Câncer do urotélio não-metastático
ASCO GU 2018 Best presentations

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Câncer do urotélio não metastático
ASCO GU 2018

1. **tumor não músculo invasivo**
2. **tumor músculo invasivo**
3. **guidelines**

Tumor não músculo invasivo da bexiga: Evolução em 5 anos

	recidiva (%)	progressão (%)
G1	50	2
G2	60	10
G3	80	50

	progressão (%)
Ta	3
T1	24

Dalbagni, Herr. Urol.Clin.N. Amer.27:137, 2000
Messing, 2003

Qual classificação histopatológica é a recomendada em 2018?

sistemas não são intercambiáveis

WHO 1973	G1	G2	G3
WHO 2004	NUBPM	baixo grau	alto grau

WHO 1973	NICE	EAU	
WHO 2004	AUA	EAU	NCCN

Woldu SL, Bagrodia A, Lotan Y. Guideline of Guidelines - Non-Muscle Invasive Bladder Cancer. BJU Int. 2017 Jan 6. doi: 10.1111/bju.13760

AUA:
Estratificação de risco no tumor de bexiga não músculo invasivo

Baixo risco	Risco Intermediário	Alto risco
• TA BG ≤ 3 cm único	• TA AG ≤ 3cm único • TA BG > 3 cm recidivado ou multifocal • T1 BG	• TA AG > 3cm recidivado ou multifocal • T1 AG • CIS • Falha BCG em AG
		Variantes histológicas
		Invasão linfo-vascular
		Invasão da uretra prostática

BG: baixo grau ; AG: alto grau

AUA guideline 2016
https://www.auanet.org/education/guidelines/non-muscle-invasive-bladder-cancer.cfm

RNA sequencing identifies 3 different molecular grades and immune checkpoint cascades with distinct clinical behavior in Non Muscle Invasive Bladder Cancer

Thenappan Chandrasekar[1,9], Alexandre R. Zlotta[3,9], Bibaswan Ghoshal[1], Jess Shen[1], Aidan P Noon[2], Annette Erlich[3], Cynthia Kuk[3], Ruoyu Ni[4], Balram Sukhu[4], Kim Chan[1], Morgan Roupret[6], Thomas Seisen, Eva Comperat[7], Joan Sweet[8], Girish S. Kulkarni[9], Neil E. Fleshner[9], Azar Azad[4], Theodorus H. van der Kwast[8], Jeffrey Wrana[1]

1Mount Sinai Hospital, Lunenfeld-Tanenbaum Research Institute, Toronto, CA, 2 University of Sheffield, Urology, Sheffield, UK,
3 Mount Sinai Hospital, Dept. of Urology, Toronto, CA, 4 Mount Sinai Hospital, Dept. of Pathology and Laboratory Medicine, Toronto, CA,
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6 Group Hospitalier La Pitié-Salpêtière, Université Pierre et Marie Curie, Dept of Urology, Paris France,
7 Group Hospitalier La Pitié-Salpêtière, Université Pierre et Marie Curie, Dept of Pathology, Paris France,
8 University Health Network, Dept. of Pathology, Toronto, CA,
9 University Health Network, Princess Margaret Cancer Centre, Dept. of Surgical Oncology, Division of Urology, Toronto, CA

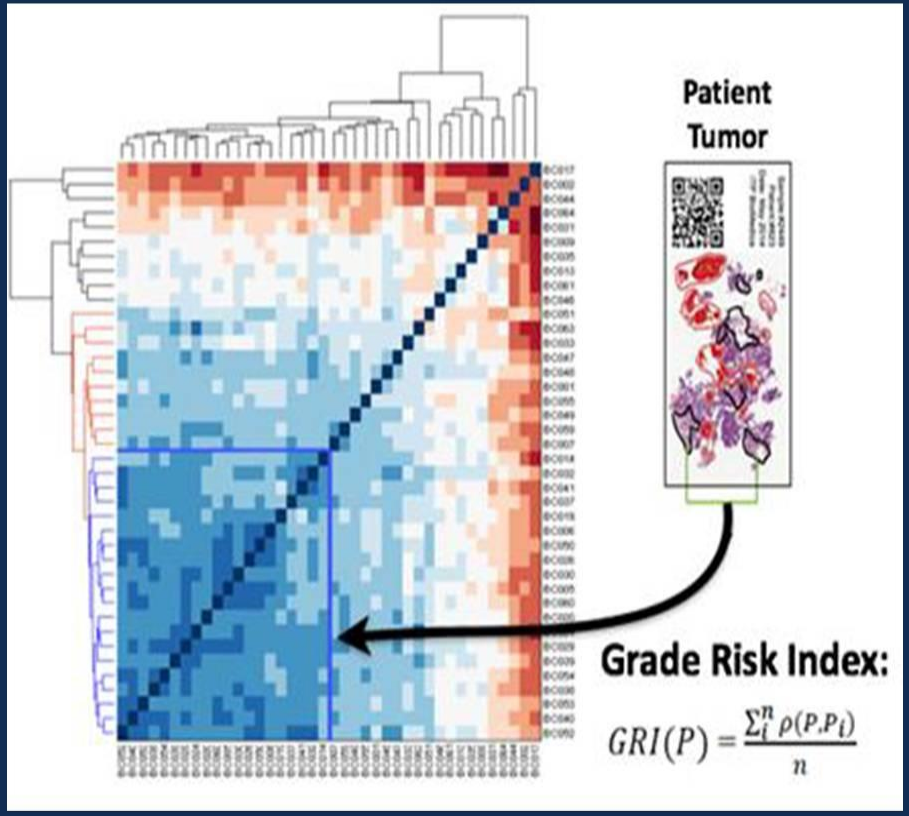
PRESENTED AT: 2018 Genitourinary Cancers Symposium | #GU18

INITIAL ANALYSIS

- Whole transcriptomic (WT) analysis of 178 bladder tumors
  - 158 NMIBC and 20 MIBC
  - Discovery cohort (n=38)
  - 2 validation cohorts (n= 40 and 80)
  - Integrated and tested for correlations with pathological grading and clinical outcomes
- Conventional pathological grading (WHO 1973 [grade 1, 2 and 3] and 2004 [low grade-LG vs high grade-HG])
- Validation cohort: independent RNA-Sequencing dataset (n=209, Hedegaard et al. 2016) Cancer Cell

Defining a Molecular Grade Risk Index (MGRI).

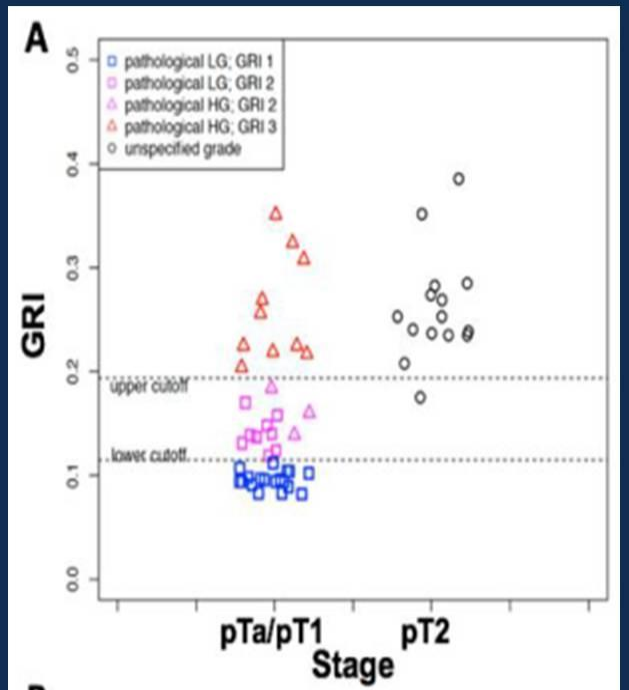
Pathologist Selection:
- No necrosis
- No hemorrhage
- Clear bladder cancer



Molecular Clustering – NMIBC and MIBC

- Analysis of discovery and validation cohorts reveal three GRI clusters (GRI 1-3) that distinguish LG, intermediate, and HG groups, respectively
  - Strong association between GRI and tumor grade
  - ROC analyses demonstrated high performance at predicting grade (AUC=0.96)

