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Advanced urothelial carcinoma: Expert guidance to navigate an evolving therapeutic landscape

Practice aid for advanced urothelial carcinoma

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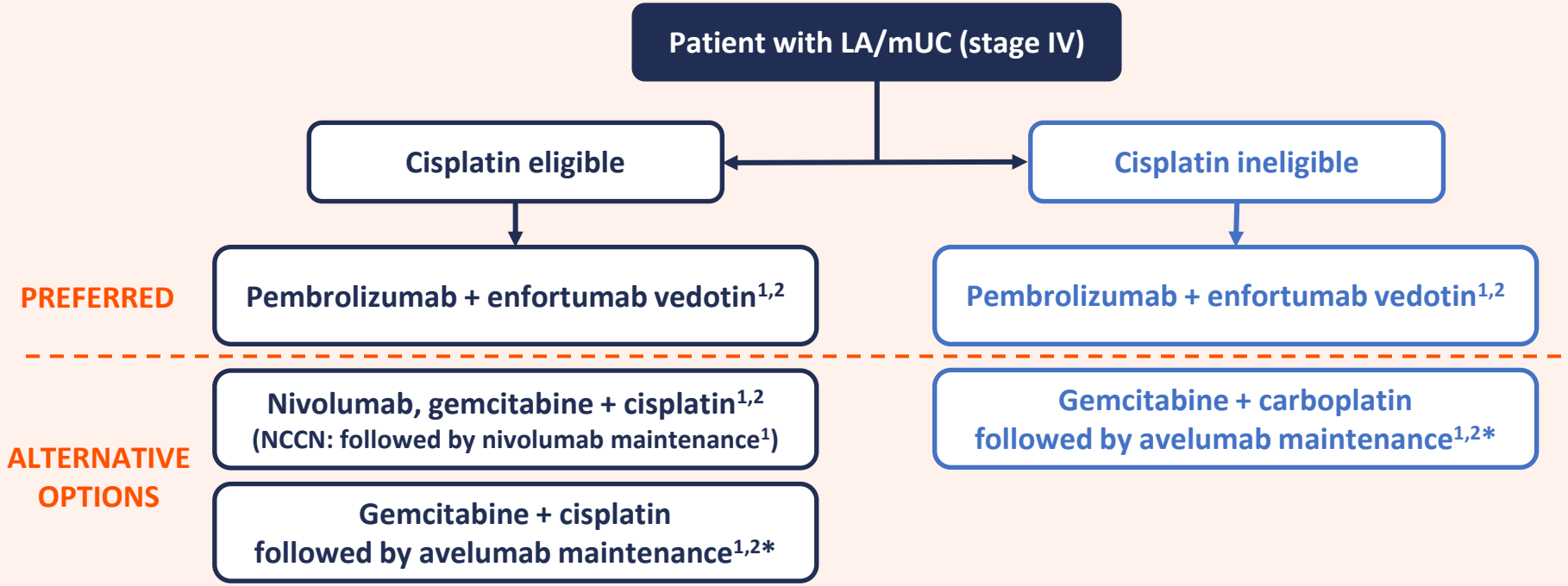
First-line treatment recommendations in ESMO and NCCN guidelines[1,2]

