

Conservative Treatment of Muscle-Invasive Bladder Cancer

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GETUC – Grupo de Estudos em Tumores Urológicos do Ceará

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- I participate as a speaker of company events: *AstraZeneca, Merck, Janssen, Astellas, Roche, Bristol*
- I am a member of the Advisory Board of Companies: *Janssen and Bristol*
- I participate in clinical trials sponsored by the companies: *Merck, Bristol, Roche*
- I do not own shares of any of these companies

Gold Standart

- Neoadjuvant CT
- **CYSTECTOMY**
- Lymphadenectomy
- Urinary Reconstruction



Conservative treatment

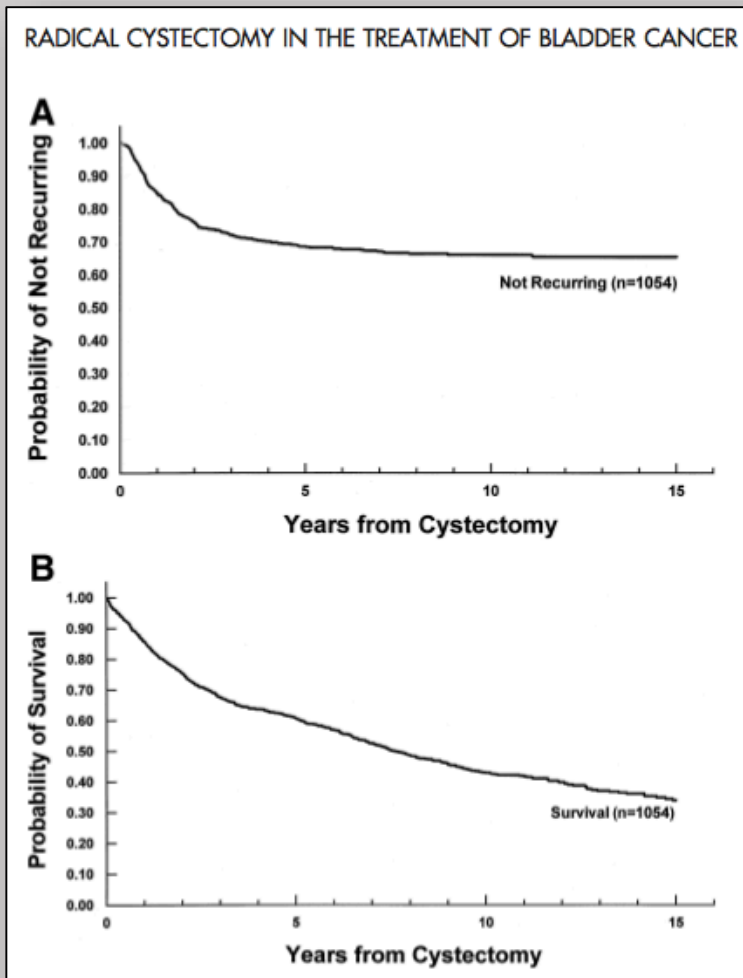
- Patients not candidates for cystectomy
- Patients who do not accept cystectomy



- Transurethral Resection
- Partial Cistectomy
- External Beam Radiation Therapy (w/ Brachytherapy)
- **TURBT + Chemoradiation**

Cystectomy

(University of Southern California)



Radical Cystectomy in the Treatment of Invasive Bladder Cancer: Long-Term Results in 1,054 Patients

By John P. Stein, Gary Lieskovsky, Richard Cote, Susan Groshen, An-Chen Feng, Stuart Boyd, Eila Skinner, Bernard Bochner, Duriyai Thangathurai, Maged Mikhail, Derek Raghavan, and Donald G. Skinner

1054 pcts (37% “superficial”) / 94% high grade

	5 y	10 y
Recurrence Free	68 %	66 %
Overall Survival	60%	43 %

Surgical mortality = 3%

JAMA[®]

Treatment of Invasive Bladder Cancer by Cisplatin and Radiation in Patients Unsuitable for Surgery

William U. Shipley, MD; George R. Prout, Jr, MD; Albert B. Einstein, MD; L. Jean Coombs, PhD;
Zev Wajsman, MD; Mark S. Soloway, MD; Leonore Englander, MD;
Bruce A. Barton, PhD; Mark D. Hafermann, MD

