MUSCLE INVASIVE BLADDER CANCER : BLADDER CONSERVATION PROTOCOLS

OVERVIEW

INTRODUCTION

MANAGEMENT OF MUSCLE INVASIVE BLADDER CANCER

BLADDER CONSERVATION PROTOCOLS

QUALITY OF LIFE ASSESSEMENT

RADIATION THERAPY TECHNIQUE

CONCLUSIONS

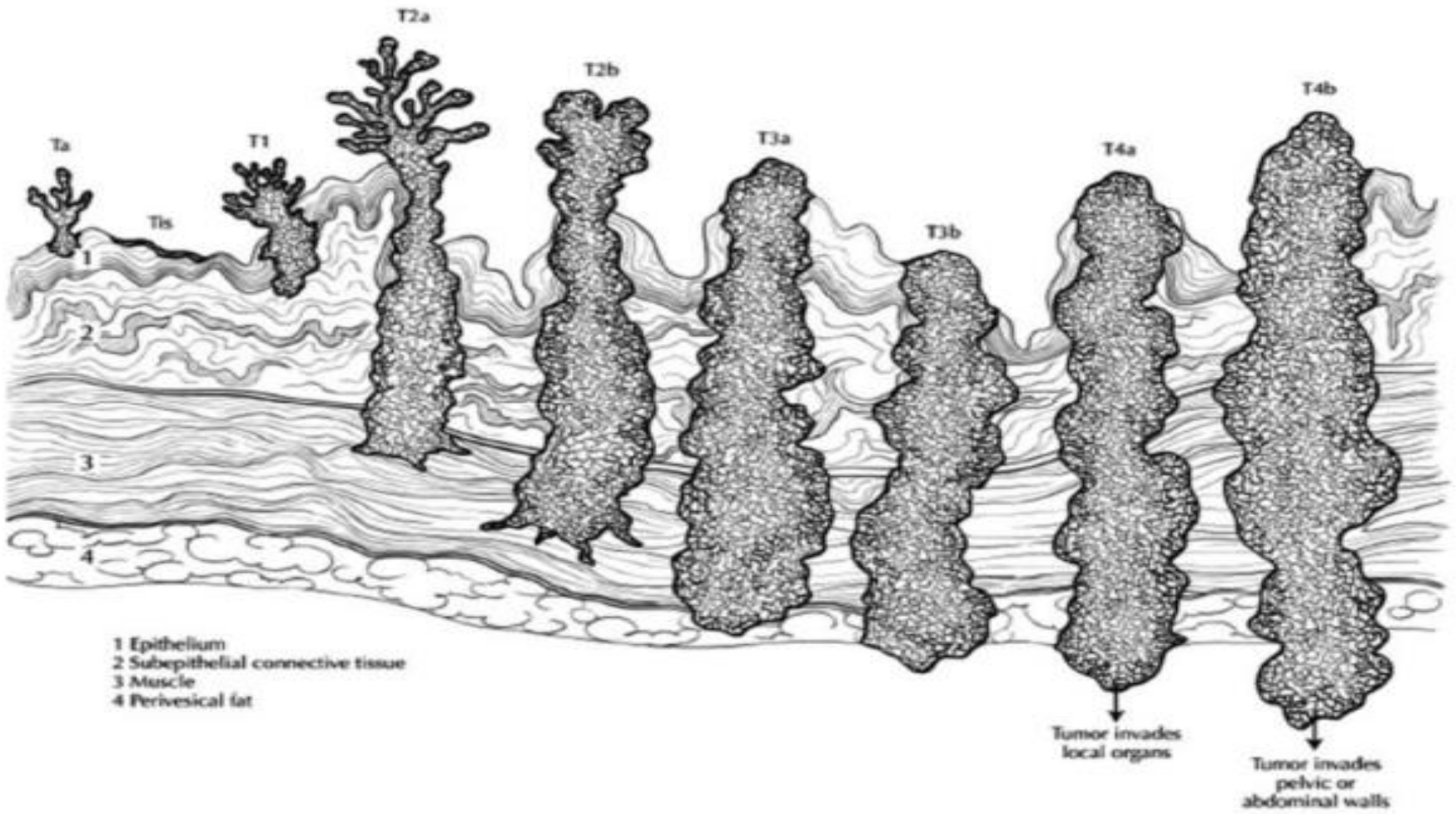
INTRODUCTION

What is Muscle Invasive Bladder Cancer ?

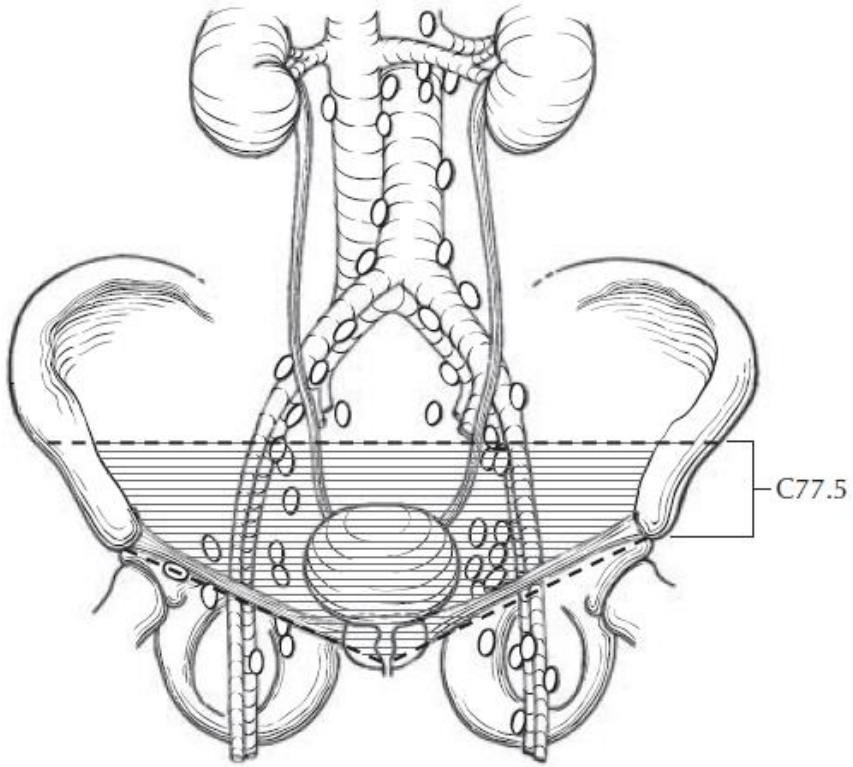
T Staging for Bladder tumors

- Tx - Primary tumour cannot be assessed
- T0 - No evidence of primary tumour
- Ta - Non-invasive papillary carcinoma
- Tis - Carcinoma in situ: ‘flat tumour’
- T1 - Tumour invades subepithelial connective tissue
- T2 - Tumour invades muscle
  - T2a - Tumour invades superficial muscle (inner half)
  - T2b - Tumour invades deep muscle (outer half)
- T3 - Tumour invades perivesical tissue:
  - T3a - microscopically
  - T3b - macroscopically (extravesical mass)
- T4 - Tumour invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
  - T4a - Tumour invades prostate stroma, seminal vesicles, uterus, or vagina
  - T4b - Tumour invades pelvic wall or abdominal wall

Extent of Primary Bladder Cancer AJCC - 2010



LYMPHATICS FOR BLADDER CANCER



N0 - No regional lymph node metastasis
N1- Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral)
N2 - Metastasis in multiple lymph nodes in the true pelvis (hypogastric, obturator, external iliac, or presacral)
N3 - Metastasis in a common iliac lymph node(s)

Correlation of pathological T stage with LN metastases

Study	Poulsen et al. [31]	Viewg et al. [12]	Stein et al. [15]	Madersbacher et al. [17]	Leissner et al. [5]	Vazina et al. [10]	Abdel-Latif et al. [11]	Hautmann et al. [20]	Ghoneim and Abol-Enein [32]
Year	1998	1999	2001	2003	2004	2004	2004	2006	2008
period	1990–1997	1980–1990	1971–1997	1985–2000	1999–2002	1992–2002	1997–1999	1986–2003	1971–2000
Total no. of patients	191	686	1054	507	290	176	418	788	2720
% of LN metastasis									
pT0, pTis, and pT1	3	10	5	2	2	4	4	1	2
pT2a	18	9	18	17	13	16	7	10	8
T2b	25	23	27	34	22	40	25	41	19
pT3	51	43	45	41	44	50	48	44	39
pT4	44	41	45		50		65		36
Total	26	28	23	24	28	24	26	18	20

Reference : Lymphadenectomy in management of Invasive Bladder Cancer; Ramy F. Youssef and Ganesh V. Raj; International Journal of Surgical Oncology ;Volume 2011

