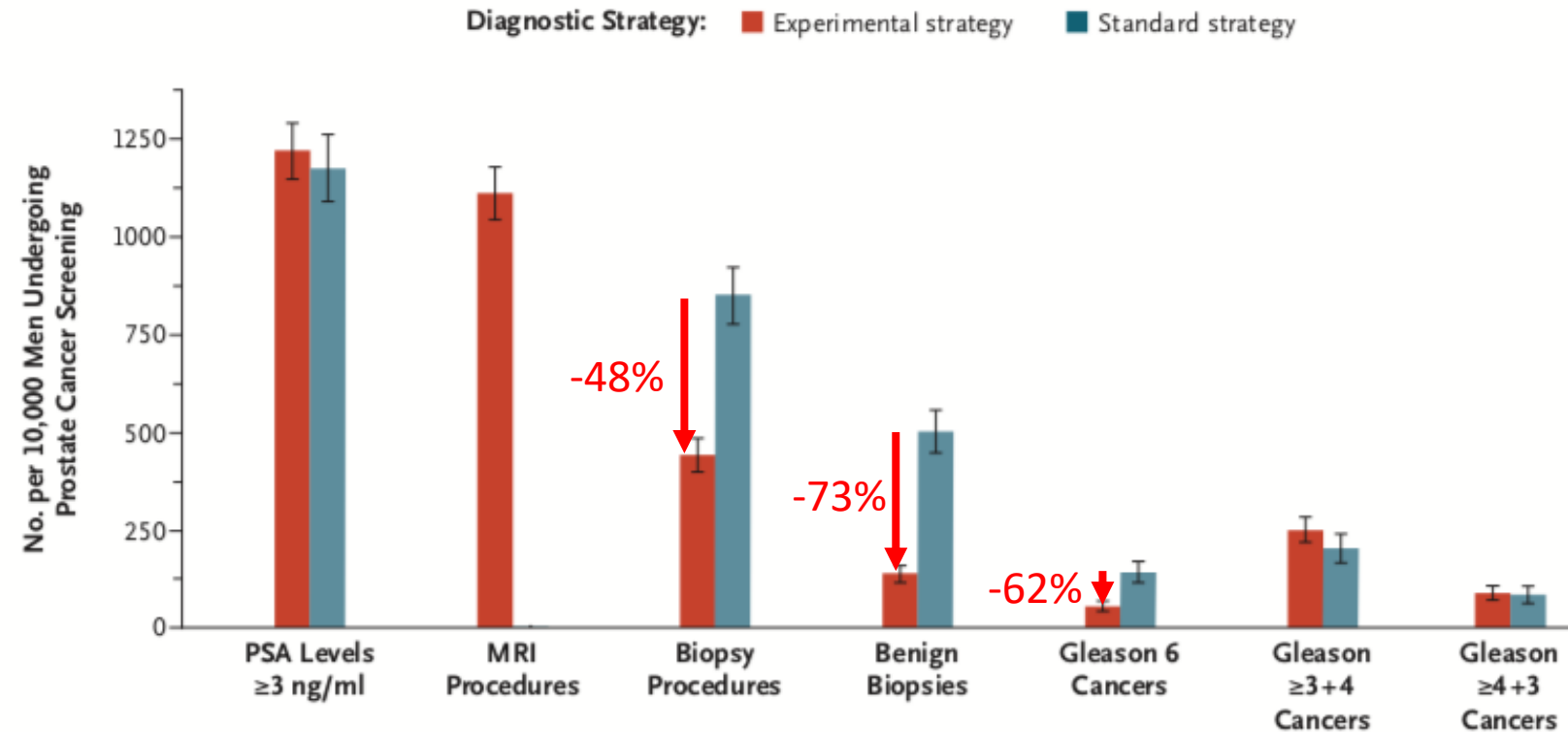
Figure 1 Study design overview of STHLM3MRI Main Study.

Stockholm3 – MRI trial



	Enrolled participants	Randomised participants		
	All (n=12750)*	All (n=2293)	Standard group (n=921)	Experimental group (n=1372)
Age, years	61 (55–67)	66 (61–71)	67 (61–71)	66 (61–71)
Family history of prostate cancer	1947 (15.7%)	413 (18.0%)	176 (19.1%)	237 (17.3%)
Previous benign biopsy	533 (4.2%)	252 (11.0%)	98 (10.6%)	154 (11.2%)
On 5- α reductase inhibitor treatment	255 (2.0%)	78 (3.4%)	25 (2.7%)	53 (3.9%)
PSA at inclusion, ng/mL	1.0 (0.6–1.9)	3.5 (2.6–4.9)	3.5 (2.6–4.9)	3.5 (2.6–4.8)
Stockholm3 at inclusion†	..	0.14 (0.10–0.20)	0.14 (0.10–0.20)	0.14 (0.10–0.20)
Prostate volume, mL‡	..	40 (30–55)	39 (30–52)	40 (31–55)
PI-RADS score				
≤2	..	..	0	815 (59.4%)
3	..	..	0	261 (19.0%)
4	..	..	0	115 (8.4%)
5	..	..	1 (0.1%)	69 (5.0%)
No MRI done	..	..	920 (99.9%)	112 (8.2%)

Stockholm3 – MRI trial



Experimental Strategy — no.	1221	1112	444	138	54	252	88
Standard Strategy — no.	1175	2	853	504	142	206	84
Absolute Difference	0.5	—	-4.1	-3.7	-0.9	0.5	0.0
(95% CI) — percentage points	(-0.7 to 1.6)	—	(-5.0 to -3.2)	(-4.3 to -3.0)	(-1.2 to -0.5)	(-0.1 to 1.0)	(-0.3 to 0.4)
Relative Difference	1.04	—	0.52	0.27	0.38	1.22	1.05
(95% CI)	(0.94 to 1.14)	—	(0.45 to 0.60)	(0.22 to 0.34)	(0.26 to 0.55)	(0.97 to 1.55)	(0.72 to 1.54)

Stockholm3 – MRI trial



- Population-based invited prostate cancer screening
- Blood test => MRI => prostate biopsy
- Less unnecessary biopsies
- Less insignificant cancers found => less overtreatment
- As much significant cancers found
- Implications for development of national and international prostate cancer screening programs

LAPRO trial 8y update



- Prospective non-randomized trial
- Open (n=885) versus Robot (2699) radical prostatectomy (2008-2011)
- 14 Swedish centres

Prostate Cancer

Functional and Oncological Outcomes After Open Versus Robot-assisted Laparoscopic Radical Prostatectomy for Localised Prostate Cancer: 8-Year Follow-up

Anna Lantz^{a,b,}, David Bock^c, Olof Akre^a, Eva Angenete^{c,d}, Anders Bjartell^{e,f}, Stefan Carlsson^a, Katarina Koss Modig^{g,h}, Martin Nyberg^{e,f}, Karin Stinesen Kollberg^{g,i}, Gunnar Steineck^j, Johan Stranne^{g,h}, Peter Wiklund^{a,k}, Eva Haglind^{c,d}*

LAPRO trial 8y update



- Robotic surgery = improved short-term outcomes
 - ↓ blood loss
 - ↓ pain
 - ↓ complications
 - Shorter hospital stay
- What about oncologic outcome ?
 - 1 Australian RCT: 2y-BCR 9% open vs 4% robot (P=0.02)
 - Long term ??

LAPRO trial 8y update

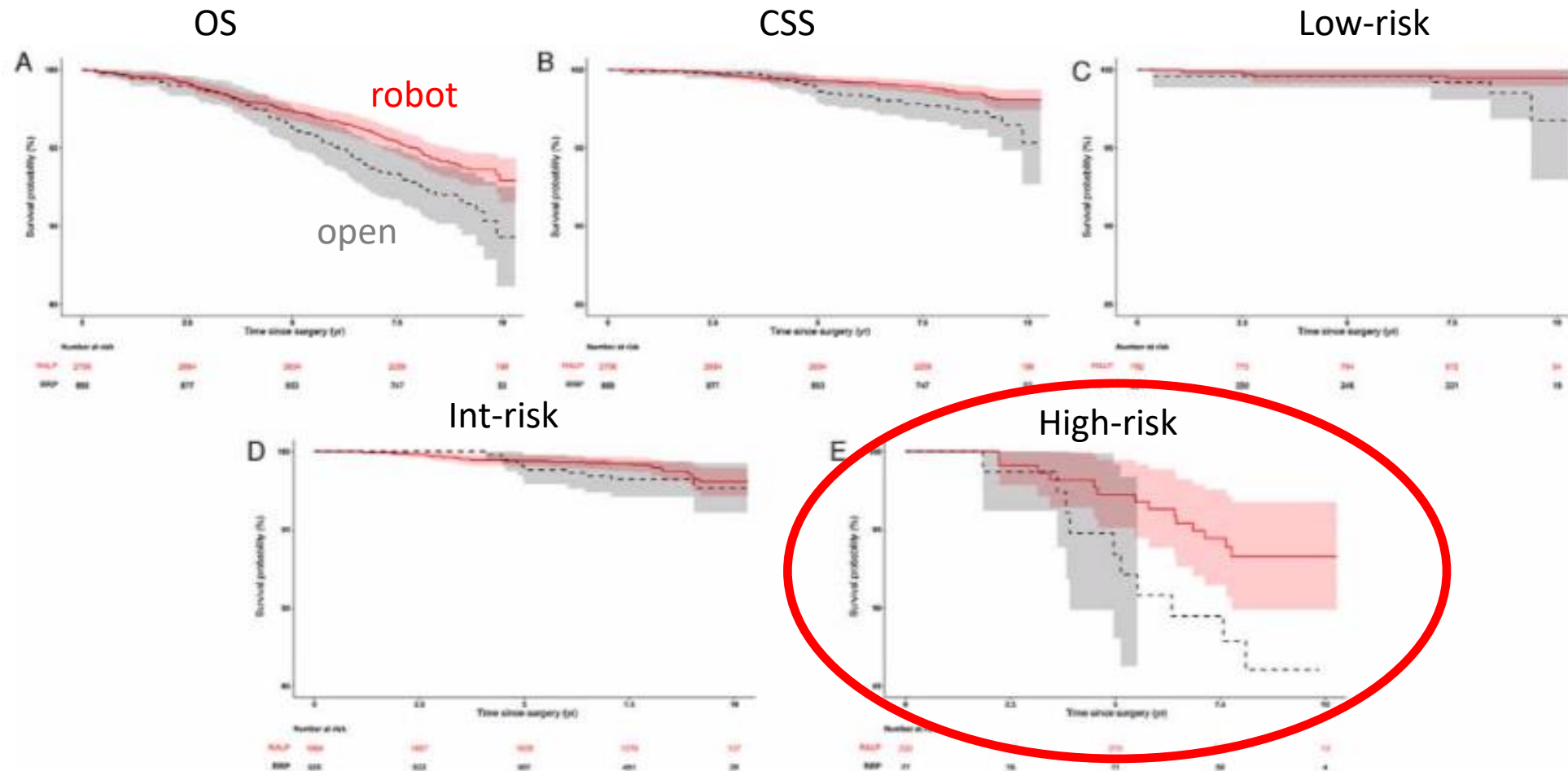


Fig. 2 – (A) All-cause mortality for RALP versus RRP. Prostate cancer-specific mortality for (B) RALP versus RRP and for D’Amico (C) low-risk, (D) intermediate-risk, and (E) high-risk groups. CI = confidence interval; HR = hazard ratio; RALP = robot-assisted laparoscopic prostatectomy; RRP = open retropubic radical prostatectomy.

