THE ROLE OF SURGERY IN METASTATIC BLADDER CANCER

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I have no conflict of interest to disclose with this presentation
Metastatic/Unresectable BC: Definition

- "Bladder cancer invading into the pelvic or abdominal wall (T4b, N+/M+)

- The vast majority of these patients have incurable disease: even with Platinum based chemotherapy and the introduction of Immunotherapy the median OS is poor with 5-year survival of 15%
Metastatic Bladder Cancer

- Lymph-node metastasis diagnosed by Imaging (CT, CT-Pet, MRI, PSMA-CT)
- Metastases in distant organs (Lung, Liver, Cutaneous ....)
M+Disease: EAU Guidelines 2019 Recommendations

- Use Cis-platinum-containing combination chemotherapy with GC,MVAC, preferably with G-CSF,HD-MVAC with G-CSF or PCG  *(SR Strong)*
- Do not offer Carboplatin and non-platinum combination chemotherapy  *(SR Strong)*
- **First line treatment in patients ineligible (unfit) for Cisplatin:**
  Offer check-point inhibitors Pembrolizumab or Atezolizumab depending on PDL-1 status  *(SR Weak)*
  Offer carboplatin combination chemo if PD-L1 is neg  *(SR Strong)*
- **Second-line treatment:** offer checkpoint inhibitors Pembrolizumab or Atezolizumab to patients progressing during or after platinum-based combination chemotherapy for M+ disease. Alternatively: clinical trials  *(SR Strong)*
Radical Local Surgery for M+ BCa: EAU Guidelines Recommendations 2019

- Offer radical cystectomy as palliative treatment to patients with inoperable locally advanced tumors (T4b) (*SR: Weak*)

- Offer palliative cystectomy to patients with symptoms (*SR Weak*)

- Intestinal or non-intestinal forms of urinary diversion can be used, with or without palliative Radical Cystectomy
ESMO Guidelines on Urogenital Cancer 2018: Management of Advanced and M+ Bladder Cancer

- Cisplatin-containing combination chemo with GC or MVAC is standard in pts. with advanced, surgical unresectable and M+ disease able to tolerate cisplatin
- High-dose intensity MVAC with G-CSF is an option for fit patients with limited advanced disease
- Paclitaxel plus GC should be considered in patients with the bladder as the primary disease origin
- Patients unfit for cisplatin-based chemo offer carbo-based regimen or single-agent taxane or Gem; recently the PD-1 Ab Pembrolizumab and Atezolizumab approved by EMA
- Nivolumab as monotherapy approved by EMA for these patients
- Palliative RT is an option to reduce symptoms such as pain and bleeding
- Surgery ....
  « Selected patients with locally advanced disease(T4b N1-2) may be offered cystectomy and lymph node dissection or definitive radiotherapy following systemic therapy»
Surgery for Locally Advanced (T3b-T4a), N+/M+ Bladder Cancer

- Is it feasible?........ Complication rate
- Is it indicated?
- Is the diagnosis always correct?
  Limitation of CT in the diagnosis of Lymphnode disease……
- In the elderly (>75)?
Clinical case: 71-y-old pt. with Tcc of the bladder involving GI tract (bowel occlusion), enlarged pelvic LNs at CT and T invading the pelvic wall considered unresectable by a Urological Center. Stage cT4bN+
Surgery
Radical cysectomy with extended LND. Resection of terminal ileum 30 cm from cecal valve and end to end ileal anastomosis. The tumor was stocked to the pelvic bone but not infiltrating Ureterocutaneostomy bilateral Omentum into the pelvis
Clinical Case

**Specimen:** Bladder with prostate and seminal vesicles

**Path. Report:**
TCCHG of the bladder invading the prostate and seminal vesicles bilat.
Invasion of the terminal ileum.
Margins negative
47 lymphnodes: obturator, internal, external, common iliac and pre-sacral nodes: **NO Cancer**

*Stage PT4aHG(G3)R0N0M0*
Unresectable Bladder Cancer

- The definition of unresectable tumor is relative. For surgeons with a great surgical experience, able to manage vascular damages, GI tract cancer infiltration (GI resections) and also bone invasion this term may not be appropriate.

