Bladder-Sparing Trimodality Therapy for Muscle-Invasive Bladder Cancer

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October 29, 2011
Organ conservation in contemporary oncology

- Anal carcinoma
- Breast carcinoma
- Esophageal carcinoma
- Laryngeal carcinoma
- Limb sarcomas
Muscle-invading TCC bladder

Cystectomy

Cystectomy alternatives

Bladder removal and reconstruction

Bladder conservation

Goals:
- cure patient and optimize survival
- prevention of pelvic failure and distant metastasis
- functional urinary reservoir and high QOL
So what’s the modern alternative to cystectomy?

Trimodality therapy

- Maximal TURBT
- Radiation therapy
- Chemotherapy
TURBT

XRT (40Gy) + Concomitant Chemotherapy

Cystoscopic response evaluation

CR

Consolidation Chemo-radiation (64Gy) +/- adjuvant chemo

Non-CR

Radical Cystectomy +/- adjuvant chemo
Importance of early salvage cystectomy

XRT (40Gy) + Concomitant Chemotherapy

Consolidation Chemo-radiation (64Gy)

Cystoscopy response evaluation

CR

Consolidation Chemo-radiation (64Gy)

Non-CR

Radical cystectomy

Frequent cystoscopy
Bladder Cancer - Lymphatic Pathway of Spread

Perivesical LN: 75%
Common iliac nodes: 19%
External iliac nodes: 65%
Internal iliac nodes: 15%
Perivesical LN: 75%

Nodal disease is present in 20-40% at diagnosis
Nodal RT fields (40 to 45Gy) are designed to conserve small bowel for urinary diversions should they be needed.
Tumor boost fields by 3-D

- Only partial bladder to high dose (total 65 Gy)
- Incorporate all TURBT and radiographic info
- Simulate and treat with empty bladder
Bladder Conservation: Evolution of the MGH and RTOG approach

1986-93
Neoadjuvant chemo
Response evaluation

1994-98
Accelerated radiation
Adjuvant chemotherapy

1999-2002
Enhanced Radiation sensitization
Adjuvant chemotherapy

MCVx2
RT + C

bidRT+C/5Fu
MCV x 3

bidRT+C/Tax
G + C x 4
Long-term MGH Experience 1986-2006

• N = 348
• Clinical stages T2-T4a
• Treated on protocols 1986-2006
• Median age 66.3 years (range 27.3–88.6)
• Median FU for those alive 7.7 years
• Actuarial endpoints included: OS, DSS
Long-term MGH Experience 1986-2006
Background Characteristics (n=348)

Gender
- Male 74%
- Female 26%

Clinical Stage
- T2 54%
- T3 38%
- T4a 8%

Visibly complete TURBT
- Yes 65%
- No 33%

Hydronephrosis
- Yes 17%
- No 83%

Efstathiou et al  ASCO GU 2010
### Long-term MGH Experience 1986-2006

#### Outcomes

<table>
<thead>
<tr>
<th>CR rate</th>
<th>72%</th>
</tr>
</thead>
</table>

**Overall Survival**

| 5 yrs  | 52% |
| 10 yrs | 35% |
| 15 yrs | 22% |

**Disease Specific Survival**

| 5 yrs  | 64% |
| 10 yrs | 59% |
| 15 yrs | 57% |

| % undergoing Cystectomy* | 29% |
| Immediate (non-CR)       | 17% |
| Salvage                   | 12% |

*No patient required cystectomy due to treatment-related toxicity

_Efstathiou et al  ASCO GU 2010_
Long-term MGH Experience 1986-2006

80% of those alive at 5 years still have native bladder

Disease-specific survival

Follow-up time (years)

Number at risk

348 213 149 101 67 44 24

95% CI  Survivor function
Long-term MGH Experience 1986-2006
Influence of Age

Disease-specific survival

Log-rank test: p = 0.6

Followup time (years)