LAPRO trial 8y update



	High risk	
	RALP (n = 220)	RRP (n = 77)
PSM, n/N (%)	44/210 (21)	25/73 (34)
Risk ratio (95% CI)		
Unadjusted	0.61 (0.41–0.92)	
Adjusted ^b	0.66 (0.44–1.00)	
Adjusted ^b + PE		
Adjusted ^b + AC		
Residual disease, n/N (%)	14/214 (6.5)	14/70 (20)
Risk ratio (95% CI)		
Unadjusted	0.33 (0.16–0.65)	
Adjusted ^c	No convergence	
Adjusted ^c + PE		
Adjusted ^c + AC		
BCR, n/N (%)	80/158 (51)	38/55 (69)
Risk ratio (95% CI)		
Unadjusted	0.73 (0.58–0.93)	
Adjusted ^c	0.80 (0.62–1.03)	
Adjusted ^c + PE		
Adjusted ^c + AC		
Overall mortality, n/N (%)	26/220 (12)	16/77 (21)
Hazard ratio (95% CI)		
Unadjusted	0.56 (0.30–1.04)	
Adjusted ^d	0.56 (0.30–1.06)	
Adjusted ^e	0.54 (0.28–1.01)	
Adjusted ^d + PE		
Adjusted ^d + AC		
PCSM, n/N (%)	14/220 (6.3)	11/77 (14)

LAPRO trial 8y update



Better oncological outcome with robot-assisted radical prostatectomy

Hypothesis:

Better visualisation + improved dexterity

More precise surgery

Better surgical plane

Increased chance of radical tumor removal

Lower PSM rate

Lower BCR

Lower mortality



Experienced surgeons in both groups

Prospective data

Long follow-up



Non-randomized

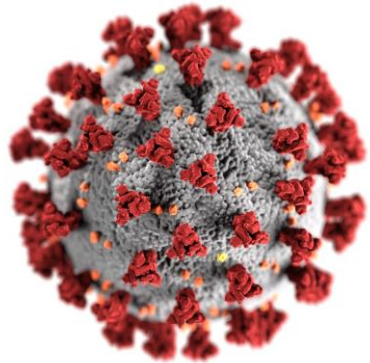
=> Longer follow-up awaited + data from (only 1!) RCT

A teal-colored header image featuring a microscopic view of cells, likely cancer cells, with a curved bottom edge.

Bladder Cancer

“Treatment going viral”

Impact of delayed diagnosis



- Reduction in 10-year net survival incurred from a **3-month delay** of diagnosis

	Age group (years)					
	30-39	40-49	50-59	60-69	70-79	≥80
Bladder	15.79%	14.95%	14.29%	15.48%	17.15%	17.03%
Brain	11.75%	14.15%	17.82%	18.24%	16.64%	16.70%
Breast	4.88%	3.27%	2.49%	2.14%	3.71%	7.70%
Cervix	5.59%	9.03%	12.20%	15.73%	17.98%	15.52%
Colorectal	10.22%	11.38%	10.82%	10.59%	13.10%	16.36%
Kidney	5.01%	6.50%	8.53%	10.53%	13.10%	17.41%
Larynx	11.07%	14.29%	13.45%	14.94%	15.86%	16.79%
Liver	16.68%	17.29%	16.17%	14.67%	11.89%	14.78%
Lung	16.87%	18.26%	16.80%	15.37%	11.78%	6.70%
Melanoma of skin	3.13%	3.96%	4.89%	5.66%	7.32%	12.56%
Pancreas	12.86%	11.76%	12.11%	9.00%	7.18%	10.74%
Prostate	0.68%	0.67%	0.32%	0%	0%	3.69%
Stomach	18.58%	18.54%	18.03%	17.34%	16.11%	8.85%
Testis	0.58%	0.36%	0.76%	0.35%	0.63%	1.62%

Nadofaragene firadenovec in NMIBC



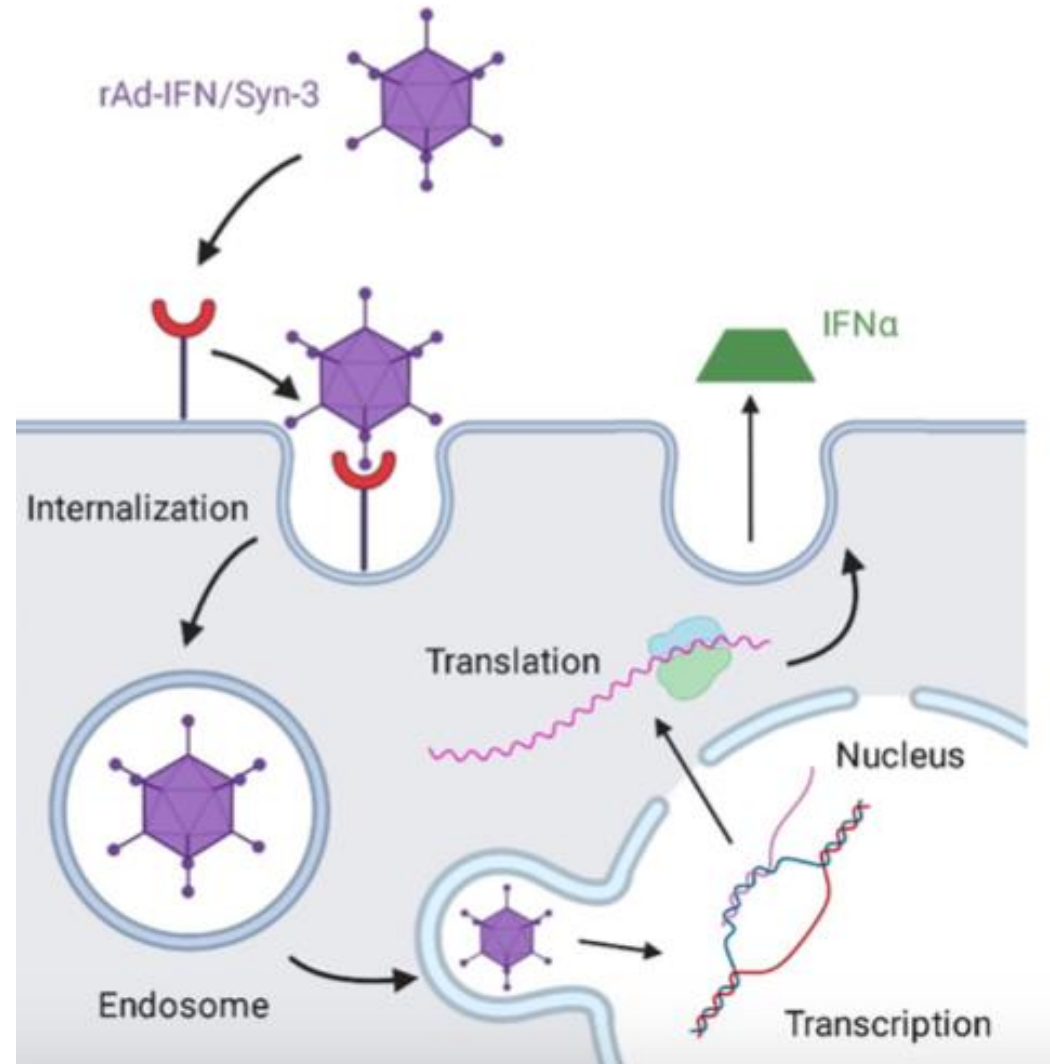
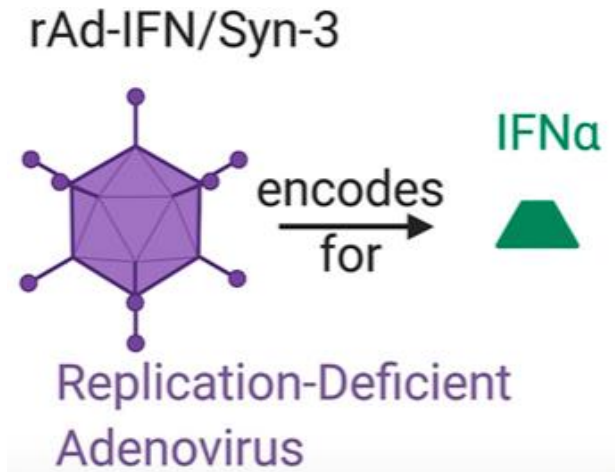
High-risk non-muscle invasive bladder cancer (NMIBC)

- Intravesical Bacillus Calmeté Guérin (BCG)
- >50% will develop BCG-unresponsive disease
- **Standard of care = radical cystectomy**

Bladder-sparing strategies ?

- Immunotherapy (phase III trials, pembrolizumab FDA approved)
- **Intravesical Nadofaragene firadenovec**

Nadofaragene firadenovec in NMIBC



Nadofaragene firadenovec in NMIBC



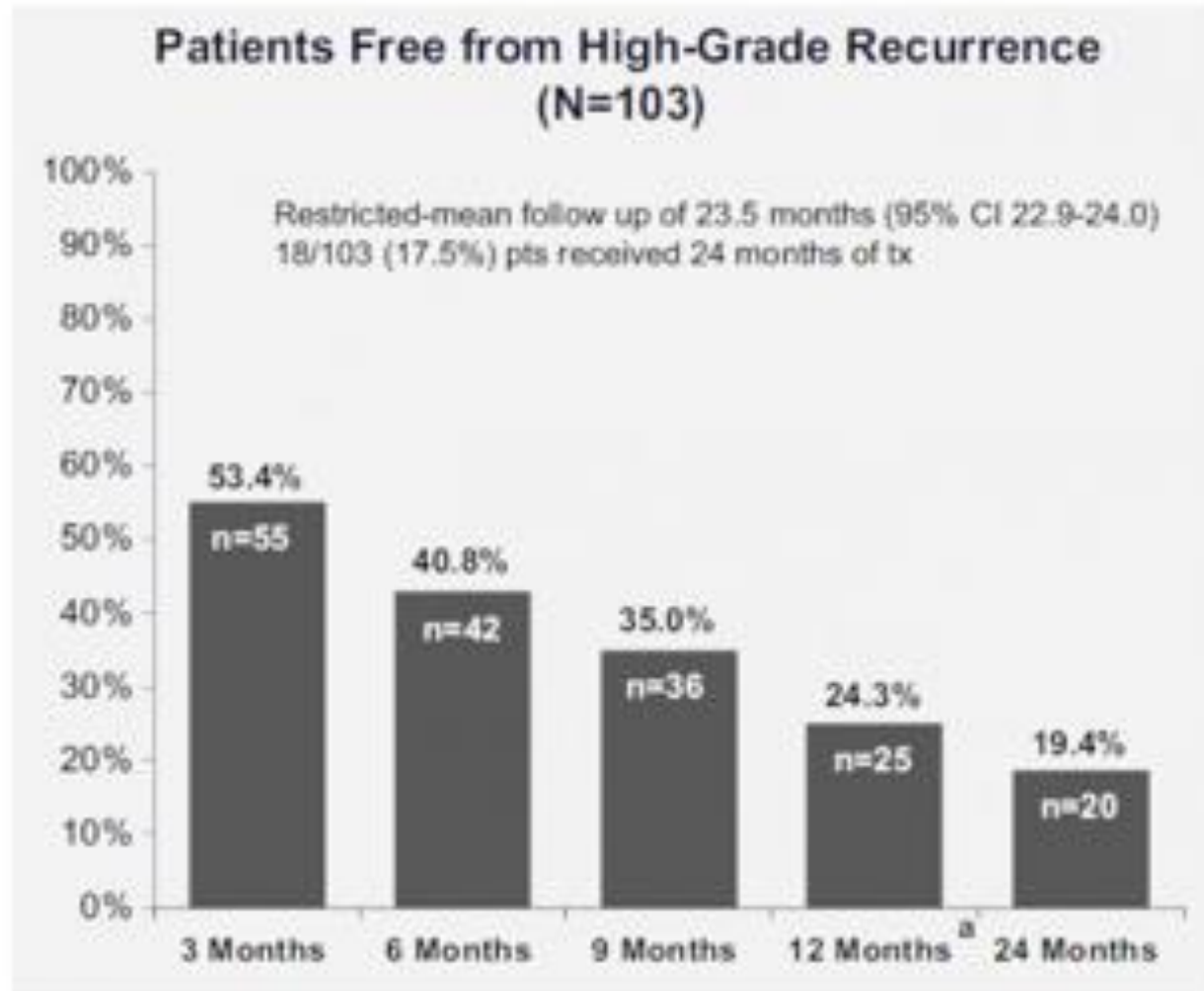
[a] BCG-unresponsive NMIBC is defined as: (1) persistent high-grade T1 recurrence ≤12 months after BCG initiation; (2) relapse with CIS after initial complete response ≤12 months after last BCG treatment; or (3) relapse with high-grade Ta/T1 NMIBC ≤6 months after last BCG treatment.¹