- GRI scores for MIBC tumors cluster in GRI 3



B

	GRI 1	GRI 2	GRI 3
HG	0	3	10
LG	18	9	0

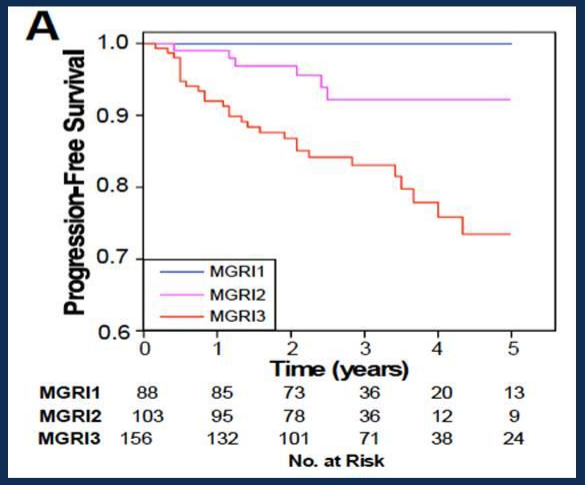
C

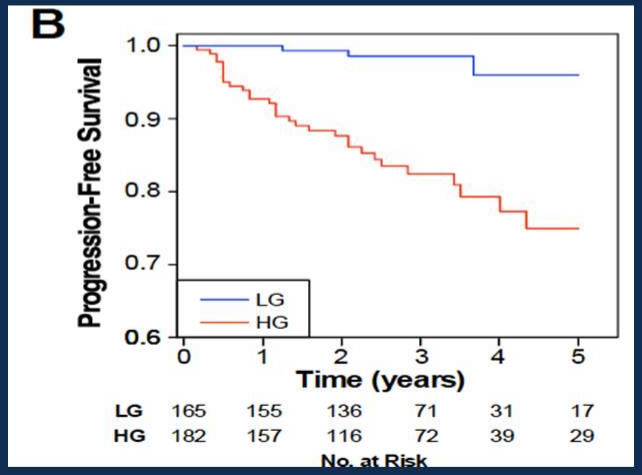
	GRI 1	GRI 2	GRI 3
HG	0	7	8
LG	14	12	0

Melhor estratificação nos grupos de baixo grau

GRI Molecular Grade + Risk of Progression to MIBC disease

- 347 NMIBC patients; Median FU time of 37 months (range 4-149)
- 31 progressions to MIBC (41% in the first year)
- GRI scores for progressors were significantly
- GRI independently predicted progression (HR=2.96, 95%CI=1.70-5.13, p=1.20x10-04)



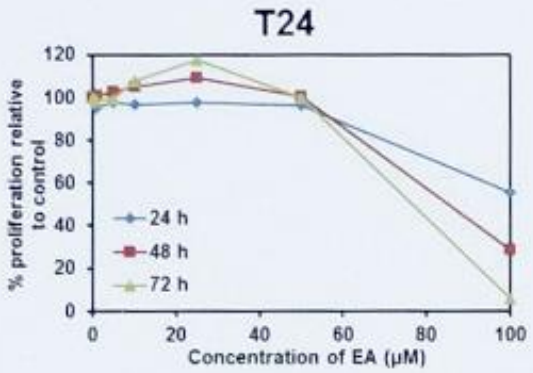


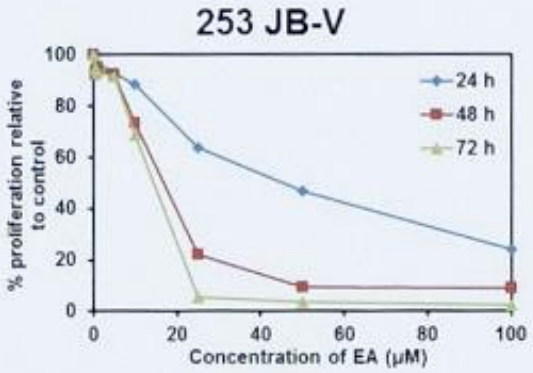
REPURPOSING ETHACRYNIC ACID FOR THE TREATMENT OF BLADDER CANCER

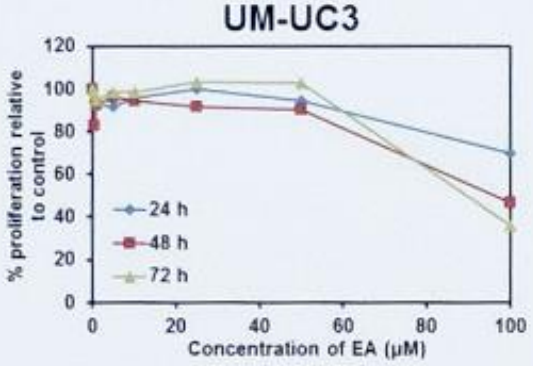
Eugene K. Lee, MD[1], Gregory A. Reed, PhD[2,5], Prasad Dandawate, PhD[3], Gaurav Kaushik, PhD[3], Dharmalingam Subramaniam, PhD[3,5], Jeffrey M. Holzbeierlein, MD[1], Shrikant Anant, PhD[3,5], Scott Weir, PharmD, PhD[2,4,5]

Department of Urology[1], Department of Pharmacology, Toxicology and Therapeutics[2], Department of Surgery[3], Institute for Advancing Medical Innovation[4], The University of Kansas Cancer Center[5], The University of Kansas Medical Center, Kansas City, KS 66160

EA inhibits proliferation of bladder cancer cell lines







IC_{50} value (μM)	24 h	48 h	72 h
T24	>100	86	78
253 JB-V	43	16	14
UM-UC3	>100	100	92

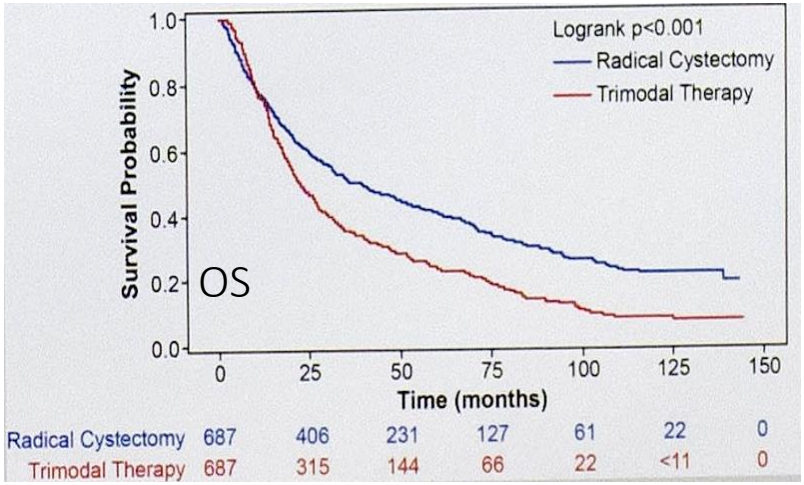
Edecrin = diurético de alça [oral ou ev] antigo

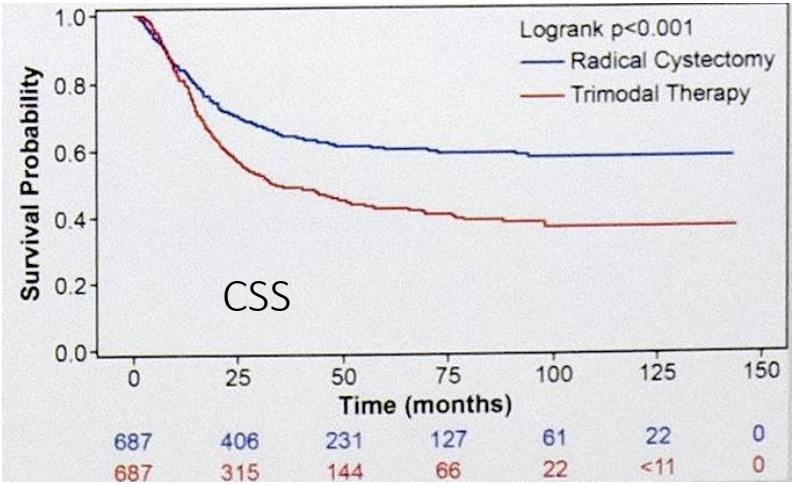
Radical Cystectomy Provides Improved Survival Outcomes and Decreased Costs Compared With Trimodal Therapy for Patients Diagnosed With Localized Muscle-Invasive Bladder Cancer

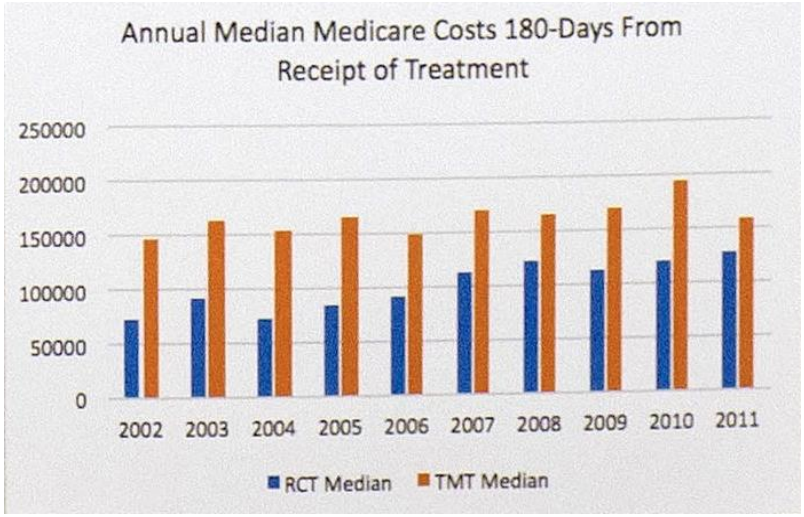
utmb Health

Stephen B. Williams[1], William Tabayoyong[2], Yong Shan[1], Usama Jazzar[1], Hemalkumar B. Mehta[3], Jacques G. Baillargeon[4], Jinhai Huo[5], Anthony J. Senagore[3], Eduardo Orihuela[1], Douglas S. Tyler[3], Todd A. Swanson[6], Ashish M. Kamat[2]