- **However the question is not if the tumor is surgically resectable or not, but, if the indication for an aggressive major surgery exists**

- For these patients a multidisciplinary approach is a must. This involves urologists, general and vascular surgeons and orthopedics, sometime gynecologists and a **Pre-OP MDT EVALUATION by**

![Diagram showing the multidisciplinary team involved in the management of unresectable bladder cancer]
Unresectable Bladder Cancer

- **PATIENTS** related (co-morbidities, age)
- **TUMOUR** related (aggressive tumor biology or massive adjacent organ/pelvic/abdominal wall infiltration or N+/M+)
- **SURGEON** related (surgeon with insufficient experience) and Institution Type related
Rationale for Palliative RC and LND in T4bBC

- **Debulking** (removing the bladder with tumor and all the tissue in the pelvis together with the lymph-nodes) trying to have neg. margins
- **Reducing local recurrence**
- **Preventing further complications** (ureteral stenosis, bowel occlusion ....)
- **Improving QoL**
- **Survival ???**
RC AND E-LND FOR LOCALLY ADVANCED AND N+ TCC OF THE BLADDER: ONCOLOGICAL RESULTS
5-YEAR DS SURVIVAL IN LOCALLY ADVANCED AND M+ BLADDER CANCER WITH RC ALONE

- pT4: 28% - 36%
- N+: 19.9% - 35%

- Studer U et al JCO 2003
- Nishiyama et al Eur. Urol 2004
- Hautmann et al J. Urol 2005
- Brausi et al Eur Urol 2014
- Wirth et al Eur Urol 2016
5-YEAR DS SURVIVAL IN LOCALLY ADVANCED AND M+ BLADDER CANCER AFTER RC AND RT-CT

pT4 : 19% - 50%

N+ : 23.4 % - 35%

Ghoneim et al J Urol 1997
Stein JP et al JCO 2001
Fair W et al Eur Urol 2002

Conclusions: RC may have a role in these patients (pT4b, N+)
Rationale of an E-LND

- Removing a larger number of pelvic lymph nodes during cystectomy is strongly correlated with improved overall survival both in lymph node negative and lymph node positive metastasis

- Vieweg J et al J Urol 1999
- Lerner SP et al J Urol 1993
- Mills RD et al J Urol 2001
- Stein JP et al BJU Int 2003
- Herr HW et al Urology 2003
LND

**Limited**: nodes of the obturator fossa

**Extended**: obturator, int., ext, common iliac, presacral.

**Super-Extended**: until the aortic bifurcation (Brausi 2018)

**Super-Super Extended**: until the inf. mesenteric artery

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Roth B  
Eur Urol 57 : 205, 2010
- Extended LND in patient with T4b bladder cancer (Brausi et al 2014)
- Extended LND in patient with T4b bladder cancer (Brausi 2014)
In T4b/N+ BC LND can be extended to the periaortic/pericaval interaortocaval space
<table>
<thead>
<tr>
<th>Variable</th>
<th>Survival</th>
<th>Local Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At Risk</td>
<td>Deaths</td>
</tr>
<tr>
<td>PLND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>Limited</td>
<td>98</td>
<td>63</td>
</tr>
<tr>
<td>Standard</td>
<td>146</td>
<td>79</td>
</tr>
<tr>
<td>Surgeon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urologist</td>
<td>153</td>
<td>98</td>
</tr>
<tr>
<td>Urologic oncologist</td>
<td>115</td>
<td>61</td>
</tr>
<tr>
<td>Institution type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Academic</td>
<td>137</td>
<td>72</td>
</tr>
<tr>
<td>Community</td>
<td>84</td>
<td>52</td>
</tr>
<tr>
<td>VA/military</td>
<td>47</td>
<td>35</td>
</tr>
<tr>
<td>Urinary diversion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileal Conduit</td>
<td>191</td>
<td>126</td>
</tr>
<tr>
<td>Continent stoma or orthotopic</td>
<td>77</td>
<td>33</td>
</tr>
</tbody>
</table>

H.W. Herr et al., J Clin Oncol 22:2781-2789, 2004
Recurrence after RC in Locally Advanced BC