STAGE GROUPING FOR BLADDER TUMORS

	T1	T2a	T2b	T3a	T3b	T4a	T4b
N0	I	II	II	III	III	III	IV
N1	IV	IV	IV	IV	IV	IV	IV
N2	IV	IV	IV	IV	IV	IV	IV
N3	IV	IV	IV	IV	IV	IV	IV
M1	IV	IV	IV	IV	IV	IV	IV

Stage	Relative 5 year survival rates
I	88%
II	63%
III	46%
IV	15%

MANAGEMENT OF MUSCLE INVASIVE BLADDER CANCER

Staging workup

Cystoscopy

Transurethral Resection of Bladder Tumor (TURBT) – For pathological diagnosis

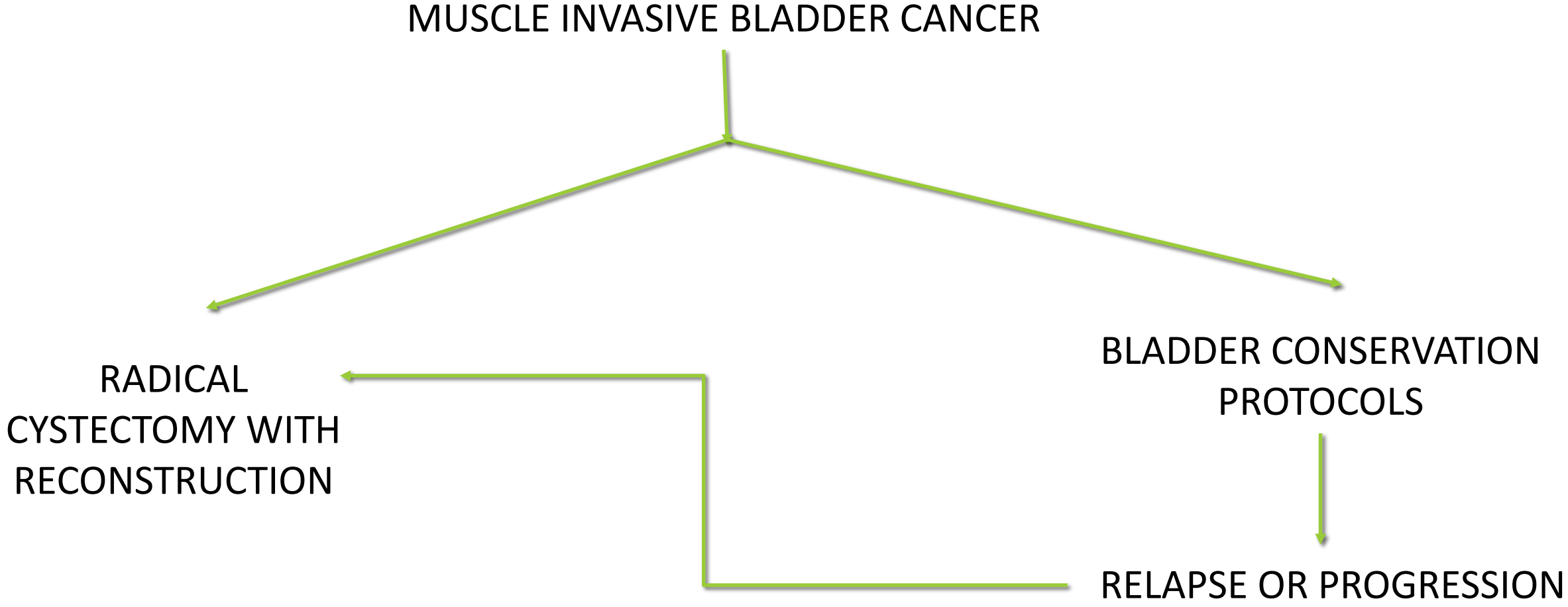
Imaging :

- Ultrasound Abdomen/Pelvis
- CT scan
- MRI

Bone scan

Goals of Treatment

- Cure patient
- Optimize survival
- Prevention of Pelvic failure and Distant metastasis
- Functional Urinary reservoir and High Quality Of Life (QoL)

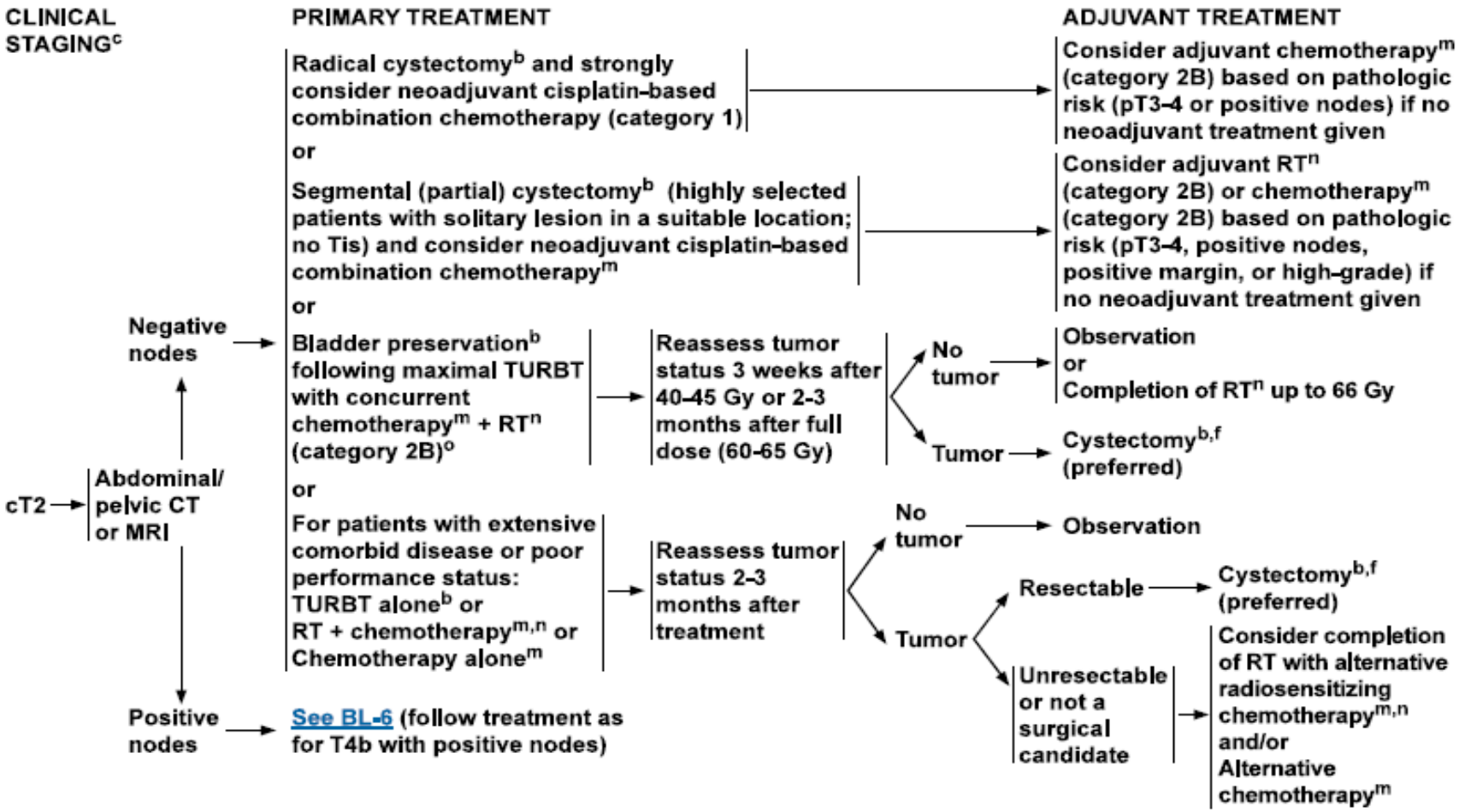

MUSCLE INVASIVE BLADDER CANCER
RADICAL CYSTECTOMY WITH RECONSTRUCTION
BLADDER CONSERVATION PROTOCOLS
RELAPSE OR PROGRESSION

Surgery

- Treatment of choice
- Radical cystectomy with pelvic lymphadenectomy is considered the standard of care.
  - Includes perivesicular fat and urethra
  - In women, the anterior wall of the vagina, the ovary and the uterus are also taken
  - In men, the prostate and seminal vesicles are taken
- Bladder reconstruction : Neo Bladder or Ileal Conduit

