Case Study Challenge in Advanced Bladder Cancer: Tailoring Treatment to Individual Patients

Key Clinical Summaries From a Leading Expert on Bladder Cancer

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In this video CE activity, Alison Birtle, FRCP, FRCR, MD, explores individualising first-line management of advanced bladder cancer. Watch at the URL below, or you may review the key clinical summaries of the most salient science presented as part of the activity.

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Activity Description and Educational Objectives
In this activity, an expert discusses tailoring treatments and individualising first-line management of advanced bladder cancer.

Upon completion of this activity, participants should be better able to:
- Assess the clinical implications of clinical trial data and real-world evidence evaluating available treatment regimens for the first-line management of advanced bladder cancer
- Formulate individualised management plans for the first-line management of advanced bladder cancer considering factors such as patient age, fitness, goals of therapy and eligibility for cisplatin and carboplatin

Target Audience
This activity has been designed to meet the educational needs of oncologists, urologists, and other clinicians involved in the management of patients with bladder cancer.

Accreditation
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Media: Enduring Material
Release and Expiration Dates: 8 July 2025 – 7 July 2027
Time to Complete: 30 minutes

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Tailoring First-Line Therapeutic Options for Patients With aUC

First-line therapeutic options for patients with advanced urothelial carcinoma (aUC) include platinum-based combination chemotherapy (PBC; gemcitabine plus cisplatin [GemCis] or gemcitabine plus carboplatin [GemCarbo]) followed by avelumab maintenance.

- This is based on the results of the JAVELIN BLADDER 100 that compared maintenance avelumab with best supportive care (BSC), in patients previously treated with 4 to 6 cycles of PBC, and whose disease did not progress at the end of chemotherapy treatment.[1]
- Long-term results of this study showed an approximately 25% reduction in the risk of death and a 45% reduction in the risk of progression in patients treated with avelumab maintenance vs BSC alone.[2]
- This therapeutic option has been the standard of care (SoC) for patients with aUC who can tolerate PBC. Patients not eligible for PBC include those who have a European Cooperative Oncology Group Performance Status (ECOG PS) of 3, a creatinine clearance (CrCl) of less than 30 mL/min, existing peripheral neuropathy (PN ≥2), or poor heart function (New York Heart Association Heart Failure [NYHA HF] class III).[3]
- Several real-world studies looking at the effectiveness of first-line maintenance therapy in patients with aUC mirror the results of the JAVELIN BLADDER 100 trial. As an example, a recent Japanese study with 453 patients presented at the 2025 Annual Meeting of the American Society of Clinical Oncology (ASCO) Symposium showed a 1-year overall survival (OS) rate of 78%.[4]

Atezolizumab or Pembrolizumab:

- These two agents are indicated for patients who are cisplatin ineligible and PD-L1–positive.
- Atezolizumab is no longer approved in the US but is still available in Europe for this indication, while pembrolizumab is approved in both the US and Europe for this indication.[5]

Enfortumab vedotin in combination with pembrolizumab (EV/P)

- This therapeutic combination is based on the results of the randomised EV-302 study, which compared the safety and efficacy of EV/P vs PBC (GemCis or GemCarbo). EV/P showed a 55% reduction in the risk of progression and a 53% reduction in the risk of death compared with PBC.[6]
- These results led to an update in the European Society for Clinical Oncology (ESMO) guidelines regarding the new SoC for first-line aUC.[7]
- The most common treatment-related adverse event (TRAE) with EV/P was peripheral neuropathy. TRAEs of grade 3 or higher included maculopapular rash, hyperglycaemia, and neutropenia (4.8%) in the EV/P group. In the chemotherapy group, TRAEs of grade 3 or higher included anaemia, neutropenia, and thrombocytopenia.[7]

Nivolumab (nivo) plus GemCis followed by nivo maintenance

- This therapeutic combination is based on the results of the CheckMate-901 study, which compared the safety and efficacy of nivo plus GemCis with GemCis as first-line treatment in cisplatin-eligible patients, followed by nivo maintenance after 6 cycles of initial therapy. The results showed a 22% reduction in the risk of death and a 28% reduction in the risk of progression.[8]
- Incidence of adverse events was similar between the two treatment arms, with the exception of immune-related events, which were reported at a higher frequency in the nivo plus GemCis group and included pruritus, rash, diarrhoea, and hypothyroidism.[8]
- Selecting the right treatment involves multiple considerations beyond clinical efficacy. Clinicians must weigh safety and side effect profiles, taking into account patient tolerability, treatment burden (eg, frequency of hospital visits), and individual preferences; in particular, the importance that many patients place on quality of life over survival. Guideline placement, strength of supporting evidence, and both financial and personal costs (including time off work for patients and caregivers) also play crucial roles. Additionally, treatment planning must consider subsequent options in the second-line setting.[9]

Reference(s):

1. Powles T et al. *N Engl J Med*. 2020;383:1218-1230.
2. Powles T et al. *J Clin Oncol*. 2023;41:3486-3492.
3. Gupta S et al. Defining "platinum-ineligible" patients with metastatic urothelial cancer (mUC). *JCO*. 2022;40:4577-4577.
4. Kikuchi E et al. 2025 Annual Meeting of the American Society of Clinical Oncology (ASCO) Symposium. Abstract 4561.
5. Vuky J et al. *J Clin Oncol*. 2020;38:2658-2666.
6. Powles T et al. *N Engl J Med*. 2024;390:875-888.
7. Powles T et al. *Ann Oncol*. 2024;35:485-490.
8. van der Heijden MS et al. *N Engl J Med*. 2023;389:1778-1789.
9. PeerVoice Activity; Alison Birtle, FRCP, FRCR, MD; June 2025.

