

A large, stylized orange grid graphic that resembles a globe or a network, composed of thick, curved lines that intersect to form a grid pattern. It is positioned in the background, partially obscured by a dark grey horizontal band at the bottom.

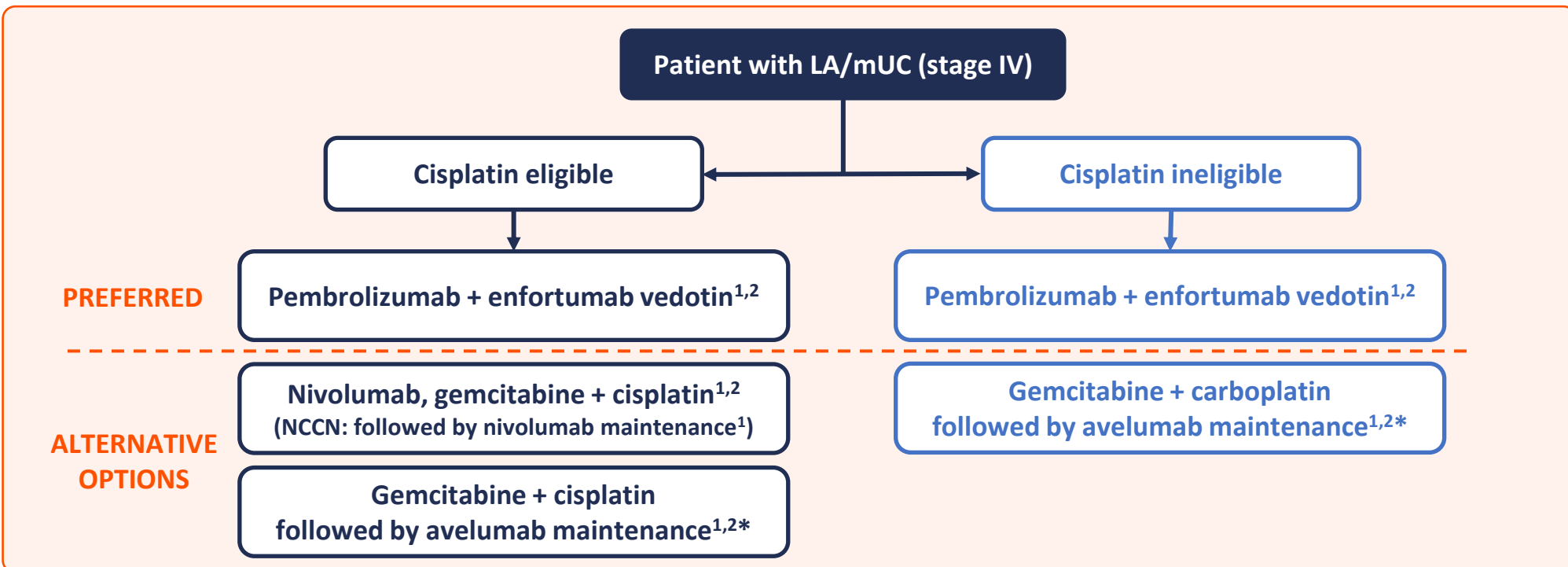
## Advanced urothelial carcinoma: Expert guidance to navigate an evolving therapeutic landscape

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**Practice aid for advanced urothelial carcinoma**