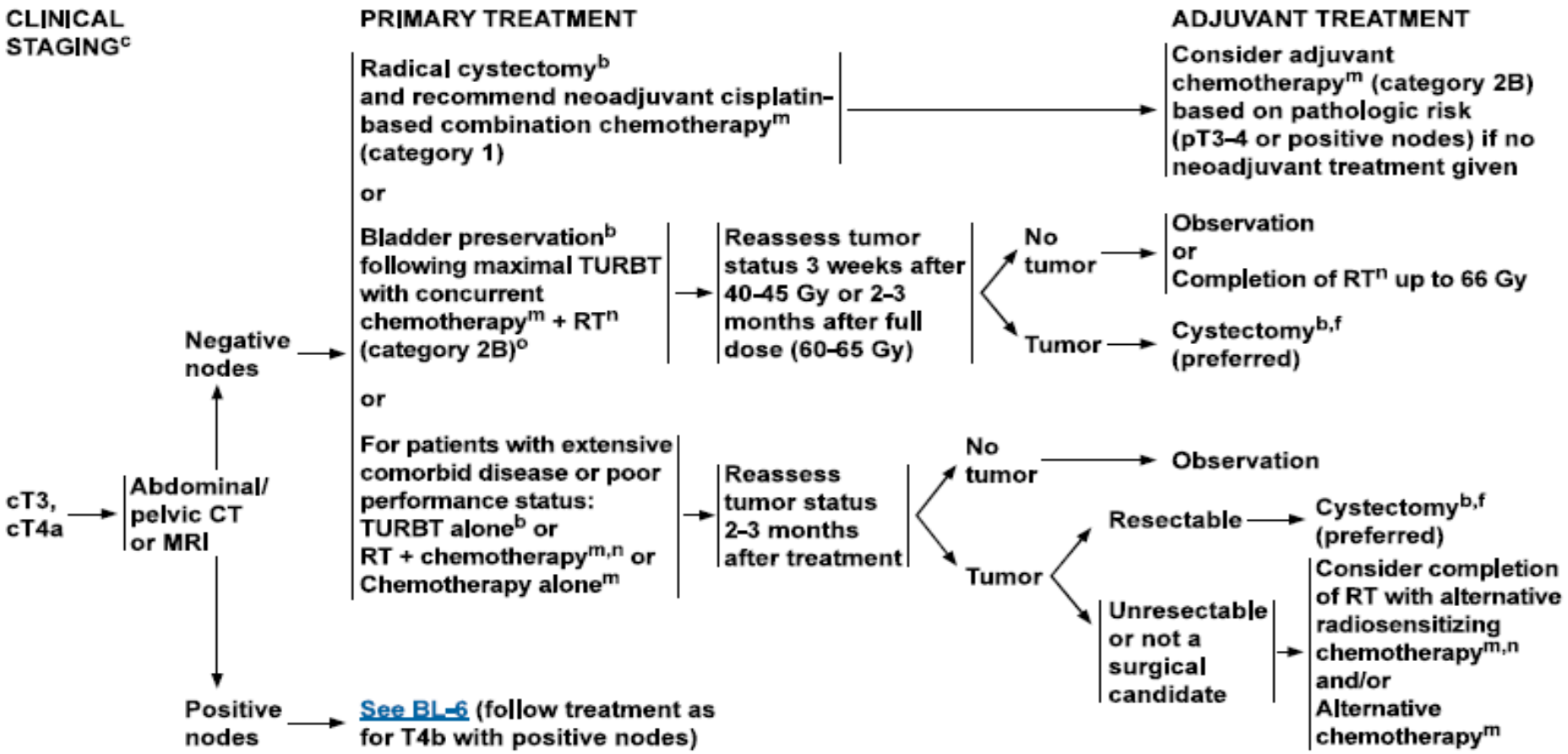
National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2014
Bladder Cancer



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2014
Bladder Cancer



BLADDER CONSERVATION PROTOCOLS

Methods of Conservation

Conservative Surgery
- Partial Cystectomy
- Trans Urethral Resection of Bladder Tumor (TURBT) alone

Radical External Beam Radiation Therapy

Interstitial Brachytherapy

Combined modality treatment
- Chemotherapy and Local Therapy
- Trimodality Therapy

No trials have till date directly compared Cystectomy and Bladder-preservation

Bladder Conservation approach

2 main concerns about bladder preservation compared with radical cystectomy :

- Toxicity of radiation therapy on bladder function
- Field cancerization effect :
  - 30-50% of patients experience a local recurrence (~50% invasive and ~50% superficial), either in the area of tumor or in a different part of bladder
  - If bladder preservation is selected, close surveillance is critical

Partial Cystectomy

6% to 19% of patients with primary, muscle-invading bladder cancer are potential candidates

Local recurrence rates : 38% to 78%

Half of the recurrences appear in the first year and two thirds by 2 years

Partial Cystectomy

Careful patient selection

- Solitary lesion
- Located in a region of the bladder that allows for complete excision with a 2-cm tumor-free margin (Bladder dome)

Partial Cystectomy

Contraindications :

- Association with *carcinoma in situ* in other sites of the bladder
- Prostatic urethral involvement
- Prior recurrent bladder or upper tract tumors
- Bladder neck or trigone tumors (Ureteral reimplantation would be required to achieve an adequate margin)

Transurethral Resection of Bladder Tumor (TURBT) alone

Clinical complete response rates (assessed cystoscopically with repeat biopsy 3 weeks after initial TURBT) for T2 and T3 cancers : 10% to 20%

5 year Overall Survival - 27%

TURBT alone is not sufficient as monotherapy in muscle-invading bladder cancer

Radical External Beam Radiation Therapy

Historically, External Beam Radiation therapy was used as monotherapy for muscle invasive bladder cancer which were medically inoperable

5-year local control rate

- 31% to 50% for the entire patient population
- 49% to 79% for the subgroup of patients with a complete response

External Beam Irradiation Alone for Muscle-Invasive Bladder Cancer

Study	Year	No. Patients	5-yr Survival Rate by T Category (%)			
			T2	T3 (T3a/T3b)	T4	Overall
Duncan[163]	1986	963	40	26	12	30
Blandy[164]	1988	614	27	38	9	—
Jenkins*[165]	1988	182	46	35	—	40
Gospodarowicz*[168]	1991	355	50	(38/28)	—	46
Jahnson*[169]	1991	319	31	16	6	28
Davidson*[174]	1990	709	49	28	2	25
Greven[166]	1990	116	59	10	0	—
Smaaland[167]	1991	146	26	10†	—	—
Fossa[170]	1993	308	38‡	14§	—	24
Pollack[171]	1994	135	42	20	0	26
Moonen[172]	1998	379	25	17	—	22
Borgaonkar*[175]	2002	163	48	26	—	45

Radical External Beam Radiation Therapy

Factors having significant favourable effect on local control with Radiotherapy:

- Early clinical stage (T2 and T3a)
- Absence of ureteral obstruction
- Complete response
- Visibly complete TURBT
- Absence of coexisting *carcinoma in situ*
- Small tumor size (<5 cm maximum diameter)
- Solitary tumors
- Tumor configuration (Papillary / Sessile)
- Haemoglobin level (>10 mg/dL)

Interstitial Brachytherapy

It has been combined with EBRT to provide a radiation boost to the primary tumor

Appropriate candidates for brachytherapy :

- Solitary TCC with a diameter of less than 5 cm
- Stage T1 disease (with high grade) to T3a disease (muscle invasion but no extension through the wall)

Treatment Outcome for Brachytherapy in Combination with External Beam Irradiation

Study*	Local Control (5-yr)	Overall Survival (5-yr)	Disease-Specific Survival (5-yr)	Survival with Preserved Bladder (5-yr)
Moonen[181]	84%	86%	—	90%
Wijnmaalen I[182]	88%	48%	69%	—
Van der Steen[121]	70%	—	T1 80% T2 60%	— —
Mazeron[184]	77%	72%	73%	95%
Rozan[185]	—	67%	83%	96.1%
Pernot[186]	73%	71%	77%	—
Pos[187]	73%	62%	73%	90%

Interstitial Brachytherapy

Five-year local control rates for selected patients treated with brachytherapy in combination with EBRT appear to be excellent

- 70% and 90%

High rates of bladder preservation

Acute toxicity :

- Fistula formation with wound leakage

Chemotherapy and Local Therapy

Chemotherapy and Conservative Surgery

- Chemotherapy has been used in combination with TURBT in highly selected population
- 5-year local control rates of up to 48%
- Complete response rates after chemotherapy and TURBT range from 45% to 54%
- Studies have shown that addition on MVAC to TURBT gives local control advantage over either alone

Chemotherapy and Conservative Surgery

- In a highly selected patient population, chemotherapy followed by partial cystectomy in conjunction with pelvic lymphadenectomy has been used in an attempt to spare the bladder
- 5-year survival rate is high ~ 50%
- Bladder preservation is possible in less than half of these patients

