

## Urothelial Cancer Guidance

The American Society of Clinical Oncology offers the following clinical guidance on treatment alternatives during shortages of antineoplastic agents. Decisions should be based on specific goals of the therapy where evidence-based medicine has shown survival outcomes and life-extending benefits in both early and advanced stages. For more information on ASCO's general principles during drug shortages, please visit ASCO's [Clinical Guidance page](#). For further consideration of ethical guidance, please visit ASCO's [Ethical Principles and Implementation Strategies page](#).

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\* Multiple factors can potentially limit the ability to safely receive cisplatin, including but not limited to comorbidities such as renal insufficiency, grade  $\geq 2$  neuropathy or hearing loss, symptomatic heart failure, and ECOG performance status  $\geq 2$ .<sup>1</sup>

### **1. Neoadjuvant Chemotherapy**

#### **A. Cisplatin eligible**

For patients who are eligible for cisplatin, recommended treatment options include:

- Dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC) with growth factor support
- Gemcitabine and cisplatin

ALTERNATIVES: While there are no other equally effective alternatives, other options include:

- Radical cystectomy alone
- Definitive radiation with concurrent chemotherapy (as an alternative to neoadjuvant chemotherapy followed by radical cystectomy in appropriately selected patients)

### **2. Adjuvant Therapy**

#### **A. Cisplatin eligible and no previous cisplatin-based neoadjuvant therapy**

Recommended options for patients with  $\geq$ ypT3 or pN+

- ddMVAC with growth factor support
- Gemcitabine and cisplatin

ALTERNATIVES: While there are no equally effective alternatives for this setting, other options include:

- Nivolumab<sup>2</sup>

- Nivolumab is recommended for patients with no previous platinum-based neoadjuvant therapy ( $\geq$ pT3 or pN+) or for patients with previous platinum-based neoadjuvant therapy ( $\geq$ ypT2 or pN+)

**B. Cisplatin eligible and previous cisplatin-based neoadjuvant therapy**

Recommended options for patients with  $\geq$ ypT2 or pN+

- Nivolumab<sup>2</sup>

**C. Cisplatin ineligible**

- I. Nivolumab
- II. For patients with upper tract disease who did not receive neoadjuvant cisplatin-based chemotherapy, gemcitabine plus carboplatin is an option<sup>3</sup>

**3. First-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)**

**A. Cisplatin eligible**

Recommended options:

- Gemcitabine and cisplatin followed by avelumab maintenance therapy
- ddMVAC with growth factor support followed by avelumab maintenance therapy

ALTERNATIVES:

- Enfortumab vedotin and pembrolizumab (EV/pembro)
- Pembrolizumab

**B. Cisplatin ineligible**

Recommended options:

- Gemcitabine and carboplatin followed by avelumab maintenance therapy
- Enfortumab vedotin and pembrolizumab (EV/pembro)

ALTERNATIVES:

- Pembrolizumab
- Gemcitabine
- Gemcitabine + paclitaxel
- Ifosfamide, doxorubicin, and gemcitabine are options for patients with good kidney function and good performance status

**4. Second-Line<sup>+</sup> Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)**

**A. After chemotherapy**

Recommended options:

- Pembrolizumab
- Nivolumab
- Avelumab
- Enfortumab Vedotin
- Enfortumab vedotin and pembrolizumab (EV/pembro)
- Erdafitinib (only in patients with FGFR2/3 alterations)
- Sacituzumab govitecan (SG)

**B. After first-line EV/Pembro**

- Gemcitabine/carboplatin

- Gemcitabine/cisplatin
- Erdafitinib (only in patients with FGFR2/3 alterations)
- SG

ALTERNATIVES:

- Docetaxel
- Gemcitabine
- Ifosfamide, doxorubicin, and gemcitabine for patients with good kidney function and good performance status

**2) After immune checkpoint inhibition alone**

- Enfortumab vedotin
- Gemcitabine/carboplatin
- Gemcitabine/cisplatin

ALTERNATIVES:

- Erdafitinib (only in patients with FGFR2/3 alterations)
- Sacituzumab govitecan
- Docetaxel
- Gemcitabine
- Ifosfamide, doxorubicin, and gemcitabine for patients with good kidney function and good performance status

**References**

1. Galsky MD, Hahn NM, Rosenberg J, et al: Treatment of Patients With Metastatic Urothelial Cancer “Unfit” for Cisplatin-Based Chemotherapy. *Journal of Clinical Oncology* 29:2432-2438, 2011
2. Bajorin DF, Witjes JA, Gschwend JE, et al: Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma. *New England Journal of Medicine* 384:2102-2114, 2021
3. Birtle A, Johnson M, Chester J, et al: Adjuvant chemotherapy in upper tract urothelial carcinoma (the POUT trial): a phase 3, open-label, randomised controlled trial. *Lancet* 395:1268-1277, 2020