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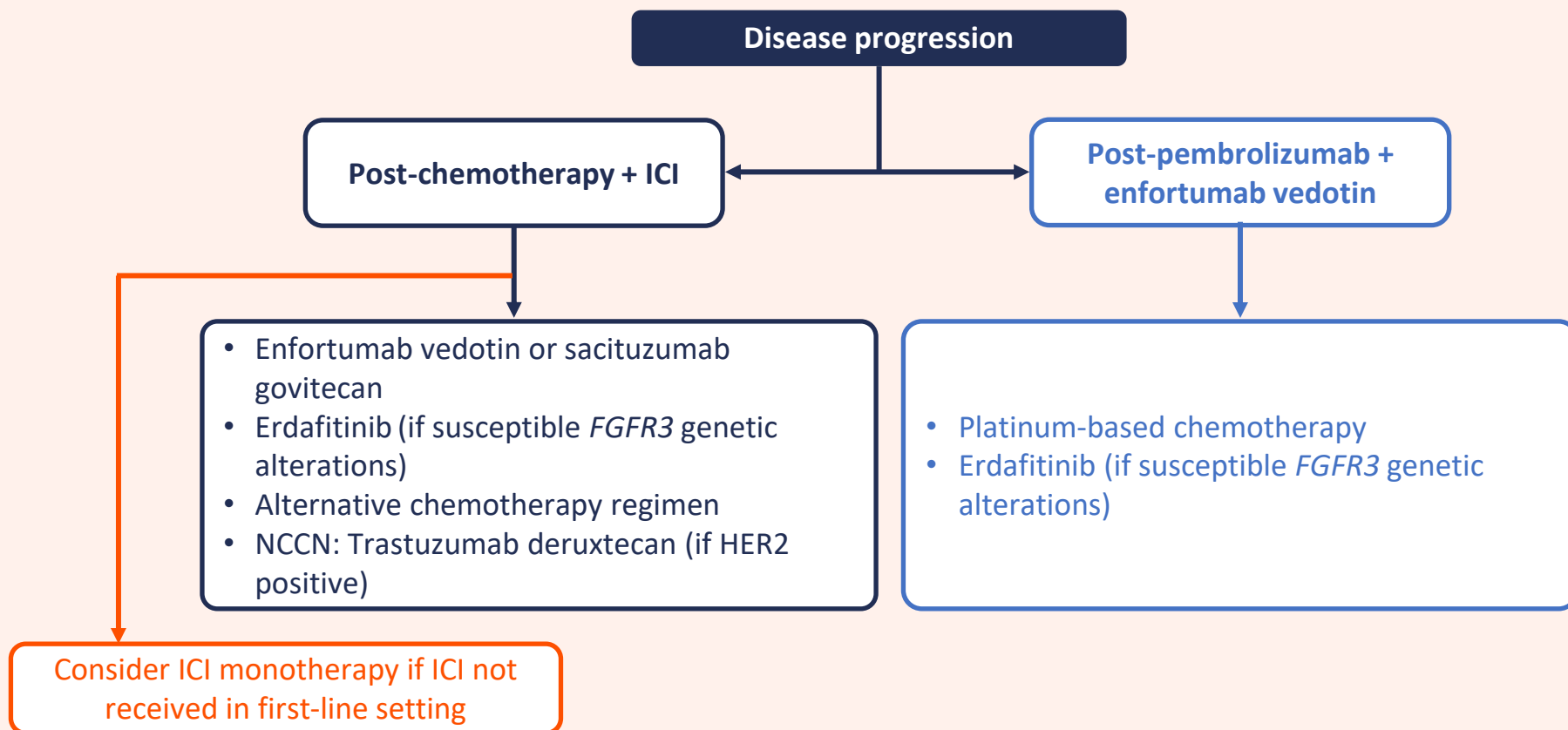
## First-line treatment recommendations in ESMO and NCCN guidelines<sup>1,2</sup>



### 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<sup>3</sup>
- **Peripheral neuropathy, hyperglycaemia and DKA** have occurred in patients treated with enfortumab vedotin<sup>4</sup>
  - Patients with pre-existing peripheral neuropathy grade  $\geq 2$  were excluded from clinical trials<sup>4</sup>
  - Patients with baseline HbA1c  $\geq 8\%$  were excluded from clinical trials<sup>4</sup>
- Patients with **previous autoimmune disease** for which they had **received systemic treatment** in the previous 2 years were excluded from the EV-302 trial<sup>3</sup>

\*Avelumab maintenance only if no progression on first-line platinum-containing chemotherapy.<sup>1,2</sup>

Second-line treatment recommendations in ESMO and NCCN guidelines<sup>1,2</sup>

## Enfortumab vedotin AEs of special interest<sup>4</sup>

 **Peripheral neuropathy**  Musculoskeletal and neurological assessments



- Grade 2: withhold until grade  $\leq 1$
- Grade  $\geq 3$ : 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  $\leq 1$

 **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  $\leq 13.9$  mmol/L ( $\leq 250$  mg/dL)

## Sacituzumab govitecan AEs of special interest<sup>5</sup>

 **Diarrhoea**  Patient reported



- If non-infectious cause, initiate loperamide
- Grade 3/4 at time of scheduled treatment: withhold and resume when resolved to grade  $\leq 1$
- 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  $\leq 1$
- 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

ICI AEs of special interest<sup>6-9</sup>

## Colitis



Monitor for signs and symptoms



## Hepatitis



Monitor ALT, AST and bilirubin



## Nephritis



Monitor serum creatinine



## Pneumonitis



Monitor for signs and symptoms



Management strategies include corticosteroids, withholding drug and treatment discontinuation, depending on grade



## 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<sup>10</sup>

## Nail and skin reactions



Patient reported



- Grade 3: withhold until grade  $\leq 1$  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  $\geq 9.0$  mg/dL, withhold treatment until level returns to  $<7.0$  mg/dL

Refer to product information for dose modifications

## 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

1. NCCN. Bladder Cancer V4.2024. Available at: [www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](http://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf) (accessed 31 May 2024).
2. Powles T, et al. *Ann Oncol*. 2024:S0923-7534(24)00075-9 (online ahead of print).
3. Powles TB, et al. *N Engl J Med*. 2024;390:875–88.
4. EMA. Enfortumab vedotin SmPC.
5. FDA. Sacituzumab govitecan PI. Available at: <https://bit.ly/4c0gD71> (accessed 23 April 2024).
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9. EMA. Nivolumab SmPC.
10. FDA. Erdafitinib PI. Available at: <https://bit.ly/4aHWK3Q> (accessed 23 April 2024).

All SmPC available at: [www.ema.europa.eu/en](http://www.ema.europa.eu/en) (accessed 23 April 2024).

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