Chemotherapy and Conservative Surgery

- **Criteria to be considered for such treatment:**
  - Complete or major response to chemotherapy
  - Solitary lesion in the dome or the anterior wall of the bladder
  - No history of prior invasive bladder cancer
  - No CIS
  - Good bladder capacity

Chemotherapy and Radical Local Therapy

- **Neoadjuvant chemotherapy** prior to definitive local therapy
  - Advantage :
    - To assess the response of the primary lesion
    - For tumor down staging
- Neoadjuvant chemotherapy seems to improve survival rates only marginally
- There is significant impact in terms of tumor down staging
- Complete clinical response - as evaluated by repeat cystoscopy and biopsy after chemotherapy, ranges from 25% to 57%

Neoadjuvant Chemotherapy

- Response to Neoadjuvant therapy certainly seems to predict survival

- 5 year Survival rates
  - 62% to 75% among responders
  - 20% to 26% among non responders

Randomized Phase III Trials of Neoadjuvant Chemotherapy

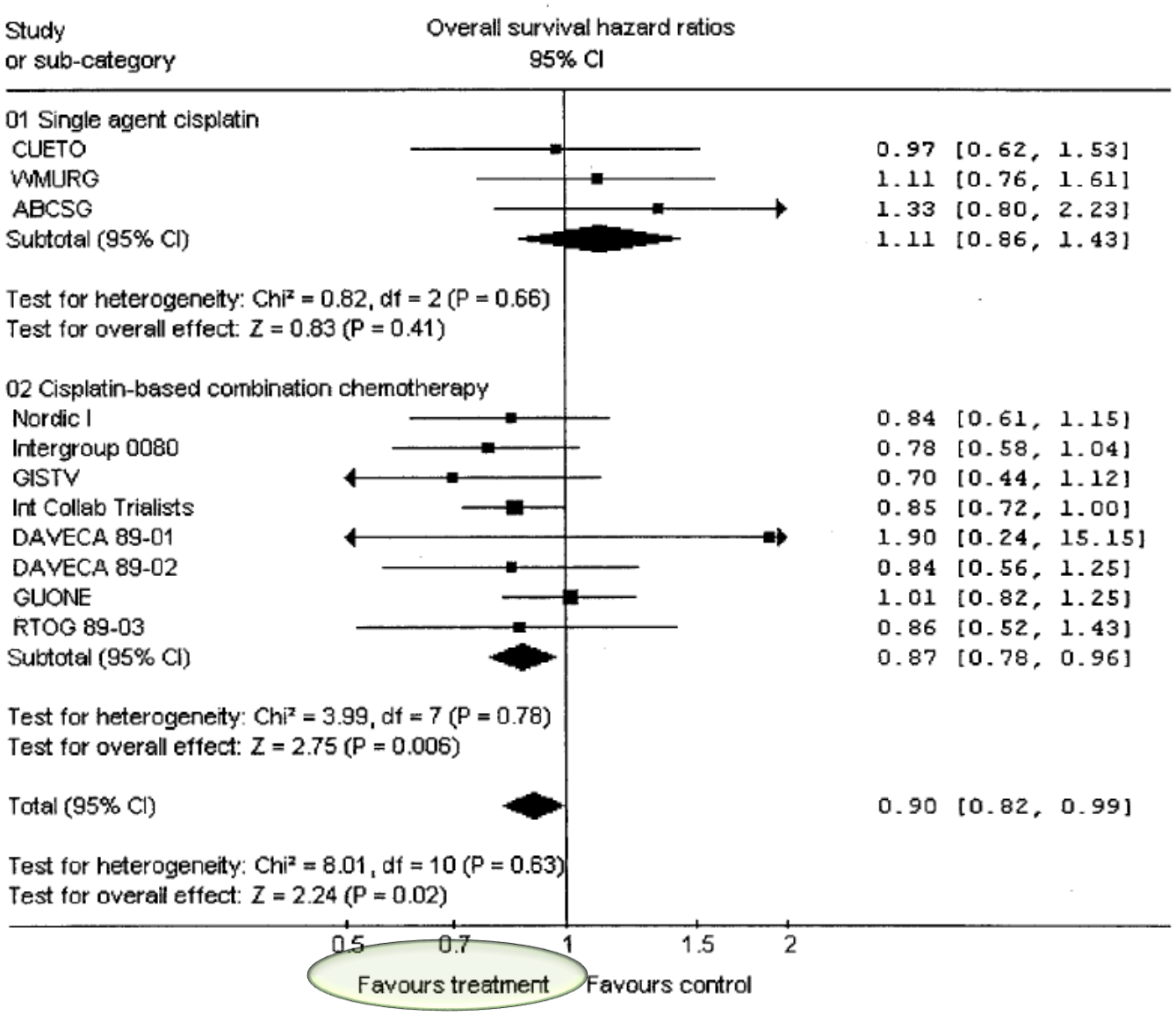
Study	Neoadjuvant Arm	Standard Arm	No. Patients	Survival
Cisplatin Trials				
Australia/UK[205]	DDP/RT	RT	255	No difference
Canada/NCI[215]	DDP/RT or preoperative RT + cystectomy	RT or preoperative RT + cystectomy	99	No difference
Spain (CUETO)[207]	DDP/cystectomy	Cystectomy	122	No difference
Combination Chemotherapy				
EORTC/MRC[210]	MCV/RT or cystectomy	RT or cystectomy	976	5.5% difference in favor of MCV
RTOG[209]	MCV/RT + C	RT + C	126	No benefit
SWOG Intergroup[216]	MVAC/cystectomy	Cystectomy	317	Benefit with MVAC
Italy (GUONE)[214]	MVAC/cystectomy	Cystectomy	206	No difference
Italy (GISTV)[208]	MVEC/cystectomy	Cystectomy	171	No difference
Genoa[211]	DDP/5-FU/RT/cystectomy	Cystectomy	104	No difference
Nordic 1[206]	ADM/DDP/RT/cystectomy	RT/cystectomy	325	No difference, 15% benefit with ADM + DDP in T3-T4a
Nordic 2[212]	MTX/DDP/cystectomy	Cystectomy	317	No difference
Abol-Enein[213]	CarboplatinMV/ cystectomy	Cystectomy	194	Benefit with carboplatinMV

NEOADJUVANT CHEMOTHERAPY FOR TRANSITIONAL CELL CARCINOMA OF THE BLADDER: A SYSTEMATIC REVIEW AND META-ANALYSIS

ERIC WINQUIST,*,† TRICIA S. KIRCHNER, ROANNE SEGAL, JOSEPH CHIN‡ AND HIMU LUKKA§
ON BEHALF OF THE GENITOURINARY CANCER DISEASE SITE GROUP OF CANCER CARE ONTARIO PROGRAM IN EVIDENCE-BASED CARE PRACTICE GUIDELINES INITIATIVE‖

THE JOURNAL OF UROLOGY®
Vol. 171, 561–569, February 2004

Absolute Survival benefit of 6.5% for Neoadjuvant chemotherapy


Study
or sub-category
Overall survival hazard ratios
95% CI
01 Single agent cisplatin
CUETO
WMURG
ABCSG
Subtotal (95% CI)
0.97 [0.62, 1.53]
1.11 [0.76, 1.61]
1.33 [0.80, 2.23]
1.11 [0.86, 1.43]
Test for heterogeneity: Chi² = 0.82, df = 2 (P = 0.66)
Test for overall effect: Z = 0.83 (P = 0.41)
02 Cisplatin-based combination chemotherapy
Nordic I
Intergroup 0080
GISTV
Int Collab Trialists
DAVECA 89-01
DAVECA 89-02
GUONE
RTOG 89-03
Subtotal (95% CI)
0.84 [0.61, 1.15]
0.78 [0.58, 1.04]
0.70 [0.44, 1.12]
0.85 [0.72, 1.00]
1.90 [0.24, 15.15]
0.84 [0.56, 1.25]
1.01 [0.82, 1.25]
0.86 [0.52, 1.43]
0.87 [0.78, 0.96]
Test for heterogeneity: Chi² = 3.99, df = 7 (P = 0.78)
Test for overall effect: Z = 2.75 (P = 0.006)
Total (95% CI)
0.90 [0.82, 0.99]
Test for heterogeneity: Chi² = 8.01, df = 10 (P = 0.63)
Test for overall effect: Z = 2.24 (P = 0.02)
0.5
0.7
1
1.5
2
Favours treatment
Favours control

Neoadjuvant Chemotherapy

There have been two large randomized Neoadjuvant chemotherapy studies in muscle-invasive bladder cancer – SWOG Intergroup study and MRC/EORTC study

