Surgery:
Metastatic bladder cancer
(non organ confined)

Lee Lui Shiong
Senior Consultant and Head of Department, Department of Urology, Sengkang General Hospital
Senior Consultant, Department of Urology, Singapore General Hospital
Visiting Consultant, Surgical Oncology, National Cancer Centre

Lee.lui.shiong@singhealth.com.sg
Disclosures

• Advisory board
  – Janssen
  – Bayer
  – MSD
  – BMS
  – Astellas

• Clinical trial funding
  – Janssen
• Clinical N+
  – Below aortic bifurcation

• Clinical M1
• Most available evidence for surgery is case series

• Level III-IV

• The quality of imaging is crucial

• Choice limited by renal function

• FDG PET
  – Slightly better than CT for extravesical disease
  – Sensitivity 80%, sensitivity 90%

Eur J Radio 2012; 81: 2411-2416
Clinically N+

- Clinical N+ - systemic disease, poor prognosis

- Surgery alone with no systemic therapy
  - Relapse inevitable
  - Zehnder et al. median RFS 18 months
Clinical N+

• Consider neoadjuvant chemoTx
• Those with clinical response
  – Consider RC with LND

• SD or progressive disease
  – Poor prognosis
  – Surgery in selected patients
<table>
<thead>
<tr>
<th>Reports</th>
<th>Patients (n)</th>
<th>Study population</th>
<th>Chemotherapy</th>
<th>Surgery</th>
<th>Pathologic response rate</th>
<th>Median follow up (mo)</th>
<th>Rate (%)</th>
<th>Median survival time (mo)</th>
<th>Survival</th>
<th>Other findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herr et al [15] 2001</td>
<td>80</td>
<td>Unresectable or regionally metastatic BCa</td>
<td>MVAC: 75%</td>
<td>RC, PLND with or without RPLND</td>
<td>pCR: 62.5%</td>
<td>60</td>
<td>5-yr OS: 42%</td>
<td>NR</td>
<td>Complete response to CHT and surgery: 41%</td>
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<td>Nieuwenhuijzen et al. [12] 2005</td>
<td>52</td>
<td>Histologically proven pN+ by aspiration (40%) or by PLND (60%)</td>
<td>MVAC: 59%</td>
<td>RC with PLND: 19 (36.5%) Only RC 21 (40.4%)</td>
<td>pCR: 73%</td>
<td>68</td>
<td>Overall 5-yr CSS: 23%</td>
<td>15.4</td>
<td>cCR (HR 8) and post CHT of any, cN0 (HR 2.8) were independently associated with better CSS</td>
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<td>Kayouf et al. [16] 2009</td>
<td>37</td>
<td>pTX any, pN+ pts who received preoperative CHT. 18 (48.6%) pts were cN+</td>
<td>Platinum-based: 30</td>
<td>RC with PLND</td>
<td>All pN+ Only one pT0</td>
<td>50</td>
<td>2-yr OS: 20%</td>
<td>OS: 13</td>
<td>Variant histology was associated with shorter OS (p = 0.01) and RFS (p = 0.036) Female sex was associated with OS (HR 0.25, p = 0.006)</td>
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<td>Ghadjar et al. [17] 2011</td>
<td>30</td>
<td>T4cN0cM0: 20% ≤T4cN+cM0: 70% ≤T4cN0cM+: 10%</td>
<td>GC: 64%</td>
<td>RC with PLND</td>
<td>pCR (pT0: 30%)</td>
<td>28</td>
<td>5-yr DFS: 42%</td>
<td>NR</td>
<td>pT0 was significantly associated with both increased DFS (HR 0.08) and increased OS (HR 0.21)</td>
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<td>Meijer et al [13] 2014</td>
<td>149</td>
<td>cN+M0: 78% cNx, M1: 22%</td>
<td>MVAC: 21%</td>
<td>RC with PLND</td>
<td>pCR: 26.8%</td>
<td>57</td>
<td>Overall 5-yr CSS: 29.2%</td>
<td>CSS for total group: 20 CSS in cRR: 127 CSS in cCR: 36</td>
<td>In patients with cCR, residual disease was present in 38.5% pPR (HR 2.31) and pSD (HR 4.02) were independently associated with CSS pN0 (HR 6.8), absence of lymphovascular invasion (HR 3.3), negative surgical margins (HR 5.1) and more LN's removed (HR 3.0) were independent post surgical prognostic factors for OS in the surgical group</td>
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</table>
Mixed bag of N+ and M1
NAC -> RC + PLND
OS 25-46%
RFS 13-39%
Best responders: cCR, cT0, pN0, negative margins
N+ / M1 selection

