

Bladder cancer session

How to assess and how to deal with complete response after neo-adjuvant CT/IO?

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Holiday Inn Brussels Airport

bmuc.be/bmuc-2026

**13th Belgian Multidisciplinary
Meeting on Urological Cancers**

Conflicts of interest

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

Speaker for a pharmaceutical company: BMS, MSD, Johnson&Johnson, Astellas, Astra zeneca

Support from a pharmaceutical company for participation in a national or international congress: Bouchara Recordati, BMS, MSD, Johnson&Johnson, Ipsen, Astellas, Photocure, Astra zeneca

Consultant : Johnson&Johnson, BMS, MSD, Photocure, Karl Storz, Merck Serono

Principal investigator of a pharmaceutical industry trial: MSD, Johnson&Johnson, Fidia, Steba Biotech, Astra zeneca, Astellas

Shares in a pharmaceutical laboratory: None

How do you currently assess patient after neo-adjuvant CT/IO prior local treatment? (multiple choice possible)

- I usually don't reassess and go straight to the initial plan
- CT-Scan
- FDG PET
- MRI
- TURBT
- In office Cystoscopy
- ct/utDNA

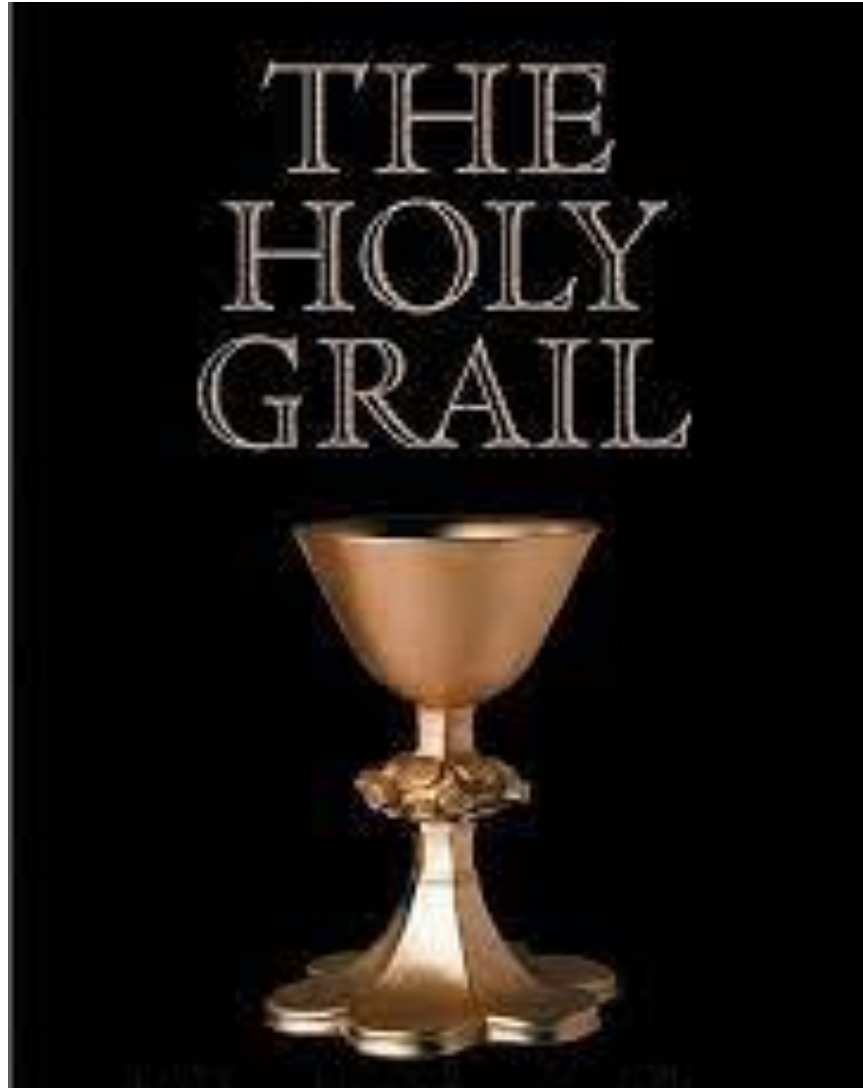


Guidelines – MIBC staging

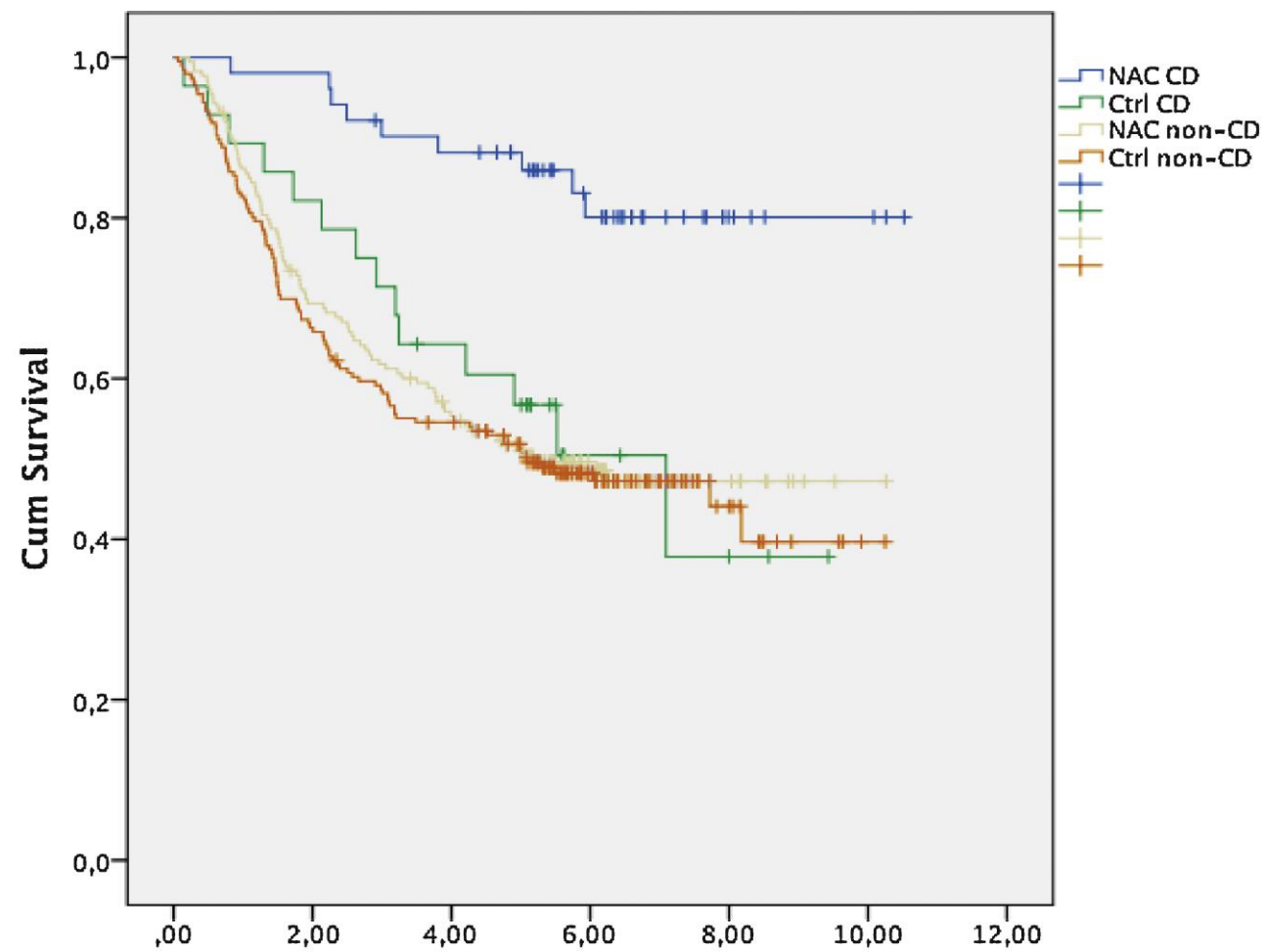
Summary of evidence	LE
Imaging as part of staging in MIBC provides information about prognosis and assists in selection of the most appropriate treatment.	2b
The diagnosis of upper tract UC depends on CT urography and, if needed, ureteroscopy.	2b
In local staging, MRI is superior to CT in terms of differentiating T1 from T2 disease.	2b
Magnetic resonance imaging is accurate for the assessment of tumour response to systemic therapy.	3
¹⁸ F-fluorodeoxy glucose-positron emission tomography with CT can provide additional information to guide treatment.	2b