- **The recurrence rate in T3-T4 BCs is high even if an extended surgery is performed.**
- 5-y RR in 1110 patients treated with RC and LND:
  - For T3 = 56%  **T4 = 64%**. Local R = 21.5%  Distant R = 69%  Secondary UC = 9.5%
  - Peritoneal carinomatosis : 5.1%
- 5-y RR in
  - N0 patients  = 33%
  - N1  = 62%
  - N2  = 75%
- About 50% of patients died within 1 year after recurrence
  - Median CSM after recurrence : 18 mos
  - *(Moschini et al EJSO 2016)*
Locally-advanced/Metastatic UBC (T4b, T\text{any}N+, T\text{any}N\text{any}M+)

“Induction” systemic therapy

Post-operative “adjuvant” systemic therapy

surgical/radiotherapy options

Stratification according to the extent of metastatic disease:
- T4b/cN+ (curative window?)
- cM+ (e.g., palliative cystectomy, metastasectomy)
Neo-Adjuvant Chemo Improves Survival for Patients with MIBC: Level 1 Evidence

Only about 20% of eligible patients receive the recommended care.

Winquist et al, J Urol 171:561, 2004
Which Chemotherapy

- **DD-MVAC and GP** are considered nowadays standard regimens for patients with metastatic urothelial cancer and normal renal function (EAU-AUA Guidelines 2017-2018)
Is NAC For Everyone?

- Meta-analysis reveals only a modest benefit for NAC and only 20-25% of unselected patients benefit.

- We cannot yet predict response prior to treatment and only those that respond dramatically benefit (30-40%). *(This would be acceptable if chemo was free from cost and toxicity).*

- In this era of precision medicine we should try to select patients who can be eligible for chemo
Genetic Alterations Predicting Response to Chemotherapy

- **ERBB2** mutations characterize a subgroup of muscle invasive bladder cancers with excellent response to neo-adjuvant chemotherapy
  
  Groenendijk FH et al Eur Urol 2016;69:384

- Alterations in ATM, RB1 and FANCC correlates with survival after NAC
  
  Van Allen, Cancer Discov 2014, Plimack, Eur Urol 2015
MDACC: 3 molecular subtypes of MIBC

Validated in 3 independent cohorts.

Choi et al, Cancer Cell 2014
Molecular Subtypes

- Basal versus Luminal
  - GSC, UNC, MDA, TCGA, Lund

- Basal tumors most sensitive to neoadjuvant chemotherapy

https://media.nature.com/full/nature-assets/nrurol/journal/v11/n7/images/nrurol.2014.129-f2.jpg
Survival for Basal Tumors Improved by NAC

Post Chemo Surgery in Patients with Unresectable or Regionally Metastatic Bladder Cancer
Herr et al J.Urol 2001

- Population:
  207 pts. with unresectable or regionally metastatic BC
  80/207 (39%) received surgery after chemo (Platinum based)

- Objective
  To assess the CR rate and Relapse-free Survival

- Results
  24/80 cases (30%) had a pathologically confirmed CR after Chemo.
  14/24 (58%) pts survived from 9 mos to 5 years
  Residual cancer was completely re-resected in 49 pts (61%) with a CR rate
  20 pts (41%) survived
  Post-Chemo surgery did not benefit those who failed to achieve a major Complete or Partial response to chemo

- Only 1/12 pts (8%) who refused surgery remained alive
THE ROLE OF CONSOLIDATIVE SURGERY IN PATIENTS WITH REGIONALLY METASTATIC BC

- Chemotherapy + Surgery in highly selected patients: 5-year survival = 24%
- Phase II study: Retroperitoneal LND in patients who responded to chemo:
  Results: 4-year DSS and RF Survival: 36% and 27%
- Clinically N+ BC who received Chemo + Surgery: 5-year survival = 29%.
  Median CSS rate: 22 months
- Clinically N+ BC who received Chemo + Surgery: 5-year survival = 66%

- De Vries et al Eur J Surg 2009
- Sweeney et al J Urol 2003
- Meiyer et al Urology 2013
- Ho et al Urol Oncol 2015
Conclusion: In well selected patients with UC like those who achieved a clinical benefit with chemotherapy and had nodal metastatic disease, there was a survival advantage in removal of disease residuals.
Effectiveness of Post Chemo-LND