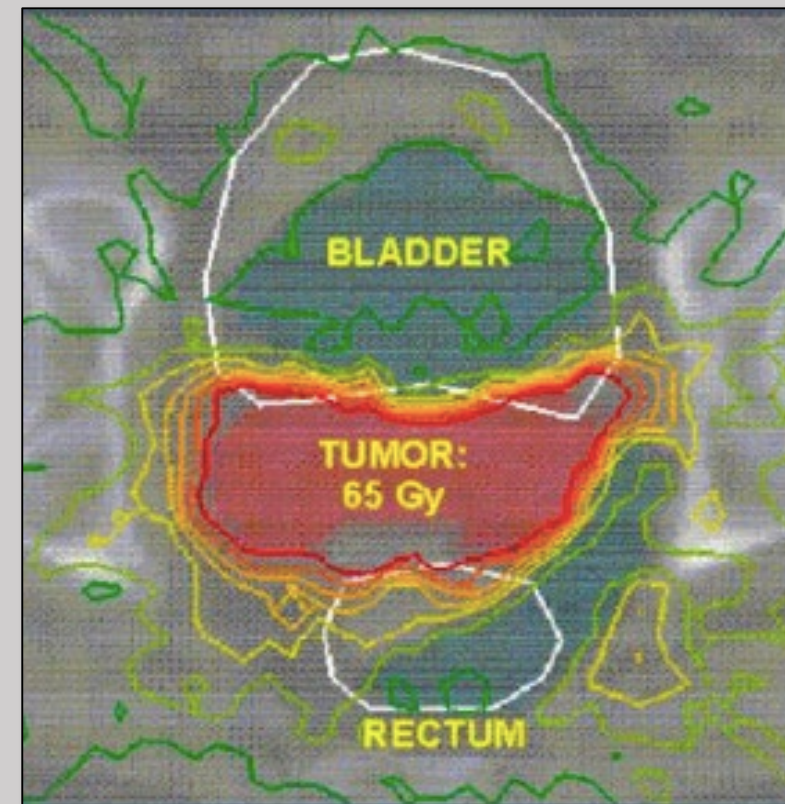
JAMA. 1987;258(7):931-935. doi:10.1001/jama.1987.03400070069037

National Bladder Cancer Group Trial

70 patients

77% Total regression

73% Bladder preservation in responders



Trial	Stage	N	OS 5y	OS 10y
Cystectomy				
USC, 2001	pT2-pT4a	633	48 %	32%
MSKCC, 2001	pT2-pT4a	181	36 %	27%
SWOG / ECOG / CALGB, 2001	cT2-cT4a	307	50%	34%
Trimodal Therapy				
Univ. Erlangen, 2002	cT2-cT4a	415	45%	29%
MGH, 2002	cT2-cT4a	190	54%	36%
RTOG, 1998	cT2-cT4a	123	49%	-
Italy, 2002	cT2-cT4a	104	60%	-

Fase 3 Trials	Stage	N	CT	OS 5y
Trimodal Therapy				
James, 2012	pT2-pT4a	182	5FU+ MMC	48%
Tunio, 2012	pT2-pT4	181	CDDP	52%
Shipley, 1998	cT2-cT4a	123	CDDP	49%
Housset, 1993	cT2-cT4	54	CDDP+5FU	59%

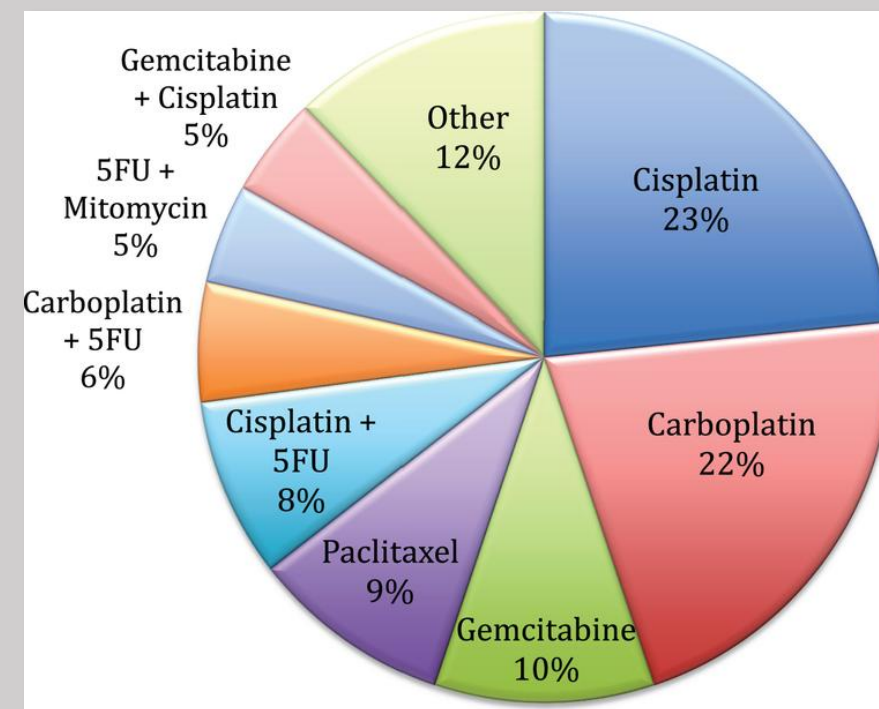
Bladder Cancer 2 (2016) 405–413
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IOS Press

405

Research Report

Patterns of Bladder Preservation Therapy Utilization for Muscle-Invasive Bladder Cancer

Tracy L. Rose^{a,*}, Allison M. Deal^a, Sylvain Ladoire^b, Gilles Créhanche^b, Matthew D. Galsky^c, Jonathan E. Rosenberg^d, Joaquim Bellmunt^e, Akhila Wimalasingham^f, Yu-Ning Wong^g, Lauren C. Harshman^h, Simon Chowdhury^b, Guenter Niegischⁱ, Michalis Liontos^j, Evan Y. Yu^k, Sumanta K. Pal^l, Ronald C. Chen^a, Andrew Z. Wang^a, Matthew E. Nielsen^a, Angela B. Smith^a, Matthew I. Milowsky^a and the Retrospective International Study of Cancers of the Urothelial Tract (RISC) Investigators