Recommendations	Strength rating
If magnetic resonance imaging (MRI) is performed for local staging of bladder cancer (BC), it should be carried out before transurethral resection of the bladder tumour.	Strong
In patients with confirmed muscle-invasive BC, use computed tomography (CT) of the chest, abdomen and pelvis for staging, including some form of CT urography with designated phases for optimal urothelial evaluation.	Strong
Offer MRI to assess the local response to systemic therapy.	Weak

Clinical complete Response Assessment

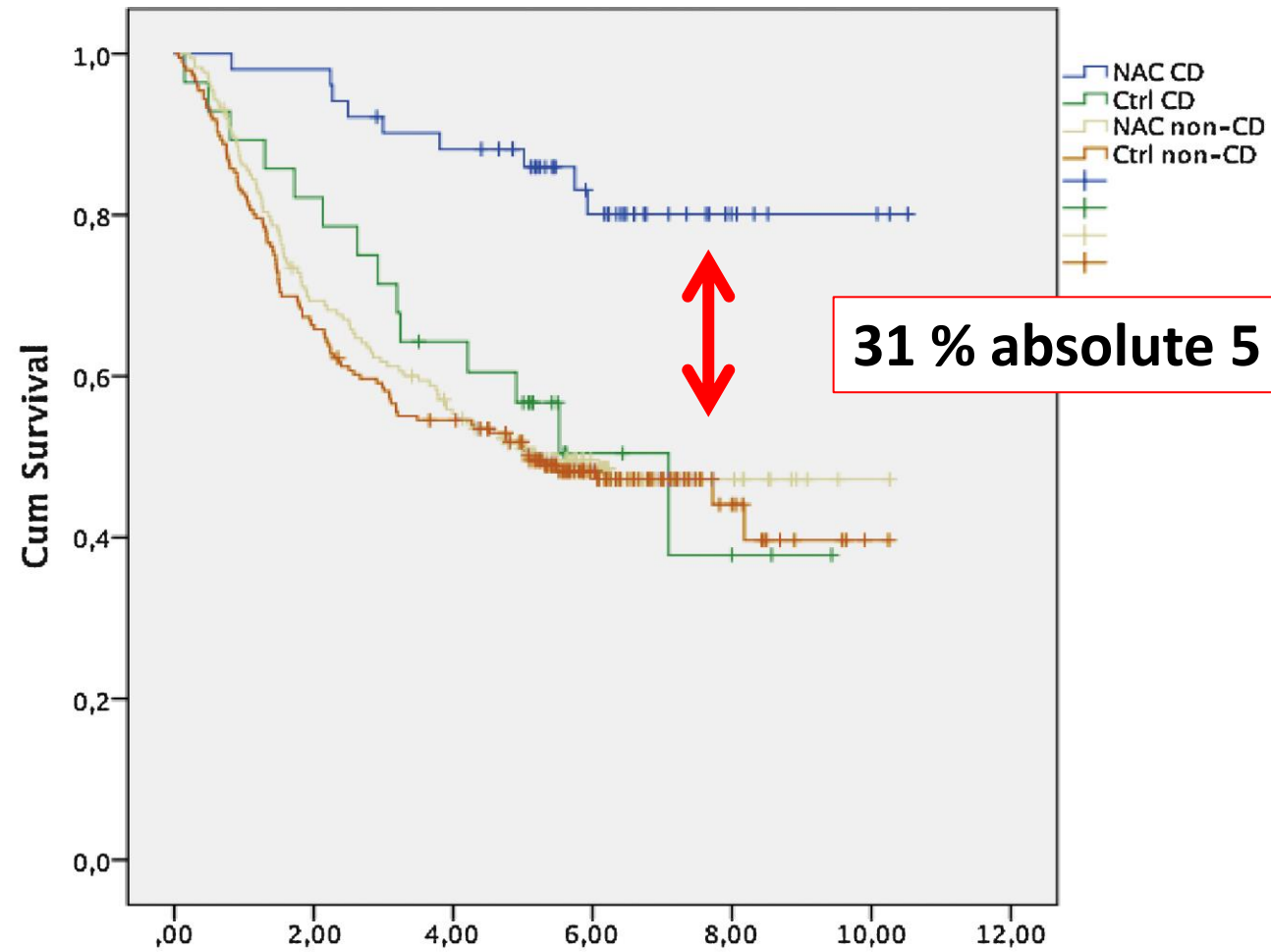


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Year	At risk	Cum No death	At risk	Cum No death	At risk	Cum No death	At risk	Cum No death	At risk	Cum No death	At risk	Cum No death
0			1		2		3		4		5	
NAC CD	51	-	50	1	50	1	45	5	44	6	40	6
Ctrl CD	28	-	25	3	23	5	20	8	17	10	15	12
NAC non-CD	174	-	149	24	119	53	106	66	93	77	78	84
Ctrl non-CD	196	-	162	34	130	66	114	81	105	89	90	95
Total	449	-	386	62	322	125	285	160	259	182	223	197

Rosenblatt R et al. Eur Urol. Jun 2012.

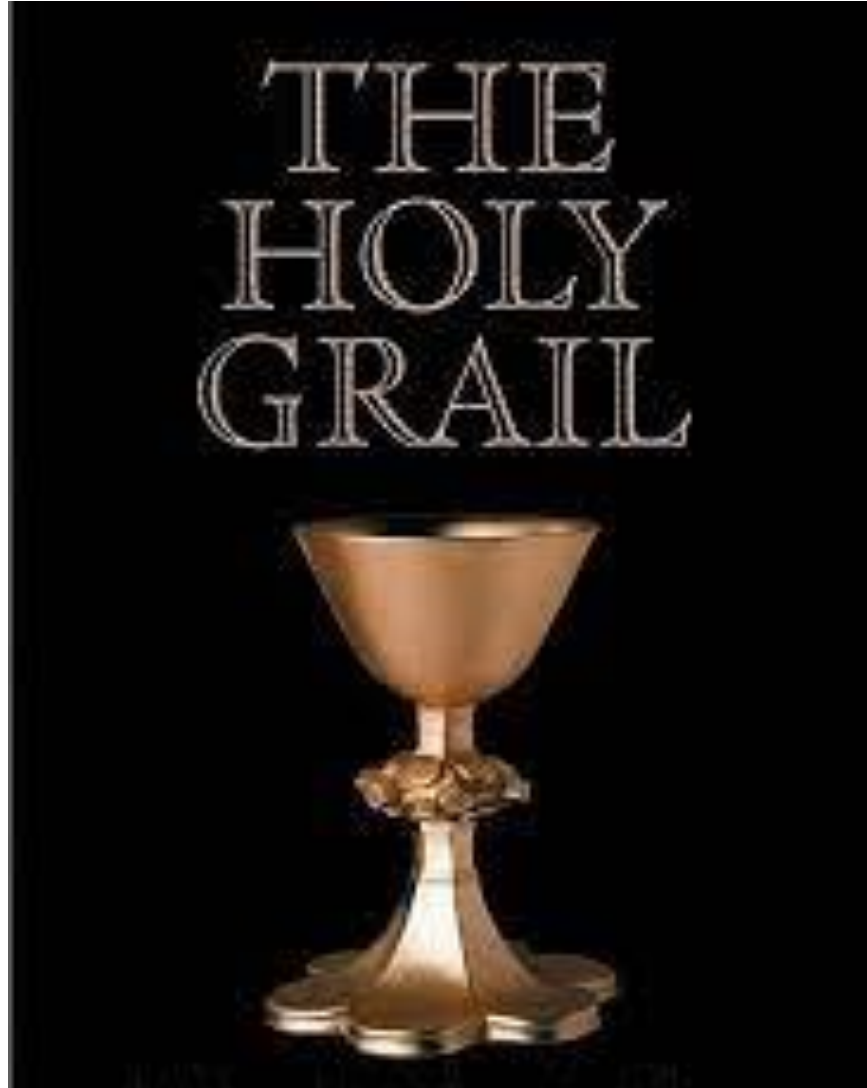


31 % absolute 5 yr OS benefit !