Intravesical NF every 3 months for up to 4 doses (+ cystoscopy/cytology)

After 1 year: 5-site bladder biopsies

In case of complete response: possibility of continued treatment every 3 months

Nadofaragene firadenovec in NMIBC



CIS (+/- Ta-T1) cohort

53% complete response

At 24 months:

- 32% underwent cystectomy (5% for T2)
- 94,4% OS

Subgroup analysis: no difference

- Age
- Sex
- Number of prior treatments

Nadofaragene firadenovec in NMIBC



Good tolerability !

Only 2 patients discontinued treatment

Adverse events:

- Instillation discharge (24%)
- Fatigue (23%)
- Bladder spasm (18%)
- Urgency (17%)

Future:

- FDA / EMA approval awaited
- Efficacy in earlier NMIBC stages ?



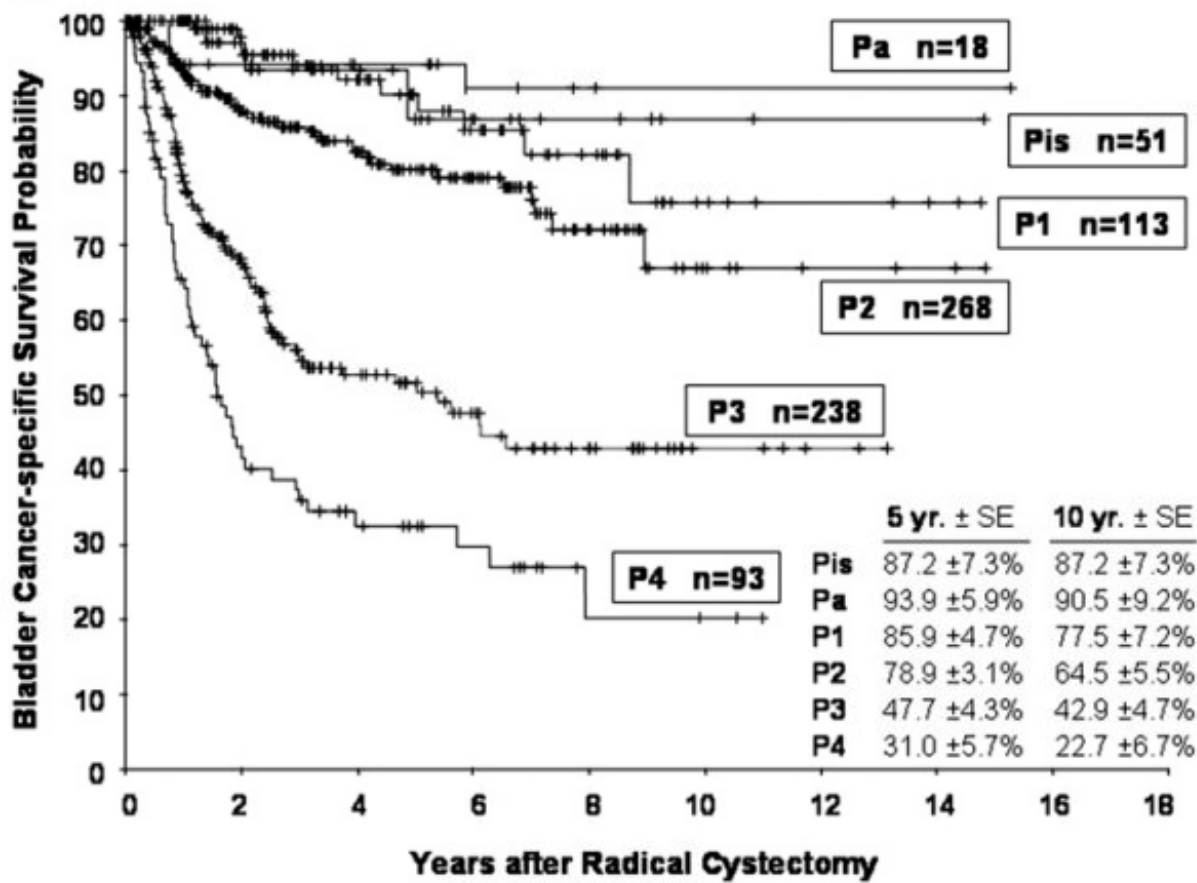
- Very promising therapy, BUT ...



ctDNA in MIBC



CSS following radical cystectomy (RC) for muscle-invasive bladder cancer (MIBC)

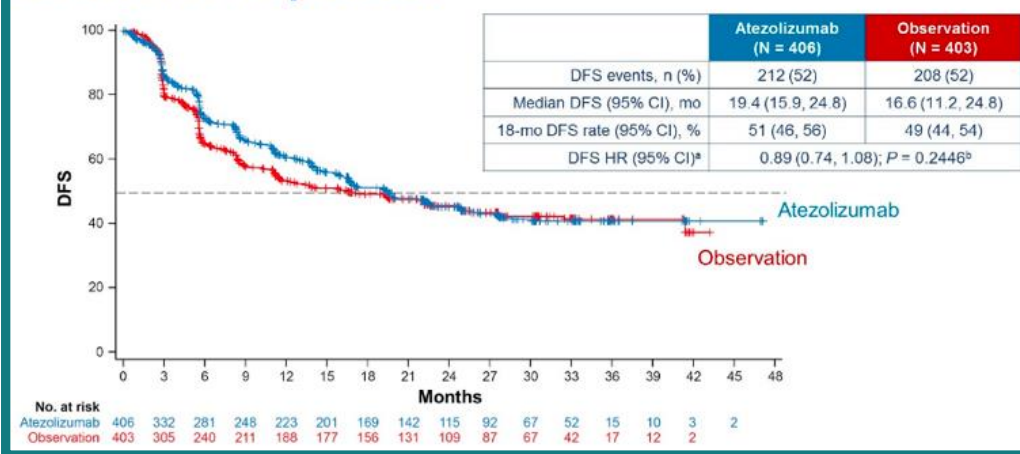


ctDNA in MIBC

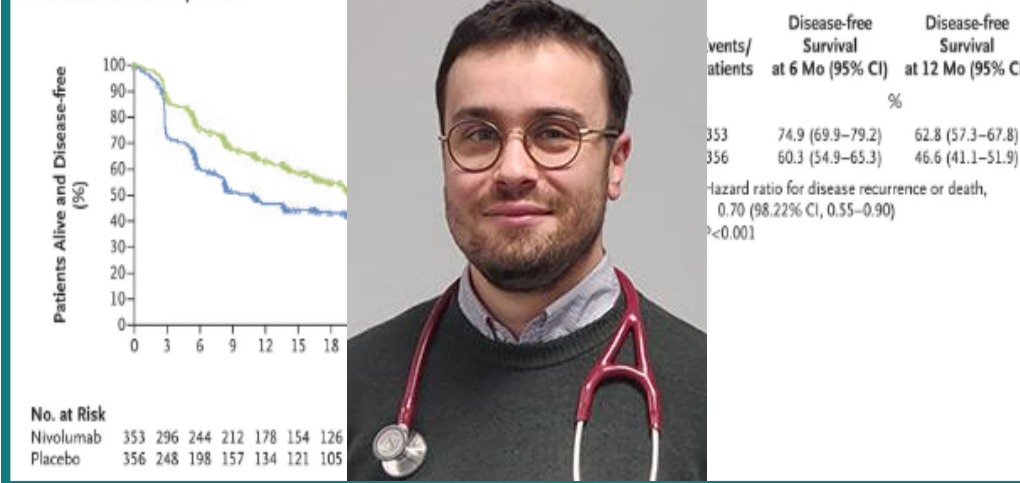
Benefit of adjuvant immunotherapy ?

- Atezolizumab (IMVIGOR-010): negative
- Nivolumab (Checkmate-274): positive !