- Both showing significant survival advantage

However, Neoadjuvant chemotherapy is still not considered as standard of care for Muscle Invasive Bladder cancer – Unlike other malignancies

Neoadjuvant Chemotherapy

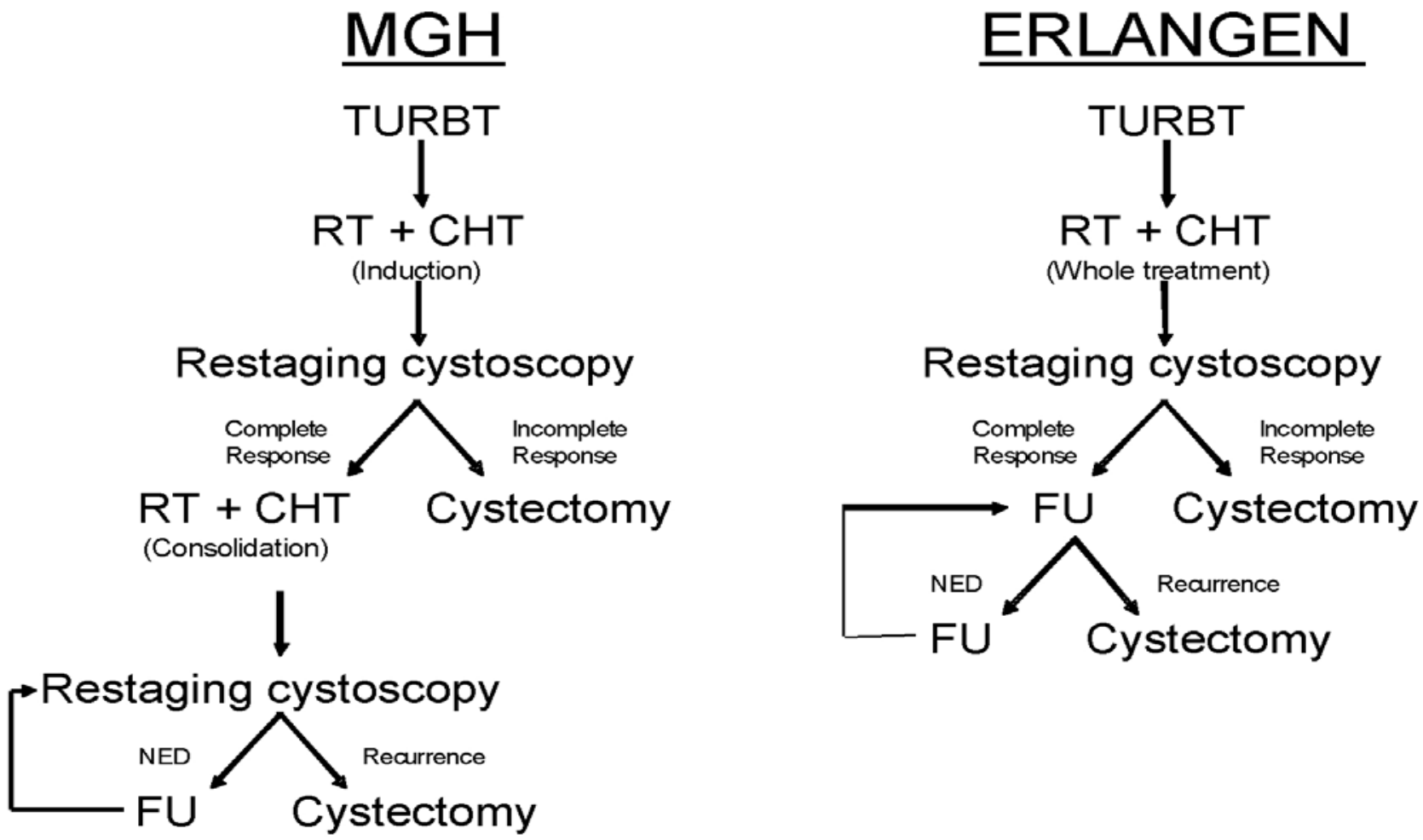
Reasons :

- Selection of patients in the trial setting is different from the patients seen in clinical setting
- Most are old with impaired renal functioning
- Also, regimes require in-patient treatment with hydration – Affects Quality of Life

Trimodality Therapy

- Combination of Limited Resection, Chemotherapy, and Irradiation in Bladder Preservation
  - Best results till date in bladder preservation when the 3 modalities are combined together
  - Based on both **single institutional data** and large **randomised control trials**

PIONEERING SINGLE INSTITUTION STUDIES OF TRIMODALITY TREATMENT



TRIALS ON BLADDER CONSERVATION WITH DIFFERENT MODALITIES

Investigators	Stage	Treatment	No. of Patients	Survival With Intact Bladder
Shipley et al[9]	T2-T4a	TURBT + chemotherapy + radiation therapy	190	45% (10-yr DSS with intact bladder)
Rödel et al[10]	T1-T4	TURBT + chemotherapy + radiation therapy	415	42% (5-yr OS with intact bladder)
Housset et al[11]	T2-T4	TURBT + chemotherapy + radiation therapy	54	Not reported (62% 3-yr DSS)
Sternberg et al[12]	T2-T4	Neoadjuvant M-VAC + TURBT	104	44% (5-yr OS, with intact bladder)
Herr[13]	T2	TURBT alone	99	57% (10-yr with intact bladder; includes only patients selected for bladder sparing)

TURBT = transurethral resection of the bladder tumor
M-VAC = methotrexate, vinblastine, doxorubicin, and cisplatin
DSS = disease-specific survival
OS = overall survival

RTOG TRIALS ON TRIMODALITY TREATMENT

RTOG Study	Radiation Therapy	Radiosensitizing Chemotherapy	No. of Patients	5-Year Survival (%)
85-12[3]	Daily (64.8 Gy)	Cisplatin	42	52
88-02[5]	Daily (64.8 Gy)	Cisplatin	91	62
89-03[6]	Daily (64.8 Gy)	Cisplatin	123	49
95-06[7]	Hypofractionated	Cisplatin and 5-fluorouracil	34	N/A
97-06[8]	Hyperfractionated	Cisplatin	52	N/A
99-06	Hyperfractionated	Cisplatin and paclitaxel	84	N/A