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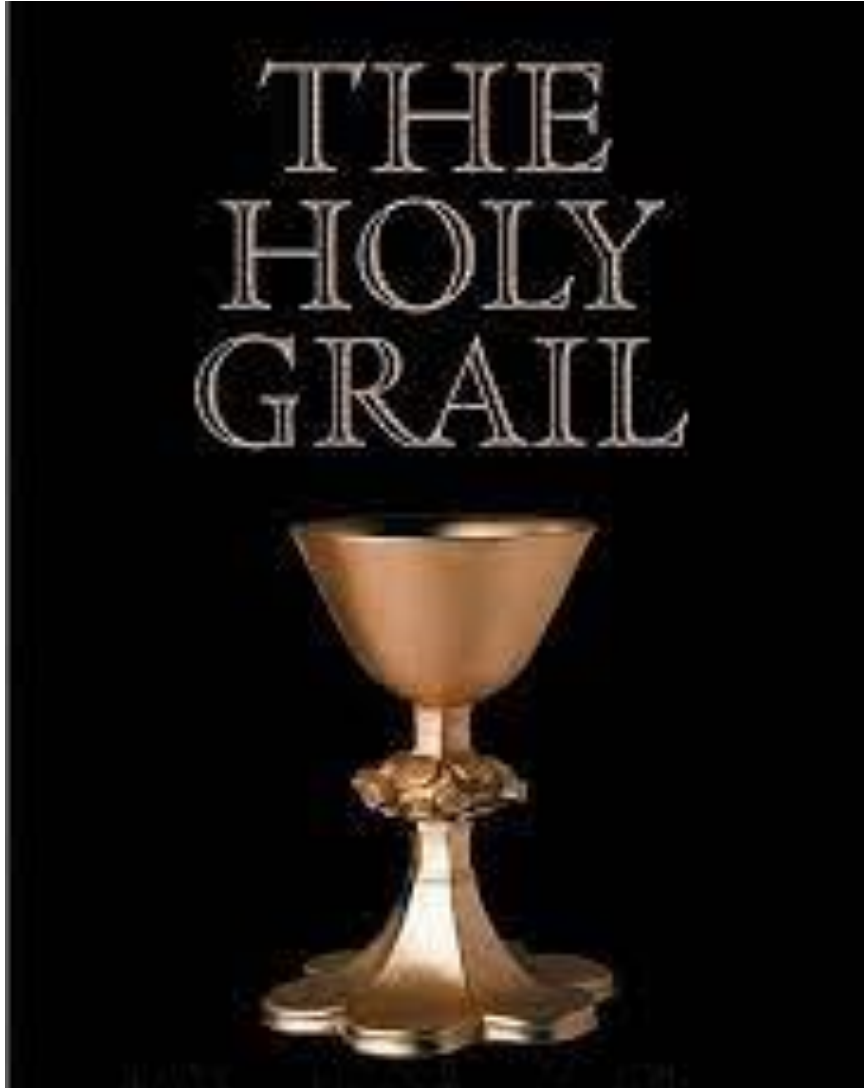
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Does a test accurately predict Clinical complete Response?



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Clinical complete Response Assessment



TURBT?

Does TURBT help?

A All patients with TUR restaging (N = 114)

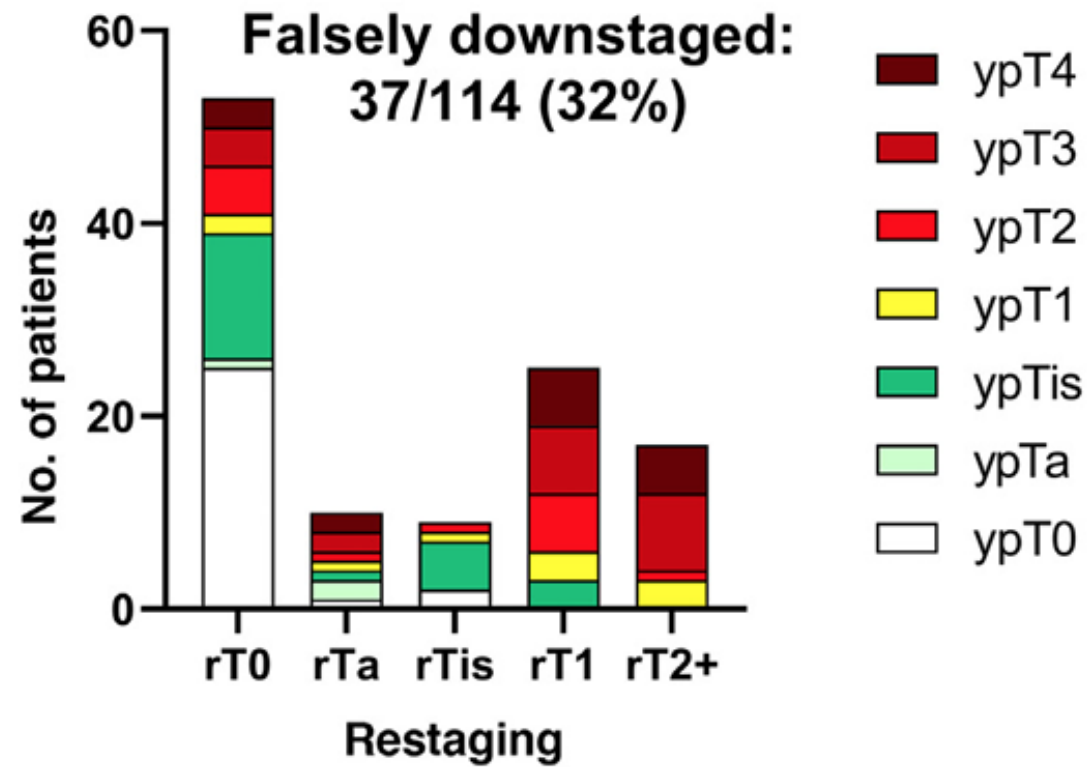


Table 3 – Stage-for-stage comparison of post-NAC TUR pathology (rT) with final cystectomy specimen pathology (ypT)

	ypT0	ypTa	ypTis	ypT1	ypT2	ypT3	ypT4	Total
<i>All patients undergoing post-NAC restaging TUR (n = 114)</i>								
rT0	25 (47)	1 (2)	13 (25)	2 (4)	5 (9)	4 (8)	3 (6)	53 (100)
rTa	1 (10)	2 (20)	1 (10)	1 (10)	1 (10)	2 (20)	2 (20)	10 (100)
rTis	2 (22)	0 (0)	5 (56)	1 (11)	1 (11)	0 (0)	0 (0)	9 (100)
rT1	0 (0)	0 (0)	3 (12)	3 (12)	6 (24)	7 (28)	6 (24)	25 (100)
≥rT2	0 (0)	0 (0)	0 (0)	3 (18)	1 (6)	8 (47)	5 (29)	17 (100)
Total	28	3	22	10	14	21	16	114
<i>All patients with visually negative post-NAC cystoscopy undergoing TUR (n = 21)</i>								
rT0	10 (59)	0 (0)	1 (6)	2 (12)	1 (6)	2 (12)	1 (6)	17 (100)
rTa	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)
rTis	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)
rT1	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	1 (50)	0 (0)	2 (100)
≥rT2	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (–)
Total	10	1	2	3	1	3	1	21
<i>All patients with tumor sequencing (n = 49)</i>								
rT0	8 (50)	0 (0)	2 (13)	1 (6)	1 (6)	4 (25)	0 (0)	16 (100)
rTa	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)
rTis	1 (20)	1 (20)	2 (40)	0 (0)	1 (20)	0 (0)	0 (0)	5 (100)
rT1	1 (14)	0 (0)	0 (0)	3 (43)	0 (0)	3 (43)	0 (0)	7 (100)
≥rT2	0 (0)	0 (0)	1 (5)	0 (0)	3 (15)	13 (65)	3 (15)	20 (100)
Total	10	2	5	4	5	20	3	49 (100)

NAC = neoadjuvant cisplatin-based chemotherapy; TUR = transurethral resection.