Criteria for patient selection

- T Stage
- Size
- Hydronephrosis
- TURBT
- CIS
- Complete Response
- Recurrence

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Combined-Modality Treatment and Selective Organ Preservation in Invasive Bladder Cancer: Long-Term Results

Journal of Clinical Oncology, Vol 20, No 14 (July 15), 2002: pp 3061-3071

By Claus Rödel, Gerhard G. Grabenbauer, Reinhard Kühn, Thomas Papadopoulos, Jürgen Dunst, Martin Meyer, Karl M. Schrott, and Rolf Sauer

ADULT UROLOGY

UROLOGY 60: 62-68, 2002. © 2002, Elsevier



SELECTIVE BLADDER PRESERVATION BY COMBINED MODALITY PROTOCOL TREATMENT: LONG-TERM OUTCOMES OF 190 PATIENTS WITH INVASIVE BLADDER CANCER

W. U. SHIPLEY, D. S. KAUFMAN, E. ZEHR, N. M. HENEY, S. C. LANE, H. K. THAKRAL,
A. F. ALTHAUSEN, AND A. L. ZIETMAN



European Association of Urology

EUROPEAN UROLOGY 61 (2012) 705–711

Platinum Priority – Bladder Cancer

Editorial by Giuseppe Simone and Michele Gallucci on pp. 712–713 of this issue

Long-Term Outcomes of Selective Bladder Preservation by Combined-Modality Therapy for Invasive Bladder Cancer: The MGH Experience

Jason A. Efstathiou^{a,*}, Daphna Y. Spiegel^a, William U. Shipley^a, Niall M. Heney^b, Donald S. Kaufman^c, Andrzej Niemierko^a, John J. Coen^a, Rafi Y. Skowronski^a, Jonathan J. Paly^a, Francis J. McGovern^b, Anthony L. Zietman^a

ANTICANCER RESEARCH 31: 985-990 (2011)

15-Year Survival Rates after Transurethral Resection and Radiochemotherapy or Radiation in Bladder Cancer Treatment

FRENS STEFFEN KRAUSE^{1,2,*}, BERNHARD WALTER^{1,*}, OLIVER JOSEF OTT³, LOTHAR HÄBERLE⁴, CHRISTIAN WEISS⁵, CLAUD RÖDEL⁵, BERND WULLICH¹ and ROLF SAUER³

Departments of ¹Urology and ³Radiation Oncology, University Clinic, Erlangen, Germany;

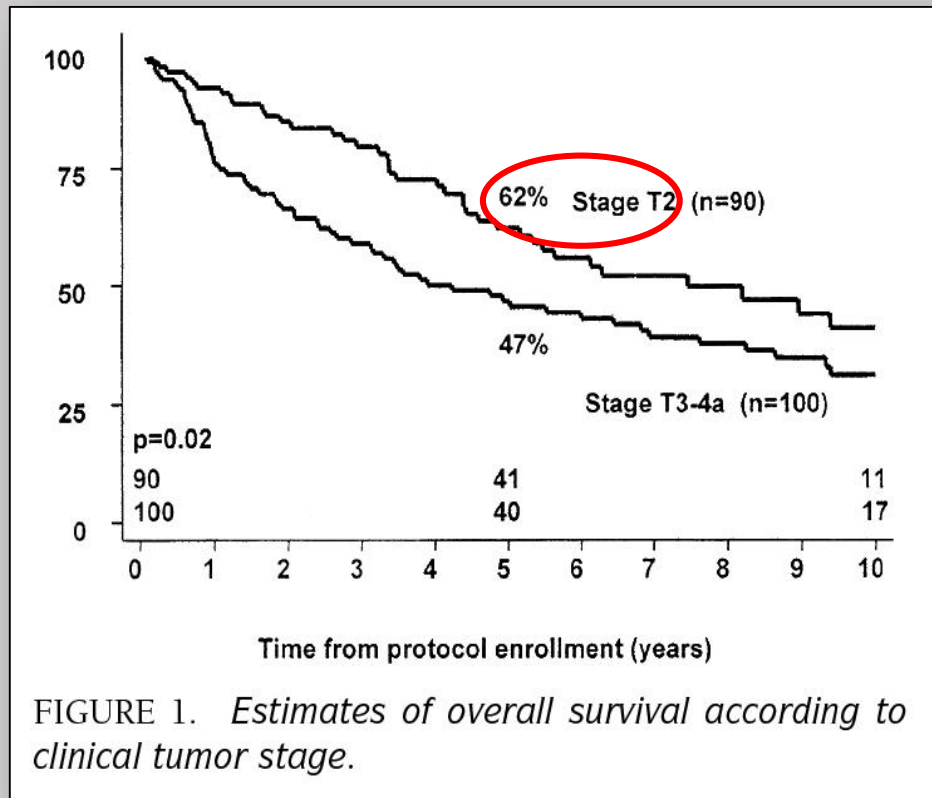
²Department of Urology, AKH-General Hospital, Linz, Austria;