Navigating First-Line Therapy for Advanced Urothelial Carcinoma in the Elderly: Two Clinical Scenarios

Two clinical cases of patients with locally advanced (LA)/metastatic urothelial carcinoma (UC) were presented and discussed.

Case 1:
Tara, a biologically fit 75-year-old woman with locally advanced bladder cancer and a solitary liver metastasis, presented as eligible for both platinum-based chemotherapy (PBC) and enfortumab vedotin plus pembrolizumab (EV/P). Despite her age, her robust European Cooperative Oncology Group Performance Status (ECOG PS; 0), daily activity level, and manageable comorbidities meant she was well placed for systemic treatment. Given her independence and distance from specialist care, the consultation focused on balancing treatment efficacy with logistical feasibility and support needs. While both EV/P and chemotherapy followed by switch maintenance avelumab were considered as viable treatment options, discussions centred on treatment scheduling, side effect management, and access to experienced centres for toxicity support. The clinician explored Tara's preferences, potential neuropathy risks, access to transportation, and her tolerance for uncertainty in the second-line setting. Ultimately, Tara opted for EV/P, prioritising maximum clinical benefit over logistical concerns. The shared decision-making process underscored the importance of tailoring therapy not just to biological eligibility, but also to a patient's lifestyle, support systems, and informed preferences.

Case 2:
Liam, an 81-year-old man with LA UC, presented with haematuria and back pain. Despite his age, he had a PS of 1 and frailty score of 3, but several comorbidities, including diabetes (requiring insulin), chronic kidney disease (CKD), anaemia, and pre-existing peripheral neuropathy. He was also the primary caregiver for his wife with dementia, which also impacted the feasibility of treatment logistics. While EV/P was considered, concerns around exacerbation of neuropathy and the potential for difficult-to-manage hyperglycaemia made this option less suitable. Instead, the preferred approach was gemcitabine plus carboplatin (GemCarbo), avoiding cisplatin due to neuropathy risk, followed by switch maintenance avelumab if disease control was achieved. This treatment choice balanced known toxicity profiles, logistical scheduling, and Liam's role as a caregiver. The decision was grounded in clinical appropriateness rather than chronological age, with an emphasis on aligning treatment with the patient's health status, life responsibilities, and manageable adverse effect expectations.

Reference(s):
PeerVoice Activity; Alison Birtle, FRCP, FRCR, MD; June 2025.
Powles T et al. *Ann Oncol.* 2024;35:485-490.
Powles T et al. *J Clin Oncol.* 2023;41:3486-3492.
Powles TB et al. *Ann Oncol.* 2025; May29:S0923-7534(25)00762-8. [Epub ahead of print].
Brower B et al. *Front Oncol.* 2024;14:1326715.

Therapeutic Individualisation in Urothelial Cancer: A Focus on Comorbidities and Patient Goals

Two clinical cases of patients with locally advanced (LA)/metastatic urothelial carcinoma (UC) were presented and discussed.

Case 1:
Christopher, a 56-year-old man with newly diagnosed metastatic micropapillary UC, initially declined treatment due to poor European Cooperative Oncology Group Performance Status (ECOG PS; 3), multiple comorbidities, and personal challenges, including chronic obstructive pulmonary disease (COPD), heart failure, substance dependence, and significant liver dysfunction. Following acute interventions (transurethral resection of bladder tumour [TURBT] and nephrostomies), his renal function stabilised, but he required transfusions due to recurrent haematuria. Although initially favouring best supportive care, a sensitive discussion clarified his limited prognosis and explored whether his decision was informed or fear-driven. Given his comorbidities and haematological fragility, enfortumab vedotin plus pembrolizumab (EV/P) was excluded, and gemcitabine plus carboplatin (GemCarbo) chemotherapy was cautiously administered in conjunction with palliative care. While he initially showed a positive clinical and radiological response, severe marrow suppression ultimately precluded further dosing or transition to maintenance immunotherapy. This case highlights the importance of nuanced, compassionate dialogue with patients who have complex needs and limited therapeutic windows, ensuring shared decision-making and integration of palliative support from the outset to align disease management with patient values and clinical realities.

Case 2:
Roger, an 83-year-old man with node-positive, LA UC (T4N1), presented with a strong desire for active treatment despite significant medical complexity. He had a history of polymyalgia rheumatica (inactive and steroid-free for 2 years), stable angina, and a critically low glomerular filtration rate (GFR) of 25 mL/min/1.73 m^2, rendering him unsuitable for EV/P or chemotherapy. His tumour was PD-L1–positive and he suffered from severe lower urinary tract symptoms, making radiotherapy poorly tolerated. With no viable chemotherapy options and concerns about his bladder capacity, a checkpoint inhibitor was considered. Given his stable autoimmune background and growing clinical experience supporting immunotherapy in such settings, he was offered atezolizumab in the UK (with pembrolizumab as an alternative where licensed). Roger accepted the potential risk of autoimmune flare, prioritising treatment. This case illustrates the importance of aligning therapy with patient preference and clinical constraints, embracing shared decision-making even in advanced age and comorbidity-laden scenarios.

Reference(s):
PeerVoice Activity; Alison Birtle, FRCP, FRCR, MD; June 2025.
Powles T et al. *Ann Oncol.* 2024;35:485-490.
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Vuky J et al. *J Clin Oncol.* 2020;38:2658-2666.

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