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

Conflict of Interest Disclosures

• RTOG grant U10 CA21661 (NCI)
• CCOP grant U10 CA37422 (NCI)
Bladder Conservation:
Evolution of the organ-sparing therapy

- 1974–1981: Radiation
  - 1986–1993: Neoadjuvant chemotherapy, Response evaluation

1. RT → RT + C
2. RT + C → RT + C
3. bid RT + C/5-FU
4. bid RT + C/Tax
5. MCV × 2
6. MCV × 3
7. Novel chemotherapy G + C × 4
Maximal TURBT

Radiation (40 Gy) + Concurrent Chemotherapy

Cystoscopic evaluation

CR

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

Non-CR

Radical Cystectomy +/- Adjuvant Chemo
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
Cisplatin 70mg/m2
Days 1, 8, 15, q28days
**RTOG 0233 (n=97)**

**TURBT**

**Induction:** Paclitaxel, Cisplatin
bid radiation

*Re-evaluation*

**Consolidation:** Paclitaxel, Cisplatin
Bid radiation

**Adjuvant:** Gemcitabine, Cisplatin, paclitaxel x 4

**Induction:** 5-FU, Cisplatin
bid radiation

*Re-evaluation*

**Consolidation:** 5-FU, Cisplatin
Bid radiation

**Adjuvant:** Gemcitabine, Cisplatin, paclitaxel x 4
Radiation details

**Induction**
- Small pelvis: 1.6 Gy am
- Whole bladder: 1.5 Gy pm
- Small pelvis: 1.6 Gy am
- Tumor boost: 1.5 Gy pm, 40.3 Gy

**Consolidation**
- Small pelvis: 1.5 Gy bid, 8 days, 24.0 Gy

Total Dose to Bladder Tumor: 64.3 Gy
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
## Baseline characteristics

<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>Age (years)</strong></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><strong>Gender</strong></td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Male</td>
<td>89 ( 88.1%)</td>
<td>16 ( 88.9%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12 (11.9%)</td>
<td>2 (11.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Zubrod Performance Score</strong></td>
<td></td>
<td></td>
<td>0.29</td>
</tr>
<tr>
<td>0</td>
<td>96 (95.0%)</td>
<td>16 (88.9%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5 (5.0%)</td>
<td>2 (11.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>T stage</strong></td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>T2</td>
<td>94 (93.1%)</td>
<td>17 (94.4%)</td>
<td></td>
</tr>
<tr>
<td>T3-T4</td>
<td>7 (6.9%)</td>
<td>1 (5.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Q1 = first quartile; Q3 = third quartile.

*Fisher’s exact test is used*
Overall Survival

Overall Survival (%)

Years after Randomization

Patients at Risk

T0

Tis/Ta

Dead

Total

p = 0.1198 (Log-Rank)
## Bladder Recurrence

<table>
<thead>
<tr>
<th>Any Bladder Recurrence</th>
<th>T0 (n=101)</th>
<th>Tis/Ta (n=18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>65 (64.4%)</td>
<td>13 (72.2%)</td>
<td>0.52</td>
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<tr>
<td>Yes</td>
<td>36 (35.6%)</td>
<td>5 (27.8%)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Invasive Bladder Recurrence</th>
<th>T0 (n=36)</th>
<th>Tis/Ta (n=5)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>13 (36.1%)</td>
<td>1 (20.0%)</td>
<td>0.53</td>
</tr>
<tr>
<td>No</td>
<td>19 (52.8%)</td>
<td>4 (80.0%)</td>
<td></td>
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</tbody>
</table>
Conclusion

• 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 RTOG and CCOP institutions
• RTOG HQ Staff
• Patients and their families