Number at risk

<75 262 184 138 105 79 59
>75 86 51 33 21 16 8

<75 years old  >75 years old

Efstathiou et al. ASCO GU 2010
Long-term MGH Experience 1986-2006

• In **univariate** analyses the following were significant:

  low clinical T stage \( (HR \ 0.53, \ p=0.001) \)
  visibly complete TURBT \( (HR \ 0.67, \ p=0.029) \)
  lack of hydronephrosis \( (HR \ 0.48, \ p=0.001) \)
  CR to induction therapy \( (HR \ 0.37, \ p<0.001) \)

• In **multivariate** analyses the following were significant:

  low clinical T stage \( (HR \ 0.56, \ p=0.01) \)
  CR to induction therapy \( (HR \ 0.41, \ p=<0.001) \)

Efstathiou et al  ASCO GU 2010
Long-term MGH Experience 1986-2006
Importance of Clinical Stage

Disease-specific survival

Number at risk
T3-T4 159 83 56 41 28 21 14
T2 188 129 92 60 39 23 10

Follow-up time (years)

Log-rank test: p = 0.0004

Efstathiou et al ASCO GU 2010
Long-term MGH Experience 1986-2006
Importance of a Complete Response

Disease-specific Survival
T2-T4a

Log-rank test: p < 0.0001

Followup time (years)

Number at risk
No CR 91 51 33 23 16 13
CR 231 173 133 100 77 52

No CR CR 95% CI 95% CI

72% 69% 47% 36%
Long-term MGH Experience 1986-2006
Neoadjuvant chemotherapy

Overall survival

Disease-specific survival

Cumulative incidence of distant metastases

Log-rank test: $p = 0.8$

Log-rank test: $p = 0.9$

Log-rank test: $p = 0.9$
No Level 1 (Phase III) data indicating cisplatin-based neoadjuvant chemotherapy given before definitive local treatment by RT or RT and concurrent chemotherapy significantly improves survival.

- **RTOG 89-03** trial (n=123) negative (5 year survivals of 49% and 50%)
- **Danish Cancer Group** trial (n=113) negative (NCT had 5.6% lower survival)
- **RT subgroup of MRC trial** (n=413) trended insignificant in favor of NCT
- **Meta-analysis negative** (survival 30.4% vs 28.1%)
Meta-Analysis of Neoadjuvant Chemotherapy in Invasive Bladder Cancer

Phase III series with RADIATION THERAPY
(A total of 526 patients)

<table>
<thead>
<tr>
<th></th>
<th>Events / patients</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NeoCT</td>
<td>Control</td>
</tr>
<tr>
<td>Radical RT</td>
<td>132/206</td>
<td>142/207</td>
</tr>
<tr>
<td>MRCb</td>
<td>51/57</td>
<td>47/56</td>
</tr>
<tr>
<td>Sengelov</td>
<td>183/263</td>
<td>189/263</td>
</tr>
</tbody>
</table>

**P=0.334**

European Urology 48: 202-206, 2005
What is the importance of an aggressive TURBT for “Cystectomy Avoidance”?

“The TURBT must be done with the determination to resect all visible tumor. Nothing less will suffice.”

NM Heney et al NATURE Rev Clin Oncol 2009
Long-term MGH Experience 1986-2006
The value of complete TURBT

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>TURBT complete</th>
<th>TURBT not complete</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>343</td>
<td>227</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>CR rate</td>
<td>72%</td>
<td>79%</td>
<td>57%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5 year outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Survival</td>
<td>52%</td>
<td>57%</td>
<td>43%</td>
<td>0.003</td>
</tr>
<tr>
<td>DSS</td>
<td>64%</td>
<td>68%</td>
<td>56%</td>
<td>0.03</td>
</tr>
<tr>
<td>% undergoing cystectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>29%</td>
<td>22%</td>
<td>42%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Immediate (non-CR)</td>
<td>17%</td>
<td>11%</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>Salvage</td>
<td>12%</td>
<td>11%</td>
<td>13%</td>
<td></td>
</tr>
</tbody>
</table>