The values in parentheses indicate the percentage of patients within each restaging clinical stage that were found to be a specific pathologic stage. Gray shading indicates falsely downstaged patients.

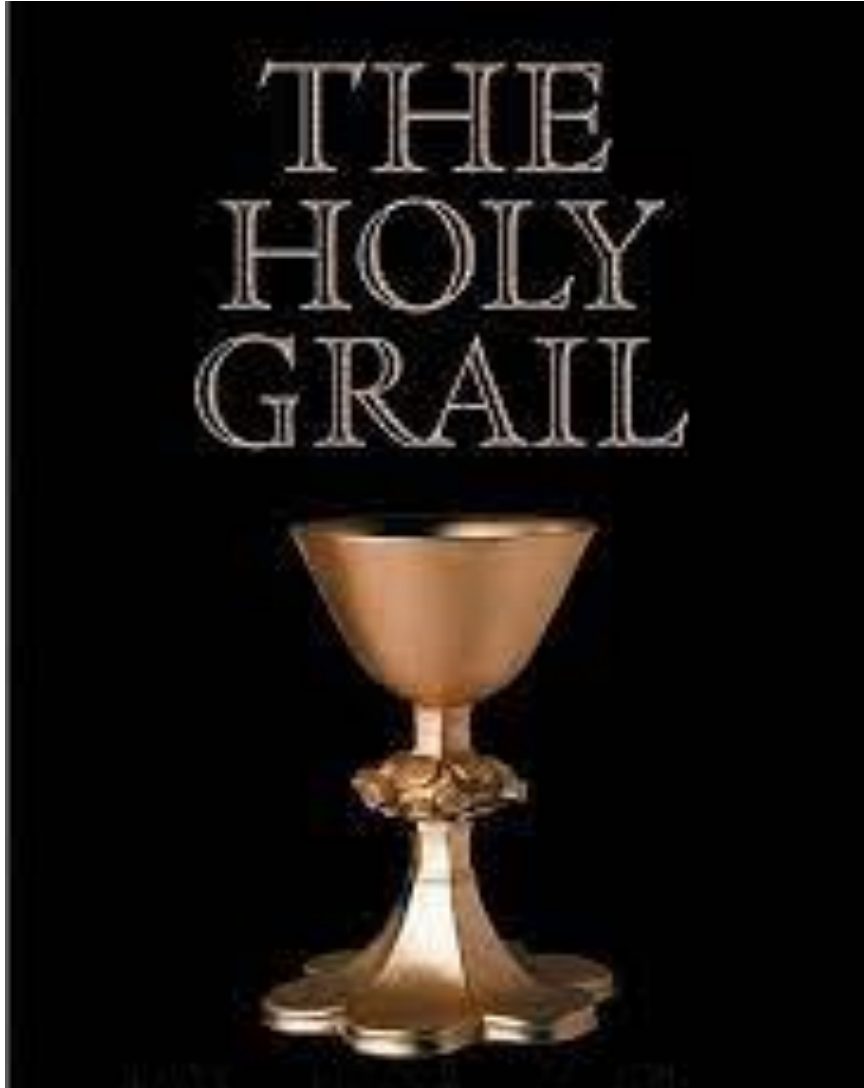
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rT1	1 (14)	0 (0)	0 (0)	3 (43)	0 (0)	3 (43)	0 (0)	7 (100)
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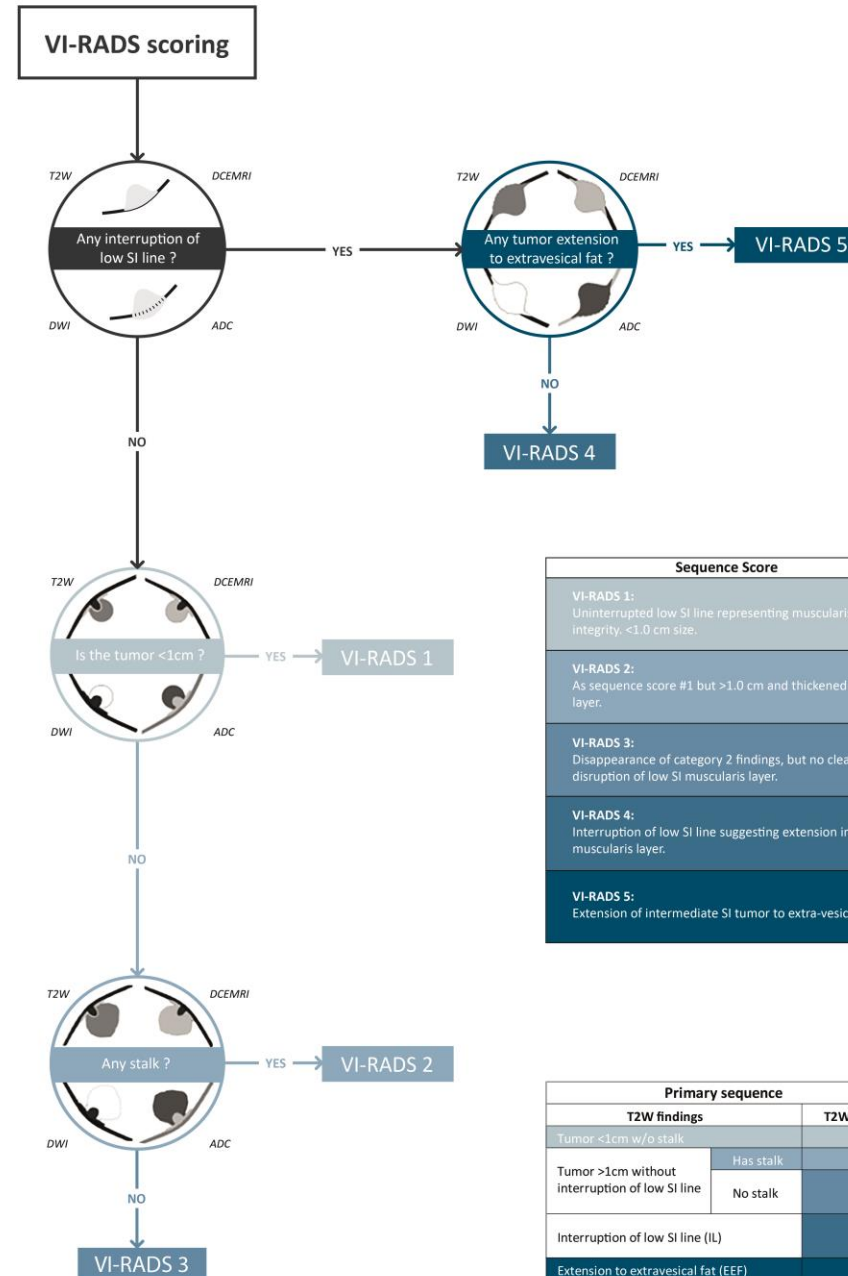
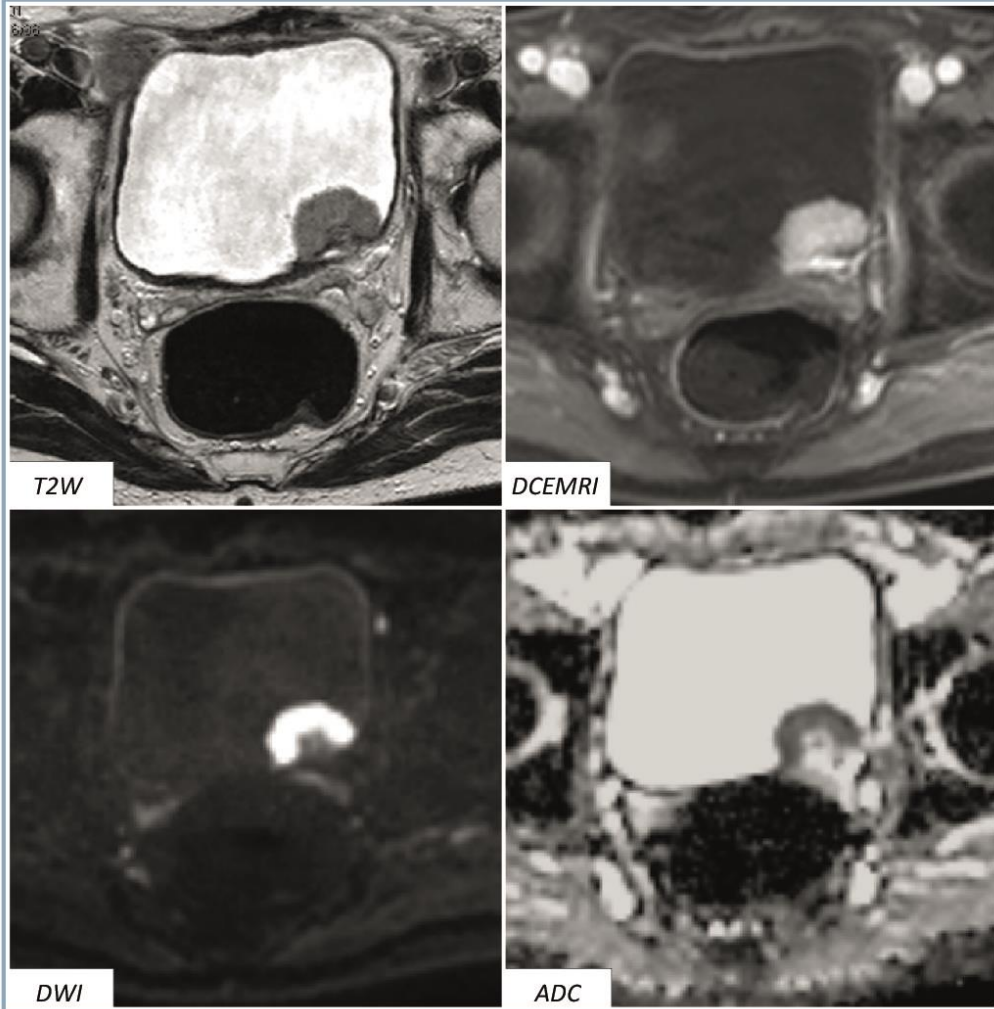
Clinical complete Response Assessment