The Role of Surgery in Metastatic Bladder Cancer: A Systematic Review
Abufaraj et al Eur Urol 2018

- **Objective**
The contemporary literature on the surgical management of metastatic BCa and factors associated with outcomes to support the development of clinical guidelines as well as informed clinical decision-making was reviewed

- **Evidence acquisition**
A systematic search of English language literature using PubMed-Medline and Scopus from 1999 to 2016 was performed
<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>Survival</th>
<th>Median survival time (mo)</th>
<th>Other findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bekku et al. 2013 [23]</td>
<td>Original cohort: 47 Study population: 12</td>
<td>Patients with cPR to CHT who underwent surgery, cM+ BcA (8) and UTUC (4)</td>
<td>GCP/MVAC 9 (75%) patients received adjuvant CHT</td>
<td>3</td>
<td>cCR: 9% cPR: 57%</td>
<td>Primary surgery: 50% RPLND: 83% Pulmonary resection: 17%</td>
<td>pCR after RPLND: 8 (80%) patients who underwent salvage surgery: 39.8% 3-year PFS without salvage surgery: 0% 3-year OS in surgery group: 71.6% 3-year OS without surgery group: 12.1%</td>
<td>33.6</td>
<td>3-year PFS in patients with pulmonary metastasis: one (50%) patient</td>
<td>Time to progression in patients undergoing salvage surgery: 23 CSS in patients undergoing salvage surgery: 47.2</td>
</tr>
<tr>
<td>Sweeney et al. 2003 [35]</td>
<td>11</td>
<td>cM1 BcA patients</td>
<td>Not standardized</td>
<td>8</td>
<td>cCR: 8.5% cPR: 57.4%</td>
<td>RC, PLND and bilateral RPLND concurrent RC and RPLND: 64%</td>
<td>18%</td>
<td>4-year CSS: 36% 4-year RFS: 27%</td>
<td>Time to recurrence: 7 RFS: 7 CSS: 14</td>
<td>No perioperative mortality Viable tumor in ≥2 LNs correlated with better CSS and RFS</td>
</tr>
<tr>
<td>De Vries et al. 2009 [36]</td>
<td>14</td>
<td>cM1 BcA patients</td>
<td>MVAC: 57% HD-MVAC: 36% GC: 7%</td>
<td>4</td>
<td>cCR: 36% cPR: 64%</td>
<td>RC, PLND, and bilateral RPLND</td>
<td>pCR: 80% In cPR: pCR in bladder: 33% pCR in LN: 56%</td>
<td>30</td>
<td>3-year survival: 36% 5-year survival: 24%</td>
<td>10.1</td>
</tr>
<tr>
<td>Necchi et al. 2013 [37]</td>
<td>Original cohort: 59 Study population: 28</td>
<td>Locally advanced or metastatic BcA (17) and UTUC (11) with at least SD post CHT</td>
<td>Modified MVAC</td>
<td>4-6</td>
<td>cCR: 25% cPR: 61% SD: 14%</td>
<td>PLND: 14 RPLND: 11 Both: 3</td>
<td>28.6%</td>
<td>5-year PFS: 35.2% 5-year OS: 48.7%</td>
<td>PFS: 18 OS: 37</td>
<td>cCR was independent predictor of PFS (HR: 2.42) Post CHT surgery was independently associated with better PFS (HR 0.43) and OS (HR 0.37); pCR did not affect PFS or OS (p = 0.1 and 0.3, respectively)</td>
</tr>
<tr>
<td>Abe et al. 2014 [31]</td>
<td>42</td>
<td>cM+ BcA: 21, UTUC: 18 synchronous BcA and UTUC: 3</td>
<td>MVAC Preoperative CHT: 91% Adjuvant CHT: 16%</td>
<td>RPLND 36% (below and above bifurcation of Aorta (40% and 60%), respectively) Distant LN: 12% Pulmonary resection: 29% Other: 33%</td>
<td>29%</td>
<td>For all patients: 28 For metastasectomy group: 22</td>
<td>5-year OS after metastasectomy: 31% OS for all patients: 29 OS from metastasectomy: 26</td>
<td>No perioperative mortality Patient who had metastasectomy in solitary LN or solitary lung lesion had significantly longer survival (81 vs 19 mo)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The Role of Surgery in metastatic Bladder Cancer: A Systematic Review
Abufaraj et al Eur Urol 2018