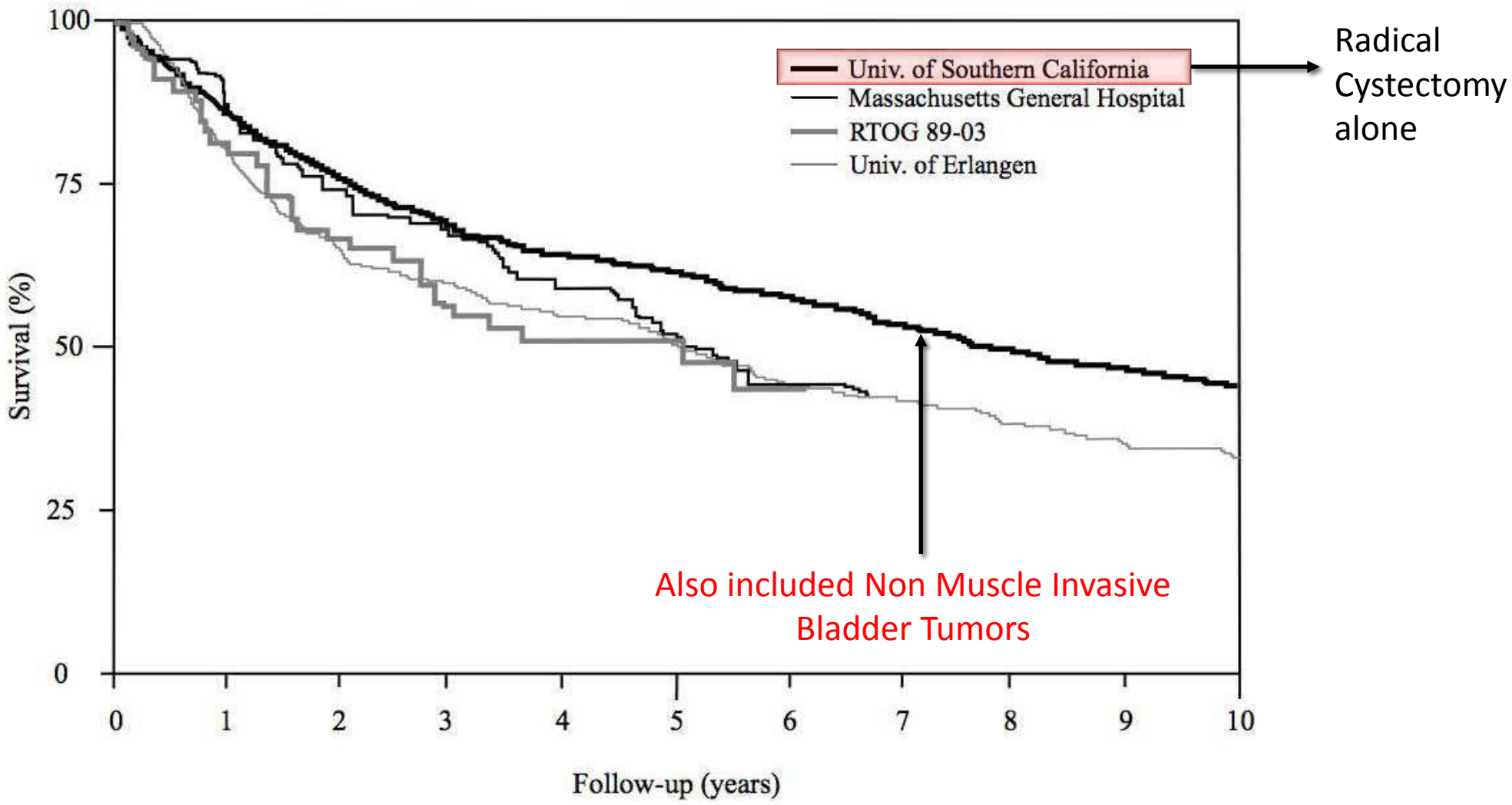
Trial	Induction RT	Induction chemo	Planned break	Consolidative RT	Consolidative chemo	Total RT dose	pCR	Survival
RTOG 99-06	40.3/26	cisplatin/taxol	3 weeks	24/16	cis/taxol, cis/gem x4	64.3/42	81%	5y: 56%
RTOG 97-06	40.8/24	cisplatin	3 weeks	24/16	cisplatin	64.8/40	74%	3y: 61%
RTOG 95-06	24/8	cisplatin/5-FU	3-4 weeks	20/8	cisplatin/5-FU	44/16	67%	3y: 86%
RTOG 89-03	39.6/22	±MCV x2 alone, then cisplatin	4 weeks	25.2/14	cispaltin	64.8/36	61%	5y: 48%
RTOG 88-02	39.6/22	MCV x2 alone, then cisplatin	2 weeks	25.2/14	cispaltin	64.8/36	80%	4y: 62%
RTOG 85-12	40/20	cisplatin	2 weeks	24/12	cisplatin	64/32	74%	3y: 59%
Harvard; 1993	39.6/22	MCV x2 alone, then cisplatin	2 weeks?	25.2/14	cispaltin	64.8/36	77%	5y: 48%
Paris; 1993	24/8	cisplatin/5-FU	6 weeks	20/8	cisplatin/5-FU	44/16	67%	3y: 64%

SURVIVAL DATA OF RADICAL CYSTECTOMY AND SELECTIVE BLADDER PRESERVATION

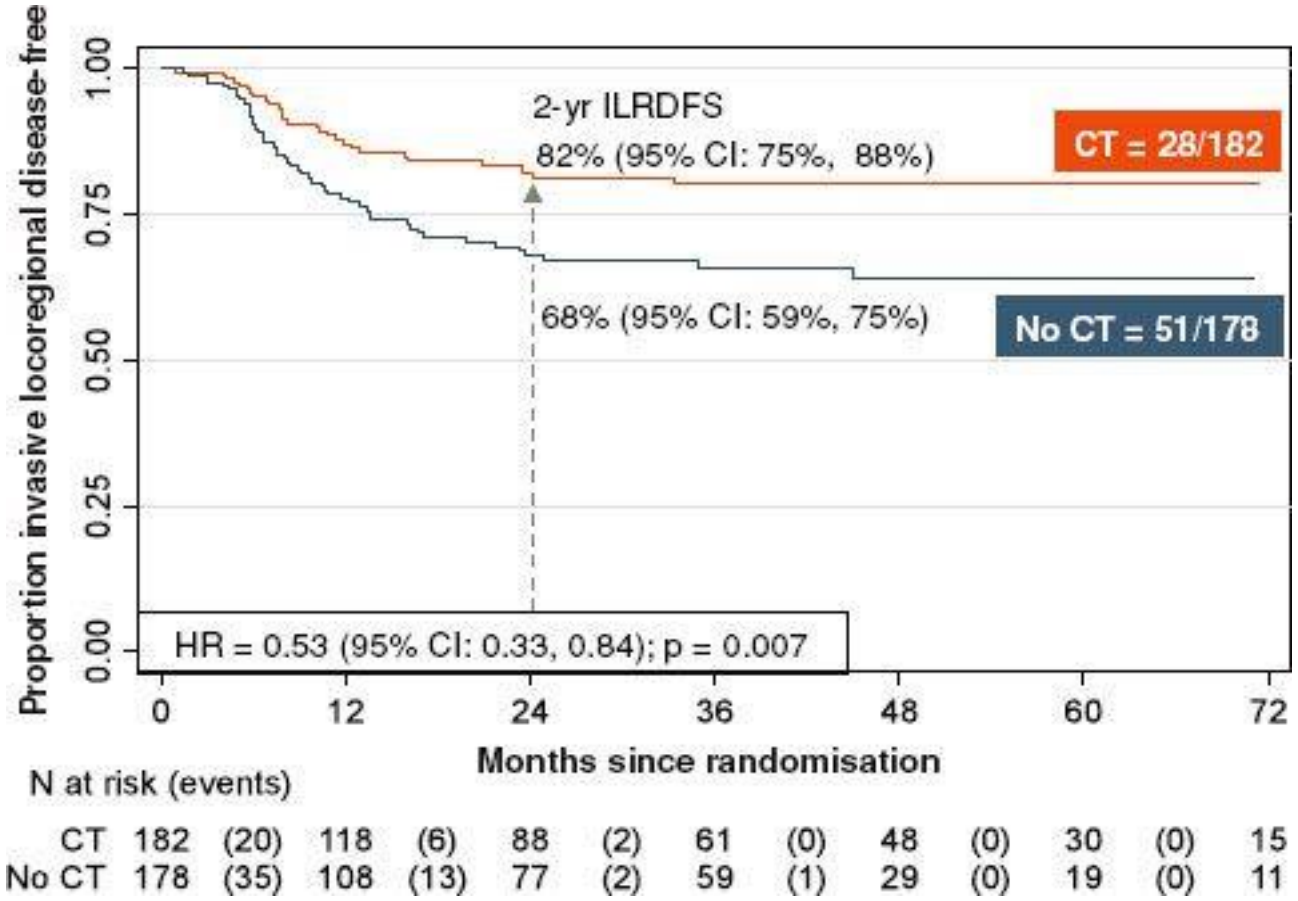
Series	Year	Category	No. Patients	Overall Survival	
				5-yr	10-yr
Cystectomy					
USC[136]	2001	pT2-pT4a	633	48%	32%
MSKCC[137]	2001	pT2-pT4a	181	36%	27%
SWOG/ECOG/CALGB*†[216]	2002	cT2-cT4a	317	49%	34%
Selective Bladder Preservation					
University of Erlangen*[123,234]	2002	cT2-cT4a	326	45%	29%
MGH*[233]	2009	cT2-cT4a	348	52%	35%
RTOG*[209]	1998	cT2-cT4a	123	49%	—

COMPARABLE

KAPLAN – MEIER GRAPH OF SURVIVAL IN MUSCLE INVASIVE BLADDER CANCER



KAPLAN - MEIER GRAPH SHOWING IMPROVED LOCOREGIONAL DISEASE FREE SURIVAL WITH ADDITION OF CONCURRENT CHEMOTHERAPY IN MUSCLE INVASIVE BLADDER CANCER : BC2001 TRIAL



Trimodality Treatment

Ideal candidates for Bladder preservation with Trimodality treatment :

- Solitary T2 or early T3 tumors < 6 cm
- No tumor-associated hydronephrosis
- Tumors allowing a visibly complete TURBT
- Invasive tumors not associated with extensive *carcinoma in situ*
- Adequate renal function to allow cisplatin concurrent with radiation
- TCC histology
- Willing for being on close surveillance
- Willing for cystectomy in case of progression or relapse