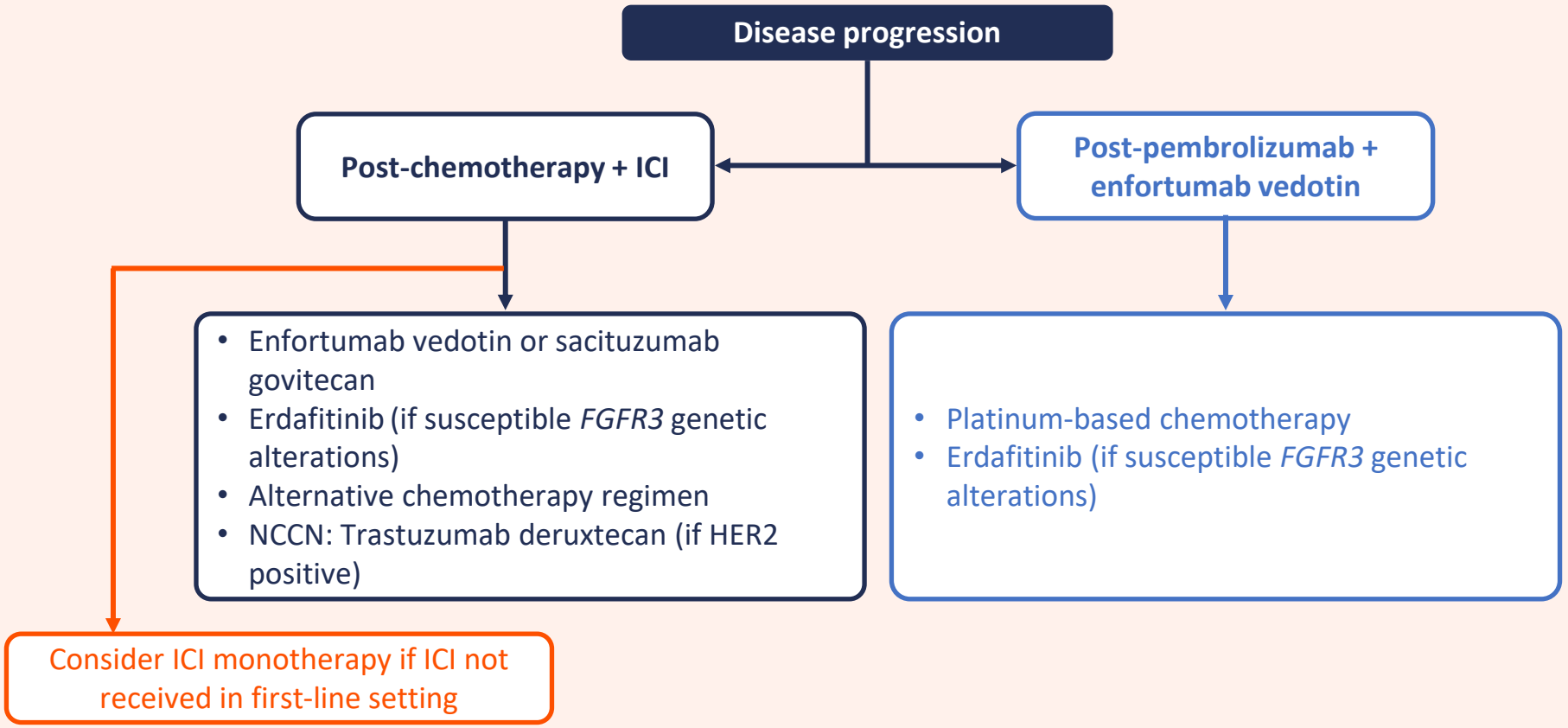


Eligibility considerations for pembrolizumab and enfortumab vedotin

- Patients with an **ECOG Performance status >2** were excluded from the EV-302 trial investigating pembrolizumab plus enfortumab vedotin[3]
- **Peripheral neuropathy, hyperglycaemia** and **DKA** have occurred in patients treated with enfortumab vedotin[4]
  - Patients with pre-existing peripheral neuropathy grade ≥2 were excluded from clinical trials[4]
  - Patients with baseline HbA1c ≥8% were excluded from clinical trials[4]
- Patients with **previous autoimmune disease** for which they had **received systemic treatment** in the previous 2 years were excluded from the EV-302 trial[3]

*Avelumab maintenance only if no progression on first-line platinum-containing chemotherapy.[1,2]

Second-line treatment recommendations in ESMO and NCCN guidelines[1,2]



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Enfortumab vedotin AEs of special interest[4]