DFS in ITT Population

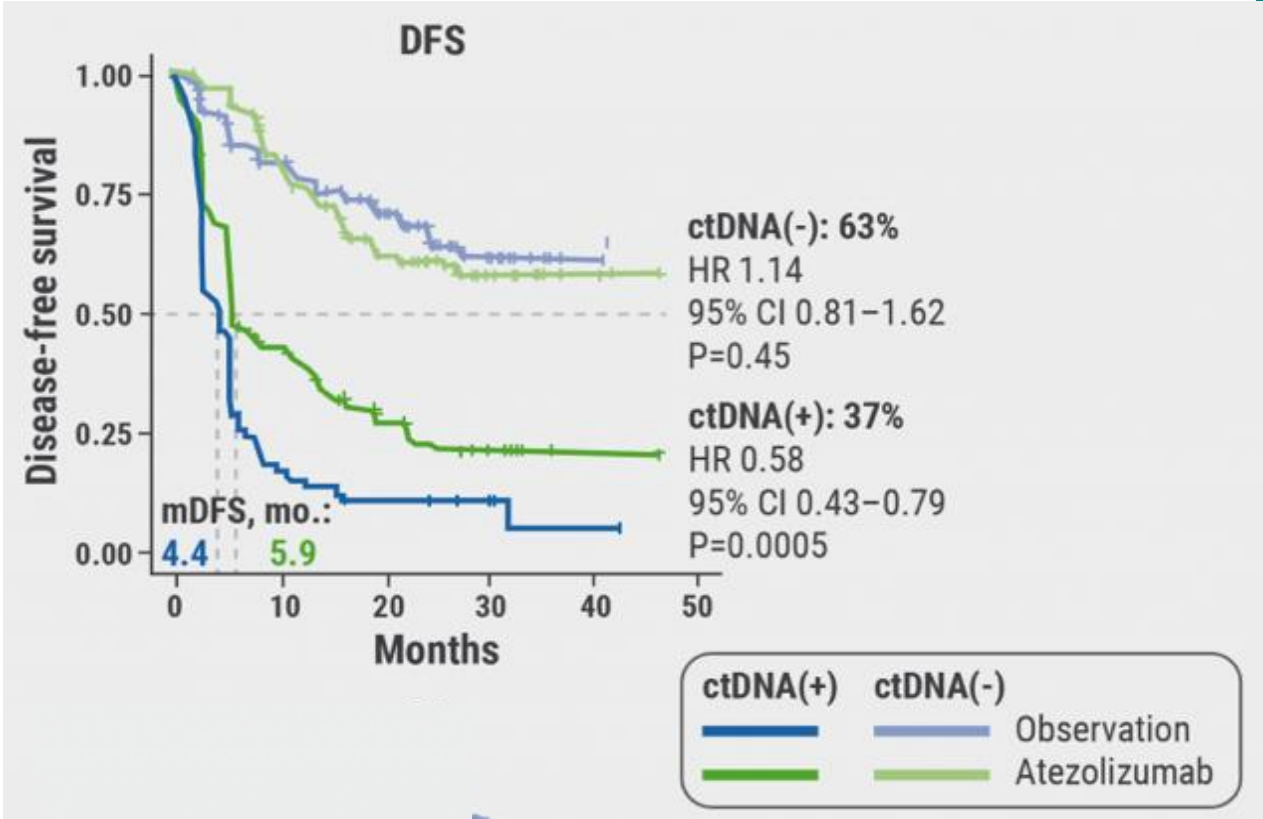


A Intention-to-Treat Population

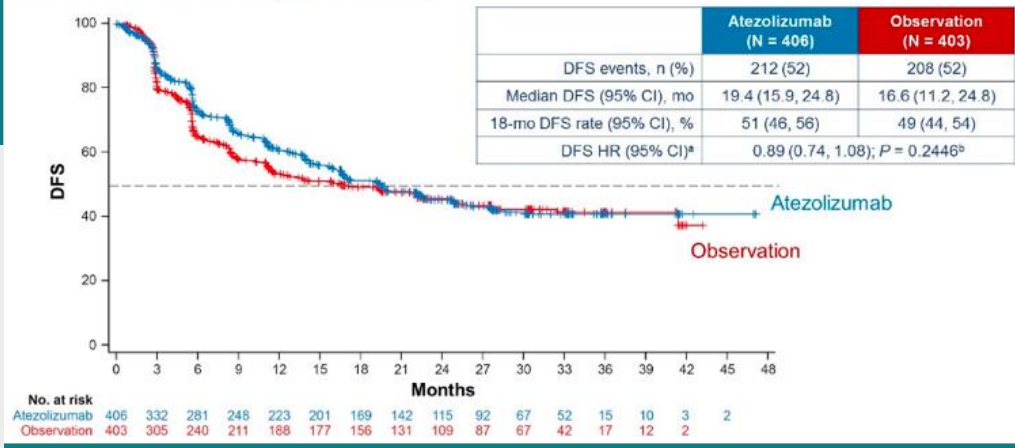


ctDNA in MIBC

- IMVIGOR-010



DFS in ITT Population

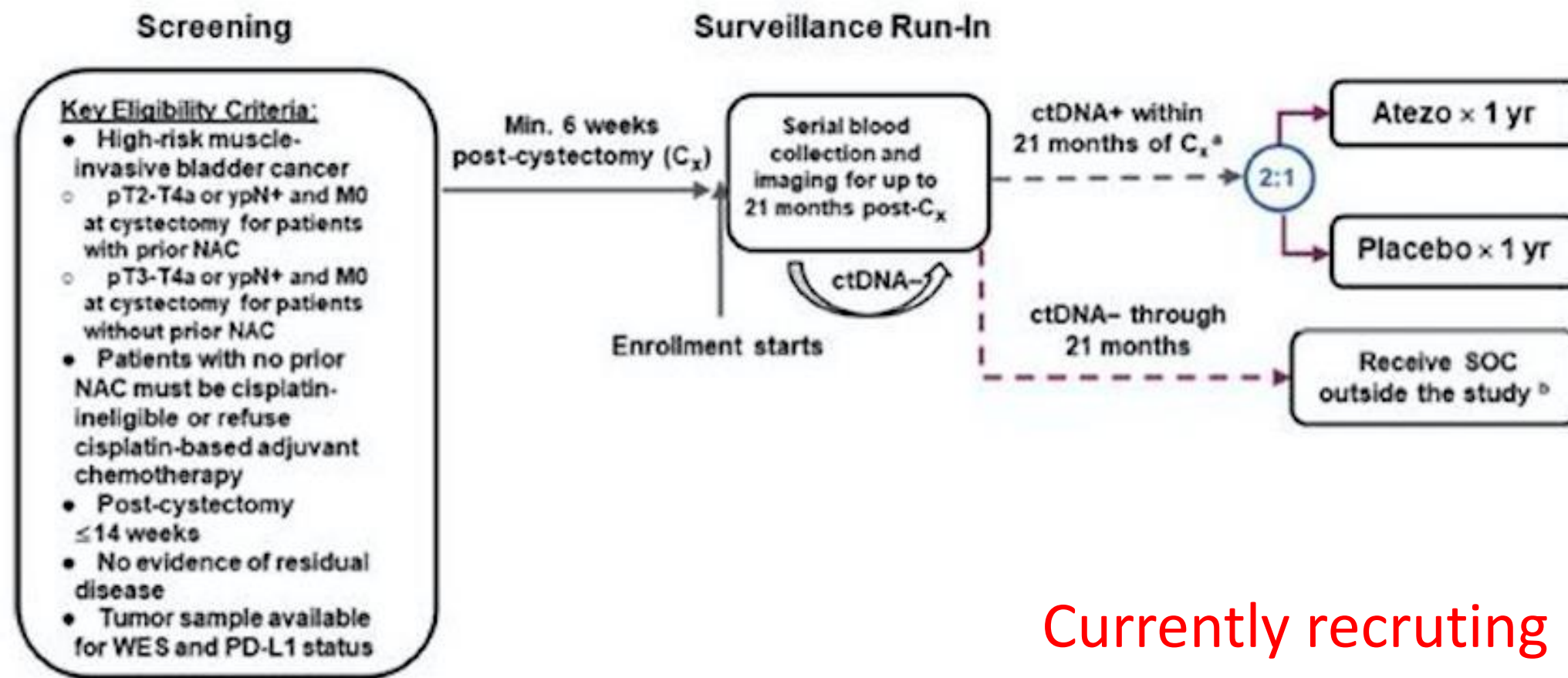


ctDNA = worse outcome = PROGNOSTIC

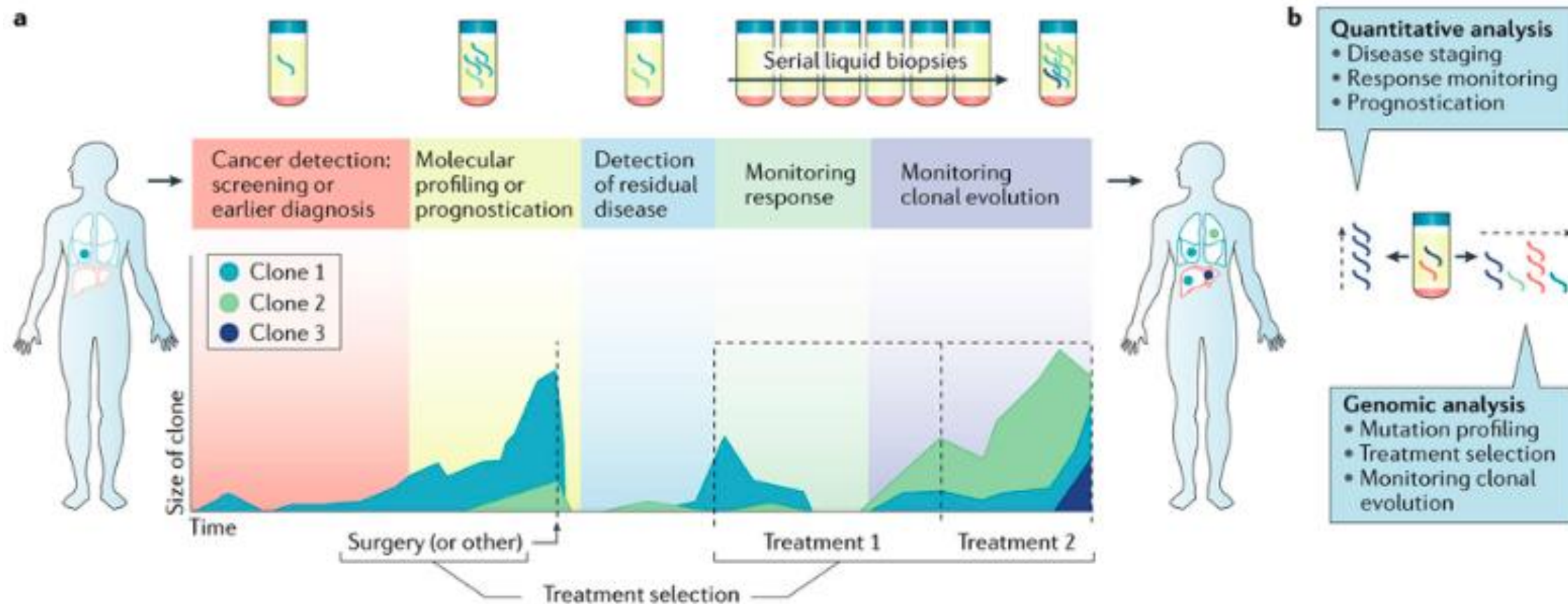
ctDNA = atezolizumab benefit = PREDICTIVE

ctDNA in MIBC

- IMVIGOR-011 (currently enrolling)



ctDNA in MIBC

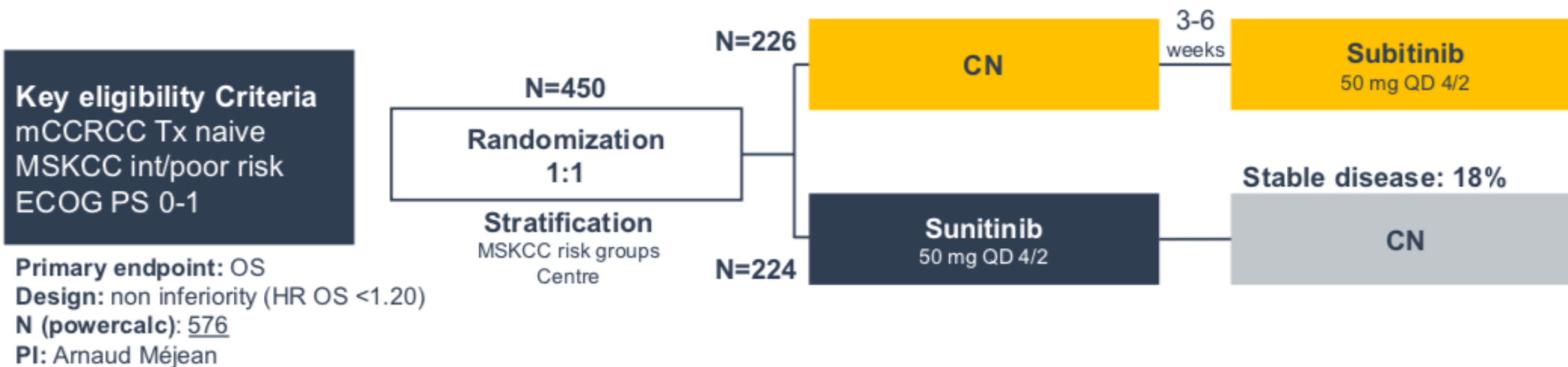


A microscopic image of renal cell carcinoma tissue, showing a dense cluster of cells with prominent nuclei and some cytoplasmic clearing, characteristic of clear cell renal cell carcinoma. The image is overlaid with a teal gradient.