⁴Department of Biometry/Epidemiology, University of Erlangen/Nuremberg, Erlangen, Germany;

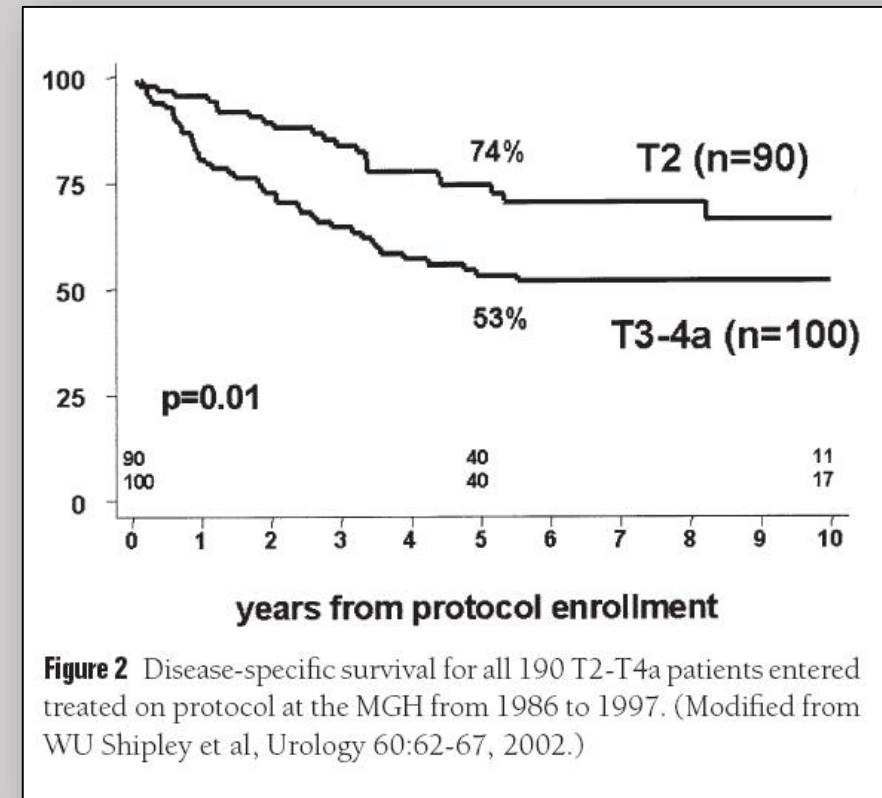
⁵Department Radiation Therapy, University Clinic, Frankfurt, Germany