From the The Department of Surgery, Division of Urology, The University of Texas Medical Branch, Galveston, TX[1]; Department of Urology, The University of Texas MD Anderson Cancer Center, Houston, TX[2]; Department of Surgery, The University of Texas Medical Branch at Galveston, Galveston, TX[3]; Department of Medicine, Division of Epidemiology, Sealy Center on Aging, The University of Texas Medical Branch at Galveston, Galveston, TX[4]; Department of Health Services Research, Management and Policy, The University of Florida, Gainesville, FL[5]; Department of Radiation Oncology, The University of Texas Medical Branch, Galveston, TX[6]







Terapia trimodal para preservação vesical: cura menos e gasta mais

Racional para preservação vesical
Problemas peri-operatórios da cistectomia radical

- tempo mediano de internação hospitalar: 7-14 dias
- 2ª maior taxa de complicação entre todas as cirurgias de alto risco
  - re-internação em 90 dias: 32-64%
  - mortalidade 90 dias após alta hospitalar: 6%

Shabsigh A et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. Eur Urol 2009; 55: 164–74

Problemas com a preservação vesical seletiva

- doença é pan-urotelial:
  - maioria recidiva na bexiga
  - ≈ 25% recidivam com tumor superficial
- progressão para cistectomia radical: 1/3
  - cirurgia ainda mais complexa??
- complicações da QT- RTX grau ≥ 3
  - agudas: até 21%
  - tardias: até 8.8%

Smith ZL.BJU International |2013: 112, 13–25

Preservação vesical seletiva: Quem é o candidato ideal?

Fatores prognósticos de melhor resposta

- **bom estado geral**
- **ClCr > 60 ml/min**
- **função vesical normal**
- **RTU visualmente completa**
- **tumor único < 3 cm**
- **ausência de cis**
- **sem hidronefrose**

< 20% do total de pacientes com tumor músculo-invasivo

Gakis G et al. Eur Urol. 2013;63(1):45-57.

Selective Bladder Preservation with Twice-Daily Radiation plus 5-Flourouracil/Cisplatin or Daily Radiation plus Gemcitabine for Patients with Muscle Invasive Bladder Cancer – Primary Results of NRG/RTOG 0712: A Randomized Phase 2 Multicenter Trial

John J Coen, MD[1], Peixin Zhang, PhD[2], Philip J Saylor, MD[3], Cheryl T. Lee, MD[4], Chin-Lee Wu, MD, PhD[3], William Parker, MS[5], Tim Lautenschlaeger, MD[6], Anthony Zietman, MD[7], Jason Efstathiou, MD, DPhil[7], Ashesh B Jani, MD[8], Omer Kucuk, MD[9], Luis Souhami, MD[5], Joseph P Rodgers[2], Howard M Sandler, MD[10], William U Shipley, MD[7]

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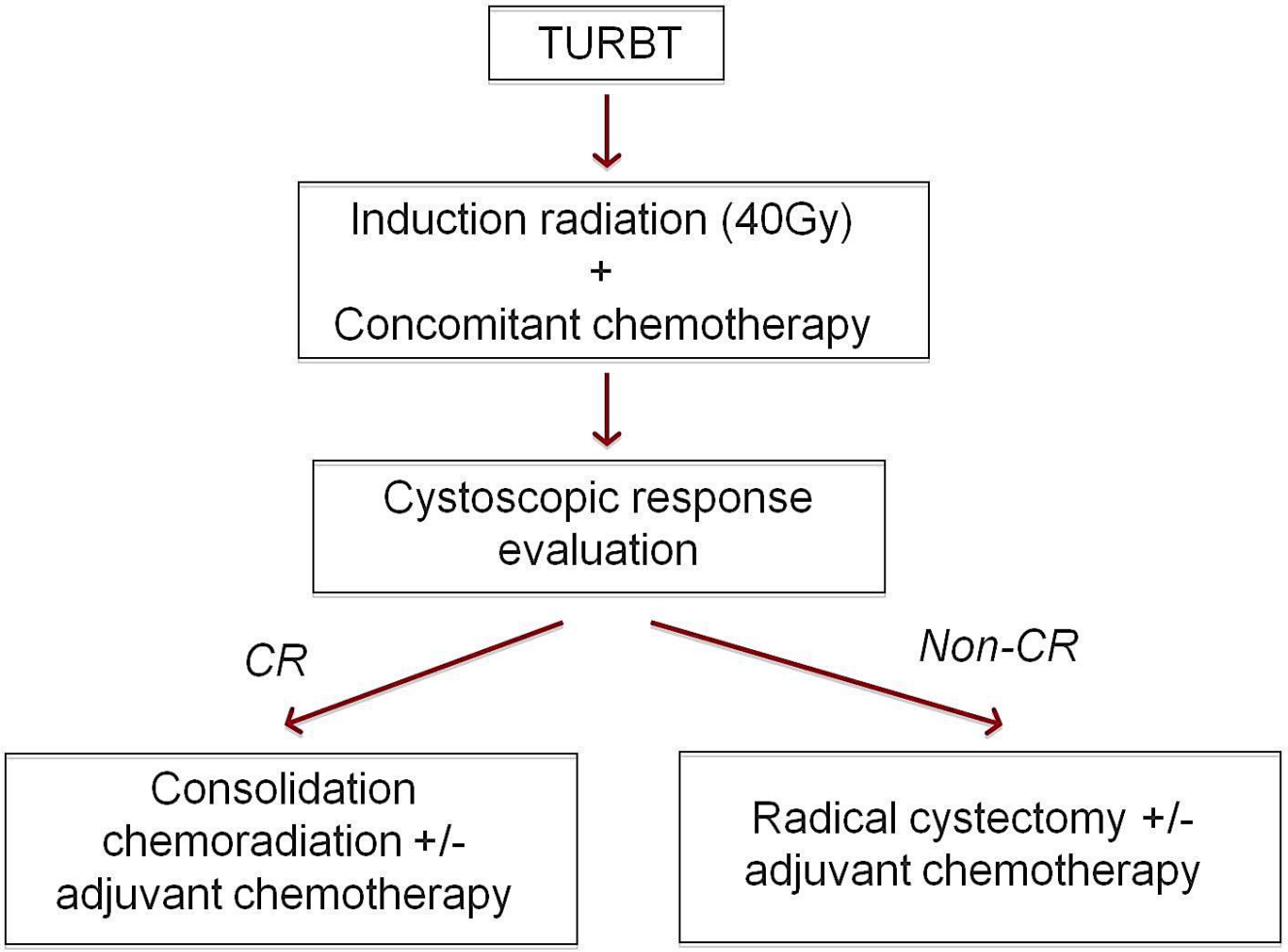
GU ASCO
February 9, 2018