Renal cell carcinoma

“Harmony between surgery and systemic therapy”

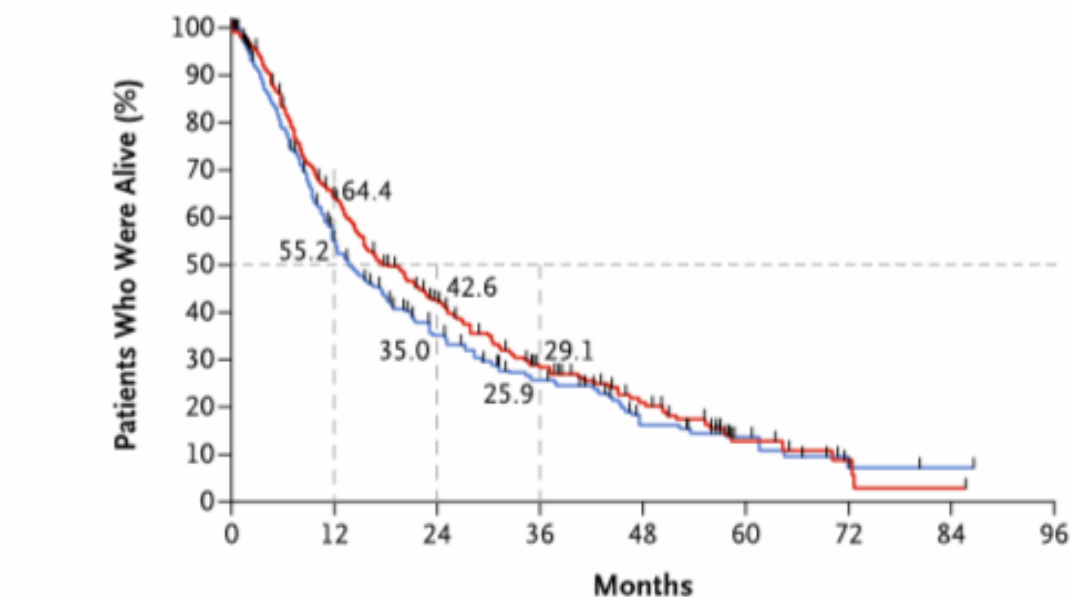
Carmena update



Carmena update

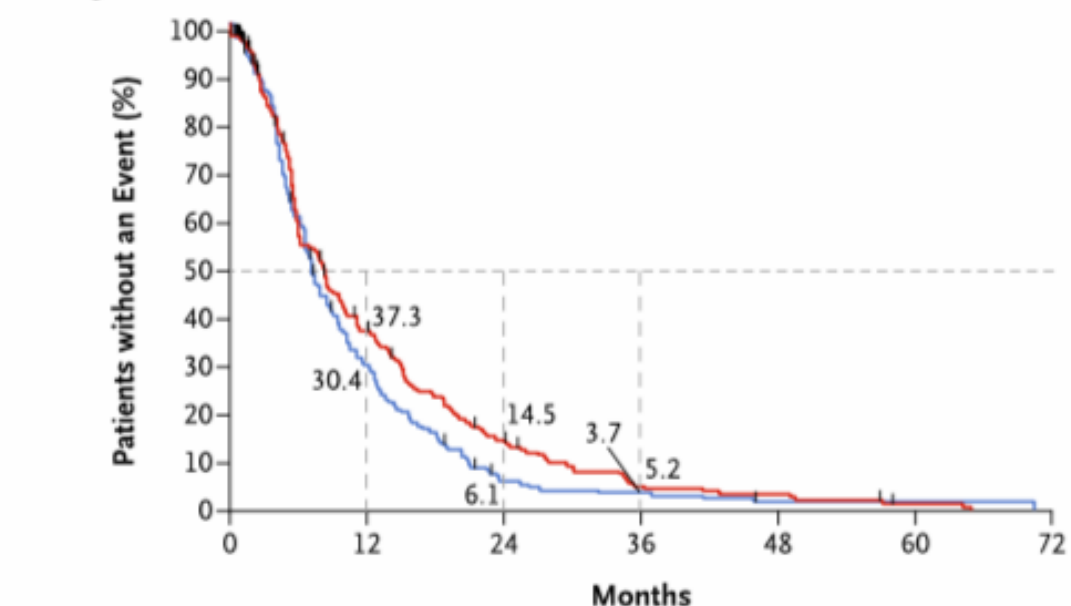


A Overall Survival



No. at Risk									
Nephrectomy+ sunitinib	226	110	61	40	19	11	4	1	0
Sunitinib alone	224	128	76	44	26	8	3	1	0

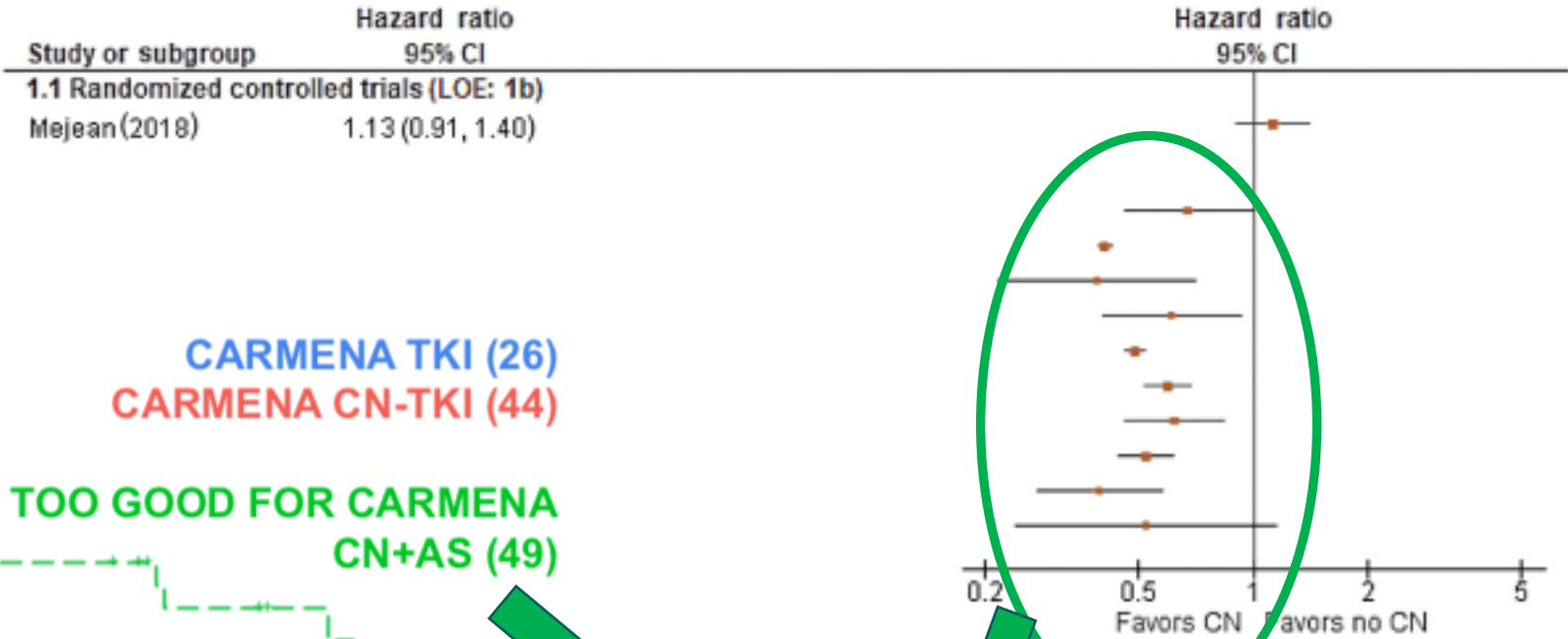
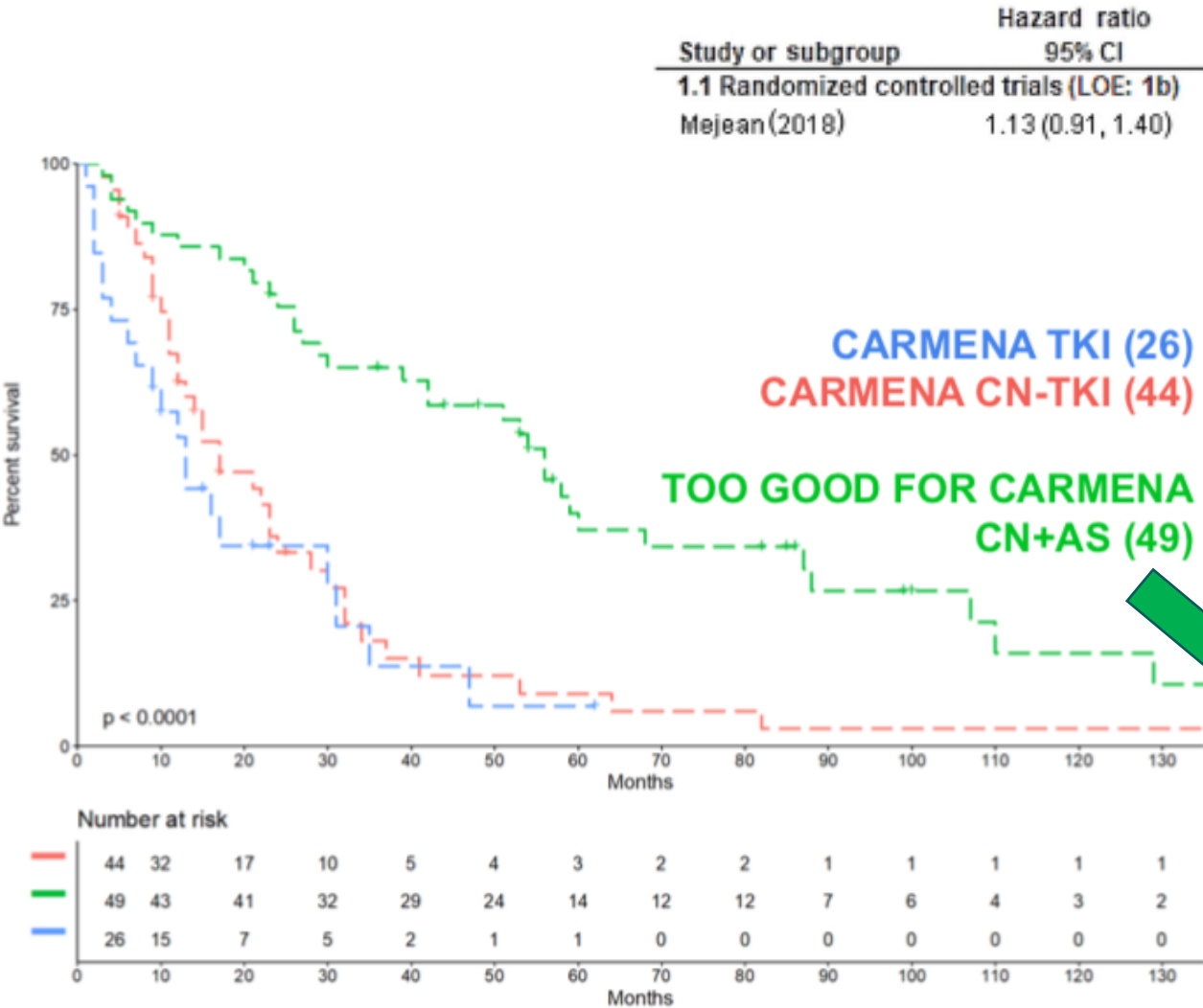
B Progression-free Survival