T Stage

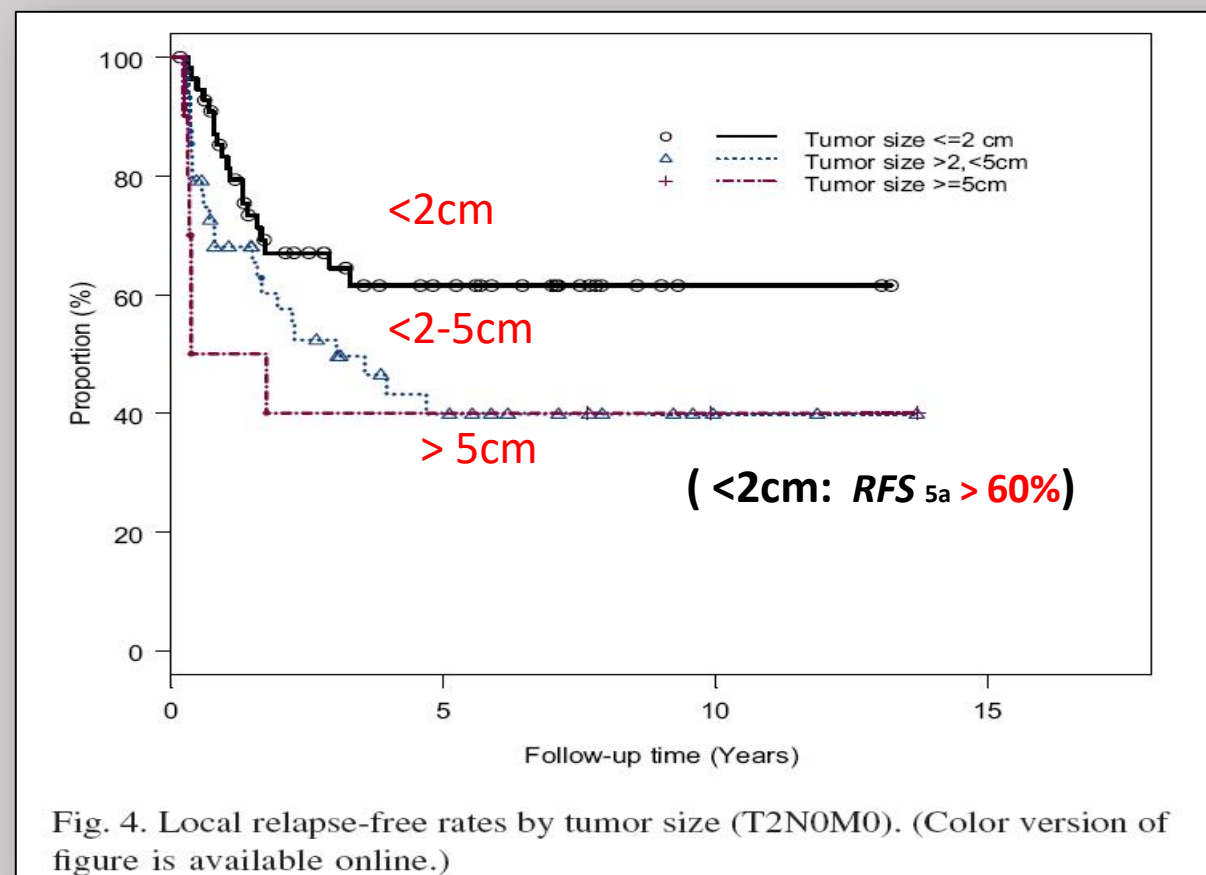
Overall Survival



Disease Specific Survival



Tumor Size



Hydronephrosis

(Absent: CR = 68%)

% Complete Response

Present	37 %
Absent	68 %

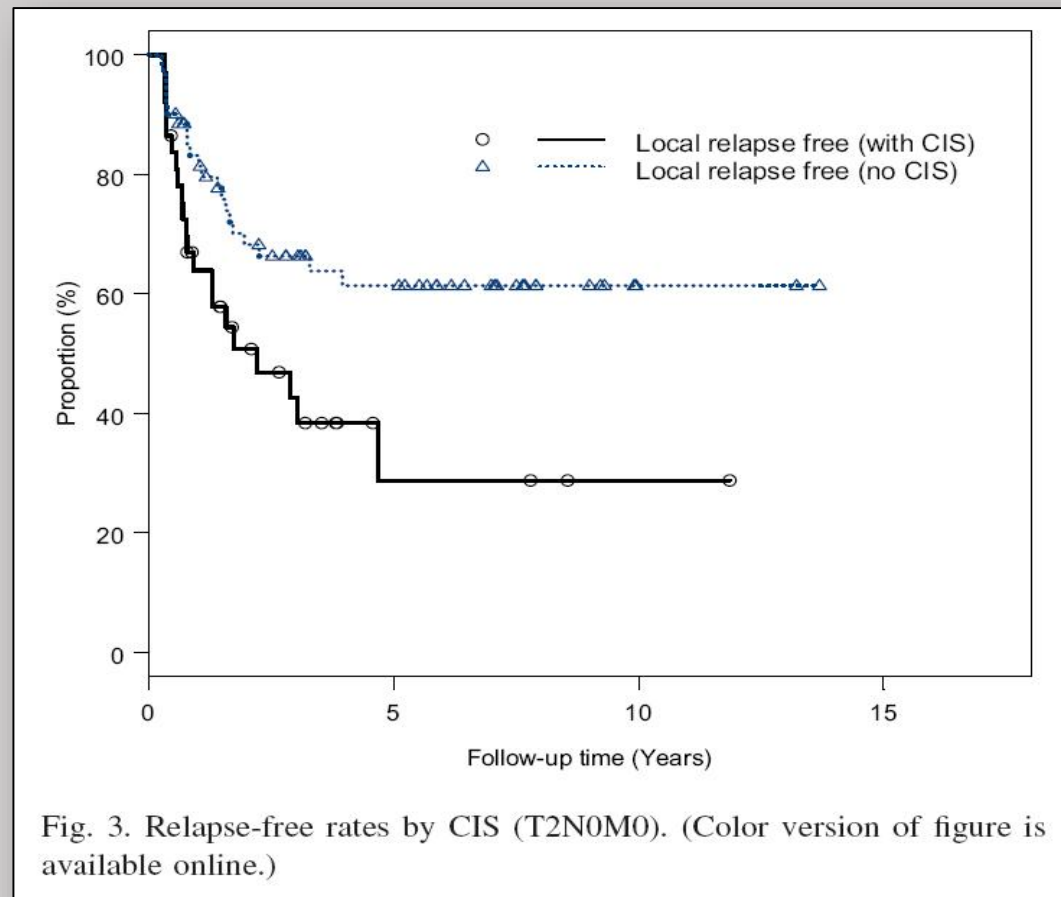
Complete TURBT

(RTU R0: $OS_{5a} = 76\%$)

	R 0	R 1	R 2	<i>p</i>
% Cystectomy	29 %	42%	50 %	<0.01
5 y OS	76 %	52 %	34 %	0.003
10 y OS	50 %	33 %	18 %	0.003