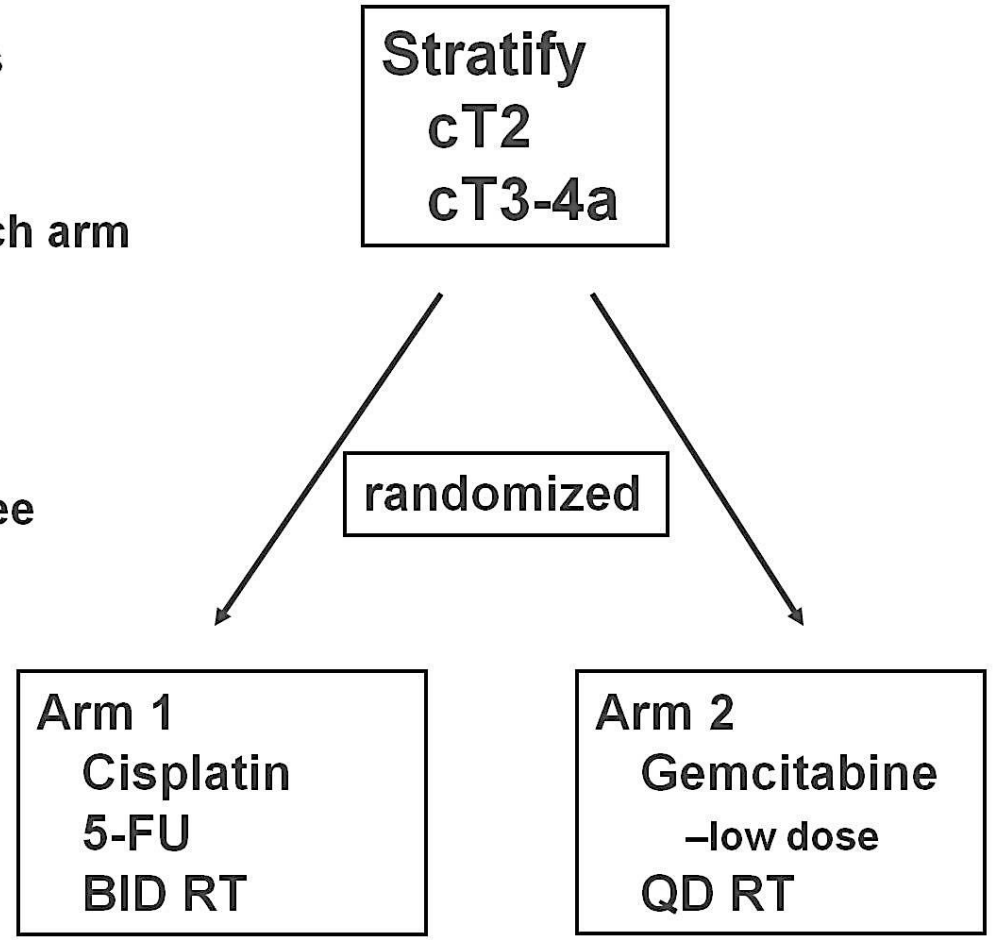
Selective Bladder Preservation Paradigm



NRG ONCOLOGY™

RTOG 0712

- Phase II randomized trial
  - 2 concurrent chemoRT arms
- Primary endpoint
  - DM rate at 3 years for each arm
- Secondary endpoints
  - Acute and late toxicity
  - Tumor response
  - 5-yr Bladder intact DM free survival
- Adjuvant chemotherapy
  - Gemcitabine
  - Paclitaxel



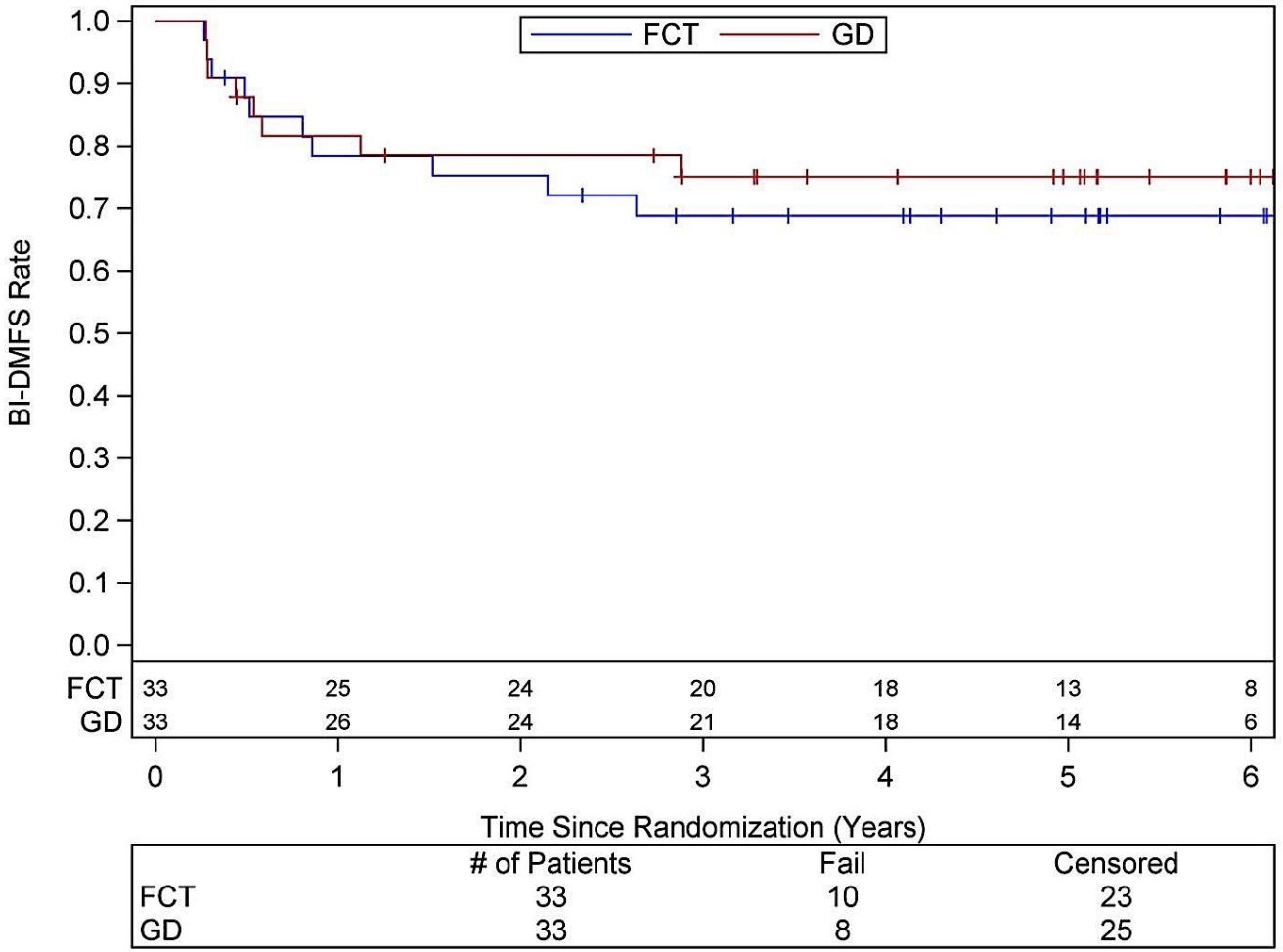
NRG ONCOLOGY™

RTOG 0712
BI-DMFS at 3 years

Bladder Intact Metastatic Disease Free Survival at Three Year Follow-up on Evaluable Patients		
	5 Fluorouracil and Cisplatin + BID Irradiation (n=30)	Gemcitabine + QD Irradiation (n=29)
Bladder Intact Metastatic Disease Free Survival at 3 years		
Yes	20 (66.7%)	20 (69.0%)
No	10 (33.3%)	9 (31.0%)
Type of Failure (First, if Multiple Occurred)	(n=10)	(n=9)
Distant metastasis	5 (50.0%)	3 (33.3%)
Death	2 (20.0%)	1 (11.1%)
Undergoing Cystectomy	3 (30.0%)	5 (55.6%)

NRG ONCOLOGY™

RTOG 0712
BI-DMFS



	# of Patients	Fail	Censored
FCT	33	10	23
GD	33	8	25

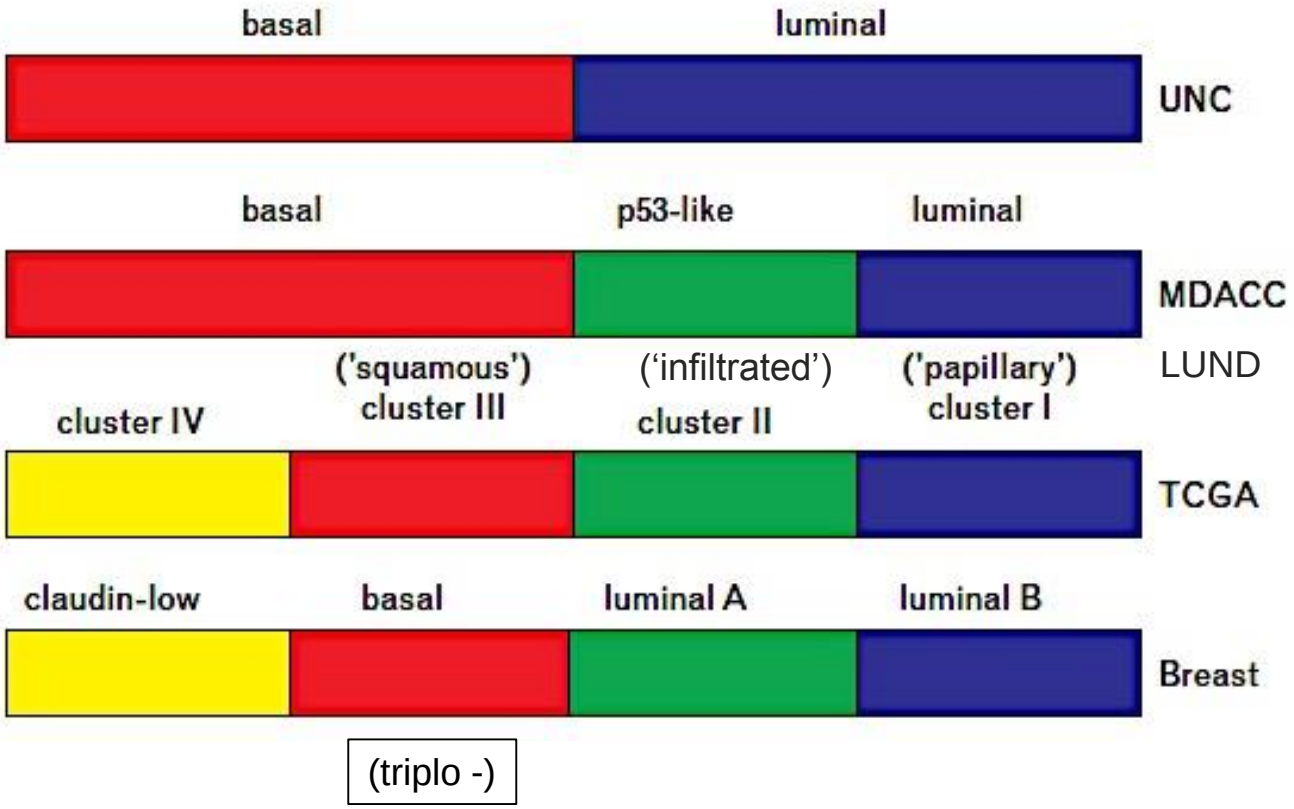
NRG ONCOLOGY™

RTOG 0712 Conclusions

- DM rate at 3 years was similar in both arms and comparable to surgical series
- Both FCI and GI arms were well tolerated
- CR rates were high in both arms
- Bladder preservation rates were high and equal

