

BLADDER CANCER

The selection, dosing, and administration of anti-cancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anti-cancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The chemotherapy regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

General treatment notes:

- NCCN recommends considering neoadjuvant and adjuvant chemotherapy based on risk factors and nodal status.¹
- No standard second-line therapy exists for metastatic bladder cancer; enrollment in clinical trials recommended.

REGIMEN

DOSING

First-Line Chemotherapy (Neoadjuvant, Adjuvant, and Metastatic)

Gemcitabine (Gemzar) + cisplatin (Platinol; CDDP) ^{1,2}	Days 1, 8 and 15: Gemcitabine 1,000mg/m ² IV over 30–60 min, plus Day 2: Gemcitabine 1,000mg/m ² IV over 30–60 min + cisplatin 70mg/m ² . Repeat cycle every 4 weeks. *Standard first-line regimen for most patients; similar ORR, PFS and overall survival as MVAC, but more favorable safety profile.
MVAC (methotrexate [MTX] + vinblastine [Velban] + doxorubicin [Adriamycin]) ^{1,2}	Days 1, 15 and 22: Methotrexate 30mg/m ² IV, plus Days 2, 15 and 22: Vinblastine 3mg/m ² IV, plus Day 2: Doxorubicin 30mg/m ² IV and cisplatin 70mg/m ² IV as a 1–8 hr infusion. Repeat cycle every 4 weeks.
CMV (cisplatin + methotrexate + vinblastine) ³	Day 1: Methotrexate 30mg/m ² IV bolus + vinblastine 4mg/m ² IV bolus, followed by Day 2: Cisplatin 100mg/m ² IV infusion before hydration; followed by folinic acid 15mg IV or orally after hydration, administered 24 hrs after methotrexate every 6 hrs for 4 doses, followed by Day 8: Methotrexate 30mg/m ² IV bolus + vinblastine 4mg/m ² IV bolus, followed by Day 9: Folinic acid 15mg IV or orally every 6 hrs for 4 doses. Repeat cycle every 3 weeks for 3 cycles.

Renal Impairment or Comorbidities

Split dose cisplatin ¹	Days 1 and 2 OR Days 1 and 8: Cisplatin 35mg/m ² . *For patients with borderline/minimal renal dysfunction.
Doxorubicin + gemcitabine and paclitaxel (Taxol) + carboplatin (Paraplatin) ⁴	Sequential doublets of doxorubicin 50mg/m ² IV + gemcitabine 2,000mg/m ² IV every other week for 5 cycles followed by Paclitaxel 65mg/m ² IV + carboplatin AUC=1.7mg/mL/min IV weekly for 12 cycles.

Second-Line Chemotherapy (Metastatic)

Palliative single-agent treatment ¹	<table style="width: 100%; border: none;"> <tr> <td style="width: 33%;">Bleomycin (Blenoxane)</td> <td style="width: 33%;">Doxorubicin</td> <td style="width: 33%;">Methotrexate</td> </tr> <tr> <td>Carboplatin</td> <td>5-fluorouracil (5-FU)</td> <td>Paclitaxel</td> </tr> <tr> <td>Cisplatin</td> <td>Gemcitabine</td> <td>Pemetrexed (Alimta)</td> </tr> <tr> <td>Docetaxel (Taxotere)</td> <td>Ifosfamide (Ifex)</td> <td>Vinblastine</td> </tr> </table>	Bleomycin (Blenoxane)	Doxorubicin	Methotrexate	Carboplatin	5-fluorouracil (5-FU)	Paclitaxel	Cisplatin	Gemcitabine	Pemetrexed (Alimta)	Docetaxel (Taxotere)	Ifosfamide (Ifex)	Vinblastine
Bleomycin (Blenoxane)	Doxorubicin	Methotrexate											
Carboplatin	5-fluorouracil (5-FU)	Paclitaxel											
Cisplatin	Gemcitabine	Pemetrexed (Alimta)											
Docetaxel (Taxotere)	Ifosfamide (Ifex)	Vinblastine											

First-Line Radiosensitizing Chemotherapy (Concurrent with radiotherapy for selective bladder preservation)

Cisplatin ± 5-FU ± paclitaxel ^{1, 5}	Age ≥70 and Karnofsky performance status (KPS) <80 Days 1 and 8: Cisplatin 35mg/m ² IV + 5-FU 2,000mg/m ² IV + leucovorin 300mg/m ² IV as a continuous infusion for 24 hrs. Repeat every 3 weeks for 3 cycles. Age <70 and Karnofsky performance status (KPS) ≥80 Days 1 and 8: Paclitaxel 70mg/m ² IV over 1 hr, plus Days 2 and 9: Cisplatin 35mg/m ² IV + 5-FU 2,000mg/m ² IV + leucovorin 300mg/m ² IV as a continuous infusion for 24 hrs. Repeat every 3 weeks for 3 cycles.
Mitomycin C (Mutamycin; MTC) + 5-FU ^{1, 6, 7}	Day 1 of radiotherapy: Mitomycin 12mg/m ² IV, plus Week 1 (f1–5) and Week 4 (f16–20) of radiotherapy: 5-FU 500mg/m ² continuous IV infusion (10 days total).