Efstathiou et al  ASCO GU 2010
For cT2, complete TURBT, no hydro; CR probability = 79%
For cT3, incomplete TURBT, no hydro; CR probability = 51%
For cT2, complete TURBT, no hydro; 5 yr DSS probability = 78%
For cT3, incomplete TURBT, no hydro; 5 yr DSS probability = 53%
Selection is Key

Tumor presentations with the highest success rates:

- 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
How does bladder preservation by combined modality therapy compare with radical cystectomy?
Cystectomy versus ChemoRT

Comparing cure rates of modern selective bladder preserving approaches with salvage cystectomy to contemporary cystectomy series is difficult.

- Retrospective cystectomy series do not report by “intention to treat”
- Outcome results are confounded by discordance between clinical (TURBT) staging and pathologic (cystectomy) staging
- Best approach is to compare the results of prospective protocols in which the eligibility is based on clinical staging and all entered patients are reported for outcome
## Survival after curative therapy

<table>
<thead>
<tr>
<th>Institution</th>
<th>Stage</th>
<th>Number</th>
<th>5 year OS</th>
<th>10 year OS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cystectomy</strong> USC 2001</td>
<td>pT2-4a</td>
<td>633</td>
<td>48%</td>
<td>32%</td>
</tr>
<tr>
<td>MSKCC 2001</td>
<td>pT2-4a</td>
<td>181</td>
<td>36%</td>
<td>27%</td>
</tr>
<tr>
<td>SWOG 2003</td>
<td>cT2-3</td>
<td>303</td>
<td>49%</td>
<td>-</td>
</tr>
<tr>
<td><strong>Chemo-RT</strong> RTOG 1998</td>
<td>cT2-4a</td>
<td>123</td>
<td>49%</td>
<td>-</td>
</tr>
<tr>
<td>Erlangen 2002</td>
<td>cT2-4</td>
<td>326</td>
<td>45%</td>
<td>29%</td>
</tr>
<tr>
<td>MGH 2011</td>
<td>cT2-4a</td>
<td>348</td>
<td>52%</td>
<td>35%</td>
</tr>
</tbody>
</table>
Contemporary Co-operative Group Trials in Invasive Bladder Cancer— all in clinically staged patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>number</th>
<th>5 yr survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWOG</td>
<td>Cystectomy + NCT</td>
<td>317</td>
<td>47%</td>
</tr>
<tr>
<td>Italian**</td>
<td>Cystectomy + NCT</td>
<td>206</td>
<td>54%</td>
</tr>
<tr>
<td>RTOG*</td>
<td>TURBT, XRT, Cisplatin + NCT</td>
<td>123</td>
<td>49%</td>
</tr>
<tr>
<td>SWOG*</td>
<td>TURBT, XRT+ both Cisplatin + 5-FU</td>
<td>25</td>
<td>45%</td>
</tr>
</tbody>
</table>

* All patients were “cystectomy candidates”

MRC “SPARE” Bladder Protocol

TURBT

Gemcitabine and Cisplatin – 3 cycles

Cystoscopic assessment of treatment response

Incomplete response

Complete response

Radical cystectomy

Definitive Radiation ± Chemo
MRC “SPARE” Bladder Protocol

Life and death of spare (selective bladder preservation against radical excision): reflections on why the spare trial closed.