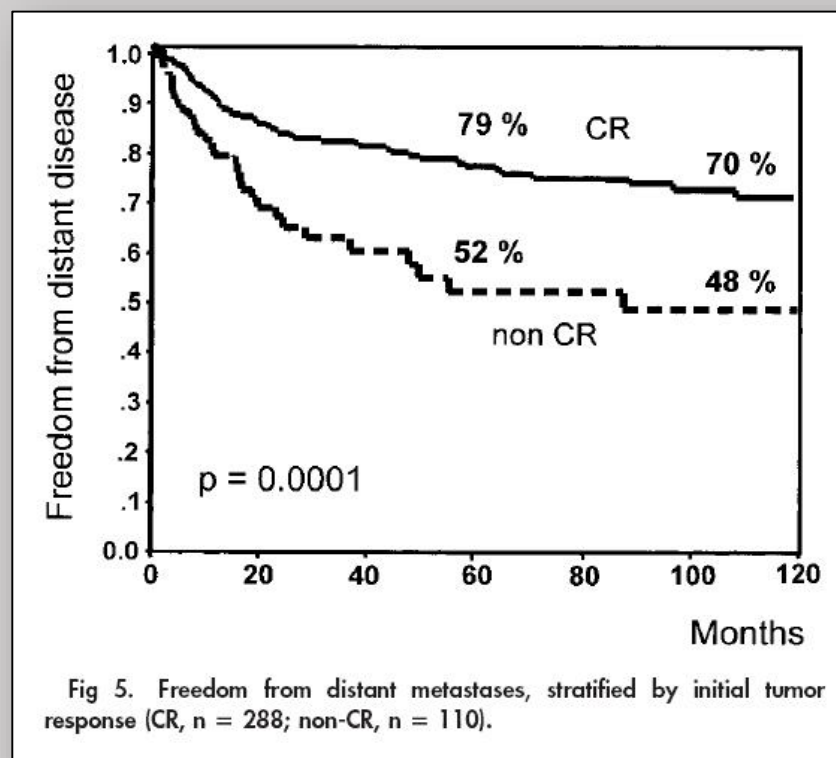
CIS

(Absent: *RFS* > 60%)



Complete Response

(CR: $MFS_{5a} = 79\%$)