NRG ONCOLOGY™

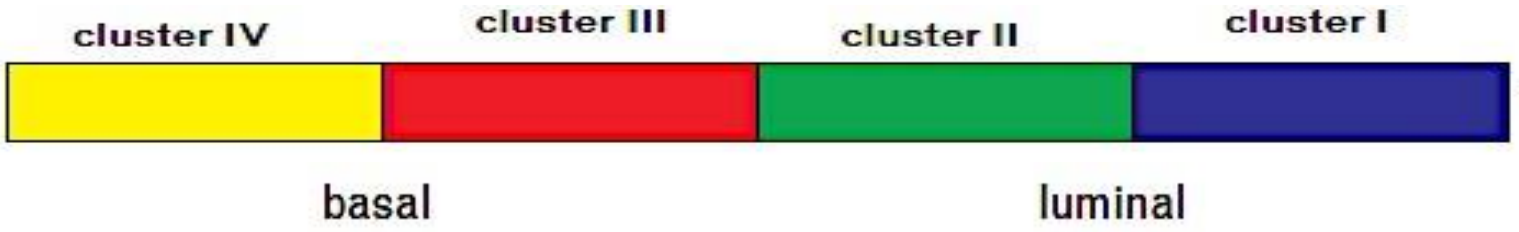
Subtipos intrínsecos de câncer de bexiga músculo-invasivo e semelhança com carcinoma da mama e do pulmão



UNC: University of North Caroline
MDACC: MD Anderson Cancer Center
LUND : Suécia (squamous = SCC = carcinoma espino-celular do pulmão)
TCGA: Cancer genomic atlas network - NIH

Curr Opin Urol 2015, 25:449–458
EBioMedicine. 2016 12: 105–117

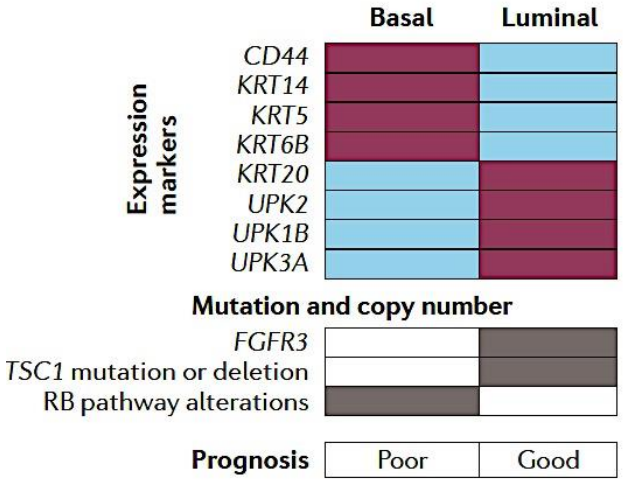
The Cancer Genome Atlas subtipos de câncer urotelial Implicação clínica



KRT5/6+ KRT14+ CD44+ EGFR+	P53 +	FGFR3 +/PPAR +

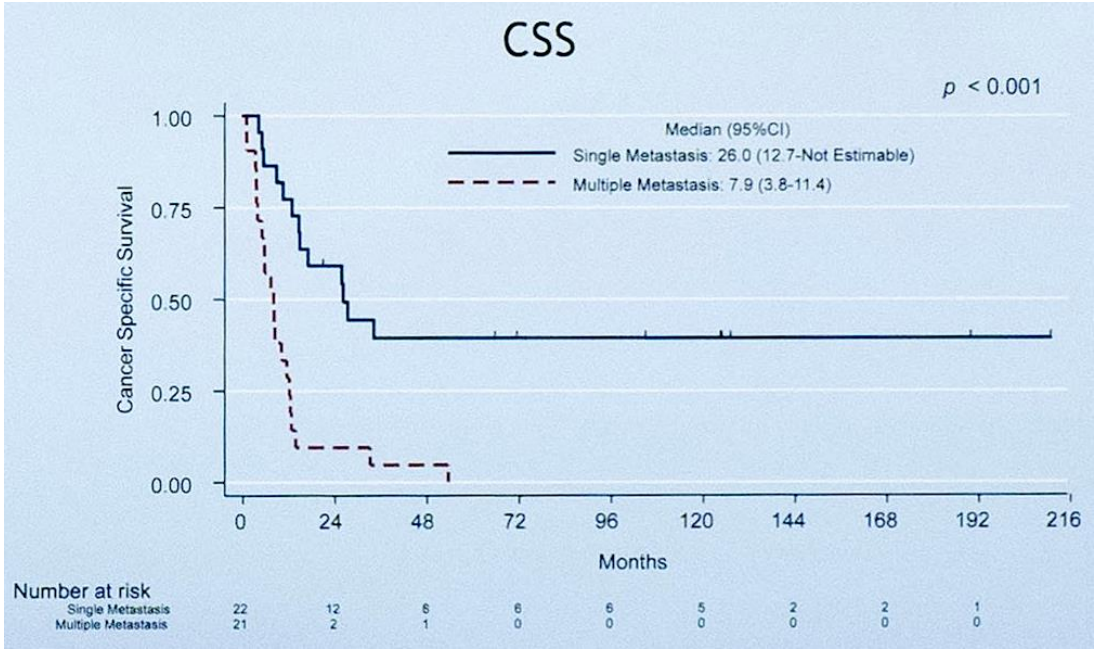
Prognóstico pior = QT neo ?
Subtipo SCC “like” letal (Cluster 3) : EGFR + = Erlotinibe?
Potencial de identificar T1?

QT neo pouco impacto (menor proliferação; quiescência celular)
Novas drogas ?



The Role of Metastatic Burden in Cytoreductive Radical Cystectomy

Roger Li MD, Janet Kukreja MD, Michael Metcalfe MD, Firas Petros MD, Matthew Campbell MD, Justin Nguyen BS, Graciela M. Nogueras MPH, Ashish M. Kamat MD, Louis Pisters MD, Colin P. Dinney MD, Neema Navai MD
The University of Texas, M.D. Anderson Cancer Center, Houston, TX



Evaluation of the Timing of Adjuvant Mitomycin C Following Nephroureterectomy for Urothelial Carcinoma of the Upper Urinary Tract

Blake Noennig, Shahab Bozorgmehri, Russell Terry, Brandon Otto, Michael Blute Jr., Li-Ming Su, Paul Crispen
University of Florida College of Medicine, Department of Urology, Gainesville, FL

UF Department of Urology UNIVERSITY of FLORIDA

Chance de câncer de bexiga após nefroureterectomia diminuiu se mitomicina foi inserida intravesical no po imediato mas não após 24 hs