Huddart et al BJU Int 2010
Which chemotherapy with radiation?
NCI-Canada Phase III Trial of RT +/- concurrent Cisplatin
Role of Concurrent Chemotherapy

The active radiosensitizing drugs include:

- Cisplatin, Paclitaxel, 5-FU, Mitomycin C, Gemcitabine and tumor hypoxia-reducing drugs
## Concurrent Chemotherapy + Twice-Daily RT

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Induction treatment</th>
<th>Patients</th>
<th>Complete Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>95-06</td>
<td>TURBT, 5-FU plus CP + BID RT</td>
<td>34</td>
<td>67%</td>
</tr>
<tr>
<td>97-06</td>
<td>TURBT, CP + BID RT adj MCV</td>
<td>52</td>
<td>74%</td>
</tr>
<tr>
<td>99-06</td>
<td>TURBT, TAX plus CP + BID RT adj CP + GEM</td>
<td>80</td>
<td>81%</td>
</tr>
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</table>
### University of Erlangen Experience

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT alone</td>
<td>98</td>
<td>57%</td>
</tr>
<tr>
<td>RT + carboplatin</td>
<td>69</td>
<td>64%</td>
</tr>
<tr>
<td>RT + cisplatin</td>
<td>115</td>
<td>81%</td>
</tr>
<tr>
<td>RT + 5-FU/cis</td>
<td>45</td>
<td>87%</td>
</tr>
</tbody>
</table>

*Rodel et al. IJROBP 2002;52:1303-9*
Phase III randomized trial of synchronous chemo-radiotherapy compared to radiotherapy alone in muscle invasive bladder cancer (BC2001 CRUK/01/004)

- 360 patients 2001 – 2008
- clinical stage T2-4aNx bladder cancer
- XRT 55 Gy/20 or 64 Gy/32
- RT ± MMC & 5-FU
- GFR > 25 ml/min
- Median follow-up 49 months

James et al, ASCO & ASTRO 2010
LRDFS in chemotherapy randomization

HR = 0.66 (95% CI: 0.46, 0.95); p=0.02

CT = 52/182
No CT = 74/178
## The Benefit of Radiation in Bladder Preservation

<table>
<thead>
<tr>
<th>Treatment</th>
<th>%CR</th>
<th>5 year survival</th>
<th>% requiring cystectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>TURBT + M-VAC* (TWO-MODALITY)</td>
<td>33-54%</td>
<td>58%</td>
<td>66%</td>
</tr>
<tr>
<td>TURBT + XRT+chemo (TRI-MODALITY)</td>
<td>64-87%</td>
<td>45%-62%</td>
<td>29-35%</td>
</tr>
</tbody>
</table>

Cystectomy rate is increased by 88-125% without radiation

RTOG PROTOCOL 02-33 (Randomized Phase II)  
(PI: AL Zietman, MD)

Stage T2 – T4a, No Hydronephrosis  
Candidate for cystectomy, if necessary

TURBT  
randomization  

bid RT  
5FU  
Cisplatin  

bid RT  
Taxol  
Cisplatin

Finished accrual 2008  
93 patients
RTOG 02-33
Overall survival following chemo-radiation

Zietman et al. ASTRO 2010
Stage T2 – T4a, No Hydronephrosis
Candidate for cystectomy, if necessary

TURBT

randomization

RTOG:
- bid RT
- 5FU
- Cisplatin

Michigan:
- qd RT
- Gemcitabine

Started accrual 2008
RTOG PROTOCOL 09-26 (Phase II)  
*(PI: D Dahl, MD)*

Stage T1 G2 or G3, Failed intravesical therapy, Cystectomy next step

1. TURBT
2. Full dose RT
   *Concurrent cisplatin*
3. Cystoscopical surveillance

*Started accrual 2010*
Personalized Care in the Era of Biomarkers and Molecular Targeted Agents

Can biomarkers be used to predict outcomes and even select an optimal treatment for subsets of muscle-invading bladder cancer patients, thus benefiting individuals?
RTOG 05-24: Phase I-II study of treatment for non-cystectomy candidates
(PI: D Michaelson, MD PhD)

Her-2 expression, identified in 57% of patients, is significantly correlated with reduced effectiveness of chemoradiation against the primary tumor (CR rate of 50% vs 81%).