- **Results**
  - The beneficial role of consolidation surgery in metastatic BCa is still unproven.
  - In presence of clinically evident lymphnode metastasis data suggest a survival advantage for pts. undergoing Post-chemo RC with e-LND, especially in those with measurable response to chemo.
  - Intra-op enlarged pelvic lymphnodes should be removed
  - Cytoreductive RC as local treatment could have a role

- Anecdotal reports of resection of pulmonary metastasis as part of multimodal approach suggest possible improved survival in well-selected patients
Surgey after Chemotherapy in N+ Bladder Cancer may have a role: Prerequisites

- 1. Good response to chemotherapy
- 2. Patient fit or accepting surgery (age is important)
- 3. Expert surgeon (removal of all the lymphatic tissue.. The N of nodes removed is a surrogate of extended surgery > 20-30)
Metastasectomy in UC: Objectives

- Cytoreduction
- “Immunosurgery”
- Subtyping
Surgery for Metastatic Urothelial Carcinoma with Curative Intent: The German Experience (AUO AB/05)

Objective:
to examine the role of surgery in older patients (> 70 y-old) with Urothelial Carcinoma in SEER DATA BASE

Methods:
70,648 patients with UC reviewed.
497 patients had at least one surgery to remove a metastatic lesion during a median follow-up of 40 months

Results:
The median OS after surgery : 19 months
3-year survival : 33%
Median length of Hospital Stay: 7 days
Complication rate: 10%

Conclusions:
In well selected patients with UC with a reasonable LE resection of M+ site is safe and associated with long-term survival and potential cures
Survival after Metastasectomy for Metastatic Urothelial Carcinoma: A Systematic Review and Meta-Analysis

Vaibhav Patel*a,1, Ana Collazo Lorduyb,c,1, Aaron Stern*, Omar Fahmyd, Rachel Pinotti*, Matthew D. Galsky* and Georgios Gakis*

Survival Improved by 37% with surgery

Bladder Cancer 2017

Table 2
Pooled patient characteristics across 17 included studies

<table>
<thead>
<tr>
<th>Type of study</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>412</td>
</tr>
<tr>
<td>Demographics, N (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>288(70)</td>
</tr>
<tr>
<td>Mean age</td>
<td>62</td>
</tr>
<tr>
<td>Tumor location, N (%)</td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>309(75)</td>
</tr>
<tr>
<td>Othera</td>
<td>103(25)</td>
</tr>
<tr>
<td>Number of metastases, N (%)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>148(36)</td>
</tr>
<tr>
<td>Single</td>
<td>148(36)</td>
</tr>
<tr>
<td>Not reported</td>
<td>116(28)</td>
</tr>
<tr>
<td>Sites of metastasectomy, N</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>181</td>
</tr>
<tr>
<td>Bone</td>
<td>21</td>
</tr>
<tr>
<td>Liver</td>
<td>16</td>
</tr>
<tr>
<td>Distant lymph nodes</td>
<td>118</td>
</tr>
<tr>
<td>Other</td>
<td>47</td>
</tr>
<tr>
<td>Peri-operative chemotherapy, N (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>325(79)</td>
</tr>
<tr>
<td>No</td>
<td>66(16)</td>
</tr>
<tr>
<td>Not reported</td>
<td>21(5)</td>
</tr>
<tr>
<td>Type of chemotherapy, N (%)</td>
<td></td>
</tr>
<tr>
<td>Platinum-based chemotherapy</td>
<td>304(88)</td>
</tr>
<tr>
<td>Other</td>
<td>21(6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>21(6)</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>Mean time from initial surgery to metastasectomyb</td>
<td>19 months</td>
</tr>
<tr>
<td>Mean time for relapse after metastasectomyc</td>
<td>14.3 months</td>
</tr>
</tbody>
</table>

a = upper tract or urethra.  b = available for 7 out of 17 studies.  c = available for 9 out of 17 studies.
LN Metastasis in the R pelvis after 3 years of RC .. without LND: he received e-LND and resection of the ileum + ileum anastomosis
ADJUVANT CHEMOTHERAPY (AC)
## Adjuvant Therapy: Current Status