No. at Risk							
Nephrectomy+ sunitinib	226	59	10	6	2	1	0
Sunitinib alone	224	74	28	9	6	2	0

— Nephrectomy-sunitinib — Sunitinib alone

Carmena update



A subgroup of patients may benefit from immediate CN

Carmena update



	MSKCC	IMDC
Karnofsky PS <80%	✓	✓
Hb < normal	✓	✓
LDH > 1,5x normal	✓	✗
Corrected Ca ²⁺ > 10 mg/dL	✓	✓
Time from diagnosis to treatment < 1 year	✓	✓
Neutrophil count > normal	✗	✓
Platelet count > normal	✗	✓

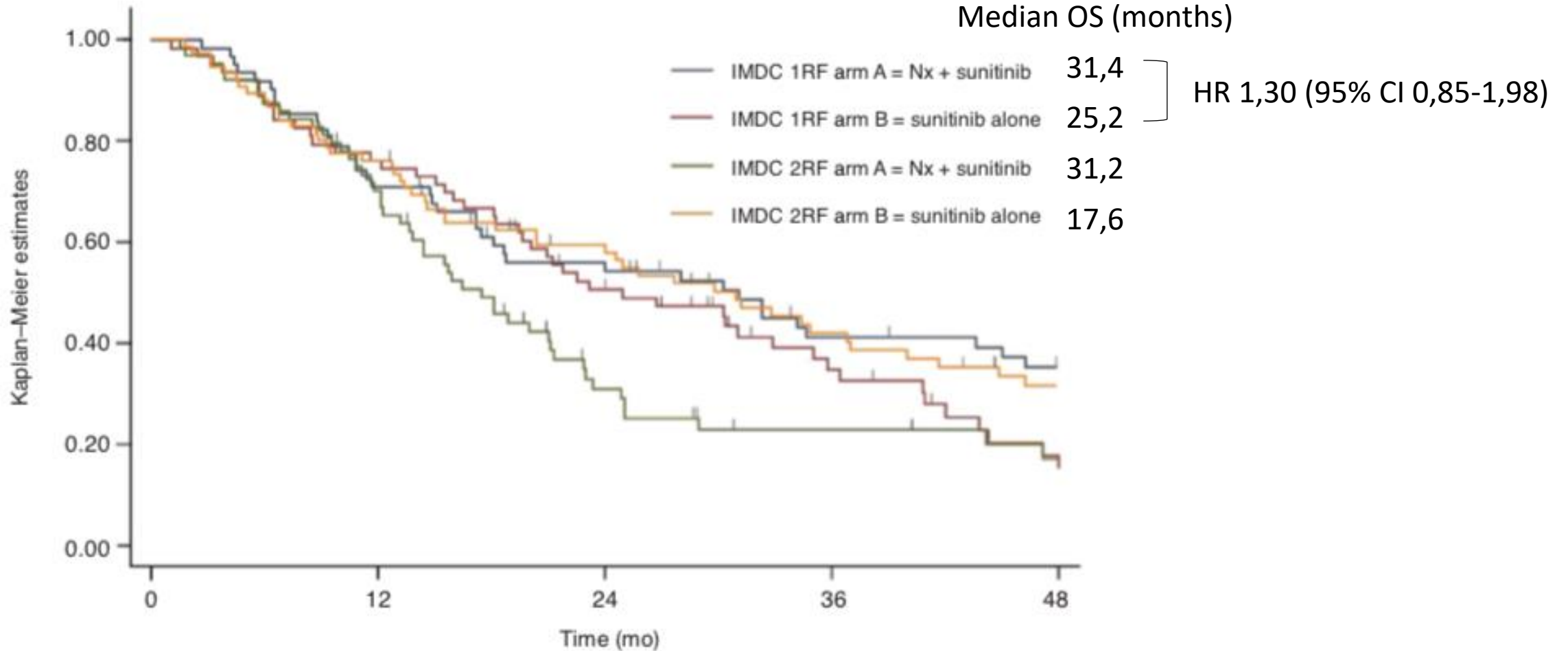
- Patient groups reclassified to IMDC
- OS update
- Stratified by
 - number of risk factors
 - number of metastases
 - delayed CN

Good prognosis: 0 risk factors (rfs)

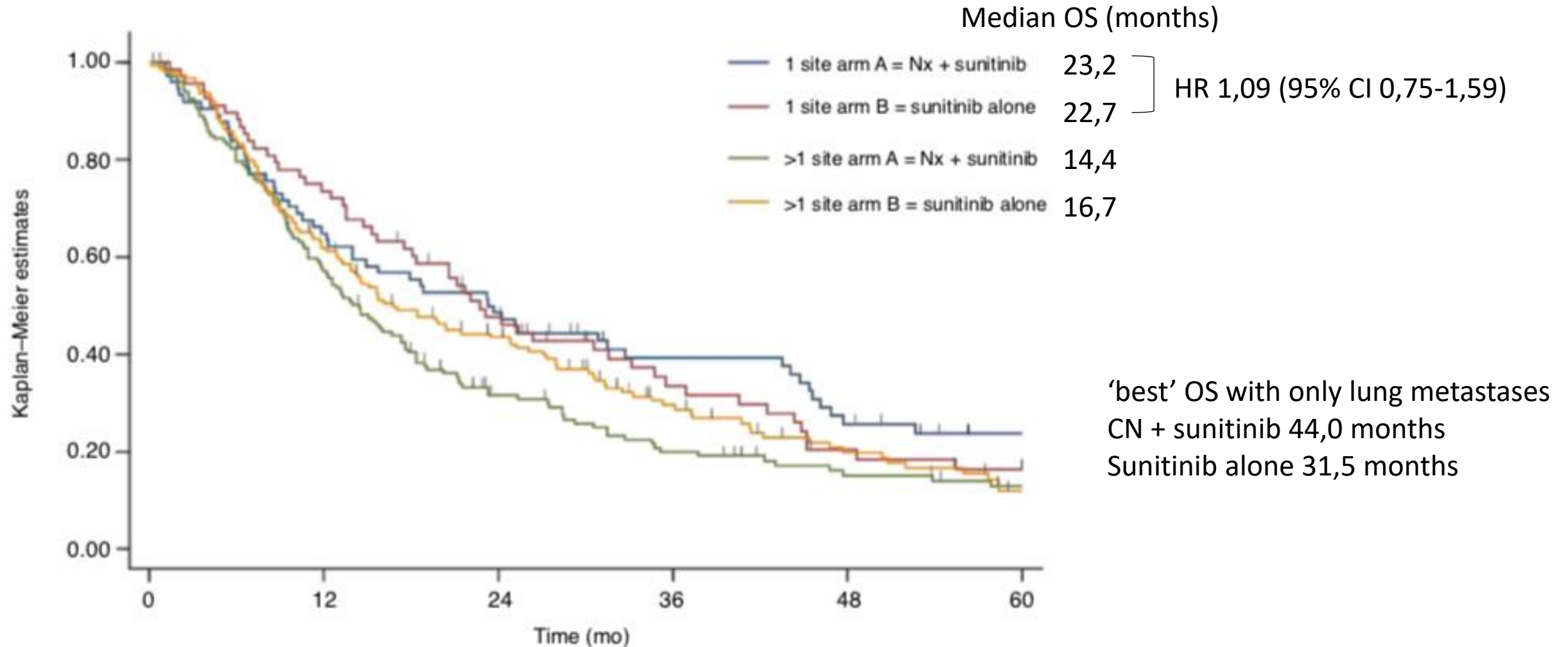
Intermediate prognostis: 1-2 rfs

Poor prognosis: >2 rfs

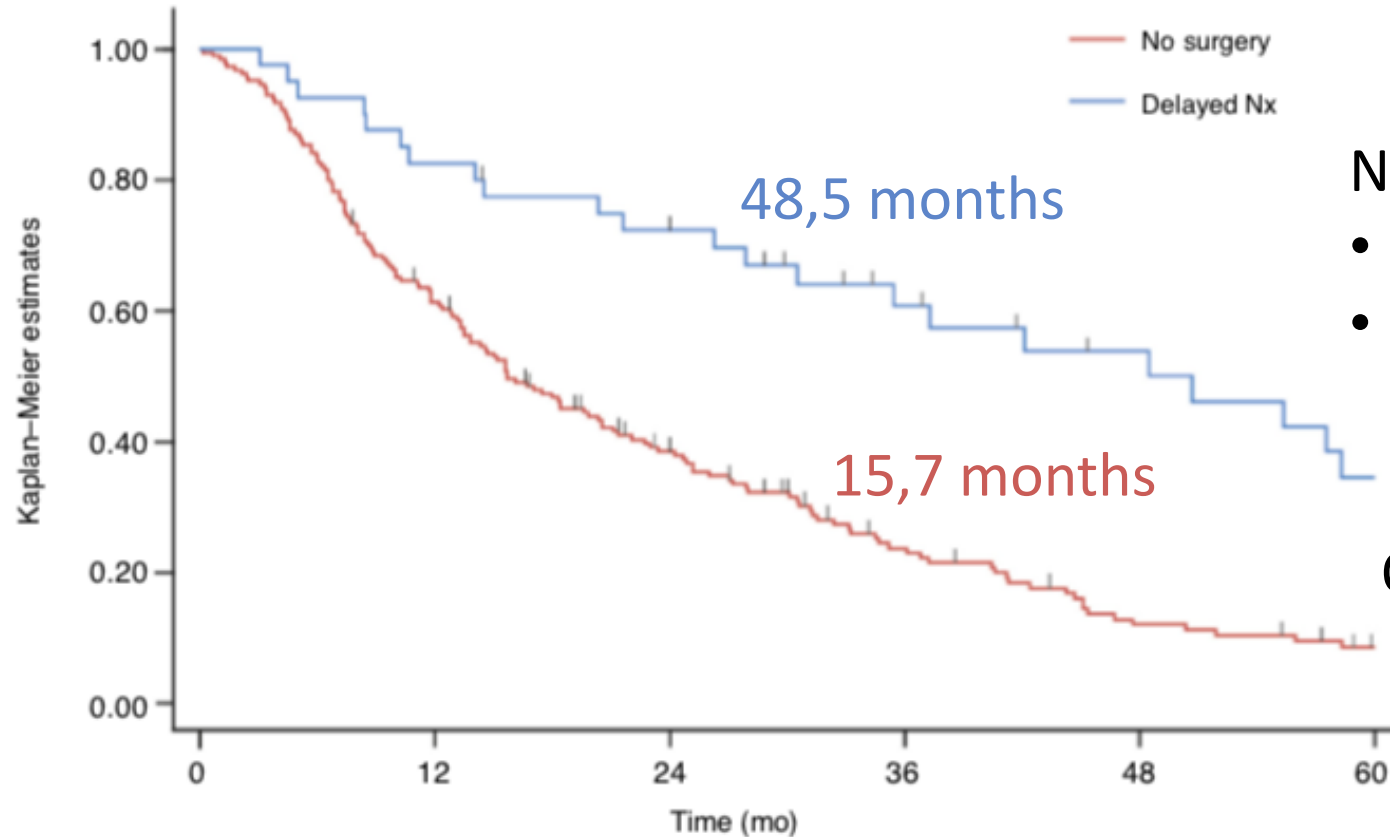
1 vs 2 or more IMDC risk factors



1 vs 2 or more metastatic sites



Delayed CN



N = 40 (18%)