Chakravarti et al IJROBP 2005
RTOG 05-24: Phase I-II study of treatment for non-cystectomy candidates
(PI: D Michaelson, MD PhD)

TURBT-------> Her-2 stain < 3+ -------> XRT + weekly taxol

TURBT-------> Her-2 stain 3+ -------> XRT + weekly taxol + HERCEPTIN

55 of 88 patients accrued
MRE11 Predictive of CSS Following Radical Radiotherapy for Muscle Invasive Bladder Cancer

- Ionizing radiation creates DNA damage sensed by the MRE11/NBS1/RAD50 (MRN) complex, which initiates cell cycle checkpoints, activates apoptosis and is involved in MRN-mediated DSB repair.

- Reduced tumor MRE11 protein expression is associated with poorer survival following radical radiotherapy for bladder cancer.

- Failure of cell cycle arrest/apoptosis responses may result in radioresistance and reduced local tumor control.

MRE11 Predictive of CSS Following Radical Radiotherapy for Muscle Invasive Bladder Cancer

**Radiation cohort**

- High MRE11
- Low MRE11

Log-rank $P < 0.001$

HR = 0.43 (95% CI: 0.26–0.71)

Numbers at risk:

- Low MRE11: 44
- High MRE11: 134

Survival from RT (mo):

- 0 25 50 75 100 125

**Cystectomy cohort**

- Low MRE11
- High MRE11

Log-rank $P = 0.46$

HR = 1.30 (95% CI: 0.65–2.64)

Numbers at risk:

- Low MRE11: 22
- High MRE11: 66

Survival from cystectomy (mo):

- 0 25 50 75 100 125

**High MRE 11 Patients**

- RT (High MRE11)
- Cystectomy (High MRE11)

Log-rank $P = 0.021$, $N = 201$

HR = 0.60 (95% CI: 0.39–0.93)

Numbers at risk:

- RT (High MRE11): 88
- Cystectomy (High MRE11): 66

Survival from treatment (mo):

- 0 25 50 75 100 125

**Low MRE 11 Patients**

- Cystectomy (Low MRE11)
- RT (Low MRE11)

Log-rank $P = 0.13$, $N = 66$

HR = 1.78 (95% CI: 0.84–3.76)

Numbers at risk:

- RT (Low MRE11): 15
- Cystectomy (Low MRE11): 22

Survival from treatment (mo):

- 0 25 50 75 100 125
Quality of life after chemo-radiation
MGH Quality of Life Study

221 patients, T2-4NX-0M0 bladder cancer, Treated on protocols 1986-2000, median f/u 6.3 years, Urodynamics 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

Zietman, Talcott, Krane et al J Urol 2003
Late Pelvic Toxicity: RTOG Results

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

Efstathiou et al J Clin Oncol 2009
QoL due to urinary symptoms after TURBT and chemoRT

*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?*

<table>
<thead>
<tr>
<th></th>
<th>delighted</th>
<th>pleased</th>
<th>mostly satisfied</th>
<th>mixed — about equally satisfied and dissatisfied</th>
<th>mostly dissatisfied</th>
<th>unhappy</th>
<th>terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>18.5%</td>
<td>51.7%</td>
<td>17.2%</td>
<td>9.1 %</td>
<td>0.8%</td>
<td>2 %</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

*Weiss et al 2005*
Quality of life after treatment of invasive bladder cancer: Cystectomy or organ-conserving therapy

2 comparative cross-sectional studies available:

Trento, Italy 1996
Incontinent diversion vs chemo-RT

Karolinska, Sweden 2002
Incont. and cont. diversions vs RT vs controls
Quality of life after treatment of invasive bladder cancer: Cystectomy or organ-conserving therapy

QOL *advantage* to chemo-RT:
- psychologic adjustment
- physical well-being
- energy
- sexual function
- urinary function