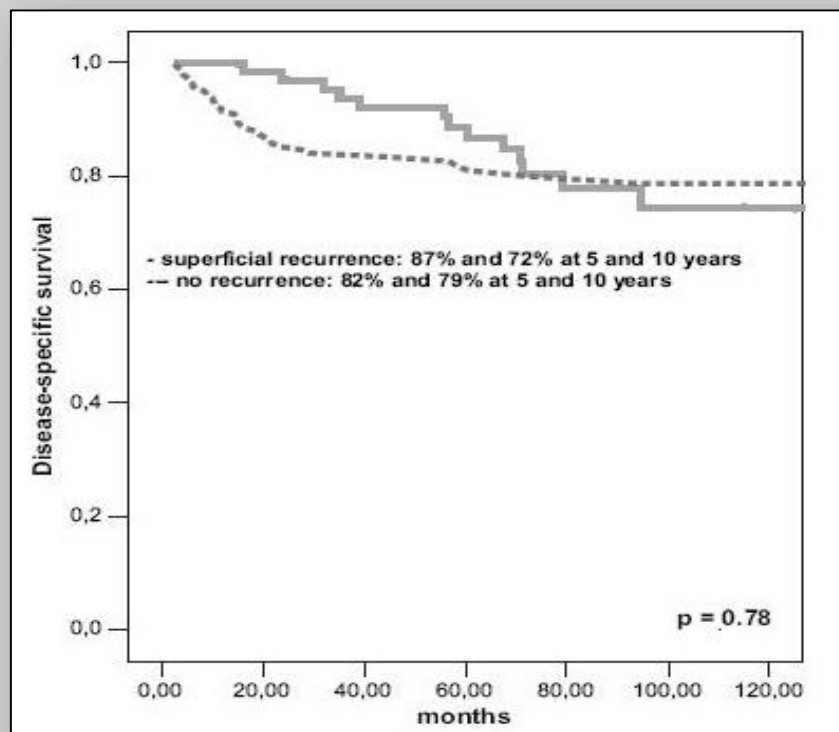


“Superficial” Recurrence vs Invasive Recurrence

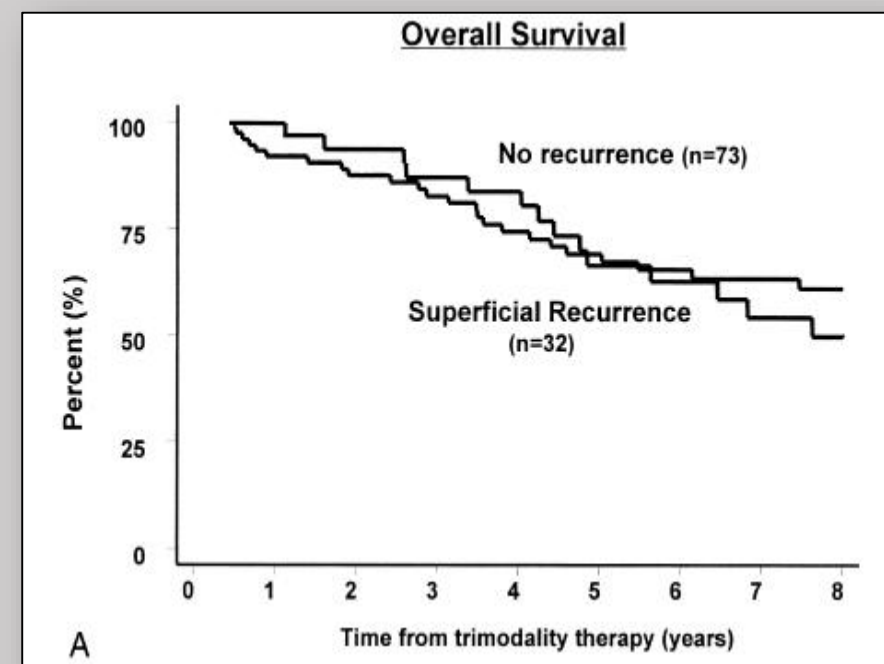
- 389/531 (75%) CR
 - 66% remained free of LR
 - 17% had Infiltrative Recurrence
 - 17% had Surface Recurrence
- Treatment of Surface Recurrence (17%)
 - TURBT ± BCG = 94%
 - Cystectomy = 6%

“Superficial” Recurrence

($OS_{5a} > 60\%$)



DSS



OS

Indications (The IDEAL candidate)

- T2
- <5cm (<2cm)
- Without Hydronephrosis
- TURBT R0
- Without CIS
- Complete response
- Superficial recurrence

And then how?

MGH

TURBT + RT + CT
(40 Gy)

2-3 week

Re-staging (Cystoscopy)

CR

Ø CR

RT + CT
(25 Gy)

Cystectomy

6 sweek

Re-staging (Cystoscopy)

SED

Recurrence

FUp

Cystectomy

CDDP + 5FU

ERLANGEN

TURBT + RT + CT
(60 Gy)

6 week

Re-staging (Cystoscopy)

CR

Ø CR

FU

Cystectomy

Recurrence

Cystectomy

Results

	MGH	Erlangen
n	190	415
Stage	T2 – T4	T1 (HR) – T4
CR	64 %	72 %
5 y OS	54 %	51 %
5 y OS w/ bladder	45 %	42 %
10 y OS	36 %	31 %
Long Term Survivors w/ bladder	83 %	82 %
% Cystectomy	35 %	20 %

Results in Invasive Tumors

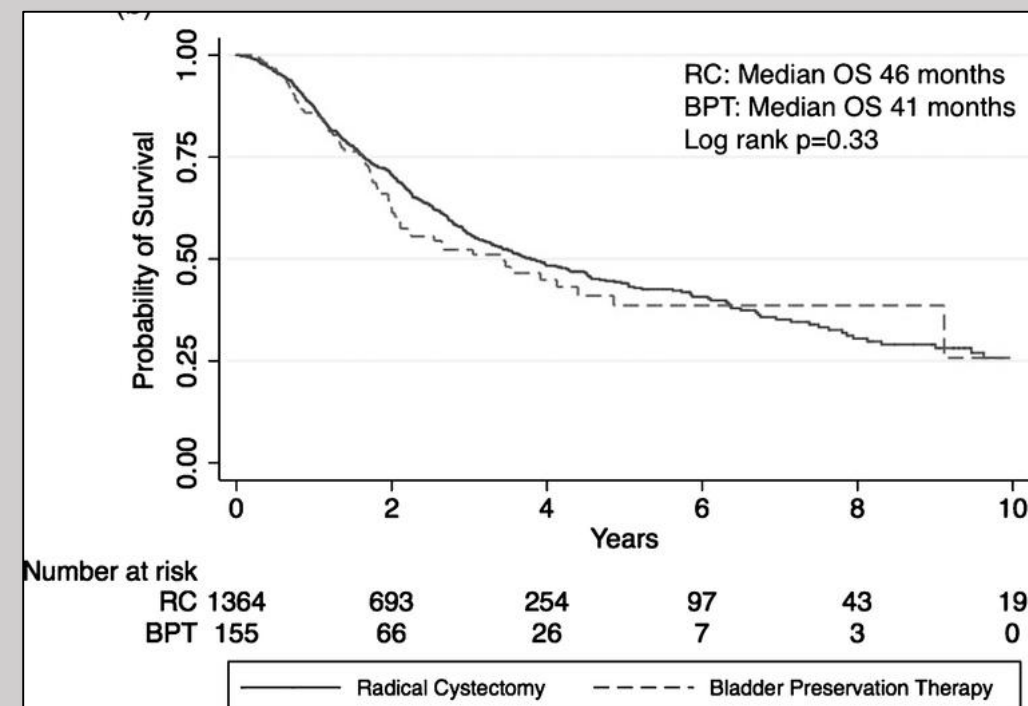
	MGH	Erlangen	Stein (Cystectomy)
n	190	415	633
Stage	cT2 – cT4a	cT2 – cT4	pT2 – pT4
5 y OS	54 %	45 %	48 %
10 y OS	36 %	29 %	32 %

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Retrospective International Study of Cancers of the Urothelial Tract (RISC)