- 7 emergency treatment of local tumor
- 33 response at metastatic sites

Only 31% continued sunitinib afterwards

A subgroup of patients may benefit from deferred CN

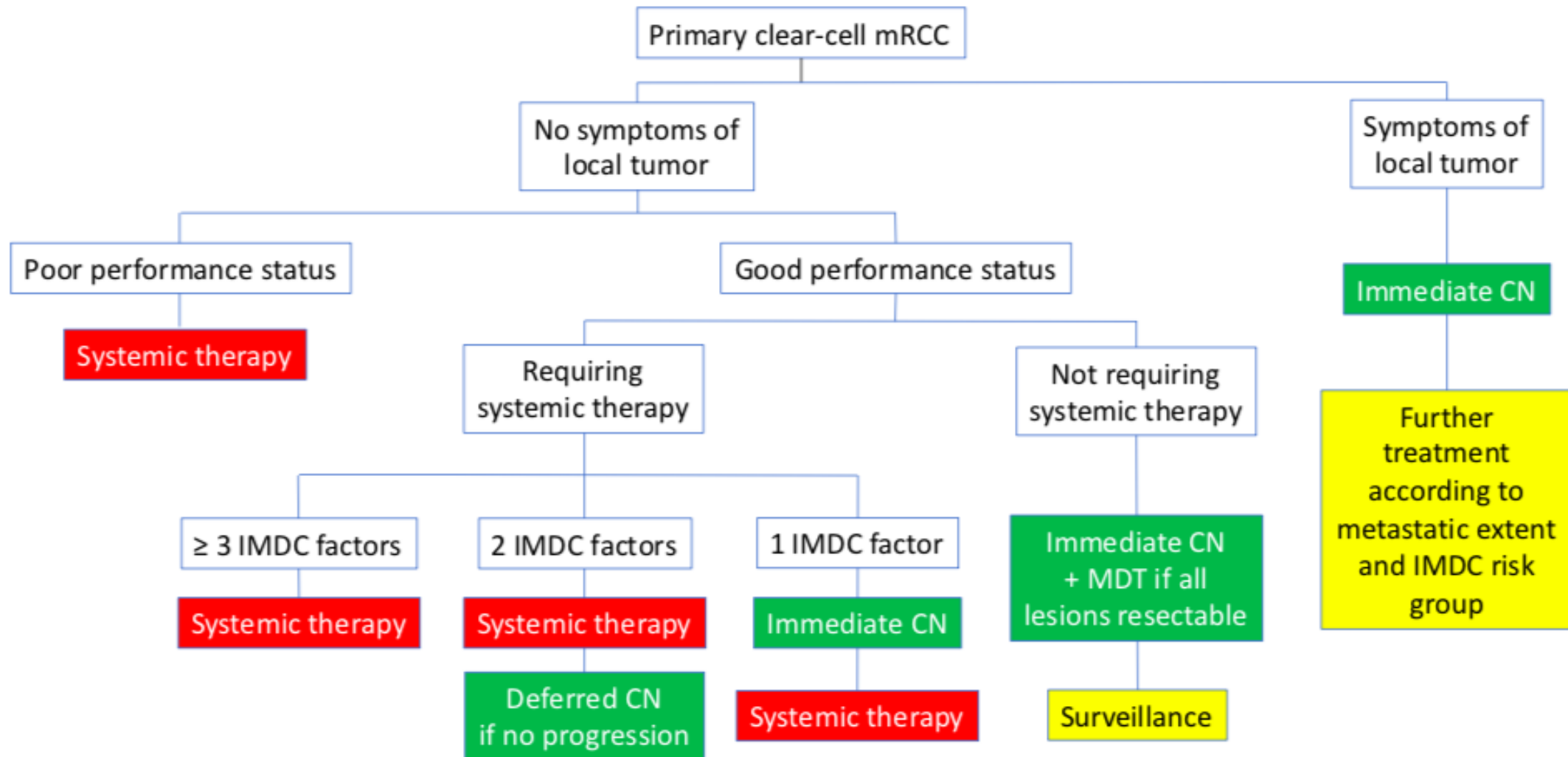
Cytoreductive nephrectomy: when and who ?



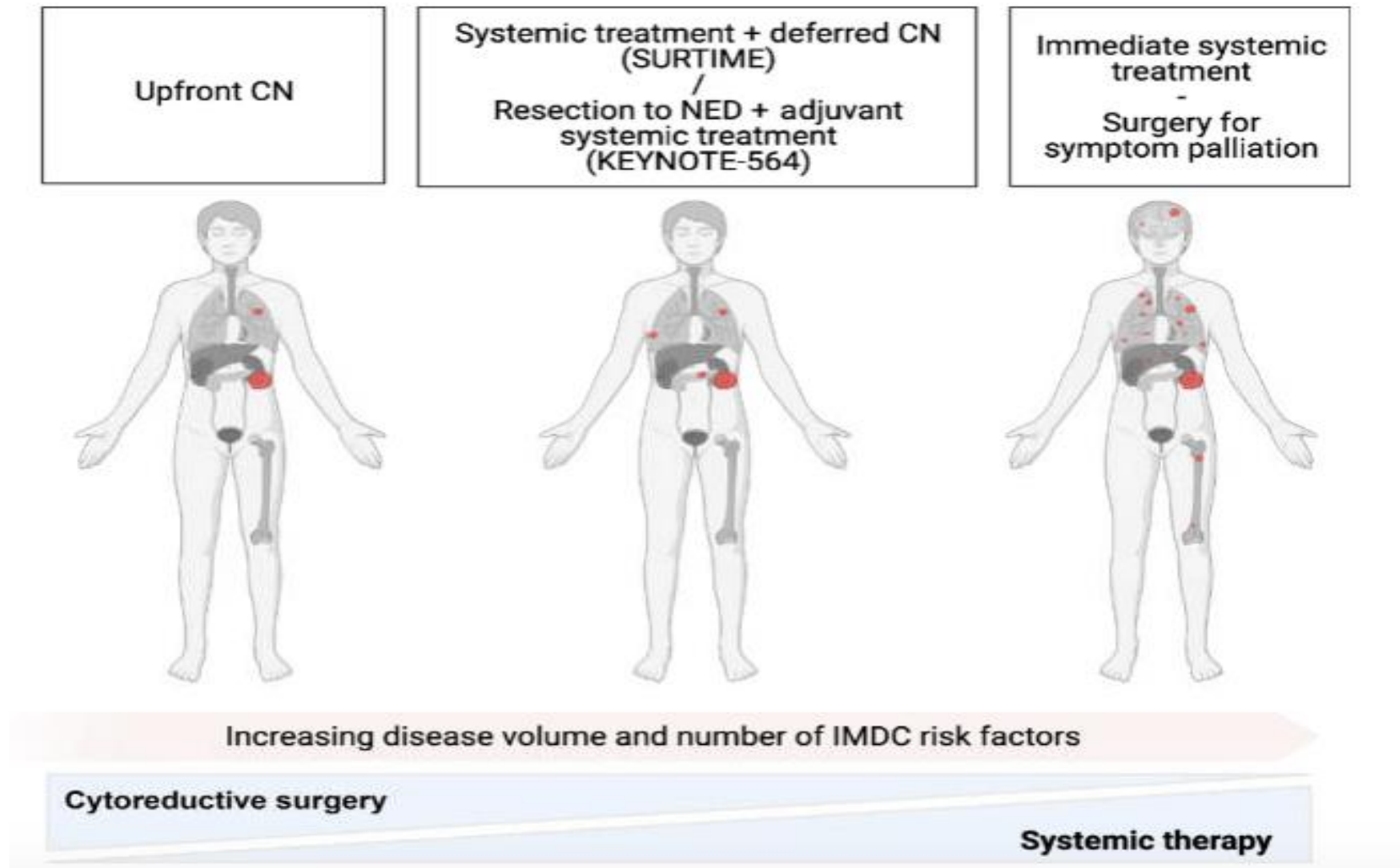
Multidisciplinary decision based on

- IMDC risk factors
- Tumor burden
- Performance status
- Symptoms

Cytoreductive nephrectomy: when and who ?



Cytoreductive nephrectomy: when ?



Neo-adjuvant therapy



Surgery = standard of care for localized and locally advanced RCC

Neo-adjuvant therapy
with TKI

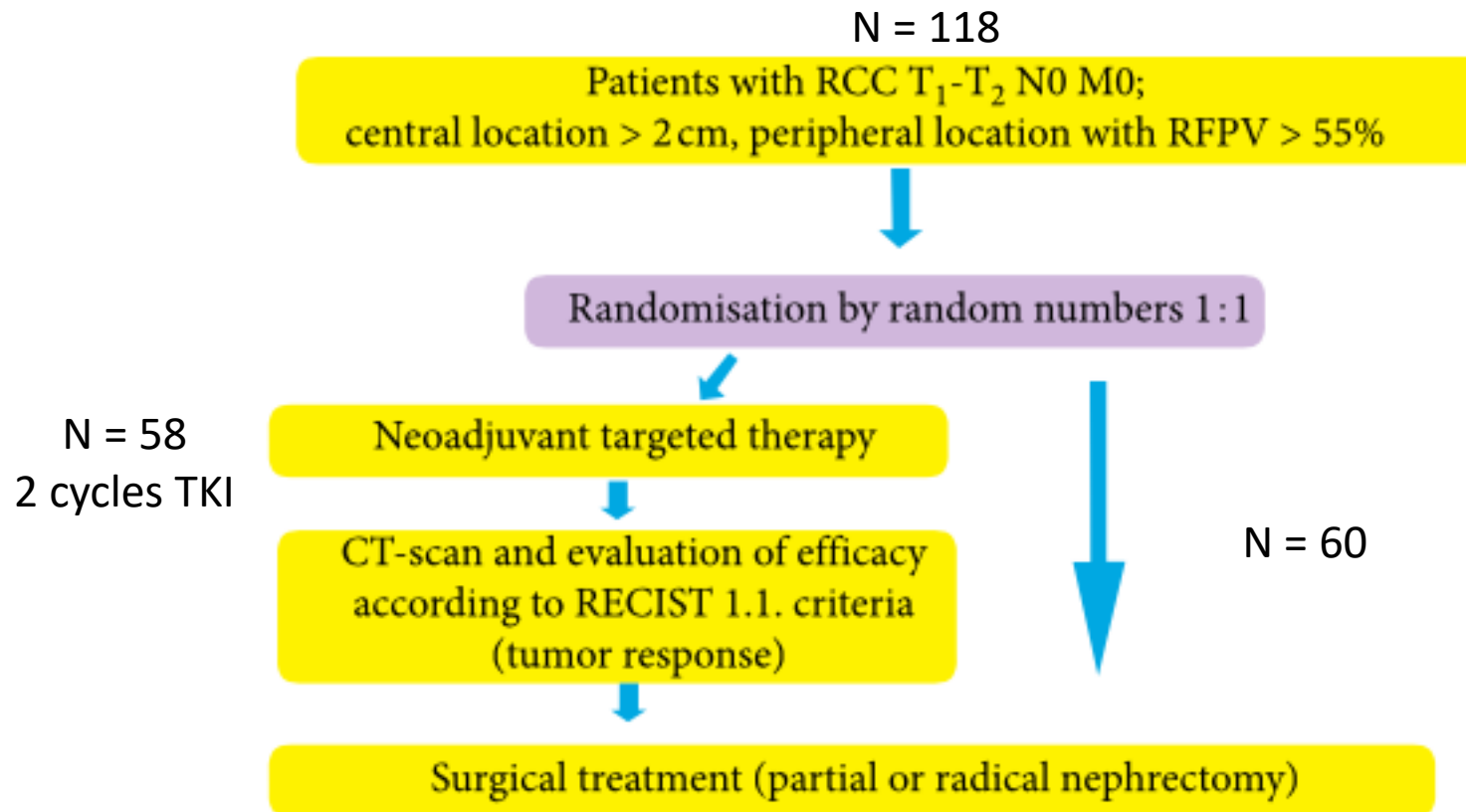
More nephron-sparing surgery

“Ukrainian RCT”