MRI?

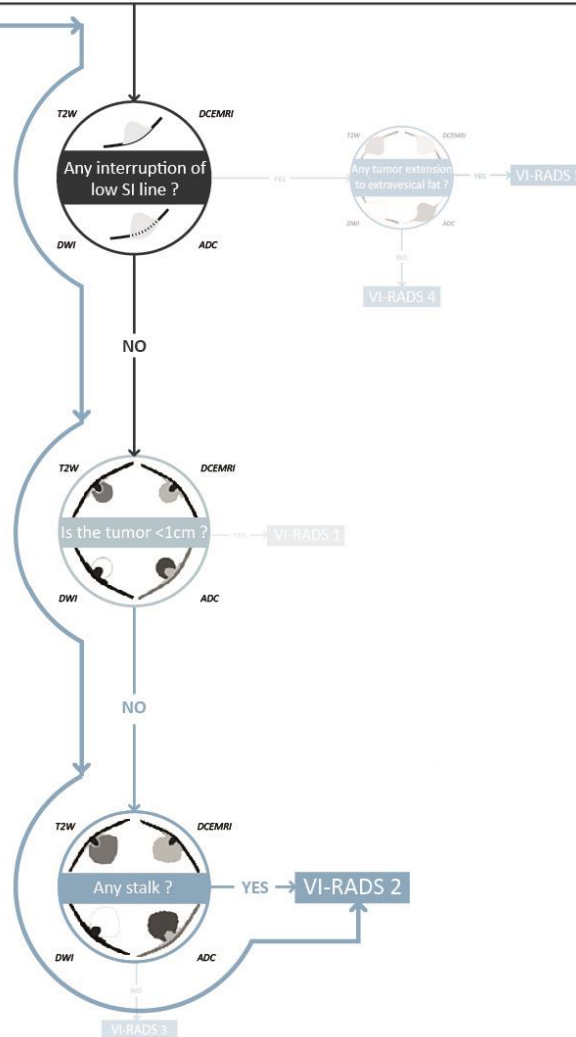
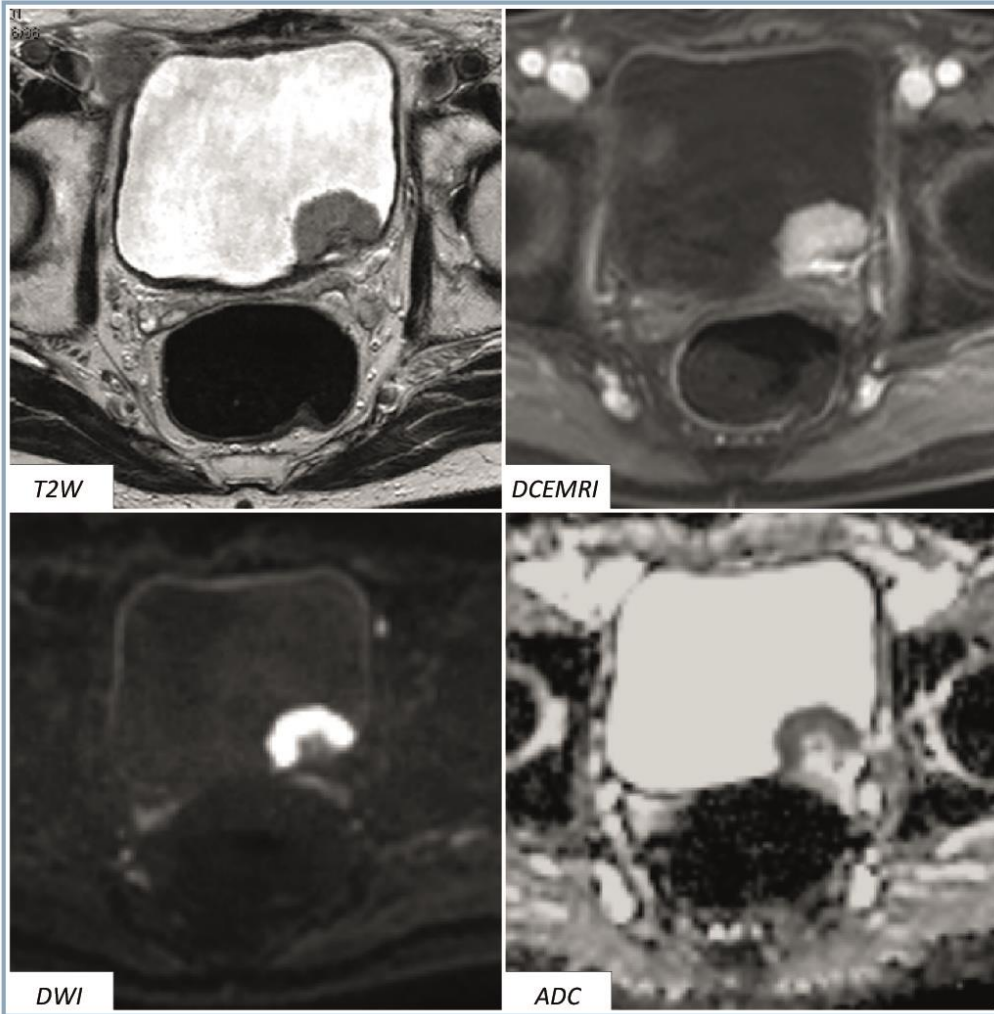
MRI in bladder cancer