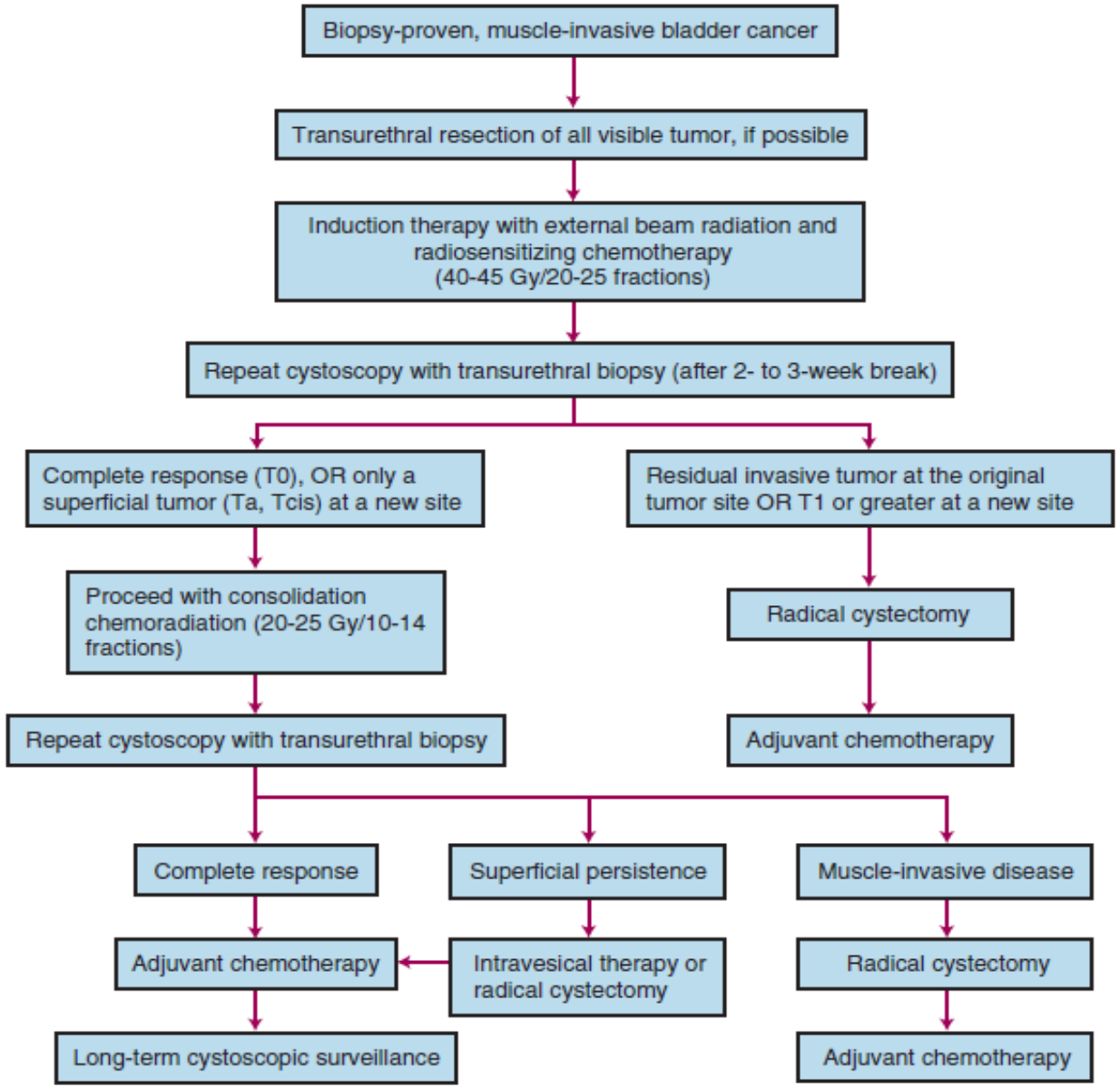
Bladder Preservation

Success rate of bladder preservation:

- TURBT alone - 20% free of invasive bladder recurrence
- Radiation Therapy alone - 41%
- Chemotherapy alone - 19%

Complete response rate:

- Radiation Therapy alone - 45%
- Chemotherapy alone - 27%
- TURBT + chemotherapy - 51%
- TURBT + chemo irradiation - 70-80%


Biopsy-proven, muscle-invasive bladder cancer
Transurethral resection of all visible tumor, if possible
Induction therapy with external beam radiation and radiosensitizing chemotherapy (40-45 Gy/20-25 fractions)
Repeat cystoscopy with transurethral biopsy (after 2- to 3-week break)
Complete response (T0), OR only a superficial tumor (Ta, Tcis) at a new site
Residual invasive tumor at the original tumor site OR T1 or greater at a new site
Proceed with consolidation chemoradiation (20-25 Gy/10-14 fractions)
Radical cystectomy
Repeat cystoscopy with transurethral biopsy
Adjuvant chemotherapy
Complete response
Superficial persistence
Muscle-invasive disease
Adjuvant chemotherapy
Intravesical therapy or radical cystectomy
Radical cystectomy
Long-term cystoscopic surveillance
Adjuvant chemotherapy

EDITORIAL

Radiotherapy and Organ Preservation in Bladder Cancer: Are We Ignoring the Evidence?

Journal of Clinical Oncology, Vol 20, No 14 (July 15), 2002: pp 3048-3050

Those involved in the management of muscle invasive bladder cancer should “take a leaf from the book” on sarcoma and breast cancer management, where multidisciplinary collaborative approach with knowledge and respect for the benefits and shortcomings of individual treatment modalities has led to a **standard of organ preservation**.

QUALITY OF LIFE ASSESSMENT

ORGAN CONSERVATION IN INVASIVE BLADDER CANCER BY TRANSURETHRAL RESECTION, CHEMOTHERAPY AND RADIATION: RESULTS OF A URODYNAMIC AND QUALITY OF LIFE STUDY ON LONG-TERM SURVIVORS

ANTHONY L. ZIETMAN,* DIANNE SACCO, URI SKOWRONSKI, PABLO GOMERY,†
DONALD S. KAUFMAN, JACK A. CLARK, JAMES A. TALCOTT AND WILLIAM U. SHIPLEY

From the Departments of Radiation Oncology (ALZ, US, WUS), Urology (DS, PG) and Medical Oncology (DSK, JAT), Massachusetts General Hospital, Harvard Medical School, and Department of Health Services (JAC), Boston University School of Public Health, Boston, Massachusetts

221 patients, T2-4Nx-0M0 bladder cancer,
Treated on protocols 1986-2000, median follow up : 6.3 years
Urodynamic study, QOL questionnaire

- 78% have compliant bladders with normal capacity and flow parameters
- 85% have no urgency or occasional urgency
- 25% have occasional to moderate bowel control symptoms
- 50% of men have normal erectile function

Late Pelvic Toxicity After Bladder-Sparing Therapy in Patients With Invasive Bladder Cancer: RTOG 89-03, 95-06, 97-06, 99-06

Jason A. Efstathiou, Kyounghwa Bae, William U. Shipley, Donald S. Kaufman, Michael P. Hagan, Niall M. Heney, and Howard M. Sandler

157 patients with Bladder Preservation who survived
2 to 13 years (Median follow-up - 5.2 years)

22% - Grade 1

10% - Grade 2

7% - Grade 3 (5.7% GU, 1.9% GI)

0% - Grade 4

0% - Grade 5

Table 4. Late Grade 3+ Pelvic Toxicity in RTOG Protocols

RTOG Protocol	Complete Response Rates (%)*	No. of Analyzable Patients	Grade 3+ Toxicity			
			GU		GI	
			No.	%	No.	%
89-03	59	56	4	7	2	4
95-06	67	24	0	0	0	0
97-06	74	24	2	8	1	4
99-06	87	53	3	6	0	0
Total		157	9	5.7	3	1.9

Abbreviations: RTOG, Radiation Therapy Oncology Group; GU, genitourinary.
*Complete response rates are for all eligible patients.

