Urothelial recurrences in patients with invasive urothelial cancers

Brant A. Inman, MD, MS
Cary N. Robertson Associate Professor
Vice Chief of Urology
Scenario 1: the NMIBC recurrence

- Did the patient fail the clinical trial?
- If not, can they get BCG?
  - What about synergistic toxicity?
  - What about synergistic efficacy?
  - Will biomarkers be affected (if assessed)?

Nephroureterectomy
pT3N1(1/12)M0R0
(12/2/2016)

Clinical trial – Adjuvant Checkpoint inhibitor
(1/12/2017)

TURBT
pTa, HG
(4/8/2017)
Scenario 2: the upper tract recurrence

- Did the patient fail the clinical trial?
- If not, nephroureterectomy?
  - What about synergistic toxicity?
  - What about treatment interruption?
  - Will biomarkers be affected (if assessed)?
Defining treatment failure is important

- Urothelial recurrences are common
  - The entire urothelium is at risk
  - Do they always represent a treatment failure?

- “Treatment failure” has consequences
  - Experimental treatment usually stops
  - Risk group changes (e.g., 1st vs 2nd line)
  - Options shrink

- Consistency is an important goal
  - Does your treatment failure definition vary?
### How common are urothelial recurrences?

<table>
<thead>
<tr>
<th>Recurrence location</th>
<th>Bladder (RC)</th>
<th>Bladder (ChemoRT)</th>
<th>Upper tract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>-</td>
<td>15% ≤T1</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20% ≥T2</td>
<td></td>
</tr>
<tr>
<td>Upper tract</td>
<td>5%</td>
<td>?</td>
<td>5%</td>
</tr>
<tr>
<td>Urethra</td>
<td>4%</td>
<td>?</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

# Urothelial recurrences after cystectomy

<table>
<thead>
<tr>
<th></th>
<th>Upper tract</th>
<th>Urethra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected by screening</td>
<td>1/3 (imaging)</td>
<td>1/3 (cytology)</td>
</tr>
<tr>
<td>Time to recurrence</td>
<td>3 years</td>
<td>1 year</td>
</tr>
<tr>
<td>Urothelium only</td>
<td>90%</td>
<td>65%</td>
</tr>
<tr>
<td>+ metastases</td>
<td>10%</td>
<td>20%</td>
</tr>
<tr>
<td>+ pelvic disease</td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>Outcome @ 5y</td>
<td>55% die</td>
<td>45% die</td>
</tr>
</tbody>
</table>

Predictors of recurrence after cystectomy

<table>
<thead>
<tr>
<th>Upper tract</th>
<th>Urethra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multifocality</td>
<td></td>
</tr>
<tr>
<td>Tis/Ta/T1</td>
<td>Positive margin</td>
</tr>
<tr>
<td>T4</td>
<td>(urethra)</td>
</tr>
<tr>
<td>(ureter)</td>
<td></td>
</tr>
</tbody>
</table>

Urine tests affect recurrence detection

- **Upper tract**
  - Positive urine test + negative cystoscopy = more testing (imaging, retrogrades, ureteroscopy)

- **Urethra**
  - Positive urethral wash = more testing (imaging, biopsy, urethrectomy)

- **Implication**: standardization required to avoid bias

- **Guideline levels of evidence are low (opinion)**

Roupret et al. Eur Urol 2017; Chang et al. AUA 2017
Bladder recurrences after chemoradiation

• Two patterns:
  1. Muscle invasive (20%)
     • Early, old tumors resistant to therapy
  2. Non-muscle invasive (15%)
     • Later, ? new tumors

• Predictors of recurrence
  – Incomplete TURBT, ≥T3, hydronephrosis, CIS

Bladder recurrence after upper tract resection

• Median time = 2 years
• 55% ≤T1 and 45% ≥T2
• Predictors of recurrence:
  – Patients: male, history of BC, CKD
  – Tumor: ureter (vs renal pelvis), multifocal, ≥T2
  – Procedure: laparoscopic, postop instillation

Fradet et al. Urol Oncol 2014
Technique affects recurrence detection

• Enhanced endoscopy is better
  – Blue light (Cysview)
  – Narrow band imaging
• Random bladder biopsies?
• Implication: endoscopy standardization required on trial to avoid bias

How to define treatment failure on trial?

- **Option 1 (a.k.a. the pessimist)**
  - Any urothelial recurrence = progression event
  - Implication: urothelial recurrence pulls you off study

- **Option 2 (a.k.a. the optimist)**
  - Urothelial recurrence = recurrence event
  - Invasive urothelial recurrence (≥T2) = progression event
  - Implication: can treat ≤T1 and remain on trial
Thank you for your attention