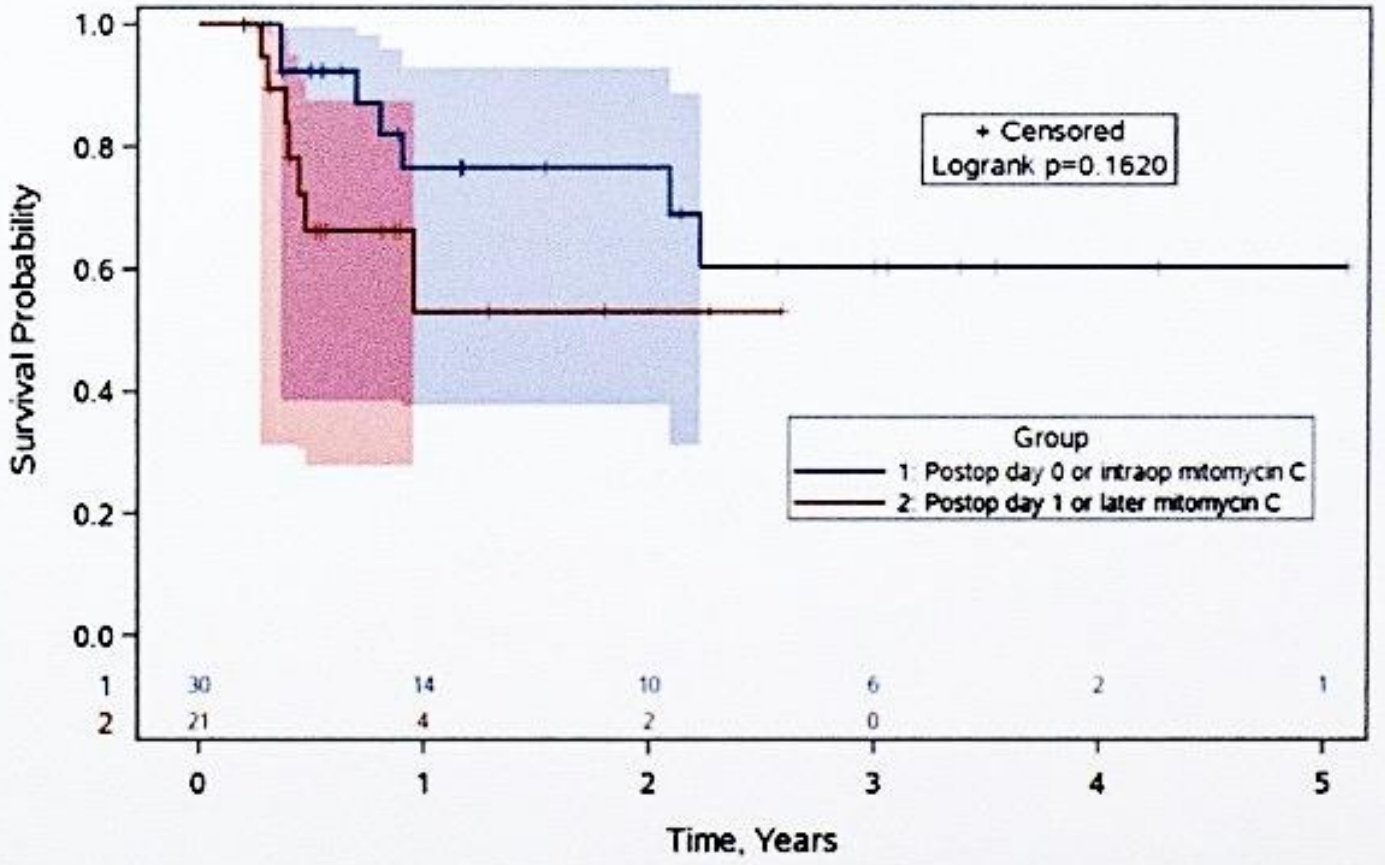


Figure 2. Kaplan-Meier survival curves for time-to-recurrence of bladder tumors at any point following radical nephroureterectomy according to two treatment groups: 1) post-operative day 0 mitomycin C and 2) post-operative day 1 or later mitomycin C.

Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/ASTRO/SUO Guideline

Summary of Recommendations

INITIAL PATIENT EVALUATION AND COUNSELING

1. Before treatment consideration, a full history and physical exam should be performed, including an exam under anesthesia, at the time of transurethral resection of bladder tumor (TURBT) for a suspected invasive cancer.

2. Before muscle-invasive bladder cancer management, clinicians should perform a complete staging evaluation, including imaging of the chest and cross sectional imaging of the abdomen and pelvis with intravenous contrast if not contraindicated. Laboratory evaluation should include a comprehensive metabolic panel (complete blood count, liver function tests, alkaline phosphatase, and renal function).

3. **An experienced genitourinary pathologist should review the pathology of a patient when variant histology is suspected or if muscle invasion is equivocal (e.g., micropapillary, nested, plasmacytoid, neuroendocrine, sarcomatoid, extensive squamous or glandular differentiation).**

Summary of Recommendations

4. For patients with newly diagnosed muscle-invasive bladder cancer, curative treatment options should be discussed before determining a plan of therapy that is based on both patient comorbidity and tumor characteristics. Patient evaluation should be completed using a multidisciplinary approach.

5. Before treatment, clinicians should counsel patients regarding complications and the implications of treatment on quality of life (e.g., impact on continence, sexual function, fertility, bowel dysfunction, metabolic problems).

Summary of Recommendations

TREATMENT NEOADJUVANT AND ADJUVANT CHEMOTHERAPY

6. **Using a multidisciplinary approach, clinicians should offer cisplatin-based neoadjuvant chemotherapy to eligible radical cystectomy patients prior to cystectomy. (Strength : strong)**

7. **Clinicians should not prescribe carboplatin-based neoadjuvant chemotherapy for clinically resectable stage cT2-T4aN0 bladder cancer. Patients ineligible for cisplatin-based neoadjuvant chemotherapy should proceed to definitive locoregional therapy. (Expert Opinion)**

8. **Clinicians should perform radical cystectomy as soon as possible following a patient's completion of and recovery from neoadjuvant chemotherapy. (Expert Opinion)**

9. **Eligible patients who have not received cisplatin-based neoadjuvant chemotherapy and have non-organ confined (pT3/T4and/or N+) disease at cystectomy should be offered adjuvant cisplatin-based**

Summary of Recommendations

RADICAL CYSTECTOMY

10. **Clinicians should offer radical cystectomy with bilateral pelvic lymphadenectomy for surgically eligible patients with ressectable non-metastatic (M0) muscle-invasive bladder cancer. (Strength : strong)**

11. **When performing a standard radical cystectomy, clinicians should remove the bladder, prostate, and seminal vesicles in males and should remove the bladder, uterus, fallopian tubes, ovaries, and anterior vaginal wall in females.**

12. **Clinicians should discuss and consider sexual function-preserving procedures for patients with organ-confined disease and absence of bladder neck, urethra, and prostate (male) involvement. (Strength : moderate)**

Summary of Recommendations

URINARY DIVERSION

13. **In patients undergoing radical cystectomy, ileal conduit, continent cutaneous, and orthotopic neobladder urinary diversions should all be discussed.**

14. **In patients receiving an orthotopic urinary diversion, clinicians must verify a negative urethral margin.**

Summary of Recommendations

PERIOPERATIVE SURGICAL MANAGEMENT

15. Clinicians should attempt to optimize patient performance status in the perioperative setting. (Expert Opinion)

16. Perioperative pharmacologic thromboembolic prophylaxis should be given to patients undergoing radical cystectomy. (Strength: strong)

17. In patients undergoing radical cystectomy, μ -opioid antagonist therapy should be used to accelerate gastrointestinal recovery, unless contraindicated. (Strength : strong)

18. **Patients should receive detailed teaching regarding care of urinary diversion before discharge from the hospital.**

Summary of Recommendations

PELVIC LYMPHADENECTOMY

19. **Clinicians must perform a bilateral pelvic lymphadenectomy at the time of any surgery with curative intent. (Strength : strong)**

20. **When performing bilateral pelvic lymphadenectomy, clinicians should remove, at a minimum, the external and internal iliac and obturator lymph nodes (standard lymphadenectomy).**

Summary of Recommendations

BLADDER PRESERVING APPROACHES

PATIENT SELECTION

21. **For patients with newly diagnosed nonmetastatic muscle-invasive bladder cancer who desire to retain their bladder, and for those with significant comorbidities for whom radical cystectomy is not a treatment option, clinicians should offer bladder-preserving therapy when clinically appropriate. (Clinical principle)**

22. **In patients under consideration for bladder-preserving therapy, maximal debulking TURBT and assessment of multifocal disease/carcinoma in situ should be performed. (Strength strong)**

Summary of Recommendations

MAXIMAL TURBT AND PARTIAL CYSTECTOMY

23. **Patients with muscle-invasive bladder cancer who are medically fit and consent to radical cystectomy should not undergo partial cystectomy or maximal TURBT as primary curative therapy. (Strength : moderate)**

PRIMARY RADIATION THERAPY

24. **For patients with muscle-invasive bladder cancer, clinicians should not offer radiation therapy alone as a curative treatment. (Strength : strong)**

Summary of Recommendations

MULTI-MODAL BLADDER PRESERVING THERAPY

25. **For patients with muscle-invasive bladder cancer who have elected multi-modal bladder preserving therapy, clinicians should offer maximal TURBT, chemotherapy combined with external beam radiation therapy, and planned cystoscopic re-evaluation. (Strength: strong)**

26. **Radiation sensitizing chemotherapy regimens should include cisplatin or 5- fluorouracil and mitomycin C. (Strength : strong)**

27. **After completion of bladder preserving therapy, clinicians should perform regular surveillance with CT scans, cystoscopy, and urine cytology. (Strength : strong)**

Summary of Recommendations

BLADDER PRESERVING TREATMENT FAILURE

28. **In patients who are medically fit and have residual or recurrent muscle-invasive disease following bladder preserving therapy, clinicians should offer radical cystectomy with bilateral pelvic lymphadenectomy. (Strengh: strong)**

29. **In patients who have a non-muscle invasive recurrence after bladder preserving therapy, clinicians may offer either local measures, such as TURBT with intravesical therapy, or radical cystectomy with bilateral pelvic lymphadenectomy. (Strength: moderate)**