QUALITY OF LIFE ASSESSMENT AFTER CONCURRENT CHEMORADIATION FOR INVASIVE BLADDER CANCER: RESULTS OF A MULTICENTER PROSPECTIVE STUDY (GETUG 97-015)

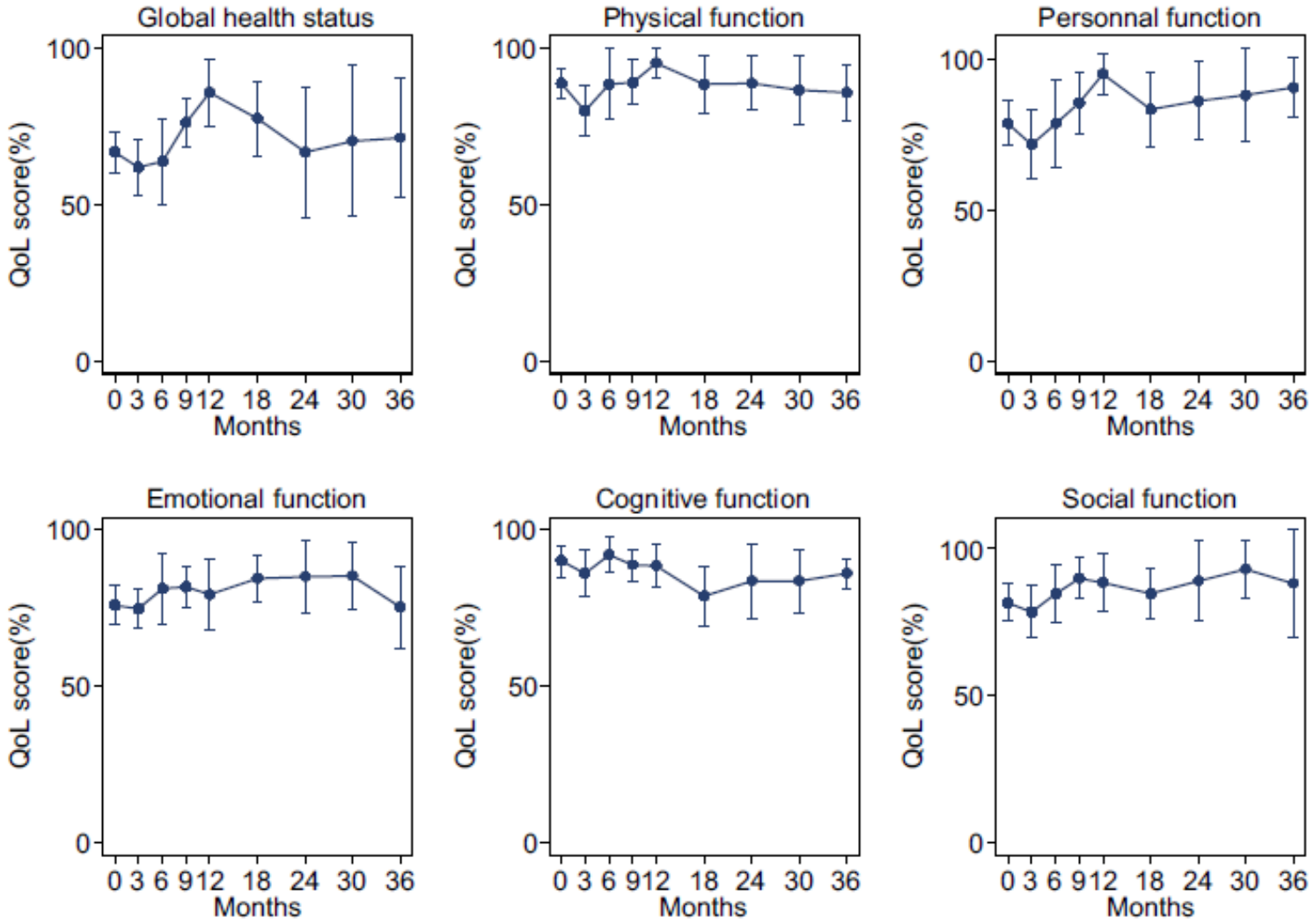
JEAN-LÉON LAGRANGE, M.D.,*† CAROLINE BASCOUL-MOLLEVI, PH.D.,‡ LIONNEL GEOFFROIS, M.D.,§ VÉRONIQUE BECKENDORF, M.D.,§ JEAN-MARC FERRERO, M.D.,† FLORENCE JOLY, M.D.,‖ NEDJILA ALLOUACHE, M.D.,‖ JEAN-MARC BACHAUD, M.D.,¶ CHRISTINE CHEVREAU, M.D.,¶ ANDREW KRAMAR, PH.D.,‡ AND BRUNO CHAUVET, M.D., # AND THE STUDY GROUP ON GENITO-URINARY TUMORS (GETUG)

Int. J. Radiation Oncology Biol. Phys., Vol. 79, No. 1, pp. 172–178, 2011

Conclusions: Concurrent chemoradiation therapy allowed bladder preservation with tumor control for 67% patients at 8 years. Quality of life and quality of bladder function were satisfactory for 67% of patients.

This prospective evaluation supports the published retrospective data suggesting good QoL for those invasive bladder cancer patients managed by bladder preservation after TUR and concurrent chemoradiotherapy. The most frequently reported sequela was an increase in moderate urinary frequency.

Patient quality of life evaluation according to the QLQ-C30 scale



QoL Assessment : Radical Cystectomy versus Organ Preservation Therapy

2 comparative cross sectional studies available :

Trento, Italy 1996 :

Retrospective study

59 patients, treated conservatively (49%) or with cystectomy (51%), who returned questionnaire (~65% rate in both)

Quality of life is better after conservative therapy than after cystectomy

Assessment of quality of life after cystectomy or conservative therapy for patients with infiltrating bladder carcinoma. A survey by a self-administered questionnaire; Caffo O, Fellin G, Graffer U, Luciani L.; Cancer 1996 Sep 1;78(5):1089-97.

QoL Assessment : Radical Cystectomy versus Organ Preservation Therapy

Karolinska, Sweden 2002 :

58 patients treated with radical RT before 1995 (63-68 Gy split course)

Compared with 251 patients with radical cystectomy and 310 general population patients

- Three quarters of long-terms survivors after radical RT had functioning urinary bladder with little or no distress from urinary tract.
- Prevalence of sexual dysfunction was lower than after surgery, with comparable GI dysfunction

Lars Henningsohn, Hans Wijkström, Paul W. Dickman, Karin Bergmark, Gunnar Steineck, Distressful symptoms after radical radiotherapy for urinary bladder cancer, Radiotherapy and Oncology, Volume 62, Issue 2, February 2002, Pages 215-22

Quality of Life after Bladder conservation Approach

ADVANTAGE OF COMBINED MODALITY TREATMENT	EQUIVALENCE TO SURGERY
Psychological adjustment	Social functioning
Physical well-being	Bowel function
Sexual function	
Urinary function	

RADIATION THERAPY TECHNIQUE

Modalities of External Beam Radiation Therapy

2D Conventional

3D Conformal Radiation therapy

Intensity Modulated Radiation Therapy (IMRT)

Patient Position and Immobilization

- The patient should be planned and treated in the same position
  - Supine with arms on their chest
  - Knee and ankle immobilization should be used to ensure patient positioning is reproducible.
- The rectum should be empty of flatus and faeces.
- Patients should be asked to empty the bladder 15 minutes prior to scan.
- While breathing normally, the patient should have a CT scan performed with 3 to 5-mm slice spacing.
- Neither intravenous nor oral contrast is beneficial.

Radiation Therapy Volumes

Gross tumor volume - Should integrate information from the staging CT or MRI as well as the TURBT.

- The use of fiducial markers or contrast medium such as lipiodol at the time of TURBT has been explored - May help identify tumor for image-guided adaptive radiotherapy.
- There are few data on the optimal radiotherapy volume.

Planning target volume : The whole bladder with a 1.5-cm margin plus extravesical extent of tumor with a 2-cm margin.

Radiation Therapy Volumes

No data to support the routine irradiation of radiologically negative lymph nodes

Nodal relapse rate in the BC2001 trial

- 3% in the chemo radiotherapy arm
- 6% in radiotherapy only arm

Radiation Therapy Volumes

All planning and treatment should be carried out with the bladder empty

- To minimize the risk of geographic miss
- To keep the treated volumes as small as possible

Patients with significant residual volumes post voiding should be considered for planning and treatment with a catheter *in situ*

Radiation Therapy Doses

Optimal radiotherapy schedule is yet to be established

Most commonly used schedule : **SPLIT SCHEDULE**

- 40-45 Gy in 1.8-2 Gy/fraction – Initially
- If good response – To go to radical dose of 64-66 Gy

Hypofractionation (55Gy in 20 fractions) – Practiced in some centres in UK

Hyperfractionation (Twice daily RT) – Also tried and used in trials

CONCLUSIONS

Conclusions

- Combined modality therapy achieves a complete response and preserves the native bladder in ~70% of patients, while offering long-term survival rates comparable to contemporary radical cystectomy series

- QoL studies have demonstrated that the retained native bladder functions well and long-term toxicity of chemo irradiation to pelvic organs is relatively low

- These results support the acceptance of modern bladder-sparing Trimodality therapy for selected patients as a proven alternative to cystectomy

Conclusions

- The optimal regimen of combined chemo irradiation, as well as the addition of rational molecular targeted therapy and personalized treatment selection, continues to be investigated

- The contribution of selective bladder sparing therapy to the quality of life of patients represents a unique opportunity for urologic surgeons, radiation oncologists, and medical oncologists to work hand in hand in a truly multidisciplinary effort


THANK YOU
THANK YOU!
THANK YOU