Peripheral neuropathy	Musculoskeletal and neurological assessments	• Grade 2: withhold until grade ≤1 • Grade ≥3: permanently discontinue
Skin reactions	Monitor from first cycle and throughout treatment	• Mild-to-moderate skin reactions: topical corticosteroids or antihistamines • Suspected SJS, TEN or bullous lesions: immediately withhold and refer to specialized care • Confirmed SJS or TEN, grade 4 or recurrent grade 3: permanently discontinue • Grade 2 worsening, grade 2 with fever or grade 3: withhold until grade ≤1
Ocular	Ophthalmological examinations	• Consider artificial tears for dry eye prophylaxis • If ocular symptoms worsen or do not resolve: ophthalmologic evaluation
Hyperglycaemia	Monitor blood glucose prior to dosing and throughout treatment	• If blood glucose elevated (>13.9 mmol/L/>250 mg/dL): withhold until ≤13.9 mmol/L (≤250 mg/dL)

Sacituzumab govitecan AEs of special interest[5]

Diarrhoea	Patient reported	• If non-infectious cause, initiate loperamide • Grade 3/4 at time of scheduled treatment: withhold and resume when resolved to grade ≤1 • Supportive measures, e.g. fluid and electrolyte substitution, as clinically indicated
Nausea and vomiting	Patient reported	• Premedicate with a two- or three-drug combination regimen • Grade 3 nausea or grade 3/4 vomiting at time of scheduled treatment: withhold and resume with additional supportive measures when resolved to grade ≤1 • Additional antiemetics and other supportive measures as clinically indicated
Hypersensitivity	Observe during infusion and for further 30 mins	• Pre-infusion treatment, including antipyretics, H1 and H2 blockers, or corticosteroids • If infusion-related reaction develops: slow or interrupt infusion; permanently discontinue if life-threatening reaction occurs
Neutropenia	Signs of infection; monitor blood cell counts	• Do not administer if absolute neutrophil count <1,500/m^3 on day 1 of any cycle or if the neutrophil count <1,000/mm^3 on day 8 of any cycle, or in cases of neutropenic fever • Administer G-CSF as clinically indicated

Refer to product information for dose modifications

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ICI AEs of special interest[6–9]

Colitis	Monitor for signs and symptoms	Management strategies include corticosteroids, withholding drug and treatment discontinuation, depending on grade
Hepatitis	Monitor ALT, AST and bilirubin	
Nephritis	Monitor serum creatinine	
Pneumonitis	Monitor for signs and symptoms	

Hypo/hyperthyroidism	Monitor thyroid function, and for signs and symptoms	• Management strategies include corticosteroids, withholding drug and treatment discontinuation, depending on grade • **For hypothyroidism:** use thyroid replacement therapy • **For hyperthyroidism:** use antithyroid medication

Erdafitinib AEs of special interest[10]

Nail and skin reactions	Patient reported	• Grade 3: withhold until grade ≤1 or baseline • Grade 4: permanently discontinue
CSR/RPED	Ophthalmological examinations	• Dry eye prophylaxis as needed • If CSR/RPED occurs, withhold; discontinue if it does not resolve within 4 weeks or if grade 4
Hyperphosphataemia	Serum phosphate level monitoring	• Dietary phosphate restriction • Consider oral phosphate binder if serum phosphate is >7.0 mg/dL • If serum phosphate ≥9.0 mg/dL, withhold treatment until level returns to <7.0 mg/dL

Refer to product information for dose modifications

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Abbreviations and references

Abbreviations

AE, adverse event; ALT, alanine transaminase; AST, aspartate transaminase; CSR, central serous retinopathy; DKA, diabetic ketoacidosis; ECOG, Eastern Cooperative Oncology Group; ESMO, European Society for Medical Oncology; EV, enfortumab vedotin; FGFR3, fibroblast growth factor receptor 3; G-CSF, granulocyte-colony stimulating factor; HER2, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; LA/mUC, locally advanced/metastatic urothelial carcinoma; NCCN, National Comprehensive Cancer Network; PI, prescribing information; RPED, retinal pigment epithelial detachment; SmPC, summary of product characteristics; SJS, Stevens-Johnson Syndrome; TEN, toxic epidermal necrolysis.

References

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