Long-term outcomes among patients who achieve complete or near-complete responses after the induction phase of bladder preserving combined modality therapy for muscle-invasive bladder cancer: A pooled analysis of RTOG 9906 and 0233


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Trial Support and Disclosures

- NCI grants: U10 CA21661, U10 CA37422
- Disclosures: none
Bladder Conservation: Evolution of the organ-sparing therapy
Maximal TURBT

Radiation (40 Gy) + Concurrent Chemotherapy

Cystoscopic evaluation

CR

Consolidation: Chemo+ RT (64 Gy) +/- Adjuvant Chemo

Non-CR

Radical Cystectomy +/- Adjuvant Chemo
Clinical Question

• Patients and physicians were not happy with the requirement of the early salvage RC for a near-complete response (Ta or Tis after induction chemo-RT)

• Last 2 Bladder RTOG trials have allowed near-CR patients to continue with bladder preservation

• This analysis was carried out to determine whether this was appropriate
RTOG 99-06 (n=80)

TURBT

Induction: Paclitaxel, Cisplatin
Bid radiation

Re-evaluation

Consolidation: Paclitaxel, Cisplatin
Bid radiation

Adjuvant: Gemcitabine, Cisplatin x 4

Chemotherapy

Induction
Paclitaxel 50mg/m2  Days 1, 8, 15
Cisplatin 20mg/m2  Days 1-2, 8-9, 15-16

Consolidation
Paclitaxel 50mg/m2  Days 1, 8
Cisplatin 20mg/m2  Days 1-2, 8-9

Adjuvant
Gemcitabine 1000mg/m2  Days 1, 8, 15, q28days
Cisplatin 70mg/m2 Day 1
Radiation details

Induction
Small pelvis 1.6Gy am
Whole bladder 1.5Gy pm
Small pelvis 1.6Gy am
Tumor boost 1.5Gy pm
Totals: 40.3Gy

Consolidation
Small pelvis 1.5Gy bid 8 days
24.0Gy

Total Dose to Bladder Tumor: 64.3Gy
Pooled Analysis

• 119 eligible patients
  – 54 on RTOG 99-06
  – 65 on RTOG 0233

• After induction chemo-RT:
  – 101 achieved T0
  – 18 achieved Ta or Tis
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>T0 (n=101)</th>
<th>Tis/Ta (n=18)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>65</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Min-Max</td>
<td>41-90</td>
<td>36-82</td>
<td></td>
</tr>
<tr>
<td>Q1-Q3</td>
<td>59-71</td>
<td>60-78</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Male</td>
<td>89 (88%)</td>
<td>16 (89%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12 (12%)</td>
<td>2 (11%)</td>
<td></td>
</tr>
<tr>
<td>Zubrod Performance Score</td>
<td></td>
<td></td>
<td>0.29</td>
</tr>
<tr>
<td>0</td>
<td>96 (95%)</td>
<td>16 (89%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5 (5%)</td>
<td>2 (11%)</td>
<td></td>
</tr>
<tr>
<td>Clinical T stage</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>cT2</td>
<td>94 (93%)</td>
<td>17 (94%)</td>
<td></td>
</tr>
<tr>
<td>cT3-cT4</td>
<td>7 (7%)</td>
<td>1 (6%)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s exact test is used
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>T0 (n=101)</th>
<th>Tis/Ta (n=18)</th>
<th>p-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal complete TURBT</td>
<td></td>
<td></td>
<td>0.59</td>
</tr>
<tr>
<td>Yes</td>
<td>93 (92%)</td>
<td>18 (100%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3 (3%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Days between induction chemo-RT and cystoscopic evaluation</td>
<td></td>
<td></td>
<td>0.47</td>
</tr>
<tr>
<td>Mean</td>
<td>28.5</td>
<td>30.3</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>28</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>15</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>51</td>
<td>57</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s exact test is used
Overall Survival

- T0: 72%
- Tis/Ta: 61%

Patients at Risk
- T0: 101
- Tis/Ta: 83
- Total: 184

Years after Randomization
- 0: 101
- 1: 97
- 2: 83
- 3: 78
- 4: 72
- 5: 58
- 6: 47

Dead
- T0: 32
- Tis/Ta: 9
- Total: 41

p = 0.1198 (Log-Rank)
### Efficacy Outcomes

<table>
<thead>
<tr>
<th>Outcome at 5 years (95% CI)</th>
<th>T0 (n=101)</th>
<th>Ta/Tis (n=18)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival</td>
<td>72% (63%, 81%)</td>
<td>61% (39%, 84%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Disease-Specific Survival</td>
<td>85% (78%, 92%)</td>
<td>67% (44%, 89%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Bladder Recurrence Free</td>
<td>68% (58%, 77%)</td>
<td>72% (51%, 94%)</td>
<td>0.70</td>
</tr>
</tbody>
</table>
## Bladder Recurrence

<table>
<thead>
<tr>
<th></th>
<th>T0 (n=101)</th>
<th>Tis/Ta (n=18)</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Bladder Recurrence</strong></td>
<td></td>
<td></td>
<td>0.52</td>
</tr>
<tr>
<td>No</td>
<td>65 (64%)</td>
<td>13 (72%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>36 (36%)</td>
<td>5 (28%)</td>
<td></td>
</tr>
<tr>
<td><strong>Recurrence</strong></td>
<td></td>
<td></td>
<td>0.63</td>
</tr>
<tr>
<td>Invasive</td>
<td>13 (41%)</td>
<td>1 (20%)</td>
<td></td>
</tr>
<tr>
<td>Non-invasive</td>
<td>19 (59%)</td>
<td>4 (80%)</td>
<td></td>
</tr>
</tbody>
</table>

* Excluded 4 patients whose recurrence was indeterminate for invasiveness.
** Fisher’s exact test is used.
Conclusions

• There is no apparent difference in the bladder recurrence and salvage cystectomy rates between complete (T0) and near-complete (Ta or Tis) responders as judged at the time of cystoscopic evaluation after induction phase of bladder preserving combined modality therapy.

• It is appropriate to recommend that patients with Ta or Tis after induction chemo-RT continue with bladder-sparing therapy.
Acknowledgements

• We would like to acknowledge participation of NRG Oncology and CCOP institutions
• NRG Oncology HQ Staff
• Patients and their families