VI-RADS scoring



MRI in bladder cancer

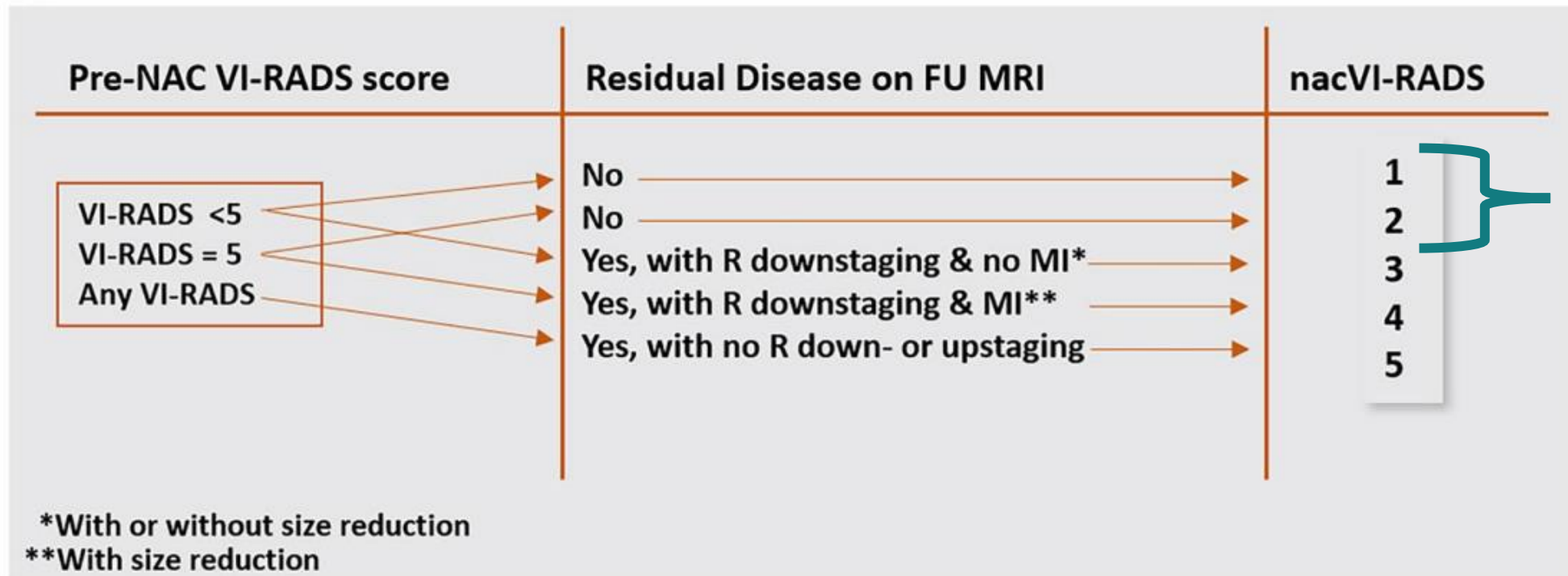
VI-RADS scoring



MRI and cCR assessment

NacVI-RADS workflow to assess the likelihood of complete response to therapy

A



= cCR?

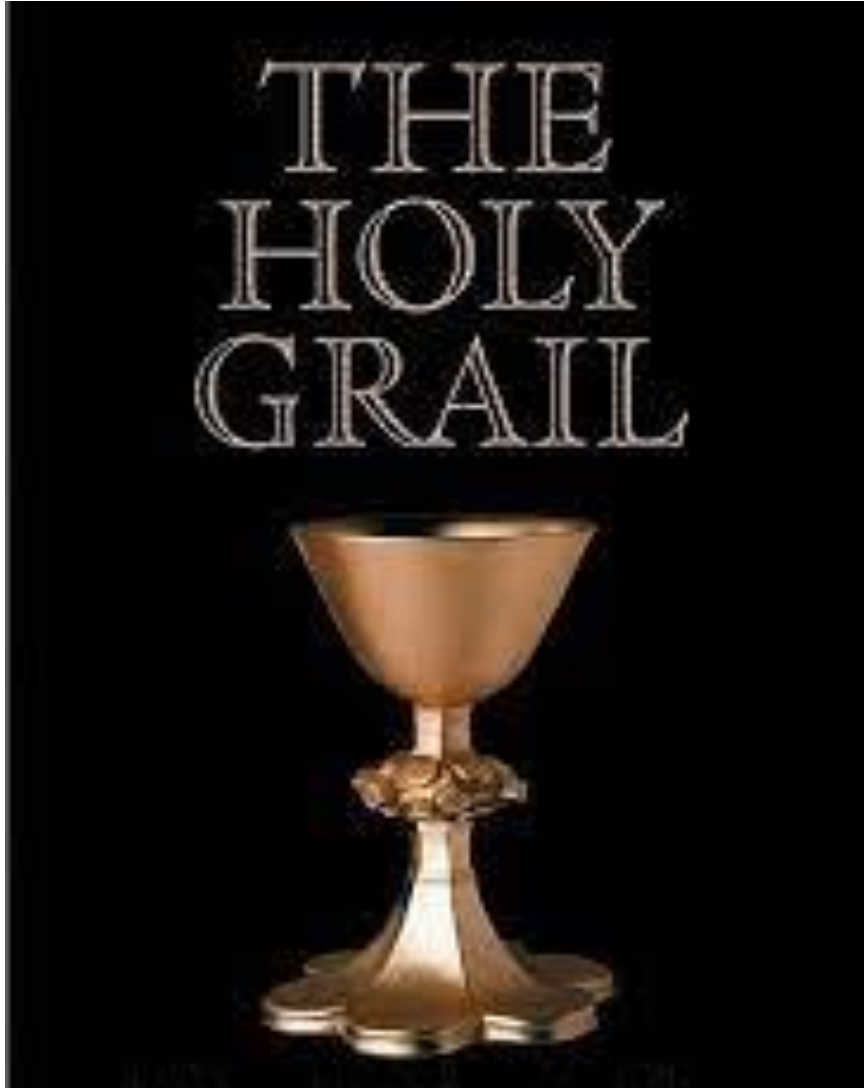
MRI and cCR assessment

Table 4: MRI Scores and Final Histopathologic Evaluation

Category	ypT0	ypT1/Ta/Tis	ypT2	ypT3–4	Total
nacVI-RADS Scores					
1	165/240 (69)	66/240 (28)	9/240 (4)	0/240 (0)	240/550 (44)
2	20/31 (65)	8/31 (26)	3/31 (10)	0/31 (0)	31/550 (6)
3	20/53 (38)	12/53 (23)	15/53 (28)	6/53 (11)	53/550 (10)
4	5/25 (20)	2/25 (8)	15/25 (60)	3/25 (12)	25/550 (5)
5	20/201 (10)	17/201 (8)	53/201 (26)	111/201 (55)	201/550 (37)

AUC nacVI-RADS for complete pathologic response (ypT0): 0.76 to 0.83

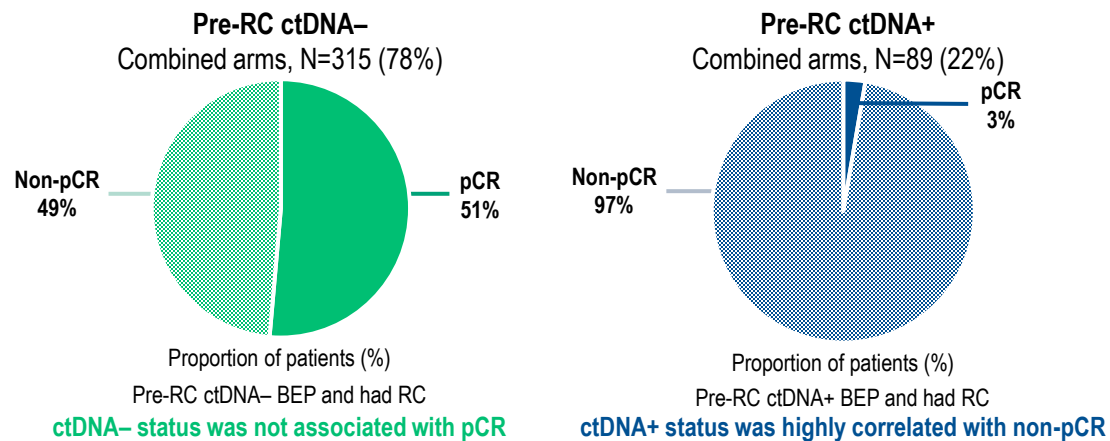
Clinical complete Response Assessment



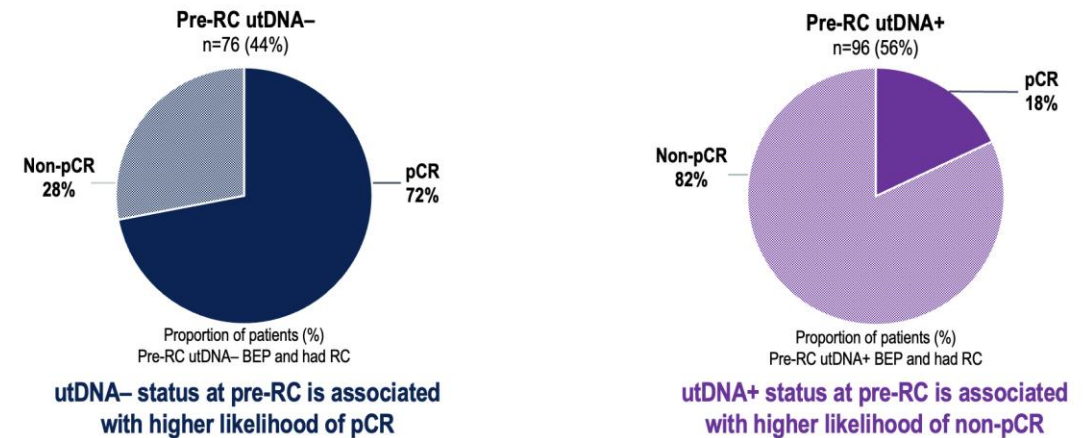
ct/ut DNA?