QOL *equivalence* chemo-RT vs surgery:
- Social functioning
- Bowel function
Quality of life after treatment of invasive bladder cancer: Cystectomy or organ-conserving therapy

Henningssohn et al 2002

**Urinary function:**
RT -  74% little or no urinary symptom distress

**Sexual function:**
RT -  38% intercourse previous month
Cyst - 13% intercourse previous month
Quality of life after treatment of invasive bladder cancer: Cystectomy or organ-conserving therapy

Henningssohn et al 2002

Bowel function:

mod or much distress

RT

Cystectomy

Controls

<table>
<thead>
<tr>
<th>Treatment</th>
<th>32%</th>
<th>24%</th>
<th>9%</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td></td>
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</tbody>
</table>

NS  Sig
The best bladder you will ever have is the one you are born with

(even if it has had an aggressive TURBT and some radiation)
Acceptance of chemoradiation used in modern bladder-sparing therapy should not be limited by concerns of high rates of late pelvic toxicity
Morbidity of primary radical cystectomy

Donat et al 2009

1142 RCs at MSKCC  1995-2005
Prospectively captured morbidity data
Reported complications within 90 days
Graded 0-5 on modified Clavien Scale
Morbidity of primary radical cystectomy

Donat et al 2009

64% More than 1 complication
13% Grade 3-5
26% Readmissions
2% 90 day mortality

Donat et al Eur Urol, 2009
## Morbidity of salvage radical cystectomy at the MGH

<table>
<thead>
<tr>
<th>Grade</th>
<th>Total</th>
<th>&lt;30 days</th>
<th>&lt;90 days</th>
<th>MSKCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>72</td>
<td>53</td>
<td>58</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>39%</td>
<td></td>
<td>26%</td>
</tr>
<tr>
<td>2</td>
<td>55</td>
<td>42</td>
<td>48</td>
<td>38%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30%</td>
<td></td>
<td>62%</td>
</tr>
<tr>
<td>3</td>
<td>52</td>
<td>11</td>
<td>18</td>
<td>14%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>28%</td>
<td></td>
<td>11%</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2%</td>
<td></td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2%</td>
</tr>
</tbody>
</table>

*Heney, Eswara et al 2010*
Current Recommendations in Cystectomy Candidates “Off-Protocol”

Stage $T_3 - T_{4a}$ with hydronephrosis: Cystectomy

Stage $T_{4a}$ (prostate stromal invasion): Cystectomy

Stage $T_2 - T_3$: TURBT and concurrent cisplatin plus XRT (QD or BID) with prompt cystectomy for failure
"Standard" Selective Bladder Sparing Therapy “Off-Protocol”

- TURBT as complete as is safely possible
- XRT to bladder & pelvic lymph nodes to 40Gy with a boost to bladder tumor to 64Gy
- Cisplatin in weeks 1, 4, and 7
- Close cystoscopic surveillance with salvage cystectomy for tumor persistence or for invasive recurrence
“Standard” Selective Bladder Sparing Therapy “Off-Protocol”

For non- cystectomy or non-Cisplatin Candidates

- TURBT as complete as is safely possible
- XRT to bladder & pelvic lymph nodes to 40Gy with a boost to bladder tumor to 64Gy in 2 Gy daily fractions
- Concurrent chemotherapy with Mitomycin C and 5-FU as in protocol BC2001
- Cystoscopic surveillance for tumor persistence or for invasive recurrence for prompt further local therapy
Closing Thoughts

• Combined modality therapy achieves a CR 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 chemoRT to pelvic organs is relatively low.

• Incidence of cystectomy performed for palliation of treatment-related toxicity has been very low and the morbidity of salvage cystectomy appears comparable to primary cystectomy.
Closing Thoughts

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

• The optimal regimen of combined chemoRT, as well as the addition of rational molecular targeted therapy and personalized treatment selection, continues to be investigated.
Closing Thoughts

• 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.