References

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| <ol style="list-style-type: none"> 1. NCCN Clinical Practice Guidelines in Oncology™. Bladder Cancer. v 2.2011. Available at: http://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed March 25, 2011. 2. von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. <i>J Clin Oncol</i>. 2005; 23:4602–4608. 3. International Collaboration of Trialists on behalf of the Medical Research Council Advanced Bladder Cancer Working Party (now the National Cancer Research Institute Bladder Cancer Clinical Studies Group), the European Organisation for Research and Treatment. International Phase III Trial Assessing Neoadjuvant Cisplatin, Methotrexate, and Vinblastine Chemotherapy for Muscle-Invasive Bladder Cancer: Long-Term Results of the BA06 30894 Trial. <i>J Clin Oncol</i>. 2011;29:2171–2177. 4. Galsky MD, Iasonos A, Mironov S, Scattergood J, Boyle MG, Bajorin DF. Phase II trial of dose-dense doxorubicin plus | <p>gemcitabine followed by paclitaxel plus carboplatin in patients with advanced urothelial carcinoma and impaired renal function. <i>Cancer</i>. 2007;109:549–555.</p> <ol style="list-style-type: none"> 5. Lin CC, Hsu CH, Cheng JC, et al. Induction cisplatin and fluorouracil-based chemotherapy followed by concurrent chemoradiation for muscle-invasive bladder cancer. <i>Int J Radiat Oncol Biol Phys</i>. 2009;75:442–448. 6. Hussain SA, Stocken DD, Peake DR, et al. Long-term results of a phase II study of synchronous chemoradiotherapy in advanced muscle invasive bladder cancer. <i>Br J Cancer</i>. 2004; 90:2106–2111. 7. James ND, Hussain SA, Hall E, et al. Results of a phase III randomized trial of synchronous chemoradiotherapy (CRT) compared to radiotherapy (RT) alone in muscle-invasive bladder cancer (MIBC) (BC2001 CRUK/01/004). <i>J Clin Oncol</i>. 2010; 28(suppl 15):4517(abstract). |
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<p>1. NCCN Clinical Practice Guidelines in Oncology™. Bladder Cancer. v 2.2011. Available at: http://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed March 25, 2011.</p> <p>2. von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. <i>J Clin Oncol.</i> 2005; 23:4602–4608.</p> <p>3. International Collaboration of Trialists on behalf of the Medical Research Council Advanced Bladder Cancer Working Party (now the National Cancer Research Institute Bladder Cancer Clinical Studies Group), the European Organisation for Research and Treatment. International Phase III Trial Assessing Neoadjuvant Cisplatin, Methotrexate, and Vinblastine Chemotherapy for Muscle-Invasive Bladder Cancer: Long-Term Results of the BA06 30894 Trial. <i>J Clin Oncol.</i> 2011;29:2171-2177.</p> <p>4. Galsky MD, Iasonos A, Mironov S, Scattergood J, Boyle MG, Bajorin DF. Phase II trial of dose-dense doxorubicin plus</p>	<p>gemcitabine followed by paclitaxel plus carboplatin in patients with advanced urothelial carcinoma and impaired renal function. <i>Cancer.</i> 2007;109:549–555.</p> <p>5. Lin CC, Hsu CH, Cheng JC, et al. Induction cisplatin and fluorouracil-based chemotherapy followed by concurrent chemoradiation for muscle-invasive bladder cancer. <i>Int J Radiat Oncol Biol Phys.</i> 2009;75:442–448.</p> <p>6. Hussain SA, Stocken DD, Peake DR, et al. Long-term results of a phase II study of synchronous chemoradiotherapy in advanced muscle invasive bladder cancer. <i>Br J Cancer.</i> 2004; 90:2106–2111.</p> <p>7. James ND, Hussain SA, Hall E, et al. Results of a phase III randomized trial of synchronous chemoradiotherapy (CRT) compared to radiotherapy (RT) alone in muscle-invasive bladder cancer (MIBC) (BC2001 CRUK/01/004). <i>J Clin Oncol.</i> 2010; 28(suppl 15):4517(abstract).</p>
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