3,024 patients **29 international centers**

2005 to 2013 **T2-T4aN0M0**

**BPT patients were older,
had poorer performance
status, and had more
comorbidities**

Clinical Investigation

Radical Cystectomy Compared to Combined Modality Treatment for Muscle-Invasive Bladder Cancer: A Systematic Review and Meta-Analysis

Vishal Vashistha, MD,* Hanzhang Wang, MS,[†] Andrew Mazzone, BS,[‡]
Michael A. Liss, MD,[†] Robert S. Svatek, MD,[†] Mary Schleicher, RN, BSN, MLIS,*
and Dharam Kaushik, MD[†]

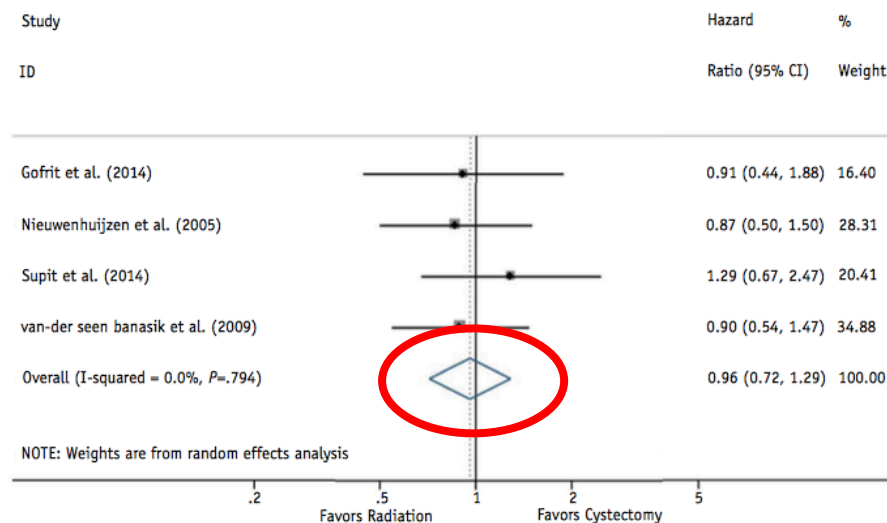
International Journal of
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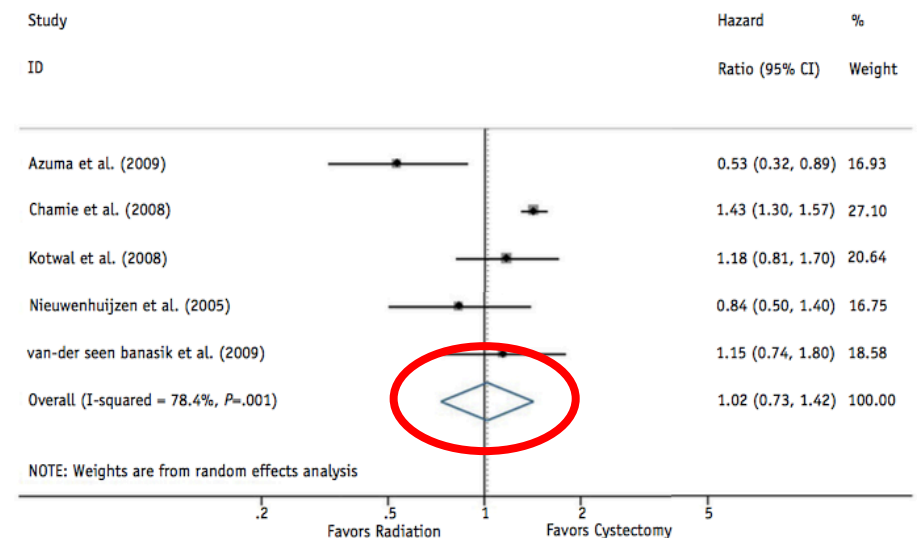
Meta-analysis of 8 studies

9,554 patients

Univariate HR of 5 year Overall Mortality Radiation vs Cystectomy



Univariate HR of 10 year Overall Mortality Radiation vs Cystectomy



Quality of Life

(quality of preserved bladder)
(neobladder quality)

Quality of Life



n=75 (living patients with preserved bladder)

90% answered the questionnaire

78% satisfied with urinary function

Table 4. Quality of life due to urinary symptoms*

Delighted	Pleased	Mostly satisfied	About equally satisfied and dissatisfied	Mostly dissatisfied	Unhappy	Terrible
19.7%	59.1%	9.9%	11.3%	0	0	0

* Of 75 patients alive with their native bladder, 71 completed the question, "If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?"

MGH : n=71 45% urodynamics
68% answered the questionnaire

75% with preserved normal-functioning bladder and satisfied with the "voiding quality"

Take Home Message

- Cystectomy remains the standard treatment for invasive muscle invasive urothelial carcinoma
- Trimodal therapy, since well indicated, offers SG and SLD rates similar to cystectomy
- Tumors T2, <2cm, without hydronephrosis or in situ component after maximum RTU will be more successful
- Satisfactory long-term quality of life
- About 30% of patients will require cystectomy
- The role of the urologist is fundamental (multidisciplinary)