ct/ut DNA - NIAGARA

ctDNA

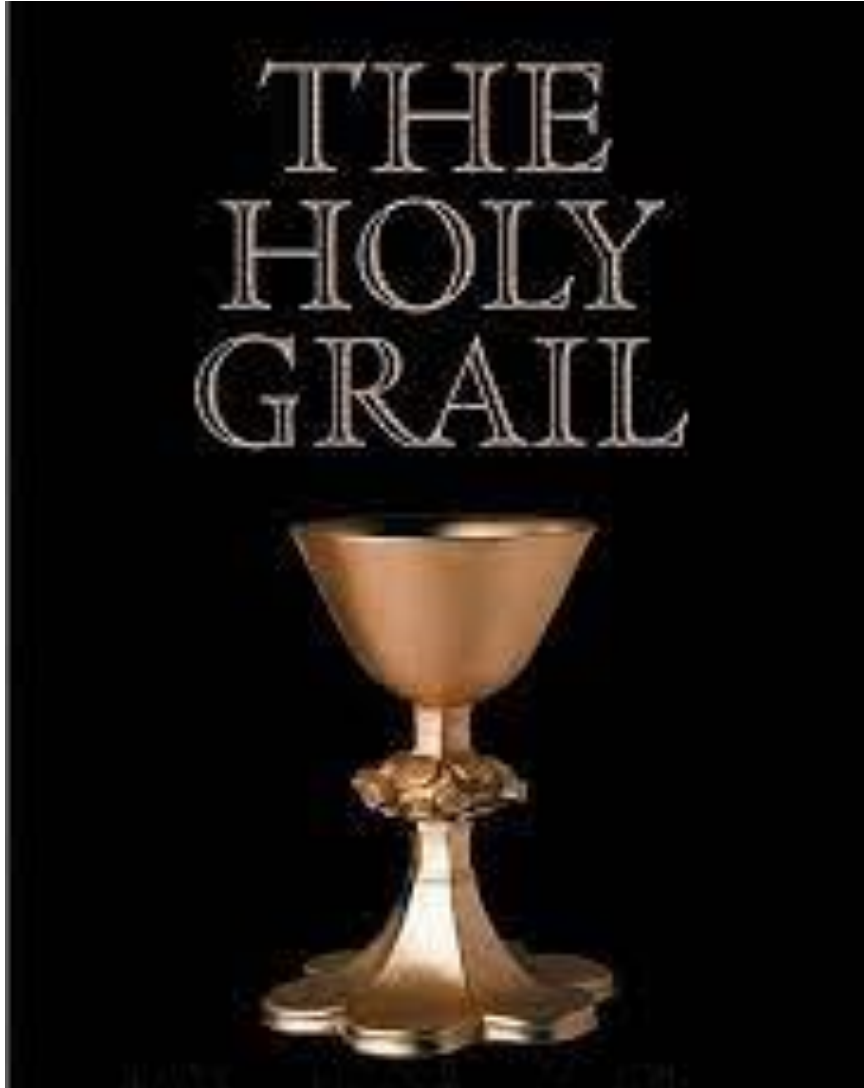


utDNA



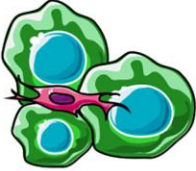
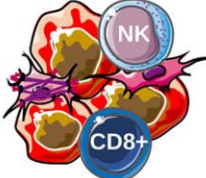
Pre-RC BEP with recorded pCR/non-pCR result, n=172 patients

Clinical complete Response Assessment



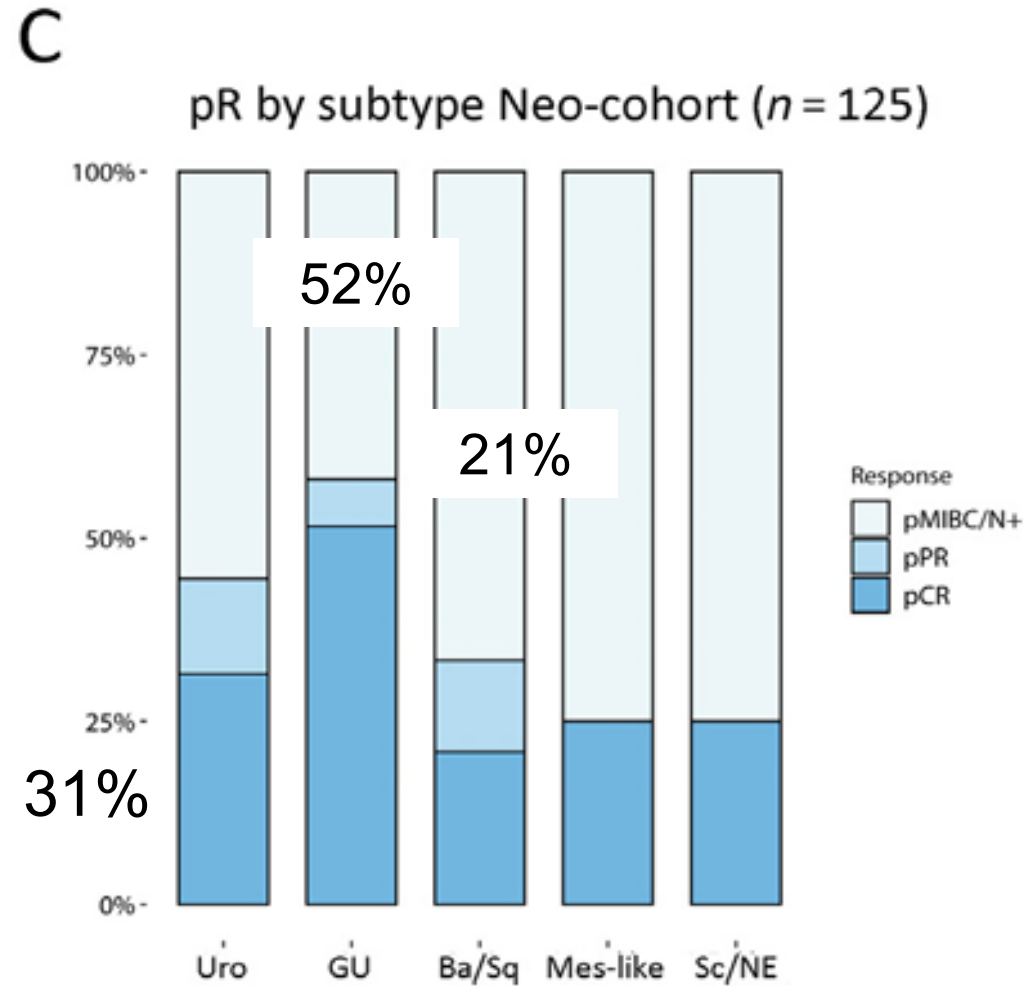
Transcriptomic?

cCR & Molecular subtypes?