Less morbid surgery

NAXIVA trial

Neo-adjuvant therapy



Neo-adjuvant therapy

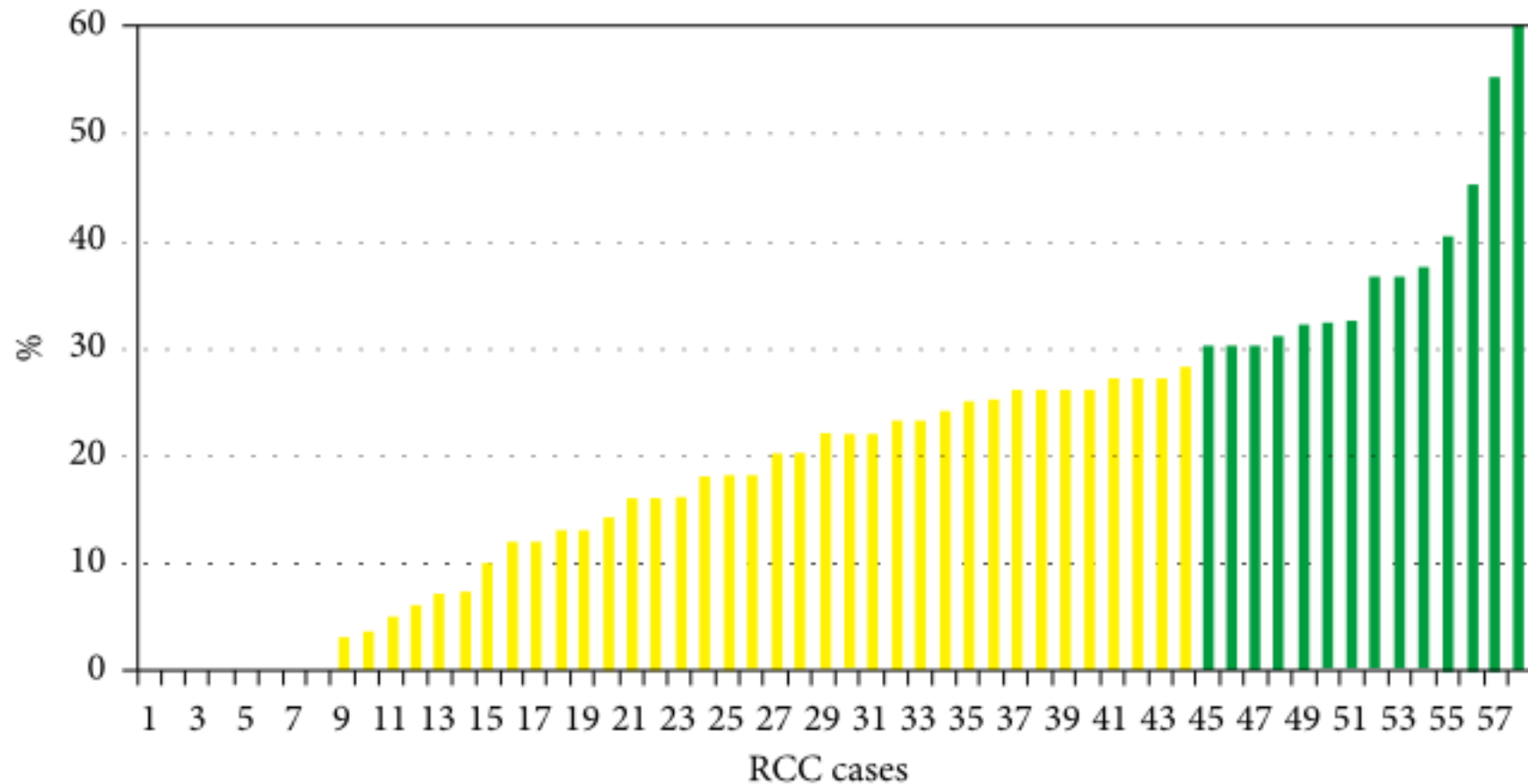


Indicator	Statistical units	Main group, $n = 58$ (%)	Control group, $n = 60$ (%)
Age, years	M $\pm$ SD (95% CI)	55.3 $\pm$ 10.3 (52.6–58)	54.5 $\pm$ 12 (51.4–57.6)
Sex	Male, n (%)	39 (67.2)	34 (56.7)
	Female, n (%)	19 (32.7)	26 (43.3)
T	1a, n (%)	7 (12.1)	5 (8.3)
	1b, n (%)	35 (60.3)	31 (51.7)
	2a, n (%)	12 (20.7)	22 (36.7)
	2b, n (%)	4 (6.9)	2 (3.3)
Kidney tumour size, mm	M $\pm$ SD (95% CI)	60.7 $\pm$ 19.8 (55.5–66)	62.5 $\pm$ 16.7 (58.2–66.9)

Neo-adjuvant therapy



% tumor volume reduction in the neo-adjuvant group (N = 58)



Median 20%
= 12mm

Max 60%

24% partial response

Neo-adjuvant therapy



	Neo-adjuvant therapy	Immediate surgery
Partial nephrectomy	53 (91%)	20 (33%)
Radical nephrectomy	5 (9%)	40 (67%)

“The surgical strategy was discussed on a multidisciplinary board” ...

No central review

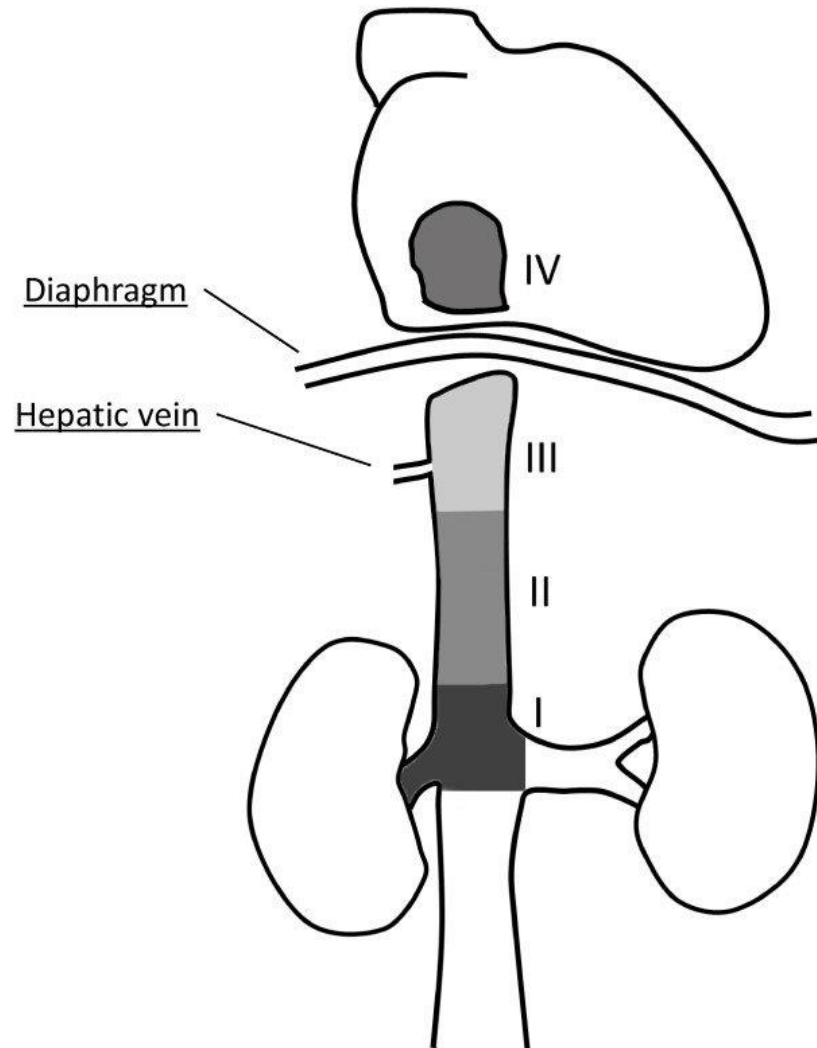
No long-term oncological outcome yet

Neo-adjuvant therapy: NAXIVA



- NAXIVA
- Phase II multicentric UK trial, 12/2017 – 01/2020
- RCC with venous tumor thrombus: T3 a-b-c, M0 or M1
- Single-arm: 8 weeks axitinib followed by surgery
- N = 21
- MRI at baseline & before surgery

Neo-adjuvant therapy: NAXIVA



Mayo classification of venous thrombus in RCC

RECIST (18/21 evaluable)

Partial response: 3

Stable disease: 13

Progressive disease: 2

Median reduction in tumor thrombus length: -21,5%

To lower Mayo grade: 6/21 (27%)



- Reduced extent of surgery
- Reduced morbidity

Complications Clavien-Dindo grade >2

- 1 grade 4
- 1 grade 5

Neo-adjuvant therapy: conclusions



Neo-adjuvant TKI in localized or locally advanced RCC

- Feasible
- Option in imperative indications (solitary kidney, 'inoperable' T3 tumor)
- Further data and long-term oncological outcome awaited

Adjuvant therapy in RCC ?

KEYNOTE-564: pembrolizumab



In summary



- Prostate cancer
 - Screening EAU update
 - Stockholm3 trial
 - Screening with MRI = better
 - LAPRO trial update
 - Better oncological outcome at 8 years with robotic radical prostatectomy in high-risk PCa

In summary



- Bladder cancer
 - NMIBC: nadofaragene firadenovec in BCG-unresponsive high-risk disease
 - MIBC: ctDNA testing in peri-operative management
- Renal cell carcinoma
 - Carmena update: still a place for immediate or deferred cytoreductive nephrectomy
 - Neo-adjuvant TKI in localized and locally advanced RCC is feasible

THANK YOU



BMUC

UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

**Post conference
meeting 2021**

Urology

Dr. Charles Van Praet
Ghent University Hospital

ANY
QUESTIONS
?