Summary of Recommendations

PATIENT SURVEILLANCE AND FOLLOW UP

IMAGING

30. **Clinicians should obtain chest imaging and cross-sectional imaging of the abdomen and pelvis with CT or MRI at 6-12 month intervals for 2-3 years and then may continue annually. (Expert Opinion)**

LABORATORY VALUES AND URINE MARKERS

31. After therapy for muscle-invasive bladder cancer, patients should undergo laboratory assessment at three to six month intervals for two to three years and then annually thereafter. (Expert Opinion)

32. After radical cystectomy in patients with a retained urethra, clinicians should monitor the urethral remnant for recurrence. (Expert Opinion)

ICR The Institute of Cancer Research

CANCER RESEARCH UK

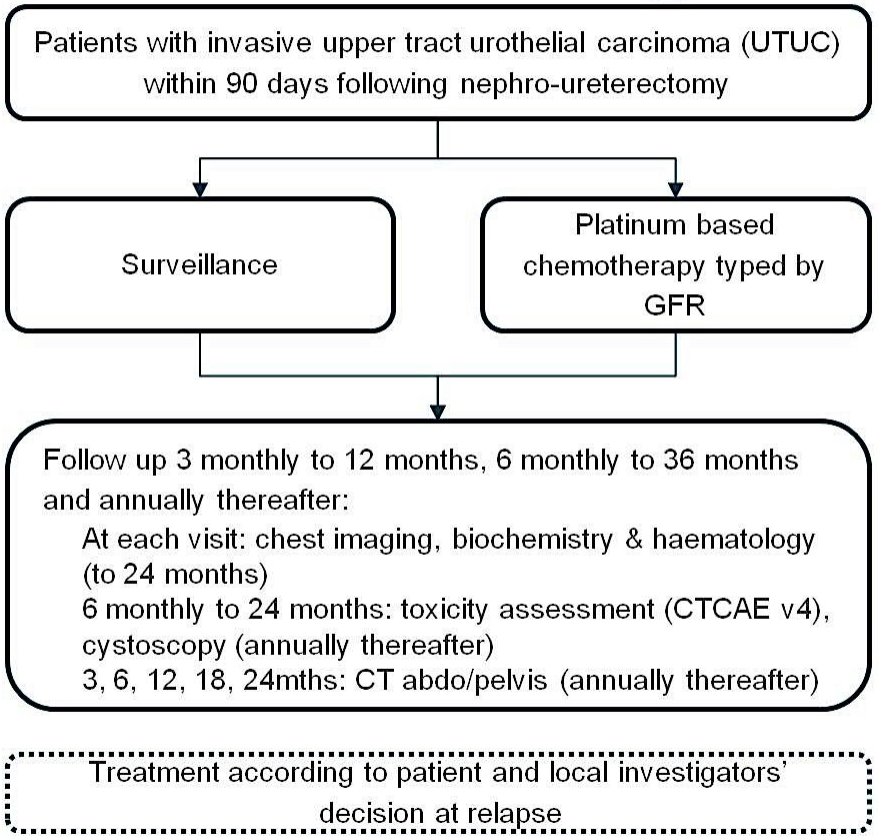
Results of POUT - A phase III randomised trial of peri-operative chemotherapy versus surveillance in upper tract urothelial cancer (UTUC)

Alison Jane Birtle*, John David Chester, Robert Jones, Mark Johnson, Michaela Hill, Richard T Bryan, James Catto, Jenny Donovan, Ann French, Chris Harris, Francis Keeley, Roger Kockelbergh, Thomas Powles, Rachel Todd, Lucy Tregellas, Caroline Wilson, Andrew Winterbottom, Rebecca Lewis, Emma Hall, on behalf of the POUT Investigators

*Chief Investigator

PRESENTED AT: **2018 Genitourinary Cancers Symposium**

POUT Trial design



Inclusion criteria:

- En-bloc radical nephro-ureterectomy
- UTUC pT2-pT4 pN0 M0 or pTany N1-3 M0 (abnormal nodes resected at surgery)
- Satisfactory haematology profile & liver function tests
- WHO performance status 0-1
- Fit to receive chemotherapy within 90 days following nephro-ureterectomy

Exclusion criteria:

- GFR <30ml/min
- Distant metastases
- Un-resected macroscopic nodal disease
- Concurrent MIBC (concurrent NMIBC acceptable)
- Other malignancy in previous 5 years
- Significant co-morbidities

POUT chemotherapy regimen

Four 21 day cycles:

All patients:

Gemcitabine

- 1000mg/m^2 day 1 & 8

With:

If GFR ≥ 50 ml/min:

Cisplatin

- 70mg/m^2 day 1

OR

If GFR 30-49ml/min:

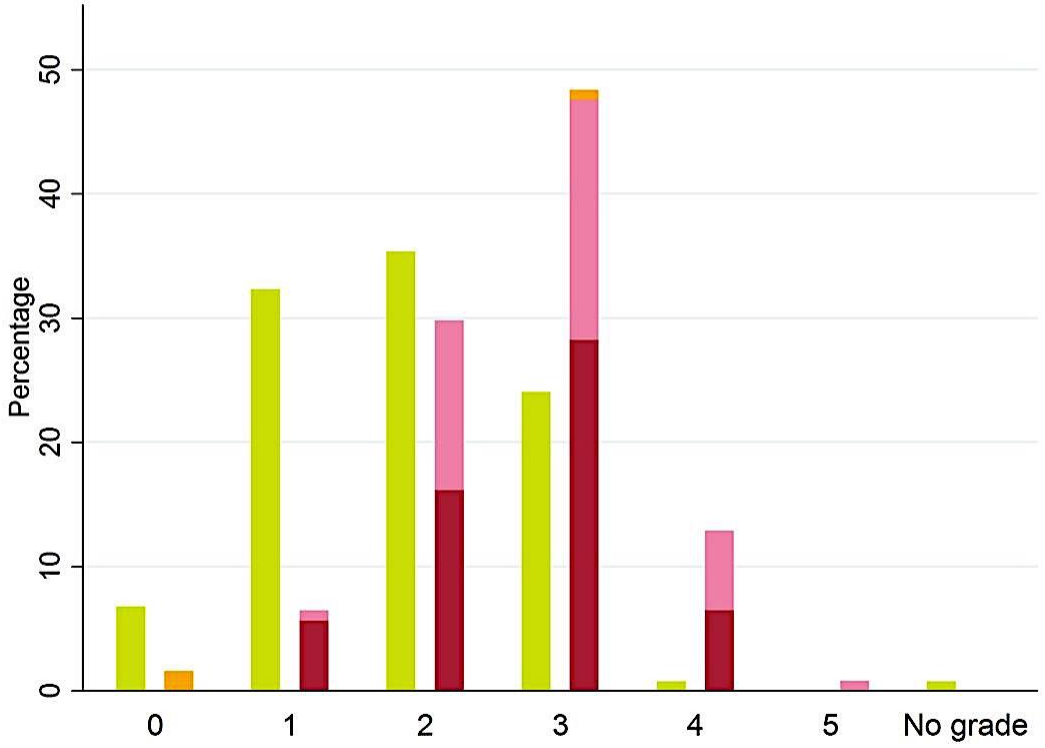
Carboplatin*

- AUC 4.5/AUC 5 day 1

*only permitted for impaired renal function

Supportive care according to local practice

Overall adverse events

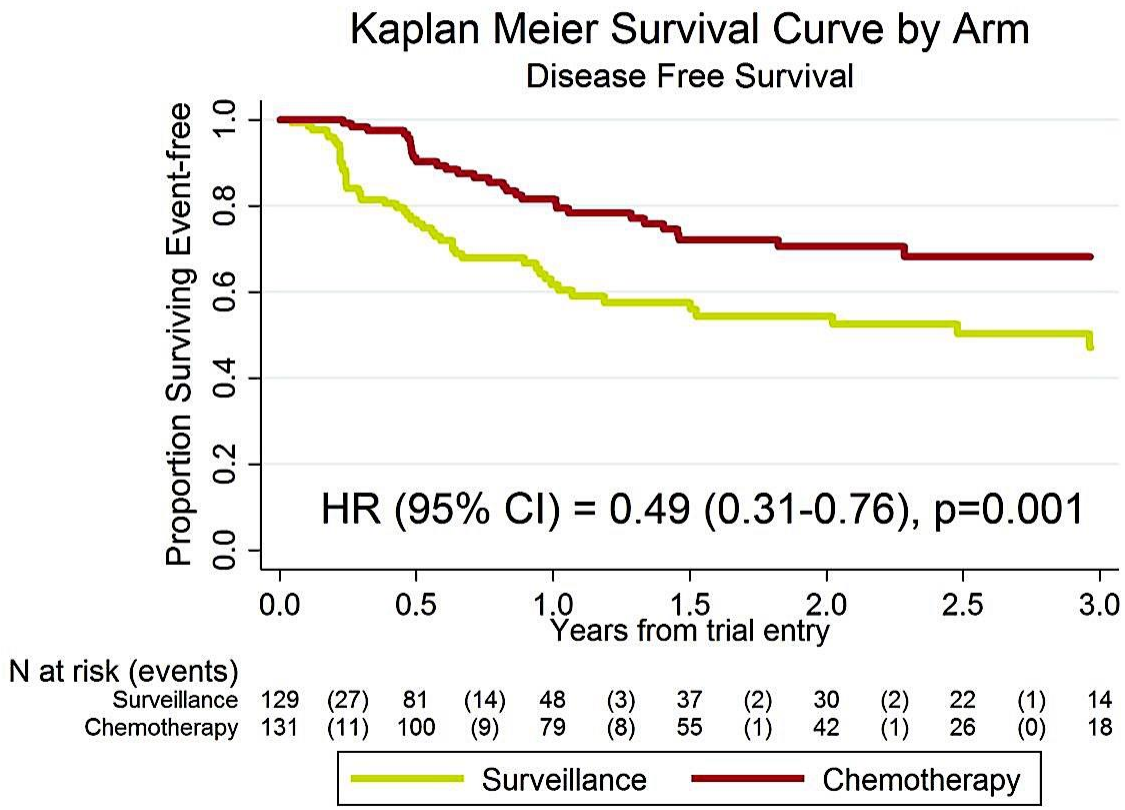


- Data are displayed by treatment received at cycle 1
- Grade≥3 toxicities:

  Surveillance: n=33/133; 24.8%

  Chemotherapy: n=77/124; 62.1%

Primary endpoint: DFS



DFS defined as time from randomisation to first of death from any cause, metastases or any ureteric or renal bed recurrence

Proportion event free at 2 years:

Chemotherapy: 0.71 (95% CI: 0.60, 0.79)

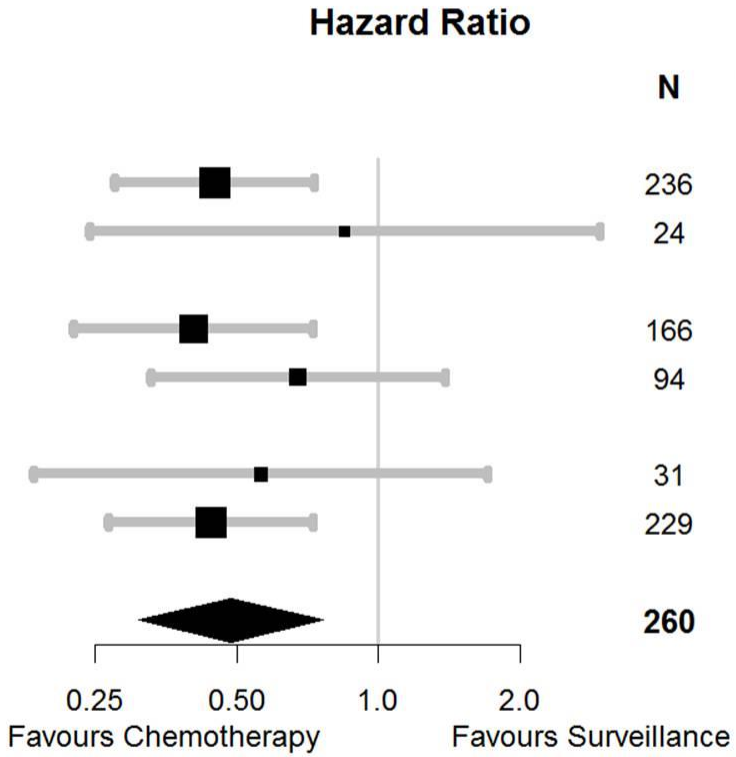
Surveillance: 0.54 (95% CI: 0.43, 0.64)

After adjustment for nodal involvement, microscopic margin status and planned chemotherapy type:

HR (95% CI) = 0.47 (0.30-0.74); p=0.001

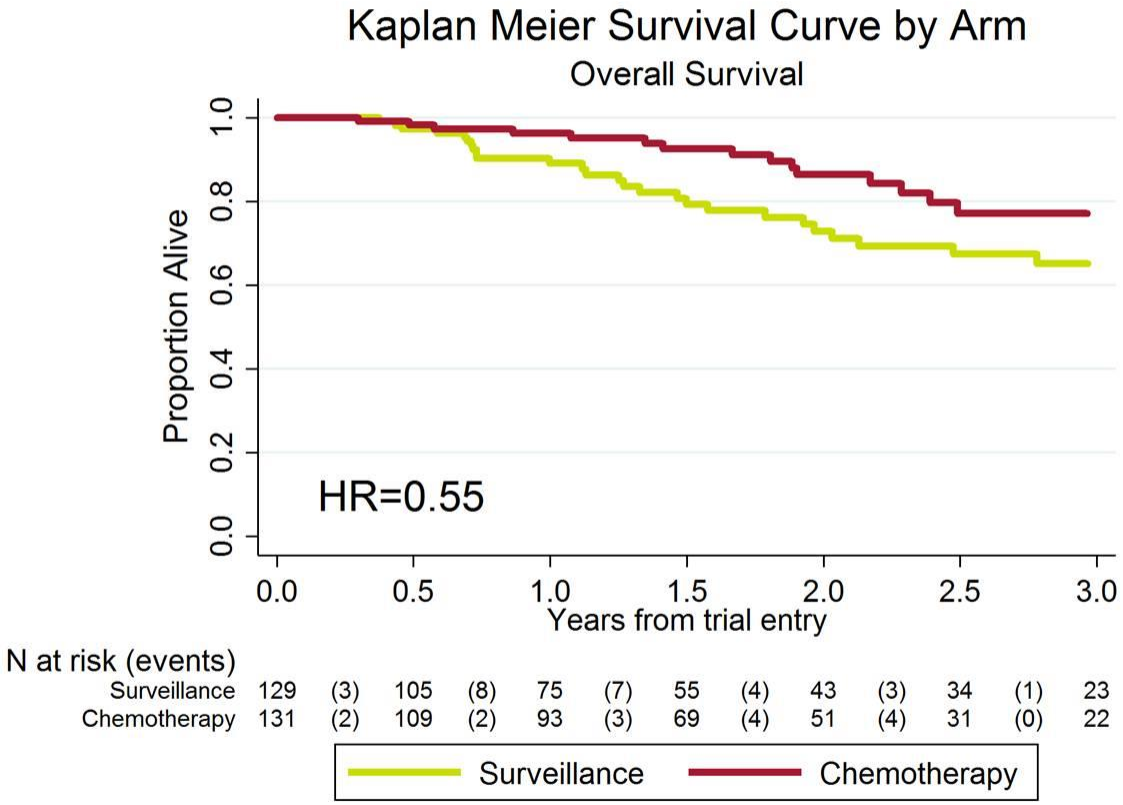
PRESENTED AT: 2018 Genitourinary Cancers Symposium

Primary: DFS



Variable	N	Univariable Hazard Ratio	p-value
Nodal involvement			
N0	236	0.45 (0.28, 0.73)	0.001
N+	24	0.85 (0.24, 2.95)	0.80
Planned chemotherapy type			
Gem-Cis	166	0.40 (0.23, 0.73)	0.003
Gem-Carbo	94	0.67 (0.33, 1.38)	0.28
Microscopic margin status			
Positive	31	0.56 (0.19, 1.71)	0.31
Negative	229	0.44 (0.27, 0.73)	0.001
Overall	**260**	**0.49 (0.31, 0.76)**	**0.001**

Secondary endpoint: OS



OS defined as time from randomisation to death from any cause

Overall survival data are currently immature and will be formally analysed after either:

- 88 deaths have occurred
- Median follow-up in patients alive has passed two years

Estudos abertos

A multicenter clinical trial of intravesical BCG in combination with ALT-803 in patients with BCG-unresponsive non-muscle invasive bladder cancer.

Session: Trials in Progress Poster Session B: Prostate Cancer, Urothelial Carcinoma, and Penile, Urethral and Testicular Cancers
Author(s): Karim Chamie, Amirali Salmasi, Charles Joel Rosser, Amy Rock, Lydia Ferguson, Hing C. Wong; University of California Los Ange...
Presenter: Karim Chamie, MD

Abstract #: TPS544

PECULIAR: An open label, multicenter, single-arm, phase 2 study of neoadjuvant pembrolizumab (PEM) and epacadostat (EPA), preceding radical cystectomy (Cy), for patients (pts) with muscle-invasive urothelial bladder cancer (MIUBC).

Session: Trials in Progress Poster Session B: Prostate Cancer, Urothelial Carcinoma, and Penile, Urethral and Testicular Cancers
Author(s): Andrea Necchi, Luigi Mariani, Andrea Anichini, Antonella Messina, Patrizia Giannatempo, Daniele Raggi, Alberto Briganti, Franc...
Presenter: Andrea Necchi, MD

Abstract #: TPS534