![Survival benefit: None - 29%](image)

<table>
<thead>
<tr>
<th>Study (year of publication)</th>
<th>TNM stage eligibility criteria (percentage of patients)</th>
<th>Planned enrolment (n)</th>
<th>Patients randomized (n)</th>
<th>Treatments (n)</th>
<th>Survival benefits demonstrated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paz-Ares et al.(^\text{23}) (2010)</td>
<td>pT3–4N0 (44%) and/or anyTpN+ (56%)</td>
<td>340</td>
<td>142</td>
<td>PCG (68) versus observation (74)</td>
<td>PCG improved DFS (P&lt;0.0001), DSS (P&lt;0.0002), and 5-year OS (60% versus 31%; P&lt;0.0009)*</td>
</tr>
<tr>
<td>Stadler et al.(^\text{24}) (2011)</td>
<td>pT1–2N0M0(^\text{+})</td>
<td>190</td>
<td>114</td>
<td>MVAC (58) versus observation (56)</td>
<td>None; DFS HR 0.78 (P = 0.62)</td>
</tr>
<tr>
<td>Cognetti et al.(^\text{25}) (2012)</td>
<td>pT2N0–2 grade 3, pT3–4N0–2, or anyTpN1–2</td>
<td>350</td>
<td>194</td>
<td>GC (102) versus observation (92)</td>
<td>None; 5-year DFS 37.2% versus 42.3% (P = 0.70); 5-year OS 43.4% versus 53.7% (P = 0.24)</td>
</tr>
<tr>
<td>Sternberg et al.(^\text{26}) (2015)</td>
<td>pT3–4N0 and/or anyTpN+</td>
<td>1,344/660(^\text{1})</td>
<td>284</td>
<td>GC, MVAC, or ddMVAC (141) versus deferred chemotherapy at relapse (143)</td>
<td>DFS only; median DFS was 3.1 years versus 0.99 years (HR 0.54, P&lt;0.0001), and 5-year DFS was 47.6% versus 31.8%; 5-year OS 54% versus 48%; 5-year DSS 39% versus 44% (P = 0.22)</td>
</tr>
</tbody>
</table>

\(^\text{ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; DFS, disease-free survival; DSS, disease-specific survival; GC, gemcitabine and cisplatin; HR, hazard ratio; MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin; n, number of patients; OS, overall survival; PCG, paclitaxel, cisplatin, and gemcitabine.}^\text{*Results presented only in abstract form.}^\text{1All patients had tumours with ≥10% nuclear reactivity for p53 on immunohistochemical analysis.}^\text{2Trial was terminated early for futility.}^\text{3Trial redesigned to reduce the target enrolment from 1,344 to 660 patients owing to poor patient accrual.}
Effectiveness of AC for Locally Advanced/N+ BC
Galsky et al JCO 2016

- **Aim**: to compare the effectiveness of AC vs O post RC in T3-4 pts. and/or pN positive

- **Methods**: National Cancer Data Base was used. OS was compared using propensity score (adjusted-stratified-weighted-matched) analyses based on patient facility and tumor-level characteristics.

  - 5,653 pts. met the inclusion criteria. 23% received AC post RC. AC pts. were younger, private insurance, higher median income, higher rate of high-school-educated, LN involvement and +SM (P< 0.05 for all comparison)
Effectiveness of AC for Locally Advanced BC

Glasky et al JCO 2016

- **Results**
  - The median F-up was 6.8 yrs in AC group vs 6.7 yrs in O group
  - 5-year OS : AC = 37% vs 29.1% O (P < 0.001)

- **Conclusions**: «In this observational study AC was associated with improved survival in patients with locally advanced BC»
Conclusions

- A multidisciplinary approach to locally advanced, N+, M+ bladder cancer is a must *(Onco Units)*
- An accurate diagnosis of the disease extension (LNs at CT) is difficult and sometime misleading
- NAC should be proposed as the first line treatment in these patients
- Post-Chemo RC with E-LND is the treatment of choice for patients with locally advanced BC and N+ who achieve a CR or PR
- The rationale for a palliative aggressive surgery (debulking, reducing RR and possible future complications) is strong
- Metastasectomy is an option and usefull in patients with solitary mets