• Surgical cohorts are selected
  – Good ECOG
  – Good response post NAC (cT0, cCR)
  – Surgically resectable

• Achieve negative margins at surgery

• Adequate LND

• Centralisation of expertise
Adequate LND
Poor prognosis of bladder cancer patients with occult lymph node metastases treated with neoadjuvant chemotherapy

Eugene K. Cha*, John P. Sfakianos†, Ranjit Sukhu†, Alyssa M. Yee*,

BJU Int 2018; 122: 627–632

NAC + RC -> node positive - worse outcome than
Upfront RC -> node positive -> AC
• Patient cohort post NAC with N+ at surgery
• Poor prognostic group

• Need adjuvant systemic therapy

• Clinical trials
Metastatectomy

• Mainly limited to lung only metastasis
• Benefits mainly those that are symptomatic, progression free survival

• Small cases series about OS benefit but highly selective cohort
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Patient Description</th>
<th>Treatment</th>
<th>Outcomes</th>
<th>Significance</th>
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<tbody>
<tr>
<td>Otto et al. 2001</td>
<td>70</td>
<td>Metastatic BCa refractory to CHT</td>
<td>M-VAC</td>
<td>3</td>
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<td>RC: 100% Pulmonary resection: 30% Peritoneal deposit resection: 14% Liver resection: 11%</td>
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<td>0%</td>
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<td>NR</td>
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<td>1-yr survival: 30% 2-yr survival: 19%</td>
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<td></td>
<td>Symptomatic patients: 73% Asymptomatic patients: 27% No survival advantage for surgery Perioperative mortality: 4%</td>
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<td>Abe et al. 2007</td>
<td>48</td>
<td>cM+ BCa (23), UTUC (16), synchronous BCa and UTUC (8), urethral carcinoma (1)</td>
<td>MVAC: 21% MEC: 63%</td>
<td>4</td>
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<td>Resection of the primary site: 75% Metastectomy: 21% (83% of them received preoperative CHT)</td>
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<td>Lung: 0% LN: 33%</td>
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<td>NR</td>
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<td>Whole cohort: 17 Patients who underwent metastectomy: 42 Patients who did not undergo metastectomy: 10</td>
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<td>Absence of liver, bone and local recurrence, ≥5 CHT cycles, and resection of metastasis were independent predictors of prolonged OS.</td>
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<td>Lehmann et al. 2009</td>
<td>44 patients</td>
<td>cM+ BCa (35) and UTUC (9)</td>
<td>Preoperative CHT: 50% Adjuvant CHT: 41%</td>
<td>NR</td>
<td>Surgery alone: 20.5% Surgery+CHT: 29.5% CHT+surgery: 36.4% CHT+surgery+CHT: 13.6%</td>
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<td>63</td>
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<td>5-yr OS survival from diagnosis: 28% 5-yr OS survival from metastasis resection: 27.7% 5-yr PFS survival from diagnosis: 23.6% 5-yr PFS survival from metastasis resection: 24%</td>
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<td>No perioperative death 7 patients survived &gt;2 yr and remained free from tumor progression Metastasis site: RPLN (57%), distant LN (11%), lung (18%) and other (14%)</td>
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<td>Nakagawa et al. 2013</td>
<td>114</td>
<td>Patients with local or distant recurrence after RC and PLND</td>
<td>Post recurrence platinum-based CHT: 53%</td>
<td>NR</td>
<td>Metastectomy: 11.4% Lung: 7% LN: 3% Ileal conduit: 0.8% Brain: 0.8%</td>
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<td>11a</td>
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<td>1-yr OS: 48% 3-yr OS: 12%</td>
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<td>11</td>
<td>Time to recurrence (≥1 yr, HR: 0.58), symptoms at recurrence (HR: 2.44), metastatic organs at recurrence (≥2, HR: 2.1), postrecurrence CHT (HR: 0.48) and metastasectomy (HR: 0.37) were independent predictors of postrecurrence OS</td>
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</table>
Palliative Procedures

- What are we palliating
- Pain, haematuria, obstruction
- Is there a least invasive option?

- Urinary diversion -> PCNs
- Urinary conduits – surgery and anastomosis
- Catheter/ ureteric stents not well tolerated
Selecting patients in 2019

• Clinical N+ patients
  – Upfront systemic therapy
  – Good responders cT0, cCR
  – Consolidate with RC and PLND

  – If N+ at PLND, need further systemic therapy -> clinical trials

• M1 patients
  – Highly selective
  – Limited to post NAC with excellent response
  – Metastatectomy – long disease free interval, solitary lung mets