% of MIBC	24%	8%	15%	15%	35%	3%
Class Name	Luminal Papillary (LumP)	Luminal Non-Specified (LumNS)	Luminal Unstable (LumU)	Stroma-rich	Basal/Squamous (Ba/Sq)	Neuroendocrine-like (NE-like)
						
Differentiation	Urothelial / Luminal				Basal	Neuroendocrine
Oncogenic mechanisms	FGFR3 + PPARG + CDKN2A -	PPARG +	PPARG + E2F3 +, ERBB2 + Genomic instability Cell cycle +		EGFR +	TP53 -, RB1 -, Cell cycle +
Mutations	<i>FGFR3</i> (40%), <i>KDM6A</i> (38%)	<i>ELF3</i> (35%)	<i>TP53</i> (76%), <i>ERCC2</i> (22%) TMB +, APOBEC +		<i>TP53</i> (61%), <i>RB1</i> (25%)	<i>TP53</i> (94%) <i>RB1</i> (39%)*
Stromal infiltrate		Fibroblasts		Smooth muscle Fibroblasts Myofibroblasts	Fibroblasts Myofibroblasts	
Immune infiltrate				B cells	CD8 T cells NK cells	
Histology	Papillary morphology (59%)	Micropapillary variant (36%)			Squamous differentiation (42%)	Neuroendocrine differentiation (72%)
Clinical	T2 stage +	Older patients + (80+)			Women + T3/T4 stage +	
Median overall survival (years)	4	1.8	2.9	3.8	1.2	1

* 94% of these tumors present either RB1 mutation or deletion

cCR & Molecular subtypes?



p=0.020

BASQ : *basal/squamous*, GU : *genomically unstable*, Mes-like : *mesenchymal like*, Sc/NE : *small cell/neuroendocrine like*, Uro : *urothelial-like*.
Sjödahl G et al. Eur Urol. 2022 May;81(5):523-532.

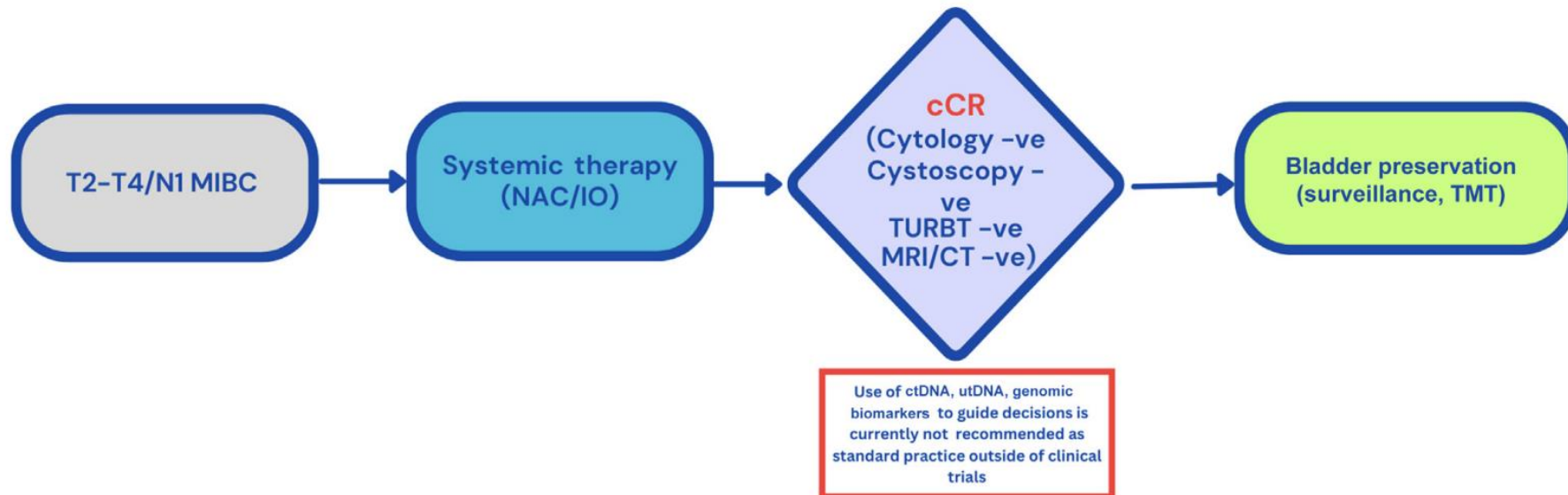
Genomic

Gene	Variant?	% with pT0	Odds ratio (IC 95%)	P-value*
ATM	Yes	56%	4.2 (1.6-11.2)	0.004
	No	25%		
ERCC2	Yes	67%	5.5 (1.8-16.6)	0.003
	No	25%		
FANCC	Yes	0%	N/A	
	No	34%		
RB1	Yes	48%	2.3 (0.9-5.9)	0.079
	No	28%		
At least 1 mutation	Yes	48%	5.4 (2-14)	0.0006
	No	14%		
* P value ajusted with stage				

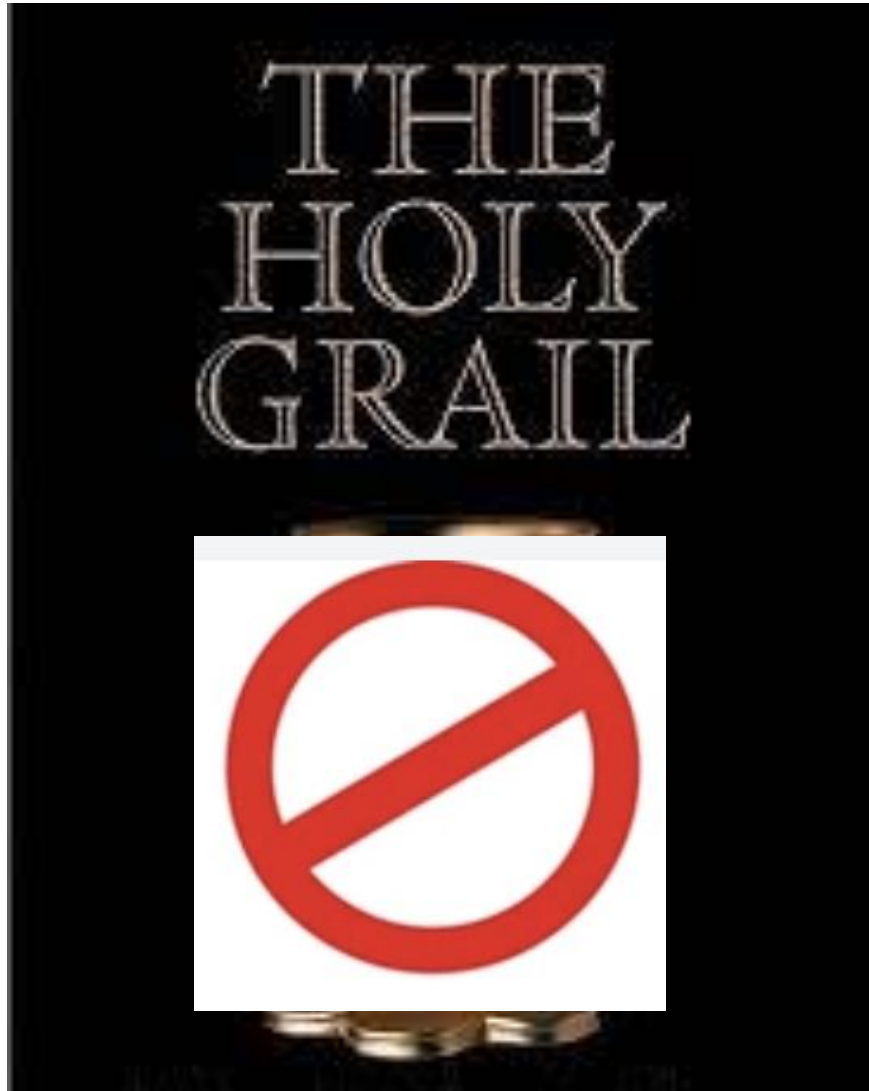
What is cCR then?



INTERNATIONAL
BLADDER CANCER
GROUP



Take home how to assess cCR in MIBC post NAT



1. Exclude obvious non-responders
CT or PET CT

2. Assess the bladder locally
Rigorous cystoscopy
Urinary Cytology
Re-TURBT (enhanced TURBT ideally)

3. Add high-quality local imaging
mpMRI with a TRAINED radiologist
nacVI-RADS ideally

4. Integrate biology when available
ctDNA
utDNA
Transcriptomic ?
Mutation profile?